RHEUMATIC FEVER

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

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

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

About the Editors

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Table of Contents

FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with rheumatic fever 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 rheumatic fever, 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 rheumatic fever, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on rheumatic fever. 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 rheumatic fever, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on rheumatic fever.

The Editors

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

CHAPTER 1. STUDIES ON RHEUMATIC FEVER

Overview

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

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and rheumatic fever, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "rheumatic fever" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **Rheumatic Fever: No Cause for Complacence**

  Source: Patient Care. 34(14): 40-42,45-46,53,57,61. July 30, 2000.

  Summary: This journal article provides health professionals with information on the epidemiology, clinical characteristics, diagnosis, treatment, and prevention of rheumatic fever. This inflammatory disorder of the connective tissue can affect the heart, joints, brain, and cutaneous and subcutaneous tissues. Cardiac damage is the only potentially chronic debilitating effect. Factors with a role in the etiology of this disease include socioeconomic status, environmental factors, and heredity. The epidemiology of rheumatic fever is linked to that of streptococcal pharyngitis because it occurs most frequently in the spring following the peak period of streptococcal pharyngitis. Clinical manifestations, which usually occur 1 to 3 weeks after the onset of pharyngitis, include arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. Diagnosis

is based on the presence of two major criteria or one major criteria and two minor criteria. Conclusive evidence of a preceding streptococcal infection must be present to confirm the diagnosis of rheumatic fever. Treatment consists of an intramuscular injection of 1.2 million U of long acting bezathine penicillin G. Aspirin should be started as soon as the diagnosis is suspected. Treatment lasts for 3 to 4 weeks, but when carditis is present, treatment may be required for 6 to 8 weeks. Corticosteroids are used primarily when severe carditis with congestive heart failure occurs. Rheumatic fever may recur with subsequent streptococcal infections, so penicillin may be administered. Sulfadiazine and erythromycin may be substituted when penicillin cannot be used. Sequelae include mild mitral insufficiency and aortic insufficiency. 3 figures, 3 tables, and 4 references.

Federally Funded Research on Rheumatic Fever

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

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

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

- **Project Title: CHARACTERIZATION OF MUCRS, A VIRULENCE REGULATOR IN GAS**

  Principal Investigator & Institution: Miller, Alita; Laboratory Animal Medicine; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, MI 481091274

  Timing: Fiscal Year 2001; Project Start 01-MAY-2000

  Summary: Streptococcus pyogenes (group A streptococcus or GA) is the causative agent of a number of human diseases, including pharyngitis, **rheumatic fever,** streptococcal toxic shock syndrome and necrotizing fasciitis. Our laboratory recently showed that mucRS is a negative regulatory of three importance virulence factor in GS. The aim of this proposal is to determine the molecular mechanisms involved in mucRS-mediated regulation of gene expression and how this relates in mucRS-mediated regulation of gene expression and how this relates to virulence in GAS. I will (i) characterize the mechanism(s) of repression of MucR, (ii) examine the role of phosphorylation of MucR, (iii) analyze the effect of MucS activity on MucR and (iv) determine the effect of a defined set of environmental conditions of MucRS activity.

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

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

- **Project Title: GROUP A STREPTOCOCCAL HYALURONATE LYASE**

  Principal Investigator & Institution: Ashbaugh, Cameron D.; Brigham and Women's Hospital 75 Francis Street Boston, MA 02115

  Timing: Fiscal Year 2001; Project Start 30-SEP-2001; Project End 29-SEP-2003

  Summary: (Verbatim from Applicant's Abstract): In the past two decades, there has been a resurgence of serious group A streptococcal (GAS) infections throughout the world. The clinical presentation of these infections has included both aggressive primary disease and the post-infectious syndrome of **rheumatic fever.** Acute invasive infections are characterized by invasion of the organism from superficial to deep foci, the frequent development of hemodynamic instability (streptococcal toxic-shock), and significant morbidity and mortality, often in previously healthy individuals. No single bacterial determinant appears to be uniquely associated with GAS virulence. Indeed, it is likely that the pathogenesis of GAS infection depends on the carefully regulated expression of a number of virulence factors. Because hyaluronic acid is an important component of human extracellular matrix, and because bacteria must negotiate the extracellular space during invasive infection, one long-standing candidate for a bacterial factor contributing to the pathogenesis of invasive GAS disease is hyaluronate lyase, an enzyme that depolymerizes hyaluronate. Although it was recognized many years ago that GAS can express hyaluronate lyase, the gene encoding the enzyme, the nature of its expression in GAS, and the demonstration of its role in virulence has not been established. Preliminary work in this laboratory has identified the chromosomal gene encoding the GAS hyaluronate lyase. The goals of this proposal are to characterize expression of the hyl gene in GAS strains representing prevalent serotypes recovered from invasive GAS disease and to determine the role of the hyl gene product in GAS virulence using several animal models that in sum capture the diverse clinical manifestations of serious human infection. The identification and characterization of novel GAS virulence determinants is a critical component in the continuing effort to understand and prevent GAS pathogenesis.

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

- **Project Title: KAWASAKI DISEASE: A LIVING HISTORY**

  Principal Investigator & Institution: Chin, Gregory; Kawasaki Disease Foundation 6 Beechwood Cir Boxford, MA 01921

  Timing: Fiscal Year 2003; Project Start 15-SEP-2003; Project End 14-SEP-2006

  Summary: (provided by applicant): Kawasaki disease (KD) is an acute, self-limited illness of infancy and early childhood that has now replaced **rheumatic fever** as the leading cause of acquired heart disease in children in the United States and Japan. Although the acute illness resolves spontaneously, permanent damage to the coronary arteries occurs in 20-25% of untreated children. The cause of KD remains unknown and there is no specific laboratory test to identify affected children. Nonetheless, an effective treatment exists that significantly reduces the risk of coronary artery damage. KD thus presents a unique dilemma: the disease may be difficult to recognize, there is no diagnostic laboratory test, there is an extremely effective therapy, and there is a 25% chance of serious cardiovascular damage or death if the therapy is not administered. This project will support the continued collaboration of an unusual multidisciplinary team with expertise in documentary film making, parent advocacy, pediatric medicine, anthropology, and the history of medicine to produce a web-based archive of interviews

and a television documentary to increase public awareness of KD and to support scholarly research on the origins of this emerging pediatric disease. Funds from this application will support three major interviewing sessions in Japan, Hawaii, and San Diego conducted under the auspices of the KD Foundation. (www.kdfoundation.org). The film will focus on 1) the importance of informed parents in establishing the timely diagnosis of KD, which permits effective treatment and prevention of complications and 2) the history of KD, showing that the ways in which it emerged as an internationally recognized disease mirror the ways in which it is now diagnosed or mis-diagnosed in our contemporary health care system. In the case of KD, informed parent advocacy can mean the difference between life and death for an affected child.

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

- **Project Title: MECHANISMS OF STREPTOCOCCAL/HOST INTERACTION**

  Principal Investigator & Institution: Zabriskie, John; Rockefeller University New York, NY 100216399

  Timing: Fiscal Year 2001

  Summary: We have now completed our studies on the nature of the nephritogenic protein using the sera and renal biopsies from patients with acute post streptococcal glomerulonephritis (APSGN). All nephritogenic strains produce a protein called nephritis plasmin binding protein (NPBP) which was isolated, sequenced and found to be identical with streptococcal proteinase or streptococcal pyrogenic exotoxin B (SPEB). Using antibodies prepared against recombinant SPEB, 65% of 20 APSGN biopsies were found to contain the antigen in the glomerulus while only 4% of 25 non APSGN biopsies were positive. None of the biopsies were positive for streptokinase, another streptococcal antigen possibly associated with APSGN. APSGN sera reacted preferentially with this antigen when compared to sera from patients with either **rheumatic fever** or uncomplicated streptococcal infections and normal controls. Furthermore, serial serum studies of APSGN patients revealed that while the titers decreased over one year they never returned to baseline values suggesting a possible protective effect against the known fact that recurrences of APSGN are extremely rare. A manuscript detailing these findings has been submitted to Kidney International. Studies involving the **rheumatic fever** marker D8/17 have proceeded along two areas of investigation. The first is concerned with the predictive role of the marker for disease susceptibility. Approximately 3,000 children ages 5-10 years who come from high risk areas of **rheumatic fever** in Mexico City have been tested for the marker. Seven percent of these unaffected children are positive for the marker. All children are being followed over time for the appearance of **rheumatic fever.** If our hypothesis is correct, only those positive for the D8/17 marker will be susceptible. The second area of investigation of the marker was unexpected. In collaboration with a group from Child Psychiatry at NIH under the direction of Dr. Sue Swedo, we have examined the presence or absence of this marker in a group of 23 children (and appropriate controls) with obsessive-compulsive disorders (OCD). In a double blind test the marker correctly identified ninety percent of the OCD patients compared to the expected 7% controls. In view of the known cross-reactions between streptococcal antigens and caudate nucleus cells, these studies suggest that other brain-streptococcal cross reactive antigens may be involved in the OCD syndrome. A manuscript detailing these findings has been sent to the J. Child Psychaitry. Our more basic approach to the exact nature of the D8/17 antigen and caudate binding antigen in the sera of Sydenham's chorea are being pursued along two main lines of investigation. Concerning the D8/17 antigen our main problem in identifying this antigen has been the fact that the antibody is the IgM class. Thus non-

specific binding of other proteins has resulted in identification of a number of bands. Secondly, this antibody does recognize other antigens expressing a coil-coiled structure. We have recently isolated a IgG clone of the D8/17 antibody and hope this will have the same specificity as the IgM molecule. We are also using the chemiluminescence technique (quite sensitive) to further identify the putative antigen. Concerning the Sydenham's caudate antigen we are screening sera from these patients both on a cDNA library of human caudate as well as immunoblots of human and mouse caudate specimens. In this respect we have identified two bands of 82 and 66 Kda that appear promising.

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

- **Project Title: MYOSIN--A LINK BETWEEN STREPTOCOCCI AND HEART**

  Principal Investigator & Institution: Cunningham, Madeleine W. Professor; Microbiology and Immunology; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, OK 73126

  Timing: Fiscal Year 2001; Project Start 01-AUG-1989; Project End 29-FEB-2004

  Summary: Rheumatic fever is a sequela of group A streptococcal infection primarily in children. Manifestations of the disease include carditis, arthritis and chorea. Our hypothesis is that autoimmune mechanisms due to molecular mimicry between the group A streptococcus and human tissues are responsible for the disease. Our data support this hypothesis. We have identified host and streptococcal antigens which react with anti-strep/heart antibodies and T cells, and we have identified streptococcal and human cardiac myosin epitopes which produce carditis and valvulitis in animal models of disease. Despite our progress, we do not know how these crossreactive autoantibodies function in the pathogenesis of acute rheumatic fever(ARF) or the exact nature and antigenic specificities of the T cells in rheumatic carditis. Therefore, the goal and objectives propose to answer questions about the potential role of antibody in disease and to investigate the nature of the T cells which are crossreactive and appear to be responsible for valvulitis. The objectives are 1) to produce a panel of cytotoxic/crossreactive monoclonal antibodies (mAbs) from humans and transgenic mice and passively transfer IgM and IgG mAbs to test for tissue deposition in vivo; 2) to determine the nucleotide sequences of crossreactive antibody V, D, and J region genes; 3) to produce transgenic mice containing the VDJ genes(H and L) of human and mouse crossreactive and/or cytotoxic mAbs; 4) to investigate the Lewis rat model of valvulitis by producing and characterizing T cell clones from rats immunized with rM6 protein and cardiac myosin and in passive transfer experiments determine if these T cells produce disease; 5) to compare valves immunohistochemically from rheumatic carditis and Lewis rat valvulitis to identify similarities. These studies will attempt to define the steps in the pathogenesis of rheumatic carditis and will continue to support the growing body of evidence that infectious agents play a role in the development of autoimmunity in man.

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

- **Project Title: PACIFIC CENTER FOR EMERGING INFECTIOUS DISEASES RESEARCH**

  Principal Investigator & Institution: Yanagihara, Richard T. Pediatrics; University of Hawaii at Manoa 2500 Campus Rd Honolulu, HI 96822

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

Summary: (provided by applicant): In response to a regional resurgence of infectious diseases and consistent with a high-priority institutional initiative to establish the Asia-Pacific Institute for Tropical Medicine and Infectious Diseases, this application proposes to develop the Pacific Center for Emerging Infectious Diseases Research at the University of Hawai'i at Manoa. By drawing on the complementary strengths and expertise within the John A. Burns School of Medicine, the Pacific Biomedical Research Center, and the Cancer Research Center of Hawai'i, as well as the State of Hawai'i Department of Health, the new Center will be anchored by the tenets of trans-disciplinary research. Projects will be linked by a unifying research focus on the molecular epidemiology and pathogenesis of infectious diseases, which are of local and regional relevance and which disproportionately affect under-served ethnic minority communities in Hawai'i and the Asia-Pacific region. Specifically, studies will be conducted on the natural history of human papillomavirus infection in heterosexual men, the immunopathogenesis of dengue fever, and the molecular epidemiology and adhesion properties on group A streptococci in relation to high-incidence acute **rheumatic fever** in Hawai'i. Newfound knowledge from these research projects will provide improved strategies for prevention and control of these regionally important infectious diseases. The overall objectives of the proposed Center will be achieved by the following specific aims: 1. Build institutional capacity by mentoring a cadre of promising young faculty to conduct research on infectious diseases of medical importance to the Asia-Pacific region. 2. Improve research competitiveness by enhancing the capacity for mentoring and expanding the capability of the technical support infrastructure. 3. Diversify the research breadth and trans-disciplinary scope of the Center through targeted recruitment and retention of funded faculty with complementary expertise and through centralization of laboratory space and research-support operations.

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

- **Project Title: PATHOGENESIS KAWASAKI DISEASE**

  Principal Investigator & Institution: Rowley, Anne H. Pediatrics; Northwestern University Office of Sponsored Programs Chicago, IL 60611

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

  Summary: Kawasaki Disease (KD) is an acute, potentially fatal vasculitis of young children which predominately affects the coronary arteries. KD affects children of all nations and ethnic groups, and has replaced acute **rheumatic fever** as the most common cause of acquired heart disease in children in the U.S. and Japan. At Children's Memorial Hospital in Chicago alone, 65 new acute KD cases were diagnosed in 1998. Despite the fact that KD has become a significant pediatric problem in the U.S. the etiology and pathogenesis remain undefined. Our long-term objective is to determine the pathogenesis of KD. The overall goal of this proposal is to investigate the role of IgA and IgA plasma cells in the development of KD vasculitis. Recent studies from our laboratory indicate that IgA1 plasma cells infiltrate the vascular wall in acute KD. Preliminary data indicate that IgA genes in the vascular wall in acute KD are oligoclonal, suggesting that the IgA response in KD is directed toward specific antigens, either those of the potential pathogen(s) causing the illness, or host antigens by a molecular mimicry mechanism. Preliminary data also indicate that IgA plasma cells are present in markedly increased numbers in the respiratory and GI tracts of KD patients when compared with age-matched controls. Other preliminary data indicate that serum IgA1 in acute KD sera is aberrently glycosylated and therefore is likely to have altered properties. Our hypothesis is that KD is an immune-mediated vasculitis triggered by a

mucosal pathogen, and that IgA plays a prominent role in pathogenesis. We propose to determine whether an oligoclonal IgA response is characteristic of KD. We will also determine glycosylation profiles of IgA l in KD sera. We will determine the distribution of IgA plasma cells in KD tissues using our established tissue repository of acute fatal KD cases. We will also characterize glycosylation profiles of IgA in the infiltrating plasma cells and determine whether these plasma cells produce matrix metalloproteinases (MMPs), matrix-degrading enzymes that participate in abdominal aortic aneurysm formation and that are produced by plasma cells in inflammatory diseases. These studies will elucidate the role of IgA and IgA plasma cells in the pathogenesis of KD, and will have important implications for potential diagnostic and treatment strategies for this increasingly recognized, potentially fatal childhood illness.

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

- **Project Title: STREP THROAT, SYDENHAM CHOREA, AND TOURETTE SYNDROME**

  Principal Investigator & Institution: Mcmahon, William M. Associate Professor; Psychiatry; University of Utah 200 S University St Salt Lake City, UT 84112

  Timing: Fiscal Year 2001; Project Start 01-MAR-2000; Project End 28-FEB-2005

  Summary: This abstract is not available.

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

- **Project Title: SYNTHESIS/ ACTIVITY OF N-AMINOTETRAHYDROPYRIDINES**

  Principal Investigator & Institution: Redda, Kinfe Ken. Professor of Medicinal Chemistry; Florida Agricultural and Mechanical Univ Tallahassee, FL 32307

  Timing: Fiscal Year 2001; Project Start 05-JUN-2000; Project End 30-APR-2005

  Summary: The primary objective is the design, synthesis and pharmacological evaluation of novel and medicinally important N-amino-1,2,3,6- tetrahydropyridine derivatives. We reported the synthesis of novel N- iminopyridium ylides using the method employed by Tamura and modified in our laboratory. Sodium borohydride reduction of the ylides afforded the stable N-amino-1, 2,3,6-tetrahydropyridines in good yields. We also recently reported preliminary pharmacological test results of a few tetrahydropyridines that exhibited analgesic and anti-inflammatory activities with no observed toxicity, even at very high dose levels. Our earlier work provides the basis for new and exciting studies so that a series of compounds related to the most active analogs could be prepared, and retested and the octanol-water partition coefficient determined. Once sufficient data are accumulated, the compounds prepared will be subjected to structure activity analysis to study the electronic, steric and lipophilic effects of substituents. The physical and pharmacologic data obtained in this study will then be used to design drugs with more beneficial biological activity. The primary focus of the pharmacological studies will be to develop and easily synthesize effective and safe non- steroidal anti-inflammatory agents for the treatment of rheumatic diseases, including rheumatoid arthritis, osteoarthritis, gout and **rheumatic fever.**

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

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "rheumatic fever" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for rheumatic fever in the PubMed Central database:

- **Association of rheumatic fever with serum albumin concentration and body iron stores in Bangladeshi children: case-control study.** by Zaman MM, Yoshiike N, Rouf MA, Haque S, Chowdhury AH, Nakayama T, Tanaka H. 1998 Nov 7; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=28708
- **Characterization of Two Novel Pyrogenic Toxin Superantigens Made by an Acute Rheumatic Fever Clone of Streptococcus pyogenes Associated with Multiple Disease Outbreaks.** by Smoot LM, McCormick JK, Smoot JC, Hoe NP, Strickland I, Cole RL, Barbian KD, Earhart CA, Ohlendorf DH, Veasy LG, Hill HR, Leung DY, Schlievert PM, Musser JM. 2002 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=133074
- **Genome sequence and comparative microarray analysis of serotype M18 group A Streptococcus strains associated with acute rheumatic fever outbreaks.** by Smoot JC, Barbian KD, Van Gompel JJ, Smoot LM, Chaussee MS, Sylva GL, Sturdevant DE, Ricklefs SM, Porcella SF, Parkins LD, Beres SB, Campbell DS, Smith TM, Zhang Q, Kapur V, Daly JA, Veasy LG, Musser JM. 2002 Apr 2; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=123705
- **Molecular Analysis of Group A Streptococcus Type emm18 Isolates Temporally Associated with Acute Rheumatic Fever Outbreaks in Salt Lake City, Utah.** by Smoot JC, Korgenski EK, Daly JA, Veasy LG, Musser JM. 2002 May; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=130927
- **Reactivity of Rheumatic Fever and Scarlet Fever Patients' Sera with Group A Streptococcal M Protein, Cardiac Myosin, and Cardiac Tropomyosin: a Retrospective Study.** by Jones KF, Whitehead SS, Cunningham MW, Fischetti VA. 2000 Dec; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=external&artid=97825
- **Repertoire of transcribed peripheral blood T-cell receptor beta chain variable-region genes in acute rheumatic fever.** by Abbott WG, Skinner MA, Voss L, Lennon D, Tan PL, Fraser JD, Simpson IJ, Ameratunga R, Geursen A. 1996 Jul; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&rendertype=abstract&artid=174152

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

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

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

- **Rheumatic fever --associated Streptococcus pyogenes isolates aggregate collagen.** by Dinkla K, Rohde M, Jansen WT, Kaplan EL, Chhatwal GS, Talay SR. 2003 Jun 15; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=161421

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[6] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

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

- **A 45-year perspective on the streptococcus and rheumatic fever: the Edward H. Kass Lecture in infectious disease history.**
  Author(s): Denny FW Jr.
  Source: Clinical Infectious Diseases : an Official Publication of the Infectious Diseases Society of America. 1994 December; 19(6): 1110-22.
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