



BETA THALASSEMIA

A 3-in-1 Medical Reference

A Bibliography and Dictionary
for Physicians, Patients,
and Genome Researchers

TO INTERNET REFERENCES

BETA THALASSEMIA

A BIBLIOGRAPHY AND
DICTIONARY
FOR PHYSICIANS, PATIENTS,
AND GENOME RESEARCHERS



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

ICON Health Publications
 ICON Group International, Inc.
 7404 Trade Street
 San Diego, CA 92121 USA

Copyright ©2007 by ICON Group International, Inc.

Copyright ©2007 by ICON Group International, Inc. All rights reserved. This book is protected by copyright. No part of it may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without written permission from the publisher.

Printed in the United States of America.

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

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

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

Cataloging-in-Publication Data

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

Beta Thalassemia: A Bibliography and Dictionary for Physicians, Patients, and Genome Researchers/ James N. Parker and Philip M. Parker, editors

p. cm.

Includes bibliographical references, glossary, and index.

ISBN: 0-497-11337-6

1. Beta Thalassemia-Popular works. I. Title.

Disclaimer

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

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

Copyright Notice

If a physician wishes to copy limited passages from this book for patient use, this right is automatically granted without written permission from ICON Group International, Inc. (ICON Group). However, all of ICON Group publications have copyrights. With exception to the above, copying our publications in whole or in part, for whatever reason, is a violation of copyright laws and can lead to penalties and fines. Should you want to copy tables, graphs, or other materials, please contact us to request permission (E-mail: iconedit@san.rr.com). ICON Group often grants permission for very limited reproduction of our publications for internal use, press releases, and academic research. Such reproduction requires confirmed permission from ICON Group International, Inc. **The disclaimer above must accompany all reproductions, in whole or in part, of this book.**

Acknowledgements

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

About the Editors

James N. Parker, M.D.

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

Philip M. Parker, Ph.D.

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

About ICON Health Publications

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

ICON Group International, Inc.
7404 Trade Street
San Diego, CA 92121 USA
Fax: 858-635-9414
Web site: www.icongrouponline.com/health

Table of Contents

FORWARD	1
CHAPTER 1. STUDIES ON BETA THALASSEMIA	3
<i>Overview</i>	3
<i>Genetics Home Reference</i>	3
<i>What Is Beta Thalassemia?</i>	3
<i>How Common Is Beta Thalassemia?</i>	4
<i>What Genes Are Related to Beta Thalassemia?</i>	4
<i>How Do People Inherit Beta Thalassemia?</i>	4
<i>Where Can I Find Additional Information about Beta Thalassemia?</i>	4
<i>References</i>	6
<i>What Is the Official Name of the HBB Gene?</i>	7
<i>What Is the Normal Function of the HBB Gene?</i>	7
<i>What Conditions Are Related to the HBB Gene?</i>	7
<i>Where Is the HBB Gene Located?</i>	8
<i>References</i>	9
<i>Federally Funded Research on Beta Thalassemia</i>	10
<i>The National Library of Medicine: PubMed</i>	15
CHAPTER 2. ALTERNATIVE MEDICINE AND BETA THALASSEMIA	38
<i>Overview</i>	38
<i>National Center for Complementary and Alternative Medicine</i>	38
<i>Additional Web Resources</i>	46
<i>General References</i>	46
CHAPTER 3. BOOKS ON BETA THALASSEMIA	47
<i>Overview</i>	47
<i>Book Summaries: Online Booksellers</i>	47
APPENDIX A. HELP ME UNDERSTAND GENETICS	49
<i>Overview</i>	49
<i>The Basics: Genes and How They Work</i>	49
<i>Genetic Mutations and Health</i>	60
<i>Inheriting Genetic Conditions</i>	66
<i>Genetic Consultation</i>	74
<i>Genetic Testing</i>	76
<i>Gene Therapy</i>	82
<i>The Human Genome Project and Genomic Research</i>	85
APPENDIX B. PHYSICIAN RESOURCES	88
<i>Overview</i>	88
<i>NIH Guidelines</i>	88
<i>NIH Databases</i>	89
<i>Other Commercial Databases</i>	92
APPENDIX C. PATIENT RESOURCES	93
<i>Overview</i>	93
<i>Patient Guideline Sources</i>	93
<i>Finding Associations</i>	96
<i>Resources for Patients and Families</i>	97
ONLINE GLOSSARIES	99
<i>Online Dictionary Directories</i>	99
BETA THALASSEMIA DICTIONARY	100
INDEX	134

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 beta thalassemia 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 beta thalassemia, 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 beta thalassemia, from the essentials to the most advanced areas of research. Special attention has been paid to present the genetic basis and pattern of inheritance of beta thalassemia. 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 beta thalassemia. 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 beta thalassemia, 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. We hope these resources will prove useful to the widest possible audience seeking information on beta thalassemia.

The Editors

¹ From the NIH, National Cancer Institute (NCI): <http://www.cancer.gov/>.

CHAPTER 1. STUDIES ON BETA THALASSEMIA

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on beta thalassemia. For those interested in basic information about beta thalassemia, we begin with a condition summary published by the National Library of Medicine.

Genetics Home Reference

Genetics Home Reference (GHR) is the National Library of Medicine's Web site for consumer information about genetic conditions and the genes or chromosomes responsible for those conditions. Here you can find a condition summary on beta thalassemia that describes the major features of the condition, provides information about the condition's genetic basis, and explains its pattern of inheritance. In addition, a summary of the gene or chromosome related to beta thalassemia is provided.²

The Genetics Home Reference has recently published the following summary for beta thalassemia:

What Is Beta Thalassemia?³

Beta thalassemia is a type of inherited blood disorder that can cause anemia (a low number of red blood cells). It affects a person's ability to produce hemoglobin, the protein in red blood cells that delivers oxygen to all parts of the body.

Signs and symptoms of beta thalassemia are severe in the form of the disorder known as thalassemia major and less severe in the form called thalassemia intermedia. Signs and symptoms of thalassemia major appear in the first 2 years of life. Infants become pale and listless, have a poor appetite, grow slowly, and often develop jaundice (yellowing of the

² This section has been adapted from the National Library of Medicine: <http://ghr.nlm.nih.gov/>.

³ Adapted from the Genetics Home Reference of the National Library of Medicine: <http://ghr.nlm.nih.gov/condition=betathalassemia>.

skin). The spleen, liver, and heart may also be enlarged. Adolescents with the severe form may experience delayed puberty. Individuals with thalassemia intermedia may have no symptoms or mild symptoms through childhood and adolescence.

How Common Is Beta Thalassemia?

Worldwide, beta thalassemia is considered a fairly common blood disorder, affecting thousands of infants each year. Beta thalassemia occurs most frequently in Mediterranean countries, North Africa, the Middle East, India, and southeast Asia. In North America, the disorder is less common; an estimated 750-1000 people have beta thalassemia.

What Genes Are Related to Beta Thalassemia?

Mutations in the **HBB** (<http://ghr.nlm.nih.gov/gene=hbb>) gene cause beta thalassemia.

The HBB gene produces one of the subunits of hemoglobin, called beta hemoglobin or the beta chain. Mutations in the HBB gene can reduce or abolish the production of beta-hemoglobin, leading to abnormal hemoglobin that cannot perform its function as an oxygen carrier.

How Do People Inherit Beta Thalassemia?

Beta thalassemia major and thalassemia intermedia are inherited in an autosomal recessive pattern, which means two copies of the gene in each cell are altered. Most often, the parents of an individual with an autosomal recessive disorder are carriers of one copy of the altered gene but do not show signs and symptoms of the disorder. Sometimes, however, carriers of the altered HBB gene have a mild anemia referred to as thalassemia minor.

In a small percentage of families, the HBB mutation is inherited in an autosomal dominant manner. In these cases, one copy of the altered gene in each cell is sufficient to cause the disorder.

Where Can I Find Additional Information about Beta Thalassemia?

You may find the following resources about beta thalassemia helpful. These materials are written for the general public.

NIH Publications - National Institutes of Health

- National Center for Biotechnology Information: Genes and Disease:
<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?call=bv.View.ShowSection&rid=gnid.section.250>
- National Heart, Lung, and Blood Institute:
http://www.nhlbi.nih.gov/health/dci/Diseases/Thalassemia/Thalassemia_WhatIs.html

- National Human Genome Research Institute:
<http://www.genome.gov/10001221>

MedlinePlus - Health Information

- Encyclopedia: Thalassemia:
<http://www.nlm.nih.gov/medlineplus/ency/article/000587.htm>
- Health Topic: Thalassemia:
<http://www.nlm.nih.gov/medlineplus/thalassemia.html>

Educational Resources - Information Pages

- Centre for Genetics Education (Australia):
<http://www.genetics.com.au/factsheet/34.htm>
- Children's Hospital Boston:
<http://www.childrenshospital.org/az/Site625/mainpageS625P0.html>
- Information Center for Sickle Cell and Thalassemic Disorders:
<http://sickle.bwh.harvard.edu>
- Madisons Foundation:
<http://www.madisonsfoundation.org/content/3/1/display.asp?did=283>
- New York Online Access to Health (NOAH):
<http://www.noah-health.org/en/blood/thalassemia/>
- Orphanet:
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=848
- University of Rochester Medical Center:
<http://www.urmc.edu/medicine/genetics/thalassemia.aspx>
- University of Virginia Health System:
http://www.healthsystem.virginia.edu/UVAHealth/adult_blood/beta.cfm

Patient Support - for Patients and Families

- Chicago Center for Jewish Genetic Disorders:
<http://www.jewishgeneticscenter.org/what/sephardi/beta.asp>
- Cooley's Anemia Foundation:
<http://www.cooleysanemia.org>
- March of Dimes:
http://www.marchofdimes.com/pnhec/4439_1229.asp
- National Organization for Rare Disorders (NORD):
http://www.rarediseases.org/search/rdbdetail_abstract.html?disname=Thalassemia%20Major

Professional Resources

You may also be interested in these resources, which are designed for healthcare professionals and researchers.

- Gene Reviews - Clinical summary:
<http://www.genetests.org/query?dz=b-thal>
- Gene Tests - DNA tests ordered by healthcare professionals:
<http://www.genetests.org/query?testid=2017>
- ClinicalTrials.gov - Linking patients to medical research:
<http://clinicaltrials.gov/search/condition=%22beta+thalassemia%22?recruiting=false>
- PubMed - Recent literature:
<http://ghr.nlm.nih.gov/condition=betathalassemia/show/PubMed;jsessionid=EB6705234BEF18B0088C8A8E7279824C>
- OMIM - Genetic disorder catalog:
<http://ghr.nlm.nih.gov/condition=betathalassemia/show/OMIM;jsessionid=EB6705234BEF18B0088C8A8E7279824C>

References

These sources were used to develop the Genetics Home Reference condition summary on beta thalassemia.

- Gene Reviews
- National Human Genome Research Institute
- Olivieri NF. The beta-thalassemias. *N Engl J Med*. 1999 Jul 8;341(2):99-109. Review. No abstract available. PubMed citation
- OMIM: Beta Thalassemia, Dominant Inclusion Body Type
- Pearson HA, Cohen AR, Giardina PJ, Kazazian HH. The changing profile of homozygous beta-thalassemia: demography, ethnicity, and age distribution of current North American patients and changes in two decades. *Pediatrics*. 1996 Mar;97(3):352-6. PubMed citation
- Rund D, Rachmilewitz E. Beta-thalassemia. *N Engl J Med*. 2005 Sep 15;353(11):1135-46. No abstract available. PubMed citation
- Thein SL. Genetic insights into the clinical diversity of beta thalassaemia. *Br J Haematol*. 2004 Feb;124(3):264-74. Review. No abstract available. PubMed citation
- Wonke B. Clinical management of beta-thalassemia major. *Semin Hematol*. 2001 Oct;38(4):350-9. Review. PubMed citation

A summary of the gene related to beta thalassemia is provided below:

What Is the Official Name of the HBB Gene?⁴

The official name of this gene is “hemoglobin, beta.”

HBB is the gene's official symbol. The HBB gene is also known by other names, listed below.

What Is the Normal Function of the HBB Gene?

The HBB gene provides instructions for making a protein chain that is a part of hemoglobin. Hemoglobin is the molecule inside red blood cells that transports oxygen throughout the body. Hemoglobin is made up of two different kinds of protein chains. One of these is made by the HBB gene and is called the beta chain of hemoglobin (sometimes called beta globin). The other part of the hemoglobin molecule is the alpha chain (or alpha globin), which is made by a different gene. Two beta chains and two alpha chains join together so that each hemoglobin molecule is composed of four protein chains.

Hemoglobin carries oxygen from the lungs to the rest of the body and then carries carbon dioxide from the body back to the lungs. Oxygen must bind to hemoglobin for transport and delivery to the tissues. Each protein chain of the hemoglobin molecule has an iron-containing center (heme group) that binds oxygen for transport. A complete hemoglobin protein, made up of four chains, is capable of carrying four oxygen molecules. Oxygen binding to hemoglobin gives blood its bright red color.

What Conditions Are Related to the HBB Gene?

Beta Thalassemia - Caused by Mutations in the HBB Gene

More than 200 HBB mutations that cause beta thalassemia have been identified. Most of the mutations involve a change in a single DNA building block (nucleotide) within or near the HBB gene. Other mutations insert or delete one to several nucleotides in the HBB gene. HBB mutations lead to reduced amounts or the absence of beta-hemoglobin. Without proper amounts of the beta chain of hemoglobin, red blood cells cannot bind enough oxygen to satisfy the body's needs.

Methemoglobinemia, Beta-Globin Type - Caused by Mutations in the HBB Gene

More than 200 HBB mutations that cause beta thalassemia have been identified. Most of the mutations involve a change in a single DNA building block (nucleotide) within or near the HBB gene. Other mutations insert or delete one to several nucleotides in the HBB gene. HBB mutations lead to reduced amounts or the absence of beta-hemoglobin. Without proper amounts of the beta chain of hemoglobin, red blood cells cannot bind enough oxygen to satisfy the body's needs.

⁴ Adapted from the Genetics Home Reference of the National Library of Medicine:
<http://ghr.nlm.nih.gov/gene=hbb;jsessionid=EB6705234BEF18B0088C8A8E7279824C>.

Sickle Cell Anemia - Caused by Mutations in the HBB Gene

Mutations in specific regions of the HBB gene cause blood cells to produce an abnormal form of hemoglobin called hemoglobin M. This form of hemoglobin disrupts the protein's interaction with iron and interferes with the delivery of oxygen to cells. As a result, people with this condition may have a bluish tint to their skin, mucous membranes, and underneath their fingernails.

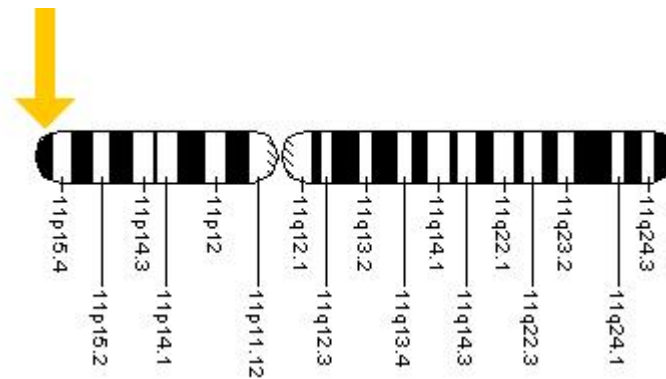
Other Disorders - Caused by Mutations in the HBB Gene

Sickle cell anemia is caused by an HBB mutation that produces an abnormal version of the hemoglobin beta chain called hemoglobin S or HbS. HbS results from a switch in building blocks (amino acids) used to make the beta chain. Specifically, the amino acid glutamic acid is replaced with the amino acid valine at position 6 in the beta chain. The shorthand for this amino acid switch is Glu6Val. Replacing glutamic acid with valine causes the abnormal HbS chains to stick together and form long, rigid molecules. The rigid HbS molecules bend red blood cells into a sickle (crescent) shape. The sickle-shaped cells die prematurely, which can lead to a shortage of red blood cells (anemia). The sickle-shaped cells can also block small blood vessels, causing pain and organ damage.

Where Is the HBB Gene Located?

Cytogenetic Location: 11p15.5

Molecular Location on chromosome 11: base pairs 5,203,271 to 5,204,876



The HBB gene is located on the short (p) arm of chromosome 11 at position 15.5.

More precisely, the HBB gene is located from base pair 5,203,271 to base pair 5,204,876 on chromosome 11.

References

These sources were used to develop the Genetics Home Reference gene summary on the HBB gene.

- Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review. *Am J Epidemiol*. 2000 May 1;151(9):839-45. Review. PubMed citation
- Flatz G, Sanguansermsri T, Sengchanh S, Horst D, Horst J. The 'hot-spot' of Hb E [β 26(B8)Glu \rightarrow Lys] in Southeast Asia: beta-globin anomalies in the Lao Theung population of southern Laos. *Hemoglobin*. 2004 Aug;28(3):197-204. PubMed citation
- Fu XH, Liu DP, Liang CC. Chromatin structure and transcriptional regulation of the beta-globin locus. *Exp Cell Res*. 2002 Aug 1;278(1):1-11. Review. PubMed citation
- Hagberg A, Barbany G, Landegren U, Birgegard G. Beta-globin mRNA increases rapidly during erythropoietin treatment. *Scand J Clin Lab Invest*. 2003;63(3):239-45. PubMed citation
- Mehanna AS. Sickle cell anemia and antisickling agents then and now. *Curr Med Chem*. 2001 Feb;8(2):79-88. Review. PubMed citation
- Nagel RL, Steinberg MH. Role of epistatic (modifier) genes in the modulation of the phenotypic diversity of sickle cell anemia. *Pediatr Pathol Mol Med*. 2001 Mar-Apr;20(2):123-36. Review. PubMed citation
- Park KW. Sickle cell disease and other hemoglobinopathies. *Int Anesthesiol Clin*. 2004 Summer;42(3):77-93. Review. No abstract available. PubMed citation
- Sadelain M, Rivella S, Lisowski L, Samakoglu S, Riviere I. Globin gene transfer for treatment of the beta-thalassemias and sickle cell disease. *Best Pract Res Clin Haematol*. 2004 Sep;17(3):517-34. Review. PubMed citation
- Scriver, Charles R; *The metabolic & molecular bases of inherited disease*; 8th ed.; New York : McGraw-Hill, c2001. p4571-4636. NLM Catalog
- Steinberg MH. Hydroxyurea treatment for sickle cell disease. *ScientificWorldJournal*. 2002 Jun 25;2:1706-28. Review. PubMed citation
- Stuart MJ, Nagel RL. Sickle-cell disease. *Lancet*. 2004 Oct 9;364(9442):1343-60. Review. PubMed citation
- Thein SL. Genetic insights into the clinical diversity of beta thalassaemia. *Br J Haematol*. 2004 Feb;124(3):264-74. Review. No abstract available. PubMed citation
- Tisdale J, Sadelain M. Toward gene therapy for disorders of globin synthesis. *Semin Hematol*. 2001 Oct;38(4):382-92. Review. PubMed citation

Federally Funded Research on Beta Thalassemia

The U.S. Government supports a variety of research studies relating to beta thalassemia. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.⁵

CRISP (Computerized Retrieval of Information on Scientific Projects)

CRISP 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 beta thalassemia.

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

- **Project Title: GENE TRANSFER TO FETAL AND NEONATAL HSC POPULATIONS**

Principal Investigator & Institution: Gaensler, Karin L.; University of California San Francisco 3333 California St., Ste. 315 San Francisco, Ca 941430962

Timing: Fiscal Year 2004

Summary: Despite intensive efforts to develop effective therapy for sickle cell anemia (SCA), this disease continues to be associated with significant morbidity and mortality. SCA affects 0.2% of African American children and young adults. In order for future gene therapy-based strategies for SCA to be successful: 1) transduction of self-renewing stem cells must be highly efficient, 2) transduced cells must have a selective or proliferative advantage, and 3) gene delivery vectors must produce stable, therapeutic levels of globin gene expression over the lifetime of the individual. Our goal is to develop procedures for efficient gene transfer into fetal liver and have already shown that high-level gene expression may be achieved following either intraperitoneal or direct intrahepatic injection of viral or non-viral vectors. We will focus on the transduction of highly proliferative HSC in the murine fetal liver. Our first hypothesis is that direct in utero delivery of gene transfer vectors will result in the transduction of higher numbers of HSCs than can be achieved in vitro, and without disrupting either the microenvironment or biology of these early HSC. We will determine the most efficient vector system for gene transfer into totipotent fetal HSC using MLV- and HIV-based retroviral vectors, and adeno-associated viral vectors. We will focus on the transduction of highly proliferative HSC in the murine fetal liver. Our first hypothesis is that direct in utero delivery of gene transfer vectors will result in the transduction of higher numbers of HSCs than can be achieved in vitro, and without disrupting either the microenvironment or biology of these early HSC. We will determine the most efficient vector system for gene transfer into totipotent fetal HSCs using MLV- and HIV-based retroviral vectors, and adeno-associated viral vectors. Our second hypothesis is

⁵ 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).

that transuterine injection provides an efficient model for rapidly screening novel globin gene vectors. We will deliver human gamma or beta gene expression. The therapeutic efficacy of gamma or beta globin vectors that direct high-level expression of globin will be tested in murine models of **beta thalassemia** and sickle cell anemia. Vectors that produce high-level globin gene expression will reduce red cell sickling and confer a survival advantage of transduced red cells. These studies will also define the fate of transduced hematopoietic stem cells and their progeny during ontogeny.

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

- **Project Title: GENETIC MODULATION OF HbF IN BETA THALASSEMIA**

Principal Investigator & Institution: Chui, David H K.; Medicine; Boston University Medical Campus 715 Albany St, 560 Boston, Ma 021182394

Timing: Fiscal Year 2005; Project Start 30-SEP-2005; Project End 31-AUG-2010

Summary: (provided by applicant): Thalassemias are man's most common Mendelian trait. Severe beta-thalassemia results from compound heterozygosity or homozygosity for mutations that abolish or impair beta-globin gene expression. The disease severity varies considerably, even among those with identical beta-thalassemia mutations and when known epistatic genetic factors, such as alpha-thalassemia, are considered. Most of this heterogeneity can be linked to the capacity to produce HbF. We hypothesize that there is genetic variation in cis-acting elements and trans-acting factors implicated in gamma-globin gene expression, in modulation of HbF concentration within erythrocytes, and in regulation of erythroid cell differentiation and proliferation. We wish to identify these genetic variations. Our 1st aim is to identify informative single nucleotide polymorphisms (SNPs) and haplotype structures in about 150 candidate genetic loci, by studying 30 family triads, each with 2 parents and 1 child. Using the haplotype tagging SNPs discovered in aim 1, our 2nd aim is to discover genetic loci and genes associated with F-cell/HbF levels, by studying about 1,000 beta-thalassemia carriers. SNP and haplotype data will be used in an F-cell/HbF quantitative trait locus (QTL) analysis. The 3rd aim is to correlate the genetic loci and genes found to be associated with F-cell/HbF levels to disease phenotypes, by studying about 320 severe beta-thalassemia patients. Our long-term goal is to identify genes of importance in HbF expression, and to investigate their biological and pathophysiological functions. A patient registry of sufficient size to accomplish these aims has been established in Hong Kong. We have formed an interactive and cohesive team of pediatricians, hematologists, geneticists, molecular biologists, epidemiologists, bioinformaticians, and statisticians who together are experienced in the proposed clinical/genetic approaches. The results of this investigation will prepare us to understand the function of potentially important genes for HbF regulation, develop prognostic guidelines and identify new therapeutic targets.

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

- **Project Title: MOLECULAR MECHANISM OF HUMAN G-GLOBIN GENE SILENCING**

Principal Investigator & Institution: Li, Qiliang; Medicine; University of Washington Office of Sponsored Programs Seattle, Wa 98105

Timing: Fiscal Year 2004; Project Start 01-APR-2003; Project End 31-MAR-2007

Summary: (provided by applicant): The goals of this research application are a) to test the hypothesis that the variable human gamma-globin gene silencing in the adult is the consequence of a dynamic equilibrium between euchromatin originating in the LCR and

heterochromatin originating in the gamma gene promoter, b) to identify gamma-globin gene specific repressors and corepressors. Our specific aims are i) To test the hypothesis that the gamma gene silencing in the adult is the consequence of a dynamic balance between euchromatin originating in the LCR and heterochromatin originating in the gamma gene promoter. This will be tested in transgenic mice carrying the human beta-globin locus yeast artificial chromosome (betaYAC) and various mutated betaYACs by examining changes of the histone code specific for heterochromatin and euchromatin. This hypothesis can be validated if changes of the histone code are correlated with the phenotypes induced by the various mutations, ii) To test whether the gammaCACCC box causes heterochromatinization in the gamma gene promoter in the adult. This will be done by relocating the gammaCACCC box in the different locations in the beta-globin locus and examining formation of heterochromatin induced by the gammaCACCC box. iii) To develop an oligonucleotide-mediated chromatin immunoprecipitation approach and using this approach to search for gamma gene specific repressors/corepressors. It is expected that these studies will lead to a unifying model explaining variable silencing of human gamma-globin gene in the adult, and will identify gamma gene specific repressors/corepressors. These studies will facilitate designing of a feasible strategy for human gamma-globin gene reactivation. Such a development will have important consequences for the treatment of patients with sickle cell disease or **beta thalassemia** syndromes.

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

- **Project Title: ORAL THERAPEUTIC FOR BETA-THALASSEMIA**

Principal Investigator & Institution: Perrine, Susan P.; Associate Professor of Medicine; Gene Regulation Laboratories, Inc. 233 Needham St, Ste 300 Newton, Ma 02464

Timing: Fiscal Year 2005; Project Start 01-SEP-2003; Project End 31-AUG-2007

Summary: (provided by applicant): The **beta thalassemia** syndromes are prevalent genetic disorders caused by molecular mutations affecting the genes for adult hemoglobin and cause early mortality from complications of blood transfusions. These conditions can be ameliorated by reactivating production of fetal hemoglobin (Hb F) in the patients' blood. Pharmacologic re-induction of HbF has been achieved in two-thirds of patients with these diseases in clinical trials, using first generation short-chain fatty acid (SCFA) therapeutics. Some of the treated patients experienced both biochemical and clinical / hematologic improvement, and became independent of blood transfusions for several years. The first SCFA therapies, butyrate and phenylbutyrate, required IV infusions or large amounts of drug (20-30 grams/day) which are difficult for long-term use. Combined therapy with rhu- EPO to stimulate erythropoiesis and with Butyrate to induce fetal globin expression produced additive effects, suggesting that both actions are necessary for an optimal definitive treatment for **beta thalassemia**. During the Phase I STTR, the applicant organization developed a new SCFA (sodium ST-7) which has substantial advantages over the first generation agents, in inducing Hb F and also stimulating erythroid cell proliferation, with oral-bioavailability, and with pharmacokinetics demonstrating feasibility for once/day oral administration at tolerable doses (0.5-1 gram for an adult). The agent has proven effective and safe in a primate model for Hb F induction and in mice transgenic for the human globin genes. In this Phase II STTR application, we propose to conduct the additional preclinical development studies required by the FDA to obtain Investigational New Drug status for Phase I clinical trials of this lead erythropoietic HbF-inducer (sodium ST-7). The goals of this proposal are: 1) To conduct the preclinical toxicology studies required for an IND for sodium ST-7 to stimulate HbF and erythropoiesis; 2) To prepare an IND application

for phase I clinical trials of the erythropoietic Hb F-inducing agent; 3) To evaluate four other novel Hb F-inducing compounds for pharmacokinetics and pharmacodynamics in baboons, as potential back-up therapeutics.

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

- **Project Title: OUTCOME MODIFYING GENES IN SICKLE CELL DISEASE**

Principal Investigator & Institution: Telen, Marilyn J.; Chief, Division of Hematology; Medicine; Duke University 2424 Erwin Rd. Durham, Nc 27705

Timing: Fiscal Year 2004; Project Start 30-SEP-2001; Project End 31-JUL-2006

Summary: (provided by applicant): Sickle cell disease (SCD) is caused by homozygosity for a single mutation of the beta hemoglobin gene. Despite the constancy of this genetic abnormality, the clinical course of patients with SCD is remarkably variable. SCD can affect the function and cause the failure of multiple organ systems through the process of vaso-occlusion. However, we as yet do not understand why the clinical course of SCD and the organs affected are so variable among patients. The process of vaso-occlusion itself appears both complex, involving multiple pathophysiological processes, as well as possibly variable from one organ system to another. This study, therefore, is designed to identify genetic factors that predispose SCD patients to develop specific end-organ complications and to experience more or less severe clinical courses. We will enroll 1000 patients with Hb SS and Hb S-beta thalassemia being followed at three regional institutions (Duke University Medical Center, University of North Carolina Medical Center, and Emory University Medical Center). Medical information obtained will identify the presence or absence of specific targeted outcomes (overall disease severity as well as specific types of end organ damage). All clinical data will be managed and stored on the PEDIGENE system and will include medical status (history, physical examination, and laboratory results) and information regarding potentially confounding environmental factors. We will also obtain blood for DNA analysis, and plasma samples potentially useful for later correlative studies (e.g. of cytokine levels or coagulation activation) will also be stored. Information on sample quality and quantity will be stored in the PEDIGENE system and linked to the clinical data obtained. Identification and development of SNPs for the candidate target genes will be performed, and the DNA samples will be analyzed for these, with results entered into the PEDIGENE system. State-of-the-art statistical methods will be used to examine the relationship between specific clinical outcomes with the SNPs, to determine which genetic characteristics predispose patients with SCD to a more or less severe overall clinical course as well as to individual organ-specific complications. Identification of such genetic factors will reveal new targets for development of therapy individualized to specific complications of SCD, thus leading eventually to improved outcomes and increased life expectancy for patients with SCD.

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

- **Project Title: PROSPECTIVE COMPARISON OF TWO REGIMENS OF DEFEROXAMINE**

Principal Investigator & Institution: Olivieri, Nancy F.; Director, Hemoglobinopathy Program; Hospital for Sick Chldrn (Toronto) 555 University Ave Toronto, on M5g 1X8

Timing: Fiscal Year 2004; Project Start 16-SEP-2004; Project End 30-JUN-2005

Summary: Since the discovery of fetal hemoglobin, augmentation of its synthesis has been proposed as a therapeutic goal in patients with **beta thalassemia**. Unfortunately, clinical trials of most pharmacologic agents have demonstrated modest clinical

responses only. Guided by previous work, the primary hypotheses of this research proposal is that augmentation of fetal hemoglobin, sufficient to increase steady-state total hemoglobin concentration and reduce transfusion requirements, will be most effective during sequential administration of selected agents to patients with specific mutations within the beta globin cluster and that responses will also be influenced by the degree of erythroid marrow expansion, with the most marked responses observed in patients in whom marrow expansion is maximized before therapy. The specific aim is to determine increases in steady-state total and fetal hemoglobin concentrations, reduction in globin chain imbalance, toxicity, and patient compliance associated with selected pharmacologic regimens with patients with genotypes selected to test the above hypotheses. To achieve this aim, 30 patients with three groups of mutations, including specific deletions or rearrangements of putatively important regulatory elements within the beta globin cluster, will be recruited. In the first study phase, patients will be treated with sodium phenylbutyrate, hydroxyurea and recombinant erythropoietin alone and in combination. In the second study phase, low-dose subcutaneous cytosine arabinoside will be offered to adult patients. The key study comparison will be made with respect to the total hemoglobin concentration; we estimate that the minimal clinically important difference between the hemoglobin concentration at baseline and after treatment will be 3 grams/deciliter. Compliance with oral therapy will be monitored using computerized pill containers, and with subcutaneous therapy using counts for syringes returned each visit. This study represents an attempt to provide definitive therapy for the primary abnormality in severe **beta thalassemia**, severe imbalance of globin chains, and to reduce or eliminate transfusions in selected patients.

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

- **Project Title: SECONDARY HEMOCHROMATOSIS IN BETA THALASSEMIA AND SCD**

Principal Investigator & Institution: Vichinsky, Elliott P.; Director; Children's Hospital & Res Ctr at Oakland 747 52Nd St Oakland, Ca 946091809

Timing: Fiscal Year 2004; Project Start 01-AUG-2000; Project End 31-MAY-2006

Summary: (adapted from the application) The purpose of this study is to determine whether the pathologic effects of iron overload secondary to hypertransfusion are different in SCD and **beta thalassemia**. Iron-related organ injury and death are common in patients with **beta thalassemia**. Similar organ pathology and mortality have not been reported in SCD after hypertransfusion. Differences in organ and cellular iron localization, cellular processing of iron, inflammatory state, or the generation of reactive low molecular weight iron might explain the differences in disease response. Pilot data shows that the severity of iron overload is similar in hypertransfused patients with SCD and **beta thalassemia**, yet the rate of organ dysfunction (heart, endocrine) is much greater in **beta thalassemia**. The primary hypothesis of this study is that hypertransfused patients with SCD show less organ damage than patients with **beta thalassemia**. The specific aims of the study are: 1) to determine the organ and cellular distribution of iron in hypertransfused patients with **beta thalassemia** and SCD, 2) to determine whether severe organ damage occurs less frequently in hypertransfused patients with SCD than in patients with **beta thalassemia** and to evaluate whether markers for early organ dysfunction can be identified and used to guide chelation therapy, 3) to determine the molecular differences in ferritin between SCD and **beta thalassemia** which could account for a difference in iron deposition in response to chronic RBC transfusion. Organ and cellular iron distribution will be determined 1) post-mortem by histologic and chemical analyses of tissues obtained from

hypertransfused patients with SCD or beta-thalassemia matched for age, transfusion volume, sex, and 2) pre-mortem, at an earlier stage of morbidity, by quantitative and histologic analyses of liver biopsy and bone marrow aspirates. Quantitative CT will be used to compare the organ distribution of iron in the two diseases. The frequency of severe organ damage (heart disease, diabetes, spinal fracture) will be determined prospectively over 3 years in a multicenter study (200 patients) to confirm the primary hypothesis. Evidence for early organ dysfunction will be sought using sensitive markers in patients (20 patients) followed prospectively for 4 years at CHO. In summary, if this study is successful and demonstrates a strong difference in the toxicity of severe iron overload in SCD as compared to **beta thalassemia**, it will change the approach to chelation therapy in hypertransfused patients with SCD, lead to reduced chelator-related toxicity, and improve quality of life in these patients.

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

NTIS (National Technical Information Service)

The NTIS (www.ntis.gov), a service of the U.S. Department of Commerce, has published the following information on sponsored studies related to beta thalassemia:

- **"Molecular Bases of Aging in Red Blood Cells (Bases Moleculaires du Vieillissement des Globules Rouges),"** published in 1990.

Sponsored by: Institut National de la Sante et de la Recherche Medicale, Creteil (France). Unite de Recherche en Genetique Moleculaire et en Hematologie.; Direction des Recherches, Etudes et Techniques, Paris (France). Centre de Documentation de l'Armement.

Written by: Y. Beuzard.

Abstract: Erythrocyte membrane and cytosol proteins, their thiol groups, and oxidation of the proteins during aging of the cells are studied. The first paper describes the methods the team used to track in vivo oxidations in cells. The protein targets were primarily membrane proteins, particularly spectrin and ankyrin; there is good correlation between anemia and membrane protein oxidation. The second study shows that the thiol reagent N-ethyl maleimide activates dehydration of the red blood cell and that a specific co-transport inhibitor, KC1, inhibits it. The third study compares mice **Beta thalassemia** red blood cells to human red blood cells and points up the essential role of oxidation lesions in membrane proteins to explain the severe anemia and premature death of the cells. In the fourth study alpha hemoglobin chains were entrapped in normal erythrocytes, leading over time to structural and functional abnormalities very similar to those seen in beta thassalemic erythrocytes in vivo.

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

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.

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

- **A case of beta thalassemia major detected using HPLC in a child of Chinese ancestry.**
 Author(s): Berendt HL, Blakney GB, Clarke GM, Higgins TN.
 Source: Clinical Biochemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10936591&query_hl=7&itool=pubmed_docsum

- **A chronic hypercoagulable state and life-long platelet activation in beta thalassemia major.**
 Author(s): Eldor A, Maclouf J, Lellouche F, Ben-Yashar V, Barenholz Y, Durst R, Hy-Am E, Goldfarb A, Rachmilewitz E.
 Source: Southeast Asian J Trop Med Public Health.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7886616&query_hl=7&itool=pubmed_docsum

- **A family with segregating triplicated alpha globin loci and beta thalassemia.**
 Author(s): Galanello R, Ruggeri R, Paglietti E, Addis M, Melis MA, Cao A.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6313095&query_hl=7&itool=pubmed_docsum

- **A new mutation in IVS-1 of the human beta globin gene causing beta thalassemia due to abnormal splicing.**
 Author(s): Atweh GF, Wong C, Reed R, Antonarakis SE, Zhu D, Ghosh PK, Maniatis T, Forget BG, Kazazian HH Jr.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2439149&query_hl=7&itool=pubmed_docsum

- **A novel beta thalassemia gene with a single base mutation in the conserved polypyrimidine sequence at the 3' end of IVS 2.**
 Author(s): Beldjord C, Lapoumeroulie C, Pagnier J, Benabadji M, Krishnamoorthy R, Labie D, Bank A.
 Source: Nucleic Acids Research.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3387213&query_hl=7&itool=pubmed_docsum

- **A novel molecular basis for beta thalassemia intermedia poses new questions about its pathophysiology.**
 Author(s): Premawardhena A, Fisher CA, Olivieri NF, de Silva S, Sloane-Stanley J, Wood WG, Weatherall DJ.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15947092&query_hl=7&itool=pubmed_docsum
- **A simple screening test for the detection of heterozygous beta thalassemia.**
 Author(s): Thool AA, Walde MS, Shrikhande AV, Talib VH.
 Source: Indian J Pathol Microbiol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9866902&query_hl=7&itool=pubmed_docsum
- **A study of membrane protein defects and alpha hemoglobin chains of red blood cells in human beta thalassemia.**
 Author(s): Rouyer-Fessard P, Garel MC, Domenget C, Guetarni D, Bachir D, Colonna P, Beuzard Y.
 Source: The Journal of Biological Chemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2808414&query_hl=7&itool=pubmed_docsum
- **A study of serum ferritin in beta thalassemia. Iron deficiency and overload.**
 Author(s): Saraya AK, Kumar R, Choudhry VP, Kailash S, Sehgal AK.
 Source: American Journal of Clinical Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=4014070&query_hl=7&itool=pubmed_docsum
- **Acquired sea-blue histiocytosis in beta thalassemia major.**
 Author(s): Das S, Garg G, Isaacs R.
 Source: Indian J Pathol Microbiol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16761752&query_hl=7&itool=pubmed_docsum
- **Alpha globin gene triplication in severe heterozygous beta thalassemia.**
 Author(s): Henni T, Belhani M, Morle F, Bachir D, Tabone P, Colonna P, Godet J.
 Source: Acta Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3012927&query_hl=7&itool=pubmed_docsum
- **Alpha, beta thalassemia produces high levels of Hb Bart's in newborns and high HbA2 in adults.**
 Author(s): Martinez G, Colombo B.
 Source: Haematologia.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3653791&query_hl=7&itool=pubmed_docsum

- **Analysis of folate and vitamin B12 in beta thalassemia minor.**
 Author(s): Gallerani M, Cicognani I, Ballardini P, Martinelli L, Ricci A, Dall'Ara G, Faggioli M.
 Source: Riv Eur Sci Med Farmacol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2103964&query_hl=7&itool=pubmed_docsum
- **Antenatal diagnosis of beta thalassemia.**
 Author(s): Maggio A, Castellano S.
 Source: British Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6466569&query_hl=7&itool=pubmed_docsum
- **Antenatal diagnosis of severe beta thalassemia during the first trimester of pregnancy.**
 Author(s): Trent RJ, Anderson J, Boogert T, Kronenberg H.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3005951&query_hl=7&itool=pubmed_docsum
- **Application of a monoclonal antibody specific for the delta chain of hemoglobin A2 in the diagnosis of beta thalassemia.**
 Author(s): Shyamala M, Kiefer CR, Moscoso H, Garver FA.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1951320&query_hl=7&itool=pubmed_docsum
- **Application of DNA polymorphisms for prenatal diagnosis of beta thalassemia in Chinese.**
 Author(s): Chan V, Chan TK, Ghosh A, Wong LC, Ma HK, Kan YW, Todd D.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2887108&query_hl=7&itool=pubmed_docsum
- **Association of beta thalassemia, beta c, alpha thalassemia and mental retardation.**
 Author(s): Sammarco P, Cocuzza S, Maggio A, Avola G, Lo Gioco P, Giambona A, Di Marzo R, Rosella A.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3104162&query_hl=7&itool=pubmed_docsum
- **Beta thalassemia and heart disease: three decades of gradual progress.**
 Author(s): Engle MA, Ehlers KH, O'Loughlin JE, Giardina PJ, Hilgartner MW.
 Source: Trans Am Clin Climatol Assoc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6242259&query_hl=7&itool=pubmed_docsum

- **Beta thalassemia due to a novel mutation in IVS 1 sequence donor site consensus sequence creating a restriction site.**
 Author(s): Lapoumeroulie C, Pagnier J, Bank A, Labie D, Krishnamoorthy R.
 Source: Biochemical and Biophysical Research Communications.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3021139&query_hl=7&itool=pubmed_docsum
- **Beta thalassemia in Melanesia: association with malaria and characterization of a common variant (IVS-1 nt 5 G----C).**
 Author(s): Hill AV, Bowden DK, O'Shaughnessy DF, Weatherall DJ, Clegg JB.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2898955&query_hl=7&itool=pubmed_docsum
- **Beta thalassemia: an immunologic therapy?**
 Author(s): Brent L, Rayfield LS, Modell B.
 Source: Transplantation Proceedings.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6129726&query_hl=7&itool=pubmed_docsum
- **Bone marrow transplantation with T-cell depleted allografts for the treatment of severe beta thalassemia major.**
 Author(s): Or R, Naparstek E, Aker M, Cividalli G, Engelhard D, Brautbar C, Weshler Z, Weiss L, Mumcuoglu M, Rachmilewitz EA, et al.
 Source: Prog Clin Biol Res.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2675089&query_hl=7&itool=pubmed_docsum
- **Bone scintigraphic findings in a patient with beta thalassemia major and knee pain.**
 Author(s): Di Leo C, Bestetti A, Tagliabue L, Cornalba GP, Tarolo GL.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15075113&query_hl=7&itool=pubmed_docsum
- **Case report 274. Beta thalassemia affecting the facial bones and skull (intermediate form).**
 Author(s): Fernbach SK.
 Source: Skeletal Radiology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6729507&query_hl=7&itool=pubmed_docsum
- **Characteristics and distribution of beta thalassemia haplotypes in South China.**
 Author(s): Chan V, Chan TK, Cheng MY, Leung NK, Kan YW, Todd D.
 Source: Human Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3011644&query_hl=7&itool=pubmed_docsum

- **Chorionic villous sampling for prenatal diagnosis in beta thalassemia.**
Author(s): Dubey AP, Sudha S.
Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15923706&query_hl=7&itool=pubmed_docsum
- **Coinheritance of Rotor syndrome, G-6-PD deficiency, and heterozygous beta thalassemia: a possible genetic interaction.**
Author(s): Fretzayas A, Koukoutsakis P, Moustaki M, Stavrinadis C, Karpathios T.
Source: Journal of Pediatric Gastroenterology and Nutrition.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11568527&query_hl=7&itool=pubmed_docsum
- **Comparison of cost effectiveness between measuring the serum erythropoietin level and reticulocyte count for monitoring thalassemic patients: a note in Thai beta thalassemia/Hb E subjects.**
Author(s): Wiwanitkit V.
Source: Hematology (Amsterdam, Netherlands).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15621741&query_hl=7&itool=pubmed_docsum
- **Comparison of organ dysfunction in transfused patients with SCD or beta thalassemia.**
Author(s): Vichinsky E, Butensky E, Fung E, Hudes M, Theil E, Ferrell L, Williams R, Louie L, Lee PD, Harmatz P.
Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16138345&query_hl=7&itool=pubmed_docsum
- **Comparison of red cell distribution width and a red cell discriminant function incorporating volume dispersion for distinguishing iron deficiency from beta thalassemia trait in patients with microcytosis.**
Author(s): Lima CS, Reis AR, Grotto HZ, Saad ST, Costa FF.
Source: Sao Paulo Medical Journal = Revista Paulista De Medicina.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9239926&query_hl=7&itool=pubmed_docsum
- **Cyclosporin A and mini short-term methotrexate vs cyclosporin A as graft-versus-host disease prophylaxis in patients with beta thalassemia major undergoing allogeneic blood and marrow transplantation.**
Author(s): Iravani M, Mousavi A, Gholibeikian S, Bahar B, Samiee S, Ashouri A, Eghbal L, Ghavamzadeh A.
Source: Bone Marrow Transplantation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15821773&query_hl=7&itool=pubmed_docsum

- **Cytochemical evaluation of neutrophil components in beta thalassemia hemoglobin E.**
 Author(s): Trewatcharegon S, Apibal S, Bunyaratvej A, Fucharoen S.
 Source: J Med Assoc Thai.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2738488&query_hl=7&itool=pubmed_docsum
- **Decreased bone magnesium in beta thalassemia with spinal osteoporosis.**
 Author(s): Cohen L, Bitterman H, Froom P, Aghai E.
 Source: Magnesium.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3959597&query_hl=7&itool=pubmed_docsum
- **Deferiprone (L1) associated neutropenia in beta thalassemia major: an Indian experience.**
 Author(s): Pati HP, Choudhry VP.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10530416&query_hl=7&itool=pubmed_docsum
- **Delta beta thalassemia and hereditary persistence of fetal hemoglobin.**
 Author(s): Bollekens JA, Forget BG.
 Source: Hematology/Oncology Clinics of North America.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1713909&query_hl=7&itool=pubmed_docsum
- **Delta-aminolevulinic acid levels in the serum and urine of persons with heterozygous and homozygous beta thalassemia.**
 Author(s): Mehta BC, Rao MS, Agarwal MB.
 Source: The Indian Journal of Medical Research.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6874021&query_hl=7&itool=pubmed_docsum
- **Detection of beta and delta globin gene mutations by PCR and direct DNA sequencing in an individual with normal HbA2 beta thalassemia.**
 Author(s): Trent RJ, Thein SL.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1349739&query_hl=7&itool=pubmed_docsum
- **Diagnosis of beta thalassemia trait.**
 Author(s): Agarwal MB.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2090609&query_hl=7&itool=pubmed_docsum

- **Differing erythrocyte membrane skeletal protein defects in alpha and beta thalassemia.**
 Author(s): Shinar E, Rachmilewitz EA, Lux SE.
 Source: The Journal of Clinical Investigation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2521488&query_hl=7&itool=pubmed_docsum
- **Echocardiographic features in patients with beta thalassemia/hemoglobin E: a combining effect of anemia and iron load.**
 Author(s): Intragumtornchai T, Minaphinant K, Wanichsawat C, Somabutr C, Posayachinda M, Watananukul P, Chinayon C.
 Source: J Med Assoc Thai.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7798836&query_hl=7&itool=pubmed_docsum
- **Effects of beta thalassemia minor on results of six glycated hemoglobin methods.**
 Author(s): Polage C, Little RR, Rohlfing CL, Cole TG, Roberts WL.
 Source: Clinica Chimica Acta; International Journal of Clinical Chemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15530468&query_hl=7&itool=pubmed_docsum
- **Efficacy and safety of oral iron chelating agent deferiprone in beta-thalassemia and hemoglobin E-beta thalassemia.**
 Author(s): Adhikari D, Roy TB, Biswas A, Chakraborty ML, Bhattacharya B, Maitra TK, Basu AK, Chandra S.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8635827&query_hl=7&itool=pubmed_docsum
- **Efficacy of erythropoietin on dialysis in patients with beta thalassemia minor.**
 Author(s): Di Iorio B, De Nicola L, Bellizzi V, Minutolo R, Zamboli P, Rubino R, Fuiano G, Conte G.
 Source: Blood Purification.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15359104&query_hl=7&itool=pubmed_docsum
- **Elastic tissue abnormalities resembling pseudoxanthoma elasticum in beta thalassemia and the sickling syndromes.**
 Author(s): Aessopos A, Farmakis D, Loukopoulos D.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11756149&query_hl=7&itool=pubmed_docsum
- **Elevated G gamma:A gamma globin chain ratio in homozygous beta thalassemia.**
 Author(s): Ponnazhagan S, Betsy J, Sarkar R.
 Source: Clinical Biochemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1705184&query_hl=7&itool=pubmed_docsum

- Elevated RDW in delta beta thalassemia.**
 Author(s): Donoghue AP.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3588020&query_hl=7&itool=pubmed_docsum
- Entrapment of purified alpha-hemoglobin chains in normal erythrocytes. A model for beta thalassemia.**
 Author(s): Scott MD, Rouyer-Fessard P, Lubin BH, Beuzard Y.
 Source: The Journal of Biological Chemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2211672&query_hl=7&itool=pubmed_docsum
- Erythrocyte P antigen in beta thalassemia major patients with human parvovirus-B19 infection.**
 Author(s): Akar N, Sipahi T, Akar E.
 Source: Pediatric Hematology and Oncology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8940744&query_hl=7&itool=pubmed_docsum
- Evaluation of alpha hemoglobin stabilizing protein (AHSP) as a genetic modifier in patients with beta thalassemia.**
 Author(s): Viprakasit V, Tanphaichitr VS, Chinchang W, Sangkla P, Weiss MJ, Higgs DR.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14715623&query_hl=7&itool=pubmed_docsum
- Evaluation of soluble transferrin receptor levels in children with iron deficiency and beta thalassemia trait, and in newborns and their mothers.**
 Author(s): Polat A, Kaptanoglu B, Aydin K, Keskin A.
 Source: Turk J Pediatr.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12458802&query_hl=7&itool=pubmed_docsum
- Expression of a beta thalassemia gene with abnormal splicing.**
 Author(s): Lapoumeroulie C, Acuto S, Rouabhi F, Labie D, Krishnamoorthy R, Bank A.
 Source: Nucleic Acids Research.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3671081&query_hl=7&itool=pubmed_docsum
- First observation of homozygous hemoglobin hamadan (B 56 (D7) GLY-ARG) and beta thalassemia (-29 G>A)- hemoglobin Hamadan combination in a Turkish family.**
 Author(s): Akar E, Ozdemir S, Hakki Timur I, Akar N.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14635211&query_hl=7&itool=pubmed_docsum

- Fractures in transfusion dependent beta thalassemia—an Indian study.**
 Author(s): Basanagoudar PL, Gill SS, Dhillon MS, Marwaha RK.
 Source: Singapore Med J.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11513055&query_hl=7&itool=pubmed_docsum
- Functional analysis of a beta-globin gene containing a TATA box mutation from a Kurdish Jew with beta thalassemia.**
 Author(s): Surrey S, Delgrosso K, Malladi P, Schwartz E.
 Source: The Journal of Biological Chemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2987224&query_hl=7&itool=pubmed_docsum
- Genetic heterogeneity of Beta thalassemia in Lebanon reflects historic and recent population migration.**
 Author(s): Makhoul NJ, Wells RS, Kaspar H, Shbaklo H, Taher A, Chakar N, Zalloua PA.
 Source: Annals of Human Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15638828&query_hl=7&itool=pubmed_docsum
- Genetic heterogeneity of beta thalassemia in western Sicily.**
 Author(s): Pirrone A, Maggio A, Gambino R, Hauser D, Acuto S, Romano V, Buttice G, Caronia F.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6819188&query_hl=7&itool=pubmed_docsum
- Glutathione S-transferase activity influences busulfan pharmacokinetics in patients with beta thalassemia major undergoing bone marrow transplantation.**
 Author(s): Poonkuzhali B, Chandy M, Srivastava A, Dennison D, Krishnamoorthy R.
 Source: Drug Metabolism and Disposition: the Biological Fate of Chemicals.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11181493&query_hl=7&itool=pubmed_docsum
- Hematological phenotype of the double heterozygous state for alpha and beta thalassemia.**
 Author(s): Rosatelli C, Falchi AM, Scalas MT, Tuveri T, Furbetta M, Cao A.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6202659&query_hl=7&itool=pubmed_docsum
- Heme arginate therapy for beta thalassemia: in vitro versus in vivo effects.**
 Author(s): Rund D, Fibach E, Goldfarb A, Friedberg A, Rachmilewitz E.
 Source: Acta Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9792937&query_hl=7&itool=pubmed_docsum

- **Hemoglobin Chesterfield (beta 28 Leu----Arg) produces the phenotype of inclusion body beta thalassemia.**
 Author(s): Thein SL, Best S, Sharpe J, Paul B, Clark DJ, Brown MJ.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1675132&query_hl=7&itool=pubmed_docsum
- **Hemoglobin Setif and in vitro pseudosickling noted in a family with co-existent alpha and beta thalassemia.**
 Author(s): Raik E, Powell E, Fleming P, Gordon S.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6674875&query_hl=7&itool=pubmed_docsum
- **Hemoglobin-Q-India (64 (E13) Asp-His) and beta thalassemia: a case report from Punjab (North India)**
 Author(s): Dash S, Huisman TH.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3356245&query_hl=7&itool=pubmed_docsum
- **Hemorheological changes in blood transfusion-treated beta thalassemia major patients.**
 Author(s): Mangalani M, Lokeshwar MR, Banerjee R, Nageswari K, Puniyani RR.
 Source: Clinical Hemorheology and Microcirculation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9699030&query_hl=7&itool=pubmed_docsum
- **Hepatic iron overload does not prevent a sustained virological response to interferon-alpha therapy: a long term follow-up study in hepatitis C-infected patients with beta thalassemia major.**
 Author(s): Sievert W, Pianko S, Warner S, Bowden S, Simpson I, Bowden D, Locarnini S.
 Source: The American Journal of Gastroenterology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12003436&query_hl=7&itool=pubmed_docsum
- **Heterocellular hereditary persistence of fetal hemoglobin (HPFH). Molecular mechanisms of abnormal gamma-gene expression in association with beta thalassemia and linkage relationship with the beta-globin gene cluster.**
 Author(s): Giampaolo A, Mavilio F, Sposi NM, Care A, Massa A, Cianetti L, Petrini M, Russo R, Cappellini MD, Marinucci M.
 Source: Human Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6201431&query_hl=7&itool=pubmed_docsum

- **Heterogeneity of beta thalassemia.**
 Author(s): Schiliro G, Russo A.
 Source: American Journal of Medical Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2422933&query_hl=7&itool=pubmed_docsum
- **Heterozygous beta thalassemia. A case report.**
 Author(s): Gore AL.
 Source: Ala Med.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6731209&query_hl=7&itool=pubmed_docsum
- **Homozygous beta thalassemia and cancer.**
 Author(s): Miniero R, Pastore G, Saracco P, Terracini B.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3924763&query_hl=7&itool=pubmed_docsum
- **Homozygous beta thalassemia in an African-American pediatric patient.**
 Author(s): DeBall S, Gordy FM.
 Source: J Clin Pediatr Dent.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9484118&query_hl=7&itool=pubmed_docsum
- **Homozygous beta thalassemia presenting as neonatal jaundice.**
 Author(s): Hazir T, Qazi SA, Abbas KA.
 Source: J Pak Med Assoc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8920616&query_hl=7&itool=pubmed_docsum
- **Image interpretation session: 1999. Extramedullary hematopoiesis in a patient with beta thalassemia.**
 Author(s): Dunnick NR.
 Source: Radiographics : a Review Publication of the Radiological Society of North America, Inc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10682787&query_hl=7&itool=pubmed_docsum
- **Impact of beta globin gene mutations on the clinical phenotype of beta thalassemia in India.**
 Author(s): Colah R, Nadkarni A, Gorakshakar A, Phanasgaonkar S, Surve R, Subramaniam PG, Bondge N, Pujari K, Ghosh K, Mohanty D.
 Source: Blood Cells, Molecules & Diseases.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15315795&query_hl=7&itool=pubmed_docsum

- **Inadequate utilization of routine electronic RBC counts to identify beta thalassemia carriers.**
 Author(s): Shalev O, Yehezkel E, Rachmilewitz EA.
 Source: American Journal of Public Health.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3177725&query_hl=7&itool=pubmed_docsum
- **Indication of genotype of beta thalassemia based on hemoglobins A2 and F.**
 Author(s): Kumar R, Saraya AK, Choudhry VP.
 Source: Journal of Tropical Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6204062&query_hl=7&itool=pubmed_docsum
- **Indications and results for splenectomy for beta thalassemia in two hundred and twenty-one pediatric patients.**
 Author(s): Pinna AD, Argioliu F, Marongiu L, Pinna DC.
 Source: Surg Gynecol Obstet.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3400027&query_hl=7&itool=pubmed_docsum
- **Induction of hemoglobin F synthesis in patients with beta thalassemia.**
 Author(s): Ley TJ, Nienhuis AW.
 Source: Annual Review of Medicine.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2581500&query_hl=7&itool=pubmed_docsum
- **Intraoperative blood salvage during cesarean delivery in a patient with beta thalassemia intermedia.**
 Author(s): Waters JH, Lukauskiene E, Anderson ME.
 Source: Anesthesia and Analgesia.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14633564&query_hl=7&itool=pubmed_docsum
- **Iron deficiency amongst family members in relation to carrier state of beta thalassemia trait.**
 Author(s): Mehta BC, Bhargava AB.
 Source: Indian Journal of Medical Sciences.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6654442&query_hl=7&itool=pubmed_docsum
- **Iron overload and left ventricular performance in beta thalassemia.**
 Author(s): Kremastinos DT, Toutouzas PK, Vyssoulis GP, Venetis CA, Avgoustakis DG.
 Source: Acta Cardiol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6609505&query_hl=7&itool=pubmed_docsum

- **Iron status of beta thalassemia carriers.**
 Author(s): Mehta BC, Pandya BG.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3812467&query_hl=7&itool=pubmed_docsum
- **Is hemoglobin instability important in the interaction between hemoglobin E and beta thalassemia?**
 Author(s): Rees DC, Clegg JB, Weatherall DJ.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9731073&query_hl=7&itool=pubmed_docsum
- **Isolated thrombocytopenia associated with hydroxyurea/deferiprone (L1) therapy in a sickle beta thalassemia patient.**
 Author(s): Sheikh-Taha M, Koussa S, Taher A.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16785128&query_hl=7&itool=pubmed_docsum
- **Juvenile myelomonocytic leukemia (JMML) with the hematologic phenotype of severe beta thalassemia.**
 Author(s): Honig GR, Suarez CR, Vida LN, Lu SJ, Liu ET.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9590152&query_hl=7&itool=pubmed_docsum
- **Laparoscopic versus open splenectomy in patients with beta thalassemia major.**
 Author(s): Konstadoulakis MM, Lagoudianakis E, Antonakis PT, Albanopoulos K, Gomatos I, Stamou KM, Leandros E, Manouras A.
 Source: Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16494539&query_hl=7&itool=pubmed_docsum
- **L-Carnitine treatment in beta thalassemia major.**
 Author(s): Yesilipek MA, Hazar V, Yegin O.
 Source: Acta Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9858797&query_hl=7&itool=pubmed_docsum
- **Management of beta thalassemia.**
 Author(s): Goyal R.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10820563&query_hl=7&itool=pubmed_docsum

- Molecular basis of beta thalassemia in south China. Strategy for DNA analysis.**
 Author(s): Zhang JZ, Cai SP, He X, Lin HX, Lin HJ, Huang ZG, Chehab FF, Kan YW.
 Source: Human Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3338793&query_hl=7&itool=pubmed_docsum
- Molecular basis of beta thalassemia in the south of Thailand.**
 Author(s): Laosombat V, Fucharoen SP, Panich V, Fucharoen G, Wongchanchailert M, Sriroongrueng W, Nopparatana C, Kenpitak K, Maipang M, Fukumaki Y.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1415194&query_hl=7&itool=pubmed_docsum
- Molecular characterization of a high A2 beta thalassemia by direct sequencing of single strand enriched amplified genomic DNA.**
 Author(s): Thein SL, Hesketh C, Brown JM, Anstey AV, Weatherall DJ.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2920214&query_hl=7&itool=pubmed_docsum
- Molecular diagnosis and carrier screening for beta thalassemia.**
 Author(s): Cao A, Saba L, Galanello R, Rosatelli MC.
 Source: Jama : the Journal of the American Medical Association.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9333270&query_hl=7&itool=pubmed_docsum
- Molecular genetic diagnosis of beta thalassemia in Pakistan.**
 Author(s): Khan SN, Zafar AU, Riazuddin S.
 Source: J Pak Med Assoc.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7596015&query_hl=7&itool=pubmed_docsum
- Molecular mechanisms associated with increased fetal hemoglobin G gamma-type in part-aboriginal family with beta thalassemia.**
 Author(s): Motum PI, Lammi A, Trent RJ.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2483259&query_hl=7&itool=pubmed_docsum
- Molecular pathology of beta thalassemia intermedia.**
 Author(s): Lu CY, Ragusa A, Goncalves I, Lapoumeroulie C, Krishnamoorthy R.
 Source: Nouv Rev Fr Hematol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7687777&query_hl=7&itool=pubmed_docsum

- **Mouse beta thalassemia, a model for the membrane defects of erythrocytes in the human disease.**
 Author(s): Rouyer-Fessard P, Leroy-Viard K, Domenget C, Mrad A, Beuzard Y.
 Source: The Journal of Biological Chemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2243088&query_hl=7&itool=pubmed_docsum
- **Multi-organ failure associated with acute parvovirus infection and exercise in a patient with sickle beta thalassemia.**
 Author(s): Nguyen H, Le C.
 Source: Southern Medical Journal.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15586616&query_hl=7&itool=pubmed_docsum
- **NESTROFT: a screening test for beta thalassemia trait.**
 Author(s): Mehta BC.
 Source: Indian Journal of Medical Sciences.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14510336&query_hl=7&itool=pubmed_docsum
- **'NESTROFT'--an effective screening test for beta thalassemia trait.**
 Author(s): Manglani M, Lokeshwar MR, Vani VG, Bhatia N, Mhaskar V.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9492398&query_hl=7&itool=pubmed_docsum
- **Non-anemic homozygous beta(o) thalassemia in an African-American family: association of high fetal hemoglobin levels with beta thalassemia alleles.**
 Author(s): Divoky V, Mrug M, Thornley-Brown D, Divoka M, Prchal JT.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11559936&query_hl=7&itool=pubmed_docsum
- **Ocular abnormalities in patients with beta thalassemia.**
 Author(s): Gartaganis S, Ismiridis K, Papageorgiou O, Beratis NG, Papanastasiou D.
 Source: American Journal of Ophthalmology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2596550&query_hl=7&itool=pubmed_docsum
- **Oligonucleotide screening of beta thalassemia mutations in the south east of France.**
 Author(s): Milland M, Berge-Lefranc JL, Lena D, Cartouzou G.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3667319&query_hl=7&itool=pubmed_docsum

- **Oral sodium phenylbutyrate therapy in homozygous beta thalassemia: a clinical trial.**
 Author(s): Collins AF, Pearson HA, Giardina P, McDonagh KT, Brusilow SW, Dover GJ.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7528572&query_hl=7&itool=pubmed_docsum
- **Permanent and panerythroid correction of murine beta thalassemia by multiple lentiviral integration in hematopoietic stem cells.**
 Author(s): Imren S, Payen E, Westerman KA, Pawliuk R, Fabry ME, Eaves CJ, Cavilla B, Wadsworth LD, Beuzard Y, Bouhassira EE, Russell R, London IM, Nagel RL, Leboulch P, Humphries RK.
 Source: Proceedings of the National Academy of Sciences of the United States of America.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12391330&query_hl=7&itool=pubmed_docsum
- **Pictorial CME. beta Thalassemia intermedia.**
 Author(s): Kulkarni V, Kamath S, Bichile SK.
 Source: J Assoc Physicians India.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11229188&query_hl=7&itool=pubmed_docsum
- **Plasma exchange in refractory autoimmune anemia in a child with systemic vasculitis associated with homozygote beta thalassemia.**
 Author(s): Besbas N, Ozen S, Bakkaloglu A, Gurgey A, Kanra T, Saatci U.
 Source: Turk J Pediatr.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7825242&query_hl=7&itool=pubmed_docsum
- **Pregnancy and homozygous beta thalassemia major.**
 Author(s): Surbek DV, Glanzmann R, Holzgreve W.
 Source: British Journal of Obstetrics and Gynaecology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10426266&query_hl=7&itool=pubmed_docsum
- **Presidential address. Iron deficiency--a cause of high prevalence of beta thalassemia in India?**
 Author(s): Mehta BC.
 Source: J Assoc Physicians India.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=4044494&query_hl=7&itool=pubmed_docsum
- **Prevalence of the H63D mutation of the HFE in north India: its presence does not cause iron overload in beta thalassemia trait.**
 Author(s): Garewal G, Das R, Ahluwalia J, Marwaha RK.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15777346&query_hl=7&itool=pubmed_docsum

- **Prophylactic cholecystectomy during splenectomy for beta thalassemia homozygous in Greece.**
 Author(s): Feretis CB, Legakis NC, Apostolidis NS, Katergiannakis VA, Philippakis MG.
 Source: Surg Gynecol Obstet.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3964971&query_hl=7&itool=pubmed_docsum
- **Pulmonary function tests in beta thalassemia.**
 Author(s): Arora M, Chandra J, Suri JC, Narayan S, Dutta AK.
 Source: Indian J Pediatr.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11338220&query_hl=7&itool=pubmed_docsum
- **Quantitative determinations of microcytic-hypochromic red blood cell population and glycerol permeability in iron-deficiency anemia and beta thalassemia minor.**
 Author(s): Yermiahu T, Ben-Shalom M, Porath A, Vardi H, Boantz A, Mazor D, Meyerstein N.
 Source: Annals of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10550558&query_hl=7&itool=pubmed_docsum
- **Rapid detection of a 13.4-kb deletion causing delta beta thalassemia in an Egyptian family by polymerase chain reaction.**
 Author(s): Craig JE, Barnetson R, Weatherall DJ, Thein SL.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8427978&query_hl=7&itool=pubmed_docsum
- **Rapid detection of deletions causing delta beta thalassemia and hereditary persistence of fetal hemoglobin by enzymatic amplification.**
 Author(s): Craig JE, Barnetson RA, Prior J, Raven JL, Thein SL.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7510147&query_hl=7&itool=pubmed_docsum
- **Rapid diagnosis of beta thalassemia mutations in Mediterraneans by PCR and restriction analysis of natural or created sites.**
 Author(s): Le Denmat C, Duchassaing D.
 Source: Clinical Biochemistry.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9253521&query_hl=7&itool=pubmed_docsum
- **Rapid prenatal diagnosis of beta thalassemia using DNA amplification and nonradioactive probes.**
 Author(s): Cai SP, Chang CA, Zhang JZ, Saiki RK, Erlich HA, Kan YW.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2917180&query_hl=7&itool=pubmed_docsum

- **Recombinant human erythropoietin for anemia of end-stage renal failure in beta thalassemia trait.**
 Author(s): Kagan A, Sinay-Trieman L, Bar-Khayim Y.
 Source: Nephron.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1436320&query_hl=7&itool=pubmed_docsum
- **Scoliosis in beta thalassemia.**
 Author(s): Papageorgiou O, Papanastasiou DA, Beratis NG, Korovessis P, Oikonomopoulos A.
 Source: Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1861937&query_hl=7&itool=pubmed_docsum
- **Serum carnitine levels in patients with homozygous beta thalassemia: a possible new role for carnitine?**
 Author(s): Tsagris V, Liapi-Adamidou G.
 Source: European Journal of Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15717177&query_hl=7&itool=pubmed_docsum
- **Serum erythropoietin levels in patients with beta thalassemia major and intermedia.**
 Author(s): Nisli G, Kavakli K, Aydinok Y, Oztop S, Cetingul N.
 Source: Pediatric Hematology and Oncology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9089744&query_hl=7&itool=pubmed_docsum
- **Sexual performance and fertility potential in patients with beta thalassemia major.**
 Author(s): Katz M, De Sanctis V, Wonke B, Vullo C, Bagni B, Zucchi F, Hoffbrand AV.
 Source: Prog Clin Biol Res.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2780751&query_hl=7&itool=pubmed_docsum
- **Sickle cell beta thalassemia with absence of spleen (a case report).**
 Author(s): Hardikar JV, Nadkarni SV.
 Source: Journal of Postgraduate Medicine.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6672184&query_hl=7&itool=pubmed_docsum
- **Sodium butyrate enhances fetal globin gene expression in erythroid progenitors of patients with Hb SS and beta thalassemia.**
 Author(s): Perrine SP, Miller BA, Faller DV, Cohen RA, Vichinsky EP, Hurst D, Lubin BH, Papayannopoulou T.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2473801&query_hl=7&itool=pubmed_docsum

- **Soluble transferrin receptor following bone marrow transplantation from donors heterozygous for beta thalassemia.**
 Author(s): Centis F, Delfini C, Agostinelli F, Tonucci P, Gaziev J, Annibali M, Lucarelli G.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7843631&query_hl=7&itool=pubmed_docsum
- **Spectrum of beta thalassemia mutations and HbF levels in the heterozygous Moroccan population.**
 Author(s): Lemsaddek W, Picanco I, Seuanes F, Mahmal L, Benchekroun S, Khattab M, Nogueira P, Osorio-Almeida L.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12827652&query_hl=7&itool=pubmed_docsum
- **Spectrum of beta thalassemia mutations and their linkage to beta-globin gene haplotypes in the Indo-Mauritians.**
 Author(s): Kotea N, Ramasawmy R, Lu CY, Fa NS, Gerard N, Beesoon S, Ducrocq R, Surrin SK, Nagel RL, Krishnamoorthy R.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10602161&query_hl=7&itool=pubmed_docsum
- **Structure and expression of two beta genes in a beta thalassemia homozygote.**
 Author(s): Young K, Margulies L, Donovan-Peluso M, Clyne J, Driscoll MC, Dobkin C, Leibowitz D, Russo G, Schiliro G, Bank A.
 Source: J Mol Appl Genet.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=4009093&query_hl=7&itool=pubmed_docsum
- **Successful correction of the human Cooley's anemia beta-thalassemia major phenotype using a lentiviral vector flanked by the chicken hypersensitive site 4 chromatin insulator.**
 Author(s): Malik P, Arumugam PI, Yee JK, Puthenveetil G.
 Source: Annals of the New York Academy of Sciences.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16339671&query_hl=7&itool=pubmed_docsum
- **Synergic effect of chronic hepatitis C infection and beta thalassemia major with marked hepatic iron overload on liver fibrosis: a retrospective cross-sectional study.**
 Author(s): Ardalan FA, Osquei MR, Toosi MN, Irvanloo G.
 Source: BMC Gastroenterology [electronic Resource].
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15307893&query_hl=7&itool=pubmed_docsum

- **The activity of superoxide dismutase in hydroxyurea-treated E beta thalassemia.**
 Author(s): Ajanta H, Chakraborty S, Madhusnata D, Bhattacharya DK, Manisha D.
 Source: J Assoc Physicians India.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12421025&query_hl=7&itool=pubmed_docsum
- **The effect of the beta thalassemia mutation on the clinical severity of the sickle beta thalassemia syndrome.**
 Author(s): Perseu L, Ristaldi MS, Dibenedetto SP, Testa R, Schiliro G, Pirastu M, Cao A.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2507407&query_hl=7&itool=pubmed_docsum
- **The frequency of anaemia, iron deficiency, hemoglobin S and beta thalassemia in the south of Turkey.**
 Author(s): Kocak R, Alparslan ZN, Agridag G, Baslamisli F, Aksungur PD, Koltas S.
 Source: European Journal of Epidemiology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7672073&query_hl=7&itool=pubmed_docsum
- **The inactive beta globin gene on a gamma delta beta thalassemia chromosome has a normal structure and functions normally in vitro.**
 Author(s): Curtin PT, Kan YW.
 Source: Blood.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=3345345&query_hl=7&itool=pubmed_docsum
- **The pathophysiology and molecular genetics of beta thalassemia.**
 Author(s): Forget BG.
 Source: The Mount Sinai Journal of Medicine, New York.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8469250&query_hl=7&itool=pubmed_docsum
- **The regulation of beta globin gene expression and beta thalassemia.**
 Author(s): Ho PJ.
 Source: Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10643000&query_hl=7&itool=pubmed_docsum
- **The silent carrier allele: beta thalassemia without a mutation in the beta-globin gene or its immediate flanking regions.**
 Author(s): Semenza GL, Delgrosso K, Poncz M, Malladi P, Schwartz E, Surrey S.
 Source: Cell.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6091904&query_hl=7&itool=pubmed_docsum

- **Thromboembolic complications in beta thalassemia major.**
 Author(s): Michaeli J, Mittelman M, Grisaru D, Rachmilewitz EA.
 Source: Acta Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1585774&query_hl=7&itool=pubmed_docsum
- **Thromboembolic events in beta thalassemia major: an Italian multicenter study.**
 Author(s): Borgna Pignatti C, Carnelli V, Caruso V, Dore F, De Mattia D, Di Palma A, Di Gregorio F, Romeo MA, Longhi R, Mangiagli A, Melevendi C, Pizzarelli G, Musumeci S.
 Source: Acta Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9554453&query_hl=7&itool=pubmed_docsum
- **Understanding the basics of beta thalassemia major.**
 Author(s): Martin MB, Butler RB.
 Source: Pediatric Nursing.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8502496&query_hl=7&itool=pubmed_docsum
- **Unique features of laparoscopic cholecystectomy in Beta thalassemia patients.**
 Author(s): Katz R, Goldfarb A, Muggia M, Gimmon Z.
 Source: Surgical Laparoscopy, Endoscopy & Percutaneous Techniques.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=14571167&query_hl=7&itool=pubmed_docsum
- **Unusual combination of genetic defects in a Sicilian boy: G gamma delta beta thalassemia, G gamma A gamma heterocellular HPFH, beta (0) thalassemia, and albinism.**
 Author(s): Schiliro G, Pavone L, Romeo MA, Russo A, Musumeci S, Russo G.
 Source: American Journal of Medical Genetics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=6192718&query_hl=7&itool=pubmed_docsum
- **Visual failure caused by suprasellar extramedullary hematopoiesis in beta thalassemia: case report.**
 Author(s): Aarabi B, Haghshenas M, Rakeii V.
 Source: Neurosurgery.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9574659&query_hl=7&itool=pubmed_docsum
- **Vitamin B12, folate, and iron studies in homozygous beta thalassemia.**
 Author(s): Kumar R, Saraya AK, Choudhyr VP, Sundaram KR, Kailash S, Sehgal AK.
 Source: American Journal of Clinical Pathology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=4061393&query_hl=7&itool=pubmed_docsum

- **Whole blood viscosity in beta thalassemia minor.**
 Author(s): Crowley JP, Metzger JB, Merrill EW, Valeri CR.
 Source: Ann Clin Lab Sci.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1503390&query_hl=7&itool=pubmed_docsum

- **Yersinia enterocolitica infection in a boy with beta thalassemia major.**
 Author(s): Monno R, Valenza MA, Quarto M, Sabato V, De Mattia D, Paradies G, Montinaro L, Fumarola D.
 Source: The Pediatric Infectious Disease Journal.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8177635&query_hl=7&itool=pubmed_docsum

- **Zinc status and zinc therapy in beta thalassemia.**
 Author(s): Arcasoy A.
 Source: Am J Pediatr Hematol Oncol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2751077&query_hl=7&itool=pubmed_docsum

CHAPTER 2. ALTERNATIVE MEDICINE AND BETA THALASSEMIA

Overview

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

National Center for Complementary and Alternative Medicine

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

- **A randomized controlled study evaluating the safety and efficacy of deferiprone treatment in thalassemia major patients from Hong Kong.**
Author(s): Ha SY, Chik KW, Ling SC, Lee AC, Luk CW, Lam CW, Ng IO, Chan GC.
Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798652&query_hl=1&itool=pubmed_docsum
- **Angioid streaks in homozygous beta thalassemia.**
Author(s): Aessopos A, Stamatelos G, Savvides P, Kavouklis E, Gabriel L, Rombos I, Karagiorga M, Kaklamanis P.
Source: American Journal of Ophthalmology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2801854&query_hl=1&itool=pubmed_docsum

- Cardiac status in well-treated patients with thalassemia major.**
 Author(s): Aessopos A, Farmakis D, Hatziliami A, Fragodimitri C, Karabatsos F, Joussef J, Mitilineou E, Diamanti-Kandaraki E, Meletis J, Karagiorga M.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15458515&query_hl=1&itool=pubmed_docsum
- Comparison of oral and subcutaneous iron chelation therapies in the prevention of major endocrinopathies in beta-thalassemia major patients.**
 Author(s): Wang CH, Wu KH, Tsai FJ, Peng CT, Tsai CH.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798651&query_hl=1&itool=pubmed_docsum
- Current management of homozygous beta thalassemia.**
 Author(s): Choudhry VP, Desai N, Pati HP, Nanu A.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1724659&query_hl=1&itool=pubmed_docsum
- Deferiprone or deferoxamine vs. combination therapy in patients with beta-thalassemia major: a case study in Taiwan.**
 Author(s): Peng CT, Wu KH, Wu SF, Liang DC, Yang CP, Jang RC, Wang LY, Hsiao CC.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16540425&query_hl=1&itool=pubmed_docsum
- Effect of deferiprone on urinary zinc excretion in multiply transfused children with thalassemia major.**
 Author(s): Bartakke S, Bavdekar SB, Kondurkar P, Muranjan MN, Manglani MV, Sharma R.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15767711&query_hl=1&itool=pubmed_docsum
- Effects of silymarin on the proliferation and glutathione levels of peripheral blood mononuclear cells from beta-thalassemia major patients.**
 Author(s): Alidoost F, Gharagozloo M, Bagherpour B, Jafarian A, Sajjadi SE, Hourfar H, Moayedi B.
 Source: International Immunopharmacology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16782543&query_hl=1&itool=pubmed_docsum
- Effects of zinc supplementation on somatomedin-C level, in beta thalassemia.**
 Author(s): Akar N, Berberoglu M, Arcasoy A.
 Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1415179&query_hl=1&itool=pubmed_docsum

- **Enlargement of hepatoduodenal ligament lymph nodes in beta thalassemia children receiving multiple transfusions: a common observation.**
 Author(s): Chu WC, Metreweli C, Chik KW, Lam WW, Chan YL, Li CK.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=12161366&query_hl=1&itool=pubmed_docsum
- **Entrapment of purified alpha-hemoglobin chains in normal erythrocytes as a model for human beta thalassemia.**
 Author(s): Scott MD.
 Source: Advances in Experimental Medicine and Biology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1295299&query_hl=1&itool=pubmed_docsum
- **Evaluation of survival in medically treated patients with homozygous beta thalassemia by the quick hit method.**
 Author(s): Iacovino JR.
 Source: J Insur Med.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=10150804&query_hl=1&itool=pubmed_docsum
- **Exchange blood transfusions for the treatment of leg ulcerations in thalassemia intermedia.**
 Author(s): Aessopos A, Kati M, Tsironi M, Polonifi E, Farmakis D.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16709519&query_hl=1&itool=pubmed_docsum
- **Fertility and pregnancy in thalassemia major.**
 Author(s): Tuck SM.
 Source: Annals of the New York Academy of Sciences.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16339678&query_hl=1&itool=pubmed_docsum
- **Glutathione S-transferase M1 gene polymorphisms are associated with cardiac iron deposition in patients with beta-thalassemia major.**
 Author(s): Wu KH, Chang JG, Ho YJ, Wu SF, Peng CT.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798650&query_hl=1&itool=pubmed_docsum
- **Growth of children with beta-thalassemia major.**
 Author(s): Low LC.
 Source: Indian J Pediatr.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15758540&query_hl=1&itool=pubmed_docsum

- **Heart failure in beta thalassemia: a 5-year follow-up study.**
 Author(s): Kremastinos DT, Tsetsos GA, Tsiapras DP, Karavolias GK, Ladis VA, Kattamis CA.
 Source: The American Journal of Medicine.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=11583636&query_hl=1&itool=pubmed_docsum
- **Hypothalamic-pituitary-gonadal function in adolescent females with beta-thalassemia major.**
 Author(s): Al-Rimawi HS, Jallad MF, Amarin ZO, Obeidat BR.
 Source: International Journal of Gynaecology and Obstetrics: the Official Organ of the International Federation of Gynaecology and Obstetrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15913630&query_hl=1&itool=pubmed_docsum
- **Impact of excess weight and estrogen receptor gene polymorphisms on clinical course of homozygous beta thalassemia.**
 Author(s): Ferrara M, Matarese SM, Borrelli B, Francese M, Perrotta A, Simeone G, Greco N, Iarussi D, Capozzi L, Esposito L.
 Source: Hematology (Amsterdam, Netherlands).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16273733&query_hl=1&itool=pubmed_docsum
- **Insulin resistance and beta cell function in chronically transfused patients of thalassemia major.**
 Author(s): Suvarna J, Ingle H, Deshmukh CT.
 Source: Indian Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16735760&query_hl=1&itool=pubmed_docsum
- **Iron overload and desferrioxamine chelation therapy in beta-thalassemia intermedia.**
 Author(s): Cossu P, Toccafondi C, Vardeu F, Sanna G, Frau F, Lobrano R, Cornacchia G, Nucaro A, Bertolino F, Loi A, De Virgiliis S, Cao A.
 Source: European Journal of Pediatrics.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=7318837&query_hl=1&itool=pubmed_docsum
- **Lack of prognostic value of normalized integrated backscatter analysis of myocardium in patients with thalassemia major: a long-term follow-up study.**
 Author(s): Jambrik Z, Derchi G, Picano E, Ait-Ali L, Forni G, Bellotti P.
 Source: Echocardiography (Mount Kisco, N.Y.).
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15725159&query_hl=1&itool=pubmed_docsum
- **L-carnitine deficiency and red blood cell mechanical impairment in beta-thalassemia major.**
 Author(s): Toptas B, Baykal A, Yesilipek A, Isbir M, Kupesiz A, Yalcin O, Baskurt OK.

Source: Clinical Hemorheology and Microcirculation.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16899956&query_hl=1&itool=pubmed_docsum

- **Liver fibrosis and iron levels during long-term deferiprone treatment of thalassemia major patients.**

Author(s): Wu SF, Peng CT, Wu KH, Tsai CH.

Source: Hemoglobin.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798646&query_hl=1&itool=pubmed_docsum

- **Longitudinal study of survival and causes of death in patients with thalassemia major in Greece.**

Author(s): Ladis V, Chouliaras G, Berdousi H, Kanavakis E, Kattamis C.

Source: Annals of the New York Academy of Sciences.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16339695&query_hl=1&itool=pubmed_docsum

- **Long-term trials of deferiprone in Cooley's anemia.**

Author(s): Olivieri NF, Brittenham GM.

Source: Annals of the New York Academy of Sciences.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9668542&query_hl=1&itool=pubmed_docsum

- **Low bone mass in prepubertal children with thalassemia major: insights into the pathogenesis of low bone mass in thalassemia.**

Author(s): Vogiatzi MG, Autio KA, Schneider R, Giardina PJ.

Source: J Pediatr Endocrinol Metab.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15526720&query_hl=1&itool=pubmed_docsum

- **Malnutrition and growth abnormalities in children with beta thalassemia major.**

Author(s): Tienboon P, Sanguansermisri T, Fuchs GJ.

Source: Southeast Asian J Trop Med Public Health.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9280002&query_hl=1&itool=pubmed_docsum

- **Methods for noninvasive measurement of tissue iron in Cooley's anemia.**

Author(s): Sheth S, Tang H, Jensen JH, Altmann K, Prakash A, Printz BF, Hordof AJ, Tosti CL, Azabagic A, Swaminathan S, Brown TR, Olivieri NF, Brittenham GM.

Source: Annals of the New York Academy of Sciences.

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16339684&query_hl=1&itool=pubmed_docsum

- **Non-Hodgkin disease in beta-thalassemia major.**

Author(s): Otrrock ZK, Shamseddine AI, Taher AT.

Source: American Journal of Hematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16369971&query_hl=1&itool=pubmed_docsum

- **Non-transferrin-bound iron during blood transfusion cycles in beta-thalassemia major.**
 Author(s): Grosse R, Lund U, Caruso V, Fischer R, Janka GE, Magnano C, Engelhardt R, Durken M, Nielsen P.
 Source: Annals of the New York Academy of Sciences.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16339692&query_hl=1&itool=pubmed_docsum
- **Overview of the beta thalassemias: genetic and clinical aspects.**
 Author(s): Schwartz E, Cohen A, Surrey S.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=2463234&query_hl=1&itool=pubmed_docsum
- **Pilot study on parental stress and behavioral adjustment to the thalassemia major disease process in children undergoing iron-chelation in western Taiwan.**
 Author(s): Kuo HT, Peng CT, Tsai MY.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798655&query_hl=1&itool=pubmed_docsum
- **Pilot study on the "quality of life" as reflected by psychosocial adjustment of children with thalassemia major undergoing iron-chelating treatment in western Taiwan.**
 Author(s): Kuo HT, Tsai MY, Peng CT, Wu KH.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798654&query_hl=1&itool=pubmed_docsum
- **Pregnancy in patients treated for beta thalassemia major in two centers (Ali Asghar Children's Hospital and Thalassemia Clinic): outcome for mothers and newborn infants.**
 Author(s): Ansari S, Kivan AA, Tabaroki A.
 Source: Pediatric Hematology and Oncology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16326410&query_hl=1&itool=pubmed_docsum
- **Prevalence of growth and puberty failure with respect to growth hormone and gonadotropins secretion in beta-thalassemia major.**
 Author(s): Moayeri H, Oloomi Z.
 Source: Arch Iran Med.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=17061604&query_hl=1&itool=pubmed_docsum

- **Prognostic factors in bone marrow transplantation for beta thalassemia major: experiences from Iran.**
 Author(s): Ghavamzadeh A, Nasser P, Eshraghian MR, Jahani M, Baybordi I, Nateghi J, Khodabandeh A, Sadjadi AR, Mohyeddin M, Khademi Y.
 Source: Bone Marrow Transplantation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9894719&query_hl=1&itool=pubmed_docsum
- **Quality of life and survival of patients with beta-thalassemia major.**
 Author(s): Cao A.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15477196&query_hl=1&itool=pubmed_docsum
- **Reevaluation of iron absorption and serum ferritin in beta-thalassemia intermedia.**
 Author(s): Gumruk F, Gurgey A, Duru F, Altay C.
 Source: Pediatric Hematology and Oncology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=1467169&query_hl=1&itool=pubmed_docsum
- **Regression of myocardial dysfunction after switching from desferrioxamine to deferiprone therapy in beta-thalassemia major patients.**
 Author(s): Huang YC, Chang JS, Wu KH, Peng CT.
 Source: Hemoglobin.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16798648&query_hl=1&itool=pubmed_docsum
- **Reversal of heart failure in thalassemia major by combined chelation therapy: a case report.**
 Author(s): Tsironi M, Deftereos S, Andriopoulos P, Farmakis D, Meletis J, Aessopos A.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15613114&query_hl=1&itool=pubmed_docsum
- **Rheumatoid arthritis in thalassemia intermedia: coincidence or association?**
 Author(s): Giakoumi X, Tsironi M, Floudas C, Polymeropoylos E, Papalambros E, Aessopos A.
 Source: Isr Med Assoc J.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16259351&query_hl=1&itool=pubmed_docsum
- **Risk factors for death in patients with beta-thalassemia major: results of a case-control study.**
 Author(s): Ceci A, Baiardi P, Catapano M, Felisi M, Cianciulli P, De Sanctis V, Del Vecchio GC, Magnano C, Meo A, Maggio A.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16963395&query_hl=1&itool=pubmed_docsum

- **Serum ferritin level as a predictor of impaired growth and puberty in thalassemia major patients.**
 Author(s): Shalitin S, Carmi D, Weintrob N, Phillip M, Miskin H, Kornreich L, Zilber R, Yaniv I, Tamary H.
 Source: European Journal of Haematology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15654898&query_hl=1&itool=pubmed_docsum
- **Serum superoxide dismutase levels of beta thalassemia patients and effects of high dosage of intravenous desferrioxamine treatment on superoxide dismutase levels.**
 Author(s): Tekin M, Akar N, Egin Y, Cin S.
 Source: Pediatric Hematology and Oncology.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9658440&query_hl=1&itool=pubmed_docsum
- **Thalassemia heart disease: a comparative evaluation of thalassemia major and thalassemia intermedia.**
 Author(s): Aessopos A, Farmakis D, Deftereos S, Tsironi M, Tassiopoulos S, Moyssakis I, Karagiorga M.
 Source: Chest.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=15888823&query_hl=1&itool=pubmed_docsum
- **Thalassemia intermedia: revisited.**
 Author(s): Taher A, Isma'eel H, Cappellini MD.
 Source: Blood Cells, Molecules & Diseases.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16737833&query_hl=1&itool=pubmed_docsum
- **The effect of dietary magnesium supplementation on the cellular abnormalities of erythrocytes in patients with beta thalassemia intermedia.**
 Author(s): De Franceschi L, Cappellini MD, Graziadei G, Manzato F, Olivieri O, Corrocher R, Fiorelli G, Beuzard Y, Brugnara C.
 Source: Haematologica.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=9549922&query_hl=1&itool=pubmed_docsum
- **The effect of folic acid supplementation in beta-thalassemia major: a randomized placebo-controlled clinical trial.**
 Author(s): Mojtahedzadeh F, Kosaryan M, Mahdavi MR, Akbari J.
 Source: Arch Iran Med.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=16859064&query_hl=1&itool=pubmed_docsum

- **The management of patients with Cooley's anemia: transfusions and splenectomy.**
 Author(s): Piomelli S.
 Source: Semin Hematol.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Retrieve&dopt=AbstractPlus&list_uids=8560283&query_hl=1&itool=pubmed_docsum

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://health.aol.com/healthyliving/althealth>
- Chinese Medicine: <http://www.newcenturynutrition.com/>
- drkoop.com[®]: <http://www.drkoop.com/naturalmedicine.html>
- Family Village: http://www.familyvillage.wisc.edu/med_altn.htm
- Google: <http://directory.google.com/Top/Health/Alternative/>
- Healthnotes: <http://www.healthnotes.com/>
- Open Directory Project: <http://dmoz.org/Health/Alternative/>
- Yahoo.com: http://dir.yahoo.com/Health/Alternative_Medicine/

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 3. BOOKS ON BETA THALASSEMIA

Overview

This chapter provides bibliographic book references relating to beta thalassemia. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, the National Library of Medicine is an excellent source for book titles on beta thalassemia. Your local medical library also may have these titles available for loan.

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 **beta thalassemia** at online booksellers' Web sites, you may discover non-medical books that use the generic term "beta thalassemia" (or a synonym) in their titles. The following is indicative of the results you might find when searching for **beta thalassemia** (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Sixth Cooley's Anemia Symposium (Annals of the New York Academy of Sciences, Vol 612)** Arthur Bank (1991); ISBN: 0897666356;
<http://www.amazon.com/exec/obidos/ASIN/0897666356/icongroupinterna>

APPENDICES

APPENDIX A. HELP ME UNDERSTAND GENETICS

Overview

This appendix presents basic information about genetics in clear language and provides links to online resources.⁷

The Basics: Genes and How They Work

This section gives you information on the basics of cells, DNA, genes, chromosomes, and proteins.

What Is a Cell?

Cells are the basic building blocks of all living things. The human body is composed of trillions of cells. They provide structure for the body, take in nutrients from food, convert those nutrients into energy, and carry out specialized functions. Cells also contain the body's hereditary material and can make copies of themselves.

Cells have many parts, each with a different function. Some of these parts, called organelles, are specialized structures that perform certain tasks within the cell. Human cells contain the following major parts, listed in alphabetical order:

- **Cytoplasm:** The cytoplasm is fluid inside the cell that surrounds the organelles.
- **Endoplasmic reticulum (ER):** This organelle helps process molecules created by the cell and transport them to their specific destinations either inside or outside the cell.
- **Golgi apparatus:** The golgi apparatus packages molecules processed by the endoplasmic reticulum to be transported out of the cell.
- **Lysosomes and peroxisomes:** These organelles are the recycling center of the cell. They digest foreign bacteria that invade the cell, rid the cell of toxic substances, and recycle worn-out cell components.

⁷ This appendix is an excerpt from the National Library of Medicine's handbook, *Help Me Understand Genetics*. For the full text of the *Help Me Understand Genetics* handbook, see <http://ghr.nlm.nih.gov/handbook>.

- **Mitochondria:** Mitochondria are complex organelles that convert energy from food into a form that the cell can use. They have their own genetic material, separate from the DNA in the nucleus, and can make copies of themselves.
- **Nucleus:** The nucleus serves as the cell's command center, sending directions to the cell to grow, mature, divide, or die. It also houses DNA (deoxyribonucleic acid), the cell's hereditary material. The nucleus is surrounded by a membrane called the nuclear envelope, which protects the DNA and separates the nucleus from the rest of the cell.
- **Plasma membrane:** The plasma membrane is the outer lining of the cell. It separates the cell from its environment and allows materials to enter and leave the cell.
- **Ribosomes:** Ribosomes are organelles that process the cell's genetic instructions to create proteins. These organelles can float freely in the cytoplasm or be connected to the endoplasmic reticulum.

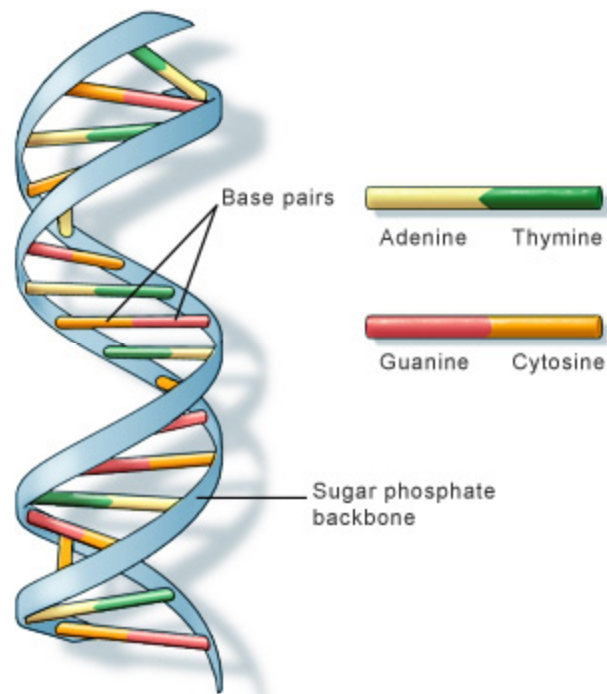
What Is DNA?

DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms. Nearly every cell in a person's body has the same DNA. Most DNA is located in the cell nucleus (where it is called nuclear DNA), but a small amount of DNA can also be found in the mitochondria (where it is called mitochondrial DNA or mtDNA).

The information in DNA is stored as a code made up of four chemical bases: adenine (A), guanine (G), cytosine (C), and thymine (T). Human DNA consists of about 3 billion bases, and more than 99 percent of those bases are the same in all people. The order, or sequence, of these bases determines the information available for building and maintaining an organism, similar to the way in which letters of the alphabet appear in a certain order to form words and sentences.

DNA bases pair up with each other, A with T and C with G, to form units called base pairs. Each base is also attached to a sugar molecule and a phosphate molecule. Together, a base, sugar, and phosphate are called a nucleotide. Nucleotides are arranged in two long strands that form a spiral called a double helix. The structure of the double helix is somewhat like a ladder, with the base pairs forming the ladder's rungs and the sugar and phosphate molecules forming the vertical sidepieces of the ladder.

An important property of DNA is that it can replicate, or make copies of itself. Each strand of DNA in the double helix can serve as a pattern for duplicating the sequence of bases. This is critical when cells divide because each new cell needs to have an exact copy of the DNA present in the old cell.



U.S. National Library of Medicine

DNA is a double helix formed by base pairs attached to a sugar-phosphate backbone.

What Is Mitochondrial DNA?

Although most DNA is packaged in chromosomes within the nucleus, mitochondria also have a small amount of their own DNA. This genetic material is known as mitochondrial DNA or mtDNA.

Mitochondria are structures within cells that convert the energy from food into a form that cells can use. Each cell contains hundreds to thousands of mitochondria, which are located in the fluid that surrounds the nucleus (the cytoplasm).

Mitochondria produce energy through a process called oxidative phosphorylation. This process uses oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source. A set of enzyme complexes, designated as complexes I-V, carry out oxidative phosphorylation within mitochondria.

In addition to energy production, mitochondria play a role in several other cellular activities. For example, mitochondria help regulate the self-destruction of cells (apoptosis). They are also necessary for the production of substances such as cholesterol and heme (a component of hemoglobin, the molecule that carries oxygen in the blood).

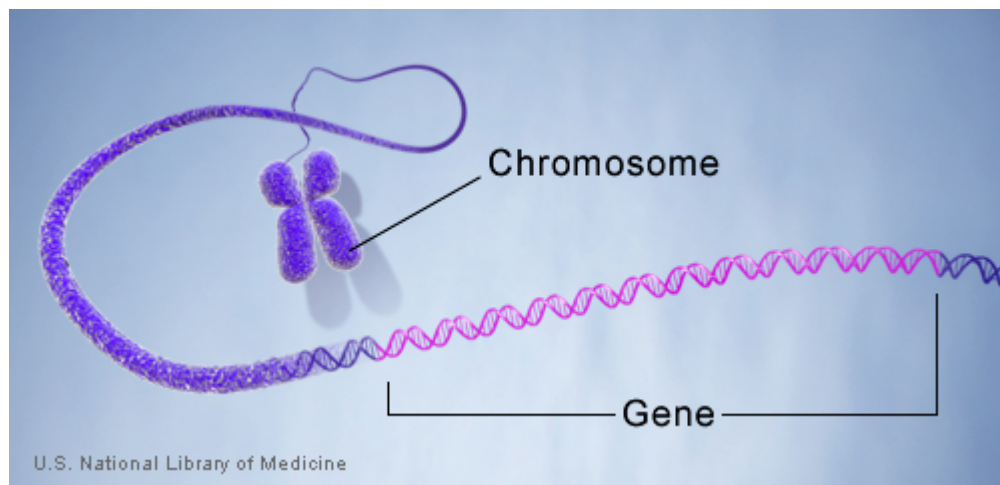
Mitochondrial DNA contains 37 genes, all of which are essential for normal mitochondrial function. Thirteen of these genes provide instructions for making enzymes involved in oxidative phosphorylation. The remaining genes provide instructions for making molecules called transfer RNAs (tRNAs) and ribosomal RNAs (rRNAs), which are chemical cousins of

DNA. These types of RNA help assemble protein building blocks (amino acids) into functioning proteins.

What Is a Gene?

A gene is the basic physical and functional unit of heredity. Genes, which are made up of DNA, act as instructions to make molecules called proteins. In humans, genes vary in size from a few hundred DNA bases to more than 2 million bases. The Human Genome Project has estimated that humans have between 20,000 and 25,000 genes.

Every person has two copies of each gene, one inherited from each parent. Most genes are the same in all people, but a small number of genes (less than 1 percent of the total) are slightly different between people. Alleles are forms of the same gene with small differences in their sequence of DNA bases. These small differences contribute to each person's unique physical features.



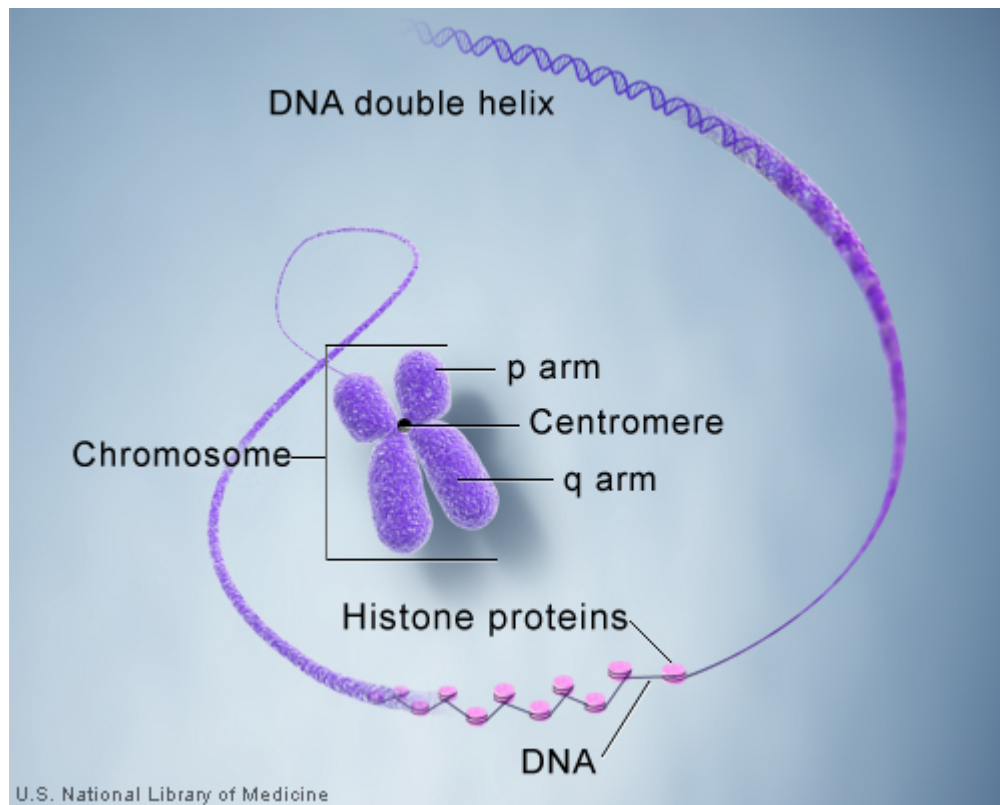
Genes are made up of DNA. Each chromosome contains many genes.

What Is a Chromosome?

In the nucleus of each cell, the DNA molecule is packaged into thread-like structures called chromosomes. Each chromosome is made up of DNA tightly coiled many times around proteins called histones that support its structure.

Chromosomes are not visible in the cell's nucleus—not even under a microscope—when the cell is not dividing. However, the DNA that makes up chromosomes becomes more tightly packed during cell division and is then visible under a microscope. Most of what researchers know about chromosomes was learned by observing chromosomes during cell division.

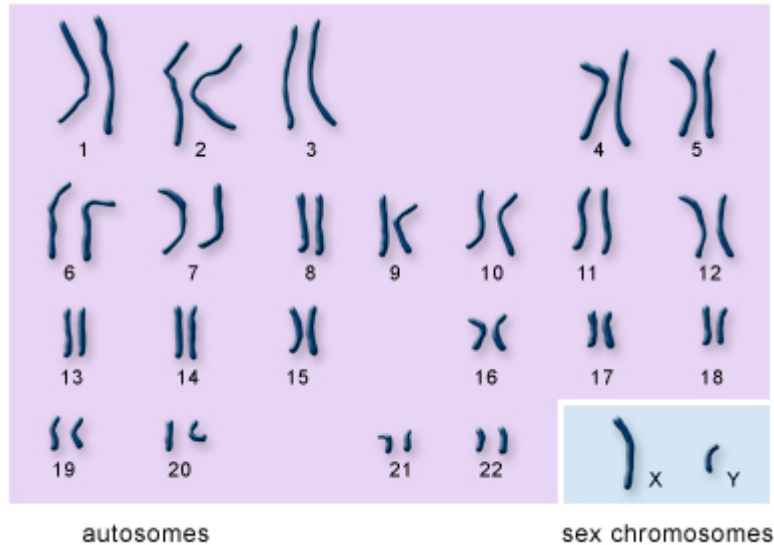
Each chromosome has a constriction point called the centromere, which divides the chromosome into two sections, or "arms." The short arm of the chromosome is labeled the "p arm." The long arm of the chromosome is labeled the "q arm." The location of the centromere on each chromosome gives the chromosome its characteristic shape, and can be used to help describe the location of specific genes.



DNA and histone proteins are packaged into structures called chromosomes.

How Many Chromosomes Do People Have?

In humans, each cell normally contains 23 pairs of chromosomes, for a total of 46. Twenty-two of these pairs, called autosomes, look the same in both males and females. The 23rd pair, the sex chromosomes, differ between males and females. Females have two copies of the X chromosome, while males have one X and one Y chromosome.



U.S. National Library of Medicine

The 22 autosomes are numbered by size.

The other two chromosomes, X and Y, are the sex chromosomes.

This picture of the human chromosomes lined up in pairs is called a karyotype.

How Do Geneticists Indicate the Location of a Gene?

Geneticists use maps to describe the location of a particular gene on a chromosome. One type of map uses the cytogenetic location to describe a gene's position. The cytogenetic location is based on a distinctive pattern of bands created when chromosomes are stained with certain chemicals. Another type of map uses the molecular location, a precise description of a gene's position on a chromosome. The molecular location is based on the sequence of DNA building blocks (base pairs) that make up the chromosome.

Cytogenetic Location

Geneticists use a standardized way of describing a gene's cytogenetic location. In most cases, the location describes the position of a particular band on a stained chromosome:

17q12

It can also be written as a range of bands, if less is known about the exact location:

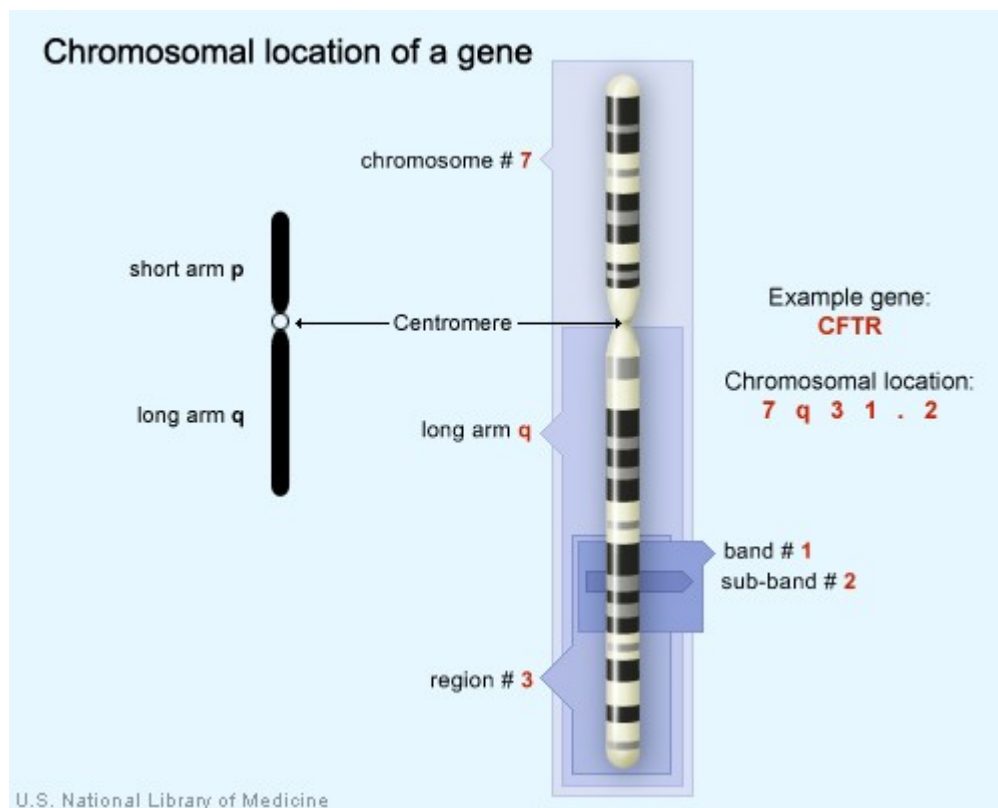
17q12-q21

The combination of numbers and letters provide a gene's "address" on a chromosome. This address is made up of several parts:

- The chromosome on which the gene can be found. The first number or letter used to describe a gene's location represents the chromosome. Chromosomes 1 through 22 (the autosomes) are designated by their chromosome number. The sex chromosomes are designated by X or Y.

- The arm of the chromosome. Each chromosome is divided into two sections (arms) based on the location of a narrowing (constriction) called the centromere. By convention, the shorter arm is called p, and the longer arm is called q. The chromosome arm is the second part of the gene's address. For example, 5q is the long arm of chromosome 5, and Xp is the short arm of the X chromosome.
- The position of the gene on the p or q arm. The position of a gene is based on a distinctive pattern of light and dark bands that appear when the chromosome is stained in a certain way. The position is usually designated by two digits (representing a region and a band), which are sometimes followed by a decimal point and one or more additional digits (representing sub-bands within a light or dark area). The number indicating the gene position increases with distance from the centromere. For example: 14q21 represents position 21 on the long arm of chromosome 14. 14q21 is closer to the centromere than 14q22.

Sometimes, the abbreviations "cen" or "ter" are also used to describe a gene's cytogenetic location. "Cen" indicates that the gene is very close to the centromere. For example, 16pcen refers to the short arm of chromosome 16 near the centromere. "Ter" stands for terminus, which indicates that the gene is very close to the end of the p or q arm. For example, 14qter refers to the tip of the long arm of chromosome 14. ("Tel" is also sometimes used to describe a gene's location. "Tel" stands for telomeres, which are at the ends of each chromosome. The abbreviations "tel" and "ter" refer to the same location.)



The CFTR gene is located on the long arm of chromosome 7 at position 7q31.2.

Molecular Location

The Human Genome Project, an international research effort completed in 2003, determined the sequence of base pairs for each human chromosome. This sequence information allows researchers to provide a more specific address than the cytogenetic location for many genes. A gene's molecular address pinpoints the location of that gene in terms of base pairs. For example, the molecular location of the APOE gene on chromosome 19 begins with base pair 50,100,901 and ends with base pair 50,104,488. This range describes the gene's precise position on chromosome 19 and indicates the size of the gene (3,588 base pairs). Knowing a gene's molecular location also allows researchers to determine exactly how far the gene is from other genes on the same chromosome.

Different groups of researchers often present slightly different values for a gene's molecular location. Researchers interpret the sequence of the human genome using a variety of methods, which can result in small differences in a gene's molecular address. For example, the National Center for Biotechnology Information (NCBI) identifies the molecular location of the APOE gene as base pair 50,100,901 to base pair 50,104,488 on chromosome 19. The Ensembl database identifies the location of this gene as base pair 50,100,879 to base pair 50,104,489 on chromosome 19. Neither of these addresses is incorrect; they represent different interpretations of the same data. For consistency, Genetics Home Reference presents data from NCBI for the molecular location of genes.

What Are Proteins and What Do They Do?

Proteins are large, complex molecules that play many critical roles in the body. They do most of the work in cells and are required for the structure, function, and regulation of the body's tissues and organs.

Proteins are made up of hundreds or thousands of smaller units called amino acids, which are attached to one another in long chains. There are 20 different types of amino acids that can be combined to make a protein. The sequence of amino acids determines each protein's unique 3-dimensional structure and its specific function.

Examples of Protein Functions

Proteins can be described according to their large range of functions in the body, listed in alphabetical order:

Function	Description	Example
Antibody	Antibodies bind to specific foreign particles, such as viruses and bacteria, to help protect the body.	Immunoglobulin G (IgG)
Enzyme	Enzymes carry out almost all of the thousands of chemical reactions that take place in cells. They also assist with the formation of new molecules by reading the genetic information stored in DNA.	Phenylalanine hydroxylase
Messenger	Messenger proteins, such as some types of hormones, transmit signals to coordinate biological processes between different cells, tissues, and organs.	Growth hormone
Structural component	These proteins provide structure and support for cells. On a larger scale, they also allow the body to move.	Actin
Transport/storage	These proteins bind and carry atoms and small molecules within cells and throughout the body.	Ferritin

How Does a Gene Make a Protein?

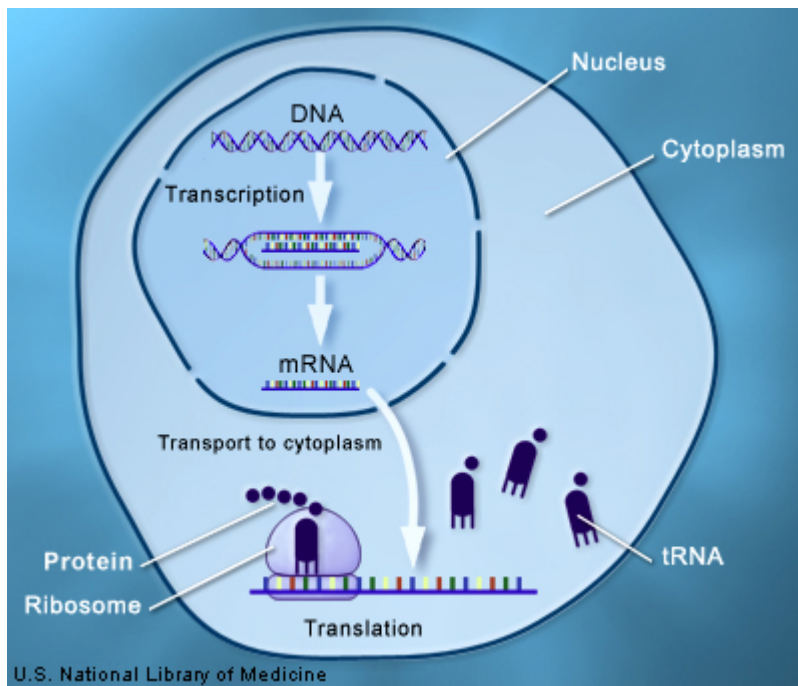
Most genes contain the information needed to make functional molecules called proteins. (A few genes produce other molecules that help the cell assemble proteins.) The journey from gene to protein is complex and tightly controlled within each cell. It consists of two major steps: transcription and translation. Together, transcription and translation are known as gene expression.

During the process of transcription, the information stored in a gene's DNA is transferred to a similar molecule called RNA (ribonucleic acid) in the cell nucleus. Both RNA and DNA are made up of a chain of nucleotide bases, but they have slightly different chemical properties. The type of RNA that contains the information for making a protein is called messenger RNA (mRNA) because it carries the information, or message, from the DNA out of the nucleus into the cytoplasm.

Translation, the second step in getting from a gene to a protein, takes place in the cytoplasm. The mRNA interacts with a specialized complex called a ribosome, which "reads" the sequence of mRNA bases. Each sequence of three bases, called a codon, usually codes for

one particular amino acid. (Amino acids are the building blocks of proteins.) A type of RNA called transfer RNA (tRNA) assembles the protein, one amino acid at a time. Protein assembly continues until the ribosome encounters a “stop” codon (a sequence of three bases that does not code for an amino acid).

The flow of information from DNA to RNA to proteins is one of the fundamental principles of molecular biology. It is so important that it is sometimes called the “central dogma.”



Through the processes of transcription and translation, information from genes is used to make proteins.

Can Genes Be Turned On and Off in Cells?

Each cell expresses, or turns on, only a fraction of its genes. The rest of the genes are repressed, or turned off. The process of turning genes on and off is known as gene regulation. Gene regulation is an important part of normal development. Genes are turned on and off in different patterns during development to make a brain cell look and act different from a liver cell or a muscle cell, for example. Gene regulation also allows cells to react quickly to changes in their environments. Although we know that the regulation of genes is critical for life, this complex process is not yet fully understood.

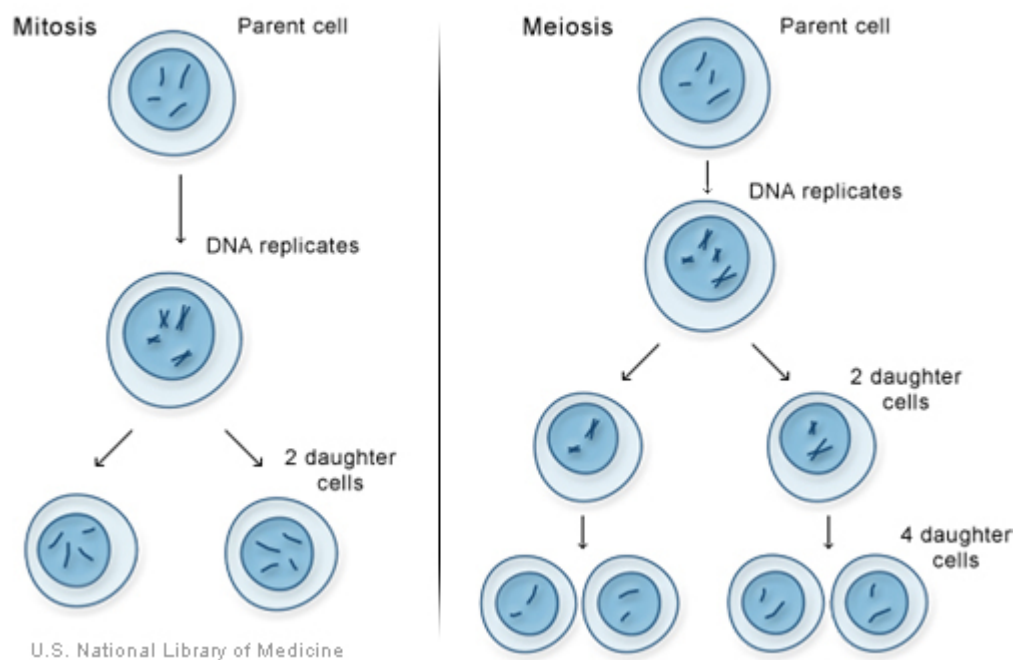
Gene regulation can occur at any point during gene expression, but most commonly occurs at the level of transcription (when the information in a gene's DNA is transferred to mRNA). Signals from the environment or from other cells activate proteins called transcription factors. These proteins bind to regulatory regions of a gene and increase or decrease the level of transcription. By controlling the level of transcription, this process can determine the amount of protein product that is made by a gene at any given time.

How Do Cells Divide?

There are two types of cell division: mitosis and meiosis. Most of the time when people refer to “cell division,” they mean mitosis, the process of making new body cells. Meiosis is the type of cell division that creates egg and sperm cells.

Mitosis is a fundamental process for life. During mitosis, a cell duplicates all of its contents, including its chromosomes, and splits to form two identical daughter cells. Because this process is so critical, the steps of mitosis are carefully controlled by a number of genes. When mitosis is not regulated correctly, health problems such as cancer can result.

The other type of cell division, meiosis, ensures that humans have the same number of chromosomes in each generation. It is a two-step process that reduces the chromosome number by half—from 46 to 23—to form sperm and egg cells. When the sperm and egg cells unite at conception, each contributes 23 chromosomes so the resulting embryo will have the usual 46. Meiosis also allows genetic variation through a process of DNA shuffling while the cells are dividing.



Mitosis and meiosis, the two types of cell division.

How Do Genes Control the Growth and Division of Cells?

A variety of genes are involved in the control of cell growth and division. The cell cycle is the cell's way of replicating itself in an organized, step-by-step fashion. Tight regulation of this process ensures that a dividing cell's DNA is copied properly, any errors in the DNA are repaired, and each daughter cell receives a full set of chromosomes. The cycle has checkpoints (also called restriction points), which allow certain genes to check for mistakes and halt the cycle for repairs if something goes wrong.

If a cell has an error in its DNA that cannot be repaired, it may undergo programmed cell death (apoptosis). Apoptosis is a common process throughout life that helps the body get rid of cells it doesn't need. Cells that undergo apoptosis break apart and are recycled by a type of white blood cell called a macrophage. Apoptosis protects the body by removing genetically damaged cells that could lead to cancer, and it plays an important role in the development of the embryo and the maintenance of adult tissues.

Cancer results from a disruption of the normal regulation of the cell cycle. When the cycle proceeds without control, cells can divide without order and accumulate genetic defects that can lead to a cancerous tumor.

Genetic Mutations and Health

This section presents basic information about gene mutations, chromosomal changes, and conditions that run in families.⁸

What Is a Gene Mutation and How Do Mutations Occur?

A gene mutation is a permanent change in the DNA sequence that makes up a gene. Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome.

Gene mutations occur in two ways: they can be inherited from a parent or acquired during a person's lifetime. Mutations that are passed from parent to child are called hereditary mutations or germline mutations (because they are present in the egg and sperm cells, which are also called germ cells). This type of mutation is present throughout a person's life in virtually every cell in the body.

Mutations that occur only in an egg or sperm cell, or those that occur just after fertilization, are called new (de novo) mutations. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell, but has no family history of the disorder.

Acquired (or somatic) mutations occur in the DNA of individual cells at some time during a person's life. These changes can be caused by environmental factors such as ultraviolet radiation from the sun, or can occur if a mistake is made as DNA copies itself during cell division. Acquired mutations in somatic cells (cells other than sperm and egg cells) cannot be passed on to the next generation.

Mutations may also occur in a single cell within an early embryo. As all the cells divide during growth and development, the individual will have some cells with the mutation and some cells without the genetic change. This situation is called mosaicism.

Some genetic changes are very rare; others are common in the population. Genetic changes that occur in more than 1 percent of the population are called polymorphisms. They are common enough to be considered a normal variation in the DNA. Polymorphisms are

⁸ This section has been adapted from the National Library of Medicine's handbook, *Help Me Understand Genetics*, which presents basic information about genetics in clear language and provides links to online resources: <http://ghr.nlm.nih.gov/handbook>.

responsible for many of the normal differences between people such as eye color, hair color, and blood type. Although many polymorphisms have no negative effects on a person's health, some of these variations may influence the risk of developing certain disorders.

How Can Gene Mutations Affect Health and Development?

To function correctly, each cell depends on thousands of proteins to do their jobs in the right places at the right times. Sometimes, gene mutations prevent one or more of these proteins from working properly. By changing a gene's instructions for making a protein, a mutation can cause the protein to malfunction or to be missing entirely. When a mutation alters a protein that plays a critical role in the body, it can disrupt normal development or cause a medical condition. A condition caused by mutations in one or more genes is called a genetic disorder.

In some cases, gene mutations are so severe that they prevent an embryo from surviving until birth. These changes occur in genes that are essential for development, and often disrupt the development of an embryo in its earliest stages. Because these mutations have very serious effects, they are incompatible with life.

It is important to note that genes themselves do not cause disease—genetic disorders are caused by mutations that make a gene function improperly. For example, when people say that someone has “the cystic fibrosis gene,” they are usually referring to a mutated version of the CFTR gene, which causes the disease. All people, including those without cystic fibrosis, have a version of the CFTR gene.

Do All Gene Mutations Affect Health and Development?

No, only a small percentage of mutations cause genetic disorders—most have no impact on health or development. For example, some mutations alter a gene's DNA base sequence but do not change the function of the protein made by the gene.

Often, gene mutations that could cause a genetic disorder are repaired by certain enzymes before the gene is expressed (makes a protein). Each cell has a number of pathways through which enzymes recognize and repair mistakes in DNA. Because DNA can be damaged or mutated in many ways, DNA repair is an important process by which the body protects itself from disease.

A very small percentage of all mutations actually have a positive effect. These mutations lead to new versions of proteins that help an organism and its future generations better adapt to changes in their environment. For example, a beneficial mutation could result in a protein that protects the organism from a new strain of bacteria.

For More Information about DNA Repair and the Health Effects of Gene Mutations

- The University of Utah Genetic Science Learning Center provides information about genetic disorders that explains why some mutations cause disorders but others do not. (Refer to the questions in the far right column.)
See <http://learn.genetics.utah.edu/units/disorders/whataregd/>.

- Additional information about DNA repair is available from the NCBI Science Primer. In the chapter called “What Is A Cell?”, scroll down to the heading “DNA Repair Mechanisms.” See http://www.ncbi.nlm.nih.gov/About/primer/genetics_cell.html.

What Kinds of Gene Mutations Are Possible?

The DNA sequence of a gene can be altered in a number of ways. Gene mutations have varying effects on health, depending on where they occur and whether they alter the function of essential proteins. The types of mutations include:

- **Missense mutation:** This type of mutation is a change in one DNA base pair that results in the substitution of one amino acid for another in the protein made by a gene.
- **Nonsense mutation:** A nonsense mutation is also a change in one DNA base pair. Instead of substituting one amino acid for another, however, the altered DNA sequence prematurely signals the cell to stop building a protein. This type of mutation results in a shortened protein that may function improperly or not at all.
- **Insertion:** An insertion changes the number of DNA bases in a gene by adding a piece of DNA. As a result, the protein made by the gene may not function properly.
- **Deletion:** A deletion changes the number of DNA bases by removing a piece of DNA. Small deletions may remove one or a few base pairs within a gene, while larger deletions can remove an entire gene or several neighboring genes. The deleted DNA may alter the function of the resulting protein(s).
- **Duplication:** A duplication consists of a piece of DNA that is abnormally copied one or more times. This type of mutation may alter the function of the resulting protein.
- **Frameshift mutation:** This type of mutation occurs when the addition or loss of DNA bases changes a gene’s reading frame. A reading frame consists of groups of 3 bases that each code for one amino acid. A frameshift mutation shifts the grouping of these bases and changes the code for amino acids. The resulting protein is usually nonfunctional. Insertions, deletions, and duplications can all be frameshift mutations.
- **Repeat expansion:** Nucleotide repeats are short DNA sequences that are repeated a number of times in a row. For example, a trinucleotide repeat is made up of 3-base-pair sequences, and a tetranucleotide repeat is made up of 4-base-pair sequences. A repeat expansion is a mutation that increases the number of times that the short DNA sequence is repeated. This type of mutation can cause the resulting protein to function improperly.

Can Changes in Chromosomes Affect Health and Development?

Changes that affect entire chromosomes or segments of chromosomes can cause problems with growth, development, and function of the body’s systems. These changes can affect many genes along the chromosome and alter the proteins made by those genes. Conditions caused by a change in the number or structure of chromosomes are known as chromosomal disorders.

Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes in each cell. A change in the number of chromosomes leads to a chromosomal disorder. These changes can occur during the formation of reproductive cells (eggs and sperm) or in early fetal development. A gain or loss of chromosomes from the normal 46 is called aneuploidy.

The most common form of aneuploidy is trisomy, or the presence of an extra chromosome in each cell. “Tri-” is Greek for “three”; people with trisomy have three copies of a particular chromosome in each cell instead of the normal two copies. Down syndrome is an example of a condition caused by trisomy – people with Down syndrome typically have three copies of chromosome 21 in each cell, for a total of 47 chromosomes per cell.

Monosomy, or the loss of one chromosome from each cell, is another kind of aneuploidy. “Mono-” is Greek for “one”; people with monosomy have one copy of a particular chromosome in each cell instead of the normal two copies. Turner syndrome is a condition caused by monosomy. Women with Turner syndrome are often missing one copy of the X chromosome in every cell, for a total of 45 chromosomes per cell.

Chromosomal disorders can also be caused by changes in chromosome structure. These changes are caused by the breakage and reunion of chromosome segments when an egg or sperm cell is formed or in early fetal development. Pieces of DNA can be rearranged within one chromosome, or transferred between two or more chromosomes. The effects of structural changes depend on their size and location. Many different structural changes are possible; some cause medical problems, while others may have no effect on a person’s health.

Many cancer cells also have changes in their chromosome number or structure. These changes most often occur in somatic cells (cells other than eggs and sperm) during a person’s lifetime.

Can Changes in Mitochondrial DNA Affect Health and Development?

Mitochondria are structures within cells that convert the energy from food into a form that cells can use. Although most DNA is packaged in chromosomes within the nucleus, mitochondria also have a small amount of their own DNA (known as mitochondrial DNA or mtDNA). In some cases, inherited changes in mitochondrial DNA can cause problems with growth, development, and function of the body’s systems. These mutations disrupt the mitochondria’s ability to generate energy efficiently for the cell.

Conditions caused by mutations in mitochondrial DNA often involve multiple organ systems. The effects of these conditions are most pronounced in organs and tissues that require a lot of energy (such as the heart, brain, and muscles). Although the health consequences of inherited mitochondrial DNA mutations vary widely, frequently observed features include muscle weakness and wasting, problems with movement, diabetes, kidney failure, heart disease, loss of intellectual functions (dementia), hearing loss, and abnormalities involving the eyes and vision.

Mitochondrial DNA is also prone to noninherited (somatic) mutations. Somatic mutations occur in the DNA of certain cells during a person’s lifetime, and typically are not passed to future generations. Because mitochondrial DNA has a limited ability to repair itself when it is damaged, these mutations tend to build up over time. A buildup of somatic mutations in mitochondrial DNA has been associated with some forms of cancer and an increased risk of certain age-related disorders such as heart disease, Alzheimer disease, and Parkinson disease. Additionally, research suggests that the progressive accumulation of these mutations over a person’s lifetime may play a role in the normal process of aging.

What Are Complex or Multifactorial Disorders?

Researchers are learning that nearly all conditions and diseases have a genetic component. Some disorders, such as sickle cell anemia and cystic fibrosis, are caused by mutations in a single gene. The causes of many other disorders, however, are much more complex. Common medical problems such as heart disease, diabetes, and obesity do not have a single genetic cause—they are likely associated with the effects of multiple genes in combination with lifestyle and environmental factors. Conditions caused by many contributing factors are called complex or multifactorial disorders.

Although complex disorders often cluster in families, they do not have a clear-cut pattern of inheritance. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been identified. By 2010, however, researchers predict they will have found the major contributing genes for many common complex disorders.

What Information about a Genetic Condition Can Statistics Provide?

Statistical data can provide general information about how common a condition is, how many people have the condition, or how likely it is that a person will develop the condition. Statistics are not personalized, however—they offer estimates based on groups of people. By taking into account a person's family history, medical history, and other factors, a genetics professional can help interpret what statistics mean for a particular patient.

Common Statistical Terms

Some statistical terms are commonly used when describing genetic conditions and other disorders. These terms include:

Statistical Term	Description	Examples
<i>Incidence</i>	The incidence of a gene mutation or a genetic disorder is the number of people who are born with the mutation or disorder in a specified group per year. Incidence is often written in the form "1 in [a number]" or as a total number of live births.	About 1 in 200,000 people in the United States are born with syndrome A each year. An estimated 15,000 infants with syndrome B were born last year worldwide.

<i>Prevalence</i>	The prevalence of a gene mutation or a genetic disorder is the total number of people in a specified group at a given time who have the mutation or disorder. This term includes both newly diagnosed and pre-existing cases in people of any age. Prevalence is often written in the form “1 in [a number]” or as a total number of people who have a condition.	Approximately 1 in 100,000 people in the United States have syndrome A at the present time. About 100,000 children worldwide currently have syndrome B.
<i>Mortality</i>	Mortality is the number of deaths from a particular disorder occurring in a specified group per year. Mortality is usually expressed as a total number of deaths.	An estimated 12,000 people worldwide died from syndrome C in 2002.
<i>Lifetime risk</i>	Lifetime risk is the average risk of developing a particular disorder at some point during a lifetime. Lifetime risk is often written as a percentage or as “1 in [a number].” It is important to remember that the risk per year or per decade is much lower than the lifetime risk. In addition, other factors may increase or decrease a person’s risk as compared with the average.	Approximately 1 percent of people in the United States develop disorder D during their lifetimes. The lifetime risk of developing disorder D is 1 in 100.

Naming Genetic Conditions

Genetic conditions are not named in one standard way (unlike genes, which are given an official name and symbol by a formal committee). Doctors who treat families with a particular disorder are often the first to propose a name for the condition. Expert working groups may later revise the name to improve its usefulness. Naming is important because it allows accurate and effective communication about particular conditions, which will ultimately help researchers find new approaches to treatment.

Disorder names are often derived from one or a combination of sources:

- The basic genetic or biochemical defect that causes the condition (for example, alpha-1 antitrypsin deficiency)
- One or more major signs or symptoms of the disorder (for example, sickle cell anemia)
- The parts of the body affected by the condition (for example, retinoblastoma)

- The name of a physician or researcher, often the first person to describe the disorder (for example, Marfan syndrome, which was named after Dr. Antoine Bernard-Jean Marfan)
- A geographic area (for example, familial Mediterranean fever, which occurs mainly in populations bordering the Mediterranean Sea)
- The name of a patient or family with the condition (for example, amyotrophic lateral sclerosis, which is also called Lou Gehrig disease after a famous baseball player who had the condition).

Disorders named after a specific person or place are called eponyms. There is debate as to whether the possessive form (e.g., Alzheimer's disease) or the nonpossessive form (Alzheimer disease) of eponyms is preferred. As a rule, medical geneticists use the nonpossessive form, and this form may become the standard for doctors in all fields of medicine. Genetics Home Reference uses the nonpossessive form of eponyms.

Genetics Home Reference consults with experts in the field of medical genetics to provide the current, most accurate name for each disorder. Alternate names are included as synonyms.

Naming genes

The HUGO Gene Nomenclature Committee (HGNC) designates an official name and symbol (an abbreviation of the name) for each known human gene. Some official gene names include additional information in parentheses, such as related genetic conditions, subtypes of a condition, or inheritance pattern. The HGNC is a non-profit organization funded by the U.K. Medical Research Council and the U.S. National Institutes of Health. The Committee has named more than 13,000 of the estimated 20,000 to 25,000 genes in the human genome.

During the research process, genes often acquire several alternate names and symbols. Different researchers investigating the same gene may each give the gene a different name, which can cause confusion. The HGNC assigns a unique name and symbol to each human gene, which allows effective organization of genes in large databanks, aiding the advancement of research. For specific information about how genes are named, refer to the HGNC's Guidelines for Human Gene Nomenclature.

Genetics Home Reference describes genes using the HGNC's official gene names and gene symbols. Genetics Home Reference frequently presents the symbol and name separated with a colon (for example, FGFR4: Fibroblast growth factor receptor 4).

Inheriting Genetic Conditions

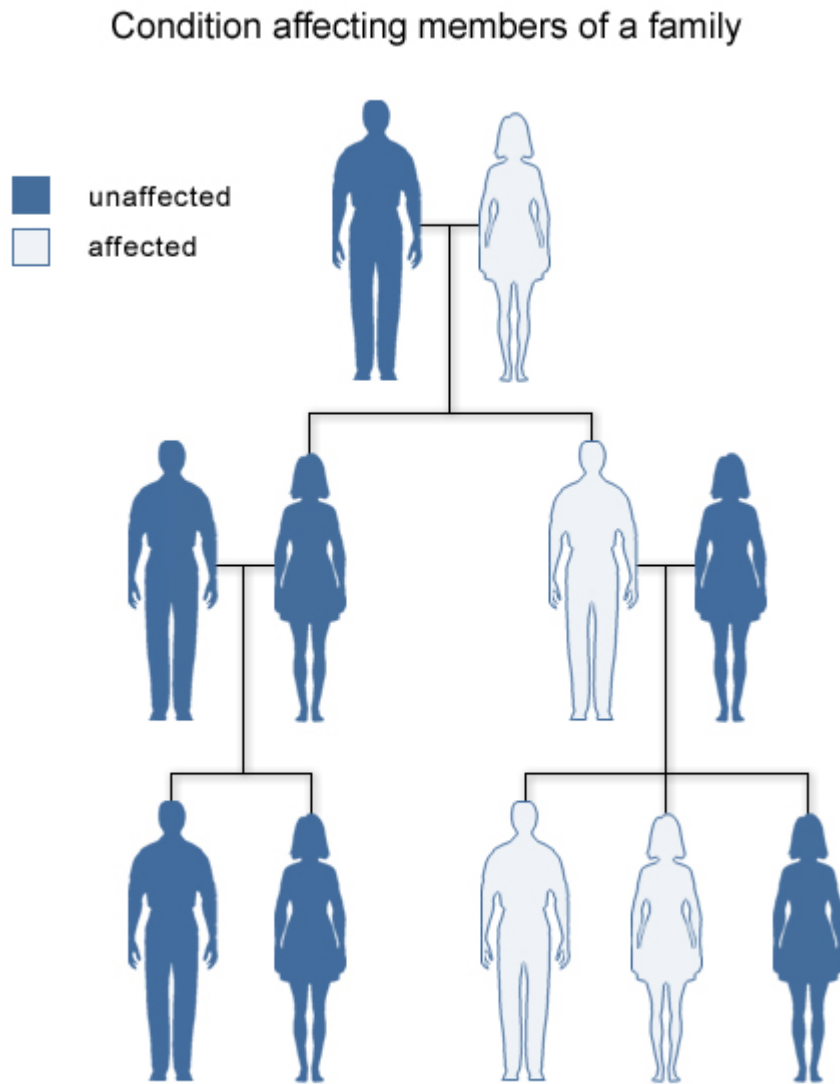
This section gives you information on inheritance patterns and understanding risk.

What Does It Mean If a Disorder Seems to Run in My Family?

A particular disorder might be described as "running in a family" if more than one person in the family has the condition. Some disorders that affect multiple family members are caused by gene mutations, which can be inherited (passed down from parent to child). Other conditions that appear to run in families are not inherited. Instead, environmental factors

such as dietary habits or a combination of genetic and environmental factors are responsible for these disorders.

It is not always easy to determine whether a condition in a family is inherited. A genetics professional can use a person's family history (a record of health information about a person's immediate and extended family) to help determine whether a disorder has a genetic component.



U.S. National Library of Medicine

Some disorders are seen in more than one generation of a family.

Why Is It Important to Know My Family Medical History?

A family medical history is a record of health information about a person and his or her close relatives. A complete record includes information from three generations of relatives,

including children, brothers and sisters, parents, aunts and uncles, nieces and nephews, grandparents, and cousins.

Families have many factors in common, including their genes, environment, and lifestyle. Together, these factors can give clues to medical conditions that may run in a family. By noticing patterns of disorders among relatives, healthcare professionals can determine whether an individual, other family members, or future generations may be at an increased risk of developing a particular condition.

A family medical history can identify people with a higher-than-usual chance of having common disorders, such as heart disease, high blood pressure, stroke, certain cancers, and diabetes. These complex disorders are influenced by a combination of genetic factors, environmental conditions, and lifestyle choices. A family history also can provide information about the risk of rarer conditions caused by mutations in a single gene, such as cystic fibrosis and sickle cell anemia.

While a family medical history provides information about the risk of specific health concerns, having relatives with a medical condition does not mean that an individual will definitely develop that condition. On the other hand, a person with no family history of a disorder may still be at risk of developing that disorder.

Knowing one's family medical history allows a person to take steps to reduce his or her risk. For people at an increased risk of certain cancers, healthcare professionals may recommend more frequent screening (such as mammography or colonoscopy) starting at an earlier age. Healthcare providers may also encourage regular checkups or testing for people with a medical condition that runs in their family. Additionally, lifestyle changes such as adopting a healthier diet, getting regular exercise, and quitting smoking help many people lower their chances of developing heart disease and other common illnesses.

The easiest way to get information about family medical history is to talk to relatives about their health. Have they had any medical problems, and when did they occur? A family gathering could be a good time to discuss these issues. Additionally, obtaining medical records and other documents (such as obituaries and death certificates) can help complete a family medical history. It is important to keep this information up-to-date and to share it with a healthcare professional regularly.

What Are the Different Ways in which a Genetic Condition Can Be Inherited?

Some genetic conditions are caused by mutations in a single gene. These conditions are usually inherited in one of several straightforward patterns, depending on the gene involved:

Inheritance Pattern	Description	Examples
Autosomal dominant	One mutated copy of the gene in each cell is sufficient for a person to be affected by an autosomal dominant disorder. Each affected person usually has one affected parent. Autosomal dominant disorders tend to occur in every generation of an affected family.	Huntington disease, neurofibromatosis type 1

Autosomal recessive	Two mutated copies of the gene are present in each cell when a person has an autosomal recessive disorder. An affected person usually has unaffected parents who each carry a single copy of the mutated gene (and are referred to as carriers). Autosomal recessive disorders are typically not seen in every generation of an affected family.	cystic fibrosis, sickle cell anemia
X-linked dominant	X-linked dominant disorders are caused by mutations in genes on the X chromosome. Females are more frequently affected than males, and the chance of passing on an X-linked dominant disorder differs between men and women. Families with an X-linked dominant disorder often have both affected males and affected females in each generation. A striking characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons (no male-to-male transmission).	fragile X syndrome
X-linked recessive	X-linked recessive disorders are also caused by mutations in genes on the X chromosome. Males are more frequently affected than females, and the chance of passing on the disorder differs between men and women. Families with an X-linked recessive disorder often have affected males, but rarely affected females, in each generation. A striking characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons (no male-to-male transmission).	hemophilia, Fabry disease
Codominant	In codominant inheritance, two different versions (alleles) of a gene can be expressed, and each version makes a slightly different protein. Both alleles influence the genetic trait or determine the characteristics of the genetic condition.	ABO blood group, alpha-1 antitrypsin deficiency
Mitochondrial	This type of inheritance, also known as maternal inheritance, applies to genes in mitochondrial DNA. Mitochondria, which are structures in each cell that convert molecules into energy, each contain a small amount of DNA. Because only egg cells contribute mitochondria to the developing embryo, only females can pass on mitochondrial conditions to their children. Mitochondrial disorders can appear in every generation of a family and can affect both males and females, but fathers do not pass mitochondrial traits to their children.	Leber hereditary optic neuropathy (LHON)

Many other disorders are caused by a combination of the effects of multiple genes or by interactions between genes and the environment. Such disorders are more difficult to analyze because their genetic causes are often unclear, and they do not follow the patterns of inheritance described above. Examples of conditions caused by multiple genes or gene/environment interactions include heart disease, diabetes, schizophrenia, and certain types of cancer. Disorders caused by changes in the number or structure of chromosomes do not follow the straightforward patterns of inheritance listed above. Other genetic factors can also influence how a disorder is inherited.

If a Genetic Disorder Runs in My Family, What Are the Chances That My Children Will Have the Condition?

When a genetic disorder is diagnosed in a family, family members often want to know the likelihood that they or their children will develop the condition. This can be difficult to predict in some cases because many factors influence a person's chances of developing a genetic condition. One important factor is how the condition is inherited. For example:

- **Autosomal dominant inheritance:** A person affected by an autosomal dominant disorder has a 50 percent chance of passing the mutated gene to each child. The chance that a child will not inherit the mutated gene is also 50 percent.
- **Autosomal recessive inheritance:** Two unaffected people who each carry one copy of the mutated gene for an autosomal recessive disorder (carriers) have a 25 percent chance with each pregnancy of having a child affected by the disorder. The chance with each pregnancy of having an unaffected child who is a carrier of the disorder is 50 percent, and the chance that a child will not have the disorder and will not be a carrier is 25 percent.
- **X-linked dominant inheritance:** The chance of passing on an X-linked dominant condition differs between men and women because men have one X chromosome and one Y chromosome, while women have two X chromosomes. A man passes on his Y chromosome to all of his sons and his X chromosome to all of his daughters. Therefore, the sons of a man with an X-linked dominant disorder will not be affected, but all of his daughters will inherit the condition. A woman passes on one or the other of her X chromosomes to each child. Therefore, a woman with an X-linked dominant disorder has a 50 percent chance of having an affected daughter or son with each pregnancy.
- **X-linked recessive inheritance:** Because of the difference in sex chromosomes, the probability of passing on an X-linked recessive disorder also differs between men and women. The sons of a man with an X-linked recessive disorder will not be affected, and his daughters will carry one copy of the mutated gene. With each pregnancy, a woman who carries an X-linked recessive disorder has a 50 percent chance of having sons who are affected and a 50 percent chance of having daughters who carry one copy of the mutated gene.
- **Codominant inheritance:** In codominant inheritance, each parent contributes a different version of a particular gene, and both versions influence the resulting genetic trait. The chance of developing a genetic condition with codominant inheritance, and the characteristic features of that condition, depend on which versions of the gene are passed from parents to their child.
- **Mitochondrial inheritance:** Mitochondria, which are the energy-producing centers inside cells, each contain a small amount of DNA. Disorders with mitochondrial inheritance result from mutations in mitochondrial DNA. Although mitochondrial

disorders can affect both males and females, only females can pass mutations in mitochondrial DNA to their children. A woman with a disorder caused by changes in mitochondrial DNA will pass the mutation to all of her daughters and sons, but the children of a man with such a disorder will not inherit the mutation.

It is important to note that the chance of passing on a genetic condition applies equally to each pregnancy. For example, if a couple has a child with an autosomal recessive disorder, the chance of having another child with the disorder is still 25 percent (or 1 in 4). Having one child with a disorder does not “protect” future children from inheriting the condition. Conversely, having a child without the condition does not mean that future children will definitely be affected.

Although the chances of inheriting a genetic condition appear straightforward, factors such as a person’s family history and the results of genetic testing can sometimes modify those chances. In addition, some people with a disease-causing mutation never develop any health problems or may experience only mild symptoms of the disorder. If a disease that runs in a family does not have a clear-cut inheritance pattern, predicting the likelihood that a person will develop the condition can be particularly difficult.

Estimating the chance of developing or passing on a genetic disorder can be complex. Genetics professionals can help people understand these chances and help them make informed decisions about their health.

Factors that Influence the Effects of Particular Genetic Changes

Reduced penetrance and variable expressivity are factors that influence the effects of particular genetic changes. These factors usually affect disorders that have an autosomal dominant pattern of inheritance, although they are occasionally seen in disorders with an autosomal recessive inheritance pattern.

Reduced Penetrance

Penetrance refers to the proportion of people with a particular genetic change (such as a mutation in a specific gene) who exhibit signs and symptoms of a genetic disorder. If some people with the mutation do not develop features of the disorder, the condition is said to have reduced (or incomplete) penetrance. Reduced penetrance often occurs with familial cancer syndromes. For example, many people with a mutation in the BRCA1 or BRCA2 gene will develop cancer during their lifetime, but some people will not. Doctors cannot predict which people with these mutations will develop cancer or when the tumors will develop.

Reduced penetrance probably results from a combination of genetic, environmental, and lifestyle factors, many of which are unknown. This phenomenon can make it challenging for genetics professionals to interpret a person’s family medical history and predict the risk of passing a genetic condition to future generations.

Variable Expressivity

Although some genetic disorders exhibit little variation, most have signs and symptoms that differ among affected individuals. Variable expressivity refers to the range of signs and

symptoms that can occur in different people with the same genetic condition. For example, the features of Marfan syndrome vary widely— some people have only mild symptoms (such as being tall and thin with long, slender fingers), while others also experience life-threatening complications involving the heart and blood vessels. Although the features are highly variable, most people with this disorder have a mutation in the same gene (FBN1).

As with reduced penetrance, variable expressivity is probably caused by a combination of genetic, environmental, and lifestyle factors, most of which have not been identified. If a genetic condition has highly variable signs and symptoms, it may be challenging to diagnose.

What Do Geneticists Mean by Anticipation?

The signs and symptoms of some genetic conditions tend to become more severe and appear at an earlier age as the disorder is passed from one generation to the next. This phenomenon is called anticipation. Anticipation is most often seen with certain genetic disorders of the nervous system, such as Huntington disease, myotonic dystrophy, and fragile X syndrome.

Anticipation typically occurs with disorders that are caused by an unusual type of mutation called a trinucleotide repeat expansion. A trinucleotide repeat is a sequence of three DNA building blocks (nucleotides) that is repeated a number of times in a row. DNA segments with an abnormal number of these repeats are unstable and prone to errors during cell division. The number of repeats can change as the gene is passed from parent to child. If the number of repeats increases, it is known as a trinucleotide repeat expansion. In some cases, the trinucleotide repeat may expand until the gene stops functioning normally. This expansion causes the features of some disorders to become more severe with each successive generation.

Most genetic disorders have signs and symptoms that differ among affected individuals, including affected people in the same family. Not all of these differences can be explained by anticipation. A combination of genetic, environmental, and lifestyle factors is probably responsible for the variability, although many of these factors have not been identified. Researchers study multiple generations of affected family members and consider the genetic cause of a disorder before determining that it shows anticipation.

What Is Genomic Imprinting?

Genomic imprinting is a factor that influences how some genetic conditions are inherited.

People inherit two copies of their genes—one from their mother and one from their father. Usually both copies of each gene are active, or “turned on,” in cells. In some cases, however, only one of the two copies is normally turned on. Which copy is active depends on the parent of origin: some genes are normally active only when they are inherited from a person’s father; others are active only when inherited from a person’s mother. This phenomenon is known as genomic imprinting.

In genes that undergo genomic imprinting, the parent of origin is often marked, or “stamped,” on the gene during the formation of egg and sperm cells. This stamping process, called methylation, is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. These molecules identify which copy of a gene was inherited

from the mother and which was inherited from the father. The addition and removal of methyl groups can be used to control the activity of genes.

Only a small percentage of all human genes undergo genomic imprinting. Researchers are not yet certain why some genes are imprinted and others are not. They do know that imprinted genes tend to cluster together in the same regions of chromosomes. Two major clusters of imprinted genes have been identified in humans, one on the short (p) arm of chromosome 11 (at position 11p15) and another on the long (q) arm of chromosome 15 (in the region 15q11 to 15q13).

What Is Uniparental Disomy?

Uniparental disomy is a factor that influences how some genetic conditions are inherited.

Uniparental disomy (UPD) occurs when a person receives two copies of a chromosome, or part of a chromosome, from one parent and no copies from the other parent. UPD can occur as a random event during the formation of egg or sperm cells or may happen in early fetal development.

In many cases, UPD likely has no effect on health or development. Because most genes are not imprinted, it doesn't matter if a person inherits both copies from one parent instead of one copy from each parent. In some cases, however, it does make a difference whether a gene is inherited from a person's mother or father. A person with UPD may lack any active copies of essential genes that undergo genomic imprinting. This loss of gene function can lead to delayed development, mental retardation, or other medical problems.

Several genetic disorders can result from UPD or a disruption of normal genomic imprinting. The most well-known conditions include Prader-Willi syndrome, which is characterized by uncontrolled eating and obesity, and Angelman syndrome, which causes mental retardation and impaired speech. Both of these disorders can be caused by UPD or other errors in imprinting involving genes on the long arm of chromosome 15. Other conditions, such as Beckwith-Wiedemann syndrome (a disorder characterized by accelerated growth and an increased risk of cancerous tumors), are associated with abnormalities of imprinted genes on the short arm of chromosome 11.

Are Chromosomal Disorders Inherited?

Although it is possible to inherit some types of chromosomal abnormalities, most chromosomal disorders (such as Down syndrome and Turner syndrome) are not passed from one generation to the next.

Some chromosomal conditions are caused by changes in the number of chromosomes. These changes are not inherited, but occur as random events during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in reproductive cells with an abnormal number of chromosomes. For example, a reproductive cell may accidentally gain or lose one copy of a chromosome. If one of these atypical reproductive cells contributes to the genetic makeup of a child, the child will have an extra or missing chromosome in each of the body's cells.

Changes in chromosome structure can also cause chromosomal disorders. Some changes in chromosome structure can be inherited, while others occur as random accidents during the formation of reproductive cells or in early fetal development. Because the inheritance of these changes can be complex, people concerned about this type of chromosomal abnormality may want to talk with a genetics professional.

Some cancer cells also have changes in the number or structure of their chromosomes. Because these changes occur in somatic cells (cells other than eggs and sperm), they cannot be passed from one generation to the next.

Why Are Some Genetic Conditions More Common in Particular Ethnic Groups?

Some genetic disorders are more likely to occur among people who trace their ancestry to a particular geographic area. People in an ethnic group often share certain versions of their genes, which have been passed down from common ancestors. If one of these shared genes contains a disease-causing mutation, a particular genetic disorder may be more frequently seen in the group.

Examples of genetic conditions that are more common in particular ethnic groups are sickle cell anemia, which is more common in people of African, African-American, or Mediterranean heritage; and Tay-Sachs disease, which is more likely to occur among people of Ashkenazi (eastern and central European) Jewish or French Canadian ancestry. It is important to note, however, that these disorders can occur in any ethnic group.

Genetic Consultation

This section presents information on finding and visiting a genetic counselor or other genetics professional.

What Is a Genetic Consultation?

A genetic consultation is a health service that provides information and support to people who have, or may be at risk for, genetic disorders. During a consultation, a genetics professional meets with an individual or family to discuss genetic risks or to diagnose, confirm, or rule out a genetic condition.

Genetics professionals include medical geneticists (doctors who specialize in genetics) and genetic counselors (certified healthcare workers with experience in medical genetics and counseling). Other healthcare professionals such as nurses, psychologists, and social workers trained in genetics can also provide genetic consultations.

Consultations usually take place in a doctor's office, hospital, genetics center, or other type of medical center. These meetings are most often in-person visits with individuals or families, but they are occasionally conducted in a group or over the telephone.

Why Might Someone Have a Genetic Consultation?

Individuals or families who are concerned about an inherited condition may benefit from a genetic consultation. The reasons that a person might be referred to a genetic counselor, medical geneticist, or other genetics professional include:

- A personal or family history of a genetic condition, birth defect, chromosomal disorder, or hereditary cancer.
- Two or more pregnancy losses (miscarriages), a stillbirth, or a baby who died.
- A child with a known inherited disorder, a birth defect, mental retardation, or developmental delay.
- A woman who is pregnant or plans to become pregnant at or after age 35. (Some chromosomal disorders occur more frequently in children born to older women.)
- Abnormal test results that suggest a genetic or chromosomal condition.
- An increased risk of developing or passing on a particular genetic disorder on the basis of a person's ethnic background.
- People related by blood (for example, cousins) who plan to have children together. (A child whose parents are related may be at an increased risk of inheriting certain genetic disorders.)

A genetic consultation is also an important part of the decision-making process for genetic testing. A visit with a genetics professional may be helpful even if testing is not available for a specific condition, however.

What Happens during a Genetic Consultation?

A genetic consultation provides information, offers support, and addresses a patient's specific questions and concerns. To help determine whether a condition has a genetic component, a genetics professional asks about a person's medical history and takes a detailed family history (a record of health information about a person's immediate and extended family). The genetics professional may also perform a physical examination and recommend appropriate tests.

If a person is diagnosed with a genetic condition, the genetics professional provides information about the diagnosis, how the condition is inherited, the chance of passing the condition to future generations, and the options for testing and treatment.

During a consultation, a genetics professional will:

- Interpret and communicate complex medical information.
- Help each person make informed, independent decisions about their health care and reproductive options.
- Respect each person's individual beliefs, traditions, and feelings.

A genetics professional will NOT:

- Tell a person which decision to make.
- Advise a couple not to have children.

- Recommend that a woman continue or end a pregnancy.
- Tell someone whether to undergo testing for a genetic disorder.

How Can I Find a Genetics Professional in My Area?

To find a genetics professional in your community, you may wish to ask your doctor for a referral. If you have health insurance, you can also contact your insurance company to find a medical geneticist or genetic counselor in your area who participates in your plan.

Several resources for locating a genetics professional in your community are available online:

- GeneTests from the University of Washington provides a list of genetics clinics around the United States and international genetics clinics. You can also access the list by clicking on “Clinic Directory” at the top of the GeneTests home page. Clinics can be chosen by state or country, by service, and/or by specialty. State maps can help you locate a clinic in your area. See <http://www.genetests.org/>.
- The National Society of Genetic Counselors offers a searchable directory of genetic counselors in the United States. You can search by location, name, area of practice/specialization, and/or ZIP Code. See <http://www.nsgc.org/resource/link.cfm>.
- The National Cancer Institute provides a Cancer Genetics Services Directory, which lists professionals who provide services related to cancer genetics. You can search by type of cancer or syndrome, location, and/or provider name at the following Web site: http://cancer.gov/search/genetics_services/.

Genetic Testing

This section presents information on the benefits, costs, risks, and limitations of genetic testing.

What Is Genetic Testing?

Genetic testing is a type of medical test that identifies changes in chromosomes, genes, or proteins. Most of the time, testing is used to find changes that are associated with inherited disorders. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. Several hundred genetic tests are currently in use, and more are being developed.

Genetic testing is voluntary. Because testing has both benefits and limitations, the decision about whether to be tested is a personal and complex one. A genetic counselor can help by providing information about the pros and cons of the test and discussing the social and emotional aspects of testing.

What Are the Types of Genetic Tests?

Genetic testing can provide information about a person’s genes and chromosomes. Available types of testing include:

- **Newborn screening** is used just after birth to identify genetic disorders that can be treated early in life. Millions of babies are tested each year in the United States. All states currently test infants for phenylketonuria (a genetic disorder that causes mental retardation if left untreated) and congenital hypothyroidism (a disorder of the thyroid gland). Most states also test for other genetic disorders.
- **Diagnostic testing** is used to identify or rule out a specific genetic or chromosomal condition. In many cases, genetic testing is used to confirm a diagnosis when a particular condition is suspected based on physical signs and symptoms. Diagnostic testing can be performed before birth or at any time during a person's life, but is not available for all genes or all genetic conditions. The results of a diagnostic test can influence a person's choices about health care and the management of the disorder.
- **Carrier testing** is used to identify people who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in certain ethnic groups with an increased risk of specific genetic conditions. If both parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition.
- **Prenatal testing** is used to detect changes in a fetus's genes or chromosomes before birth. This type of testing is offered during pregnancy if there is an increased risk that the baby will have a genetic or chromosomal disorder. In some cases, prenatal testing can lessen a couple's uncertainty or help them make decisions about a pregnancy. It cannot identify all possible inherited disorders and birth defects, however.
- **Preimplantation testing**, also called preimplantation genetic diagnosis (PGD), is a specialized technique that can reduce the risk of having a child with a particular genetic or chromosomal disorder. It is used to detect genetic changes in embryos that were created using assisted reproductive techniques such as in-vitro fertilization. In-vitro fertilization involves removing egg cells from a woman's ovaries and fertilizing them with sperm cells outside the body. To perform preimplantation testing, a small number of cells are taken from these embryos and tested for certain genetic changes. Only embryos without these changes are implanted in the uterus to initiate a pregnancy.
- **Predictive and presymptomatic types of testing** are used to detect gene mutations associated with disorders that appear after birth, often later in life. These tests can be helpful to people who have a family member with a genetic disorder, but who have no features of the disorder themselves at the time of testing. Predictive testing can identify mutations that increase a person's risk of developing disorders with a genetic basis, such as certain types of cancer. Presymptomatic testing can determine whether a person will develop a genetic disorder, such as hemochromatosis (an iron overload disorder), before any signs or symptoms appear. The results of predictive and presymptomatic testing can provide information about a person's risk of developing a specific disorder and help with making decisions about medical care.
- **Forensic testing** uses DNA sequences to identify an individual for legal purposes. Unlike the tests described above, forensic testing is not used to detect gene mutations associated with disease. This type of testing can identify crime or catastrophe victims, rule out or implicate a crime suspect, or establish biological relationships between people (for example, paternity).

How Is Genetic Testing Done?

Once a person decides to proceed with genetic testing, a medical geneticist, primary care doctor, specialist, or nurse practitioner can order the test. Genetic testing is often done as part of a genetic consultation.

Genetic tests are performed on a sample of blood, hair, skin, amniotic fluid (the fluid that surrounds a fetus during pregnancy), or other tissue. For example, a procedure called a buccal smear uses a small brush or cotton swab to collect a sample of cells from the inside surface of the cheek. The sample is sent to a laboratory where technicians look for specific changes in chromosomes, DNA, or proteins, depending on the suspected disorder. The laboratory reports the test results in writing to a person's doctor or genetic counselor.

Newborn screening tests are done on a small blood sample, which is taken by pricking the baby's heel. Unlike other types of genetic testing, a parent will usually only receive the result if it is positive. If the test result is positive, additional testing is needed to determine whether the baby has a genetic disorder.

Before a person has a genetic test, it is important that he or she understands the testing procedure, the benefits and limitations of the test, and the possible consequences of the test results. The process of educating a person about the test and obtaining permission is called informed consent.

What Is Direct-to-Consumer Genetic Testing?

Traditionally, genetic tests have been available only through healthcare providers such as physicians, nurse practitioners, and genetic counselors. Healthcare providers order the appropriate test from a laboratory, collect and send the samples, and interpret the test results. Direct-to-consumer genetic testing refers to genetic tests that are marketed directly to consumers via television, print advertisements, or the Internet. This form of testing, which is also known as at-home genetic testing, provides access to a person's genetic information without necessarily involving a doctor or insurance company in the process.

If a consumer chooses to purchase a genetic test directly, the test kit is mailed to the consumer instead of being ordered through a doctor's office. The test typically involves collecting a DNA sample at home, often by swabbing the inside of the cheek, and mailing the sample back to the laboratory. In some cases, the person must visit a health clinic to have blood drawn. Consumers are notified of their results by mail or over the telephone, or the results are posted online. In some cases, a genetic counselor or other healthcare provider is available to explain the results and answer questions. The price for this type of at-home genetic testing ranges from several hundred dollars to more than a thousand dollars.

The growing market for direct-to-consumer genetic testing may promote awareness of genetic diseases, allow consumers to take a more proactive role in their health care, and offer a means for people to learn about their ancestral origins. At-home genetic tests, however, have significant risks and limitations. Consumers are vulnerable to being misled by the results of unproven or invalid tests. Without guidance from a healthcare provider, they may make important decisions about treatment or prevention based on inaccurate, incomplete, or misunderstood information about their health. Consumers may also experience an invasion of genetic privacy if testing companies use their genetic information in an unauthorized way.

Genetic testing provides only one piece of information about a person's health—other genetic and environmental factors, lifestyle choices, and family medical history also affect a person's risk of developing many disorders. These factors are discussed during a consultation with a doctor or genetic counselor, but in many cases are not addressed by at-home genetic tests. More research is needed to fully understand the benefits and limitations of direct-to-consumer genetic testing.

What Do the Results of Genetic Tests Mean?

The results of genetic tests are not always straightforward, which often makes them challenging to interpret and explain. Therefore, it is important for patients and their families to ask questions about the potential meaning of genetic test results both before and after the test is performed. When interpreting test results, healthcare professionals consider a person's medical history, family history, and the type of genetic test that was done.

A positive test result means that the laboratory found a change in a particular gene, chromosome, or protein of interest. Depending on the purpose of the test, this result may confirm a diagnosis, indicate that a person is a carrier of a particular genetic mutation, identify an increased risk of developing a disease (such as cancer) in the future, or suggest a need for further testing. Because family members have some genetic material in common, a positive test result may also have implications for certain blood relatives of the person undergoing testing. It is important to note that a positive result of a predictive or presymptomatic genetic test usually cannot establish the exact risk of developing a disorder. Also, health professionals typically cannot use a positive test result to predict the course or severity of a condition.

A negative test result means that the laboratory did not find a change in the gene, chromosome, or protein under consideration. This result can indicate that a person is not affected by a particular disorder, is not a carrier of a specific genetic mutation, or does not have an increased risk of developing a certain disease. It is possible, however, that the test missed a disease-causing genetic alteration because many tests cannot detect all genetic changes that can cause a particular disorder. Further testing may be required to confirm a negative result.

In some cases, a negative result might not give any useful information. This type of result is called uninformative, indeterminate, inconclusive, or ambiguous. Uninformative test results sometimes occur because everyone has common, natural variations in their DNA, called polymorphisms, that do not affect health. If a genetic test finds a change in DNA that has not been associated with a disorder in other people, it can be difficult to tell whether it is a natural polymorphism or a disease-causing mutation. An uninformative result cannot confirm or rule out a specific diagnosis, and it cannot indicate whether a person has an increased risk of developing a disorder. In some cases, testing other affected and unaffected family members can help clarify this type of result.

What Is the Cost of Genetic Testing, and How Long Does It Take to Get the Results?

The cost of genetic testing can range from under \$100 to more than \$2,000, depending on the nature and complexity of the test. The cost increases if more than one test is necessary or if multiple family members must be tested to obtain a meaningful result. For newborn

screening, costs vary by state. Some states cover part of the total cost, but most charge a fee of \$15 to \$60 per infant.

From the date that a sample is taken, it may take a few weeks to several months to receive the test results. Results for prenatal testing are usually available more quickly because time is an important consideration in making decisions about a pregnancy. The doctor or genetic counselor who orders a particular test can provide specific information about the cost and time frame associated with that test.

Will Health Insurance Cover the Costs of Genetic Testing?

In many cases, health insurance plans will cover the costs of genetic testing when it is recommended by a person's doctor. Health insurance providers have different policies about which tests are covered, however. A person interested in submitting the costs of testing may wish to contact his or her insurance company beforehand to ask about coverage.

Some people may choose not to use their insurance to pay for testing because the results of a genetic test can affect a person's health insurance coverage. Instead, they may opt to pay out-of-pocket for the test. People considering genetic testing may want to find out more about their state's privacy protection laws before they ask their insurance company to cover the costs.

What Are the Benefits of Genetic Testing?

Genetic testing has potential benefits whether the results are positive or negative for a gene mutation. Test results can provide a sense of relief from uncertainty and help people make informed decisions about managing their health care. For example, a negative result can eliminate the need for unnecessary checkups and screening tests in some cases. A positive result can direct a person toward available prevention, monitoring, and treatment options. Some test results can also help people make decisions about having children. Newborn screening can identify genetic disorders early in life so treatment can be started as early as possible.

What Are the Risks and Limitations of Genetic Testing?

The physical risks associated with most genetic tests are very small, particularly for those tests that require only a blood sample or buccal smear (a procedure that samples cells from the inside surface of the cheek). The procedures used for prenatal testing carry a small but real risk of losing the pregnancy (miscarriage) because they require a sample of amniotic fluid or tissue from around the fetus.

Many of the risks associated with genetic testing involve the emotional, social, or financial consequences of the test results. People may feel angry, depressed, anxious, or guilty about their results. In some cases, genetic testing creates tension within a family because the results can reveal information about other family members in addition to the person who is tested. The possibility of genetic discrimination in employment or insurance is also a concern.

Genetic testing can provide only limited information about an inherited condition. The test often can't determine if a person will show symptoms of a disorder, how severe the symptoms will be, or whether the disorder will progress over time. Another major limitation is the lack of treatment strategies for many genetic disorders once they are diagnosed.

A genetics professional can explain in detail the benefits, risks, and limitations of a particular test. It is important that any person who is considering genetic testing understand and weigh these factors before making a decision.

What Is Genetic Discrimination?

Genetic discrimination occurs when people are treated differently by their employer or insurance company because they have a gene mutation that causes or increases the risk of an inherited disorder. People who undergo genetic testing may be at risk for genetic discrimination.

The results of a genetic test are normally included in a person's medical records. When a person applies for life, disability, or health insurance, the insurance company may ask to look at these records before making a decision about coverage. An employer may also have the right to look at an employee's medical records. As a result, genetic test results could affect a person's insurance coverage or employment. People making decisions about genetic testing should be aware that when test results are placed in their medical records, the results might not be kept private.

Fear of discrimination is a common concern among people considering genetic testing. Several laws at the federal and state levels help protect people against genetic discrimination; however, genetic testing is a fast-growing field and these laws don't cover every situation.

How Does Genetic Testing in a Research Setting Differ from Clinical Genetic Testing?

The main differences between clinical genetic testing and research testing are the purpose of the test and who receives the results. The goals of research testing include finding unknown genes, learning how genes work, and advancing our understanding of genetic conditions. The results of testing done as part of a research study are usually not available to patients or their healthcare providers. Clinical testing, on the other hand, is done to find out about an inherited disorder in an individual patient or family. People receive the results of a clinical test and can use them to help them make decisions about medical care or reproductive issues.

It is important for people considering genetic testing to know whether the test is available on a clinical or research basis. Clinical and research testing both involve a process of informed consent in which patients learn about the testing procedure, the risks and benefits of the test, and the potential consequences of testing.

Gene Therapy

This section presents information on experimental techniques, safety, ethics, and availability of gene therapy.

What Is Gene Therapy?

Gene therapy is an experimental technique that uses genes to treat or prevent disease. In the future, this technique may allow doctors to treat a disorder by inserting a gene into a patient's cells instead of using drugs or surgery. Researchers are testing several approaches to gene therapy, including:

- Replacing a mutated gene that causes disease with a healthy copy of the gene.
- Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
- Introducing a new gene into the body to help fight a disease.

Although gene therapy is a promising treatment option for a number of diseases (including inherited disorders, some types of cancer, and certain viral infections), the technique remains risky and is still under study to make sure that it will be safe and effective. Gene therapy is currently only being tested for the treatment of diseases that have no other cures.

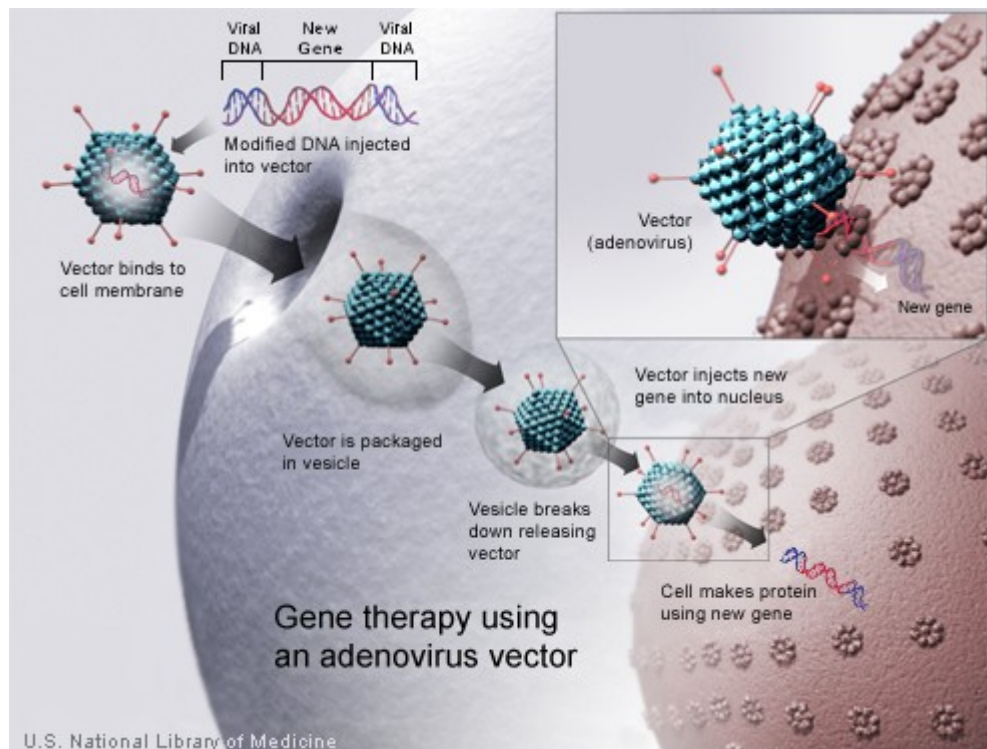
How Does Gene Therapy Work?

Gene therapy is designed to introduce genetic material into cells to compensate for abnormal genes or to make a beneficial protein. If a mutated gene causes a necessary protein to be faulty or missing, gene therapy may be able to introduce a normal copy of the gene to restore the function of the protein.

A gene that is inserted directly into a cell usually does not function. Instead, a carrier called a vector is genetically engineered to deliver the gene. Certain viruses are often used as vectors because they can deliver the new gene by infecting the cell. The viruses are modified so they can't cause disease when used in people. Some types of virus, such as retroviruses, integrate their genetic material (including the new gene) into a chromosome in the human cell. Other viruses, such as adenoviruses, introduce their DNA into the nucleus of the cell, but the DNA is not integrated into a chromosome.

The vector can be injected or given intravenously (by IV) directly into a specific tissue in the body, where it is taken up by individual cells. Alternately, a sample of the patient's cells can be removed and exposed to the vector in a laboratory setting. The cells containing the vector are then returned to the patient. If the treatment is successful, the new gene delivered by the vector will make a functioning protein.

Researchers must overcome many technical challenges before gene therapy will be a practical approach to treating disease. For example, scientists must find better ways to deliver genes and target them to particular cells. They must also ensure that new genes are precisely controlled by the body.



A new gene is injected into an adenovirus vector, which is used to introduce the modified DNA into a human cell. If the treatment is successful, the new gene will make a functional protein.

Is Gene Therapy Safe?

Gene therapy is under study to determine whether it could be used to treat disease. Current research is evaluating the safety of gene therapy; future studies will test whether it is an effective treatment option. Several studies have already shown that this approach can have very serious health risks, such as toxicity, inflammation, and cancer. Because the techniques are relatively new, some of the risks may be unpredictable; however, medical researchers, institutions, and regulatory agencies are working to ensure that gene therapy research is as safe as possible.

Comprehensive federal laws, regulations, and guidelines help protect people who participate in research studies (called clinical trials). The U.S. Food and Drug Administration (FDA) regulates all gene therapy products in the United States and oversees research in this area. Researchers who wish to test an approach in a clinical trial must first obtain permission from the FDA. The FDA has the authority to reject or suspend clinical trials that are suspected of being unsafe for participants.

The National Institutes of Health (NIH) also plays an important role in ensuring the safety of gene therapy research. NIH provides guidelines for investigators and institutions (such as universities and hospitals) to follow when conducting clinical trials with gene therapy. These guidelines state that clinical trials at institutions receiving NIH funding for this type of research must be registered with the NIH Office of Biotechnology Activities. The protocol, or plan, for each clinical trial is then reviewed by the NIH Recombinant DNA Advisory Committee (RAC) to determine whether it raises medical, ethical, or safety issues that warrant further discussion at one of the RAC's public meetings.

An Institutional Review Board (IRB) and an Institutional Biosafety Committee (IBC) must approve each gene therapy clinical trial before it can be carried out. An IRB is a committee of scientific and medical advisors and consumers that reviews all research within an institution. An IBC is a group that reviews and approves an institution's potentially hazardous research studies. Multiple levels of evaluation and oversight ensure that safety concerns are a top priority in the planning and carrying out of gene therapy research.

What Are the Ethical Issues surrounding Gene Therapy?

Because gene therapy involves making changes to the body's set of basic instructions, it raises many unique ethical concerns. The ethical questions surrounding gene therapy include:

- How can "good" and "bad" uses of gene therapy be distinguished?
- Who decides which traits are normal and which constitute a disability or disorder?
- Will the high costs of gene therapy make it available only to the wealthy?
- Could the widespread use of gene therapy make society less accepting of people who are different?
- Should people be allowed to use gene therapy to enhance basic human traits such as height, intelligence, or athletic ability?

Current gene therapy research has focused on treating individuals by targeting the therapy to body cells such as bone marrow or blood cells. This type of gene therapy cannot be passed on to a person's children. Gene therapy could be targeted to egg and sperm cells (germ cells), however, which would allow the inserted gene to be passed on to future generations. This approach is known as germline gene therapy.

The idea of germline gene therapy is controversial. While it could spare future generations in a family from having a particular genetic disorder, it might affect the development of a fetus in unexpected ways or have long-term side effects that are not yet known. Because people who would be affected by germline gene therapy are not yet born, they can't choose whether to have the treatment. Because of these ethical concerns, the U.S. Government does not allow federal funds to be used for research on germline gene therapy in people.

Is Gene Therapy Available to Treat My Disorder?

Gene therapy is currently available only in a research setting. The U.S. Food and Drug Administration (FDA) has not yet approved any gene therapy products for sale in the United States.

Hundreds of research studies (clinical trials) are under way to test gene therapy as a treatment for genetic conditions, cancer, and HIV/AIDS. If you are interested in participating in a clinical trial, talk with your doctor or a genetics professional about how to participate.

You can also search for clinical trials online. ClinicalTrials.gov, a service of the National Institutes of Health, provides easy access to information on clinical trials. You can search for

specific trials or browse by condition or trial sponsor. You may wish to refer to a list of gene therapy trials that are accepting (or will accept) patients.

The Human Genome Project and Genomic Research

This section presents information on the goals, accomplishments, and next steps in understanding the human genome.

What Is a Genome?

A genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.

What Was the Human Genome Project and Why Has It Been Important?

The Human Genome Project was an international research effort to determine the sequence of the human genome and identify the genes that it contains. The Project was coordinated by the National Institutes of Health and the U.S. Department of Energy. Additional contributors included universities across the United States and international partners in the United Kingdom, France, Germany, Japan, and China. The Human Genome Project formally began in 1990 and was completed in 2003, 2 years ahead of its original schedule.

The work of the Human Genome Project has allowed researchers to begin to understand the blueprint for building a person. As researchers learn more about the functions of genes and proteins, this knowledge will have a major impact in the fields of medicine, biotechnology, and the life sciences.

What Were the Goals of the Human Genome Project?

The main goals of the Human Genome Project were to provide a complete and accurate sequence of the 3 billion DNA base pairs that make up the human genome and to find all of the estimated 20,000 to 25,000 human genes. The Project also aimed to sequence the genomes of several other organisms that are important to medical research, such as the mouse and the fruit fly.

In addition to sequencing DNA, the Human Genome Project sought to develop new tools to obtain and analyze the data and to make this information widely available. Also, because advances in genetics have consequences for individuals and society, the Human Genome Project committed to exploring the consequences of genomic research through its Ethical, Legal, and Social Implications (ELSI) program.

What Did the Human Genome Project Accomplish?

In April 2003, researchers announced that the Human Genome Project had completed a high-quality sequence of essentially the entire human genome. This sequence closed the gaps from a working draft of the genome, which was published in 2001. It also identified the locations of many human genes and provided information about their structure and organization. The Project made the sequence of the human genome and tools to analyze the data freely available via the Internet.

In addition to the human genome, the Human Genome Project sequenced the genomes of several other organisms, including brewers' yeast, the roundworm, and the fruit fly. In 2002, researchers announced that they had also completed a working draft of the mouse genome. By studying the similarities and differences between human genes and those of other organisms, researchers can discover the functions of particular genes and identify which genes are critical for life.

The Project's Ethical, Legal, and Social Implications (ELSI) program became the world's largest bioethics program and a model for other ELSI programs worldwide.

What Were Some of the Ethical, Legal, and Social Implications Addressed by the Human Genome Project?

The Ethical, Legal, and Social Implications (ELSI) program was founded in 1990 as an integral part of the Human Genome Project. The mission of the ELSI program was to identify and address issues raised by genomic research that would affect individuals, families, and society. A percentage of the Human Genome Project budget at the National Institutes of Health and the U.S. Department of Energy was devoted to ELSI research.

The ELSI program focused on the possible consequences of genomic research in four main areas:

- Privacy and fairness in the use of genetic information, including the potential for genetic discrimination in employment and insurance.
- The integration of new genetic technologies, such as genetic testing, into the practice of clinical medicine.
- Ethical issues surrounding the design and conduct of genetic research with people, including the process of informed consent.
- The education of healthcare professionals, policy makers, students, and the public about genetics and the complex issues that result from genomic research.

What Are the Next Steps in Genomic Research?

Discovering the sequence of the human genome was only the first step in understanding how the instructions coded in DNA lead to a functioning human being. The next stage of genomic research will begin to derive meaningful knowledge from the DNA sequence. Research studies that build on the work of the Human Genome Project are under way worldwide.

The objectives of continued genomic research include the following:

- Determine the function of genes and the elements that regulate genes throughout the genome.
- Find variations in the DNA sequence among people and determine their significance. These variations may one day provide information about a person's disease risk and response to certain medications.
- Discover the 3-dimensional structures of proteins and identify their functions.
- Explore how DNA and proteins interact with one another and with the environment to create complex living systems.
- Develop and apply genome-based strategies for the early detection, diagnosis, and treatment of disease.
- Sequence the genomes of other organisms, such as the rat, cow, and chimpanzee, in order to compare similar genes between species.
- Develop new technologies to study genes and DNA on a large scale and store genomic data efficiently.
- Continue to explore the ethical, legal, and social issues raised by genomic research.

What Is Pharmacogenomics?

Pharmacogenomics is the study of how genes affect a person's response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that will be tailored to a person's genetic makeup.

Many drugs that are currently available are "one size fits all," but they don't work the same way for everyone. It can be difficult to predict who will benefit from a medication, who will not respond at all, and who will experience negative side effects (called adverse drug reactions). Adverse drug reactions are a significant cause of hospitalizations and deaths in the United States. With the knowledge gained from the Human Genome Project, researchers are learning how inherited differences in genes affect the body's response to medications. These genetic differences will be used to predict whether a medication will be effective for a particular person and to help prevent adverse drug reactions.

The field of pharmacogenomics is still in its infancy. Its use is currently quite limited, but new approaches are under study in clinical trials. In the future, pharmacogenomics will allow the development of tailored drugs to treat a wide range of health problems, including cardiovascular disease, Alzheimer disease, cancer, HIV/AIDS, and asthma.

APPENDIX B. 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 Institute⁹:

- National Institutes of Health (NIH); guidelines consolidated across agencies available at <http://health.nih.gov/>
- National Institute of General Medical Sciences (NIGMS); fact sheets available at <http://www.nigms.nih.gov/Publications/FactSheets.htm>
- 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/cancertopics/pdq>
- National Eye Institute (NEI); guidelines available at <http://www.nei.nih.gov/health/>
- 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/HealthInformation/Publications/>
- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at <http://www.niaaa.nih.gov/Publications/>

⁹ These publications are typically written by one or more of the various NIH Institutes.

- 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.nidcr.nih.gov/HealthInformation/>
- 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/healthinformation/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 Biomedical Imaging and Bioengineering; general information at <http://www.nibib.nih.gov/HealthEdu>
- 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.¹⁰ 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

¹⁰ Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINEplus (<http://medlineplus.gov/> or <http://www.nlm.nih.gov/medlineplus/databases.html>).

citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine¹¹:

- **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/aidsinfo.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/index.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
- **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

¹¹ See <http://www.nlm.nih.gov/databases/index.html>.

The NLM Gateway¹²

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.¹³ To use the NLM Gateway, simply go to the search site at <http://gateway.nlm.nih.gov/gw/Cmd>. Type **beta thalassemia** (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	7318
Books / Periodicals / Audio Visual	14
Consumer Health	49
Meeting Abstracts	2
Other Collections	0
Total	7383

HSTAT¹⁴

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.¹⁵ 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.¹⁶ Simply search by **beta thalassemia** (or synonyms) at the following Web site: <http://text.nlm.nih.gov>.

Coffee Break: Tutorials for Biologists¹⁷

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.

¹² Adapted from NLM: <http://gateway.nlm.nih.gov/gw/Cmd?Overview.x>.

¹³ 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).

¹⁴ Adapted from HSTAT: <http://www.nlm.nih.gov/pubs/factsheets/hstat.html>.

¹⁵ The HSTAT URL is <http://hstat.nlm.nih.gov/>.

¹⁶ 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.

¹⁷ Adapted from <http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html>.

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.¹⁸ 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.¹⁹ This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: <http://www.ncbi.nlm.nih.gov/Coffeebreak/>.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **MD Consult:** Access to electronic clinical resources, see <http://www.mdconsult.com/>.
- **Medical Matrix:** Lists over 6000 medical Web sites and links to over 1.5 million documents with clinical content, see <http://www.medmatrix.org/>.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see <http://www.mwsearch.com/>.

¹⁸ 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.

¹⁹ After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

APPENDIX C. 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 beta thalassemia 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

This section directs you to sources which either publish fact sheets or can help you find additional guidelines on topics related to beta thalassemia. 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 beta thalassemia. 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 **beta thalassemia**:

Anemia

<http://www.nlm.nih.gov/medlineplus/anemia.html>

Blood and Blood Disorders

<http://www.nlm.nih.gov/medlineplus/bloodandblooddisorders.html>

Blood Transfusion and Donation

<http://www.nlm.nih.gov/medlineplus/bloodtransfusionanddonation.html>

Hemochromatosis

<http://www.nlm.nih.gov/medlineplus/hemochromatosis.html>

Laboratory Tests

<http://www.nlm.nih.gov/medlineplus/laboratorytests.html>

Newborn Screening

<http://www.nlm.nih.gov/medlineplus/newbornscreening.html>

Sickle Cell Anemia

<http://www.nlm.nih.gov/medlineplus/sicklecellanemia.html>

Thalassemia

<http://www.nlm.nih.gov/medlineplus/thalassemia.html>

Within the health topic page dedicated to beta thalassemia, the following was listed:

- Diagnosis/Symptoms

Thalassemia: Laboratory Tests

Source: American Association for Clinical Chemistry

<http://www.labtestsonline.org/understanding/conditions/thalassemia-3.html>

- Treatment

Focus on a Cure

Source: Cooley's Anemia Foundation

http://www.cooleysanemia.org/sections.php?sec=1&tab=7&cooleys_sess=97059e603331ad7642e40c328d2a758a

Treating Thalassemia

Source: Northern California Comprehensive Thalassemia Center

http://www.thalassemia.com/treat_thal.html

- Nutrition

Diet for Thalassemia

Source: Cooley's Anemia Foundation

<http://www.cooleysanemia.org/sections.php?sec=2&tab=10&sub=117>

- Children

Thalassemias

Source: Nemours Foundation

<http://kidshealth.org/parent/medical/heart/thalassemias.html>

- From the National Institutes of Health

Learning about Thalassemia

Source: National Human Genome Research Institute

<http://www.genome.gov/page.cfm?pageID=10001221>

Thalassemia

Source: National Heart, Lung, and Blood Institute

http://www.nhlbi.nih.gov/health/dci/Diseases/Thalassemia/Thalassemia_WhatIs.html

- Organizations

Cooley's Anemia Foundation

<http://www.cooleysanemia.org/>

National Heart, Lung, and Blood Institute

<http://www.nhlbi.nih.gov/>

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.

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:

- **geneticalliance.org**

Source: www.geneticalliance.org

http://www.geneticalliance.org/ws_display.asp?filter=resources_family_history&char=C&s_Diseases=

- **Iron Disorders Institute - About Iron**

Summary: Patients might like to contact organizations such as Cooley's Anemia Foundation or the Iron Disorders Institute for patient comments about their experiences.

Source: www.irondisorders.org

<http://www.irondisorders.org/Disorders/about.asp>

- **Learning More about Your Disease -- leukemia and other blood.**

Source: www.marrow.org

http://www.marrow.org/PATIENT/Undrstnd_Disease_Treat/Lrn_about_Disease/

- **NORD - National Organization for Rare Disorders, Inc.**

Source: www.rarediseases.org

http://www.rarediseases.org/search/rdblist.html?query_start=1001

- **Thalassemia, Hereditary Blood Disorders, DD, NCBDDD, CDC**

Summary: The most severe of these disorders is Cooley's Anemia. For more information. Locate a thalassemia care center. Organizations. Cooley's Anemia Foundation.

Source: www.cdc.gov

<http://www.cdc.gov/ncbddd/hbd/thalassemia.htm>

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 beta thalassemia. 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://health.nih.gov/index.asp>. Under **Search Health Topics**, type **beta thalassemia** (or synonyms) into the search box, and click **Search**.

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:

- 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://www.webmd.com/diseases_and_conditions/default.htm

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to beta thalassemia. By consulting all of the associations listed in this chapter, you will have nearly exhausted all sources for patient associations concerned with beta thalassemia.

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 beta thalassemia. 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://sis.nlm.nih.gov/dirline.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. Simply type in **beta thalassemia** (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://healthhotlines.nlm.nih.gov/>. 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 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 **beta thalassemia** (or a synonym) into the search box, and click **Submit Query**.

Resources for Patients and Families

The following are organizations that provide support and advocacy for patient with genetic conditions and their families²⁰:

- Genetic Alliance: <http://geneticalliance.org>
- Genetic and Rare Diseases Information Center:
http://rarediseases.info.nih.gov/html/resources/info_cntr.html
- Madisons Foundation: <http://www.madisonsfoundation.org/>
- March of Dimes: <http://www.marchofdimes.com>
- National Organization for Rare Disorders (NORD): <http://www.rarediseases.org/>

²⁰ Adapted from the National Library of Medicine: <http://ghr.nlm.nih.gov/ghr/resource/patients>.

For More Information on Genetics

The following publications offer detailed information for patients about the science of genetics:

- What Is a Genome?: http://www.ncbi.nlm.nih.gov/About/primer/genetics_genome.html
- A Science Called Genetics: <http://publications.nigms.nih.gov/genetics/science.html>
- Genetic Mapping: <http://www.genome.gov/10000715>

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/archive/20040831/nichsr/ta101/ta10108.html>

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).

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>
- 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>

BETA THALASSEMIA DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

3-dimensional: 3-D. A graphic display of depth, width, and height. Three-dimensional radiation therapy uses computers to create a 3-dimensional picture of the tumor. This allows doctors to give the highest possible dose of radiation to the tumor, while sparing the normal tissue as much as possible. [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]

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]

Adaptability: Ability to develop some form of tolerance to conditions extremely different from those under which a living organism evolved. [NIH]

Adenine: A purine base and a fundamental unit of adenine nucleotides. [NIH]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adenosine Triphosphate: Adenosine 5'-(tetrahydrogen triphosphate). An adenine nucleotide containing three phosphate groups esterified to the sugar moiety. In addition to its crucial roles in metabolism adenosine triphosphate is a neurotransmitter. [NIH]

Adenovirus: A group of viruses that cause respiratory tract and eye infections. Adenoviruses used in gene therapy are altered to carry a specific tumor-fighting gene. [NIH]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

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]

Age Distribution: The frequency of different ages or age groups in a given population. The distribution may refer to either how many or what proportion of the group. The population is usually patients with a specific disease but the concept is not restricted to humans and is not restricted to medicine. [NIH]

Age Groups: Persons classified by age from birth (infant, newborn) to octogenarians and older (aged, 80 and over). [NIH]

Albinism: General term for a number of inherited defects of amino acid metabolism in which there is a deficiency or absence of pigment in the eyes, skin, or hair. [NIH]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [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]

Allografts: A graft of tissue obtained from the body of another animal of the same species but with genotype differing from that of the recipient; tissue graft from a donor of one genotype to a host of another genotype with host and donor being members of the same species. [NIH]

Alpha-1: A protein with the property of inactivating proteolytic enzymes such as leucocyte collagenase and elastase. [NIH]

Alpha-Thalassemia: A disorder characterized by reduced synthesis of the alpha chains of hemoglobin. The severity of this condition can vary from mild anemia to death, depending on the number of genes deleted. [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]

Ameliorated: A changeable condition which prevents the consequence of a failure or accident from becoming as bad as it otherwise would. [NIH]

Amino Acid Motifs: Commonly observed structural components of proteins formed by simple combinations of adjacent secondary structures. A commonly observed structure may be composed of a conserved sequence which can be represented by a consensus sequence. [NIH]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Amino Acid Substitution: The naturally occurring or experimentally induced replacement of one or more amino acids in a protein with another. If a functionally equivalent amino acid is substituted, the protein may retain wild-type activity. Substitution may also diminish or

eliminate protein function. Experimentally induced substitution is often used to study enzyme activities and binding site properties. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH₂) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Amino Acids: Organic compounds that generally contain an amino (-NH₂) and a carboxyl (-COOH) group. Twenty alpha-amino acids are the subunits which are polymerized to form proteins. [NIH]

Aminolevulinic Acid: A compound produced from succinyl-CoA and glycine as an intermediate in heme synthesis. [NIH]

Amnion: The extraembryonic membrane which contains the embryo and amniotic fluid. [NIH]

Amniotic Fluid: Amniotic cavity fluid which is produced by the amnion and fetal lungs and kidneys. [NIH]

Amplification: The production of additional copies of a chromosomal DNA sequence, found as either intrachromosomal or extrachromosomal DNA. [NIH]

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]

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]

Aneuploidy: The chromosomal constitution of cells which deviate from the normal by the addition or subtraction of chromosomes or chromosome pairs. In a normally diploid cell the loss of a chromosome pair is termed nullisomy (symbol: 2N-2), the loss of a single chromosome is monosomy (symbol: 2N-1), the addition of a chromosome pair is tetrasomy (symbol: 2N+2), the addition of a single chromosome is trisomy (symbol: 2N+1). [NIH]

Angioid Streaks: Small breaks in the elastin-filled tissue of the retina. [NIH]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anomalies: Birth defects; abnormalities. [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]

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]

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]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antisickling Agents: Agents used to prevent or reverse the pathological events leading to sickling of erythrocytes in sickle cell conditions. [NIH]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anuria: Inability to form or excrete urine. [NIH]

Anus: The opening of the rectum to the outside of the body. [NIH]

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]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Asymptomatic: Having no signs or symptoms of disease. [NIH]

Atypical: Irregular; not conformable to the type; in microbiology, applied specifically to strains of unusual type. [EU]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccid, rodlike or bacillary, and spiral or spirochetal. [NIH]

Base: In chemistry, the nonacid part of a salt; a substance that combines with acids to form salts; a substance that dissociates to give hydroxide ions in aqueous solutions; a substance whose molecule or ion can combine with a proton (hydrogen ion); a substance capable of donating a pair of electrons (to an acid) for the formation of a coordinate covalent bond. [EU]

Base Sequence: The sequence of purines and pyrimidines in nucleic acids and polynucleotides. It is also called nucleotide or nucleoside sequence. [NIH]

Beta-Thalassemia: A disorder characterized by reduced synthesis of the beta chains of hemoglobin. There is retardation of hemoglobin A synthesis in the heterozygous form (thalassemia minor), which is asymptomatic, while in the homozygous form (thalassemia major, Cooley's anemia, Mediterranean anemia, erythroblastic anemia), which can result in severe complications and even death, hemoglobin A synthesis is absent. [NIH]

Bewilderment: Impairment or loss of will power. [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 Pigments: Pigments that give a characteristic color to bile including: bilirubin, biliverdine, and bilicyanin. [NIH]

Bioavailability: The degree to which a drug or other substance becomes available to the target tissue after administration. [EU]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Biological response modifier: BRM. A substance that stimulates the body's response to infection and disease. [NIH]

Biopsy: Removal and pathologic examination of specimens in the form of small pieces of tissue from the living body. [NIH]

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]

Blastocyst: The mammalian embryo in the post-morula stage in which a fluid-filled cavity, enclosed primarily by trophoblast, contains an inner cell mass which becomes the embryonic disc. [NIH]

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 transfusion: The administration of blood or blood products into a blood vessel. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a

network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood Viscosity: The internal resistance of the blood to shear forces. The in vitro measure of whole blood viscosity is of limited clinical utility because it bears little relationship to the actual viscosity within the circulation, but an increase in the viscosity of circulating blood can contribute to morbidity in patients suffering from disorders such as sickle cell anemia and polycythemia. [NIH]

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]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Buffers: A chemical system that functions to control the levels of specific ions in solution. When the level of hydrogen ion in solution is controlled the system is called a pH buffer. [NIH]

Busulfan: An anticancer drug that belongs to the family of drugs called alkylating agents. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH₂O)_n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Cardiac: Having to do with the heart. [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]

Carrier State: The condition of harboring an infective organism without manifesting symptoms of infection. The organism must be readily transmissible to another susceptible host. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Cause of Death: Factors which produce cessation of all vital bodily functions. They can be analyzed from an epidemiologic viewpoint. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

Cell Death: The termination of the cell's ability to carry out vital functions such as metabolism, growth, reproduction, responsiveness, and adaptability. [NIH]

Cell Differentiation: Progressive restriction of the developmental potential and increasing specialization of function which takes place during the development of the embryo and leads to the formation of specialized cells, tissues, and organs. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell 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]

Central Nervous System: The main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges. [NIH]

Centromere: The clear constricted portion of the chromosome at which the chromatids are joined and by which the chromosome is attached to the spindle during cell division. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Chelation: Combination with a metal in complexes in which the metal is part of a ring. [EU]

Chin: The anatomical frontal portion of the mandible, also known as the mentum, that contains the line of fusion of the two separate halves of the mandible (symphysis menti). This line of fusion divides inferiorly to enclose a triangular area called the mental protuberance. On each side, inferior to the second premolar tooth, is the mental foramen for the passage of blood vessels and a nerve. [NIH]

Cholecystectomy: Surgical removal of the gallbladder. [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]

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]

Chromosome Banding: Staining of bands, or chromosome segments, allowing the precise identification of individual chromosomes or parts of chromosomes. Applications include the determination of chromosome rearrangements in malformation syndromes and cancer, the chemistry of chromosome segments, chromosome changes during evolution, and, in conjunction with cell hybridization studies, chromosome mapping. [NIH]

Chromosome Fragility: Susceptibility of chromosomes to breakage and translocation or other aberrations. Chromosome fragile sites are regions that show up in karyotypes as a gap (uncondensed stretch) on the chromatid arm. They are associated with chromosome break sites and other aberrations. A fragile site on the X chromosome is associated with fragile X syndrome. Fragile sites are designated by the letters "FRA" followed by the designation for

the specific chromosome and a letter which refers to the different fragile sites on a chromosome (e.g. FRAXA). [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Cirrhosis: A type of chronic, progressive liver disease. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at <http://cis.nci.nih.gov>. [NIH]

Clear cell carcinoma: A rare type of tumor of the female genital tract in which the inside of the cells looks clear when viewed under a microscope. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Coagulation: 1. The process of clot formation. 2. In colloid chemistry, the solidification of a sol into a gelatinous mass; an alteration of a disperse phase or of a dissolved solid which causes the separation of the system into a liquid phase and an insoluble mass called the clot or curd. Coagulation is usually irreversible. 3. In surgery, the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation. [EU]

Codon: A set of three nucleotides in a protein coding sequence that specifies individual amino acids or a termination signal (codon, terminator). Most codons are universal, but some organisms do not produce the transfer RNAs (RNA, transfer) complementary to all codons. These codons are referred to as unassigned codons (codons, nonsense). [NIH]

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus. [NIH]

Colonoscopy: Endoscopic examination, therapy or surgery of the luminal surface of the colon. [NIH]

Combination Therapy: Association of 3 drugs to treat AIDS (AZT + DDC or DDI + protease inhibitor). [NIH]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin system) and complement regulatory proteins are known by semisystematic or trivial names.

Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Concentric: Having a common center of curvature or symmetry. [NIH]

Conception: The onset of pregnancy, marked by implantation of the blastocyst; the formation of a viable zygote. [EU]

Confounding: Extraneous variables resulting in outcome effects that obscure or exaggerate the "true" effect of an intervention. [NIH]

Confusion: A mental state characterized by bewilderment, emotional disturbance, lack of clear thinking, and perceptual disorientation. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Consciousness: Sense of awareness of self and of the environment. [NIH]

Consensus Sequence: A theoretical representative nucleotide or amino acid sequence in which each nucleotide or amino acid is the one which occurs most frequently at that site in the different sequences which occur in nature. The phrase also refers to an actual sequence which approximates the theoretical consensus. A known conserved sequence set is represented by a consensus sequence. Commonly observed supersecondary protein structures (amino acid motifs) are often formed by conserved sequences. [NIH]

Conserved Sequence: A sequence of amino acids in a polypeptide or of nucleotides in DNA or RNA that is similar across multiple species. A known set of conserved sequences is

represented by a consensus sequence. Amino acid motifs are often composed of conserved sequences. [NIH]

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]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Controlled clinical trial: A clinical study that includes a comparison (control) group. The comparison group receives a placebo, another treatment, or no treatment at all. [NIH]

Controlled study: An experiment or clinical trial that includes a comparison (control) group. [NIH]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Corpuscle: A small mass or body; a sensory nerve end bulb; a cell, especially that of the blood or the lymph. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cyanosis: A bluish or purplish discoloration of the skin and mucous membranes due to an increase in the amount of deoxygenated hemoglobin in the blood or a structural defect in the hemoglobin molecule. [NIH]

Cytochrome: Any electron transfer hemoprotein having a mode of action in which the transfer of a single electron is effected by a reversible valence change of the central iron atom of the heme prosthetic group between the +2 and +3 oxidation states; classified as cytochromes a in which the heme contains a formyl side chain, cytochromes b, which contain protoheme or a closely similar heme that is not covalently bound to the protein, cytochromes c in which protoheme or other heme is covalently bound to the protein, and cytochromes d in which the iron-tetrapyrrole has fewer conjugated double bonds than the hemes have. Well-known cytochromes have been numbered consecutively within groups and are designated by subscripts (beginning with no subscript), e.g. cytochromes c, c1, C2, . New cytochromes are named according to the wavelength in nanometres of the absorption maximum of the a-band of the iron (II) form in pyridine, e.g., c-555. [EU]

Cytokine: Small but highly potent protein that modulates the activity of many cell types, including T and B cells. [NIH]

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]

Cytosine: A pyrimidine base that is a fundamental unit of nucleic acids. [NIH]

De novo: In cancer, the first occurrence of cancer in the body. [NIH]

Death Certificates: Official records of individual deaths including the cause of death certified by a physician, and any other required identifying information. [NIH]

Deferoxamine: Natural product isolated from *Streptomyces pilosus*. It forms iron complexes

and is used as a chelating agent, particularly in the form of its mesylate. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydration: The condition that results from excessive loss of body water. [NIH]

Deletion: A genetic rearrangement through loss of segments of DNA (chromosomes), bringing sequences, which are normally separated, into close proximity. [NIH]

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]

Demography: Statistical interpretation and description of a population with reference to distribution, composition, or structure. [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]

Deoxyribonucleic: A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

Deoxyribonucleic acid: A polymer of subunits called deoxyribonucleotides which is the primary genetic material of a cell, the material equivalent to genetic information. [NIH]

Deoxyribonucleotides: A purine or pyrimidine base bonded to a deoxyribose containing a bond to a phosphate group. [NIH]

DES: Diethylstilbestrol. A synthetic hormone that was prescribed from the early 1940s until 1971 to help women with complications of pregnancy. DES has been linked to an increased risk of clear cell carcinoma of the vagina in daughters of women who used DES. DES may also increase the risk of breast cancer in women who used DES. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [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]

Disorientation: The loss of proper bearings, or a state of mental confusion as to time, place, or identity. [EU]

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]

Elastic: Susceptible of resisting and recovering from stretching, compression or distortion applied by a force. [EU]

Electrocoagulation: Electrosurgical procedures used to treat hemorrhage (e.g., bleeding ulcers) and to ablate tumors, mucosal lesions, and refractory arrhythmias. [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]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Emollient: Softening or soothing; called also malactic. [EU]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

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]

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]

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]

Erythropoiesis: The production of erythrocytes. [EU]

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]

Estrogen: One of the two female sex hormones. [NIH]

Estrogen receptor: ER. Protein found on some cancer cells to which estrogen will attach. [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]

Euchromatin: Chromosome regions that are loosely packaged and more accessible to RNA polymerases than heterochromatin. These regions also stain differentially in chromosome banding preparations. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Excitatory: When cortical neurons are excited, their output increases and each new input they receive while they are still excited raises their output markedly. [NIH]

Excrete: To get rid of waste from the body. [NIH]

Exhaustion: The feeling of weariness of mind and body. [NIH]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Extracellular: Outside a cell or cells. [EU]

Extremity: A limb; an arm or leg (membrum); sometimes applied specifically to a hand or foot. [EU]

Eye Color: Color of the iris. [NIH]

Eye Infections: Infection, moderate to severe, caused by bacteria, fungi, or viruses, which occurs either on the external surface of the eye or intraocularly with probable inflammation, visual impairment, or blindness. [NIH]

Facial: Of or pertaining to the face. [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]

Fathers: Male parents, human or animal. [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]

Ferritin: An iron-containing protein complex that is formed by a combination of ferric iron with the protein apoferritin. [NIH]

Fetal Hemoglobin: The major component of hemoglobin in the fetus. This hemoglobin has two alpha and two gamma polypeptide subunits in comparison to normal adult hemoglobin, which has two alpha and two beta polypeptide subunits. Fetal hemoglobin concentrations can be elevated (usually above 0.5%) in children and adults affected by leukemia and several types of anemia. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Folate: A B-complex vitamin that is being studied as a cancer prevention agent. Also called folic acid. [NIH]

Folic Acid: N-(4-(((2-Amino-1,4-dihydro-4-oxo-6-pteridiny)l)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]

Forearm: The part between the elbow and the wrist. [NIH]

Frameshift: A type of mutation which causes out-of-phase transcription of the base sequence; such mutations arise from the addition or deletion of nucleotide(s) in numbers other than 3 or multiples of 3. [NIH]

Frameshift Mutation: A type of mutation in which a number of nucleotides not divisible by three is deleted from or inserted into a coding sequence, thereby causing an alteration in the reading frame of the entire sequence downstream of the mutation. These mutations may be induced by certain types of mutagens or may occur spontaneously. [NIH]

Gallbladder: The pear-shaped organ that sits below the liver. Bile is concentrated and stored in the gallbladder. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastrin: A hormone released after eating. Gastrin causes the stomach to produce more acid. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes

are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Products, rev: Trans-acting nuclear proteins whose functional expression are required for HIV viral replication. Specifically, the rev gene products are required for processing and translation of the HIV gag and env mRNAs, and thus rev regulates the expression of the viral structural proteins. rev can also regulate viral regulatory proteins. A cis-acting antirepression sequence (CAR) in env, also known as the rev-responsive element (RRE), is responsive to the rev gene product. rev is short for regulator of virion. [NIH]

Gene Silencing: Interruption or suppression of the expression of a gene at transcriptional or translational levels. [NIH]

Gene Therapy: The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells in vivo (e.g., bone marrow) or in vitro (e.g., fibroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particularly for leukemia. [NIH]

Genes, env: DNA sequences that form the coding region for the viral envelope (env) proteins in retroviruses. The env genes contain a cis-acting RNA target sequence for the rev protein (= gene products, rev), termed the rev-responsive element (RRE). [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]

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]

Germline mutation: A gene change in the body's reproductive cells (egg or sperm) that becomes incorporated into the DNA of every cell in the body of offspring; germline mutations are passed on from parents to offspring. Also called hereditary mutation. [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]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glutamate: Excitatory neurotransmitter of the brain. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glycerol: A trihydroxy sugar alcohol that is an intermediate in carbohydrate and lipid metabolism. It is used as a solvent, emollient, pharmaceutical agent, and sweetening agent.

[NIH]

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]

Gonad: A sex organ, such as an ovary or a testicle, which produces the gametes in most multicellular animals. [NIH]

Gonadal: Pertaining to a gonad. [EU]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

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-versus-host disease: GVHD. A reaction of donated bone marrow or peripheral stem cells against a person's tissue. [NIH]

Granule: A small pill made from sucrose. [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]

Guanine: One of the four DNA bases. [NIH]

Hair Color: Color of hair or fur. [NIH]

Haplotypes: The genetic constitution of individuals with respect to one member of a pair of allelic genes, or sets of genes that are closely linked and tend to be inherited together such as those of the major histocompatibility complex. [NIH]

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]

Hematopoiesis: The development and formation of various types of blood cells. [NIH]

Hematopoietic Stem Cells: Progenitor cells from which all blood cells derive. [NIH]

Hemochromatosis: A disease that occurs when the body absorbs too much iron. The body stores the excess iron in the liver, pancreas, and other organs. May cause cirrhosis of the liver. Also called iron overload disease. [NIH]

Hemodialysis: The use of a machine to clean wastes from the blood after the kidneys have failed. The blood travels through tubes to a dialyzer, which removes wastes and extra fluid. The cleaned blood then flows through another set of tubes back into the body. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal concentration. 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 A: Normal adult human hemoglobin. The globin moiety consists of two alpha and two beta chains. [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]

Hemoglobin H: An abnormal hemoglobin composed of four beta chains. It is caused by the reduced synthesis of the alpha chain. This abnormality results in alpha-thalassemia. [NIH]

Hemoglobin M: A group of abnormal hemoglobins in which amino acid substitutions take place in either the alpha or beta chains but near the heme iron. This results in facilitated oxidation of the hemoglobin to yield excess methemoglobin which leads to cyanosis. [NIH]

Hemoglobinopathies: A group of inherited disorders characterized by structural alterations within the hemoglobin molecule. [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]

Hemophilia: Refers to a group of hereditary disorders in which affected individuals fail to make enough of certain proteins needed to form blood clots. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hepatic: Refers to the liver. [NIH]

Hepatitis: Inflammation of the liver and liver disease involving degenerative or necrotic alterations of hepatocytes. [NIH]

Hepatocytes: The main structural component of the liver. They are specialized epithelial cells that are organized into interconnected plates called lobules. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Hereditary mutation: A gene change in the body's reproductive cells (egg or sperm) that becomes incorporated into the DNA of every cell in the body of offspring; hereditary mutations are passed on from parents to offspring. Also called germline mutation. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Heterochromatin: The portion of chromosome material that remains condensed and is transcriptionally inactive during interphase. [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]

Histiocytosis: General term for the abnormal appearance of histiocytes in the blood. Based on the pathological features of the cells involved rather than on clinical findings, the histiocytic diseases are subdivided into three groups: Langerhans cell histiocytosis, non-Langerhans cell histiocytosis, and malignant histiocytic disorders. [NIH]

Histones: Small chromosomal proteins (approx 12-20 kD) possessing an open, unfolded structure and attached to the DNA in cell nuclei by ionic linkages. Classification into the various types (designated histone I, histone II, etc.) is based on the relative amounts of arginine and lysine in each. [NIH]

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]

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]

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]

Hydroxyurea: An antineoplastic agent that inhibits DNA synthesis through the inhibition of ribonucleoside diphosphate reductase. [NIH]

Hyperbilirubinemia: Pathologic process consisting of an abnormal increase in the amount of bilirubin in the circulating blood, which may result in jaundice. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [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]

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]

Immunosuppressant: An agent capable of suppressing immune responses. [EU]

Impairment: In the context of health experience, an impairment is any loss or abnormality of psychological, physiological, or anatomical structure or function. [NIH]

Implantation: The insertion or grafting into the body of biological, living, inert, or radioactive material. [EU]

In 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]

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]

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]

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]

Informed Consent: Voluntary authorization, given to the physician by the patient, with full comprehension of the risks involved, for diagnostic or investigative procedures and medical and surgical treatment. [NIH]

Infusion: A method of putting fluids, including drugs, into the bloodstream. Also called intravenous infusion. [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Insulator: Material covering the metal conductor of the lead. It is usually polyurethane or silicone. [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]

Interphase: The interval between two successive cell divisions during which the chromosomes are not individually distinguishable and DNA replication occurs. [NIH]

Intracellular: Inside a cell. [NIH]

Intracellular Membranes: Membranes of subcellular structures. [NIH]

Intrahepatic: Within the liver. [NIH]

Intraperitoneal: IP. Within the peritoneal cavity (the area that contains the abdominal organs). [NIH]

Intravenous: IV. Into a vein. [NIH]

Involuntary: Reaction occurring without intention or volition. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Iris: The most anterior portion of the uveal layer, separating the anterior chamber from the posterior. It consists of two layers - the stroma and the pigmented epithelium. Color of the iris depends on the amount of melanin in the stroma on reflection from the pigmented epithelium. [NIH]

Jaundice: A clinical manifestation of hyperbilirubinemia, consisting of deposition of bile pigments in the skin, resulting in a yellowish staining of the skin and mucous membranes. [NIH]

Karyotype: The characteristic chromosome complement of an individual, race, or species as defined by their number, size, shape, etc. [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 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]

Kinetic: Pertaining to or producing motion. [EU]

Lectin: A complex molecule that has both protein and sugars. Lectins are able to bind to the outside of a cell and cause biochemical changes in it. Lectins are made by both animals and plants. [NIH]

Leg Ulcer: Ulceration of the skin and underlying structures of the lower extremity. About 90% of the cases are due to venous insufficiency (varicose ulcer), 5% to arterial disease, and the remaining 5% to other causes. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Leucocyte: All the white cells of the blood and their precursors (myeloid cell series, lymphoid cell series) but commonly used to indicate granulocytes exclusive of lymphocytes. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Life Expectancy: A figure representing the number of years, based on known statistics, to which any person of a given age may reasonably expect to live. [NIH]

Ligament: A band of fibrous tissue that connects bones or cartilages, serving to support and strengthen joints. [EU]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Lipid: Fat. [NIH]

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]

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]

Lymphocytes: White blood cells formed in the body's lymphoid tissue. The nucleus is round or ovoid with coarse, irregularly clumped chromatin while the cytoplasm is typically pale blue with azurophilic (if any) granules. Most lymphocytes can be classified as either T or B (with subpopulations of each); those with characteristics of neither major class are called null cells. [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]

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]

Malaria: A protozoan disease caused in humans by four species of the genus *Plasmodium* (*P. falciparum* (malaria, falciparum), *P. vivax* (malaria, vivax), *P. ovale*, and *P. malariae*) and transmitted by the bite of an infected female mosquito of the genus *Anopheles*. Malaria is endemic in parts of Asia, Africa, Central and South America, Oceania, and certain Caribbean islands. It is characterized by extreme exhaustion associated with paroxysms of high fever, sweating, shaking chills, and anemia. Malaria in animals is caused by other species of plasmodia. [NIH]

Malaria, Falciparum: Malaria caused by *Plasmodium falciparum*. This is the severest form of malaria and is associated with the highest levels of parasites in the blood. This disease is characterized by irregularly recurring febrile paroxysms that in extreme cases occur with acute cerebral, renal, or gastrointestinal manifestations. [NIH]

Malaria, Vivax: Malaria caused by *Plasmodium vivax*. This form of malaria is less severe than malaria, falciparum, but there is a higher probability for relapses to occur. Febrile paroxysms often occur every other day. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Mammography: Radiographic examination of the breast. [NIH]

Medical Records: Recording of pertinent information concerning patient's illness or illnesses. [NIH]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

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]

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 Proteins: Proteins which are found in membranes including cellular and intracellular membranes. They consist of two types, peripheral and integral proteins. They include most membrane-associated enzymes, antigenic proteins, transport proteins, and drug, hormone, and lectin receptors. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Mental: Pertaining to the mind; psychic. 2. (L. mentum chin) pertaining to the chin. [EU]

Mental Retardation: Refers to sub-average general intellectual functioning which originated during the developmental period and is associated with impairment in adaptive behavior. [NIH]

Metabolic disorder: A condition in which normal metabolic processes are disrupted, usually because of a missing enzyme. [NIH]

Methotrexate: An antineoplastic antimetabolite with immunosuppressant properties. It is an inhibitor of dihydrofolate reductase and prevents the formation of tetrahydrofolate, necessary for synthesis of thymidylate, an essential component of DNA. [NIH]

Mice Minute Virus: The type species of parvovirus prevalent in mouse colonies and found as a contaminant of many transplanted tumors or leukemias. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

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]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Milk Thistle: The plant *Silybum marianum* in the family Asteraceae containing the bioflavonoid complex silymarin. For centuries this has been used traditionally to treat liver disease. [NIH]

Miscarriage: Spontaneous expulsion of the products of pregnancy before the middle of the second trimester. [NIH]

Mitochondria: Parts of a cell where aerobic production (also known as cell respiration) takes place. [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]

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]

Mononuclear: A cell with one nucleus. [NIH]

Monosomy: The condition in which one chromosome of a pair is missing. In a normally diploid cell it is represented symbolically as $2N-1$. [NIH]

Morphological: Relating to the configuration or the structure of live organs. [NIH]

Mosaicism: The occurrence in an individual of two or more cell populations of different chromosomal constitutions, derived from a single zygote, as opposed to chimerism in which the different cell populations are derived from more than one zygote. [NIH]

Multicenter study: A clinical trial that is carried out at more than one medical institution. [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]

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]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at <http://cancer.gov>. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [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]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, γ -aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Neutropenia: An abnormal decrease in the number of neutrophils, a type of white blood cell. [NIH]

Neutrophil: A type of white blood cell. [NIH]

Nuclear: A test of the structure, blood flow, and function of the kidneys. The doctor injects a mildly radioactive solution into an arm vein and uses x-rays to monitor its progress through the kidneys. [NIH]

Nuclear Envelope: The membrane system of the cell nucleus that surrounds the nucleoplasm. It consists of two concentric membranes separated by the perinuclear space.

The structures of the envelope where it opens to the cytoplasm are called the nuclear pores (nuclear pore). [NIH]

Nuclear Pore: An opening through the nuclear envelope formed by the nuclear pore complex which transports nuclear proteins or RNA into or out of the cell nucleus and which, under some conditions, acts as an ion channel. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nurse Practitioners: Nurses who are specially trained to assume an expanded role in providing medical care under the supervision of a physician. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysosomes; plastids; and vacuoles. [NIH]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Ovaries: The pair of female reproductive glands in which the ova, or eggs, are formed. The ovaries are located in the pelvis, one on each side of the uterus. [NIH]

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 Phosphorylation: Electron transfer through the cytochrome system liberating free energy which is transformed into high-energy phosphate bonds. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Pancreatic: Having to do with the pancreas. [NIH]

Particle: A tiny mass of material. [EU]

Parvovirus: A genus of the family Parvoviridae, subfamily Parvovirinae, infecting a variety of vertebrates including humans. Parvoviruses are responsible for a number of important diseases but also can be non-pathogenic in certain hosts. The type species is mice minute virus. [NIH]

Paternity: Establishing the father relationship of a man and a child. [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 Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

PDQ: Physician Data Query. PDQ is an online database developed and maintained by the National Cancer Institute. Designed to make the most current, credible, and accurate cancer information available to health professionals and the public, PDQ contains peer-reviewed summaries on cancer treatment, screening, prevention, genetics, and supportive care; a registry of cancer clinical trials from around the world; and directories of physicians, professionals who provide genetics services, and organizations that provide cancer care. Most of this information is available on the CancerNet Web site, and more specific information about PDQ can be found at <http://cancernet.nci.nih.gov/pdq.html>. [NIH]

Pelvis: The lower part of the abdomen, located between the hip bones. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peripheral blood: Blood circulating throughout the body. [NIH]

Peripheral stem cells: Immature cells found circulating in the bloodstream. New blood cells develop from peripheral stem cells. [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]

Pharmacodynamics: The study of the biochemical and physiological effects of drugs and the mechanisms of their actions, including the correlation of actions and effects of drugs with their chemical structure; also, such effects on the actions of a particular drug or drugs. [EU]

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]

Phenylbutyrate: An anticancer drug that belongs to the family of drugs called differentiating agents. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nerves, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Phosphorylation: The introduction of a phosphoryl group into a compound through the formation of an ester bond between the compound and a phosphorus moiety. [NIH]

Photocoagulation: Using a special strong beam of light (laser) to seal off bleeding blood vessels such as in the eye. The laser can also burn away blood vessels that should not have grown in the eye. This is the main treatment for diabetic retinopathy. [NIH]

Physical Examination: Systematic and thorough inspection of the patient for physical signs of disease or abnormality. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair. [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; absence of nervous and sensory systems; and an alteration of haploid and diploid generations. [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]

Plasticity: In an individual or a population, the capacity for adaptation: a) through gene changes (genetic plasticity) or b) through internal physiological modifications in response to changes of environment (physiological plasticity). [NIH]

Plastids: Self-replicating cytoplasmic organelles of plant and algal cells that contain pigments and may synthesize and accumulate various substances. Plastids are used in phylogenetic studies. [NIH]

Platelet Activation: A series of progressive, overlapping events triggered by exposure of the platelets to subendothelial tissue. These events include shape change, adhesiveness, aggregation, and release reactions. When carried through to completion, these events lead to the formation of a stable hemostatic plug. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Pneumonia: Inflammation of the lungs. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3' direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymorphism: The occurrence together of two or more distinct forms in the same population. [NIH]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

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]

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]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prenatal Diagnosis: Determination of the nature of a pathological condition or disease in the postimplantation embryo, fetus, or pregnant female before birth. [NIH]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Progeny: The offspring produced in any generation. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

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 S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

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]

Protozoan: 1. Any individual of the protozoa; protozoon. 2. Of or pertaining to the protozoa; protozoal. [EU]

Pseudoxanthoma: A rare disease of the skin characterized by the appearance of elevated yellowish papules or plaques, particularly on the neck, chest and abdomen and infrequently on the eyelids. [NIH]

Pseudoxanthoma Elasticum: A rare, progressive inherited disorder resulting from extensive basophilic degeneration of elastic tissue, usually presenting after puberty and involving the skin, eye, and cardiovascular system. Characteristic manifestations are small, circumscribed

yellowish patches at sites of considerable movement of the skin, angioid streaks in the retina, and a tendency towards hemorrhage and arterial insufficiency. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [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]

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]

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]

Pyrimidines: A family of 6-membered heterocyclic compounds occurring in nature in a wide variety of forms. They include several nucleic acid constituents (cytosine, thymine, and uracil) and form the basic structure of the barbiturates. [NIH]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

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]

Reactivation: The restoration of activity to something that has been inactivated. [EU]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to

crossing-over. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Reductase: Enzyme converting testosterone to dihydrotestosterone. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Refractory: Not readily yielding to treatment. [EU]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Reproductive cells: Egg and sperm cells. Each mature reproductive cell carries a single set of 23 chromosomes. [NIH]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Reticulocyte Count: Determination of the number of reticulocytes in a measured volume of blood. Values for reticulocytes are expressed as a percentage of the erythrocyte count or in the form of a so-called "corrected" reticulocyte "index". An increase in circulating reticulocytes, often referred to as reticulocytosis, is among the simplest and most reliable signs of accelerated erythrocyte production. Reticulocytosis, or an increased reticulocyte count, occurs during active blood regeneration (stimulation of red bone marrow) and in certain anemias, particularly congenital hemolytic anemia. [NIH]

Reticulocytes: Immature erythrocytes. In humans, these are erythroid cells that have just undergone extrusion of their cell nucleus. They still contain some organelles that gradually decrease in number as the cells mature. ribosomes are last to disappear. Certain staining techniques cause components of the ribosomes to precipitate into characteristic "reticulum" (not the same as the endoplasmic reticulum), hence the name reticulocytes. [NIH]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinoblastoma: An eye cancer that most often occurs in children younger than 5 years. It occurs in hereditary and nonhereditary (sporadic) forms. [NIH]

Retrospective: Looking back at events that have already taken place. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Ribonucleic acid: RNA. One of the two nucleic acids found in all cells. The other is deoxyribonucleic acid (DNA). Ribonucleic acid transfers genetic information from DNA to proteins produced by the cell. [NIH]

Ribonucleoside Diphosphate Reductase: An enzyme of the oxidoreductase class that catalyzes the formation of 2'-deoxyribonucleotides from the corresponding ribonucleotides using NADPH as the ultimate electron donor. The deoxyribonucleoside diphosphates are used in DNA synthesis. (From Dorland, 27th ed) EC 1.17.4.1. [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]

Scatter: The extent to which relative success and failure are divergently manifested in qualitatively different tests. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [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]

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]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

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]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Silymarin: A mixture of flavonoids extracted from seeds of the milk thistle, *Silybum marianum*. It consists primarily of three isomers: silicristin, silidianin, and silybin, its major component. Silymarin displays antioxidant and membrane stabilizing activity. It protects various tissues and organs against chemical injury, and shows potential as an antihepatotoxic agent. [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]

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]

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 cells: All the body cells except the reproductive (germ) cells. [NIH]

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]

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]

Spectrin: A high molecular weight (220-250 kDa) water-soluble protein which can be extracted from erythrocyte ghosts in low ionic strength buffers. The protein contains no lipids or carbohydrates, is the predominant species of peripheral erythrocyte membrane proteins, and exists as a fibrous coating on the inner, cytoplasmic surface of the membrane. [NIH]

Sperm: The fecundating fluid of the male. [NIH]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Splenectomy: An operation to remove the spleen. [NIH]

Sporadic: Neither endemic nor epidemic; occurring occasionally in a random or isolated manner. [EU]

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]

Stillbirth: The birth of a dead fetus or baby. [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]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stool: The waste matter discharged in a bowel movement; feces. [NIH]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

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]

Superoxide: Derivative of molecular oxygen that can damage cells. [NIH]

Superoxide Dismutase: An oxidoreductase that catalyzes the reaction between superoxide anions and hydrogen to yield molecular oxygen and hydrogen peroxide. The enzyme protects the cell against dangerous levels of superoxide. EC 1.15.1.1. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Supportive care: Treatment given to prevent, control, or relieve complications and side effects and to improve the comfort and quality of life of people who have cancer. [NIH]

Suppression: A conscious exclusion of disapproved desire contrary with repression, in which the process of exclusion is not conscious. [NIH]

Systemic: Affecting the entire body. [NIH]

Terminator: A DNA sequence sited at the end of a transcriptional unit that signals the end of transcription. [NIH]

Thalassemia: A group of hereditary hemolytic anemias in which there is decreased synthesis of one or more hemoglobin polypeptide chains. There are several genetic types with clinical pictures ranging from barely detectable hematologic abnormality to severe and fatal anemia. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytopenia: A decrease in the number of blood platelets. [NIH]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroid Gland: A highly vascular endocrine gland consisting of two lobes, one on either side of the trachea, joined by a narrow isthmus; it produces the thyroid hormones which are concerned in regulating the metabolic rate of the body. [NIH]

Thyroid Hormones: Hormones secreted by the thyroid gland. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicokinetics: Study of the absorption, distribution, metabolism, and excretion of test substances. [NIH]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxins: Specific, characterizable, poisonous chemicals, often proteins, with specific biological properties, including immunogenicity, produced by microbes, higher plants, or animals. [NIH]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

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]

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]

Trinucleotide Repeat Expansion: DNA region comprised of a variable number of repetitive, contiguous trinucleotide sequences. The presence of these regions is associated with diseases such as Fragile X Syndrome and myotonic dystrophy. Many chromosome fragile sites (chromosome fragility) contain expanded trinucleotide repeats. [NIH]

Trinucleotide Repeats: Microsatellite repeats consisting of three nucleotides dispersed in the euchromatic arms of chromosomes. [NIH]

Trisomy: The possession of a third chromosome of any one type in an otherwise diploid cell. [NIH]

Ultraviolet radiation: Invisible rays that are part of the energy that comes from the sun. UV radiation can damage the skin and cause melanoma and other types of skin cancer. UV radiation that reaches the earth's surface is made up of two types of rays, called UVA and UVB rays. UVB rays are more likely than UVA rays to cause sunburn, but UVA rays pass deeper into the skin. Scientists have long thought that UVB radiation can cause melanoma and other types of skin cancer. They now think that UVA radiation also may add to skin damage that can lead to skin cancer and cause premature aging. For this reason, skin specialists recommend that people use sunscreens that reflect, absorb, or scatter both kinds of UV radiation. [NIH]

Uremia: The illness associated with the buildup of urea in the blood because the kidneys are not working effectively. Symptoms include nausea, vomiting, loss of appetite, weakness, and mental confusion. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Vaccine: A substance or group of substances meant to cause the immune system to respond to a tumor or to microorganisms, such as bacteria or viruses. [NIH]

Vacuoles: Any spaces or cavities within a cell. They may function in digestion, storage, secretion, or excretion. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

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]

Varicose: The common ulcer in the lower third of the leg or near the ankle. [NIH]

Varicose Ulcer: Ulcer due to varicose veins. Chronic venous insufficiency in the deep veins of the legs leads to shunting the venous return into the superficial veins, in which pressure and flow rate, as well as oxygen content, are increased. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vasculitis: Inflammation of a blood vessel. [NIH]

Vector: Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venous: Of or pertaining to the veins. [EU]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Ventricular: Pertaining to a ventricle. [EU]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Villi: The tiny, fingerlike projections on the surface of the small intestine. Villi help absorb nutrients. [NIH]

Villous: Of a surface, covered with villi. [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]

Viscosity: A physical property of fluids that determines the internal resistance to shear forces. [EU]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [NIH]

Womb: A hollow, thick-walled, muscular organ in which the impregnated ovum is developed into a child. [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]

Zygote: The fertilized ovum. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

INDEX

3

3-dimensional, 64, 96, 110

A

Abdomen, 110, 132, 137, 140, 145, 149

Abdominal, 110, 130, 137

Acceptor, 110, 136

Adaptability, 110, 117

Adenine, 58, 110, 141

Adenosine, 59, 110, 138

Adenosine Triphosphate, 59, 110, 138

Adenovirus, 92, 110

Adjustment, 46, 110

Adolescence, 4, 110

Adverse Effect, 110, 143

Aerobic, 110, 134

Affinity, 111, 144

Age Distribution, 6, 111

Age Groups, 111

Albinism, 38, 111

Algorithms, 111, 115

Alkylating Agents, 111, 116

Alleles, 32, 60, 78, 111, 129

Allogeneic, 21, 111

Allografts, 20, 111

Alpha-1, 74, 78, 111

Alpha-Thalassemia, 11, 111, 127

Alternative medicine, 54, 111

Ameliorated, 13, 112

Amino Acid Motifs, 112, 120

Amino Acid Sequence, 112, 113, 120

Amino Acid Substitution, 112, 127

Amino Acids, 8, 60, 64, 70, 112, 118, 120, 137, 139, 140, 143, 147

Aminolevulinic Acid, 22, 112

Amnion, 112

Amniotic Fluid, 87, 90, 112

Amplification, 34, 112

Anaemia, 37, 112, 133

Anaesthesia, 112, 129

Anatomical, 112, 117, 129, 143

Anemic, 32, 112

Aneuploidy, 71, 113

Angioid Streaks, 113, 140

Anions, 113, 131, 146

Annealing, 113, 139

Anomalies, 9, 113

Antibodies, 65, 113, 128

Antibody, 19, 65, 111, 113, 119, 128, 129, 130, 135, 141

Anticoagulant, 113, 140

Antigen, 24, 111, 113, 119, 128, 129, 130

Antimetabolite, 113, 134

Antineoplastic, 111, 113, 129, 134

Antioxidant, 113, 143

Antisickling Agents, 9, 113

Antiviral, 113, 130

Anuria, 114, 131

Anus, 114, 119

Apoptosis, 59, 68, 114

Aqueous, 114, 121, 129

Arginine, 114, 128

Arterial, 114, 129, 131, 140

Arteries, 114, 115, 120

Arterioles, 114, 115

Asymptomatic, 114

Atypical, 82, 114

B

Bacteria, 57, 65, 70, 113, 114, 124, 128, 134, 147, 148

Base, 8, 9, 17, 58, 59, 62, 64, 68, 69, 70, 94, 95, 110, 114, 121, 122, 124, 131

Base Sequence, 69, 114, 124

Beta-Thalassemia, 6, 9, 11, 15, 23, 36, 41, 43, 44, 45, 46, 47, 49, 114

Bewilderment, 114, 120

Bile, 114, 125, 131, 132

Bile Pigments, 114, 131

Bioavailability, 13, 115

Biochemical, 13, 19, 74, 111, 113, 115, 131, 138

Biological response modifier, 115, 130

Biopsy, 15, 115

Biotechnology, 4, 16, 54, 64, 93, 95, 100, 115

Biotransformation, 115

Bladder, 115, 148

Blastocyst, 115, 120

Blood Glucose, 115, 127

Blood Platelets, 115, 146

Blood pressure, 77, 115, 116, 129, 134, 144

Blood transfusion, 13, 26, 42, 45, 115

Blood vessel, 8, 80, 115, 116, 117, 128, 132, 138, 144, 145, 146, 148

Blood Viscosity, 38, 115

Body Fluids, 115, 144

Bone Marrow, 15, 21, 25, 35, 46, 47, 93, 116, 123, 125, 126, 132, 142

Bone Marrow Transplantation, 21, 25, 35,
46, 47, 116
Buccal, 87, 90, 116
Buffers, 116, 145
Busulfan, 25, 116

C

Carbohydrate, 116, 126, 139
Carbon Dioxide, 7, 116, 142
Carcinogenic, 111, 116, 130, 140
Cardiac, 41, 43, 116, 135
Cardiovascular, 97, 116, 140
Cardiovascular disease, 97, 116
Cardiovascular System, 116, 140
Carnitine, 30, 35, 44, 116
Carrier State, 29, 116
Case report, 20, 26, 27, 35, 38, 47, 116, 118
Cause of Death, 116, 121
Cell Cycle, 68, 117
Cell Death, 68, 114, 117, 135
Cell Differentiation, 11, 117
Cell Division, 60, 67, 69, 81, 82, 114, 117,
130, 133, 134, 138
Cell proliferation, 13, 117
Cell Respiration, 117, 134, 142
Central Nervous System, 117, 125, 126
Centromere, 61, 63, 117
Cerebrovascular, 116, 117
Chelation, 15, 41, 44, 46, 47, 117
Chin, 117, 134
Cholecystectomy, 33, 38, 117
Cholesterol, 59, 114, 117, 121
Chromatin, 9, 12, 36, 114, 117, 132
Chromosomal, 68, 71, 82, 83, 84, 86, 112,
113, 117, 128, 135
Chromosome Banding, 117, 123
Chromosome Fragility, 118, 147
Chronic, 15, 17, 36, 118, 123, 130, 131, 145,
148
Cirrhosis, 118, 127
CIS, 11, 118, 125
Clear cell carcinoma, 118, 122
Clinical Medicine, 96, 118, 139
Clinical study, 118, 120
Clinical trial, 10, 13, 14, 32, 93, 94, 97, 100,
118, 120, 135, 137, 140, 141
Cloning, 115, 118
Coagulation, 14, 115, 118, 146
Codon, 66, 118
Colon, 75, 119
Colonoscopy, 77, 119
Combination Therapy, 41, 119
Complement, 119, 131, 133

Complementary and alternative
medicine, 40, 49, 119

Complementary medicine, 40, 119

Computational Biology, 100, 119

Concentric, 119, 136

Conception, 67, 120, 124, 144

Confounding, 14, 120

Confusion, 74, 120, 122, 148

Connective Tissue, 105, 116, 120, 124, 125,
132

Consciousness, 120, 122

Consensus Sequence, 19, 112, 120

Conserved Sequence, 112, 120

Constriction, 61, 63, 120

Consultation, 83, 84, 87, 88, 120

Contraindications, ii, 120

Controlled clinical trial, 49, 120

Controlled study, 40, 120

Coronary, 116, 120

Coronary heart disease, 116, 120

Corpuscle, 121, 123

Curative, 121, 146

Cyanosis, 121, 127

Cytochrome, 121, 136

Cytokine, 14, 121

Cytoplasm, 57, 58, 59, 65, 66, 114, 121, 126,
132, 136, 143

Cytosine, 14, 58, 121, 141

D

De novo, 68, 121

Death Certificates, 77, 121

Deferoxamine, 41, 121

Degenerative, 121, 128

Dehydration, 16, 121

Deletion, 34, 70, 114, 121

Dementia, 72, 121

Demography, 6, 122

Denaturation, 122, 139

Deoxyribonucleic, 58, 122, 143

Deoxyribonucleic acid, 58, 122, 143

Deoxyribonucleotides, 122, 143

DES, 16, 122

Diabetes Mellitus, 122, 127

Diagnostic procedure, 54, 122

Digestion, 114, 122, 132, 145, 148

Diploid, 113, 122, 135, 138, 147

Direct, iii, 11, 22, 30, 87, 88, 89, 118, 122,
142

Discrimination, 90, 96, 122

Disorientation, 120, 122

E

Efficacy, 11, 23, 40, 122

Elastic, 23, 122, 140
 Electrocoagulation, 118, 122
 Electrolyte, 122, 131, 144
 Electrons, 113, 114, 122, 131, 136, 141
 Embryo, 67, 68, 69, 78, 112, 115, 117, 123, 129, 139
 Emollient, 123, 126
 Endemic, 123, 133, 145
 End-stage renal, 34, 123
 Environmental Health, 99, 100, 123
 Enzymatic, 34, 119, 123, 139
 Enzyme, 59, 65, 112, 123, 125, 134, 139, 140, 142, 143, 146, 149, 150
 Erythrocyte Membrane, 23, 123, 145
 Erythrocytes, 11, 16, 24, 31, 42, 48, 112, 113, 116, 123, 127, 128, 142
 Erythropoiesis, 13, 123
 Erythropoietin, 9, 14, 21, 23, 34, 35, 123
 Estrogen, 43, 123
 Estrogen receptor, 43, 123
 Ethnic Groups, 83, 86, 123
 Euchromatin, 12, 123
 Eukaryotic Cells, 123, 136
 Excitatory, 123, 126
 Excrete, 114, 123, 131
 Exhaustion, 123, 133
 Exogenous, 115, 124
 Extracellular, 120, 124, 144
 Extremity, 124, 131
 Eye Color, 69, 124
 Eye Infections, 110, 124
F
 Facial, 20, 124
 Family Planning, 100, 124
 Fat, 116, 120, 124, 132, 144
 Fathers, 78, 124
 Fatigue, 124, 127
 Ferritin, 15, 18, 47, 48, 65, 124
 Fetal Hemoglobin, 13, 14, 22, 27, 31, 32, 34, 124
 Fetus, 86, 87, 90, 94, 123, 124, 139, 145, 148
 Fibrosis, 36, 44, 69, 72, 77, 124, 143
 Folate, 18, 38, 124
 Folic Acid, 49, 124
 Forearm, 115, 124
 Frameshift, 70, 124
 Frameshift Mutation, 70, 124
G
 Gallbladder, 110, 117, 125
 Ganglia, 125, 135
 Gas, 116, 125, 129
 Gastric, 116, 125

Gastrin, 125, 129
 Gene Expression, 10, 11, 27, 35, 37, 65, 66, 125
 Gene Products, rev, 125
 Gene Silencing, 12, 125
 Gene Therapy, 10, 91, 92, 93, 94, 110, 125
 Genes, env, 76, 125
 Genetic testing, 80, 84, 85, 86, 87, 88, 89, 90, 91, 96, 125, 139
 Genomics, 96, 125
 Genotype, 28, 111, 126, 138
 Germ Cells, 68, 94, 126, 133, 144
 Germline mutation, 68, 126, 128
 Gland, 126, 132, 137, 143, 146
 Glucose, 115, 122, 126, 127
 Glutamate, 126
 Glutamic Acid, 8, 124, 126, 127, 135
 Glycerol, 33, 126
 Glycine, 112, 126, 135
 Gonad, 126
 Gonadal, 43, 126
 Governing Board, 126, 139
 Graft, 21, 111, 126
 Graft-versus-host disease, 21, 126
 Granule, 126, 143
 Granulocytes, 126, 131, 149
 Grasses, 124, 126
 Guanine, 58, 127, 141
H
 Hair Color, 69, 127
 Haplotypes, 20, 36, 127
 Heart attack, 116, 127
 Heart failure, 43, 47, 127
 Hematopoiesis, 28, 38, 127
 Hematopoietic Stem Cells, 11, 32, 127
 Hemochromatosis, 87, 104, 127
 Hemodialysis, 127, 131
 Hemoglobinopathies, 9, 106, 125, 127
 Hemolysis, 123, 128
 Hemolytic, 128, 142, 146
 Hemophilia, 78, 128
 Hemorrhage, 122, 128, 140, 145
 Hepatic, 27, 36, 128
 Hepatitis, 27, 36, 128
 Hepatocytes, 128
 Hereditary, 22, 27, 34, 57, 58, 68, 78, 84, 106, 126, 128, 142, 146
 Hereditary mutation, 68, 126, 128
 Heredity, 60, 125, 128
 Heterochromatin, 12, 123, 128
 Heterogeneity, 11, 25, 27, 111, 128
 Histiocytosis, 18, 128

Histones, 60, 117, 128
 Homologous, 111, 125, 128
 Homozygote, 33, 36, 129
 Hormone, 46, 65, 122, 123, 125, 129, 133, 146
 Hydrogen, 110, 114, 116, 122, 129, 134, 136, 146
 Hydrogen Peroxide, 129, 146
 Hydroxyurea, 10, 14, 29, 36, 129
 Hyperbilirubinemia, 129, 131
 Hypertension, 116, 129

I

Immune response, 113, 129, 133, 146, 149
 Immune system, 129, 132, 148, 149
 Immunologic, 20, 129
 Immunosuppressant, 111, 129, 134
 Impairment, 44, 114, 124, 129, 134
 Implantation, 120, 129
 In vitro, 11, 26, 37, 115, 125, 129, 139
 In vivo, 16, 26, 125, 129
 Induction, 13, 28, 129
 Infancy, 97, 129
 Infection, 24, 31, 36, 39, 115, 116, 124, 130, 132, 135, 137, 145, 149
 Inflammation, 93, 124, 128, 130, 139, 148
 Informed Consent, 87, 91, 96, 130
 Infusion, 130, 147
 Initiation, 130, 147
 Insulator, 36, 130
 Interferon, 27, 130
 Interferon-alpha, 27, 130
 Interphase, 128, 130
 Intracellular, 130, 133
 Intracellular Membranes, 130, 133
 Intrahepatic, 11, 130
 Intraperitoneal, 11, 130
 Intravenous, 48, 130
 Involuntary, 130, 135
 Ions, 114, 116, 122, 129, 130
 Iris, 124, 131

J

Jaundice, 3, 27, 129, 131

K

Karyotype, 62, 131
 Kb, 34, 131
 Kidney Failure, 72, 123, 131
 Kidney Failure, Acute, 131
 Kidney Failure, Chronic, 131
 Kinetic, 131

L

Lectin, 131, 133
 Leg Ulcer, 42, 131

Lesion, 131, 132
 Leucocyte, 111, 131
 Leukemia, 29, 106, 124, 125, 132
 Life Expectancy, 14, 132
 Ligament, 42, 132
 Linkage, 27, 36, 132
 Lipid, 126, 132
 Liver, 3, 11, 15, 36, 44, 66, 110, 114, 116, 118, 123, 124, 125, 127, 128, 130, 132, 134
 Localization, 15, 132
 Localized, 130, 132, 138
 Lymph, 42, 121, 132
 Lymph node, 42, 132
 Lymphatic, 130, 132, 145
 Lymphatic system, 132, 145
 Lymphocytes, 113, 132, 145, 149
 Lysine, 127, 128, 132

M

Macrophage, 68, 132
 Major Histocompatibility Complex, 127, 132
 Malaria, 20, 133
 Malaria, Falciparum, 133
 Malaria, Vivax, 133
 Malignant, 113, 128, 133
 Mammography, 77, 133
 Medical Records, 77, 90, 133
 MEDLINE, 100, 133
 Megaloblastic, 124, 133
 Meiosis, 67, 133
 Melanoma, 133, 148
 Membrane, 16, 18, 31, 58, 112, 119, 123, 133, 136, 142, 143, 145, 147
 Membrane Proteins, 16, 133
 Memory, 121, 133
 Mental, iv, 10, 19, 82, 84, 86, 99, 101, 117, 120, 121, 122, 124, 133, 134, 140, 143, 148
 Mental Retardation, 19, 82, 84, 86, 134
 Metabolic disorder, 106, 134
 Methotrexate, 21, 134
 Mice Minute Virus, 134, 137
 Microbe, 134, 147
 Microbiology, 114, 134
 Microorganism, 134, 149
 Migration, 25, 134
 Milk Thistle, 134, 143
 Miscarriage, 90, 134
 Mitochondria, 58, 59, 71, 78, 79, 134, 136
 Mitosis, 67, 114, 134
 Modification, 134, 141

Molecular, 8, 10, 12, 15, 16, 17, 27, 30, 31, 37, 62, 64, 66, 100, 102, 115, 119, 134, 144, 146
Molecule, 7, 58, 59, 60, 65, 113, 114, 119, 131, 134, 136, 141, 148
Monitor, 134, 136
Monoclonal, 19, 135, 141
Mononuclear, 41, 135
Monosomy, 71, 113, 135
Morphological, 123, 135
Mosaicism, 69, 135
Multicenter study, 15, 38, 135
Mutagens, 125, 135
Myocardium, 44, 135
Myotonic Dystrophy, 81, 105, 135, 147
N
NCI, 1, 98, 118, 135, 137
Necrosis, 114, 135
Neonatal, 27, 135
Nervous System, 81, 117, 135, 146
Neuropathy, 78, 135
Neurotransmitter, 110, 126, 135, 145
Neutropenia, 22, 135
Neutrophil, 21, 136
Nuclear, 58, 123, 125, 135, 136
Nuclear Envelope, 58, 136
Nuclear Pore, 136
Nuclei, 122, 125, 128, 134, 136
Nucleic acid, 114, 121, 135, 136, 141, 143
Nucleus, 58, 59, 60, 65, 71, 92, 94, 114, 117, 121, 123, 132, 133, 135, 136, 142, 145
Nurse Practitioners, 87, 136
O
Oliguria, 131, 136
Organelles, 57, 58, 121, 136, 138, 142
Osteoporosis, 22, 136
Ovaries, 86, 136, 143
Oxidation, 16, 110, 113, 115, 121, 127, 136
Oxidative Phosphorylation, 59, 60, 136
P
Palliative, 136, 146
Pancreas, 110, 127, 137
Pancreatic, 116, 137
Particle, 137, 147
Parvovirus, 24, 31, 134, 137
Paternity, 87, 137
Pathologic, 15, 114, 115, 120, 129, 137
Pathologic Processes, 114, 137
Pathophysiology, 17, 37, 137
Patient Compliance, 14, 137
PDQ, 98, 137
Pelvis, 110, 136, 137, 148

Penicillin, 137, 148
Peptide, 137, 139, 140
Peripheral blood, 41, 130, 137
Peripheral stem cells, 126, 137
Peritoneal, 130, 137
Peritoneal Cavity, 130, 137
Pharmacodynamics, 13, 138
Pharmacokinetic, 138
Pharmacologic, 13, 14, 138, 147
Phenotype, 26, 28, 29, 36, 138
Phenylbutyrate, 13, 14, 32, 138
Phosphorus, 138
Phosphorylation, 59, 138
Photocoagulation, 118, 138
Physical Examination, 14, 84, 138
Physiologic, 138, 141
Pigment, 111, 133, 138
Plants, 116, 126, 131, 138, 147
Plasma, 14, 33, 58, 113, 127, 131, 138
Plasticity, 127, 138
Plastids, 136, 138
Platelet Activation, 17, 138
Platelets, 138, 139
Pneumonia, 120, 139
Polymerase, 34, 139
Polymerase Chain Reaction, 34, 139
Polymorphism, 89, 139
Polypeptide, 112, 120, 124, 139, 146, 150
Polysaccharide, 113, 139
Postmenopausal, 136, 139
Postnatal, 139, 145
Practice Guidelines, 101, 139
Preclinical, 13, 139
Precursor, 123, 139, 148
Prenatal, 19, 20, 34, 86, 89, 90, 123, 139
Prenatal Diagnosis, 19, 20, 34, 139
Prevalence, 33, 46, 73, 139
Progeny, 11, 140
Progressive, 72, 117, 118, 121, 131, 135, 138, 140
Promoter, 12, 140
Prone, 72, 81, 140
Prophylaxis, 21, 140
Protease, 119, 140
Proteolytic, 111, 119, 140
Protocol, 93, 140
Protozoan, 133, 140
Pseudoxanthoma, 23, 140
Pseudoxanthoma Elasticum, 23, 140
Psychic, 134, 140
Puberty, 4, 46, 48, 140
Public Policy, 100, 140

Pulmonary, 33, 115, 131, 141, 149
 Pulmonary Artery, 115, 141, 149
 Pulmonary Edema, 131, 141
 Purines, 114, 141
 Pyrimidines, 114, 141

Q

Quality of Life, 15, 46, 141, 146

R

Race, 131, 134, 141
 Radiation, 110, 141, 148, 149
 Radiation therapy, 110, 141
 Radioactive, 129, 136, 141
 Randomized, 40, 49, 122, 141
 Reactivation, 12, 141
 Reagent, 16, 141
 Receptor, 24, 35, 75, 113, 141
 Recombinant, 14, 34, 93, 141, 148
 Recombination, 125, 142
 Rectum, 114, 119, 125, 142
 Red blood cells, 3, 7, 8, 16, 18, 123, 128, 142
 Reductase, 134, 142
 Refer, 1, 63, 67, 70, 74, 94, 111, 116, 119, 132, 142
 Refractory, 33, 122, 142
 Regeneration, 142
 Regimen, 122, 137, 142
 Reproductive cells, 71, 82, 83, 126, 128, 142
 Respiration, 116, 134, 142
 Reticulocyte Count, 21, 142
 Reticulocytes, 142
 Retina, 113, 140, 142
 Retinoblastoma, 74, 142
 Retrospective, 36, 142
 Retroviral vector, 11, 125, 143
 Ribonucleic acid, 65, 143
 Ribonucleoside Diphosphate Reductase, 129, 143
 Ribose, 110, 143
 Ribosome, 66, 143, 147

S

Scatter, 143, 148
 Schizophrenia, 78, 143
 Sclerosis, 74, 143
 Screening, 11, 18, 30, 31, 32, 77, 86, 87, 89, 104, 118, 137, 143
 Secretion, 46, 143, 148
 Senile, 136, 143
 Sequencing, 22, 30, 95, 139, 143
 Serum, 18, 21, 22, 35, 47, 48, 119, 131, 143
 Sex Characteristics, 110, 140, 143
 Side effect, 94, 97, 110, 143, 146, 147

Signs and Symptoms, 4, 80, 81, 86, 143
 Silymarin, 41, 134, 143
 Skeletal, 20, 23, 144
 Skeleton, 144
 Skull, 20, 144
 Small intestine, 129, 144, 149
 Social Environment, 141, 144
 Social Work, 83, 144
 Sodium, 13, 14, 32, 35, 144
 Soft tissue, 116, 144
 Solvent, 126, 144
 Soma, 144
 Somatic, 68, 71, 72, 83, 110, 133, 134, 144
 Somatic cells, 69, 71, 83, 133, 134, 144
 Somatic mutations, 72, 144
 Specialist, 87, 107, 144
 Species, 96, 111, 120, 131, 133, 134, 135, 137, 141, 144, 145, 147, 149
 Spectrin, 16, 144
 Sperm, 67, 68, 69, 71, 81, 82, 83, 86, 94, 117, 126, 128, 142, 144, 145
 Spinal cord, 117, 135, 145
 Spleen, 3, 35, 132, 145
 Splenectomy, 28, 30, 33, 49, 145
 Sporadic, 142, 145
 Stem Cells, 10, 123, 137, 145
 Stillbirth, 84, 145
 Stimulant, 145, 148
 Stomach, 110, 125, 129, 137, 144, 145
 Stool, 119, 145
 Strand, 30, 58, 139, 145
 Stress, 46, 145
 Stroke, 77, 99, 116, 145
 Subacute, 130, 145
 Subclinical, 130, 145
 Subcutaneous, 14, 41, 145
 Subspecies, 144, 145
 Superoxide, 36, 48, 146
 Superoxide Dismutase, 36, 48, 146
 Supplementation, 42, 48, 49, 146
 Supportive care, 137, 146
 Suppression, 125, 146
 Systemic, 33, 115, 130, 141, 146

T

Terminator, 118, 146
 Therapeutics, 13, 146
 Thermal, 139, 146
 Thrombin, 140, 146
 Thrombocytopenia, 29, 106, 146
 Thrombomodulin, 140, 146
 Thrombosis, 140, 145, 146
 Thyroid, 86, 146

Thyroid Gland, 86, 146
 Thyroid Hormones, 146
 Toxic, iv, 57, 111, 126, 135, 147
 Toxicity, 14, 15, 93, 147
 Toxicokinetics, 147
 Toxicology, 13, 100, 147
 Toxins, 113, 130, 147
 Trachea, 146, 147
 Transcription Factors, 66, 147
 Transduction, 10, 147
 Transfection, 115, 125, 147
 Transfusion, 14, 15, 25, 104, 147
 Translation, 65, 66, 125, 147
 Translational, 125, 147
 Transplantation, 20, 21, 131, 133, 147
 Trinucleotide Repeat Expansion, 81, 147
 Trinucleotide Repeats, 147
 Trisomy, 71, 113, 147
U
 Ultraviolet radiation, 69, 148
 Uremia, 131, 148
 Urethra, 148
 Urinary, 41, 136, 148
 Urine, 22, 114, 115, 131, 136, 148
 Uterus, 86, 136, 148
V
 Vaccine, 140, 148
 Vacuoles, 136, 148
 Vagina, 122, 148
 Valine, 8, 148
 Varicose, 131, 148
 Varicose Ulcer, 131, 148

Vascular, 130, 146, 148
 Vasculitis, 33, 148
 Vector, 11, 36, 92, 147, 148
 Vein, 130, 136, 148
 Venous, 131, 140, 148, 149
 Ventricle, 141, 149
 Ventricular, 29, 149
 Venules, 115, 149
 Veterinary Medicine, 100, 149
 Villi, 149
 Villous, 20, 149
 Viral, 11, 91, 125, 147, 149
 Viral vector, 11, 149
 Virulence, 147, 149
 Virus, 92, 130, 143, 147, 149
 Viscera, 144, 149
 Viscosity, 115, 149
 Vitro, 11, 86, 149
 Vivo, 16, 149
W
 White blood cell, 68, 113, 132, 135, 136, 149
 Windpipe, 146, 149
 Womb, 148, 149
X
 X-ray, 136, 141, 149
Y
 Yeasts, 138, 149
Z
 Zygote, 120, 135, 150
 Zymogen, 140, 150