CHOREA AS A MANIFESTATION OF RHEUMATIC FEVER: A LONG-TERM PERSPECTIVE

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Chorea, a common manifestation of rheumatic fever, is still a mysterious entity. Its clinical features are curious, its pathology is ill defined, and the efficacy of treatment is problematical.

We are reporting herewith a long-term perspective of this disorder as a sequel to an earlier report by Jones and Bland in 1935 based on the study of 1,000 children and adolescents followed since the 1920's.[1, 2] In addition to these data from this group other features of the illness have become apparent from collateral observations over the intervening years on a larger number of patients at the House of the Good Samaritan in Boston.

A feature of chorea of considerable interest and importance is its characteristic late appearance in the sequence of other rheumatic fever symptoms. In the majority of patients it appears as a delayed manifestation of rheumatic activity when other signs of the disease have abated or actually disappeared. This feature is well shown by the clinical chart illustrated in Figure 1. This eleven-year old boy developed severe rheumatic fever after a streptococcal throat infection (and probable scarlet fever), which was in turn followed by fever, arthritis, nodules and carditis. During four months of hospitalization he made a good recovery, only to develop chorea in the fifth month when all other measurable signs of activity had subsided. This late appearance of the central nervous system manifestation of rheumatic fever is so characteristic that it may have some subtle meaning as yet unclear in terms of tissue resistance or immunity, but the constancy of this relationship in the rheumatic fever sequence is almost as striking as the initiating streptococcal infection.

In the four decades since 1921 over 3,000 patients under the age of twenty with rheumatic fever have been hospitalized at this institution in Boston. The incidence of chorea and carditis in this group is shown in Table 1.

From this table it is to be noted that chorea occurs in about one third of children with rheumatic fever (1,057 cases) and that in a considerable number of these patients this neurological disorder is the only manifestation of their disease (382 cases), so-called pure chorea.

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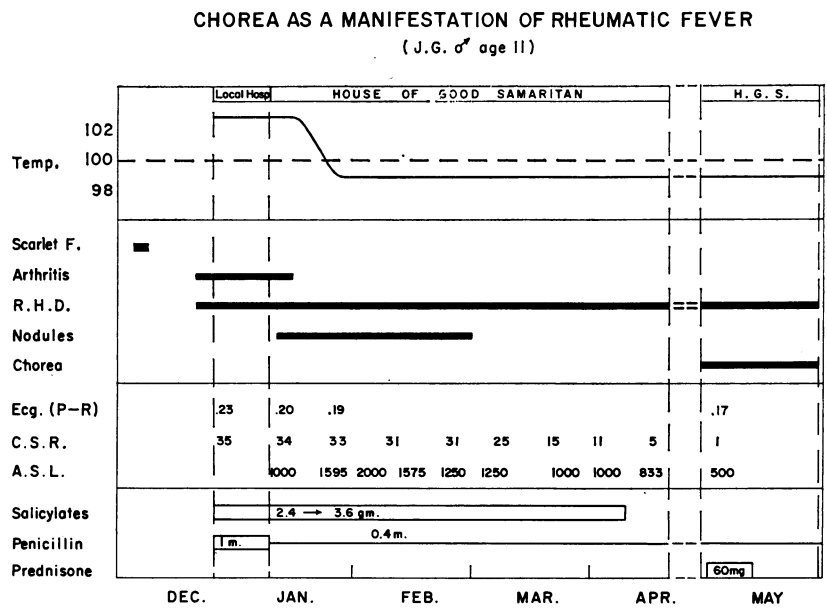

FIG. 1. Clinical chart showing the characteristic late appearance of chorea in the rheumatic fever sequence.

In our report in 1935 we noted the very small incidence (3%) of heart disease in this special group with pure chorea, and this clinical feature has been confirmed in the larger series reported herewith (4.7%). This is in striking contrast to the much higher incidence when chorea is accompanied by other signs of rheumatic disease. Our main purpose in this report is to present a follow-up of our original patients with pure chorea in terms of the insidious appearance of heart disease many years after the original illness. Our data are complete for the first twenty years and in the near future will be completed for a full three decades of follow-up.

TABLE 1

Chorea and Carditis in Rheumatic Fever Patients

(3,365 Patients—1921–61)

	Pure Chorea	Chorea and Rheumatic Fever	Rheumatic Fever
	(12%)	(21%)	(67%)
Cases	382	698	2,285
R.H.D.*	18 (4.7%)	467 (67%)	1,585 (70%)

* R.H.D. = rheumatic heart disease

TABLE 2

Delayed Appearance of Rheumatic Heart Disease After Pure Chorea: 163 *Cases**

	At the time of chorea	Years after onset			
		1–5	6–10	11–15	16–20
R.H.D.	6	3	10	10	9
Cumulative per cent	3.4	5.5	11.6	17.8	23.3

* Originally reported by Jones and Bland, J.A.M.A., 1935

In Table 2 is presented the incidence of the delayed appearance of rheumatic heart disease after pure chorea.

It is to be emphasized that the insidious development of the signs of rheumatic heart disease (usually mitral stenosis) has occurred under our continued observation in over one fifth of this special group without at any time measurable evidence of rheumatic activity other than pure chorea (recurrent in about one half). Our as yet incomplete data indicate a similar trend in the third decade of follow-up.

Summary

Two features of chorea of clinical importance have been presented.

(1) The delayed appearance of this central nervous system manifestation of rheumatic fever is emphasized. The significance of this characteristic sequence is still unclear.

(2) Rheumatic heart disease is uncommon in patients with so-called pure chorea but in a considerable number it evolves later in the form of mitral stenosis.

REFERENCES

1. Jones, T. D., and Bland, E. F. Clinical significance of chorea as a manifestation of rheumatic fever. *J.A.M.A. 105:* 571, 1935.
2. Bland, E. F., and Jones, T. D. Rheumatic fever and rheumatic heart disease: a twenty-year report on 1000 patients followed since childhood. *Circulation 4:* 836, 1951.

DISCUSSION

Dr. Francis C. Wood (Philadelphia): Do these patients take penicillin prophylactically?

Dr. J. B. Vander Veer (Philadelphia): I was interested in this subject as an intern in Montreal. We had many cases of severe rheumatic heart disease and severe rheumatic fever and shortly after entering on the medical ward service I had a 16 year old girl with severe chorea. It was called, I think, the "maniacal form," which they occasionally saw. She had had previous attacks of chorea. This patient lived only a few days and I remember she had to be shackled to the bed. We didn't, of

course, have the benefit of antibiotic therapy and recurrent infection may have played a part in her death. A post mortem was obtained and great interest was aroused. Dr. Wilder Penfield and others were there. Dr. Lawrence Rhea did the post mortem. He was interested in this field and later reported on cases with peritoneal, pleural and pulmonary involvement in rheumatic infections.

It was decided that this was chorea. There were perivascular lesions which were either typical or in keeping with this and I would guess that the sections might still be available at the Montreal General Hospital Pathology Department.

We are certainly indebted to Dr. Bland for bringing us up to date on this subject. As a student it was our idea that chorea was one of the mild manifestations of a rheumatic infection. We certainly didn't see much of it in the Midwest where I went to medical school. In Montreal we saw severe rheumatic fever and all of its manifestations. A common belief at that time was that patients with chorea frequently developed mitral stenosis but not aortic valve lesions. I wonder if this has been borne out by your study?

DR. MORTON HAMBURGER (Cincinnati): Have you followed up these patients in detail over this long period? Are you able to tell us if they did or did not have streptococcal infection?

DR. BLAND (Closing): First, Dr. Wood, about penicillin. Our studies date back to the 1930s and hence they were not on penicillin during the first decade of their disease. It was not available. We now have the policy of putting all patients even those with pure chorea on penicillin and maintaining it for an indefinite number of years.

I am very much interested in Dr. Vander Veer's remarks because of the pathology of this disease, and also its relation to pregnancy. In the past it was considered an absolute indication for the interruption of pregnancy. One rarely encounters chorea after the age of twenty, but occasionally when it did occur in the older group it was in connection with pregnancy. I have been trying to track down, Dr. Vander Veer, a case that is said to have occurred in Boston in 1922 which Dr. Charles Short remembers as a student because he wrote the patient up. This was a patient who was pregnant and developed chorea, had rheumatic heart disease and died with violent chorea. That is the one patient of which I have knowledge. In this connection I checked the records of the Boston Lying-In Hospital and within the last thirty years they have not seen chorea as a complication of pregnancy.

There is a very interesting observation by Osler who, as you recall, wrote a monograph on chorea and published it in 1894. I must say that I think most of his patients were selected from hospital records in Philadelphia. It is a little uncertain how many of these patients Dr. Osler actually saw himself, but for whatever it is worth, it was based on some 500 patients in the Philadelphia area prior to 1894 and he made the observation that of all the rheumatic fever manifestations he would rather not see chorea because it seemed to him to be associated with such a severe form of the disease and was so often fatal.

Since the time of these observations by Osler in 1894 there must have been some striking mutation of this disease in the subsequent decades.

Dr. Hamburger, would you repeat your question about the streptococci?

DR. HAMBURGER: Have you been able to follow these patients in sufficient detail to permit you to tell us whether they have or have not had streptococcal infections?

DR. BLAND: Not the early ones, but in recent years we have and I think in this connection there is the interesting report from Irvington House in which they found that if they went back far enough, three or four or maybe five months, they could demonstrate streptococcal activity which initiated the process. Thus, if we went

back to January in the clinical chart of the boy I showed we could certainly relate his subsequent course to the streptococcal infection four or five months ago.

In closing, I would like to quote you a short paragraph which has to do with the pathology of this disease and those who have been most interested have been the neuropathologists in England where Buchanan, and Greenfield have searched exhaustively the pathological material in England and Scotland and their conclusions were published in 1958:

"The histological findings in the central nervous system vary from case to case and include cellular infiltration of the brain, that is, perivascular and through all of its substance, loss of nerve cells from the cortex, basal ganglia and cerebellum and endarteritis.

"One picture which these findings seem to have in common is that they are widespread and not localized to any particular part of the central nervous system. Buchanan and others have therefore suggested that the abnormal movements originate in the cerebral cortex but only occur when the motor cortex is hyperexcitable, either congenitally or because of lesions in the circuits which normally modify the activity of the cortex."

In closing and in so far as we can tell there have been no residual neurological deficits as an aftermath of childhood chorea. The only finding that we connect with it is rheumatic heart disease, most often mitral stenosis.