THE LEUCOCYTE COUNT IN RHEUMATIC HEART DISEASE IN CHILDHOOD.

BY

C. BRUCE PERRY, M.D., M.R.C.P.

(From the University Centre of Cardiac Research, General Hospital, Bristol.)

This investigation was undertaken to see if the leucocyte count in rheumatic heart disease might serve as a useful index of activity of the infective process.

Cabot[1] stated that a leucocytosis of about 14,000 per c.mm. was the rule in children suffering from acute rheumatism. Ewing[2] considered that mild cases of rheumatism showed no leucocytosis, but that with fever and swelling of the joints a leucocytosis from 10,000 per c.mm. occurred. If the leucocytosis be greater than 20,000 per c.mm. it indicates the presence of some complication. The leucocytes return to normal in defervescence. Quoting Türk, he stated that with a total count of under 10,000 per c.mm. the differential count is not disturbed, but that with a greater leucocytosis than this the proportion of polymorphonuclears is increased, and this after defervescence, is followed by an eosinophilia. Macalister[3] in 1909 found that 8 cases of chorea all showed an eosinophilia to a greater or lesser extent. This was not found to be the case in acute rheumatism, and he considered that this indicated different causes for the two conditions. Bosc and Carrieu[4], from an examination of 12 cases of acute rheumatism, concluded that this is usually associated with a leucocytosis. There is a relative mononucleosis with a greatly increased number of 'medium, large and very large mononuclears' and occasionally of lymphocytes. In convalescence the mononucleosis persists and is accompanied by an eosinophilia. Leopold[5] in 1914 found in 20 cases of chorea an eosinophilia of from 1–16 per cent.; higher in second attacks than in the first. Berger[6] made a series of counts in 40 children with chorea aged from 7–14 years. He found that all but 5 of these showed an eosinophilia at some stage or other. The highest eosinophilia found was 26 per cent. of the total count, and the lowest 0 per cent. The average for the series was 7·6 per cent. The rise and fall of the eosinophilia was unconnected with any change in the clinical course of the illness. No other cause for an eosinophilia could be demonstrated. Swift, Miller and Boots[7], by repeated white cell counts, found that cases with a single 'monocyclic' attack of polyarthritis showed a slight leucocytosis which rapidly fell with anti-rheumatic therapy, and showed a light temporary rise on its discontinuance. In cases with a relapsing arthritis the leucocytes tended to remain above normal for a longer period, and were less influenced by therapeutic measures. In cases with a pronounced cardiac lesion, half of whom showed nodules, there was a persistent leucocytosis with occasional falls to normal, followed later by a rise again, and almost entirely uninfluenced by drugs. They conclude that :—

(1) Rheumatic fever is associated with a leucocytosis. (2) The leucocyte curve gives some idea of the severity and duration of the infection. (3) Patients with arthritis and exudative phenomena show a more marked leucocytosis than those with a proliferative reaction, such as myocarditis and nodules. (4) A leucocytosis depressed by anti-rheumatic drugs, indicates a mild infection of short duration. The persistence of the leucocytosis in spite of drugs, or its return on the discontinuance of the administration of the drug, indicates a more persistent infection. (5) Relapses are heralded by a rise in the leucocyte count.

Gulland and Goodall[8] reported in chorea a slight leucocytosis and, despite contrary reports, no evidence of the constant, or even usual, occurrence of an eosinophilia. In acute rheumatism they found a leucocytosis of 12,000 to 15,000 per c.mm., very rarely exceeding 20,000 per c.mm.

Wilson and Kopel[9] found that the average leucocyte count in children with a history of previous rheumatic infection, was 7,000 per c.mm.; in children with evidence of an organic

cardiac lesion was 7,700 per c.mm.; in children with evidence of an active infection was 9,000 per c.mm. They considered that the leucocyte count is of value as an index of activity.

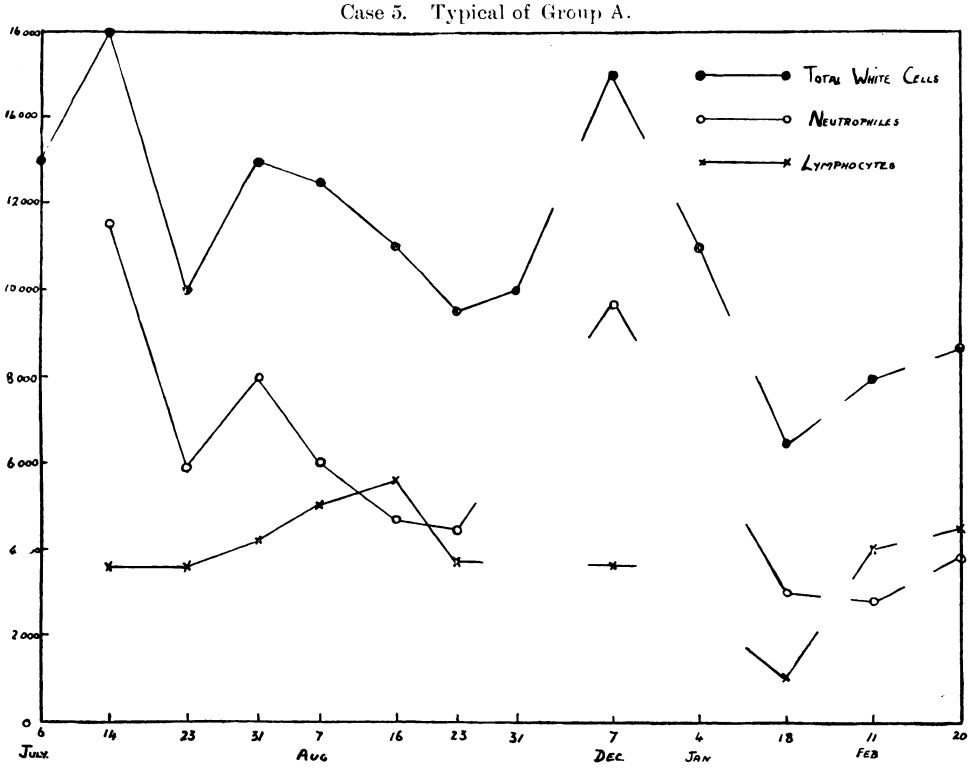
Thayer[10] reported that in 24 children with rheumatic carditis 20 showed a leucocytosis of over 10,000 per c.mm.; 11 over 20,000 per c.mm., and 5 over 30,000 per c.mm.

Piney[11] stated that acute rheumatism is associated with a slight leucocytosis which never exceeds 15,000 per c.mm. This leucocytosis often does not reappear in relapses. At the onset the eosinophiles are diminished, but reappear later and then persist throughout the rest of the illness.

Present Investigations.

In the present series repeated white cell counts were made on 41 children, 239 counts in all being made. All the cases were under the action of salicylate in some form or another, as it was not considered advisable to suspend the use

CHART I.
Case 5. Typical of Group A.



of it for the purpose of investigation. The blood was collected as nearly as possible at the same time of the day on each occasion, and all the counts were done personally. Differential counts were done in most cases. At first the neutrophils were divided into myelocytes, metamyelocytes, band forms and adult polymorphonuclears after Schilling[12], but it was seen that there was no obvious shift to the left or right, and this method was dropped in the later counts, the cells being divided simply into neutrophils, eosinophils, basophils, lymphocytes and monocytes. Various stains were used, but Leishman's was finally adopted as being most serviceable,

Results.

The cases have been divided clinically into six groups.

Group A. (*Cases* 1–6). Six cases, seen in a first acute attack of arthritis or chorea, associated with evidence of carditis.

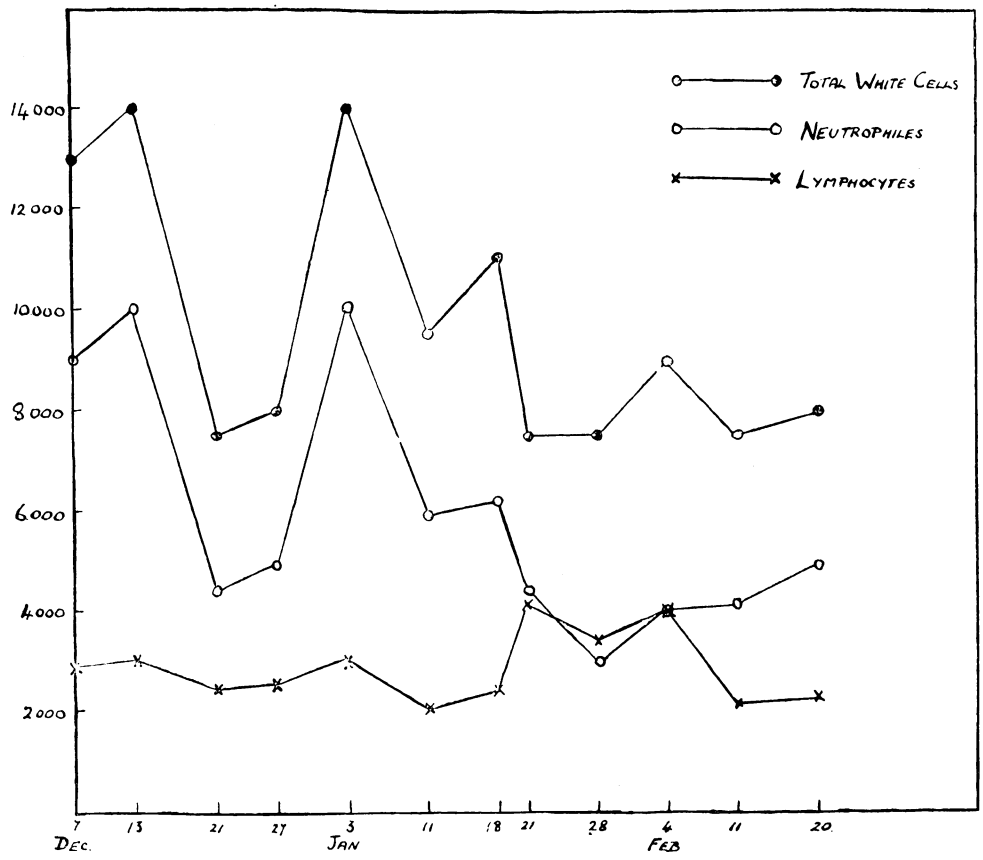
The average highest total count was 15,500 per c.mm.

The highest count made was one of 27,000 per c.mm. It was found in Case 2 late in the illness, when clinically improved.

The lowest count at the onset was 9,000 per c.mm., observed in Case 3 six days after the onset of arthritis. The count fell in 3–4 weeks to somewhere near the normal level, as determined in later examinations.

CHART II.

Case 10. Typical of Group B.



The main increase in the count is due to an increase in the neutrophils, although not entirely so, as the highest percentage of neutrophiles was 72 per cent. This tends to be followed, as the count falls, by a lymphocytosis.

There was no marked increase in the monocytes at any stage except in Case 5, which in convalescence showed a monocyte count as high as 9 per cent. of the total cells.

Case 2 in conjunction with, and preceding, the lymphocytosis showed a gradual eosinophilia reaching 7 per cent. of the total.

Chart I shows the curve of Case 5 which is typical of the group.

Group B. (*Cases* 7–10.) Four cases, seen in an acute exacerbation of a carditis whether associated with other rheumatic manifestations, or not. One of the cases was followed through two relapses.

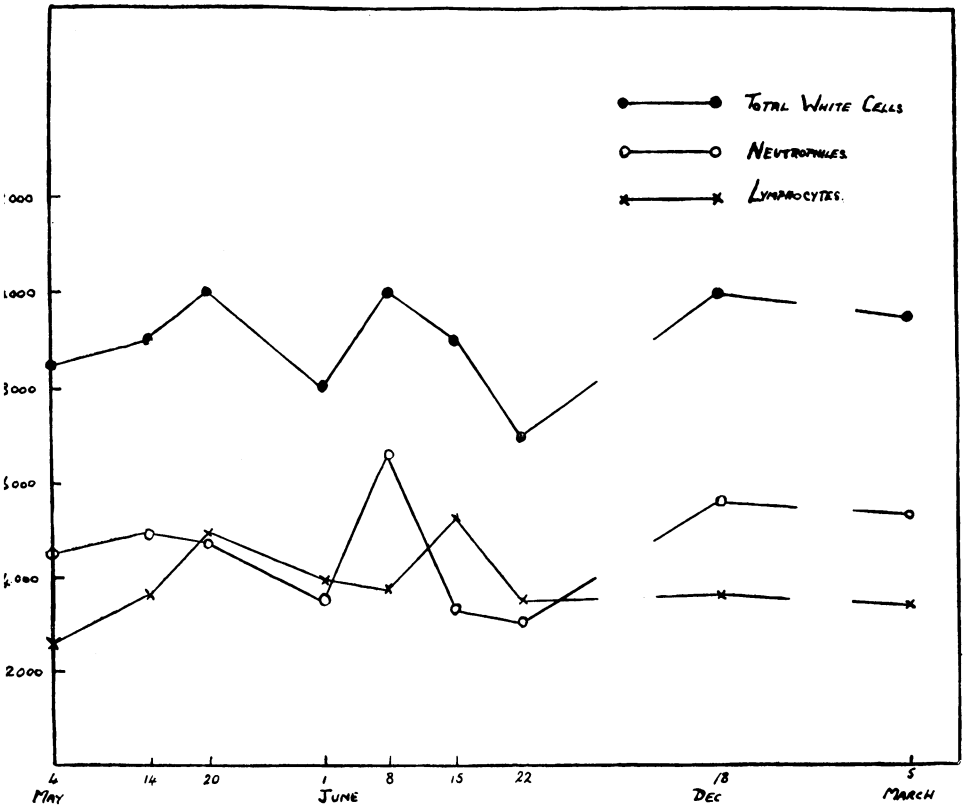
The average highest total count was 12,900 per c.mm.

The highest count observed was 28,000 per c.mm., again at the end of a recrudescence in Case 7. The highest count observed in Case 8 which terminated fatally, and was confirmed post mortem, was 17,800 per c.mm. a few days before death.

The lowest count observed, while the patient was acutely ill, was 7,000 per c.mm. in Case 9. In this case the count later rose to 11,000 per c.mm., and still later, after discharge from hospital, to 12,000 per c.mm.

CHART III.

Case 16. Typical of Group C.



The increase was mainly in the neutrophils, the highest percentage, apart from the late rise in Case 7 being 72 per cent.

There was no definite lymphocytosis or eosinophilia. The highest percentage was 5 per cent., and these cells fluctuated quite independently of the other cells. There was no monocytosis.

Chart II shows the curve of Case 10 and is fairly typical.

Group C. (Cases 11–26). Sixteen cases showing clinical evidence of a subacute and smouldering infection, such as nodules, slight fever, "sub-chorea," or occasional pains, and evidence of a cardiac lesion. Case 12 was followed through two relapses.

The average highest total count observed was 11,700 per c.mm.

The highest count made was 18,000 per c.mm. in Case 12 and this also was late in the first relapse.

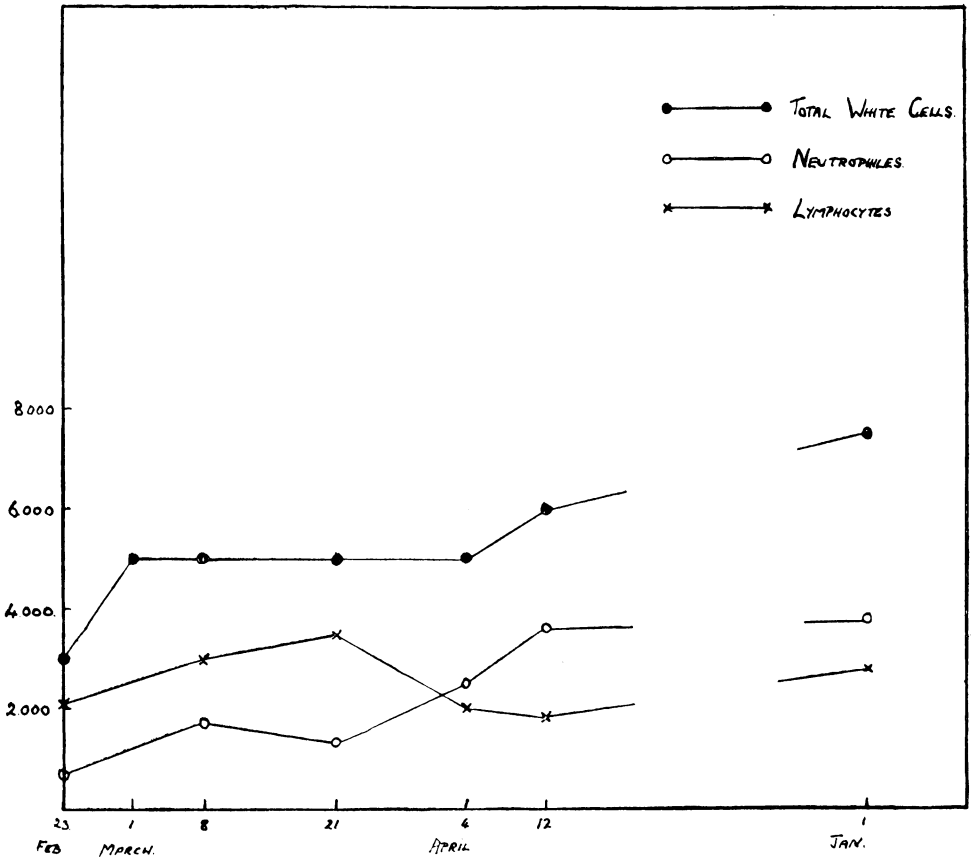
The lowest count observed when first seen (with the exception of one case) was 7,800 per c.mm. in Case 11, in which the count later rose to 9,800 per c.mm.

The count fell on improvement in varying times. The differential counts showed no definite curves. There is occasionally a tendency to a relative lymphocytosis as the count falls.

The eosinophils varied from 5 per cent. to 7 per cent. with no obvious relationship to the rest of the blood picture, or to the clinical condition.

CHART IV.

Case 22. Showing the leucopenia which was observed in this case.



A typical curve, that of Case 16, is shown in Chart III. The one case referred to above (Case 22) showed a leucopenia of 3,000 per c.mm., with a relative lymphocytosis of 70 per cent. when first seen. On improvement the count gradually rose to normal as shown in Chart IV. There was no clinical distinction between this and the other cases throughout the illness.

Group D. (*Cases* 27–37). Eleven cases admitted to hospital under the suspicion of having an active infection, but which on further investigation showed no definite evidence of this. All showed signs of cardiac involvement.

The average highest total count was 8,700 per c.mm.

The highest counts observed were 13,000 per c.mm. in cases 28 and 37.

The lowest count made, except after discharge, was 6,000 per c.mm.

There was no constant fall in the count on improvement. No significant variations in the differential count were noted. There was no eosinophilia, the highest count observed being 6 per cent. on one occasion in Case 35.

Case 38 had an average monocyte count of 7·5 per cent. No other case showed any monocytosis.

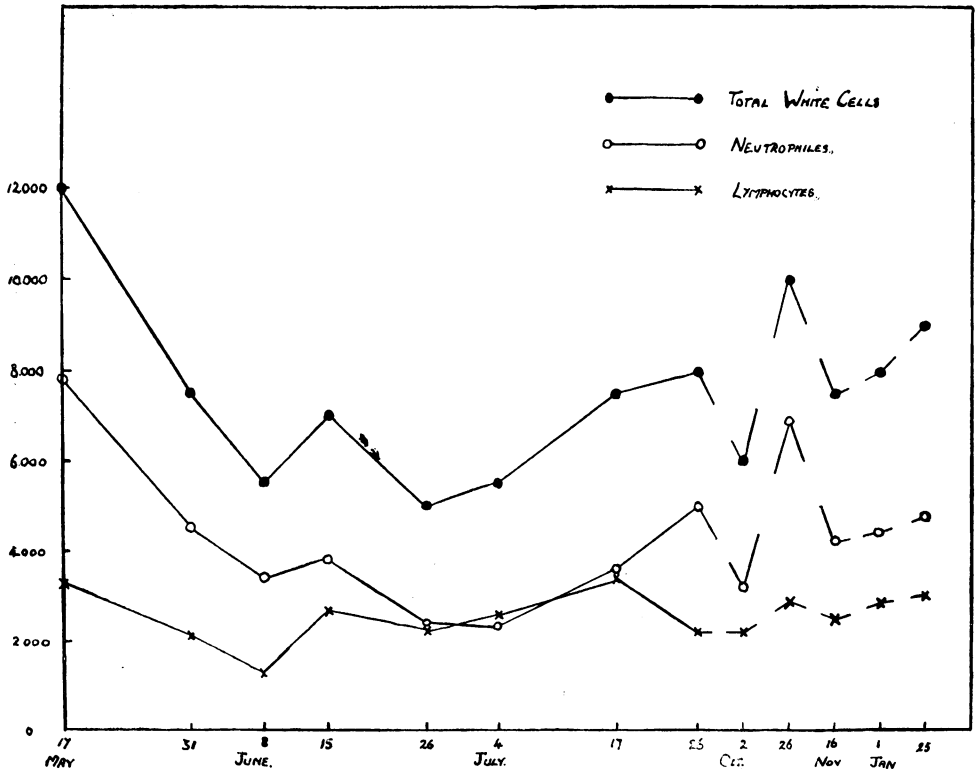
Chart V is of Case 32 and is a curve typical of the group.

Group E. (*Cases* 38 *and* 39). Two cases of chorea with no clinical evidence of carditis.

One of these cases showed a leucocytosis of 11,000 per c.mm. rising while under observation to 15,000 per c.mm. The other case had a count of 7,000 per c.mm. There was no change in the differential count.

CHART V.

Case 32. Typical of Group D.



Group F. (*Cases* 40 *and* 41.) Two cases of chronic rheumatic heart disease with no suspicion of active infection.

The highest count observed was 8,000 per c.mm. in Case 41. The count remained at a fairly constant level while under observation (see Chart VI). The eosinophils varied from 1 to 6 per cent.

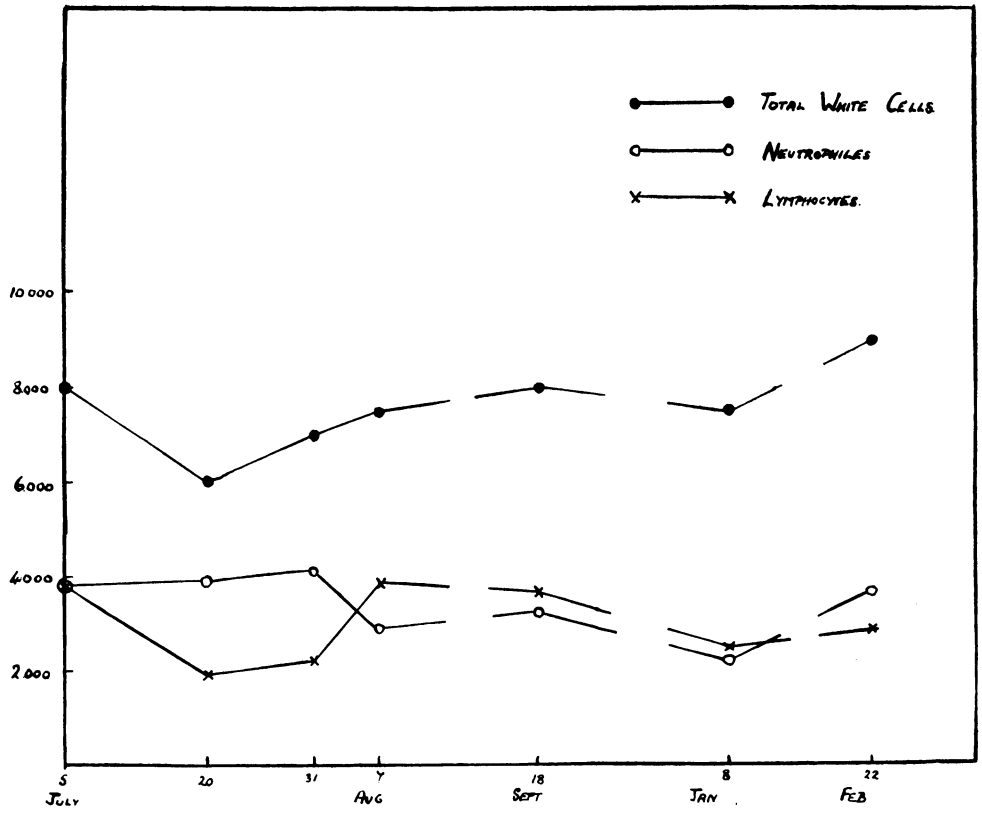
Chorea. Those cases showing definite chorea were further examined together for any evidence of an eosinophilia. There were 10 cases in all. In 6 of these the highest percentage of eosinophils recorded was 4 per cent. Of the other 4 cases the highest percentage observed in Case 21 was 8 per cent., fairly late in the course of the illness. Case 16 on two occasions had 6 per cent. of eosinophils. Cases 12 and 23 showed an eosinophilia of 7·5 per cent. and 10 per cent. respectively, occurring with a relative lymphocytosis.

Discussion.

From these figures it would appear that acute rheumatic carditis is associated with a mild leucocytosis, with a neutrophile increase. The total cells fall fairly early in convalescence and there sometimes occurs a post-infective lymphocytosis which is often accompanied by the usual eosinophilia (Piney[11]). The leucocytosis recurs with relapses. This leucocytosis is however insufficiently marked and falls to within normal limits apparently in advance of clinical improvement, so that it is of little value as a practical index of activity

CHART VI.

Case 41. Typical of Group F.



of infection. Although repeated normal white cell counts would rule out any acute activity, a single count is of no value : moreover the repeated counts would not appear likely to help in the difficult question of the advisability or not of further convalescent treatment. Further, as Fletcher and Mitchell[13] have shown, in children the fluctuations of white cells are even more marked than in adults as demonstrated by Sabin[14] and her co-workers, and by Medlar[15]. One is therefore forced to conclude that the white cell count is of no practical value as an index of activity in rheumatic heart disease in childhood.

As regards chorea, no very strong evidence of an eosinophilia is forthcoming. The only eosinophilia observed would appear to be that associated with a post-infective lymphocytosis, and in this, as in other respects, the leucocytosis in chorea does not differ from that in other rheumatic manifestations.

Summary.

1. Acute rheumatic carditis is associated with a slight leucocytosis (12,000—15,000 per c.mm.).

2. This is mainly due to a neutrophile increase.

3. Subacute smouldering infections show a varying and less constant leucocytosis.

4. The leucocyte count is of no value as an index of activity in rheumatic heart disease.

5. There is no evidence of an eosinophilia in chorea.

My thanks are due to Dr. Carey Coombs for his help and advice.

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APPENDIX.

Group A. Case 5.—Male aged 11. 30.6.28. Acute polyarthritis. 5.7.28 Pancarditis. Gradual improvement till discharge 3.9.28. ? slight relapse at the end of November, 1928. No previous attack. (*See* Chart I.)

Group B. Case 10.—Male aged 12. November, 1924, first attack of acute rheumatism. Admitted 7.12.28 with arthritis, nodules and a severe pancarditis. Very slow improvement. Discharged 23.2.29. (*See* Chart II.)

Group C. Case 16.—Female aged 11. September, 1927, Choreic movements first noticed. Improved for a time but relapsed recently. Admitted 15.5.28 with chorea; heart not enlarged, apical systolic bruit. Improved. Discharged 28.7.28. (*See* Chart III.)

Case 22.—Exhibited a leucopenia. Female aged 10. First attack of rheumatic fever, May, 1927. Scarlatina January, 1928. Since discharge from fever hospital joint pains. Admitted 21.2.28 with fever and pallor. Heart enlarged with apical systolic bruit and accentuated pulmonary second sound. Fever tended to persist. Gradual improvement. Discharged 19.4.28. (*See* Chart IV.)

Group D. Case 32.—Female aged 9. Admitted 2.5.28 with 2 years history of vague joint pains. Very slight chorea. No fever. Heart slightly enlarged with apical systolic bruit. Improved. Discharged 26.6.28. (*See* Chart V.)

Group F. Case 41.—Female aged 9. Rheumatic carditis November, 1927. Admitted 26.6.28 for tonsillectomy in quiescent stage. Operation 2.7.28. No post-operative reaction. (*See* Chart VI.)