A Clinical Study

ON

THE AVENUES OF RHEUMATIC INFECTION:

BASED UPON EXAMINATION OF 75 CASES OF SYDENHAM'S CHOREA.

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THIS study was undertaken in order to provide some data (with a view to rational treatment and prophylaxis) concerning the extent of the relation between rheumatic infection on the one hand and infective processes in the nose and throat on the other. The data put forward in it are based upon a personal and *ad hoc* examination of 75 cases of Sydenham's chorea, taken as they came; and no case has been admitted to the series if any doubt was felt as to the diagnosis.

My particular thanks are due, and I offer them, to Dr. Morley Fletcher, from whose service for diseases of children at St. Bartholomew's Hospital most of the patients were drawn, and who has helped me in many ways; also to Dr. A. E. Gow and Dr. E. A. Cockayne, Casualty Physicians to that hospital, who have been most kind in giving me access to a number of cases.

The Gravity of Rheumatic Infection.

The rheumatic affections, subacute rheumatism and chorea, constitute a graver menace to middle and later childhood than any other single disease process. Elmslie¹ has shown that more than half the deaths among children at the London County Council schools for the physically defective are due to heart disease; and it appears that some 86 per cent. of the cardiac anomalies to be met with at those schools are acquired affections.² Moreover, the *post-mortem* records of a children's hospital have shown³ that more children between the ages of 8 and 15 years die from heart disease than from any other single cause, not excepting tuberculosis. It must be accepted that rheumatic infection stands to middle and later childhood in a threatening relation not unlike that of epidemic diarrhoea and tuberculosis towards the first three years of life; and this merely on the score of present fatality. Yet no one needs to be reminded how small a part of the indictment against rheumatic infection is comprehended by its present fatality; nor how many are the victims of it who survive a childhood of intermittent invalidism with no other prospect than that of a brief and crippled maturity spent under the shadow of recurring failure of the heart. It would be difficult to exaggerate the mischief brought about by this infection.

The Present Position.

The extent of these depredations measures the extent of therapeutic failure; and it is a sense of the greatness of the failure which has prompted this attempt to collect some facts in order to clear the ground. For the present position of our efforts to combat rheumatic infection is unsatisfactory and anomalous. I submit that the sparring of bacteriologists as to the precise identity of the rheumatic agent has preoccupied clinicians to an undue extent. No serious person, I imagine, doubts any longer that the agent is a micro-organism of some kind; and if this be admitted, precise identification of it becomes a matter of secondary consequence. At all events, clinicians need not wait for this consummation before applying the common rule of conduct in the presence of infections—namely, to detect the avenue of infection, if possible, and by means of local treatment at the earliest moment to limit the mischief and obstruct its recurrence.

How do we stand as regards the detection of the avenue or avenues of rheumatic infection? I know of a good many physicians and surgeons who hold and teach that the tonsils are a common port of entry; the literature abounds with references to tonsillitis as a frequent manifestation of rheumatism, and with hints that in the tonsil we may have the starting-point of the infection. One

might expect the treatment of the tonsil to bulk large in the advice of our authoritative writers on rheumatic affections. Yet, with the single exception of Dr. Poynton,⁴ I have not met one writer in any of our leading textbooks on medicine who makes serious reference to the treatment of the pharynx. Written allusions to the importance of treating the naso-pharynx seem to be rare in medical literature generally; but of course they exist. Senator⁵ has written of the etiological relation between the nose and rheumatic arthritis. Menier⁶ has recorded "a case of chorea minor cured by the removal of adenoid vegetations." De Ponthière⁷ speaks of "the naso-pharyngeal origin of chorea." Turner and Stewart⁸ speak of hypertrophied tonsils as favouring relapse of chorea. And no doubt there are others. But it is a fact that there is no popular recognition of what so many individuals hold to be true—namely, that the infection of rheumatism gains access in a large majority of instances by way of the nose or pharynx. It seemed to me, therefore, that a collection of some facts might help to popularize this view, the acceptance of which, in my judgement, is of the greatest moment.

The Choice of Chorea for Investigation.

The origin of this investigation (if I may be permitted a brief retrospect which is not without relevance) was as follows: Some years ago, while conducting a routine examination of a school of some 500 girls for the London County Council, I met with 13 examples of acquired heart disease hitherto unsuspected. When the statistics came to be tabulated it appeared that I, having at the time no theory to establish, had recommended no fewer than 10 of the 13 for operative treatment on account of nasal obstruction or tonsillar hypertrophy. My attention was naturally engaged by the circumstance, and I set about collecting data concerning the relation of rheumatic affections to nasal and pharyngeal anomalies. But here arose the difficulty that, owing to the vagueness of articular manifestations in the rheumatism of childhood, it was frequently difficult to feel confident of the diagnosis. Moreover, even if the relation were as close as seemed likely to be the case, there was little hope of establishing the thing as a fact unless it were possible to examine a series of patients within a short interval from the beginning of symptoms; for manifestations seemingly so trivial as nasal catarrh and sore throat do not live long in the recollection, particularly of parents of the hospital class. This early examination proved to be unattainable, since the invasion of juvenile rheumatism is commonly so insidious that it is usual for weeks, and often months, to have elapsed between the commencement of symptoms and the bringing of the patient for treatment. I therefore turned to chorea as being a symptom more easily diagnosed with confidence, and one which might be expected to bring the patient before the doctor while the lesion giving entry to the infection was still in progress, or at all events in time to secure a record of such catarrhal or inflammatory antecedents as might have heralded the appearance of movements.

Relations of Chorea and Rheumatism.

It may be objected that Sydenham's chorea has not been proved to be a rheumatic manifestation. Undoubtedly, until the bacteriology of the two affections has been established demonstration must be lacking. But I think the circumstantial evidence no longer admits of reasonable doubt that the two are but different signals of one disease process. Every one admits that the relation is a close one, and some⁹ have long since declared for the unity of them. I myself had doubts before this inquiry, but they have been dissipated completely by the following considerations.

I.

The proportion of choreic children exhibiting, or having in the past exhibited, articular manifestations is put by various authors at figures ranging from 26 per cent. to 56 per cent.¹⁰ This high proportion, whichever extreme be taken, seems to admit of two solutions only. Either the diseases depend upon the same infection, or they depend upon two infections which, though distinct, are yet mutually favourable each to the other. Now, if the two were essentially independent, one would expect to see with great frequency pure cases of chorea free from borrowed rheumatic symptoms. As a fact, if inquiry be made, it is

relatively exceptional to meet cases of chorea lacking a well-defined history of pains in the limbs or joints. In the present series the results were as follows:

Reliable information in 67 cases.	
History of rheumatic fever or pains	71.5 per cent.
Doubtful history of pains	7.4 "
No pains...	20.8 "

Dr. M. Fraser's series of 300 cases at the Children's Hospital, Paddington Green,¹¹ is not dissimilar in effect.

Previous joint rheumatism	50 per cent.
Concurrent rheumatic fever or heart murmur	27 "
Total	77 "

Therefore, unless it be assumed that heart affections and pains in the limbs or joints are regular symptoms of pure chorea, or that chorea and rheumatism, though independent diseases, are yet incapable of appearing apart in more than from 20 to 30 per cent. of instances, one must conclude that the two are but varied manifestations of the same disorder. And of these three hypotheses the last is certainly the easiest to accommodate.

II.

If rheumatism and chorea be due to the same infection one might expect them to manifest the same seasonal characteristics. As a matter of fact, their seasonal prevalence is not identical. The data available for estimating the monthly incidence of chorea in this country are limited, I believe, to the charts given by Dr. Morley Fletcher, which relate to 574 cases only. Although these figures have not sufficed to produce an even curve, they show the tendency of chorea to become prevalent somewhat later in the year than does rheumatic fever. (See Chart.)

Chart of monthly incidence of rheumatic fever and chorea in London, expressed in percentage of mean monthly value. Dated from onset of symptoms. Chorea; 574 cases, adapted from Morley Fletcher, *St. Bartholomew's Hospital Reports*, vol. xxxii, p. 388. Rheumatic fever; 1,958 cases, adapted from Phillips, *Allbutt's System of Medicine*, vol. ii, part i, p. 600.

This discrepancy is susceptible of a simple and adequate explanation. Those who have examined carefully a number of cases of chorea will agree that there are commonly, if not always, two stages in the development of choreic movement. The first is a stage of potential (or, as Dr. Miller calls it, latent) chorea; the second the stage of frank movement. This prechoreic phase may endure for many weeks. It is marked by emotional irritability and fretfulness always; sometimes by obvious change in disposition; often by headaches and intellectual dullness; and is a pronounced and constant feature when it is looked for. It must be regarded as the index of some subtle factor at work upon the central nervous system. Given a nervous system thus disequibrated the moment of emergence of choreic movements becomes a matter partly of temperament, partly of chance; or, rather, a matter of the interaction between temperament and chance. For in such circumstances the most trifling emotional stress assumes a power of disturbance out of all proportion with its rights, and the more temperamentally unstable the child the lower is the limit of psychical stimulation competent to convert potential into active chorea. It is legitimate to speak in this dogmatic fashion, for the evidence

that psychical shock is an exciting cause of choreic movements is altogether too strong to be overlooked or credited to coincidence. Making allowances for the forgetfulness of the youthful patients and for the transiency (as far as overt manifestations go) of emotional outbreaks in early life, be they never so violent while they last, and making allowances also for the necessarily partial knowledge of parents in this particular, it is surprising how often a plausible story of precedent shock or abnormal excitement is forthcoming. In this series it was obtained in 41 per cent. of the cases offering reliable information on the subject. Further, the reality of this psychical relation is confirmed by the efficacy of isolation in abating the movements of choreic children who have failed to respond to mere rest in bed.

If it be admitted that emotion can, and does frequently, act as an exciting cause of choreic movement, we arrive at the following intelligible, and I think satisfying, conception of chorea. Just as the poison alcohol, or the tubercle bacillus, acts upon different susceptible individuals in different ways, attacking this tissue in one subject and that in another, so does the rheumatic infection exercise a selective action upon the tissues of those susceptible to it, venting itself mainly or wholly upon arthritic structures sometimes, sometimes upon fibro-tendinous tissues predominantly, sometimes upon the nervous system or parts of it. The subtle factor mentioned above as being responsible for the cerebral manifestations of the pre-choreic period is the infection of rheumatism (or its diffusible poison, as seems to me more likely) acting upon a specifically predisposed nervous system. It is only when the nervous system has been thus suitably prepared that the emergence of choreic movements becomes possible. Whether they will appear at all, and, if so, the moment of their appearance, are matters to be resolved by the chance incidence or absence of emotional stresses.

If the existence of a pre-choreic period be admitted—a period, that is to say, during which the rheumatic poison is slowly undermining the stability of the central nervous system—then the postponed prevalence of chorea as opposed to rheumatism becomes a witness for, rather than against, the essential unity of the two.

III.

The frequent occurrence of rheumatism and chorea in the same individual at the same time; their frequent appearance in the same individual at different times; their mutual interchangeability among the various members of a rheumatic or choreic stock; their common liability to be complicated by heart affections of identical and unique character—all these clinical commonplaces combine to supply a weight of circumstantial evidence for unity which is almost irresistible.

Pathology of Choreia.

The study of the material at my disposal has left me as completely convinced as anything short of actual demonstration can do that chorea is nothing more than a symptom led up to by the action of the rheumatic poison upon nervous tissues of an emotional, that is to say feminine, type. This conception agrees well with all the facts known to me concerning chorea, with one possible exception: I mean the undoubted fact that chorea is of more frequent occurrence among the poorer classes than among the well-to-do—a circumstance at first sight contrary to expectation. Yet it does not, I think, vitiate the conception. For the minor degrees of loss of health which are comprehended by the prechoreic phase, though they may fail to attract the attention of a hard-worked mother in the labouring class will not pass unnoticed in the case of children more favourably situated; with the result that whereas the prechoreic child of poor parents continues to be exposed daily to the efficient determining causes of choreic movement, the other is daily sheltered from them, and thus escapes more often than her poorer sister the final term in the series they have so far shared.

I think I cannot do better than conclude this section of the subject by citing a most suggestive history as regards this issue.

A man who has had rheumatic fever himself on three occasions has two daughters, aged 8 and 12 years respectively. The younger exhibits well-marked chorea and complains of pains

in the limbs, but is free from lesions of the heart. The elder complains of generalized articular pain and stiff neck, and has organic valvular disease of the heart, but is free from movements. Their history is as follows: Three months ago the younger girl developed a bad sore throat (severe enough to lead to the fear that it meant diphtheria), and movements one week later. She is described as very excitable, and is said to have had rheumatic fever at 3 years of age and chorea at 6. Two weeks after the onset of sore throat in the younger child the elder was similarly affected, and within a few days was attacked by articular pains and general stiffness but remained free from movements. This girl is described as being much less excitable than her sister. She has had two previous attacks of rheumatism, in her sixth and seventh years, but has never suffered from chorea.

On all these grounds I submit that the unity, as regards identity of the infection, of chorea and rheumatism is established beyond reasonable doubt, and that the following data concerning the naso-pharyngeal history and condition, though drawn from choreic patients, are applicable to the rheumatic infection generally, at all events during childhood.

General Considerations Relative to Paths of Infection.

Although it is probably true that an infecting agent can, on occasion, traverse an intact mucous membrane and subsequently excite a constitutional infection, it is nevertheless certain that in a vast majority of instances a local inflammation or breach of surface is a necessary intermediary. Sometimes the local lesion is pronounced, as happens with measles and scarlet fever; sometimes it is apparently trivial, as may happen with pyogenic infections and syphilis. But it exists wellnigh always. Now when we find, in the case of a common infective malady, that an immense amount of clinical observation has left the path of infection still obscure, we may be pretty certain either that the portal is some unobservable portion of the alimentary canal, or that entry occurs elsewhere under cover of some frequent and intrinsically insignificant phenomenon which has masked the more important mischief-maker. This statement has been proved to be true of malaria and the insect-borne diseases generally, and probably has a wide application. Under the circumstances which exist in this country, therefore, we are entitled *a priori* to suspect that the rheumatic infection gains an entry under cover of some common lesion of a mucous surface, and experience tells us that a sore throat is a frequent precursor of rheumatic fever. So both reason and observation make out a *prima facie* case in favour of the main thesis I am urging.

Naso-pharyngeal Data.

A. Of the 75 children, 21.2 per cent. had already been operated upon, at some time prior to the current attack of chorea, for the relief of "tonsils and adenoids." I am unable to say what proportion of ordinary school children of corresponding age and sex and class have undergone this operation. The medical officer to the Board of Education has stated, on the basis of five million examinations, that 8 per cent. of school children require it.¹² While I am confident that this is far too low an estimate, for London at least, and do not feel disposed to press the significance of this considerable proportion of previous operations among choreic children, I think the fact may be taken as unbiassed evidence that naso-pharyngeal anomalies of a pronounced kind are common among them. This evidence gains weight when one reflects how many children of this class escape operative treatment through the carelessness of their parents, however urgent be the call for it; and that if the operation has actually been performed in 21.2 per cent. of the cases one may look to find lesions calling for operation in a much larger proportion.

B. As regards nasal and pharyngeal inflammations of consequence, the following items were accepted as evidence:

1. Enlargement of the tonsils or tonsillar lymphatic glands in the neck.
2. Obvious mouth-breathing.
3. Excoriation of the nostrils, or pus in the nasal passages.

One or other of these manifestations existed in 88 per cent. of the cases, and often several of them together.

There is no standard available for strict comparison with this finding. Macleod Yearsley found,¹³ as a result of 1,246 examinations, that enlarged tonsils or adenoids were

present in 42.9 per cent. of school children, and this is the highest estimate I have met with.

The details making up the 88 per cent. are as follows:

1. Tonsils enlarged, including those previously operated upon	62 per cent.
2. Tonsillar glands enlarged	65 "
3. Existing inflammation of nasal passages (53 cases)—	
(a) Soreness or excoriation of anterior nares	11
(b) Pus in anterior nares	10
(c) Muco-pus streaming from naso-pharynx	6
Total	50 per cent.

I submit that on this evidence one is entitled to say that the active phase of the rheumatic infection is fairly consistently attended by inflammatory lesions about the naso-pharynx, whether there be a causal relationship between the two or not.

Inquiries as to this relationship yielded the following results.

A satisfactory antecedent history was forthcoming with respect to 52 attacks, 46 belonging properly to this series and 6 being previous attacks sustained by members of the series. Among these 52 there was a definite history of a closely precedent acute lesion of the nose or throat in 39, or 75 per cent. The details are as follows:

Closely precedent sore throat	36
" sore nose or nasal catarrh	12
" operation on tonsils	2
" scarlet fever (before this attack)	1
" attacks (before previous)	6
" attacks (before this attack)	5
" attacks (before previous)	1
" diphtheria (before previous)	2
" attacks (before previous)	1
" measles	1

It appears, therefore, that in a high proportion of instances with regard to which information is forthcoming, inquiry will elicit a history of closely precedent nasal or pharyngeal inflammation, sore throat being the commonest lesion, with some acute nasal affection as a good second.

Some Incidental Matters of Importance.

Firstly, it has been a frequent experience in the course of the collection of these data to find a blank denial given to the question as to precedent throat trouble, and yet to find on examination tonsils sometimes of enormous size. This suggests that historical evidence underestimates heavily the frequency of precedent throat affections sufficient in themselves to account for the entry of an infection by way of the tonsils, and also that the tonsillar inflammations productive of chronic hypertrophy are not necessarily painful to any great degree.

Secondly, excoriation of the anterior nares, often attended by scab formation on the inner aspect of them, is a fairly common event in chorea. My attention was not attracted to it until the series had advanced some distance, but when it was looked for it was found with tolerable frequency. Straton,¹⁴ in 1885, called attention to this conjunction, but I have found no later mention of it. He says that chorea in early life is characterized first by sores in the nostril or pharynx, malaise, blunted intellect, vague pains and swellings of the joints, some degree of paresis, and finally, disorderly movement. He instances three children attending the same school. One little girl had a sore nose, became stupid, developed a cardiac murmur and tender metatarsal joints, and finally chorea. Shortly afterwards another little girl exhibited precisely the same course of symptoms, ending in chorea. Presently the brother of the second child developed a sore nose, with a fissure at the anterior margin of the nares, and became more stupid than his sister, but never exhibited any movements. The choreic sequence, that is to say, was arrested in his case in the prechoreic phase. I believe this lesion is an important and not uncommon one, and has a definite relation to the entry of the rheumatic infection.

Thirdly, Authorities upon scarlet fever hold that chorea is a very rare sequel of this affection. Caiger¹⁵ does not mention it. Priestley¹⁶ puts the figure at 0.2 per cent., which gives a frequency for chorea among scarlet fever patients less, according to Osler,¹⁷ than that observed among patients at a general hospital. The matter is vital to my argument; for if it be the fact that chorea seldom follows scarlet fever, while rheumatism is known to do so

with moderate frequency, the fact would be almost conclusive evidence against the essential unity of chorea and rheumatism. In the present series only one of the current attacks could be brought into relation with immediately precedent scarlet fever. But there were five others, recurrent attacks, with regard to which it was convincingly stated that the first or (in one case) second bouts of chorea had followed close in the wake of scarlet fever. Fourteen of the 75 children had suffered from scarlet fever, and of them no less than 6 had developed chorea shortly after their return from the fever hospital. The discrepancy between these figures and those of the fever hospitals is explained by a consideration of the history of the only attack in the series which was closely associated with scarlet fever. The child returned from the fever hospital and was kept at home for three weeks, during which she exhibited no movements. She was then sent back to school, and the very next day was observed to be jerking herself about. It seems clear that the ordered placidity of a fever hospital exercised in her case, and presumably in the others, a sedative influence upon a nervous system already in a state of potential chorea, and that the withdrawal of this steadying influence combined with exposure to the chances of everyday life admitted the determining factor, emotional stress, which in the case of the child under discussion was provided by her first visit to school since her illness. There is no other assumption than this which will account for the otherwise singular fact that chorea should be actually rarer in a fever hospital than among the common run of hospital patients; but the fact chimes well with the conception of chorea given above.

Fourthly. It is quite certain that amputation of the tonsils is ineffectual for any other purpose than the removal of a physical obstruction in the airway. The tonsillar remains or tonsillar lymphatic glands were still enlarged in all but 3 of the 16 children previously operated upon, and of those 3, 1 had been treated by enucleation.

CONCLUSIONS.

1. That Sydenham's chorea and rheumatic fever are due to one and the same infecting agent.
2. That the action of the rheumatic poison upon a specifically predisposed central nervous system produces a characteristic nervous instability which may precede the appearance of choreic movements by some weeks, and may in other cases itself constitute the sole evidence of the choreic tendency, the phase of movements never becoming developed at all.
3. That the emergence of choreic movements is determined by emotional stimuli acting upon a central nervous system thus previously disequibrated.
4. That the commonest avenue of rheumatic infection is the tonsil, and next to it the nose.
5. That the first essential of rational treatment of rheumatic infection is restoration of the upper air passages to a healthy condition.
6. That irrigation and thorough cleansing of the nasal passages, combined with antiseptic treatment of the nose and pharynx, should be a routine item of antirheumatic treatment; and that the operation of enucleation should be performed without delay upon all rheumatic children who exhibit chronic enlargement of the tonsils or of the tonsillar lymphatic glands.
7. That chorea is a common sequel of scarlet fever, but that the appearance of movements is usually postponed until the patient has left the fever hospital.

STATISTICAL TABLE.

Total number of cases	...	...	...	75
Proportion of girls to boys	...	...	...	5.25 to 1
Average age	...	...	...	10 years
Family history of rheumatic fever or chorea				
(67 cases)—				
Father and mother	...	...	...	6
Father, not mother	...	...	...	9
Mother, not father	...	...	...	8
Total parental	...	...	...	23 (34.3%)
Brother, sister, uncle or aunt	...	...	...	15
Total with positive family history	...	...	...	38 (56.7%)
Colour of hair (59 cases)—				
Red or rufous	...	...	...	15
Not red or rufous	...	...	...	27
Total fair	...	...	...	42
Brown	...	...	...	8
Dark	...	...	...	9

Immediately precedent shock (51 cases)—			
Plausible history present in	...	...	41 %
Condition of heart (75 cases)—			
Normal in	...	...	30 (40%)
Organic disease in	...	...	25 (33.3%)
Doubtful murmurs in	...	...	20 (26.6%)
Relation to scarlet fever (67 cases)—			
No previous scarlet fever	...	...	53
Previous scarlet fever	...	...	14
No chorea or rheumatism as direct sequel			
Chorea as direct sequel	...	...	6
Rheumatism as direct sequel	...	...	2
Enlarged movable lymphatic glands along lower border of mandible, unexplained by condition of teeth or gums, in			
	...	...	4
Present condition with regard to tonsils and tonsillar glands of 15 cases previously operated upon by amputation—			
Tonsillar glands enlarged	...	...	13
Remnants of tonsil enlarged	...	...	7
Tonsillar region healthy	...	...	2

Table showing Age at Onset of First Attack of Chorea (70 Cases).

First attack occurred at—			
4 years of age in	2 cases.	11 years of age in	6 cases.
5	"	12	"
6	"	13	"
7	"	14	"
8	"	15	"
9	"	16	"
10	"		

Table of Recurrences (73 Cases).

The current attack was the first in	...	33 cases.
" second in	...	21 "
" third in	...	11 "
" fourth in	...	3 "
" fifth in	...	5 "

Percentage of recurrences = 54.7.

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A POSSIBLE TEST IN THE DIFFERENTIATION BETWEEN HUMAN AND BOVINE TYPES OF THE TUBERCLE BACILLUS.

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THE most reliable test which we possess in the process of differentiation between human and bovine tubercle bacilli is the inoculation of certain animals (most commonly the rabbit or the calf) with a small known quantity* of the organism under investigation. If the infection results in a rapid dissemination of the disease and the speedy death of the animal, it may be affirmed that the bovine bacillus in the organism present.

* The exact amount varies in the case of the rabbit; 0.01 mg. of the dried bacilli is the most suitable quantity (Royal Commission Reports).