EDITORIAL

Rheumatic fever: the way it was

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THE RECENT OUTBREAK of rheumatic fever in Utah brings to mind the fact that a new generation of physicians has arrived who have never seen this disease, and to today's medical students a discussion of chorea seems irrelevant. But it has not always been this way.

In the 1920s, rheumatic fever was the leading cause of death in individuals between 5 and 20 years of age and was second only to tuberculosis in those between 20 and 30. In 1938 there were more than a thousand deaths in New York City alone and 8% of the autopsies at the Presbyterian Hospital showed specific lesions of the rheumatic state. In New England, childhood rheumatism accounted for nearly half of adult heart disease, and in Boston's crowded North End hardly a family was spared; even the well-to-do were not immune.

The only treatment was salicylates and bed rest. The majority remained at home for weeks, more often for months, with a smoldering illness while the sicker children were managed in foster homes. In several large cities, special institutions took over the care of the chronically ill: the House of Good Samaritan (locally, the "HGS") in Boston (figure 1), Irvington House in New York, Larabida in Chicago, and Taplow outside London.

At the HGS, which had a capacity of 80 beds, 3500 children and adolescents were hospitalized during the four decades from 1921 to 1961. The usual stay was 3 to 6 months. In 1927 a research unit was established there under the late Dr. T. Duckett Jones (figure 1, inset) where he began his life-long study of the disease. In 1931, I joined in this endeavor and for the next two decades we followed, with the help of Benedict Massell and others, the course of the disease in this population. In particular, we set aside the original 1000 patients (admitted between 1921 and 1931) for special study and at the end of 20 years rendered a report. It was from this and other collateral studies that Dr. Jones formulated his guidelines for diagnosis now accepted as the "Jones criteria."

By 1930, the role of the streptococcus had been established by Coburn and others as the initiating agent of a disease process not well understood then or even now. As the decade advanced there were signs that the disease might be waning a bit.

However, with the advent of World War II, a formidable problem arose for the military in that with the hurried build-up of the armed forces, the assemblage of large groups provided an ideal setting for the spread of respiratory infections and epidemics of rheumatic fever. For example, at some air bases the incidence of rheumatic fever in 1943 was in excess of 25 per 1000 troops, and during the peak of the season one large post experienced rates in excess of 100 per 1000 troops. Fortunately, by this time the sulfonamides were available, and it was soon shown that they could repel an outbreak and protect 85% of susceptible recruits from infection. From this early experience in the training camps, concern was felt for the Army overseas, but subsequent reports indicated that no similar epidemics were encountered and no mass protection was undertaken.

After the war and by midcentury, the incidence and the severity of rheumatic fever had abated dramatically. At that time Paul reviewed the extensive mortality rates from the United States, Canada, England, and elsewhere and found this to be widespread and probably worldwide. Our own observations were in accord and furthermore showed that this favorable trend antedated the antibiotic era. The extent of this decline is indicated by figures from the HGS; of the first 100 admissions in 1921, eight were dead by the end of the first year and 24 had died by 5 years, whereas comparable figures for 1951 were one and three, respectively.

The clinical picture

It has been said rheumatic fever is a disease that "licks the joints and bites the heart." However, it was Cheadle who, a hundred years ago, recognized the disease as one of systemic proportions, and in his Harveian lecture of 1889 he clearly pointed out its

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widely involved in many structures beyond the joints and heart. Equally important, he admonished that "the rheumatism of childhood exhibits a marked contrast to the disease as it is seen in adult life." Incidentally, he also apologetic for choosing as his topic a disease so commonplace in 19th century London. But, as it was in Cheadle’s day, so it continued in the early decades in the United States, where the usual picture was that of a sickly child who, after a succession of respiratory infections, failed to thrive with pallor, poor appetite, mild fever, joint and muscle pains, and often nosebleeds. The diagnosis was often unsuspected until the appearance of the telltale systolic murmur of mitral regurgitation.

The sequence of tonsillitis and a latent period, followed in a week or two by the clinical syndrome, is now a well-recognized feature of the disease. These events are shown in figure 2, which is the bedside chart of a 13-year-old boy who had recovered from recent rheumatic fever. While awaiting discharge, he developed acute pharyngitis, fever briefly, positive throat cultures, a progressive rise in sedimentation rate and antistreptolysin titer and, after a 10 day interval, severe rheumatic fever. In 2 weeks the child was dead with carditis, pericarditis, and congestive heart failure—all too often the course of events in the preantibiotic era.

After the usual respiratory infection, the distinctive features of rheumatic fever were as follows:

1. Pain, the most common presenting symptom either as arthralgia or arthritis, occurred in 80% of our series. The arms and the legs and especially the joints were the usual sites of discomfort, and in young children it was often mild and mistaken for "growing pains." The severe migrating polyarthritis traditionally attributed to the disease is far more characteristic in adults than in children, and of all the symptoms of rheumatic fever pain in the joints is the most satisfactory to treat; if it does not subside in a few days on salicylate therapy the diagnosis of rheumatic fever is unlikely.

FIGURE 1. The House of The Good Samaritan in Boston with 80 beds, where 3500 children and adolescents were hospitalized with rheumatic fever between 1921 and 1961. Inset, Dr. T. Duckett Jones (1899 to 1954), founder of the research department and director for 25 years.

FIGURE 2. Bedside chart of a 13-year-old boy showing the usual sequence of sore throat, latent period, rheumatic fever and, in this instance, death.
Pain elsewhere is common, usually deep and aching in the precordium or pleuritic-like in the chest. When deep with tenderness in the abdomen, it can mimic appendicitis precisely and on rare occasions has even required surgery for clarification.

(2) Carditis is the most serious and unequivocal manifestation of rheumatic fever. When present it is usually detected early with the appearance of characteristic murmurs, the first clue being an apical systolic blow but with progressive dilatation of the heart; diastolic murmurs and a gallop rhythm are common.

In the first 1000 patients in our series, there were 653 who began their rheumatic fever with carditis, and at the end of 20 years 301, or nearly half, had died; in 90% the cause of death was related to the heart. On the other hand, in a smaller number (108) all signs of valvular disease disappeared.

(3) Chorea, present in nearly half of our patients, is the most bizarre and least well understood manifestation of the rheumatic state (figure 3, B). It is an affliction primarily of childhood, with a high predilection for girls, and is apt to appear late in convalescence when other signs of rheumatic activity have abated. It begins as an unusual form of nervousness or awkwardness, which is often first noted at school and usually becomes more pronounced later as purposeless jerking movements of the arms, legs, and face. It may even affect the speech, and sometimes physical restraint is required. The grips are firm but poorly sustained, the protruded tongue is retracted abruptly in reptilian fashion, and the peripheral reflexes are hyperactive. In sleep, no matter how violent the movements have been, all is quiet. Occasionally chorea is the only manifestation of the rheumatic state, so-called pure chorea. There are no known neurologic sequelae, but 20 years later one-fourth of those who had pure chorea have quietly developed mitral stenosis.

(4) Nodules are another curious manifestation of the rheumatic state limited to childhood (figure 3, A). They are small pea-sized structures, sometimes larger, non-tender, and present in about 10% of cases. They appear on the tendon sheaths at the elbows, knees, ankles, and fingers and often over the occiput. They ultimately disappear completely and are often overlooked unless sought specifically. Their presence signals severe rheumatic fever, cardiac involvement, and a protracted course.

(5) Rash of the erythema marginata type is occasionally seen (8%). It is pale pink, nonpruritic, usually evanescent, and nondiagnostic but is helpful in supporting the diagnosis in questionable cases (figure 3, A).

(6) Epistaxis occurred in one-third of our patients, often requiring packing but rarely transfusion.

(7) The erythrocyte sedimentation rate (ESR), antistreptolysin titer, electrocardiogram, and roentgenograms are useful adjuncts. In particular, the ESR was essential in monitoring to quiescence subsiding rheumatic fever, and when back to normal physical activity could be allowed again.

(8) Fatal rheumatic fever is usually the outcome of a protracted illness. In 250 fatal cases the duration of the terminal illness extended over a period of months before the patient succumbed to an exacerbation of toxic symptoms with increasing signs of right heart failure. Less often the initial attack progressed to a fatal termination in as little time as 3 months in three

FIGURE 3. A, The frontispiece from Cheadle's book; a sketch from life of a 4 1/2 year old boy showing nodules and rash (faintly). B, The arm and facial contortion of a young boy with chorea. C, One of five groups of chronically ill children who spent the winter in Florida. Six months later they were much improved.
of our patients and within 6 months in 25 others. In a few instances, a fulminant recrudescence was fatal in as short a period as 10 days (figure 2). It is of some interest that of the so-called major manifestations, chorea was present at the end in only two cases and arthritis in none.\footnote{The technique used was suggested by the late Granville Bennett (pathologist). Shortly after early quick fixation, the specimens were photographed under fluid to avoid glistening highlights, the fluid being alcohol to restore the natural colors.}

Pathology

The pathology of fatal rheumatic fever is consistent and specific. Initial inspection usually reveals petechiae 1 to 2 mm in size scattered over the pericardium, pleura, and sometimes the peritoneum as the first indication of the hemorrhagic nature of the disease. However, its stark pathology is shown in figure 4. These photographs were taken by the author during the rampant years, circa 1935, when the death rate at the HGS was one a month.*

In panel A is a view of the mitral valve apparatus from an adolescent who died 5 years after his original attack. The atrial wall is scarred, the valve cusps are dense and curled, and the chordae are thickened and somewhat adherent. Also present but not well seen were fibrin-platelet aggregations along the valve margins, pinhead in size, characteristic of the acute terminal phase of his illness.

In panel B is shown pericarditis of an unusual severity. This patient, an older adolescent with longstanding disease, died of rheumatic fever and congestive heart failure. In addition to the scarred valve, the deformed chordae, and the thickened ventricle, the striking finding was the extensive involvement of the pericardium with strata of hemorrhage interspersed with layers of fibrin, but with only a modest amount of fluid. One would have suspected that, in this instance, if the patient had reached adulthood pericardial constriction and possible tamponade would have ensued. However, such has not been the fate of a single patient among the 301 deaths in our 20 year series.

In panel C is a cross section showing the distinctive feature of the “rheumatic lung,” namely hemorrhage. In fulminant cases it was a common finding superimposed on congestive changes. The areas of hemorrhage were usually discrete, spotty, and bilateral, about a centimeter in size but at times confluent and even involving a lobe. The clinical counterpart of this entity was described by Paul\footnote{14} in 1928 as a flabby pneumonitis without specific sputum or hemoptysis.

In panel D is a cross-section of the liver, which shows spotty hemorrhagic lesions similar to those in the lung. Strangely, however, terminal jaundice was rare.

The myocardial lesions were studied in 40 patients who died in the hospital of fulminant rheumatic fever.\footnote{Infiltration with lymphocytes, monocytes, and fibrous tissue was present in 95% and Aschoff bodies in 72%. A lesser number showed neutrophils and eosinophils.} In this particular study these lesions were compared with 40 biopsy specimens of the atrial appendage removed at operation for mitral stenosis at the Massachusetts General Hospital. There were two surprising findings: the high incidence of Aschoff bodies in the surgical specimens (55% in our series, as high as 75% elsewhere) and the remarkable similarity of the lesions in the two series. Actually, from a pathologic standpoint the only real difference was the higher incidence of Aschoff bodies in the fatal cases, findings that lend credence to the old maxim “once rheumatic, always rheumatic.”

Treatment

Salicylates and bed rest were standard for years and diuretics were helpful in those with congestive heart failure, digitalis less so. At one time ascorbic acid in large doses (1 g four times a day) seemed to have a mild anti-inflammatory effect. Finally, a change of climate was tried by Coburn in 1929 and by the HGS in 1930. The former transported 10 patients from New York to Puerto Rico for the six winter months and noted a modest improvement. The HGS study was more extensive and involved sending four to six children per year to Miami over a 5 year period. A total of 26 patients were involved. In Florida, they improved to some degree where infections were less prevalent, but three of the group died there of recurrent rheumatic fever. In essence, the study was impractical, expensive, and not very illuminating.\footnote{The first breakthrough in therapy came in 1935 with the introduction of the sulfa drugs (initially prontosyl) by Domagh\footnote{17} in Germany. These quickly became effective in controlling streptococcal infections and in preventive programs. However, it was not until 1942 with the arrival of penicillin that a truly effective agent was available. Finally, in 1949 Hench and Kendall at a memorable meeting of the “Young Turks” (American Society for Clinical Investigation) in Atlantic City reported their discovery of ACTH (adrenocorticotropic hormone) and its remarkable anti-inflammatory action in rheumatoid arthritis.\footnote{18} Shortly thereafter we were able to obtain from them a small amount of this new material, just enough to treat one patient. We chose an 11-year-old girl at the HGS desperately ill with fever, rapid
ESR, arthritis, nodules, pericarditis, cardiac dilation, gallop rhythm, and congestive heart failure. Under these circumstances it seemed unlikely that she could long survive. She was started on full doses and the response was immediate (figure 5). The following day her temperature was normal, in 2 days her arthritis was gone, the pericardial rub and gallop disappeared in 4 days, and by then her heart size by roentgenogram was almost back to normal (figure 5). Her appetite and sense of well-being returned and the nodules were gone in 6 weeks (they usually last 4 to 6 months).

Never before had we seen such a dramatic response. However, all was not perfect. Toward the end of a month, extensive acne appeared together with moonshaped facies to an extent that her parents hardly recognized her. Fortunately, in due time these side effects subsided and her heart remains normal in size with only a faint systolic murmur at the apex. Such is the saga of the first patient to receive ACTH therapy for rheumatic fever. Since then the role and the limitations of the corticosteroids have been well documented and their value, especially in severe cases, established.19

Conclusion
In recalling the fateful years of this disease, one remembers with gratitude the notable contributions of the HGS in giving hospital care (mostly free) and providing the facility for the study of a single disease in so many for so long. And from this long association came the opportunity to share in a number of so-called “firsts.” Many a Harvard graduate looks back with nostalgia to the HGS wards where they, as second-year students, experienced for the first time the thrill of “hearing a murmur,” and it was from these wards that Jones devised his “Criteria for Diagnosis.”

In 1923, Cutler and Levine chose their first patient for valvulotomy—a 12-year-old girl from HGS with severe mitral stenosis who survived nearly 5 years after the operation.20 Six subsequent attempts failed and the procedure was abandoned; 25 years elapsed before valvulotomy became a notably successful operation, only now being supplanted in part by balloon valvuoplasty.

Next, in 1948 just before the era of valve surgery, we were beset by a small but special group of young adults, mostly women, with tight mitral stenosis and recurring

![FIGURE 4. A. The mitral valve apparatus 5 years after rheumatic fever with a terminal recurrence (see text). B. An unusual degree of pericarditis in a patient with fatal rheumatic fever. C. The “rheumatic lung,” a common finding in fulminant cases. D. Cross-section of the liver showing spotty hemorrhages reminiscent of the pulmonary findings.](https://circ.ahajournals.org/doi/10.1161/01.CIR.106.7.1194)
bouts of pulmonary edema often accompanied by hemoptysis at the time of their menstrual periods (so-called vicarious menstruation by our elders). Moved by urgency and frustration, we asked Richard Sweet (an eminent surgeon) if he could devise a spilloff from the congested pulmonary veins into the less tense and more capacious systemic circulation. He suggested a shunt into theazygos vein near thehilus of the right lung. Hence, a 17-year-old girl at the HGS who had nearly succumbed on several occasions was the first of 14 to undergo the procedure. There were no fatalities and all were improved. Fortunately, however, this palliative procedure was soon replaced by definitive operations on the valve itself.

Lastly, in 1949 as noted previously, the first child to receive ACTH for rheumatic fever was at the HGS.*

*This once stately and venerable institution (founded in 1860) has now been razed and replaced by an extension of the Brigham and Women’s Hospital.

Thus, as one contemplates the future and ponders why this remarkable demise of rheumatic fever has occurred in our world, there is hope for those in less favored regions where it is estimated that 15 to 20 million new cases per year are to be expected.22

What is the answer? No one knows, but it is clear that our times are better and our defenses stronger. Maybe the streptococcus is less aggressive or the host more resilient. Whatever the answer, there are still a few who believe in miracles.

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