Their chief argument against the toxæmic theory is that it is difficult to attribute an affection which may be unilateral to a general infection. I have attempted to show that owing to the unequal rate of development of the two sides of the brain unilateral incidence might be expected.⁴⁰ Poynton and Holmes were inclined to consider hemichorea as a result of a localised infection, but the cases investigated by them showed a generalised infection through the parts of the nervous system examined. My own view is that hemichorea could be equally well explained as the result of a general infection of the nervous system and of a general toxæmia, but their observations incline me strongly to the belief that infection plays the chief part.

If capillary embolism, or thrombosis, is ever the structural basis of chorea the explanation must be that the lesion has impaired the function of the mechanism of control. The infrequency of any pronounced permanent effects after recovery from chorea seems to argue against the view that vascular changes often take part in its production.

Importance of Fright.

Sturges looked on chorea as a disturbance of function without any gross structural change in the nervous system, and attributes to fright great importance as an ætiological factor. In 268 cases in which inquiry was made a history of fright was obtained in 66, but even this number included many in which there was great doubt as to cause and effect. Thus one child is said to have been frightened by a frog; another is said to have been awakened at night by a man shouting in the street and to have developed movement seven days later; another is said to have developed chorea because he was caned at school for fidgeting. To get 66 histories of fright out of 268 cases, such examples as these have to be included. Most children are frightened occasionally, and by the law of chance choreic children would not always escape. Fright undoubtedly exaggerates choreic movement, and consequently may at times be considered its cause without adequate reason.

To give an example of the extreme difficulty which may arise in estimating the relation of fright to chorea:

A girl, aged 11, who had previously been quite well, was chased by a goat; typical chorea, involving all limbs and the face, developed immediately, and she was admitted to hospital; a few days later she developed arthritis of the right elbow with pyrexia and evidence of mitral incompetence; she recovered after three months' treatment, but was readmitted to hospital one month after discharge with a relapse, this time without any history of fright.

Fright, or anxiety, is more easily connected with the development of chorea in older patients, especially those who have had previous attacks.

Thus a girl of 27, who had had two previous attacks of chorea, saw her step-father try to cut his throat; movements developed seven days later, but disappeared after a fortnight in hospital.

The chorea of pregnancy⁴¹ is often determined by anxiety, and the best proof of this is that the onset is commonly associated with quickening. Though fright or anxiety may often exaggerate chorea and cause a relapse in those previously attacked, yet I have not found it at all frequently as an important ætiological factor. The same may be said of overpressure at school, which is not infrequently accused of causing chorea. It is not good for a choreic child to attend school, but it is very difficult to get evidence that schooling is really responsible for making a healthy child choreic. Rheumatism appears to be by far the commonest cause of chorea, but it is not the only cause. Recently I have had under my care two patients with irregular spontaneous movements indistinguishable from those of rheumatic chorea, but developing other symptoms in the course of the disease which seemed to make it quite certain that they were suffering from lethargic or focal encephalitis.

If the views which I have urged with regard to the cause of chorea are correct we should, in diagnosing chorea, indicate by an adjective the supposed ætiology of the attack.

ACUTE RHEUMATISM IN CHILDREN

UNDER TWELVE YEARS OF AGE.¹

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AND

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IN this paper we record the results of a study at the Hospital for Sick Children, Great Ormond-street, of a severe outbreak of acute rheumatism in children under 12 years of age, which occurred between July, 1919, and June, 1920. Although we need only mention such eminent names as those of the late Dr. W. B. Cheadle, Sir Thomas Barlow, Sir Dyce Duckworth, and the late Dr. D. B. Lees to dispose of any idea that we are breaking new ground on this subject, we believe that by insisting on the gravity of this disease, and by indicating this gravity in definite terms, we shall do some service to the medical profession in this country. Such an attempt will be useful as a nucleus for a wider study of the disease, which we can hardly doubt will eventually be undertaken, for not only is rheumatism very rife in this country, but it offers the best opportunities we at present possess for the practical advancement of the treatment of heart disease.

We are not concerned here with the pathology or the treatment of rheumatism, and do not intend to enter upon the vexed questions that present themselves in a complete study of the disease. Our intention is to present the facts which this outbreak has provided—facts which we have collected during 12 months from the in-patient cases. The collection was a laborious undertaking, although the actual results have been comparatively small. Moreover, our research had obvious limitations, for during the year there must have been a considerable number of cases which, from lack of bed space, had to be treated in the out-patients or at home. Again, the age-limit of 12 years is an arbitrary one, determined by the hospital regulations. This, however, can be confidently stated: that the injuries done by this outbreak were sustained by those who had not even commenced the real struggle for existence.

Details of the Research.

Number of cases.—The total number of cases in the 12 months from July, 1919, to June, 1920, was 172; of these 84 were first attacks.

Sex-incidence.—A hundred and four were females and 68 were males, a proportion of about 3 to 2.

Locality.—Eighty cases came from North London, 47 from East London, 23 from West and South-West London, and 22 from outside the London area. The majority of all our cases came from North and North-East London.

Age-incidence.—We show two tracings on our chart (see Chart 1) to illustrate this point. The continuous

⁴⁰ Cf. Stanley Hall: Adolescence, vol. i., p. 149.

⁴¹ Cf. Wall and Andrews: Jour. of Obstetrics and Gynaecology, June, 1903.

¹ A paper read at the Medical Society of London on Nov. 22nd, 1920.

line shows the ages of all the cases at the time of their first attack of rheumatism: the interrupted line shows the ages on admission of all the cases during the 12 months. The former indicates a rapid rise in the age-incidence from 2 to 7 years, when the maximum of 31 cases is reached; then follows a steady fall to the twelfth year. The latter indicates that the maximum, again 31, has now moved from the seventh to the ninth year; this move is clearly explained by the fact that among the children admitted during the 12 months there were many recurrent attacks. This is a point of importance in the history of the disease.

Heredity.—The hereditary tendency cannot be so accurately determined in a series of hospital cases as in a series of private cases, such as was published by Dr. Cheadle, who found a family history in 58 per cent. of 180 patients. In our series the percentage was 40.

Seasonal incidence.—This was calculated from the earliest dates of the symptoms of the illnesses. In both first attacks and recurrent attacks the maximum was reached in December, 1919, and the minimum in March, 1920. November and December, 1919, were both bad months, and April, 1920, shows an outbreak of first attacks. On reference to the official meteorological reports we found that November was exceedingly cold, with frequent snow and hail, and that all December was rainy. Again, March, 1920, was exceedingly mild (the incidence of rheumatism at its minimum), but April was throughout wet and unsettled.

Results of the outbreak.—The result on leaving the hospital was as follows: Deaths, 15; chronic invalids, 17; cases of compensated heart disease, 70; recoveries, 70. Examination of these patients three months later in September, 1920, showed that the death-rate had risen to 22, the number of chronic invalids to 30, while cases of compensated heart disease had fallen to 58 and recoveries to 62. Thus in this outbreak nearly 13 per cent. died and over 17 per cent. became complete invalids.

Analysis of the 84 first attacks.—An analysis of the 84 first attacks will serve to introduce the various rheumatic manifestations of which heart disease, chorea, and arthritis are the outstanding examples, and lead us to the wider question of the details in the total number, 172. Of these 84 cases, 33 came under notice for chorea, 9 for arthritis, 5 for primary cardiac disease, and 37 for multiple manifestations. Thus it is apparent that the most frequent solitary manifestation of rheumatism is chorea, a point to which we shall allude again later. Twelve of these cases died.

The economic question.—We turn aside here for a moment to the economic side of the subject. Our medical beds in the hospital are 100 in number, and throughout the year are, as a rule, fully occupied. The average stay of each medical case in hospital is 28 days. Now if the 172 cases of rheumatism be looked upon as one case, occupying one bed in the hospital, that bed was monopolised for 10,252 days, which means that it was monopolised for from 28 to 29 years, or, to put it in another way, all the medical beds were occupied for 15 weeks. The cost of each child per week is almost exactly £2 9s., and thus in mere money the outbreak cost the hospital £4589. Further, the average stay of these cases was 60 days, as against the average of 28 days for all medical cases. How much the efficiency of the hospital as an institution for acute diseases was hampered is evident when we point out that these cases occupied beds for more than twice the average time they would have been occupied by an equal number of cases of all kinds, including rheumatic. When we recall that at least 13 per cent. of these cases died, 17 per cent. were permanent invalids, and nearly 30 per cent. had organic heart disease, we realise how serious a disease rheumatism in childhood is in this country.

Analysis of the 172 Cases of Rheumatism.

A.—Chorea.

1. *A rheumatic lesion: lesson of the air raids.*—We must now consider the manifestations in the grand total of 172 cases. The first we take is chorea, because it opens up some interesting questions in rheumatism.

Our view upon chorea is that, although not certainly always rheumatic in origin, it is best to consider every case as of this origin unless there is convincing evidence to the contrary. It was present in 104 cases—that is, 60 per cent. (Chart 2.) We believe that the majority

of physicians in this country agree in considering rheumatism to be the outstanding cause, and in our opinion the vast experiment of the air raids conclusively proved that fright, although a factor, is not the cause of chorea. In illustration of this we give the following figures showing the number of cases of chorea admitted to the hospital over a period of four years; one year was pre-war, another when the air raids were at their worst, the third coincided with the termination of the war, and the last is the 12 months we are considering in this paper. July, 1913, to June, 1914, 77 cases of chorea in 1147 medical admissions; January to December, 1917, 63 cases of chorea in 1086 admissions; July, 1918, to June, 1919, 65 cases in 978 admissions; July, 1919, to June, 1920, 104 cases in 1292 admissions.

2. *Analysis of 104 cases.*—It was noted that in 37 out of the 104 cases of chorea there was no evidence of rheumatism forthcoming. Six of these cases, however, gave a family history of rheumatism, and 11 at an earlier date had suffered from tonsillitis to the extent that removal of the tonsils had been undertaken. When we bear in mind the association of tonsillitis and rheumatism, the fact that 11 of these should have been operated upon for enucleation is interesting. Nevertheless, we are prepared to accept the criticism that we have regarded 37 out of the 104 cases of chorea as rheumatic without any definite evidence and justification. On the other hand, we can put forward from our series 12 examples of acute rheumatism in which chorea was the first and only manifestation, but which subsequently developed heart disease and arthritis. Clearly, then, because chorea occurs as a solitary symptom we cannot exclude the likelihood of its being the solitary symptom of rheumatism. Others have pointed this out, and we only dwell on it here because we have some actual figures and can give two striking examples: one a child who had five attacks of chorea and then died of carditis, and another who had four attacks of chorea and then developed acute endocarditis in an attack of acute rheumatism.

Sixty-seven cases remain over and above the 37 we have just considered, and all of these showed other rheumatic manifestations in addition to chorea. Thirty had heart disease, 18 arthritis, 12 both arthritis and endocarditis; 5 more had in addition nodules, 1 had erythema, and 1 acute tonsillitis. If 37 were examples of chorea only, 67 were examples of chorea and rheumatism, and this series affords further strong evidence in support of the rheumatic origin of chorea.

It is interesting to find that the age-incidence of these cases of chorea shows a maximum at 7 years, thus

corresponding precisely with the maximum age-incidence of all cases of rheumatism. (See Chart 3.) Similarly, the seasonal incidence shows the same maximum in December, the same minimum in March, and the same

exacerbation in April. (See Chart 4.) There seems to be no apparent reason why fright should reach its maximum at 7 years and be much more frequent in December than in March.

3. *Frequency as a solitary rheumatic sign.*—There seems little doubt that of the three great manifestations chorea is the most frequent solitary lesion. This is clearly shown in the 84 first attacks of rheumatism, for whereas chorea was solitary in 33 cases heart disease and arthritis were solitary in 5 and 10 cases respectively. Now of all the manifestations chorea is the most likely to attract attention, and the question arises whether the greater frequency of rheumatism in girls is as real an event as figures seem to show. Is it not possible that the lesser frequency of chorea in males leads to the overlooking of early cases of rheumatism in this sex, slight heart disease and transient pains being missed by the parents and their real significance not understood? The greater frequency of chorea in girls, which is unassailable and in our series was as three to one, must, we think, depend upon their more unstable nervous system, although we mention the latter with bated breath.

4. *Two types of rheumatic attacks in childhood.*—One result of the study of chorea is to lead to the recognition of two main groups of rheumatic conditions in the young. One is represented by tonsillitis, arthritis, and morbus cordis, which is more fatal; the other by chorea and endocarditis, which is more chronic and a frequent precursor of mitral stenosis.

5. *Frequency of chorea in London.*—The last point of interest concerned with chorea is this, that we found no less than 104 cases of chorea in 172 cases of rheumatism taken from the in-patients only of one hospital. It would be interesting to know the number of cases of chorea that occur in London in one year. There must be very many, and we ought to ask ourselves why. Can

it be that our educational system lacks some saving grace of humanity? We realise that in using such an old-fashioned term as this we are likely to arouse the laughter of the modern intensive school of thought, but despite that fact we feel there may be some value in raising this question.

B.—*Morbus Cordis.*

We come now to the most important manifestation, heart disease. Here we must admit there may be differences of opinion as to the earliest evidence of cardiac disturbances, and in some cases the onset is so insidious that it escapes notice at the time of the illness. The lesion may not become apparent until after the child has left the hospital, as our review of these cases in September, 1920, showed. We have, then, in their analysis dealt only with definite and clearly noted disturbances.

1. *Analysis.*—In 172 cases 114, or 66 per cent., showed some lesion: 19 had general carditis; 63 had mitral lesions, of which 22 showed definite signs of mitral stenosis; 14 had aortic and mitral disease; 15 a transient dilatation; and 3 a persistently rapid action.

2. *Results on re-examination.*—At the end of September we re-examined or obtained information about all cases that had left the hospital, and we found that 7 deaths had occurred during the interval, that 14 had become total invalids, and 12 more had lost ground from failure in good compensation. The 22 deaths in this outbreak of rheumatism were with one exception due to carditis. The exception was death from vomiting, acetonæmia, and collapse, apparently the result of pushing salicylate of soda. We lay stress on the fact that a heart affection was the most frequent event in this outbreak (see Chart 2), for it has been stated that the heart disease of rheumatism is associated with and not caused by the disease. If this is the case, then surely still more must all the other manifestations be considered in this light, for they are less frequent. If, however, we take away all the manifestations as being associated with and not caused by the disease, what is rheumatism?

C.—*Arthritis.*

Under the heading of arthritis the first point we lay stress on is the impossibility of drawing any distinction between the cases of arthritis and those with arthritic and muscular pains. It is not infrequent for a child to suffer acute pains in a joint that shows no visible changes, and such a joint may be more painful than one visibly inflamed. The total number of cases was 111, or 65 per cent. Thus, though clinically a manifestation of little gravity, it is a valuable indication of the disease, and we found that the fatal cases of rheumatism most frequently commenced with an acute arthritis, rapidly followed by carditis. In particular we would lay stress on the association of severe stiff neck with serious heart disease.

D.—*Angina Faucium.*

1. *Analysis.*—In 172 cases of rheumatism there were 22 examples of rheumatism following immediately on an attack of tonsillitis, 38 with enlarged and unhealthy tonsils, and 17 in whom the tonsils and adenoids had been previously removed. This is in great contrast to the evidence in favour of any abdominal affection as an antecedent to an attack of rheumatism, for there was not a single example of this occurrence. We venture to think that in so far as children's rheumatism is concerned, the idea that it is an infection from the bowel is an hypothesis unsupported by clinical evidence.

2. *Rheumatism and tonsillitis.*—We believe the throat to be a path of entry of the infection for these reasons: (1) Acute tonsillitis may be followed at once by severe and even fatal rheumatism; (2) guillotining of the tonsils when acutely inflamed may be followed at once by an attack of rheumatism; (3) unhealthy conditions of the throat are very frequent in the rheumatic child. This leads us to speak of the enucleation of the tonsils in the rheumatic. This, though a valuable operation in many cases, does not, however, prevent further attacks, upon which point we have valuable facts. In this series there were 17 examples of rheumatism occurring after enucleation, the operations varying in time from

just before an attack to five years previously. One of these children died of carditis six months after the operation. Two suffered from carditis, the operations having been done four years and one year respectively before the illnesses. Three developed chorea and heart disease, and 13 chorea. These figures, though few, must warn us that although enucleation is a preventive measure of importance, it is not a panacea for rheumatism.

E.—Nodules.

The older clinicians gave us very clear teaching on the grave meaning of subcutaneous nodules. This series will give strong support to this teaching, which shows some tendency to be forgotten. No doubt nodules can occur in cases which run a benign course and even in cases free from heart disease, but this does not in any way affect the general truth that their appearance is a very grave event. There were 33 examples in this series, of which 12 cases, or 37 per cent., were fatal, 15, or 47 per cent., had severe heart disease and became invalids, 4 had heart disease which later compensated, and 2 were free from heart disease.

F.—Cutaneous Manifestations.

These were 17 in number, 10 being examples of erythema and 7 of purpura; finally there were 6 cases of epistaxis, 2 of which were severe.

G.—The Fatal Cases.

The fatal cases illustrate the fact that though less frequent, rheumatism is, as a rule, more fatal in the male. In 172 cases of rheumatism 68 were males and 12, or 18 per cent., died. 104 were females and 10, or 10 per cent., died. Of the 12 cases fatal in the first attack of rheumatism 10 were boys.

1. *Absence of fever in virulent cases.*—The absence of fever in virulent cases in this outbreak was a very remarkable feature. (See Chart 5). Some cases were

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Case of rheumatic carditis with nodules, resulting in death.

characterised throughout by their steady progress to a fatal end and by their entire failure to react to any form of treatment.

2. *Remarkable taciturnity.*—Another interesting feature was the taciturnity of virulent cases. These children lay for weeks without speaking to doctors, nurses, or other children, and there is no doubt that this extreme taciturnity is a grave sign of a virulent affection of the heart.

Conclusion.

In conclusion, it appears that this analysis proves beyond dispute the extreme gravity of rheumatism in children of the class that are treated in hospitals—a fact all the more striking when we realise how comparatively infrequent such cases are in the children of the more fortunate. For those of us who are acquainted with the work done by the New York Association for the Prevention and Relief of Heart Disease, the absence of organised effort in this country for control of rheumatism and its heart disease is a matter of profound regret. Fortunately, it is never too late to mend.

It would have been impossible for us to have undertaken this research had we not received the ready assent of the three other physicians to the hospital to utilise the cases under their care. We owe our grateful thanks to Dr. G. F. Still, Dr. R. Hutchison, and Dr. J. H. Thursfield for such permission.

MANCHESTER RADIIUM INSTITUTE.—In response to the recently issued appeal for £30,000 over £6000 have already been received. Lord Doverdale subscribed £3000, Sir William Milligan £1000, two city firms £250 each, and several other firms £100 each.

SENECIO POISONING.

BY ARTHUR R. CUSHNY, M.D. ABERD., F.R.S.,

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THE very interesting paper by Drs. F. C. Willmott and G. W. Robertson in THE LANCET of Oct. 23rd, on cases of Senecio Poisoning in man in South Africa has suggested to us that the results obtained by us some years ago may interest a wider circle of readers than those of the technical journals in which our papers¹ were published. At the same time some corrections and additions may be made in the accounts of our pharmacological work.

Senecio poisoning has been known for some years to be the cause of a characteristic form of liver cirrhosis in cattle and horses, in Canada, where it is known as Pictou disease, in South Africa (Molteno disease) and in New Zealand (Winton disease). The connexion between the disease and the plants was first established by the careful experimental work of Gilruth, Chase, and Pethick, an account of whose work may be found in the paper of the senior author already cited. The chemistry of the *Senecio latifolius* was investigated by one of the present writers under Professor Wyndham R. Dunstan's direction, and resulted in the isolation of two alkaloids, senecifoline and senecifolidine, which were examined by pharmacological experiment and were found to induce the same effects in animals as had previously been described by the veterinary investigators of the disease in cattle. Very large doses caused acute poisoning marked by excitement and convulsions from stimulation of the higher divisions of the central nervous system. But these were not of so much interest as the symptoms which followed from a single medium dose, or better from small doses repeatedly given by the mouth or subcutaneously. These corresponded closely with the disease arising from feeding the plant to laboratory animals or cattle, and also with the symptoms described by Drs. Willmott and Robertson. The onset was slow, no effects following the injection of a single dose for several days; the animal then began to lose weight, diarrhoea and vomiting, general weakness, staggering gait and apathy followed, developing into stupor with low temperature and final failure of the respiration. Blood was often vomited or passed in the stools and was almost invariably found in the stomach and bowel post mortem. A certain amount of ascites was generally present in cats and sometimes this was very marked, the abdominal cavity containing large quantities of bile-stained fluid. Congestion of the stomach and duodenum with masses of black blood was present, whether the poison was given by the mouth or hypodermically. The liver was swollen and congested, and microscopically many of the liver cells were found in a state of degeneration, while the interstitial tissue was swollen and infiltrated with round cells which extended between the liver cells. The whole organ presented the appearance of early cirrhosis; the small laboratory animals did not live long enough to develop the later stages described in cattle, but there could be no doubt that the symptoms were of the same character. The gall-bladder and ducts were filled with dark very viscous bile which could be pressed into the gut only with some difficulty.

These experiments were all performed with the alkaloids of *Senecio latifolius* of South Africa, and showed conclusively that these alkaloids are responsible for the disease there known as Molteno disease. We then took up the study of the *Senecio Jacobaea* or ragwort, using samples grown in this country and in

¹ H. E. Watt: Trans. Chem. Soc., xcv., p. 466, 1909; A. R. Cushny: Journ. Pharm. and Exp. Therap., ii., p. 531, 1911, and Abstract in Proc. Roy. Soc., B. lxxxiv., p. 188, 1911.