Yale University EliScholar – A Digital Platform for Scholarly Publishing at Yale

Yale Medicine Thesis Digital Library

School of Medicine

1974

Rheumatic fever in Connecticut, 1968-1972

Harry Alan Magnes Yale University

Follow this and additional works at: http://elischolar.library.yale.edu/ymtdl

Recommended Citation

Magnes, Harry Alan, "Rheumatic fever in Connecticut, 1968-1972" (1974). Yale Medicine Thesis Digital Library. 2889. http://elischolar.library.yale.edu/ymtdl/2889

This Open Access Thesis is brought to you for free and open access by the School of Medicine at EliScholar – A Digital Platform for Scholarly Publishing at Yale. It has been accepted for inclusion in Yale Medicine Thesis Digital Library by an authorized administrator of EliScholar – A Digital Platform for Scholarly Publishing at Yale. For more information, please contact elischolar@yale.edu.

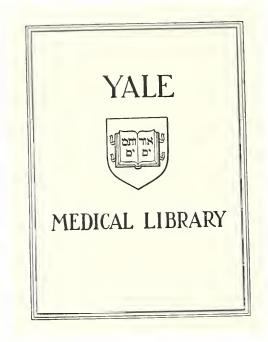


RHEUMATIC FEVER IN CONNECTICUT 1968 - 1972

15

HARRY ALAN MAGNES







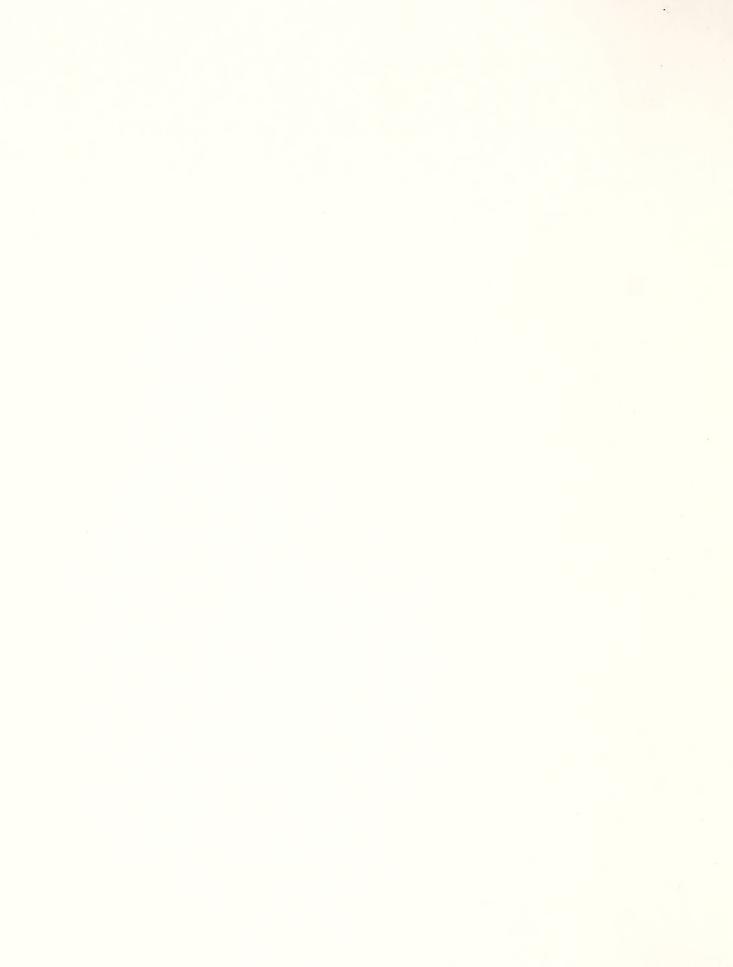




Digitized by the Internet Archive in 2017 with funding from The National Endowment for the Humanities and the Arcadia Fund



https://archive.org/details/rheumaticfeverin00magn



RHEUMATIC FEVER IN CONNECTICUT 1968 – 1972

HARRY ALAN MAGNES A.B., BROWN UNIVERSITY, 1970

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF MEDICINE

YALE UNIVERSITY SCHOOL OF MEDICINE

инеиматіс FEVER ін соммсстісчт 1968–1972

HARRY ALAM MAGNES A.B., BROWN UNIVERSITY, 1970

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE IF

3010103M RD R0T300

YALE UNIVERSITY SCHOOL OF WEDTENE

DEDICATION

TO MY PARENTS

NJITAJICH

TO MY PARENTS

TU ROZ

ACKNOWLEDGEMENTS

I wish to express my appreciation to:

- Dr. Ruth Whittemore, my advisor, who gave so openly of her time and resources, and whose support made this project both stimulating and gratifying.
- Dr. Milton Markowitz, for guidance and suggestions, and for sharing his vast experience in the field of rheumatic fever.
- The Rheumatic Fever Committee of the Connecticut Heart Association, for sponsoring this research, and for their enthusiasm and encouragement during the past six months.
- Mrs. Susan Kabakoff, for her assistance and encouragement.
- Mrs. Amelia Ramunno, Mrs. Florence Levy, and the entire staff of the Connecticut Heart Association state office, for their interest and support, and for revealing the intricacies of the Rheumatic Fever Registry to me.
- All the Medical Librarians throughout the state, for their patience, guidance, and technical assistance, and without whom this research could never have been completed.

To all of you I extend my deepest gratitude.

Introduction 1						
Materials and Methods 8						
The Coding Form 11						
Results and Comparisons 2						
Incidence 23						
Sex 30						
Race						
Age 31						
Month of Admission 34						
Length of Hospitalization 35						
Jones Criteria 36						
Supporting Evidence of Preceding Streptococcal Infection 46						
Diagnostic Validity 51						
Primary Prevention of Rheumatic Fever 54						
RHD on Discharge 59						
Secondary Prophylaxis of Rheumatic Fever - 61						
Connecticut Heart Association Rheumatic Fever Registry 66						
Discussion and Recommendations						
Summary						
Appendix						
References						



A B B R E V I A T I O N S U S E D

RF - rheumatic fever

ARF - acute rheumatic fever

RHD - rheumatic heart disease

ESR - erythrocyte sedimentation rate

CRP - C-reactive protein

ASO - anti-streptolysin O

RF → ようねについたう。 (人気化 → 作ないていてんね()(10) 主点 (* 2000) (日外江 → まりはんごうたい。 (2000) * 20 (* 2000) (日外江 → まりはんごうたい。 (2000) * 2000) * 2000 (日外二 → 成下人)(日、2000) * 2000) * 2000) * 2000

ACG - andirettarticities - CCA

INTRODUCTION

Rheumatic fever is unique among the major causes of cardiovascular disease in that it is the only one that is clearly preventable. Although the exact etiology is still in question, the undeniable association between rheumatic fever and a preceding streptococcal pharyngitis forms the basis for both primary and secondary prevention programs. To adequately treat a patient with pharyngitis proven due to group A beta-hemolytic streptococci is to reduce the likelihood of that patient's becoming a victim of RF; and by placing a patient with a well-documented attack of RF on continuous penicillin prophylaxis we can minimize the likelihood of his having further infections with streptococci and therefore reduce the chance of recurrent bouts of RF.

It is reported that, during the past 40 years, the epidemiology of RF has undergone significant changes in economically developed countries such as the U.S. Most observers believe that acute rheumatic fever is less frequent than before. (Markowitz, 1972)

Unfortunately we have reached the point where interest in RF in this country is diminishing more rapidly than the incidence of the disease. This complacency has developed from a false sense of security and achievement based on the delusion that even without additional effort, penicillin will lead us into the promised land of RF obsolescence. The unfor-

tunate byproduct of this attitude is that lack of interest and support on the part of many agencies endangers efforts to find new preventive methods and to improve and continue existing prophylaxis programs. (Markowitz, 1970)

Many physicians hold the view that RF no longer remains a significant public health problem and report that they see little or no RF in their practices. A further indication of the decreasing emphasis on RF was observed in 1967 when the Michigan State Medical Society closed its three RF centers and discontinued its RF control program. (Parker, 1969)

Here in Connecticut, the decline in interest in RF is exemplified by the loss of enthusiasm in several areas of the state for long-standing prophylaxis programs run by the Connecticut Heart Association, and can be underscored by quoting from an article appearing in <u>The Hartford Courant</u> on July 4, 1973, entitled "Rheumatic Fever Cases Expected to Set Record:" (RF is a reportable disease in Connecticut.)

A record number of rheumatic fever cases in Connecticut appears likely this year, With half the year gone, the count so far equals the highest 12-month count since the state Health Department began keeping track of cases in 1965. An Enfield elementary school student became the state's 10th case last week. There were 10 cases in 1970 and only 3 during 1972,

Belief in the accuracy of the number of reported cases in Connecticut might certainly lend strength to the argument that RF is, indeed, a conquered disease and that little effort need further be expended upon its prevention.

However, many clinicians in Connecticut both private

-2-

the second se

and hospital affiliated, had personally observed more than 3 cases of RF in 1972 in their own practices or hospital services. That a degree of underreporting existed was certain, but no one knew what the true incidence in the state was. Estimates, speculation, and debate were offered in many forums, each based on projections from local statistics, and each with varying techniques of data collection and with different criteria for diagnosis.

PURPOSE

This study was then undertaken to accurately assess the extent and clinical picture of RF in Connecticut. It was felt that accurate estimates of statewide incidence would serve many purposes, such as indicating the magnitude of the problem among the different populations at risk, identifying the regions where the problem is greatest, and providing grounds for approximating how much time, money, and effort needs to be directed toward preventive and remedial work on the problem of rheumatic fever.

EARLY PLANNING

It was realized early in the planning phase of our study that no single source of data could provide an accurate picture of the extent of RF in Connecticut.

<u>Rheumatic fever registry</u>: Many states, Connecticut included, have established registries of RF patients who receive prophylactic medication. The data from such registries are often used as the basis for gauging the incidence of RF

-3-

by counting the number of new cases entered annually in the registry. However, underreporting is a major problem. An additional problem is that most registries do not provide a method for verifying whether the cases meet the Jones Criteria. As a result, registries often include a significant number of incorrectly diagnosed cases. In view of the inaccuracies inherent in any registry system, we decided to avoid using the RF registry as our basis for estimating incidence. Instead, we compared the names of the patients on file at the registry with those we had obtained as hospitalized cases of ARF, and could then judge the degree of underreporting to the registry.

Underestimation: Sources depending upon a physician or medical institution to remember and report each case generally miss a significant proportion of the true cases in the community. The degree of underascertainment depends in some measure on the incentive for reporting. But even the best methods of ascertainment will miss those cases which do not come to medical attention. This is particularly significant in a disease such as ARF in which the case fatality rate is low, the clinical picture is variable with many mild cases, and the frequency of the disease is highest among the poor whose medical services are often extremely limited in availability and accessibility. Nothing short of a prospective study of a very large group of people can give more than a gross estimate of those cases of RF which never reach medical attention. Therefore, those cases were excluded from our

- 4 -

study whose medical care, if present, did not discover this diagnosis, and in whom treatment was therefore denied.

As for those patients who do reach medical attention, we chose for the present to deal solely with hospital admissions, and to leave for a later study those cases not hospitalized and treated as outpatients. In this way, we avoided any reliance on memory of cases, hoped to find reasonably accurate and complete records for most patients, and might then be able to give a quite accurate incidence figure for hospitalized cases.

<u>Population</u>: The populations from which cases come is often highly selected or imprecisely defined. If, for example, one looks at the number of cases of RF admitted to a single hospital, it is frequently not clear whether the hospital served a defined population, and, if so, whether the cases arising in the population might not have been admitted to other hospitals. Moreover, admissions to a single hospital are poor indications of the frequency of the disease in the general population, since they reflect the local admission policies and the changing interests of the medical staff.

Furthermore, defined populations such as insured individuals, college students, or soldiers are highly selected on the basis of medical, ethnic, and socioeconomic factors, and therefore may not be representative of the population at risk for RF. For these reasons, our population was taken to be the entire state of Connecticut, and our incidence

-- 5 --

.

2

figures were derived from RF admissions to all hospitals in the state.

<u>Validation</u>: Many sources accept the diagnosis of RF as given and have no mechanism for verifying the diagnosis. This can lead to a serious problem, since the diagnosis is on the basis of the Jones diagnostic criteria and physicians vary in their use of these guidelines. The fact that not all true cases fit the Criteria further contributes to the problem. (Okuni, 1971) In our study, each chart was reviewed and information gathered with regard to many parameters. In this way, the diagnosis could be verified and an estimate of validity given for the state.

<u>Comparison</u>: This study is neither the first nor the last to attempt to evaluate the incidence and clinical picture of ARF by using retrospective hospital chart review. Wherever possible, our results have been compared with those of similar studies reported in the past 15 years,

When reference is made to one of these studies (shown in figure 1), it will be by name of the author and date of publication. Dates during which the study was performed, age and geographic restrictions, and total number of cases in question will not be repeated in each reference. In all cases, undefined percentages refer to a number of cases out of the total in the study. (For example, when referring to Tahernia, 1971, the percentage 35% refers to 35% of the total 100 admissions, or 35 admissions, unless otherwise stated.)

-6-

Figure	1:	A Selected List of Retrospective Studies of Rheumatic
		Fever Against Which the Data from the Present Study
		can be Compared,

AUTHOR	YEARS OF Study	ADMISSIONS	AGES	REGION OR HOSPITAL UNDER STUDY
Goldring 1968	1956-1965	195	5-15	St. Louis Children's Hospital
Feinstein 1962a	1958-1960	275	5-15	* Irvington House
McCue 1970	1965-1968	142	pediatric ward	Medical College of Virginia Hospital
Brownell 1973	1963-1965	298	5-14	Lower East Side of Manhattan, N.Y.C.
Gordis 1969	1960-1964	270	5-19	Baltimore, Maryland
Hall 1961	1930 - 1954	1434	all	Malmo, Sweden
Saslaw 1962	1955-1958	83	all	greater Miami, Florida
Mayer 1963	1935-1958	792	pediatric ward	Bellevue Hospital, N.Y.C.
Sitaj 1970	1969	277	all	region in Czechoslovakia
Saksena 1969	1969	60	all	region in India
Tahernia 1971	1958-1969	100	all	region in southern Iran

* Irvington House is a regional referral hospital for the acute care and convalescence of children with rheumatic fever.

MATERIALS AND METHODS

From the <u>Journal of the American Hospital Association</u>, August 1, 1971 (45 (II):46-48), a list of all 67 hospitals in the state of Connecticut was obtained. By eliminating from this list all convalescence homes, Federal penal or military institutions, and psychiatric hospitals, we constructed a list of the 38 acute medical care hospitals in the state which were likely to represent the great majority of RF admissions (see figure 2).

A letter was drafted and sent to both the chief administrator and the chief medical librarian at each hospital (see Appendix) to acquaint them with our study, assure them of the confidentiality of any data we might obtain, stress the importance of the undertaking and the backing of the Connecticut Heart Assocation, and request their assistance and permission in reviewing all the charts in their hospital 1967-1972 with the diagnosis of acute rheumatic fever on discharge.

Approximately one week after the mailing of the letters to the hospitals (the letters were sent out in groups of 10-15), the author personally called the chief medical librarian at each institution to confirm receipt of the letter, answer any questions, and, when possible, confirm a date upon which the charts might be reviewed. It was asked that all charts with ARF as either primary or ancillary discharge diagnosis be pulled for inspection. For the majority of the hospitals

using the HICD (Hospital International Classification of Diseases), this corresponded to categories 390 (ARF without carditis), 391 (ARF with carditis), and 392 (Sydenham's chorea). The categories before modification of the HICD in 1969 were 400. 401, and 402 respectively.

As necessary, further phone calls were made to each hospital until a firm appointment for chart review could be made.

The author then personally travelled to each of the 38 hospitals in the study and reviewed the charts of all admissions for ARF from 1967-1972, using the coding form described below (see Appendix). All available data were recorded as found in the chart, except in the case of obvious inconsistencies (e.g. If the discharge summary stated that the highest ASO during the hospitalization was 500, yet there were two laboratory slips for that patient and during that hospitalization which gave values of 625, the value of 625 would have been recorded as the highest ASO during the hospitalization,)

Only hospitalizations for the acute phase of an attack were included in our study. Charts were excluded for three main reasons. Admissions for convalescence directly following discharge or a few days thereafter were excluded by comparing names and birth dates of all admissions. Also, in several charts, the discharge diagnosis did not match the coding by HICD. The majority of these were patients admitted with pericarditis, rheumatic heart disease, or a totally unrelated

··· 9 ···

•

cause, who were erroneously cataloged as 390 or 391. Finally, some admissions gave firm discharge diagnoses followed by a list of "rule-outs" which had been satisfactorily ruled out (e.g. discharge diagnosis--gouty arthritis, R/O rheumatoid arthritis, R/O ARF, R/O systemic lupus erythematosis). In this case, when it was clearly not intended to imply that ARF was one of the discharge diagnoses, the chart was excluded.

In 1955, the Connecticut Heart Association established a registry to facilitate the distribution of low-cost penicillin to RF patients for continuous prophylaxis against recurrent attacks. Currently, under agreement between the Connecticut Heart Association and the Connecticut Pharmaceutical Association, pharmacists in the state sell penicillin at low cost to persons who are registered by their physicians as having had RF. There are no age or income limits on eligibility. (Spinelli, 1961)

Following the completion of chart reviews at all 38 hospitals, the author reviewed the files of the Connecticut Rheumatic Fever Registry, for the years 1967-1972 in an effort to find how many patients known to have been admitted to hospitals in the state during that period, managed to be registered with the Heart Association, and how many were still on the active registry.

After all data was collected, it was found that there were several gaps, with a few hospitals unable to provide data on the earliest years under study. It was decided to

.

cut the time under study to the five-year period 1968-1972 to avoid the majority of the discontinuities in our information. It must, however, be noted that in addition to the unknown and hopefully small number of charts which should be included in the study but, by omission, were not pulled from the hospital records, two institutions were unable to provide any information for the year 1968: McCook Hospital and Norwalk Hospital. The former's charts are apparently in storage with the State of Connecticut and unavailable, and the latter never centrally classified their admissions with regard to discharge diagnosis prior to 1969. These two lapses hopefully only account for a handful of charts and introduce no more than a 1-2% error in any of our data.

Upon completion of data collection, all information was punched onto 80-column IBM cards, a program for analysis of the data was written in the language DATATEXT, and the program was run at the Yale University Computing Center,

THE CODING FORM

In order to facilitate computerized analysis of our data, a coding form (see Appendix) was devised which would lend itself to easy transferral of data to 80-column IBM punch cards. In general, the code 1 was defined as an unqualified positive response, 2 as an unqualified negative response, 8 as the presence of equivocal or questionable information, and 9 as the lack of sufficient information to further categorize.

The heading of the coding sheet included spaces for the

*** 1 1 ***

.

hospital name, date of the data collection, name, address, and birthdate of the patient, and dates of admission and discharge,

The body of the coding form began with <u>study number</u>, a 5-digit number uniquely identifying each patient. The first two digits represented a hospital code O1 to 38 and the fourth and fifth digits represented a patient code O1 to 99 assigned in order as charts were reviewed at each hospital. The third or middle digit was used for recording instances of multiple admissions of the same patient for ARF during the period of study. For a patient's first admission, the digit was O, for his second admission, or first readmission, the digit became 1, and so forth. When the data was transferred to punched cards, these 5 digits, as well as all further information on the coding form, were simply transferred to the first five columns of the card. (e.g. O1025 indicates the identifying number of the 25th patient reviewed at hospital O1, which was his first admission for ARF for the period under study.)

Column 6 was used for the question <u>Was the chart available?</u> the answer to which was universally yes. The coding was 1 for yes and 2 for no.

Column 7 identified the patient with respect to <u>race and</u> <u>sex</u>; 1-white male, 2-white female, 3-black male, 4-black female,

Columns 8 and 9 were used for the patient's <u>age on admis</u>-

Columns 10 and 11 were used for the month of admission, 01-January to 12-December.

m12m



Column 12 was used for the last digit of the <u>vear of</u> admission; 7-1967, 8-1968, 9-1969, 0-1970, 1-1971, 2-1972,

Colums 13-15 were used for the <u>number of days of hospit</u>-<u>alization</u>. In the cases in which a patient was discharged to a convalescent home, the length of hospitalization was taken to be the total length of the acute hospitalization, ending with transferral to the convalescent home. In the event of a recrudescence, defined in our study as rebound or reappearance of symptoms after total suppression by treatment and within 2 months of discharge, the total length of hospitalization was the sum of the initial and the recrudescent admissions, and the two were combined with regard to clinical manifestations. (e.g. A diagnosis of carditis during either the initial or readmission was sufficient to classify the patient as having carditis.)

Columns 16-22 were used for the patient's chart number,

Column 23 was used for <u>disposition</u>; 1-discharge home, 2-convalescent home or hospital, 3-died, 4-other, 9-no information.

Column 24 was used for <u>carditis</u>; 1-yes, or present, 2-no, or absent, 8-questionable, 9-no information. In cases in which the diagnosis of carditis was made in the chart a "yes" was coded unless the diagnosis was admitted in the chart to rest solely on the basis of a prolonged P-R interval on ECG, in which case, in the absence of other findings, murmur, rub,

•

or x-ray changes, the patient was coded as "no." In instances in which no mention of carditis was found, a minimal criterion for "yes" was a 2/6 systolic murmur heard at the apex and radiating to the axilla. When a "murmur" or "systolic murmur" was mentioned as an important finding with no further information, the patient was placed in the "yes" category. Questionable categorization was used mainly for charts in which the question of carditis was openly raised during hospitalization, often with several consultations and differing opinions.

Column 25 was used for <u>migratory polyarthritis</u>; 1-yes, unable to qualify further, 2-no, 3-one joint by history alone with no signs on examination, 4-more than one joint by history alone, 5-one joint <u>with</u> evidence on examination, 6-more than one joint <u>with</u> evidence on examination, 8-questionable, 9-no information. Information in this category was usually sufficient to place the patient in one of the well defined categories 3 through 6.

Columns 26, 27, and 28 were used for the remaining three major Jones criteria, respectively, <u>chorea</u>, <u>erythema marginatum</u>, and <u>subcutaneous nodules</u>. Each was scored exactly the same as column 24 and exactly as columns 29-34 with 1-yes, or present, 2-no, or absent, 8-questionable, 9-no information. The information in these areas was sparse on many charts. "Normal neurological" was allowed as sufficient evidence against chorea, and "skin-normal" as satisfactory evidence

-14-

.

against erythema marginatum and subcutaneous nodules. Although these are less frequent manifestations than either carditis or arthritis, it is difficult to measure the degree of underdiagnosis. In cases in which the history sounded suspicious but not certain (i.e. "a rash 4 days prior to admission") the petient was placed in the questionable category.

Column 29 was used for <u>fever</u>, as evidenced by any single reading greater than or equal to 100.4° F. (38° C.), This information was obtained most commonly from the temperature charts when they were available.

Column 30 was used for <u>arthralgia</u>, and was coded as present even in the presence of polyarthritis, as attempts were being made to depict the true clinical picture of the average RF patient in Connecticut. Arthralgia is eliminated as a minor criterion when polyarthritis is used as a major criterion, and this was considered in our evaluation of the Jones criteria.

Column 31 was used for <u>prior rheumatic heart disease</u>, coded as "yes" only in the event of a statement to the affirmative, with or without substantiating murmur. The descriptions of murmurs were far too imprecise to allow a retrospective decision on RHD.

Column 32 was used for <u>prolonged P-R interval on ECG</u>, and was coded as positive or negative if so mentioned by the



physician reading the ECG, or as positive if greater than 0,22 seconds. The region 0.20 to 0,22 seconds was scored as questionable without further mention in the chart.

Column 33 was used for <u>elevated white blood count</u>, greater than or equal to 12,000 per cubic millimeter on at least one occasion,

Column 34 was used for <u>recent scarlet fever</u>, and was scored as present only when such mention was found in the chart and within 2 months prior to admission.

Column 35 was used for <u>acute phase reactants</u>, or erythrocyte sedimentation rate, and C-reactive protein. The coding was 1-both ESR and CRP done, ESR elevated, CRP normal; 2-both ESR and CRP done, ESR normal, CRP positive; 3-both ESR and CRP done, both positive; 4-both ESR and CRP done, neither positive; 5-ESR only done, and elevated; 6-CRP only done, and positive; 7-ESR only done, and normal; 8-questionable or contradictory results; 9-no information. The CRP was regarded as positive if any reading other than "negative" was obtained ("trace", "1mm", or any other reading was regarded a positive). ESR was regarded as positive depending on the hospital's level of normal. In general, ESR's over 20 mm/hour (Wintrobe) were considered elevate.

Column 36 was used for <u>previous rheumatic fever</u>; 2-no 3-yes, by history alone, 4-yes, by history and hospitalization, 8-questionable, 9-no information. "History alone" was coded

- 10.7

-

-

and a second second

in cases in which the patient claimed to have had RF diagnosed by a physician, but was at most bedridden for a period. "Yes, by history and hospitalization" was coded when either the patient had a documaneted hospitalization for RF, or claimed to have been hospitalized for RF, and is thus a more certain category for previous RF.

Column 37 was used for <u>throat culture on admission</u> and was coded for the first throat cultures taken after admission (within 72 hours after admission and before inpatient antibiotics were begun); 1-positive for group A beta-hemolytic streptococci; 2-negative for group A beta-hemolytic streptococci; 3-not done; 7-negative for streptococci, but after the patient had been taking antibiotics prior to admission.

Column 38 was used for the <u>highest ASO in the hospital</u>, and corresponds to the highest ASO during the admission,; O-less than or equal to 50 Todd Units; 1-100 Todd Units; 2-125; 3-166; 4-250; 5-333; 6-500; 7-625; 8-greater than or equal to 833 Todd Units; 9-no information; X-not done. The ASO levels were coded as the closest level when they fell between coding points (150 was coded as 166). "No information" indicated that the test was ordered or mentioned, but that no results can be found in the chart. "Not done" indicates that there is no mention of the test and no order for it.

Columns 39-42 were used to deal with the question of preceding streptococcal pharyngitis.

-17-



Column 39 dealt with the question, "<u>Did the patient</u> <u>have a preceding upper respiratory infection?</u>" 2-no; 3-yes, but no further information was available; 4-yes, and he was seen by a physician; 5-yes, but he was not seen by a physician; 8-questionable; 9-no information. The answer to this and the following 3 questions was based on a combination of information from the chart (progress notes, discharge summary, and nurses'notes).

Column 40 was used for the <u>physician's diagnosis of</u> <u>the preceding respiratory infection</u>, and was only applicable for those patients who admitted in column 39 to having had such an infection; 1-a throat culture was taken and was positive for group A beta-hemolytic streptococci; 2-a throat culture was taken but was negative for group A beta-hemolytic streptococci; 3-no culture was taken, but the clinical appearance was that of streptococci; 4-no culture was taken, and the clinical appearance was <u>not</u> that of streptococci; 7-not applicable, a category including all patients who denied a prior respiratory infection and those who had a prior infection but were not seen by a physician; 8-questionable; 9-insufficient information.

Column 41 was used for the <u>physician's treatment of the</u> <u>preceding streptococcal pharyngitis</u>; O-no treatment was given; 1-treatment was given, but we do not know any further details; 2-treated with antibiotics, but for less than ten days (stopped either by the patient or on the basis of medical

-18-

•

advice); 3-antibiotics were prescribed for 10 days, but were <u>not</u> taken; 4-antibiotics were prescribed for 10 days but we do not know whether they were taken; 5-antibiotics were prescribed for 10 days and <u>were</u> taken; 6-antibiotics were given intramuscularly; 7-not applicable, including all patients denying preceding respiratory infection and those not seen by a doctor; 8-questionable; 9-no information.

Column 42 was used to show <u>where the patient was seen</u> <u>for his respiratory infection</u>; 1-personal or private physician; 2-outpatient department or emergency room of the hospital to which the patient was ultimately admitted for ARF; 3-outpatient department or emergency room of a hospital other than the one to which the patient was ultimately admitted for ARF; 4-other, usually treatment as a patient in a hospital for an unrelated complaint; 7-not applicable; 8-questionable; 9-no information.

Column 43 dealt with the question, "<u>Did the admission</u> <u>satisfy the modified Jones Criteria?</u>" with 2-no; 3-yes, with 2 major criteria; 4-yes, with 1 major and 2 minor criteria; 5-yes with Sydenham's chorea but less than 2 minor criteria; 8-questionable; 9-no information. For this question, the acceptable major manifestations were carditis, polyarthritis, chorea, erythema marginatum, and subcutaneous nodules. The acceptable minor criteria were fever, arthralgia (if not using polyarthritis as a major criterion), previous RF or rheumatic heart disease, positive acute phase

-19-

•

reaction (elevated ESR or positive CRP or elevated WBC), and prolonged P-R interval on ECG. It was not required that a patient have supporting evidence of a preceding streptococcal infection for fulfilling the Jones Criteria, as this was handled separately.

Column 44 was used for <u>attack number</u>; 1-first attack of RF; 2-second attack of RF; 3-third or greater attack; 4-recurrence unable to be more accurately categorized; 8-questionable; 9-insufficient information for an answer.

Column 45 dealt with the question, "<u>If this admission is</u> <u>a recurrence, was the patient on prophylaxis at the time of</u> <u>his admission?</u>" with 1-yes, the patient had prophylactic medication prescribed and claimed to be taking it regularly; 2yes, the patient had prophylactic medication prescribed, but admitted to occasional omissions; 3-yes the patient had prophylactic medication prescribed, but we do not know whether or not he was taking it regularly; 4-no, the patient did not have prophylactic medication prescribed; 7-not applicable; 8-questionable; 9-insufficient information.

Column 46 was used to indicate whether the patient had <u>rheumatic heart disease on discharge</u>; 1-yes; 2-no; 7-not applicable, due to the death of the patient; 8-contradictory evidence precludes a reasonable decision; 9insufficient evidence. Again, in this question, the word of the chart was taken above all, unless the evidence upon

which the diagnosis was based was stated and was clearly incorrect (e.g. "RHD on discharge diagnosed by a 2/6 systolic murmur heard at the apex.").

Column 47 was used for the <u>discharge diagnosis by HICD</u>; 1-390, ARF without carditis (400 before 1969); 2-391, ARF with carditis (401 before 1969); 3-392, Sydenham's Chorea (402 before 1969), 4-393-398 (410-416) chronic RHD; 6-other; 7-not coded by HICD, for those hospitals using other systems; 8questionable; 9-no information.

Column 48 was used for <u>discharge diagnosis</u>, 1-acute rheumatic fever, 2-question of rheumatic fever, 3-history of rheumatic fever, 4-question of history of rheumatic fever, 5-not rheumatic fever, 6-other, 8-questionable, 9-no information.

Column 49 was used to indicate whether the patient was ever <u>reported to the Connecticut Heart Association Rheumatic</u> <u>Fever Registry</u> when applying for the penicillin prophylaxis program. 1-yes, 2-no, 7-not applicable, due to the death of the patient, 8-questionable, 9-no information. These data were obtained by cross-checking the name of each patient registered with the list of names of patients hospitalized, and may contain inaccuracies due to the incorrect transcription of names or changes in names after admission to the hospital and prior to registration.

Column 50 was used to indicate the number of days from

admission to the hospital for ARF until registration with the <u>RF registry</u>; 1-less than one month; 2-one to six months; 3-six months to one year; 4-more than one year; 7-not applicable; 8-questionable; 9-no information.

Column 51 was used to indicate whether the patient was <u>currently on the active registry with the Connecticut Heart</u> <u>Association</u>, 1-yes, 2-no, 7-not applicable, 8-questionable, 9-no information.

RESULTS AND COMPARISONS

INCIDENCE

The extent of an illness such as acute rheumatic fever is better measured in terms of morbidity than mortality, because the case fatality rate, the number of people dying from RF among those who have the disease, is very low. The most frequently used morbidity indices are incidence (the number of new cases in a population during a specified time period) and prevalence (the number of persons with the disease in a specified population at a point in time.) (Markowitz, 1972)

Has there been any change in the incidence of ARF over the past decades? Unfortunately, good comparative data from different periods of time in the same population are very difficult to obtain. In different periods, varying methods of ascertainment and validation of cases are used by investigators. In addition, as a result of population shifts, studies of the same geographical area at separate time periods frequently compare dissimilar populations.

In spite of these drawbacks, a decline in the incidence of ARF during the recent past has been shown by several authors. However, reliable figures on the size of the decline are difficult to find and the uncertainties of such estimates are obvious.

In 1962, Stamler in Chicago estimated the incidence of

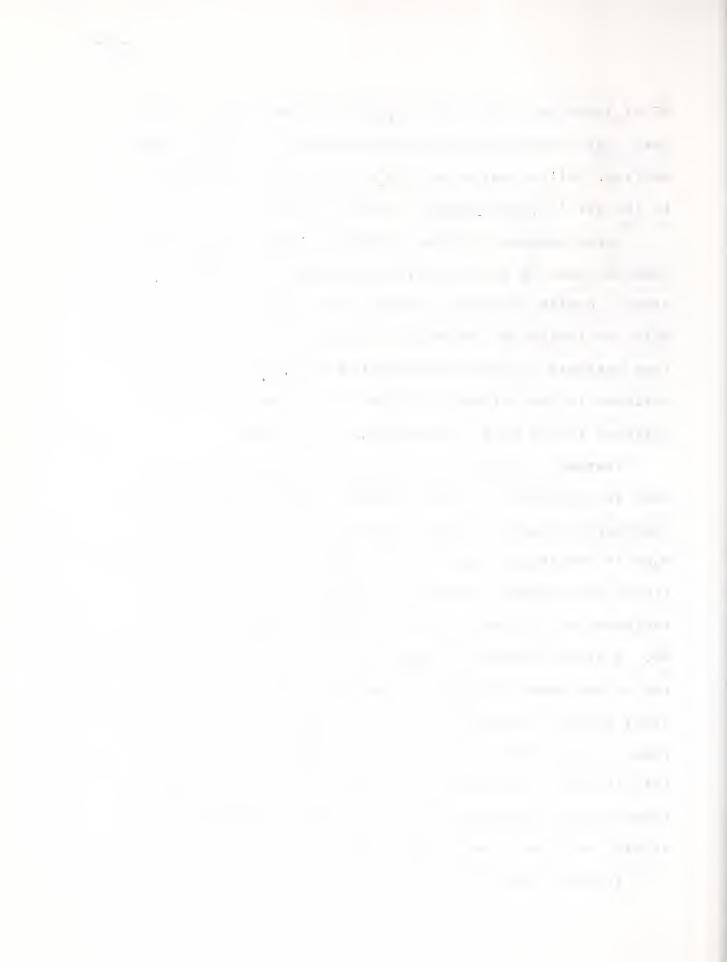
-23-

RF as 35-45 new cases per 100,000 children ages 5-15 per year, using combined data from six surveys. Twenty years earlier, Collins estimated the Chicago attack rate as 100 to 120 per 100,000 children. (McCue, 1970)

Circumstances in Malmo, Sweden, a city with a single hospital serving a well-defined population completely covered by health insurance, render this town uniquely suitable for incidence estimates. Incidence figures of hospitalized patients in Malmo declined from 34 cases per 100,000 children in the period 1930-1934 to 21 cases per 100,000 children in the period 1950-1954. (Hall, 1961)

However, the decline in reported frequency of RF as well as mortality from this disease (Quinn, 1970) does not necessarily imply a massive reduction in its prevalence. Much of the change could be attributed to diminishing severity of the disease. Necropsy analyses have reported an incidence of rheumatic valvular disease varying between 1 and 6%. A study between the years 1941 and 1955 reported this as the actual cause of death in less than 50%. This 15 year study showed no reduction in the overall incidence at necropsy, though the clinical severity showed a decline from 1941 to 1955. This suggests that subclinical and atypical forms of the disease may exist in larger numbers than previously realized. (Besterman, 1970)

In our study of hospitalized cases of ARF in the state



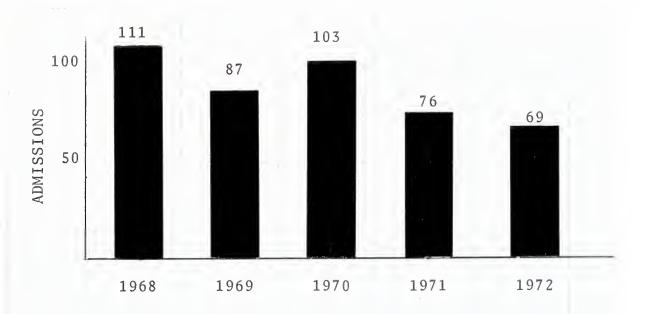


Figure 2: Hospital Admissions for Acute Rheumatic Fever in

Connecticut by Years, 1968-1972

of Connecticut for the period 1968-1972 we obtained data on 446 attacks, an average of 89 attacks per year. These admissions are broken down by years according to figure 2. There seems to be a declining trend even during the five years under study, with 111 cases in 1968 and only 69 cases in 1972. This decrease becomes even more significant when we remember that the majority of the gaps in our data, and hence the greatest degree ofunderestimation, occurred in the first year of our study. We would thus expect an even higher number of cases in 1968 were we able to obtain information on all of them.

The overall incidence figure for Connecticut over the entire 5-year period 1968-1972 (taking the total population

-25-



1 110.71



,

as 3,000,000, the actual value in 1970, the midpoint of our study) is 3.0 admissions for ARF per 100,000 total population per year. When broken down on an annual basis, using accurate population estimates for each year, we obtain a decrease from an incidence of 3.6 per 100,000 in 1968 to 2.2 per 100,000 in 1972. In any event, it is clear that there were many more cases of rheumatic fever than the 10 reported during 1970 and the 3 during 1972.

When comparing these data with other studies, we find that our incidence figures are considerably lower than almost any other with the exception of the study done in greater Miami, Florida, 1955-1958, which also reported an incidence of 3 hospitalizations per 100,000 total population. (Saslaw, 1962) The Baltimore City Study, using techniques quite similar to our own, found 15.6 admissions per year for the period 1960-1964 per 100,000 population ages 5-19 (Gordis, 1969a). Quinn studied the incidence in Nashville, Tennessee from 1963 to 1965 and reported an incidence of 12.6 per 100,000 total population (Quinn, 1967), and the incidence in the Lower East Side of Manhattan, N.Y.C. was reported, in a study from 1963-1965 to be 61 per 100,000 population ages 5-14. (Brownell, 1973)

We can explain some of the difference by the fact that all of the studies with the exception of that performed in Miami and our own dealt with a highly populated metropolitan area.

-26-



Crowding and demographic factors present in cities are known to increase the incidence of RF in a population, so perhaps we might review our data with an eye to an urban-rural differentiation. (Gordis, 1969b), (Stollerman, 1961)

If we break down the state of Connecticut into cities with populations over 85,000 and communities under 85,000, we find that 272 of the total 446 admissions occurred in cities of greater than 85,000 (New Haven, Bridgeport, Stamford, Hartford, Waterbury, New Britain), but that these cities make up only about one fourth of the state's population. This gives us a city incidence figure (averaged over the 5 years of 7.1 per year per 100,000 urban population and a noncity incidence figure of 1.5 admissions per year per 100,000 non-urban population.

In judging whether the incidence of ARF in Connecticut has changed over the past several decades, we can compare the present study with one done from 1934-1938 by the Connecticut State Department of Health (Paul and Deutch, 1941) and find that the incidence at that time was calculated to be 62 hospitalizations per year per 100,000 total population. Unfortunately, these admissions were not screened, but were obtained by questionnaire from the hospitals. It is also of interest to compare the number of admissions to each hospital 1968-1972 (figure 3) with those of 1934-1938. We find that in the earlier 5-year span, there were 1001 total ad-

Figure 3: Total Admissions for Acute Rheumatic Fever by Hospital, 1968-1972

	AI	(446) DMISSIONS	% OF TOTAL
2. 3.	Bridgeport Hospital, Bridgeport Park City Hospital, Bridgeport St. Vincent's Hospital, Bridgeport	34 11 11	7.6 2.5 2.5
5.	Bristol Hospital, Bristol Danbury Hospital, Danbury	6 20	1.4
	Griffin Hospital, Derby Greenwich Hospital, Greenwich	11 12	2.5
8.	Hartford Hospital, Hartford	35	7.9
	Mount Sinai Hospital, Hartford St. Francis Hospital, Hartford	9 25	2.0
	University of Connecticut Hospital,		
1.0	McCook Division, Hartford	8 er 6	1.8
	Manchester Memorial Hospital, Manchester Meriden-Wallingford Hospital, Meriden	9	2.0
	World War II Veterans' Memorial	<i>co</i> g	A 9
15	Hospital, Meriden Middlesex Memorial Hospital, Middletown	3 n 22	0.7 5.0
16.	Milford Hospital, Milford	2	0.5
17.	New Britain General Hospital, New Britain	28	6.3
18.	Hospital of St. Raphael, New Haven	8	1.8
	Yale-New Haven Hospital, New Haven	25	5.6
20.	Lawrence and Memorial Hospitals, New London	9	2.0
	New Milford Hospital, New Milford	4	0.9
	Newington Children's Hospital, Newington Norwalk Hospital, Norwalk	on 2 10	0.5 2.2
24.	William W. Backus Hospital, Norwich	7	1.6
	Day Kimball Hospital, Putnam Rockville General Hospital, Rockville	23 1	5.2 0.2
27.	Sharon Hospital, Sharon	4	0.9
	Bradley Memorial Hospital, Southington Cyril and Julia Johnson Memorial	1	0.2
<i>49</i> *	Hospital, Stafford Springs	1	0.2
	St. Joseph's Hospital, Stamford	10	2.2
	Stamford Hospital, Stamford Charlotte Hungerford Hospital,	13	2.9
	Torrington	4	0.9
33. 34	St. Mary's Hospital, Waterbury Waterbury Hospital, Waterbury	31 24	7.0 5.4
	Windham Community Memorial Hospital,		
76	Willimantic Winsted Memorial Hospital Winsted	$10 \\ 3$	2.2 0.7
	Winsted Memorial Hospital, Winsted Veterans Administration Hospital,	5	U o /
	West Haven	1	0.2
38.	Veterans Administration Hospital, Newington	3	0.7



missions as compared with 446 in the present study. Granted the methodologies were different, the population has changed in Connecticut (1.6 million in 1935, 3.1 million in 1972), and the diagnostic criteria for RF have been altered several times; nevertheless, the feeling remains that the incidence of ARF in the state has been declining and continues to decline.

A final correction factor that we may want to add to our incidence figures would be an estimate of the per cent of non-hospitalized cases. This is an area in which we have undertaken no direct investigation; however, several studies in the literature estimate that about 60% of all cases of ARF are hospitalized.

In Pennsylvania, a questionnaire was sent to every physician in the state and then a personal interview was conducted with a random sample of non-responders. This yielded the information that 50-75% of all cases of RF reported were hospitalized. (Spector, 1968) In Baltimore, 700 practicing physicians were surveyed to estimate the proportion of RF patients who wer treated as outpatients, and it was found that 64% were hospitalized. (Gordis, 1969a) In greater Miami, it was found that, of 83 patients studied, 51, or 61% were hospitalized. (Saslaw, 1962) Thus, if we use 60% as a correction factor, for our presumed non-hospitalized cases in Connecticut, we calculate an average of 150 total cases per year, or an incidence of 5.0 per year per 100,000 population.

-29-

	(IIgules III pare	entheses represent	o of cotal admissions
	Male	Female	Total Race
White	187 (42)	170 (38)	357 (80)
Black	39 (9)	50 (11)	89 (20)
Total Sex	226 (51)	220 (49)	446 (100)

Figure 4: Total Admissions by Race and Sex (figures in parentheses represent % of total admissions)

READMISSIONS

The 446 admissions studied represented 431 patients, 11 of whom were admitted twice during the period of study, and 2 who were admitted on three separate occasions during the study. SEX - see figure 4

We found a roughly equal number of males and females admitted in the study, 226/446 (51%) males and 220/446 (49%) females. Although it has been stated that RF is more common among girls, available data do not show such sex differences. Males and females have been found to be nearly equal in studies done in Manhattan by Brownell, 1973 (51% males, 49% females), in Bellevue by Mayer, 1963 (50% males, 50% females), in St. Louis by Gcldring, 1968 (51% males, 49% females), in Missouri by Allen, 1965 (50% males, 50% females), and by Hall in Malmo, Sweden, 1961.

RACE - see figure 4

We found a 4 to 1 ratio of Whites to Blacks in our study group with 357/446 (80%) of the admissions Whites and

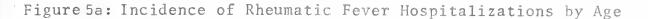


89/446 (20%) of the admissions Blacks. It has long been suggested that RF occurs more commonly in certain ethnic groups. Earlier in this century, the Irish were considered particularly prone to the disease and Blacks less susceptible. (Markowitz, 1972) However, no studies of racial liability have ever been properly controlled with respect to cultural and religious practices, housing, and the other environmental variables which are closely correlated with racial genotype and many of which are also correlated with incidence of RF. It is impossible to say what part, if any, ethnic origin per se plays in the epidemiology of the disease. (Acheson, 1965).

Reports of Black to White ratios from 2 to 1 (Quinn, 1967) to 2.5 to 1 (Gordis, 1969a) to 6 to 5 (McCue, 1970) abound in the literature; few are corrected for population distribution in the area under study and none have been able to provide any explanation or hypothesis on the basis of race. <u>AGE</u> - see figures 5a and 5b

Although ARF is accepted as a disease of childhood and adolescence, it is not sufficiently appreciated that attacks may occur in adults right up to the fourth, fifth, and even sixth decade. (Wee, 1966) For this reason, it was decided not to confine our study to children 5-15 or 5-19 as is often done.

ARF is uncommon in children under 5 years of age and very rare under 2, (Rosenthal, 1968), (Waly, 1971) In our



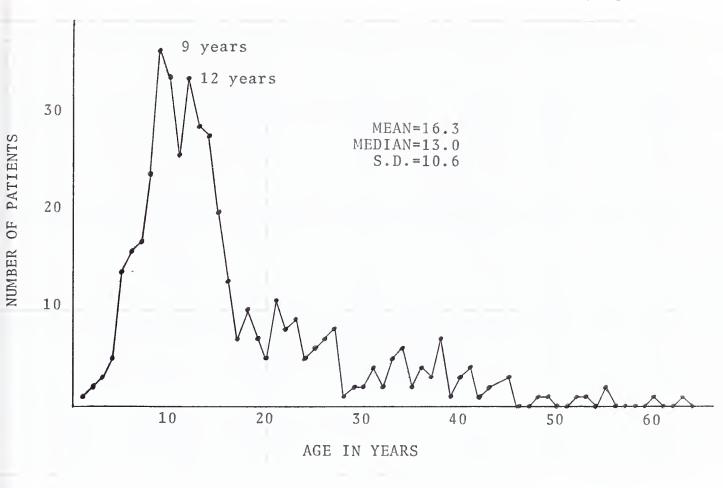
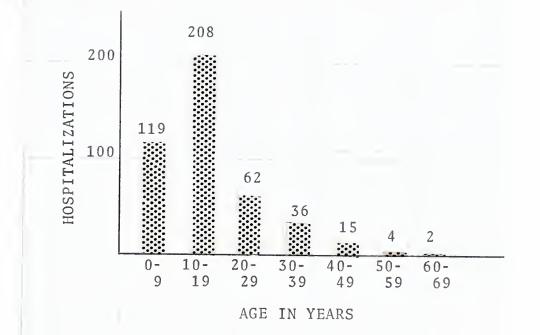


Figure 5b: Incidence of Rheumatic Fever Hospitalizations by Age Group



sure Sas Incidence of Rheymotic Rever Hechitelingtions by Ang

rigure Mat Incidence of Rheumatic Fever Hospitalizations by Age Grou

study, we found only one admission under 2 years of age and 11/446 (2.5%) under the age of 5. Hedley (1940) reported that 0.7% of 2324 patients had their initial attack under 2 years of age and 8.4% under the age of 5.

The incidence of initial attacks of RF decreases after puberty, probably because exposure to streptococci decreases during adult life. However, RF is still seen in young adults and it has been shown that susceptibility to RF remains relatively high until at least 22 year of age. (Markowitz, 1972)

We found 27% of our admissions ages 0-9 (119/446) as compared with 25% (Sievers, 1971), 23% (Saslaw, 1962), and 11% (Hall, 1961).

Forty-eight per cent of our admissions (208/446) were among the 10-19 group as compared with 23% (Sievers, 1971), 23% (Hall, 1961), and 49% (Saslaw, 1962).

In the group over 20 years of age we found 25% (119/446) of our admissions as compared with 28% (Saslaw, 1962), 22% (Allen, 1965), 18% (Gordis, 1969a), and 52% (Sievers, 1971).

Our oldest patient with ARF was 63. The peak age (mode) was 9 years, agreeing with peaks of 10 years (McCue, 1970), 11 years (Tahernia, 1971), and 10-14 (Quinn, 1967). However, our mean age of 16.3 years is a bit higher than the wellknown values of 10-12 years and can probably be explained by the fact that our curve was skewed by the number of patients .

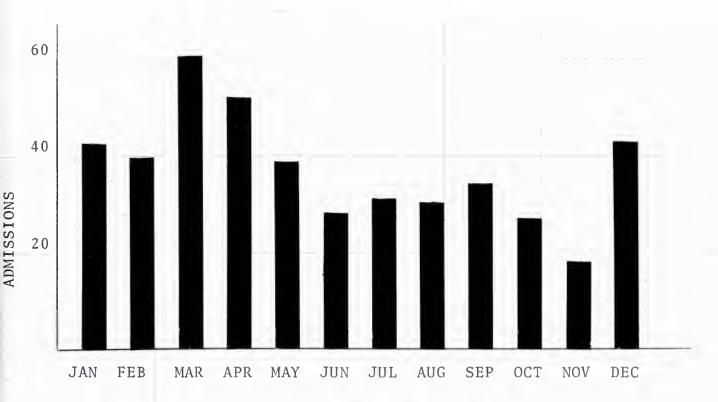


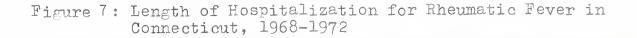
Figure 6: Incidence of Rheumatic Fever Admissions by Month (composite of all admissions 1968-1972)

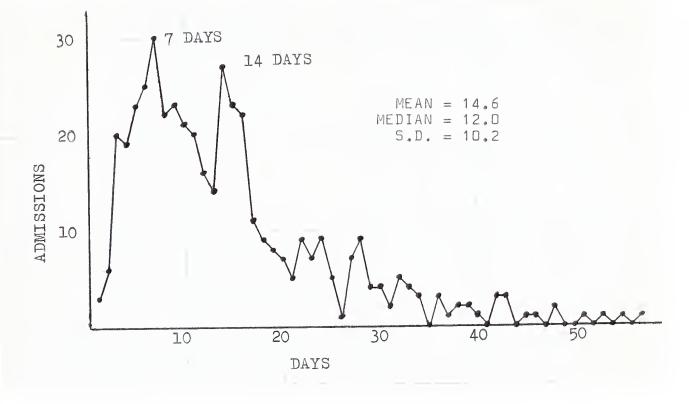
over 20 included in our survey who would not have been included in any studies of RF in children. Thus, if we calculate the mean for only our 5-25 year old admissions, we obtain 12.6, more in line with other reports.

MONTH OF ADMISSION - see figure 6

The definite seasonal incidence of RF varies in different localities. On the west coast of the U.S., it peaks in January and February, on the east coast, in March and April. In general, the seasonal variation of RF follows that of streptococcal pharyngitis. (Markowitz, 1972)







Our admissions, combined for the 5-year period under consideration, showed the expected peak in March and April, with 25% of the total admissions (113/446) occurring in those months, and following the characteristic pattern for the northeastern U.S. LENGTH OF HOSPITALIZATION - see figure 7

The average length of hospitalization for ARF in Connecticut, 1968-1972 was 14.6 days. The graph has peaks at both one and two weeks. The shortest admissions were 3 patients hospitalized for only 1 day; the longest was one patient hospitalized for 57 days. Thirty-seven patients (8%) were dis-



charged only after a month.

The duration of hospitalization in the era prior to anti-inflammatory treatment revealed 20% remaining less than 2 months, 30% remaining 2 to 4 months, and a full 50% remaining longer than 6 months (these hospitalization figures include convalescence). (Baum, 1963)

DISPOSITION

The overwhelming majority of the admissions in our study terminated with discharge of the patient to his home, 97.5% (435/446). Four of our patients, 0.9% (4/446) were discharged to convalescent homes or to other hospitals for convalescence; 1.4% (6/446) were discharged to other institutions (penal institutions, schools), and only 1 patient out of the 446 died of ARF during the years of the study. The death rate from ARF has been continually declining, partially due to a decrease in incidence and partially due to a decrease in severity of the disease.

In 1900, the estimated death rate per 100,000 population was 20 (Goldring, 1968). By 1920, the estimate had dropped in half to 10 per 100,000 (McCue, 1970). And in the early 1960's, accounts ran as low as 0.4 per 100,000 (McCue, 1970 and Goldring, 1968). The number of deaths in our study is too low to allow extrapolation for a mortality rate, but it seems to be in the expected range.

JONES CRITERIA - see figure 8

"The renowned clinical criteria, formulated in 1944 by

Figure 8: Jones Criteria Profile of All Admissions in Connecticut 1968-1972 Diagnosed as Rheumatic Fever**

MANIFESTATION	EVIDE	NT WITH NCE OF ESTATION	QUE	ABER WITH ESTIONABLE IDENCE	DUE	ABER OMITTED TO LACK INFORMATION
MAJOR Carditis	25.1	(112/446)	17	(3,8%)	0	
Polyarthritis .	87,2	(389/446)	1	(0,2%)	0	
Chorea	4,4	(18/405)	2	(0,5%)	41	(9.1%)
Erythema Marginatum	8,9	(35/395)	4	(1,0%)	51	(11.4%)
Subcutaneous Nodules	3.0	(12/395)	۵		51	(11.4%)
MINOR CLINICAL Fever (over 100.4 F)	70.5	(313/444)	0		2	(0,5%)
Arthralgia	93,1	(415/446)	0		0	
Previous Rheuma-						
tic Heart Dis- ease	6.3	(28/446)	5	(1,1%)	0	
Previous Rheuma- tic Fever	15,5	(69/446)	8	(1.8%)	0	
MINOR LABORATORY						
Elevated Sedimen- tation Rate	89,4	(397/444)	۵		2	(0,5%)
C-Reactive Protein	55,6	(180/324)	0		122	(27.4%)
Leukocytosis (over 12,000)	35,1	(156/444)	0		2	(0,5%)
Prolonged P-R	19,5	(85/436)	1	(0,2%)	10	(2,2%)
**The denominat and for the <u>n</u>	or for umber	the <u>percen</u> with questi	t w ona	ith evidence ble evidence	e of e is	manifestation

*The denominator for the <u>percent with evidence of manifestation</u> and for the <u>number with questionable evidence</u> is the number of admissions for which sufficient evidence was found to allow categorization into yes, no, and questionable categories. It was derived by subtracting the <u>number omitted due to lack of</u> <u>information</u> from the total admissions in the study (446),

T. Duckett Jones, and since then twice revised, have brought about a degree of diagnostic uniformity and provided a vitally needed standard for national and international cooperative RF studies." (Markowitz, 1972)

The major Jones Criteria for the diagnosis of ARF are carditis, polyarthritis, chorea, erythema marginatum, and subcutaneous nodules. The minor criteria are comprised of (1) fever, (2) arthralgia, (3) previous RF or RHD, (4) acute phase reactants - either leukocytosis, elevated ESR, or positive CRP, and (5) prolonged P-R interval on ECG.

<u>Carditis</u>: The prevalence of carditis in our study was 25% (112/446). This agrees well with the study performed in Malmo, Sweden which reports 26% (371/1434) admissions for ARF with evidence of carditis (Hall, 1961). Most other recent studies, however, give significantly higher values: 38% at Bellevue (Mayer, 1963), 43% in Manhattan (Brownell, 1973), 42% at Irvington House (Feinstein, 1962b), 60% at the Medical College of Virginia Hospital (McCue, 1970), 63% in Czechoslovakia (Sitaj, 1970), 83% in Southern Iran (Tahernia, 1971), 80% in greater Miami (Saslaw, 1962), 85% in St. Louis (Goldring, 1968).

Carditis is easily the most important manifestation of ARF from the point of view of diagnosis as well as serious consequences to the patient. (Bland, 1966) Its course may vary from a fulminating fatal case to a subclinical inflammation.

-38-

Figure 9: Correlation of Race with Carditis in Connecticut Hospital Admissions for Rheumatic Fever 1968-1972

WHITES BLACKS 80.0% (357/446) 20.0% (89/446)

CARDITIS DIAGNOSED 25.1% (112/446)	80/446 17.9%	32/446 7,2%
CARDITIS NOT DIAGNOSED 71.1% (317/446)	262/446 58.7%	55/446 12,3%
CARDITIS Questionable 3.8% (17/446)	15/446 3.4%	2/446 0.5%

Admissions omitted due to lack of information = 0 Chi-Square = 7.266 Significant at .027 with 2 degrees of freedom

In our study, we found no correlation between carditis and sex or age; however, we found an increased incidence of carditis in Blacks (see figure 9). Thirty-two of 112 cases of carditis (29%) were found in Blacks in spite of the fact that they made up only 20% of our total population of admissions.

<u>Polyarthritis</u>: The prevalence of polyarthritis in our study was 87% (389/446), which agrees extremely well with recent studies of ARF: 92% (Saksena, 1969), 84% (Hall, 1961),



Figure 10: Correlation of Race with Chorea in Connecticut Hospital Admissions for Rheumatic Fever 1968-1972

> WHITES BLACKS 78.8% (319/403) 21.2% (86/403)

LHUREA		
DIAGNOSED	16/403	2/403
	4.0%	0,5%
4.4% (18/403)		

CHOOP

CHOREA NUT		
DIAGNOSED	303/403	82/403
95.1% (385/403)	75.1%	20,4%

Admissions omitted due to lack of information = 43 Chi-Square = 8.522 Significant at .015 with 2 degrees of freedom

76% (Feinstein, 1962a), 80% (Sitaj, 1970), 88% (Saslaw, 1962), 69% (Mayer, 1963), 85% (Goldring, 1968).

We found no correlation between polyarthritis and sex, race, or age.

<u>Chorea</u>: The prevalence of chorea in our study was 4.4% (18/405). In this, as in all subsequent situations in which the denominator is less than the 446 total admissions, the difference represents those cases for which insufficient information was present to allow any categorization. Our figure agrees quite well with most recent studies of ARF: 4% (Tahernia, 1971), 8% (McCue, 1970), 7% (Brownell, 1973), 5% (Saksena, 1969), 7% (Hall, 1961), 4% (Feinstein, 1962a), 6% (Goldring, 1968).



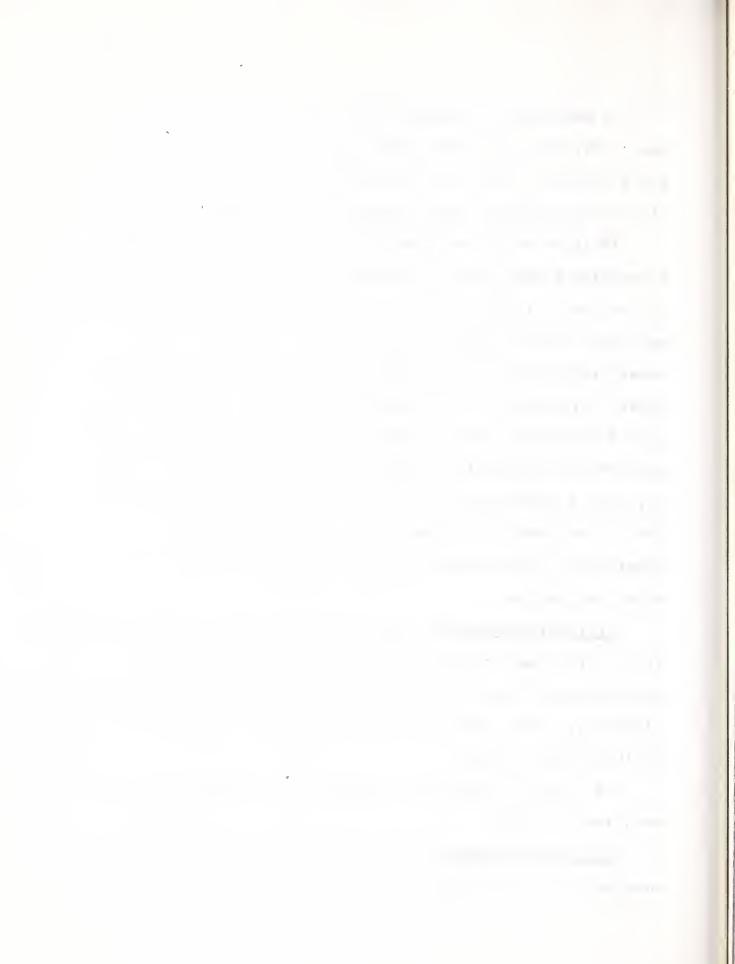
No patients with chorea were found in our study over the age of 25, and 2/3 of the cases were found in patients 6-15 years of age. This is in keeping with the known infrequency of the manifestation over the age of 16. (Massell, 1964)

In spite of the well-documented propensity for females to develop chorea, with the female to male ratio reported as 1.7 - 2.4 to 1 (Hall, 1961), we were unable to demonstrate any correlation between chorea and sex. Eight of the 18 cases (44%) of chorea occurred in males and 10 (56%) in females, very close to the expected 9 for each sex, predicted by the 51/49 male:female ratio. However, we quite unexpectedly found a correlation between chorea and race (see figure 10) with a preponderance of Whites having the manifestation: 90% of the cases of chorea, 16/18, were found in Whites, despite the fact that this group only made up 80% of the total admissions.

Erythema Marginatum: The prevalence of erythema marginatum in our study was found to be 8.9% (35/395), which agrees reasonably well with recent studies: 1.1% (Sitaj, 1970), 3% (Tahernia, 1971), 15% (Goldring, 1968), 1.6% (Saksena, 1969), 4% (Feinstein, 1962a).

We found no correlation between erythema marginatum and sex, race, or age.

Subcutaneous Nodules: The prevalence of subcutaneous nodules in our study was 3.0% (12/395) which agrees fairly



well with recent studies on ARF: 1% (Tahernia, 1971), 5% (Goldring, 1968), 8.3% (Saksena, 1969), and 1% (Feinstein, 1962a).

We found no correlation between subcutaneous nodules and sex,or age. There were no Blacks in our study reported to have nodules, but the total number of admissions having evidence of the manifestation is so small as to preclude any conclusion of significance. In addition, the lack of Blacks with this manifestation may be explained simply by the difficulty in recognizing subcutaneous nodules on black skin. (Dimitriu, 1965)

<u>Fever</u>: The prevalence of fever in our study was 70.5% (313/444) which was a bit lower than most recent reports on ARF: 98% (Sitaj, 1970), 97% (Saslaw, 1962), 91% (Feinstein, 1962a), 92% (Goldring, 1968), 73-80% (Saksena, 1969). One of the possible explanations for this result was that our definition of fever was strict (equal to or greater than 100.4° F. on at least one occasion), and may have been based on a higher temperature than were other studies. No other study clearly gave the definition of fever used.

We found no correlation between fever and race or age, but, surprisingly, found a significant correlation between fever and sex, with males having a disproportionate number of the febrile admissions (see figure 11).

Arthralgia: The prevalence of arthralgia in our study

-42-

MALES FEMALES 50.9% (226/444) 49,1% (218/444)

ADMISSIONS WITH		
FEVER	173/444	140/444
70,5% (313/444)	39.0%	31.5%

ADMISSIONS		
WITHOUT FEVER	53/444	78/444
29.5% (131/444)	11.9%	17.6%

ADMICCIONC

Admissions omitted due to lack of information = 2 Chi-Square = 8,108 Significant at ,005 with 1 degree of freedom

was 93% (313/444) which agrees reasonably well with the one other study in which it was measured in the same manner as in the present study. Our definition of arthralgia included all admissions in which arthralgia was a significant symptom, not excluding those in which polyarthritis would ultimately be used to satisfy the Jones Criteria. In the one study found in which arthralgia was similarly defined, 88% of the admissions gave evidence of the manifestation. (Saslaw, 1962) We found no correlation between arthralgia and race, sex, or age.



<u>Previous Rheumatic Heart Disease</u>: The prevalence of previous RHD in our study was 6,3% (28/446).

We found no significant correlation between previous RHD and race, sex, or age.

Previous Rheumatic Fever: The prevalence of a previous attack of RF in our study was 15.5% (69/446), a significantly lower value than those recently reported for ARF: 31% (37/118) in a study of the British Army (Slater, 1959), 65% (Saksena, 1969), 33% (Saslaw, 1962), 48% (Sitaj, 1970). The variability among studies with regard to this parameter may be simply due to geographic and population differences in the prevalence of ARF and RHD as well as differences in diagnostic criteria.

In Connecticut, of the 69 admissions mentioned as "having had" previous RF, only 49 (71%) had documented hospitalizations, while the remaining 20 (29%) merely replied in the affirmative to the question, "Did you ever have rheumatic fever?"

No significant correlation was found between previous RF and race, sex, or age.

Elevated Sedimentation Rate: The prevalence of an elevated ESR in our study was 89% (397/444) which agrees well with the 84% reported in the greater Miami area (Saslaw, 1962).

No significant correlation was found between elevated

.

ESR and race, sex, or age.

<u>Presence of C-Reactive Protein</u>: The prevalence of a positive CRP in our study was 56% (180/324) which agrees moderately well with the 71% reported in the greater Miami area (Saslaw, 1962).

No significant correlation was found between positive CRP and race, sex, or age.

Leukocytosis: The prevalence of an elevated white blood cell count (WBC) in our study was 35% (156/444). It is difficult to compare our result with that of any other studies, since "leukocytosis" is ordinarily taken to mean simply any elevation of the WBC above the normal range for the hospital involved. In regard to this parameter, our definition was "a leukocytosis of equal to or greater than 12,000 per cubic millimeter on at least one occasion."

We found no correlation between leukocytosis and race, sex, or age.

<u>Prolonged P-R Interval on ECG</u>: The prevalence of a prolonged P-R interval in our study was 19.5% (85/436). Due to the lack of a clearcut definition of a "prolonged P-R interval" in most studies, we are unable to make any cross-study comparisons.

We found no correlation between prolonged P-R interval on ECG and race or age, but found a quite significant correlation with sex, a preponderance of males in our group



Figure 12: Correlation of Sex with Prolongation of the P-R Interval in Connecticut Hospital Admissions for Rheumatic Fever 1968-1972

> MALES FEMALES 50.5% (220/435) 49,5% (216/435)

 PROLONGED P-R

 FOUND
 57/435
 28/435

 19.5% (85/435)
 13.1%
 6.4%

PROLONGED P-R		
NOT FOUND	162/435	188/435
80,3% (350/435)	37.3%	43,2%
00,300 (330/433)		

Admissions omitted due to lack of information = 11 Chi-Square = 12,790 Significant at ,002 with 1 degree of freedom

with prolonged P-R, 173/313 (55%), in spite of the fact that males made up only 51% of the total sample (see figure 12).

A prolonged P-R interval is found so frequently in other childhood illnesses that it has little weight as a diagnostic test for ARF. It is <u>not</u> a sign of acute carditis and has no real prognostic import, (McCue, 1970)

SUPPORTING EVIDENCE OF PRECEDING STREPTOCOCCAL INFECTION - see

figure 15

The modified Jones Criteria emphasize the supporting evidence of a preceding group A beta-hemolytic streptococcal infection. Verification of a recent streptococcal infection is a necessary ingredient for diagnosis. Acceptable supporting





evidence is comprised of either (1) recent recognized scarlet fever, (2) a positive throat culture for group A streptococci, or (3) an elevated anti-streptolysin O titer. (Ad Hoc Committee of the Council on Rheumatic Fever, 1965)

Recent Scarlet Fever: The prevalence of recent scarlet fever in our study was 1.6% (7/444). No significant correlation was found between recent scarlet fever and race, sex, or age.

Positive Throat Culture: The prevalence of positive throat culture in our study was 23% (75/321) which agrees well with studies in the recent literature: 39% (Saslaw, 1962), 29% (Gordis, 1969a), 23% (McCue, 1970). No correlation was found between positive throat culture and race, sex, or age.

Of the 440 admissions on which we have information, we find that throat cultures were taken on 90% (397/440) and were omitted in 10% (43/440) of the cases (see figure 13). Of the 397 cultures taken, 81% (322/397) were negative for group A beta-hemolytic streptococci and only 19% (75/397) were positive. And of those 322 cultures found to be negative, 24% (76/322) were obtained after the patient had begun antibiotic therapy, either as an outpatient or in the hospital.

These results point up the need for taking cultures from each patient in whom the diagnosis of ARF is considered, and in taking these cultures before antibiotics are begun.



Figure 13: Analysis of Inpatient Throat Cultures Among 446 Hospitalizations in Connecticut for Rheumatic Fever 1968-1972

THROAT CULTURE

6 admissions omitted due to insufficient information

> OBTAINED 90.2% (397/440) 9.8% (43/440)

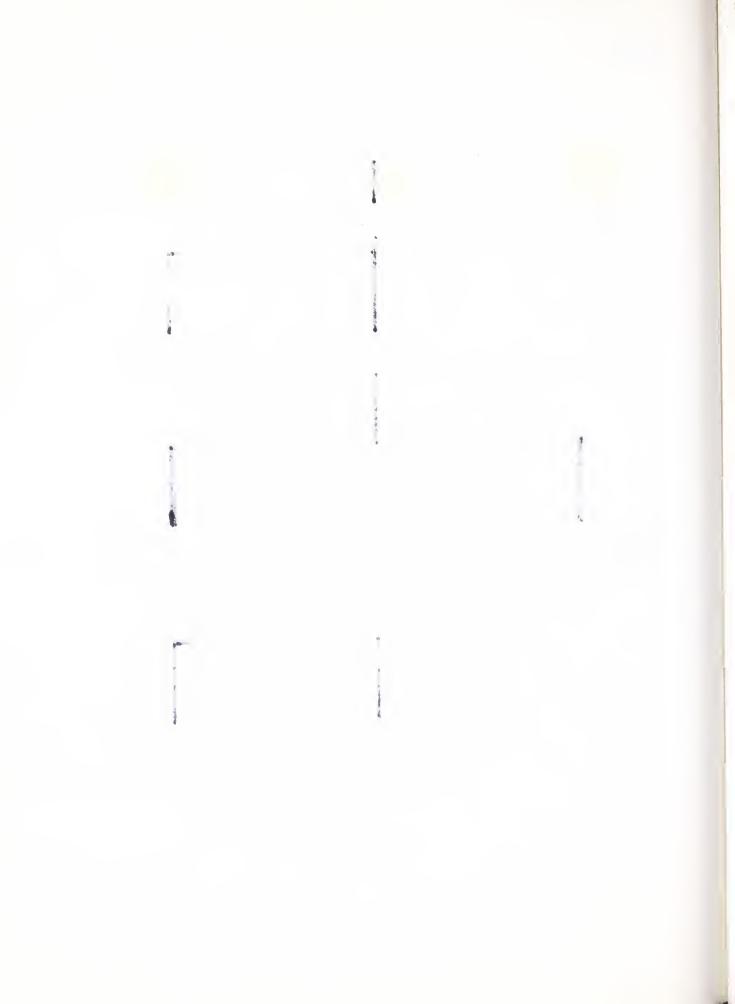
NOT OBTAINED

POSITIVE FOR GROUP A **STREPTOCOCCI** 17.1% (75/440)

NEGATIVE EOR GROUP A STREPTOCOCCI 73.2% (322/440)

CULTURED AFTER START OF ANTIBIOTICS

CULTURED BEFORE START OF ANTIBIOTICS 17.3% (76/440) 55.9% (246/440)



Elevated Antistreptolysin O: Antibody to streptolysin O begins generally to rise 7-10 days after a streptococcal infection and reaches a peak at 3-5 weeks. The antibody response is quantitatively greater in patients who develop RF but there is so much variation in the titer that the magnitude of the rise is not itself of diagnostic value. The titers return to normal in 2-4 months and therefore are usually normal in the chronic stages of rheumatic disease. (Feinstein, 1962b)

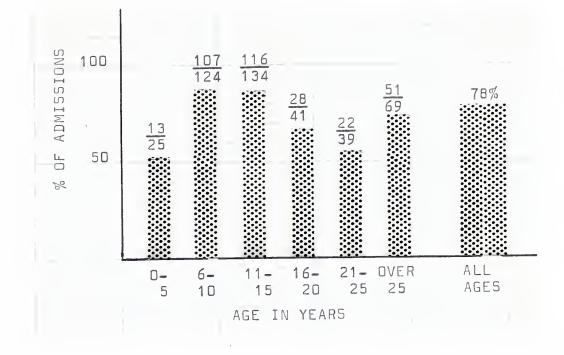
ASO can be demonstrated in 70-80% of patients following an untreated pharyngeal infection with group A streptococci. But prompt antibiotic treatment may suppress the ASO response. (McCue. 1970)

The prevalence of elevated ASO titers in our study was 78% (337/432) a value in very good accordance with other reported values: 89% (Hall, 1961), 71% (Saslaw, 1962), 78% (Gordis, 1969).

However, a single value of antibody titer, no matter how high or low, does not demonstrate or exclude a recent streptococcal infection. The important aspect of antibody titer is a change in values, rather than any single reading. A single titer can be as high as the residuum of an even higher value from an old infection, whose titer has slowly decayed, and a low or normal value might represent a rise from an even lower previous titer in that patient. (Feinstein, 1966)

-49-





No significant correlation was found between elevated ASO titer and race or sex, but an interesting variation with age was demonstrated (see figure 14). The ASO response following a streptococcal infection has been said to increase from infancy through childhood, with almost all patients over the age of 5 responding with an increased titer. (Ferencz, 1969) In our study, we found that only 52% (13/25) of the admissions of children under the age of 6 had an elevated ASO, whereas 86% (223/258) of those ages 6-15 had elevated titers. After the age of 15, the percent of positives began to drop, to 68% (28/41) ages 16-20, and 56% (22/39) ages 21-25. We can see from figure 14 that only during the years 6-15 do we find



a greater per cent of positives than the overall 78% average. DIAGNOSTIC VALIDITY - see figure 16

The widespread application of the Jones Criteria has brought major progress to the study of ARF, because the population of patients under surveillance can now be defined more precisely than ever before. They are not perfect, no arbitrary decisions about disease ever can be, but at least they enable physicians to circumscribe a zone of the different types of human illness to be considered as candidates for the diagnosis of ARF. The manifestations cited by the Jones Criteria, however, can be produced by many major diseases other than ARF. These masqueraders can oft be identified by specific diagnostic tests for gout, sickle cell disease, rheumatoid arthritis, or systemic lupus erythematosis. (Feinstein, 1966)

"The presence of two major criteria, or of one major and two minor criteria, indicates a high probability of the presence of rheumatic fever. Evidence of a preceding streptococcal infection greatly strengthens the possibility of ARF. Its absence should make the diagnosis doubtful." (Ad Hoc Committee of the Council on Rheumatic Fever, 1965)

The Jones Criteria are indeed a useful tool in helping to diagnose ARF; however, there are loudly voiced objections to overly strict adherence from some quarters (Okuni, 1971). Hence, while a discussion of the validity of diagnoses with

-51-



in All	ting Evidence of P Admissions in Con tic Fever		tococcal Infection 1972 Diagnosed as
MANIFESTATION	PERCENT WITH EVIDENCE OF MANIFESTATION	NUMBER WITH Questionable evidence	DUE TO LACK
Elevated ASO (over 166)	78,0 (337/432)	D	14 (3,1%)
Positive Throat Culture for Group A Streptococcus	23,4 (75/321)	0	49 (11,0%)
Recent Scarlet Fever	1,6 (7/444)	0	2 (0.5%)

Figure 16: Analysis of Case Validity in Connecticut Admissions 1968-1972 Diagnosed as Rheumatic Fever

	PERCENT OF ADMISSIONS SATISFYING CRITERIA	PERCENT OF ADMISSIONS NOT SATISFYING CRITERIA
Jones Criteria	94,2 (420/446)	5,8 (26/446)
Supporting Evid- ence of Strep Infection (ASO, Scarlet Fever, Culture)	81.6 (364/446)	18.4 (82/446)
Jones Criteria and Supporting Evidence	78.0 (348/446)	22.0 (98/446)

respect to the Jones Criteria must certainly be included in any complete study of ARF, we have not rejected those admissions from our study which did not fulfill them.

The prevalence of admissions which satisfied the Jones Criteria was 94% (420/446) which agrees well with previously reported figures: 95% (Spector, 1968), 80% (Gordis, 1969a), 93% (Saslaw, 1962), 90% (Hall, 1961).

Of the 420 cases satisfying the criteria, 120 (29%) had evidence of two major criteria, 291 (69%) had evidence of one major and two minor criteria, and 9 (2%) had evidence of chorea associated with less than two minor criteria.

We found no significant correlation between satisfying of the Jones Criteria and race, sex, or age,

One or more pieces of supporting evidence of a streptococcal infection was found in 82% (364/446) of the admissions under study. Of the 364 with supporting evidence, 280 (77%) had only an elevated ASO titer, 22 (6.5%) had only a positive throat culture, 5 (1.4%) had only scarlet fever, 55 (15%) had both a positive throat culture and an elevated ASO titer, and 2 (0.1%) had both scarlet fever and an elevated ASO titer.

The percentage of admissions qualifying as ARF by the strictest criteria (satisfaction of the Jones Criteria together with evidence of preceding streptococcal infection) was 78% (348/446). This means that only 22% (98/446) did not fulfill the most rigorous requirements to meet the



diagnosis of ARF, and seems quite good in a statewide study of a disease as difficult to diagnose as is ARF.

PRIMARY PREVENTION OF RHEUMATIC FEVER

Rheumatic fever occurs in 0.3 to 3.0% of untreated streptococcal pharyngitis. (Rammelkamp, 1952), (Siegel, 1961) Both initial attack and recurrence of ARF follow a characteristic pattern. A streptococcal pharyngitis, severe, mild, or subclinical occurs. When symptoms are present, they subside in 3-4 days unless there are suppurative complications. The patient appears well for a period of time. And this is followed by the appearance of ARF. (Feinstein, 1964)

Characteristically, the clinical manifestations of ARF appear 1-6 weeks after the pharyngitis. The mean duration of the latent period between the onset of the infection and the appearance of rheumatic symptoms has been reported to be 18.6 days. (Baum, 1963) It is reported that 24% of patients experience a latent period greater than 35 days; however, many of these may be reinfections. It is said that 7% have latent periods of less than 5 days and a few patients have been mentioned in whom the symptoms of ARF coincided with the onset of the respiratory illness. The length of the latent period does not appear to be related to the specific type of group A streptococcus, the height of the ASO titer, or to the clinical pattern of the rheumatic episode. (Rammelkamp, 1962)

"Primary prevention or prophylaxis of ARF refers to the



adequate treatment of a streptococcal infection in a patient who has not had RF and who will, by prompt and complete eradication of the organism, be protected from any late, non-suppurative complications." (Ferencz, 1969)

It is no secret that the battle against the streptococcus is, by and large, mounted against tremendous odds. The organism is ubiquitous; it is difficult and sometimes impossible to distinguish carrier states from true infections; (Dunlap, 1973) many infections occur in asymptomatic or mildly symptomatic children who never reach medical attention (Noble, 1972); throat cultures are not infallible; and effective treatment is difficult to achieve. (Brett, 1972), (Markowitz, 1968)

As a result of the findings during an epidemic of streptococcal pharyngitis in a military training center in 1950, it is now established that the administration of adequate doses of penicillin for ten days to patients with scarlet fever or streptococcal pharyngitis may prevent the appearance of RF (Denny, 1950). Treatment for a full 10-day period is essential to eliminate streptococci from the nasopharynx. If antibiotics are only given for a few days, the organism may persist in the throat and RF may develop.

One of the major factors limiting the prevention of initial attacks of ARF by using antibiotics is that about two thirds of the patients who develop ARF do so following

-55-

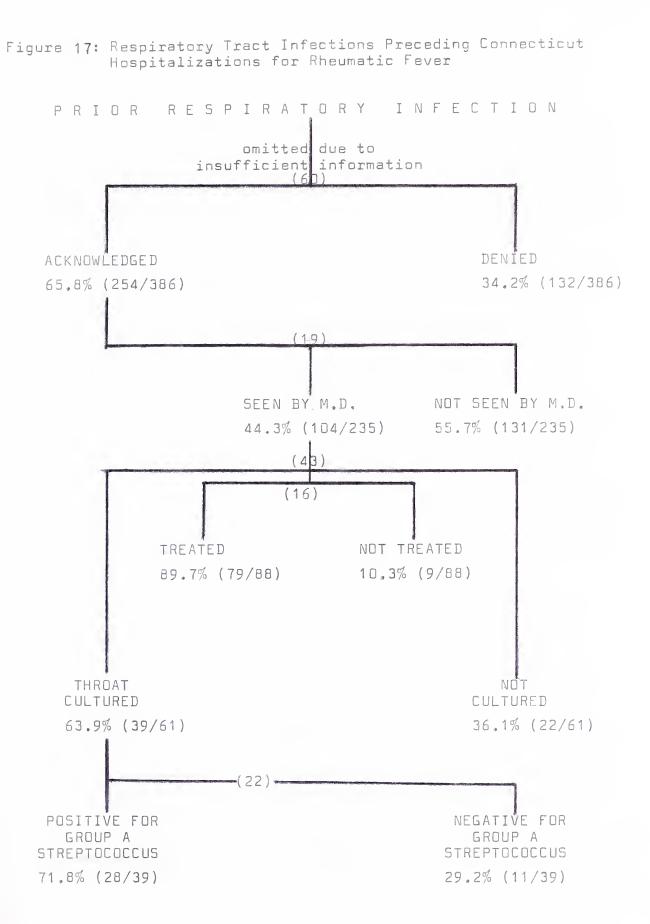


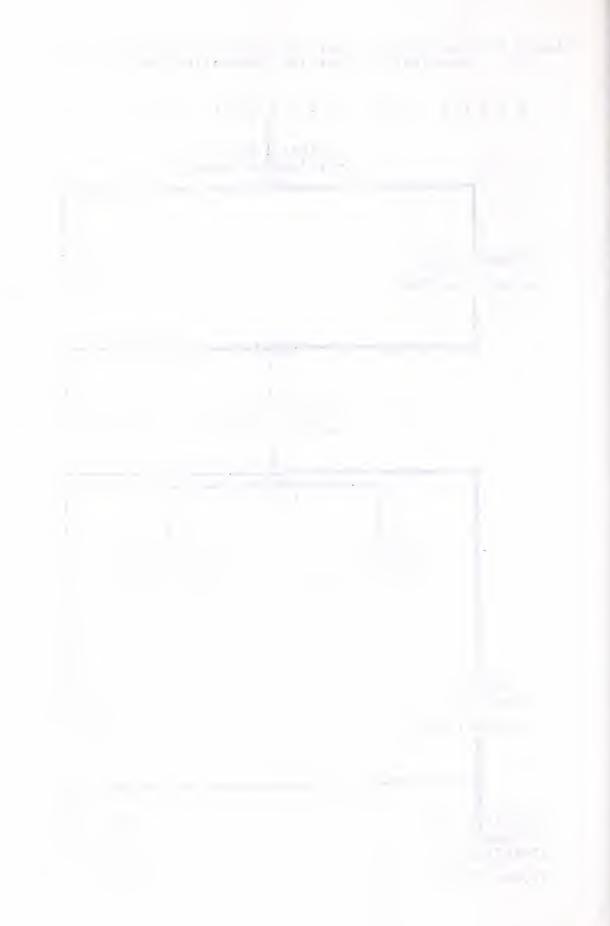
either asymptomatic or mild streptococcal infections. Furthermore the lower socioeconomic groups, in which the risk of RF is the greatest, are the least likely to receive adequate care for an acute respiratory infection. (Markowitz, 1969)

In our study, we found that 66% (254/386) of the admissions were preceded by acknowledged respiratory tract infections (see figure 17). Of our total 446 admissions, 60 were omitted due to lack of information. Our 66% figure is in exact agreement with the data from a similar study done in Baltimore in which it was found that 66% (of 261 patients) acknowledged a prior respiratory infection (Markowitz, 1970), and agrees well with other reported figures: 68% (Slater, 1959), 51% (Gordis, 1969a), 64% (Sitaj, 1970). In both the Baltimore study and our own in Connecticut, the estimate for asymptomatic or mildly symptomatic infections would thus be 34%.

Of the 235 respiratory infections in which we have information (19 of the 254 were omitted due to lack of information), we found that 44% (104/235) were seen by a physician and 56% (131/235) were not seen. Presented in a different way, we see that 27% (104/386) of the total were seen by a physician. This figure is similar to results of 34% (of 261 patients) in Baltimore (Markowitz, 1970) and 33% (35/105) in Boston (McCue, 1970).

Of the 104 seen by a physician, we have no information





regarding therapy in 16. Of the remaining 88, 90% (79/88) were "treated" and 10% (9/88) were not treated. The breakdown of the "treatment" was as follows: 12 of 88 were treated with penicillin intramuscularly (14%), 12 (14%) were "treated" with no further information, 10 (11%) claimed to have continued oral therapy for 10 full days, 32 (36%) admitted to either not taking their antibiotic at all or taking it for less than 10 days, and 22 (25%) had oral antibiotics prescribed for 10 days, but did not mention whether or not they were taken.

To evaluate patient cooperation in carrying out the recommended 10-day treatment course of penicillin prescribed for streptococcal pharyngitis or otitis media, a study was performed utilizing both a urine test for the presence of penicillin and home visits with pill counts. We find that in spite of the special attention resulting from the study itself, only about 50% of private patients and 20% of clinic patients completed the full course of treatment, although over 80% of the clinic mothers reported that the recommendations had been carried out. (Ferencz, 1969)

Of the 88 patients in our study seen by a physician for a respiratory infection, 67 (77%) were seen by private physicians and 21 (23%) were seen in hospitals, either outpatient clinics or emergency services.

We have information on 61 of the 104 patients seen by a physician with regard to throat culture (43 were excluded because of insufficient information). Sixty-four per cent

-- 58--

.

(39/61) had their throats cultured while 36% (22/61) did not. Of those who did have throats cultured, we have information on the results in 39 cases (22 were omitted because of lack of information). Of these 39, 28 or 71% were positive for group A streptococcus and 11 or 29% were negative.

Thus, 79 of our 446 admissions have at least had a history of having antibiotics prescribed for them (19%), and 12 received intramuscular therapy; yet they still developed RF. This is certainly one area in which improvements can be made both through further education of physicians and through programs to improve compliance of patients. RHEUMATIC HEART DISEASE AT TIME OF DISCHARGE - see figure 18

It has been taught for many years that 60-80% of patients with clinically detectable carditis during an attack of ARF are left with residual RHD, although in many the clinical findings of RHD may not appear until months or years after discharge. (Spagnuolo, 1971), (Baum, 1963), (Wenger, 1967)

The declining severity of RF can be judged by the decrease in cardiac involvement seen in patients hospitalized with ARF. Generally speaking, the prognosis for any child with the disease is directly related to the severity of the carditis. Mayer (1963) reported that among children discharged from Bellevue Hospital the percentage of total cases with organic heart disease had decreased to 21% between 1951-

-59-



Figure 18: Rheumatic Heart Disease at Time of Discharge in 446 Connecticut Admissions for Rheumatic Fever 1968-1972

PERCENT HAVING RHEUMATIC HEART DISEASE	13,8 (61/443)
PERCENT NOT HAVING RHEUMATIC HEART DISEASE	83,5 (370/443)
PERCENT WITH QUESTIONABLE EVIDENCE	2.7 (12/443)
NUMBER OMITTED DUE TO LACK OF INFORMATION	3/446 (0.7%)

1958 from 37% between 1935-1950. Massell (1964) found that at the House of the Good Samaritan (a regional hospital for the acute and convalescent care of RF) the population of patients with RHD decreased from 73% 1921-1930 to 51% in the period 1951-1960.

In our study, the prevalence of RHD at the time of discharge was found to be 14% (61/443) or 54% (61/112) of those manifesting carditis during hospitalization.

We found no significant correlation between RHD at discharge and sex or age, but did find an increased prevalence of RHD among Blacks (see figure 19). Thirty-three per cent (20/61) of the RHD at discharge was found in Blacks even though they made up only 20% of the total admissions.

Figure 19: Correlation of Race with Rheumatic Heart Disease at Discharge Among Connecticut Hospital Admissions for Rheumatic Fever 1968-1972

> WHITES BLACKS 80.1% (355/443) 19.9% (88/443)

HD FOUND AT DISCHARGE 13.8% (61/443)	41/443 9.3%	20/443 4,5%
RHD NOT FOUND At discharge 83.5% (370/443)	306/443 69,1%	64/443 14,5%
QUESTIONABLE		

 EVIDENCE OF RHD
 8/443
 4/443

 AT DISCHARGE
 1.8%
 0.8%

 2.7% (12/443)
 0.8%

Admissions omitted due to lack of information = 3 Chi-Square = 9.298 Significant at .010 with 2 degrees of freedom

SECONDARY PROPHYLAXIS OF RHEUMATIC FEVER

OUD FOUND AT

The prevention of streptococcal infection among patients who have had an attack of RF is of extreme importance because these patients are particularly susceptible to a rheumatic recurrence. (Gordis, 1971) It has been determined that 20-50% of susceptible patients not receiving antimicrobials might be expected to have such recurrences. (Baum, 1963), (Johnson, 1964)

Thomas Sydenham was the first to realize that rheumatic

patients were "very subject to a relapse, . . It is proper to bleed and purge the patients for some days about the same season the next year, or a little earlier."

Recurrent RF can be defined as "the reappearance of such RF manifestations as would be sufficient to make a diagnosis of a first attack, after a period of quiescence not resulting from treatment." Manifestations of RF may fluctuate and reappear after total suppression by treatment, in which case the term rebound or relapse can be used. But experience shows that such relapses fall within two months of the end of treatment and usually within two weeks. New or renewed manifestations two months or more after treatment is stopped have been shown to follow a new streptococcal infectin. (Taranta, 1967)

Secondary prevention or prophylaxis of RF refers to the protection of those with a history of RF from streptococcal infections, which might reactivate the disease. In other words, it means the maintenance of the patient in the streptococcus-free state achieved by the original treatment course. Either penicillin or sulfonamide is effective in a small daily dose as long as it is conscientiously taken. Failures occur in spite of faithful compliance, but are mostly due to patients' failure to take the medication. (Ferencz, 1969)

Antibiotic agents which can prevent beta-hemolytic streptococcal infections became available in 1936. Because of the

high recurrence rate of RF, daily doses of sulfonamides were tried as a prophylactic measure to prevent streptococcal infections in rheumatic subjects in convalescent homes and pediatric cardiology clinics. Well-controlled studies showed that by this procedure, streptococcal pharyngitis could be prevented and that the recurrence rate of RF was grossly reduced. Subsequently, similar results were obtained with a daily oral dose of penicillin. (Markowitz, 1972)

The general consensus is that a monthly injection of benzathine penicillin is by far the most effective regimen. Using this program, the recurrence rate was 0.4 per 100 patient years, as compared with a rate of 5.5 for similar patients on daily oral penicillin, and 10.7 on oral penicillin for only 10 days per month. (Spagnuolo, 1973)

Although the number of recurrent attacks has been reduced, approximately 10% of rheumatic patients still develop recurrences either because they are not on prophylaxis at all or they take their medication irregularly. (Markowitz, 1972)

In one study, we find that, after one year, only 20-60% of the patients had continued prophylaxis (by urine test). (Ferencz, 1969) In another study done in Baltimore, only 32% of the patients were found to take their medication more than 75% of the time (by urine test), and over 36% took their medication <u>less than</u> 25% of the time. (Markowitz, 1970) In a study done at Yale-New Haven Hospital, it was found that less than 1% of teenagers maintained regular prophylaxis

Figure 20: Rheumatic Fever Recurrences Among Hospitalizations in Connecticut for Rheumatic Fever 1968-1972

First Attacks	84.6% (373/441)
Recurrences	15,4% (68/441)
Second Attacks	10,4% (46/441)
Third or More	2,5% (11/441)
Undifferentiated Recurrences	2,5% (11/441)
Omitted Due to Lack of Information	5/446 (1,1%)

Figure 21: Prophylaxis Among 68 Recurrent Attacks of Rheumatic Fever in Connecticut 1968-1972

> On Rheumatic Fever Prophylaxis 53,7% (36/67) Not on Rheumatic Fever Prophylaxis 46,3% (31/67) Omitted Due to Lack of Information 1/68 (1,5%)

(Whittemore, 1966).

In our study, we found that 85% (373/441) of our admissions were for first attacks of ARF and 15% (68/441) were recurrences. This figure is in accordance with the findings of other authors: 15% (Gordis, 1969a), 20% (Brownell, 1973), 13% (Saslaw, 1962). The recurrences (figure 20) can be further broken down: 46 (10%) were documented second attacks, 11 (2.5%) were third or greater attacks, and 11 (2.5%) were not differentiated.

We must remember that recurrence rates judged by history



miss all those first attacks manifest by silent carditis and count those erroneously diagnosed. In a patient group ages 11-22 with a prior history of ARF and not on prophylaxis, the streptococcal infection rate was 24,3 per 100 patient years as measured by bimonthly serum antibody levels. Of these, 83% were asymptomatic and were not treated. (Findlan, 1970)

If we compute the recurrence incidence for Connecticut, 1968-1972, we arrive at the figure 0.5 per 100,000 total population. Considering only recurrences occurring in patients ages 5-20 we find 33 recurrences in a population of about 900,000 (Connecticut population ages 5-20, 1972 estimate), or an incidence of 3.7 per 100,000 ages 5-20. The study in Baltimore (Gordis, 1969a) reported a recurrence incidence of 2.3 per 100,000 ages 5-19.

We find that of the 68 recurrent attacks in our study, 36 (54%) occurred while "on prophylaxis" (figure 21). Thus, 36 of our total 446 admissions (8%) had at least had some type of prophylactic medication prescribed for them. This agrees extremely well with other reports: 7% (Ferencz, 1969), 10% (Brownell, 1973), 9% (Taranta, 1967).

In an effort to further differentiate our patients "on prophylaxis" we found that of the 36 claiming to be on a regimen, 17 (47%) admitted to not taking their medication regularly, only 5 (14%) claimed that they did take the medication regularly, and in 17 cases we have no information regarding

-65-

regularity,

CONNECTICUT RHEUMATIC FEVER REGISTRY - see figure 22

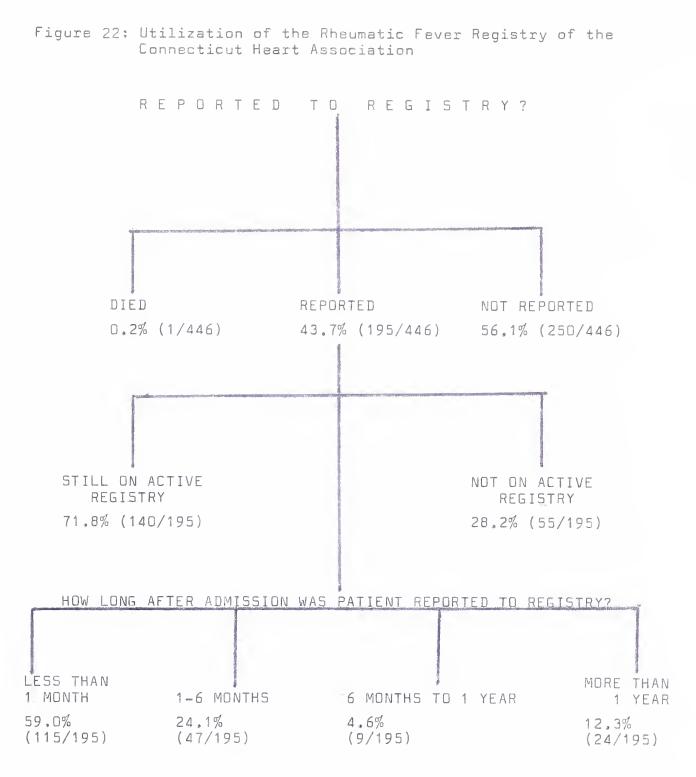
It is important to note that the Connecticut Heart Association Rheumatic Fever Registry provides only oral penicillin; therefore, it may well be that some patients have been put on other treatment regimens, and remain unregistered. (Teagle, 1963)

With regard to utilization of the registry, we found that 195 (44%) of our 446 admissions were reported to the registry, as compared to 61% reported to the Maryland registry (Gordis, 1969c). Of those reported in order to obtain low-cost penicillin prophylaxis, the majority, 59% (115/195) were reported less than a month after their admission for ARF; 24% (47/195) were reported between 1 and 6 months, 4.6% (9/195) were reported between 6 months and one year, and 12.3% (24/195) were reported a year or more after admission.

One hundred forty of the 195 originally reported to the registry (72%) were on active registry as of December, 1973. While the rate of those still registered is being measured over little more than a year for those patients admitted in 1972, it agrees well with the 68% reported in Maryland (Gordis, 1969c).

We were unable to find any significant correlation between a patient's being registered and race, sex, or age, and found that having had carditis, RHD, chorea, or a recurrence had no effect on his being registered or not.

e





DISCUSSION AND RECOMMENDATIONS

In 1930, Glover wrote that "the incidence of acute rheumatism seems to show that it, like tuberculosis, is slowly but surely being conquered. . .We seem to be seeing the same process of epidemiological obsolescence in acute rheumatism that Creighton saw in smallpox." (Markowitz, 1972) Glover's prediction of obsolescence has not yet been fulfilled, and the data presented from our study indicate that it is still a problem of considerable magnitude.

The overall incidence of ARF seems to have declined, as has its mortality rate, and severity. A much lower percentage of patients with RF seem to be presenting with carditis or ultimately developing RHD. However, we might take a note of warning from our comrades in Missouri: With no deaths from ARF in the years 1955-1966, "it was not surprising that admitting officers and staff at St. Louis Children's Hospital had been lulled into a sense of unawareness about RF. This was so until 1967 when they were jolted into the realization that the disease was very much with us when two patients admitted with fulminating ARF died." (Goldring, 1968)

(1) With RF a reportable disease in Connecticut and only 5-10% of hospitalized cases of ARF being reported to the state, and certainly an even lower proportion of total cases, the decision must be made as to whether RF should continue to be reportable. If so, measures must be taken to encourage reporting,

(2) Efforts at primary prevention should be increased. There is no current method of primary prevention for those who have had no antecedent history of respiratory infection; of those who did have an infection, but did not see a physician, there is an apparent need for increased community health education and probably increased availability of medical care. For the remaining who were seen by a physician there is no doubt that an educational program aimed at the doctors is indicated with particular reference to the appropriate use of throat cultures and a review of general medical principles for the treatment of upper respiratory infections.

The cost of RF was estimated in 1965 to be \$22,324. per patient (onset of the disease to death), or \$465 per year per patient (Saslaw, 1965). With these figures in mind, and the knowledge that the cost must be far higher in this decade, it certainly seems financially sound to continue and expand programs for primary prophylaxis of RF, those aimed at preventing initial attacks.

(3) In view of the extent and distribution of the RF problem in Connecticut, it seems well-advised to continue secondary prophylaxis programs, including the Heart Association's Registry (which, with nearly 50% of the hospitalized cases reported to it, seems to be the only fairly reliable source at present for gauging the extent of the disease). Improvements in the system might include offering intramus-

-69-

cular penicillin and oral sulfonamides as alternatives for prophylactic regimen, and stressing compliance with the help of visiting nurses or telephone calls.

(4) Equally as imprtant as any of these prophylaxis measures is the continued education of physicians with regard to diagnosis and treatment of ARF. Although the Jones diagnostic criteria have been purified, amended, and classified, we still have no pathognomonic test for RF. It is still essential that in any patient in whom the disease is considered, a good history be obtained and a thorough work-up performed, including throat culture, ASO, ESR, CRP, and ECG, before beginning antibiotics. Only by continued awareness of the disease and preparedness to make the diagnosis, can we hope to continue effective and prompt treatment in this potentially acutely fatal process.

(5) It might be worthwhile to repeat this study in several years, with the view of defining any changes over the time period and reassessing the need for and the effect of the various prophylaxis programs in the state.

-70-



SUMMARY

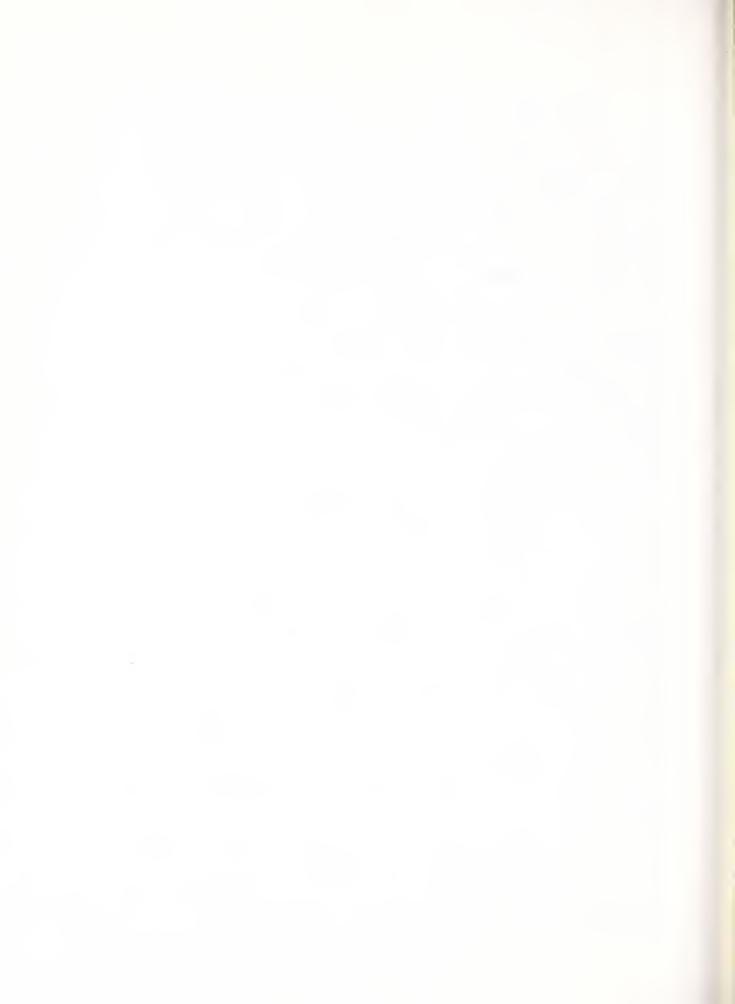
A retrospective chart review of all hospital admissions for acute rheumatic fever (by discharge diagnosis) in the state of Connecticut was performed for the years 1968 to 1972. A total of 446 admissions, representing 431 patients were found, an average of 89 admissions per year or 3.0 admissions for ARF per 100,000 total population per year.

The number of recurrences in this group was 68 (14%), giving us an incidence for recurrent RF of 0.5 per 100,000 total population, or 3.7 per 100,000 ages 5-19. Of the 68 recurrences, 31 (46%) admitted to being on some type of secondary prophylaxis regimen, but only 5 claimed to take the medication regularly.

Our sample was composed of equal numbers of males and females (51% males, 49% females), and the ratio of Whites to Blacks was found to be 4:1.

Although the peak age of admission was 9, our "average admission" was 13 years of age, and remained in the hospital for 12 days, after which he was discharged home. The most common constellation of manifestations was polyarthritis associated with fever and an elevated sedimentation rate. Only 25% (112/446) of our admissions showed evidence of carditis, and, of those, 54% (61/112) had rheumatic heart disease at the time of discharge.

Ninety-four percent of our sample (420/446) satisfied the Jones diagnostic criteria, 82% (364/446) had supporting evidence of a preceding streptococcal infection, and 78% (348/446)



fulfilled both requirements of validity.

At least 254 admissions were preceded by acknowledged respiratory tract infections; however, we know of only 104 cases in which a physician was seen, only 79 who received antibiotic treatment, and only 39 in whom a throat culture was obtained.

In our investigation of the Connecticut Heart Association Rheumatic Fever Registry, we found that 44% (195/446) of our admissions were reported to the registry for the purpose of obtaining penicillin at low cost for prophylaxis, most within one month of their hospitalization for ARF. In addition, 72% (140/195) of those reported are still on the active registry.



APPENDIX

- 1. Letter introducing our study to the Chief Administrator and the Chief Medical Librarian at each hospital
- 2. Coding form used to record all data on patients



Dear

For many years, the Connecticut Heart Association has been active in programs aimed at the prevention and control of rheumatic fever. In order to plan effectively for the future and to determine the needs of the State in this area, we are conducting a study of the number of cases of the disease in Connecticut. Since the clinical pattern and the severity or rheumatic fever has been changing through the years, we are surveying the hospital records to form a clinical profile of rheumatic fever.

We are writing you, therefore, to request permission and to acquaint you with this project. We should like to review the records of all patients at your hospital from 1967-1972 inclusive with a diagnosis of acute rheumatic fever. This information will, of course, be kept completely confidential and will be used only to help plan the Heart Association program. No attempt will be made to contact these patients.

We are requesting that a medical student, Mr. Harry Magnes, YMS '74, review these records according to our protocol. He will be under the direction of Dr. Ruth Whittemore, Clinical Professor of Pediatrics at the Yale University School of Medicine and Dr. Milton Markowitz, Professor and Director of Pediatrics at the University of Connecticut School of Medicine. Mr. Magnes will be in contact with your medical librarian in the relatively near future to arrange how he may best review records in your hospital with the diagnosis of acute rheumatic fever between 1967-1972.

The information we obtain will be invaluable in helping us plan services for prevention and control of rheumatic fever in Connecticut, and we would greatly appreciate any assistance you feel would contribute to the success of this study. If you have any questions, please do not hesitate to contact any of us listed below. Thank you for your interest and cooperation.

Sincerely yours,

Victor Hurst, M. D. Chairman, Rheumatic Fever Committee

- P.S. The address of Mr. Harry Magnes is 1 South St., New Haven 06510 Telephone numbers of
 - Dr. Hurst-Waterbury- 573-6000
 - Dr. Whittemore-New Haven-436-8310
 - Dr. Markowitz-Hartford-243-2531, ext. 351

Ruth Whittemore, M. D.



	CONNECTICUT RHEUMATIC FEVER STUDY	DY	RESP INFEC	43 MET JONES GRITERIA?	48 DISCHARGE DIAGNOSIS 1-ACUTE RF
NARE	ADDRESS	en brand in de la constant de la cons Constant de la constant de la constan		4-YES, 1 WAJOR+2 MIN.	3-HX OF RE A DIFESTION BY OF FR
BIRTHDATE	ADMITTED 19 DIS	DISCHARGED 19	S-130, NOE SEAM 8-QUESTIONABLE	9-COURSTIONABLE 9-DUESTIONABLE	11 <u>1</u> 2
5 1-5 STUDY NUMBER	24 CARDITIS , 1 2 8 9	36 PREVIOUS RF? 2-NO		44 ATTACK NUMBER	8-QUESTIONABLE 9-NO INFORMATION
6 CHART AVAILABLE?	25 POLYARTHRITIS			1-FIRST ATTACK 2-SECOND ATTACK 3-THIRD OR MORE	49
1-YES 2-NO	0	9-NO INFOLMATION	4-NO CULT-CLIN STREP 4-NO CULT-CLIN NO STREP -7-NOT APPLICABLE	4-RECURRENCE(?Number) 8-QUESTIONABLE 9-NO INFORMATION	
7 RACE AND SEX 1-White male	- 4->1 JOINT (SUBJ ONL) 5-1 JOINT (OBJ + SUB) 6->1 JOINT(OBJ + SUB)		9-WO INFORMATION	45 IF RECURRENCE, WAS	
1-White Hale 2-White female 3-Black Homale		2-NEGATIVE FOR STREP 3-NOT DONE 8-QUESTIONABLE 6-NO INFORMATION	41 MD'S RX OF STREP O-NOT TREATED	45 IF ABCOARDINGE, MAS PT. ON PROPHYLAXIS AT TIME?	50 # DAYS FROM ADEISSION TO REJISTRATION
	26 CHOREA 1 2 8 9	38 HIGHEST ASO IN HOSP.	1-RXed, NO DETAILS 2-RXed LESS THAN 10d 3-RXed 10d-NOT TAKEN	1-YES-REGULARLY 2-YES-IRREGULARLY 3-YES-REG NOT KNOWN	0
8-9 ACE ON ATMISSICH	27 ERYTHEMA MARGINATUM 1 2 8 9	0-≦50 TU	4-RXed IOd-TTAKEN 5-RXed lod-TAKEN 6-RXed IM	4-NO 7-NOT APPLICABLE 8-QUESTIONABLE	4-WOR APPLICABLE 7-WOR APPLICABLE 8-QUESTIONABLE
August marches. Como en faite a	28 SUBCULANEOUS NODULES 1 2 8 9	3-166	7-NOT A PPLICABLE 8-QUESTIONABLE	9-NO INFORMATION	9-NO INFORMATION
MAY AD EX HANN 31-01	≚100.4 8	1 0 0 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	AS WHERE SEEN FOR THES	46 RHD ON DISCHARGE?	51 PT CURRENTLY ON ACTIV REJISTRY?
13-15 # DAYS HOSP	30 ARTHRALGIA 1 2 8 9	8-≧833 9-NO INFORMATION	1-PERSONAL MD	Z-NO 7-NOT APPLICABLE 8-JUESTIONABLE	1-YES 2-NO 7-NOT APPLICABLE
	31 PRIOR KHD 1 2 8 9	x-NOT DONE	- 4-OTHER	9-NO INFORTATION	
16-22 CHART NUMBER	32 PROLONGED P-R ON EKG 1 2 8 9		7-NOT APPLICABLE 8-QUESTIONABLE 9-NO INFORMATION	47 DISCHARGE DX BY ICD? 1-390(400) s carditis	
23 DISPOSITION	33,7EC ≅ 12,000 1 2 8 9			2-391(401) c carditis 3-392(402) chorea	
1-JISCHARGE HOME 2-CONVALESCENT HOME 3-NTER	34 RECENT SCARLET FEVER 1 2 8 9			4-393-390(410-410) chronic RHD 6-OTHER	
4-OTHER 9-NO INFORMATION	35 ACUTE PHASE REACTION 1-INCREASED ESR ONLY 2-FOSITIVE CRP ONLY			7-NOT CODED BY ICD 8-QUESTIONABLE 9-NO INFOHMATION	
	3-BOTH POSITIVE 4-NEITHER POSITIVE 8-QUESTIONABLE 9-NO INFORMATION				
					1

a.	 1		and the second of
		10000000000000000000000000000000000000	

REFERENCES

- Acheson, R.M.: The epidemiology of acute rheumatic fever 1950-1964, J. Chronic Dis. 18:723, 1965.
- Ad Hoc Committee of the Council on Rheumatic Fever and Congenital Heart Disease: Jones Criteria (revised) for guidance in the diagnosis of rheumatic fever, Circ. 32:664, 1965.
- Allen, W.C., et al.: The magnitude of rheumatic fever and rheumatic heart disease in Missouri. Missouri Med. 62:835, 1965.
- Baum, D.: Rheumatic fever, Ped, Clin. N. Amer. 10:899, 1963,
- Besterman, E.: The changing face of acute rheumatic fever, Br. Heart J. 32:579, 1970.
- Bland, E.F.: Declining severity of rheumatic fever. A comparative study of the past 4 years. N.E.J.M. 262:597, 1960.
- Brett, B.: The prevention of rheumatic fever. Can. J. Pub. Health 63:486, 1972.
- Brownell, K.D., et al.: Acute rheumatic fever in children. Incidence in a borough in New York City. J.A.M.A. 224:1593, 1973.
- Collins, S.D.: The incidence of rheumatic fever as recorded in general morbidity surveys of families. Pub. Health Rep. Suppl. 198, 1947.
- Denny, F.W., et al.: Prevention of rheumatic fever: Treatment of the preceding streptococcal infection. J.A.M.A. 143:151, 1950.
- Dimitriu, C.G., et al,: Pathogenic significance and prognosis of rheumatic nodules. Rumanian Med. Rev. 19:8, 1965.
- Dunlap, M.B., et al: Subsequent health of former carriers of hemolytic streptococci, N.Y. State J. Med. 73:1875, 1973.
- Feinstein, A.R., et al.: The pattern of symptoms, pre-treatment interval, and prognosis of acute rheumatic fever, Ann, Int. Med. 57:563, 1962a.
- Feinstein, A.R.: The clinical patterns of acute rheumatic fever: A reappraisal. Medicine (Baltimore) 41:279, 1962b.



- Feinstein, A.R., et al.: Rheumatic fever in children and adolescents, A long-term epidemiologic study of subsequent prophylaxis, streptococcal infections, and clinical sequelae. I thru VII. Ann. Int. Med. 60,Suppl. 5:6, 1964.
- Feinstein, A.R., et al.: Discontinuation of anti-streptococcal prophylaxis. A double-blind study in rheumatic patients free of heart disease, J.A.M.A. 197:949, 1966.
- Feinstein, A.R.: The natural histories of rheumatic fever. Bull. Rheum. Dis. 17:423, 1966.
- Ferencz, C.: Rheumatic fever; A changing disease. Med. Times 97:112, 1969.
- Findlan, C.: Rheumatic fever and rheumatic heart disease on campus 1956-1969. J. Am. Coll. Health Assoc. 19:131, 1970.
- Goldring, P., et al.: Rheumatic fever--1967. Med. Times 96:635, 1968,
- Gordis, L., et al.: Studies in the epidemiology and preventability of rheumatic fever. I. Demographic factors and the incidence of acute attacks. J. Chron. Dis. 21:645, 1969a.
- Gordis, L., et al.: Studies in the epidemiology and preventability of rheumatic fever. II. Socio-economic factors and the incidence of acute attacks. J. Chron. Dis. 21: 655, 1969b.
- Gordis, L., et al.: An evaluation of the Maryland rheumatic fever registry, Pub. Health Rep. 84:333, 1969c.
- Gordis, L., et al.: Prevention of rheumatic fever revisited. Ped, Clin, N. Amer. 18:1243, 1971.
- Hall, P.: On the prognosis and natural history of acute rheumatic fever and rheumatic heart disease. A study based upon a 25-year material in a Swedish town served by a single hospital. Acta Med. Scand. 169, Suppl. 362:1, 1961.
- Hedley, O.F.: Rheumatic heart disease in Philadelphia hospitals, Pub. Health Rep. 55:1647, 1940,
- Johnson, E.E., et al.: Rheumatic recurrences in patients not receiving continuous prophylaxis. J.A.M.A. 190:407, 1964.

- Markowitz, M.: Rheumatic Fever, Clin. Proc. Child. Hosp. D.C. 25:268, 1969.
- Markowitz, M.: Eradication of rheumatic fever: An unfulfilled hope, Circ, 41:1077, 1970.
- Markowitz, M. and Gordis, L.: <u>Rheumatic Fever</u>. W.B. Saunders Co., Phila., 1972.
- Massell, B.F., et al.: Evolving picture of rheumatic fever. Data from 40 years at the House of the Good Samaritan. J.A.M.A. 188:287, 1964.
- Mayer, F.E.: The declining severity of first attacks of rheumatic fever. Amer. J. Dis. Child. 105:146, 1963.
- McCue, C.M.: Acute rheumatic fever in 1969. Med. Times 98: 89, 1970,
- Noble, R.C., et al.: Post streptococcal diseases I. Acute rheumatic fever. J. Ky. Med. Assoc. 70:931, 1972.
- Okuni, M.: Problems in the clinical application of the revised Jones diagnostic criteria for rheumatic fever, Jap. Heart J. 12:436, 1971.
- Parker, W.G.: The Michigan Rheumatic Fever Study: Clinical characteristics of children attending MDPH sponsored cardiac field clinics. Mich. Med. 68:795. 1969.
- Paul, J.R. and Deutch, J.V.: <u>Rheumatic Fever in Connecticut:</u> <u>A General Survey.</u> Conn. State Dept. of Health, Hartford, Conn., 1941.
- Quinn, R.W., et al.: The incidence of rheumatic fever in metropolitan Nashville 1963-1965. Pub. Health Rep. 82: 673, 1967.
- Quinn, R.W., et al.: Mortality rates for rheumatic fever and rheumatic heart disease 1940-1965. Pub. Health Rep. 85: 1091, 1970.
- Rammelkamp, C.H., et al.: Studies on the epidemiology of rheumatic fever in the armed services. In: Rheumatic fever. A symposium, page 72. Ed. Thomas, L. Univ. of Minn. Press, Minneapolis, 1952.



- Rammelkamp, C.H. Jr., et al.: The latent period before the onset of acute rheumatic fever. Yale J. Biol. Med. 34: 386, 1961.
- Rosenthal, A., et al.: Rheumatic fever under three years of age. Ped. 41:612, 1968.
- Saksena, P.N., et al.: Rheumatic fever. Clinical and epidemiological considerations. Ind. J. Ped. 36:1, 1969.
- Saslaw, M.S., et al.: Case registry for rheumatic fever in greater Miami, Florida, Pub. Health Rep. 77:17, 1962.
- Saslaw, M., et al.: The cost of rheumatic fever and of its prevention. Amer, J. Pub. Health 55:429, 1965.
- Siegel, A.C., et al.: Controlled studies of streptococcal pharyngitis in a pediatric population. I. Factors related to the attack rate of rheumatic fever. N.E.J.M. 265:559, 1961.
- Sievers, J., et al.: The incidence of acute rheumatic fever. Br, Heart J. 33:833, 1971.
- Sitaj, S., et al.: Some aspects of epidemiology and surveillance of rheumatic fever. Acta Rheum. Scand. 16:30, 1970.
- Slater, J.D.: Acute rheumatic fever in young men: A clinical and epidemiological study. Ann. Rheum. Dis. 18:285, 1959.
- Spagnuolo, M., et al.: The risk of rheumatic fever recurrences after streptococcal infections. Prospective study of clinical and social factors. N.E.J.M. 285:641, 1971.
- Spector, A.J.: Measurement of the incidence of acute rheumatic fever: A methodological study. Amer. J. Pub. Health. 58:1950, 1968.
- Spinelli, N.P.R., et al.: Operation of a cooperative statewide rheumatic fever prevention program. Amer. J. Pub. Health 51:2, 1961.
- Stamler, J.: Cardiovascular diseases in the United States. Amer. J. Cardiol. 10:319, 1962.
- Stollerman, G.H.: Factors determining the attack rate of rheumatic fever. J.A.M.A. 177:823, 1961.

- Tahernia, A.C., et al.: Some clinical observations on rheumatic fever in childhood, Patterns of the disease as seen in southern Iran. Clin, Ped. (Phila.) 10:530, 1971.
- Taranta, A.: Factors influencing recurrent rheumatic fever. Ann. Rev. Med. 18:159, 1967.
- Teagle, R.F.: Why report rheumatic fever? J, Ky, Med. Assoc. 61:1066, 1963.
- Waly, F., et al.: Rheumatic fever under three years of age. W. Va. Med. J. 67:181, 1971.
- Wee, A.S., et al.: Acute rheumatic fever and carditis in older adults. Lancet 2:239, 1966.
- Wenger, N.K.: Rheumatic fever without clinical evidence of carditis. G.P. 36:106, 1967.
- Whittemore, R.: The effectiveness of an oral rheumatic fever secondary prevention program over eighteen years. Proc. IV World Cong. of Cardiol., New Delhi, India, Oct., 1966.



YALE MEDICAL LIBRARY

Manuscript Theses

Unpublished theses submitted for the Master's and Doctor's degrees and deposited in the Yale Medical Library are to be used only with due regard to the rights of the authors. Bibliographical references may be noted, but passages must not be copted without permission of the authors, and without proper credit being given in subsequent written or published work.

This thesis by has been used by the following persons, whose signatures attest their acceptance of the above restrictions.

NAME AND ADDRESS

DATE