A Study of the Blood in Postmalarial Anaemia, as observed in the South of Spain, with seventy illustrative cases.

Thesis for the degree of M.D.,

by

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Glasgow, September, 1905.

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Introduction.

In this paper dealing with the anaemia resulting from malarial fever as observed in the South of Spain, a few general introductory remarks are necessary.

I was stationed at the town of Rio Tinto in the Province of Huelva, and the cases to be described, or analysed, were collected by me from Rio Tinto and the villages in the neighbourhood during the past two years.

Rio Tinto is situated up in the hills some 1100 feet above sea-level, and about 50 miles from the coast. Viewed from any considerable elevation the surrounding countryside presents an endless succession of small rocky hills, separated from one another by narrow gullies or "barrancos." These gullies, while they contain running water in considerable amount during the wet season, are dry in the warm months, but for occasional small pools which make excellent breeding places for the anopheles mosquito, and are to be found in close proximity to most villages.

Although formerly malaria was very prevalent in the town itself, during the past few years a great diminution in the number and severity of infections has been noted; the result of persistent active measures taken against the anopheles mosquito, and efforts to put prompt and thorough treatment within the reach

of all infected. In fact at the present time, patients living in the town and suffering from fresh infections, are almost always found to have contracted the fever out in the countryside; either when staying at their little huertas or orchards, where anopheles often abound, or in the neighbouring villages. It is in these villages that most cases are encountered, though, as the result of the measures above mentioned, (pools being filled up or drained etc), a marked improvement has also been effected.

Cases of malarial infection are most frequently seen during the warm months. Fresh infections are rare between the months of October and May, but chronic cases suffering irregularly from fever occur irrespective of season. June, July, August and September are the months during which the disease is most prevalent and the most acute cases are seen.

The average severity of the infections met with is moderate, and. though pernicious cases do occur they are uncommon. The commonest variety of fever is Quartan, next comes Malignant Tertian or Subtertian, while Benign Tertian comes last in frequency. The benign infections are as a rule single, but occasionally one meets cases doubly or trebly infected.

In the following series of cases no system of selection was employed. Cases were examined when, at the instance of the Spanish doctors, they came to the Rio Tinto Company's Hospital "consulta" or special dispensary. The patients were Spaniards of all ages, and both sexes; the majority however being men, working in the Rio Tinto Copper Mines

and living in the villages before mentioned. After getting medicine at the "consulta," few of the sufferers came back for continuation of treatment, or for re-examination: some refrained because they had a long distance to come, and being poor did not wish to leave their work; others, if the fever were kept in abeyance for some days, were quite satisfied and did not return as advised. In this way a great number of avoidable relapses resulted, as well as the loss of interesting re-examinations, and to follow a cases through improvement to recovery was difficult.

In concluding these remarks it may be added that the term Postmalarial Anaemia is in this paper used to include all cases where there is anaemia due to attacks of malaria, whether these attacks have ceased for some time, or are still actively continuing: also that in studying the subject the following subdivisions will be made:

Chapter I. Postmalarial Anaemia generally considered.

" II. Red Cells and Haemoglobin, with examples.
Abnormal red elements.

" III White Cells.
(a) Actual counts in Apyrexia
(b) Actual counts in Pyrexia } with examples.

" IV. (a) Relative counts in Apyrexia
(b) Relative counts in Pyrexia } with examples.
(c) White counts in complicated cases.

" V Abnormal white cells.

" VI Notes on diagnosis.

Chapter VII. Notes on Prognosis
" VIII. " Treatment, and
Illustrative charts.

Chapter I.

General consideration of postmalarial anaemia.

Postmalarial anaemia is essentially a secondary anaemia as it directly results from a destruction of red corpuscles by the malarial organism in the circulating blood. At present however constant features, which isolate it from other secondary anaemias, and are of great value in diagnosis.

The degree of anaemia present in any given case varies in proportion to:- (1.) the intensity of the paroxysms of fever present or recent; (2) the periodicity of these paroxysms, whether they occur daily, or with one or two whole days' intermission; (3) the length of time that the patient has suffered; and to some extent (4) the type of organism present in the blood.

As a rule one finds the severest anaemias resulting from daily paroxysms of fever, this being specially noticeable in pernicious cases, where the temperature is remittent and not intermittent; while, apart from such cases the severity is generally more marked if the infection is of the Subtertian variety, than if of a multiple benign nature.

Regarding the length of time a patient has suffered, that although important, may have its influence modified by the taking of quinine. For example: a patient has suffered for several months from malarial attacks, but by taking quinine at intervals, though without system

and in insufficient doses), he has been able to enjoy frequently a few weeks of immunity during which his blood improves considerably. His anaemia thus never becomes severe. Another patient having suffered for a shorter time but more continuously, and having taken little or no quinine would, all things being Equal, shew more marked anaemia.

The anaemia is as a rule fairly slow in becoming evident. Cases are on record where in two or three days pernicious attacks reduced the blood count enormously, but such are very rare in Spain. In a fresh infection of moderate severity and especially in the benign fevers where the intermissions are long, the first few attacks have little effect on the blood count, and there may be no appreciable anaemia present by the end of apyrexia. When however anaemia has distinctly developed, in the presence of continuing attacks or the absence of successful treatment it slowly progresses till it reaches a moderately severe degree, the blood shewing some 50% Red cells and 40% to 50% haemoglobin, while the patient suffers considerably from the associated symptoms. In a large number of cases a greater reduction than this does not occur, the blood forming centres apparently doing all they can to make good the loss. This is specially true of cases due to benign fevers. The cases where the anaemia progresses like a grave loss of red cells occurs, and perhaps a fatal result ensues, are almost always subtertian in nature. It may be added that those here reported were mostly of some duration, many were chronic and cachectic, and the majority were actually infected at the time of examination. In the most recent cases the infection dated back ten or fifteen days, in others

two years or more.

Associated Signs and Symptoms.

Summarizing the signs and symptoms associated with the anaemia, one finds that:—

(1) In cases of moderate severity complaint is made of headache, pains in the legs, tiredness and loss of appetite. There is usually considerable pallor, the face being of a dirty greyish colour, but this is not so distinctive as in cachectic cases.

(2) As the condition becomes chronic and cachexia develops, emaciation becomes noticeable; the skin is loose, and the pallor, of a peculiar grey yellow earthy tint, is very evident and distinctive. The lips and mucous membranes are pale.
The symptoms above mentioned become intensified; dyspnoea on exertion, palpitation, giddiness and nausea are frequent, and there may be vomiting and diarrhoea. Coldness and numbness of the extremities are sometimes complained of.

(3) When cachexia is marked, oedema of the feet and ankles is common, and in addition, ascites with or without albuminuria may occur. The spleen becomes hugely enlarged and is hard and smooth to palpation. At the same time the liver dulness may be increased, but never to any great extent.
The pulse is small and frequent; the heart sounds weak and rapid, while soft systolic murmurs may be heard, with their greatest intensity over the base, or bruit over the large veins in the neck. Death may result directly from the anaemia and its associated organic changes, or from intercurrent disease to which such cases are very prone.

Method of examining the blood.

The method employed in making the blood examinations of the cases reported in this paper, was as follows.-
A Thoma-Zeiss haemocytometer, and a Gower's haemoglobinometer were respectively used to estimate the percentages of red cells and haemoglobin in the peripheral circulation; Toisson's methyl violet solution being used as the diluting agent. The dilution usually employed was 1/100, and in estimating the number of red cells per mm^3, the number of cells in ten large squares of sixteen small ones each, was invariably counted. In counting the white cells per mm^3, the same pipette was used as for red cells, microscopic fields being counted instead of squares, and the number of cells present in one hundred fields being counted as a routine. This method was convenient where, as often happened, the blood was poor in leucocytes: and as an interesting point in these cases is the ratio of white to red cells, any considerable error in this ratio was thus made impossible. In staining films for differential counts, eosin and haematoxylin were used. From 800 to 1200 or more white cells were counted in estimating the relative percentages in each case, but usually the number was about 1000.
The above stains were found very serviceable, differentiating the white cells satisfactorily (with the exception of neutrophile myelocytes, which required Ehrlich's triple stain), and staining any organisms present. A considerably extended trial of eosin and methyl blue failed to give sufficiently uniform results.
Fresh films were examined in all cases with the main object of noting the presence or absence of organisms.
The blood drop was always extracted from the lobe of the ear.

Chapter II.

The Red cells and Haemoglobin.

While postmalarial anaemia varies greatly in degree, it also varies considerably in type. Four distinct types have been mentioned by Bignami and Dionisi*:—

I. Anaemia after ordinary acute malaria: loss of red cells according to degree of severity. Prognosis favourable.

II Anaemia progressive and fatal, the blood having all the characteristics of blood in pernicious anaemia.

III Anaemia rapidly fatal: at first resembling class I. but shewing no signs of regenerative power.

IV Chronic secondary anaemia: like class I but with accompanying cachexia and secondary changes in the blood-forming organs: after much malaria.

V Also slight anaemias after short infections: quick recovery.

This classification according to type, includes all the cases here to be described, the great majority coming under classes I. & IV. It has been found however most convenient to classify all under the three headings of Quartan, Benign Tertian and Subtertian, according to the type of fever producing the anaemia.

As above stated loss of red cells is met with in varying degrees. In cases of short duration, the result of benign infection, or in those of long duration where considerable periods of apyrexia have intervened, the red cells may be between 3½ million and 4 million per mm³. On the other hand, infections benign or malignant of long duration, and badly treated, are accompanied by considerable anaemia. all things being equal however,

* Quoted by Thayer: Lectures on Malarial Fevers. 1899.

Subtertian fever causes the greatest loss of red cells, counts as low as one million per mm^3 being found.
For example:-

J.J.K. aet 14. Simple tertian of 8 months duration.

Red Cells. 71% or 3565 000 per mm^3.
Haemoglobin 50%
Colour Indesc 0·7.

Here a clear day intervened between the attacks, and fever was occasionally absent for some weeks. The anaemia is therefore slight.

M.P. aet 5 Double tertian, 2½ months duration.

Red Cells. 39% or 1,950,000 per mm^3.
Haemoglbn. 32%
Colour Indesc 0·8

Two active generations of parasites were present in the boy's blood, and as the boy had suffered almost continuously, the anaemia is severe.

R.J. aet 3½ mths. Subtertian. 10 days duration.

Red Cells 40% or 2000,000 per mm^3.
Haemoglobn 30%
Colour Index 0·75.

Severe anaemia, rapidly developed in a young child.

In the following examples of loss of red cells and haemoglobin, the normal number of red cells per mm^3 is taken as 5000,000 for men, and 4500,000 for women. Sixty six cases are tabulated under the headings of quartan, benign tertian and Subtertian, the total number of examinations being ninety seven.

Quartan Anaemia.

No.	Age.	Duration.	Red Cells %.	Haemoglobin %.	Col. Index.	
1.	38	3 mths.	49·5	50	1·0	
			83	74	·9	1 month later.
			100	80	·8	2 mths "
			102	100	·98	3 mths "
2.	17	4 mths.	58	44	·76	
			56	40	·7	5 days later.
			66	52	·8	8 days "
			80	70	·87	10 days "
			84·6	70	·82	12 days " .
3.	3	6 mths.	59	44	·7	
4.	49	2 mths.	60	50	·8	
5.	30	3 mths.	60·6	50	·82	
6.	26	5 mths.	62	52	·8	
			78	66	·87	1 week later
			85	74	·87	2 weeks "
			74	65	·8	2 weks " .
7.	19	4 mths	67	50	·74	
8.	22	5 mths.	65	56	·86	
9.	14	5 mths.	66	60	·9.	
10.	29	2 years.	66	60	·9	
			98	82	·8	2 weeks later
			100	98	·98	3 months " .
11.	14	3 mths.	66·6	65	·97	
12.	27	4 mths.	72·5	50	·7	
13	19	8 mths	72	60	·8	

Quartan Anaemia (contd).

No.	Age.	Duration.	Red Cells%	Haemoglobin%	Colour Index.	
14.	9	5 mths.	71·4	58	·8	
			89	72	·8	2 weeks later.
15.	7 mths.	½ mths.	76	50	·67	
16.	44	5 mths.	75	60	·8	
17.	13	1 mth.	75	60	·8	
18.	17	1 year.	77	58	·75	
19.	40	1 mth.	80	72	·9	
20.	26	4 mths.	82·8	76	·9	
21.	33	10 days.	88	80	·9	
22.	31.	5 mths.	86	76	·88	
			84	70	·8	
23.	24.	3 mths.	92	70	·7	
			98	82	·8	2 wks. later.

Benign Tertian Anaemia.

No.	Age.	Duration	Red Cells%	Haemoglob%	Colour Index.	
24.	5	2½ mths	39	32	·8	
25.	21 mths.	1 mth	40	32	·8	
26.	50	5 mths	58	40	·7	
27.	43	12 mths	57	50	·9	
28.	6	10 mths	59	44	·7	
29.	2	11 days	70	60	·8	
30.	13	8 mths	71	50	·7	
31.	8	7 mths	78	60	·7	
			84	75	·9	9 days later

Benign Tertian Anaemia (ctd).

No.	Age	Duration	Red Cells %	Haemoglob. %	Col. Index	
31/ctd.	8	7 mths	80	72	·9	8 days later.
32.	30	2 mths.	88	70	·8	
33.	9	2 weeks.	92	60	·6	

Subtertian Anaemia.

No.	Age.	Duration.	Red Cells %	Haemoglob. %	Colour Index	
34.	2½ mths.	2 mths	21	12	·6	
35.	35	4 mths	25·3	24	·94	
			22·5	22	·98	2 days later.
36.	22	2 mths	32	26	·8	
			34	30	·87	2 weeks later.
			77·3	66	·85	9 weeks " .
37.	32	6 mths	35·1	34	·9	
38.	3½ mths	10 days.	40	30	·75	
39.	21	2 yrs	40	35	·9	
40.	13	3 mths.	46·3	38	·8	
			59·2	50	·83	5 days later.
			52·4	42	·8	8 days " .
41.	23	3 mths	50	36	·7	
42.	6	2 weeks	51·8	42	·8	
43.	21 mths	15 days.	52	44	·86	
44.	5	2 mths.	54	30	·6	
45.	34	2 mths	55	42	·76	
46.	17 mths	10 mths	54·6	46	·84.	
47.	17	3 mths	58	44	·76	
48.	10	14 mths	59	40	·7	
			48	32	·7	1 wk. later

Subtertian Anaemia. (cont'd.)

No.	Age.	Duration	Red Cells %	Haemogl. %	Colour Index.	
48(cont'd)	10	4 mths	47	30	·64	1 week later.
			35·4	25	·7	2 weeks "
			40	25	·62	2 weeks "
49.	40	2 mths	60	42	·7	
50.	36	5 mths	61·2	46	·7	
			70	65	·9	2 wks later.
51.	33	6 wks.	68	35	·5	
52.	30	8 mths.	61·6	36	·9	
53.	18	2 mths	64	56	·87	
54.	19	1 year	68	50	·7	
55.	8 mths	3 mths	70	50	·7	
56.	37	2 weeks.	71	62	·87	
57.	30	2 mths	74	52	·7	
58.	30	4 mths	72	66	·8	
			75	70	·9	1 month later
			89	88	1·0	3 weeks later.
59.	27	6 weeks.	74	62	·8	
			81	78	·96	3 weeks later.
			106	95	·8	5 weeks later.
60.	27 mths	12 mths	80	52	·6	
61.	35	1 mth.	80	60	·75	
62.	30	2 mths	85	68	·8	
63.	37	15 days	86	74	·86	
64.	11	1 year	88	70	·8	
65.	2½	2 mths	95	67	·7	
66.	17	1 mth.	97	60	·6	

In these examples, representative of post malarial anaemia in South Spain, one notes that the average severity is moderate, severe cases being very few: also, that the Quartan examples are particularly slight, while the Subtertian list contains the most marked cases.

Thus the <u>lowest counts</u> are:—

<u>Quartans.</u>	49·5%	in No 1.
	58%	in No 2.
<u>Benign Tertians.</u>	39%	in No 24.
	40%	in No 25
<u>Subtertians</u>	21%	in No 34
	22·5%	" " 35
	32%	" " 36
	35%	" " 37.

In all three lists cases occur, where the red counts are almost normal, but the haemoglobin is noticeably reduced. Cases of this kind give the blood counts a chlorotic appearance. As a rule however the haemoglobin is reduced proportionately to a greater extent than the red cells. Occasionally both are equally reduced, giving a colour index of I·0. The following are the extremes of colour indices noted, and the average C.Is in the three lists of counts.

	Lowest Col. Ind.	Highest C.I.	Average Colour Index.
Quartans.	·67, ·7	I·0	·8 for 38 examples
B. Tertians.	·6, ·7	·9	·77 " 12 "
Subtertians.	·5, ·6	I·0, ·98	·77 " 47 "

The colour index thus varies considerably, but shews a tendency to stay below I·0. Possibly this is marked here owing to the chronic nature of so many of the cases. In none is the index above I·0, as in class No III of Bignami and Dionisi, (page 8). One such case was examined, but is placed in the notes on diagnosis for reasons to be afterwards stated. It may be added that the anaemia produced in young children is often severe and developes rapidly, the colour index being as a rule low. The following observations made by writers on malaria regarding the loss of red cells and haemoglobin, are of interest, and more or less agree.

* Thayer says the red cells and haemoglobin are equally diminished, but that at times the haemoglobin suffers more reduction

* Bignami and Dionisi say that the haemoglobin is a little poorer than the red cells, and slower in regaining.

† Daniels seems to consider the colour index to be about I·0.

‖ Cabot under varieties of secondary anaemias includes the following examples of post-malarial anaemia. The colour indices (which I have calculated and inserted), are low.

Age.	Red cells	Haemogl.	Colour Index	
23.	1656,000	18	·54	
	2048,000	24	·58	1 week after.
	1808000	30	·83	2 weeks after.
35.	3070,000	35	·57	
	1931,000	35	·9	

The tendency for the haemoglobin to lag behind the red cells during convalescence, (see Bignami and Dionisi, above), is seen in cases Nos I, 10, and 48: (see charts on page 55).

* Lectures on Malaria. 1899. † Laboratory studies in Tropical Medicine. 1903.

‖ Clinical examination of the blood. 1903.

Conclusions.

The general conclusions regarding the red cells and haemoglobin in postmalarial anaemia, are:—

(1). As a rule the condition of the blood, as regards the loss of red cells and haemoglobin, differs in no striking manner from that in other secondary anaemias; e.g. after Chronic Bright Disease, malignant disease, haemorrhage etc.

(2) The anaemia is usually moderate.

(3) Marked anaemia is rare in benign infections.

(4). Extreme anaemia is very rare at any time, (in South Spain), and only occurs after pernicious attacks of Subtertian fever.

(5). The haemoglobin may be equally reduced with the red cells, but as a rule suffers a somewhat greater relative reduction. This may at times be marked, as in chlorosis.

(6). Very rarely the red cells may be reduced to a relatively greater extent than the haemoglobin, as in pernicious anaemia, this only occurring in very pernicious subtertian cases.

(7) During convalescence the haemoglobin may be slower in regaining than the red cells.

Appearances of Red cells in Postmalarial Anaemia.

In a fresh preparation one may see

(a) Pallor. When there is much anaemia, this is easily noticeable. In some cases only the edges of the red cells are coloured, and very faintly.

(b) Variations in Size. As anaemia progresses the average size of the red cells tends to become less. Megalocytes may be often seen, but marked differences in size, (anisocytosis), do not form a noticeable feature unless in very severe cases.

(c) Poikilocytosis. This in any marked degree is rare. One may

see however oval or pearshaped cells occasionally.
In stained films slight degrees of polychromatophyllia occur now and then, along with slight poikilocytosis.

In addition to these qualitative changes, abnormal red cells occur in the shape of (1) Nucleated Red Cells, and (2) Red cells containing malarial organisms

Nucleated Red Cells.

These are only found in severe cases of postmalarial anaemia, or in cases which have recently been severe. They occur both as normoblasts and megaloblasts, the former term being applied to all nucleated red cells below, and the latter to all above 10 μ in diameter. The significance of normoblasts in malarial blood seems to be the same as in other anaemias primary or secondary, namely that active efforts at blood-regeneration are going on in the bone marrow. Their complete absence in a very severe case would signify the opposite, and justify a serious prognosis. Megaloblasts are rarely seen in malarial blood, and then only in very small numbers, and almost invariably in smaller numbers than the accompanying normoblasts.
In the following table the presence of nucleated red cells is noted in 13 out of 66 cases. The white counts are included so that one may roughly calculate the number of erythroblasts per mm^3.

Nucleated Red Cells.

No.	Age	Red Cells %	Haem %	White Cells p. mm³.	Normoblasts per 1000 W.C.	Megaloblasts per 1000 W.C.	Normoblasts per mm³.	Megaloblasts per mm³.	
3.	3.	59	44	4100	13		53.3		Quartan.
15.	7m	76	50	5600	2		11.2		"
25.	21m	40	32	5100	10		51		B. Tertian
34.	2½m	21	12	19000	3		57		Subtertian
36.	22	32	26	3120	14	2	43.6	6.24	"
37.	32	35	34	2980	10		29.8		"
38.	3½m	40	30	17800	21	2	373.8	35.6	"
39.	21	40	35	3400	10		34		"
40.	13	46.3	38	10185	4		40.7		"
		39.2	50	10300	6		61.8		"
		52.4	42	17450	5		87.2		"
42.	6	52	42	4810	4		19.2		"
44.	5	54	30	2800	9		25.2		"
48.	10	48	32	5400	2		10.8		"
		47	30	6800	6		40.8		"
		35	25	3820	2		7.6		"
		40	25	2670	5	1	13.3	2.6	"
53.	8m	70	50	15400	8		123.2		"
									"

Of the thirteen cases in the above table, it will be seen that ten are subtertian, two are quartan, and one benign tertian. Almost all are cases of severe anaemia, and five are very young children.

The largest number of normoblasts in any case is 373.8 per mm³. In cases where leucopenia exists the ratio of nucleated to normal red cells is found to be comparatively low: but where, as in a few cases above, leucocytosis is present, the ratio is

greater than appears at first sight.
In three cases megaloblasts were found, but in very small numbers, and with an accompanying greater proportion of normoblasts. All were very severe cases, two ending fatally. If, as rarely happens, megaloblasts occur in greater numbers than normoblasts, it is only in these malignant and progressively fatal infections (Bignami and Dionisi), where the blood resembles that of pernicious anaemia in all details. Their presence in post-malarial anaemia seems of serious import.

(2). Red Cells containing Malarial Organisms

A description of these organisms is unnecessary and beyond the scope of this paper. In cases of anaemia due to Benign fevers and especially in Quartans, the specific amoeba was very frequently found in fresh and stained specimens, in varying stages of development. In Subtertian cases they were much less commonly found, though crescents were very frequently seen. Of the 66 cases here analysed, 42 shewed organisms at one time or another.

The Leucocytes. Chapter III.

The study of the leucocytes in post malarial anaemia presents points of greater interest than that of the red cells and haemoglobin. This interest lies to some extent in the actual counts of white cells per cubic millimetre, but especially in the differential counts and their important bearing on the question of diagnosis, actual and differential.

For, while the state of the red cells and haemoglobin presents no striking differences from what is seen in other secondary anaemias, on examining the leucocytes constant and unique changes are met with, separating post malarial anaemia from all other secondary anaemias or cachectic conditions.

In trying to arrange this section so that, without the loss of important detail, the matter should be as concise as possible, a little difficulty has been experienced, and it has been found necessary to make many subdivisions.

The actual numbers of white cells per cubic millimetre in the cases examined will be studied first, examples being given during apyrexia and pyrexia. Then the differential or relative white counts will also be given in apyrexia and pyrexia; followed by a few cases of complicated malaria, shewing how the white counts are affected. In conclusion a few remarks will be made on the varieties of white cells in malarial blood.

In discussing the actual white counts, the terms <u>leucopenia</u> and <u>leucocytosis</u> will be frequently used, and it is necessary to explain the significance here given to them. The terms are

used relatively to what the red count happens to be in any case under consideration: (see Stephens and Christophers "Practical Study of Malaria," 1903, where Examples similar to those below are given). Thus the ratio of white to red cells in normal blood is taken here as 1 : 500, (10,000 white cells to 5000,000 red cells); and this is also taken as the normal ratio in all cases here reported, apart from the actual numbers of white and red cells per $mm.^3$ in each case.

Therefore if in any case the ratio of white to red cells is less than 1:500 it is called leucopenia.

E.G. Red cells = 50%
White cells = 3000 per $mm.^3$
W.C. : R.C. = 1/83 (i.e. leucopenia).

While if in any case the proportion of white to red cells is greater than 1 : 500 we have leucocytosis.

E.G. Red cells = 30%
White cells = 10,000 per $mm.^3$
W.C. : R.C. = 1/50 (i.e. leucocytosis).

In other words the term leucocytosis is here interpreted to mean any increase in the normal ratio of white to red cells in the peripheral circulation, whether an absolute increase of white cells above the normal number per $mm.^3$ (10,000), be present or not in the case under consideration.

The following main points will be noticed in the lists of cases to be given:—

During Apyrexia. (1) Leucopenia is almost invariably present in uncomplicated malaria, (any exceptions shewing a normal ratio of white to red cells) (2) leucocytosis never occurs.

During Pyrexia. (1) The apyretic leucopenia may persist, or

leucocytosis, sudden and of short duration, may occur, to be succeeded by leucopenia on the return to apyrexia. Also complications of an inflammatory nature can cause a leucocytosis bearing no relation to the malarial infection.

Diurnal White Counts in Apyrexia.

No.	Red Cells	Haemo	White cells	W.C./R.C.	Organisms	
1.	49.5	50	4220	1/587	Yes.	
	83	74	5600	1/741	No.	1 mth later
	100	80	4100	1/1220	No.	2 mths. "
	102	100	5300	1/962.	No	3 mths " .
3.	59	44	4100	1/720	Yes.	
4.	60	50	2700	1/1100	"	
5.	60.6	50	3390	1/890	"	
6.	62	52	3565	1/847		
	78	66	5350	1/732	No.	1 wk. Later
	85	74	4100	1/1040	"	2 wks "
	74	65	4500	1/827	"	2 wks "
7.	67	50	5120	1/654	Yes.	
8.	65	56	2290	1/1419	"	
9.	66	60	5720	1/576	"	
10.	66	60	6210	1/533	"	
	98	82	5000	1/980	No	2 weeks later
	100	98	6000	1/840	No	3 months "
11.	66.6	65	2866	1/1160	Yes.	
12.	72.5	50	4500	1/800	"	
13.	72	60	4000	1/900	No	
14.	71.4	58	6900	1/517	Yes.	
	89	72	3530	1/1260	No.	2 weeks later.

Quartan White Counts in Apyrexia. (cont'd)

No.	Red Cells %	Haem.° %	White cells	W.C/R.C	Organisms	
15.	76	50	5600	1/678	Yes.	
16.	75	60	4000	1/937	"	
17.	75	60	4200	1/892	"	
18.	77	58	5770	1/670	"	
19.	80	72	5940	1/660	"	
20.	83	76	6115	1/677	"	
21.	88	80	6310	1/697	No.	
22.	86	76	4300	1/1000	Yes.	
	84	70	3800	1/1100	Yes.	
23.	92	70	5730	1/800	Yes	
	98	82	9000	1/540	No.	2 weeks later.

Benign Tertian White Counts in Apyrexia.

No.	Red Cells %	Haemo.°	White Cells	W.C/R.C.	Organisms.	
24.	39	32	4000	1/490	Yes.	Double infection
25.	40	32	4200	1/476	"	
27.	57	50	5400	1/527	No.	
28.	59	44	2950	1/1006	Yes.	
29.	70	60	5940	1/588	"	
30.	71	50	2500	1/1420	"	
31.	78	60	6000	1/650	"	
32.	88	70	4800	1/920	"	
33.	92	60	4780	1/962	"	

In the above 42 examples of benign infections it is at once evident that in no case in apyrexia is there leucocytosis. There is either a fairly normal ratio of white to red cells, or,

and much more commonly a distinct leucopenia. This is at times very marked, giving a very low W.C.:R.C. Good examples are Nos 8, 11, 14, and 22; No 8 shewing W.C/R.C. of 1/420.
The leucopenia is also seen to be very persistent, continuing during convalescence and being still present when the red cells and haemoglobin are normal. At times the white cells may even diminish further as the red cells and haemoglobin improve.
These points are seen in cases, Nos 1, 6, 10, and 14.

Subtertian White counts in apyrexia.

No.	Red cells%	Haemo.%	White cells	W.C./R.C.	Organisms	
36.	32	26	3120	1/514	Yes.	
	34	30	3260	1/521	No	2 weeks after.
	77·3	66	3820	1/1011	"	9 wks. "
37.	35·1	34	2980	1/588	"	
39.	40	35	3400	1/588	Yes	
42.	52	42	4810	1/538	"	
43.	52	44	3020	1/860	"	
44.	54	30	2800	1/966	Yes	
45.	55	42	2800	1/990	No	
46	55	46	6740	1/404	"	
47.	58	44	5400	1/536	Yes	
48.	59	40	3820	1/781	No	
50.	61	46	7878	1/390	Yes	
	70	65	6100	1/573	No	2 wks after.
51.	68	35	3850	1/883	No	
52.	62	56	4074	1/756	No	
54.	68	50	6110	1/570	Yes.	

Subtertian White Counts in Apyrexia. (cont^d.)

No.	Red Cells %	Haemog^n %	White Cells	W.C./R.C.	Organisms.	
56.	71	62	2164	1/644	Yes	
57.	74	52	3602	1/666	"	
58.	72	66	6000	1/600	"	
	75	70	6400	1/390	No.	1 month later
	89	88	7600	1/384	No.	3 weeks later
59.	74	62	5252	1/706	Yes	
	81	78	6900	1/624	No.	3 weeks later.
	106	95	7800	1/679	No.	5 weeks " .
61.	80	60	5000	1/800	Yes	
62.	85	68	3950	1/1074	No.	
63.	86	74	6100	1/704	Yes.	
64.	88	70	6410	1/702	No.	
65.	95	67	10,000	1/475	No.	

In these 30 Subtertian examples the leucopenia is again noticeable. In one case, No. 56, it is very marked, giving W.C./R.C. of 1/644. The high ratio in No. 50 of 1/390, suggests either inaccuracy, or some unnoticed complicating influence. In Nos 36, 58, and 59 there is evidence of the persistence of the leucopenia before noted.

The following are <u>isolated</u> examples of white counts <u>during pyrexia</u>.

Isolated White Counts during Pyrexia

No.	Red Cells%	Haemoglo%	White Cells	W.C./R.C.	Organisms.	
25.	58	40	8900	1/327	Yes.	
33.	21	12	19000	1/35	"	Comatose.
36.	40	30	178000	1/12	"	Moribund.
39.	50	36	9170	1/272	"	
46.	48	32	5400	1/444	No	
	47	30	6800	1/346	"	1 week later
	35·4	25	3820	1/463	"	2 wks "
	40	25	2673	1/746	"	2 wks "
47.	60	42	3310	1/906	"	Dying. Temp 105°F.
53.	70	50	15400	1/227	Yes	Collapsed.
57.	64.	36	6824	1/468	"	Fever subsiding.
58.	80	52	27,000	1/148	Yes	
64.	97	60	12000	1/404	No.	

These few examples are only of interest by their variety. In some the ratio of white to red cells is almost normal: in others there is distinct leucopenia, as in case No. 47, whose white count is in great contrast to that of No. 33, where there is great leucocytosis.

In judging the significance however of white counts in pyrexia, one must take into consideration the stage of pyrexia at which the count is made. For the leucocytosis unless of the 'terminal' variety, (as in Nos. 33, 36, and 58), is very temporary and may be missed, either leucopenia or a normal W.C./R.C. being found instead. For example, in No. 47 above mentioned, the temperature was 106°F one hour previous to examination and it is quite possible

that some leucocytosis was then present. Therefore while these counts are of interest by their variety, more is to be learned by doing repeated counts in one case, starting at the end of apyrexia, continuing through pyrexia, and finishing at the succeeding apyrexia.

The following examples shew at what point in the malarial cycle leucocytosis begins, when it reaches its highest, and when it disappears.

	Age	Red Cells	Haemogl.	Time of examination	Temperature	White Cells	W. Cells / Red Cells	Remarks
A.D.C.	30	71	58		98·6°F	5100	1/622	Apyretic. Quartan.
		70·2	60	4·45 p.m	101°F	6000	1/601	2 days later.
				5·40 p.m.	104°F	9110	1/396	height of rigor.
				7·45 p.m	103°F	6290	1/573	temp. descending
				10·30 p.m	98·4°F	4560	1/760	Apyretic.
B.L.		73·3	48	2·30 p.m	98·6°F	3280	1/1117	Subtertian.
				8 p.m.	103°F	7520	1/487	no shivering
S.F.		65	56	3 pm.	98·2°F	2290	1/1419	Double Quartan.
				8 pm.	103·2°	2170	1/1497	No shivering
				8·50 pm.	104·2°	8643	1/376	Slight shivering
				10 pm.	98·6°F	2340	1/1397	Apyretic.
S.L.D.	12	80	64	9 am.	98·4°F	3740	1/1069	Quartan.
				2 pm.	102·6°	4340	1/921	Starting rigor.
				3 pm.	104°	5900	1/677	height of rigor
				4 pm.	103·8	3820	1/1047	
				9 am.	98·2	3670	1/1089	

White counts in pyrexia. (cont'd.)

	Age.	Red Cells	Haemog.	Time of Examination.	Temperat^re	White Cells	W.C./R.C.	
D.A.	29	60	50	10 am	98·4°F	3390	1/890	Quartan.
				4 pm	104·4°F	6560	1/462	

although leucocytosis is not very marked in these examples, a marked contrast is shewn between the ratio of white to red cells during apyrexia and pyrexia. A slight increase in the white count may occur as the temperature begins to rise, but the leucocytosis is most marked with the full development of the shivering, or the height of the attack. With the close of the shivering and the beginning of the temperature to descend, the white count at once begins to come down to its former condition of leucopenia which may be reached even before the temperature is normal. The actual white count may therefore be said to rise and fall with the temperature.

Regarding the observations made by various authorities on the white counts in malarial blood,

*Marchiafava and Bignami say that in malaria the leucocytes decrease relatively and absolutely except in pernicious cases, when the absence of this decrease is only temporary. They also quote the statement of Dionisi, that the white cells follow the red cells in their reduction, but occasionally become greatly reduced while the red cells tend to become normal.

†Mannaberg states that the leucocytes are often diminished, quoting a case of Kelsch's, where there was a W.C./R.C. of 1/2000, this being noted in a case of malarial cachexia; and that only in very pernicious malaria was a high ratio like 1/45 obtained.

*March. and Bignami on Malaria. New Sydenham Society, 1894. chap. 9, p 174.

†Mannaberg on Malarial Fevers. 1894. New Sydenham Society.

*Billings says the leucocytes are subnormal in number unless in pernicious cases. Also, that there is a slight increase at the beginning of a paroxysm, followed by a rapid fall to the end of pyrexia, when the greatest degree of leucopenia is seen: and that from this point a gradual increase begins till the start of next paroxysm, when things are repeated.

†Stephens and Christophers in their interesting book on malaria state that leucopenia is present in apyrexia, and that with the onset of a paroxysm there is a sudden leucocytosis of short duration, the white count being at its highest when the temperature is highest, and then subsiding with the temperature till there is leucopenia again at the close of the attack. In contrast to Billings they find the most marked leucopenia immediately before the next paroxysm.

Conclusions. regarding actual white counts.

(1). Leucopenia is constant in apyrexia in uncomplicated post-malarial anaemia, the white cells suffering a relatively greater reduction than the red cells.

(2). Rarely the white cells suffer an equal reduction with the red cells.

(3). These conditions, (1), or (2), may persist during pyrexia.

(4). Usually however in pyrexia there is an increase in the normal W.C./R.C., i.e. a leucocytosis. This is sudden and of short duration, most marked at the height of the rigor, or in its absence when the temperature is highest, and quickly subsiding with the falling temperature till leucopenia is again reached in apyrexia, if not before that. In other words, the white count rises and falls with the temperature

* Johns Hopkins Bulletin 1894.

† Practical Study of Malaria 1903.

(5). In pernicious cases where the patient is collapsed or dying a marked leucocytosis may occur, — so-called terminal leucocytosis - which is not of the temporary nature above noted.

(6). The persistence of the apyretic leucopenia is very marked; it may last for two months or longer, and may even be present when the red cells and haemoglobin are normal. Sometimes leucopenia becomes more marked as the red cells improve.

Chapter IV
The Differential White Counts.

The normal relative percentages of the different varieties of white cells in the blood are here taken as:—

Polymorphonuclear	from 65%	to 70%
Lymphocytes, or small mononuclear	" 20%	" 25%
Large mononuclear, or large hyaline with transitional cells	" 4%	" 10%
Eosinophile	" 2%	" 4%

The transitional cells included above in the large mononuclear class are large cells, whose nuclei approach in shape those of polymorphonuclear cells, but which in other respects resemble the mononuclear variety.

In postmalarial anaemia one finds variations from the above standard percentages, of a kind seldom, and to a degree perhaps never seen in any other disease. The constancy and persistence of these variations are also remarkable. The striking feature is an abnormally large relative increase of the large mononuclear and transitional cells, this usually constituting an absolute increase, even when leucopenia is present. Accompanying

this there is a corresponding relative (and absolute) reduction of polymorphonuclear cells.

Various observations have been made on this matter by writers on malarial fever.

Thus *Bastianelli found that while there is a diminution of polymuclear neutrophile cells, there exists instead a relative increase of large mononuclear and transitional cells. That this is specially noticeable in cases of advanced infection and in those of pernicious type, and is less observed in the incubal period and during first paroxysms.

According to †Cabot "the differential count shews a lymphocytosis whenever the white cells are subnormal, the large forms of lymphocytes being especially numerous while the polymorphonuclears and eosinophiles are scanty".

§Daniels says that the relative increase of large mononuclear cells "appears to be constant, and it is rarely less than 20%, though it may be twice as great. It occurs in all forms of malaria and persists after all the signs and symptoms of malaria have disappeared. It is found sometimes three months or more after an attack, and rarely disappears or even diminishes in a month.

Again, ‖Stephens and Christophers say; "the main characteristic change is, that there is an increase in the percentage of large mononuclears, so that at times they may even outnumber the polymuclear cells. This change is specially well marked in periods of apyrexia. When there is leucocytosis, the increase in the mononuclears may not be apparent."

*Quoted by Marchiafava and Bignami op. cit.

†Clinical examination of the blood 1903

§Op. cit. ‖Op. cit.

These observers all agree as to the nature of the principal change found. Daniels notes it "in all forms of malaria"; and Bastianelli, "especially noticed in cases of advanced infection and in those of pernicious type." Cabot, and Stephens and Christophers however mention the influence which the presence or absence of fever has on the differential count; the former noting the increase "whenever the white cells are subnormal," (i.e. in apyrexia); while the latter say "it is specially well marked in apyrexia and may not be apparent when there is leucocytosis" (i.e. in pyrexia). These writers do not mention what variety of white cell being increased constitutes the leucocytosis of pyrexia in cases where the mononuclear increase is not apparent; but from the differential counts to be presently stated, it will be seen that the increase is mainly of the reduced polymorphonuclears and the resulting percentages are those of normal blood.

*Ellanchiafava and Bignami believe that there is no proper leucocytosis in malaria, and that any leucocytosis occurring, due to increase in polynuclear neutrophile cells is not uncomplicated malaria. Also that the presence of a true leucocytosis, (a marked increase in polynuclear cells), in malarial blood, may justify one in suspecting complications of an inflammatory nature. They add however that leucocytosis may occur where collapse is present, or during the failure of vital power immediately preceeding death.

Regarding the statement made on page 30, that the relative increase of large mononuclear and transitional cells usually constituted an absolute increase, it is necessary to state what is here meant by the latter term. The writer defines it as:- An increase per mm^3 in any case of the large mononuclear and transitional

* Op. cit.

cells, above the number per mm^3 which would be found in the same case at normal percentages, if the ratio of white to red cells were 1:500. (the percentage of red cells in the case remaining constant). After the previous interpretations of the terms leucopenia and leucocytosis, the normal standard thus arrived at is the only possible one.

For example, with the percentages on page we find normally

Polymorphonuclears 6500 - 7000 per mm^3.
Lymphocytes 2000 - 2500 " "
Large Mono^{rs} & Transit^{ls} 400 - 1000 " "
Eosinophiles 200 - 400 " "

If we take a case where the Red Cells are 40%
" " White Cells . 2000 per mm^3
then W.C./R.C. = 1/1000 a leucopenia; and if the differential count shews large mononucleaus 30%, we have 600 cells of this variety per mm^3.

But with the red cells at 40%, 4000 white cells per mm^3 would be required to give us the normal W.C./R.C of 1/500, and this number at normal percentages gives us 160 - 400 large mononucleaus per mm^3. Therefore 600 constitutes a small absolute increase of large mononuclear cells for the case under consideration. To take 10,000 white cells as our standard of comparison, instead of 4000 as mentioned, would be wrong, as 10,000 white cells would represent a leucocytosis in this case.

In the following differential counts, the actual numbers of large mononuclear and transitional cells per mm^3 will be included and also in each case the standard of comparison arrived at as above stated. As a rule the polymorphonuclear cells are absolutely diminished. This is naturally always the case in leucopenia and occasionally so in leucocytosis.

Quartan Differential Counts. — Apyrexia.

No.	Red Cells%	White Cells.	W.C. / R.C.	Large Mononuclear	Lymphocy*	Polymorphs.	Eosins.	Myelocytes		Large Mononuclears per cubic millimetre.	Normal Standard of comparison
1.	49·5	4220	1/587	22·6	23·5	53·3	·6			953	198 - 495.
	83	5600	1/741	24	18·7	56·7	·6		1 week later	1344	322 - 829.
	100	4100	1/1220	18·7	22·5	57·9	·9		3 wks later	766	400 - 1000.
	102	5300	1/962	19·1	19·3	60·5	1·1		1 mth later	1052	408 - 1020.
3.	59	4100	1/720	27·1	30·3	42·2	·4			1111	236 - 590.
4.	60	2700	1/1100	22·1	23·7	53·9	·3			596	237 - 594.
5.	60·6	3390	1/890	29·3	20·2	50	·5			993	241 - 603.
6.	62	3565	1/847	27·6	21·6	50·4	·4			983	244 - 608.
	78	5350	1/732	24·3	18·3	56·6	·8		1 wk. later	1300	313 - 783
	85	4100	1/1040	17·5	19·8	61·7	1·0		3 wks "	717	341 - 852.
	74	4500	1/827	30·1	10·3	58·9	·7		relapse	1354	297 - 744.
7.	67	5120	1/654	31	16	50·8	·2			1587	268 - 669.
8.	65	2290	1/1419	24·6	23·6	50·4	1·4			563	260 - 649.
9.	66	5720	1/576	29	23	47·7	·3			1658	271 - 679.
10.	66	6210	1/533	20·5	16·3	62·6	·6			1242	265 - 662.
	98	5000	1/980	23·4	10	65·1	1·5		6 wks later.	1170	392 - 980
	100	6000	1/840	26	12·2	60·8	1·0		3 wks "	1560	403 - 1008.
11.	66	2866	1/1160	40	12·5	46·6	·9			1146	265 - 664.
12.	72	4500	1/800	25·2	4·4	69	1·4			1134	288 - 720.
13.	72	4000	1/900	18	29	52·1	·9			720	288 - 720
14.	71·4	6900	1/517	19·5	18·7	60·8	1·0			1345	281 - 713
	89	3530	1/1260	15	33	50·6	1·4		3 wks after.	529	356 - 889
15.	76	5600	1/678	13·8	43·2	42	1·0			772	304 - 759
16.	75	4000	1/937	17·3	18·6	63·8	·3			692	300 - 750
17.	75	4200	1/892	28·5	20·4	49·5	1·6			1197	299 - 749
18.	77	5770	1/670	31·2	20	47·7	1·1			1800	309 - 773.
19.	80	5940	1/660	22·3	17·1	58·3	2·3			1324	313 - 784

Quartan Differential Counts. (contin^d)

No.	Red cells %	White cells.	W.C. / R.C.	Large Mononuclears	Lympho-cytes.	Polymorphs.	Eosino^s.	Myeloc^s.	Large Mononuclears per cubic millimetre.	Normal Standard.
20.	83	6115	1/677	23·4	16·8	59·6	·2		1430	331 - 827.
21.	88	6310	1/697	18·4	19·2	61·5	·9		1161	352 - 879.
22.	86	4300	1/1000	29·2	21·9	48·2	·7		1255	344 - 860.
	84	3800	1/1100	23·4	20·5	55	1·1		889	374 - 836.
23.	92	5730	1/800	23·2	16·4	60·2	·2		1329	367 - 918
	98	9000	1/340	12·2	18·2	68	1·6		1098	388 - 972.

Benign Tertian
Differential Counts in Apyrexia

No.	Red cells %	White cells.	W.C. / R.C.	Large Mononuclears	Lympho-cytes.	Polymorphs.	Eosino^s.	Myeloc^s.	Large Mononuclears per cubic millimetre.	Normal Standard.
24.	39	4000	1/490	27·6	22·6	48·3	1·5		1104	157 - 392.
25.	40	4200	1/476	32·6	12·6	54·3	·5		1369	159 - 399.
27.	57	5400	1/527	32·3	23·8	43·7	·2		1744	227 - 369.
28.	59	2950	1/1006	28·2	15·2	56·1	·5		602	284 - 710.
29.	70	5940	1/588	31·1	27·8	40·9	·2		1847	279 - 698.
30.	71	2500	1/1420	24·1	21·8	53·6	·5		602	284 - 710.
31.	78	6000	1/650	31·9	28·4	39·1	·6		1914	312 - 780.
32.	88	4800	1/920	20·7	16·1	62·3	·9		993	353 - 883.
33.	92	4780	1/962	27·9	19·5	52·4	·2		1333	368 - 919.

Subcutaneous Differential Counts in Apyrexia.

No.	Red cells %	White cells per mm³	W.C. / R.C.	Large Mononuclears	Lymphocytes	Polymorphs.	Eosinos.	Myelocytes		Large Mononuclears per cub. millimetre	Normal Standard.
36.	32	3120	1/14	34·1	11·1	54·5	·3			1063	107 - 318.
	34	3260	1/21	26·2	16·1	57·4	·3		2 wks after	854	111 - 326.
	77·3	3820	1/11	19·1	22·4	58	·5		9 wks after.	729	309 - 772.
37.	35	2980	1/88	12·5	14·9	72	·6	·1		372	140 - 350.
39.	40	3400	1/88	29·5	16·1	53	·7	·7		1003	152 - 399.
42.	52	4810	1/38	28·1	33·3	37·2	1·2	·2		1352	207 - 517.
44.	54	2800	1/66	35·7	25·1	38·5	·3	·4		999	216 - 540.
45.	55	2800	1/90	29·1	18	52·6	·3			814	221 - 554.
46.	54·6	6740	1/04	28·2	20·3	50·4	1·1			1900	218 - 548.
47.	58	5400	1/36	29·7	23·6	45·4	1·3			1603	231 - 578.
48.	59	3820	1/81	19·4	17·8	62·5	·3			741	239 - 596.
50.	61	7878	1/90	20·4	14·1	64·3	1·2			1607	245 - 614.
	70	6100	1/73	22·8	15·1	61·7	·4		2 wks after.	1390	279 - 699.
51.	68	3850	1/83	20	25·4	53·4	1·2			770	271 - 677.
52.	61·6	4074	1/56	17·3	18·8	62·1	1·8			704	246 - 616.
54.	68	6110	1/70	24·8	22	52·6	·6			1512	271 - 677.
56.	71	2164	1/644	19·2	17·5	61·3	2·0			415	288 - 711.
57.	74	5602	1/66	24·1	18·2	56·3	1·4			1350	298 - 746.
58.	72	6000	1/60	25·7	13·7	58·7	1·9			1542	288 - 720.
	75	6400	1/90	26·3	14·2	58·3	1·2		1 mth. after	1683	302 - 755.
	89	7600	1/84	18·4	19·3	60·9	1·4		3 wks after.	1398	363 - 887.
59.	74	5252	1/76	36·1	11	52·3	·6			1895	298 - 746.
	81	6900	1/24	28·6	6	64·4	1·0		3 wks after	1973	343 - 859.
	106	7800	1/79	26·6	9·8	59·9	3·7		5 wks after	2074	423 - 1059.
61.	80	5000	1/80	21·6	28·5	47·8	2·1			1080	320 - 800
62.	85	3950	1/74	17·6	23·8	58·2	·4			695	339 - 848.
63.	86	6100	1/04	21·4	22·5	55·3	·8			1305	343 - 858.
64.	88	6410	1/02	26·6	13·9	57·7	1·8			1673	360 - 900.
65.	95	10,000	1/75	25·2	24·6	48	2·2			2520	380 - 950.

In these examples taken during apyrexia, the great relative increase of the large mononuclear and transitional cells is well seen, and also the corresponding relative diminution of the polymorphonuclear cells. The highest percentages noted are:—

40% in a quartan case
36·1% " subtertian "
32·6% " benign tertian "

The lowest percentage, 12·2% is in case No 23, a very mixed quartan, almost well.

In the following table is given the average percentages of the various classes of white cells in the total number of apyretic counts (71), and also the averages under each variety of infection.

	Large Mononuclears %	Lymphocytes %	Polymorphon.rs %	Eosinoph.s %
Average percentages in 71 cases.	24·6	19·5	54	0·93
Average percentages in 33 quartans.	23·5	19·9	55·4	0·86
Average percentages in 9 benign tertians.	28·4*	20·8	50·06	0·6
Average percentages in 29 Subtertians.	24·6	18·5	53·5	1·12

*The benign tertian average, taken from so few cases, is probably rather high.

Regarding the <u>absolute</u> increase of large mononuclear and transitional cells in Apyrexia, we find (interpreting the term as before stated);—

	Absolute increase.	No absolute increase.
Quartans	19.	11.
B. Tertians	7.	2.
Sub-tertians	22.	5.

The largest numbers of large mononuclear cells per mm^3, are 2520 and 2074. Frequently the number lies between 1000 and 2000 per mm^3.

It will also be noticed that the relative, (and at times absolute) increase of large mononuclear cells is as persistent as the leucopenia; being found sometimes still present when the red cells and haemoglobin have reached normal limits: (e.g. Nos 1, 10, 58, and 59).

Regarding the other varieties of white cells:—

The lymphocytes may be diminished, but as a rule are little affected.

The eosinophiles are almost always greatly diminished.

Differential Counts in Pyrexia

No.	Red cells %	White cells	W.C. / R.C.	Large Mononuclrs.	Lympho-cytes.	Poly-morphons.	Eosins.	Myelocyts.	
25.	58	8900	1/327	12	11·7	75·8	·5		
33.	21	19000	1/55	24·2	25·3	49·2	·6	·7	comatose.
36.	40	17800	1/112	45·6	19·6	34·7	·1	·1	dying.
39.	50	9170	1/272	10·6	8·6	78·7	2·1		
46.	48	5400	1/444	14·6	18	66·3	1·1		
	47	6800	1/346	15·1	13·1	71·4	·4		1 week later.
	35·4	3820	1/463	12·9	20·9	65·8	·4	·3	2 wks. " .
	40	2673	1/746	15·9	14·2	68·8	1·1		2 wks " .
47.	60	3310	1/906	29·5	19·8	50·4	·3		Dying: temp 105° F.
53.	70	15400	1/227	12·9	18·3	68·5	·3	·2	collapsed.
57.	64	6824	1/468	19·1	22·4	58	·5		Fever subsiding.
58.	80	27000	1/148	45·	13·6	40·6	·8	·3	
64.	97	12000	1/404	18	11·4	70·3	·3		Slight attack.

These are the same isolated examples whose actual counts in pyrexia have already been considered, (page 26), and the statement there made applies here as well, that one must take into consideration the stage of pyrexia at which the count is made: otherwise the results obtained (as in the above cases, which are at varying stages of pyrexia!), are confusing. For, while the changes in the actual white count during pyrexia are of a temporary nature, so also are those in the relative count.

It may be noticed however that where there is a rise in the white count, there is frequently a fall in the percentage of large mononuclear cells to an almost normal level, with a corresponding rise in polymorphonuclears. Also, that when leucopenia persists, the abnormally high mononuclear percentage also persists. This is very marked in case No 47.

In three cases with distinct leucocytosis — viz: 33, 36, and 38 — there is a great relative increase of large mononuclear cells, amounting to a huge absolute increase. In these cases, the leucocytosis was "terminal", and one might rather have expected an increase of polymorphonuclear cells. Kelsch and Ewing have noticed however (Cabot) that in severe malignant tertian attacks the leucocytosis may consist of an increase mononuclear cells. It may be added that these three cases were aged 3½ months, 2½ months, and 27 months respectively.

In the following table are the changes in the differential count as they occur at varying stages of pyrexia. These changes are seen to more or less coincide with those occurring in the actual count.

Differential White counts in Pyrexia. (ctd.)

	Red cells %	Time of examinat.	Temperature	White cells.	U. Cell / R cells	Large Mononuclr.	Lymphocytes.	Polymorphos.	Eosinophs.	
A.D.C.	71		98·4°F	5100	1/622	27·3	20·2	52	·5	Quartan.
	70·2	4.45 pm	101°F	6000	1/601	14·6	22·6	61	1·8	Two days later
		5.40 "	104°F	9110	1/396	14·2	20·4	64·6	·8	Height of rigor & fever.
		7.45 "	103°F	6290	1/573	14·3	22·2	62·8	·7	Temperat. falling.
		10.30 "	98·4°F	4560	1/760	24·9	23·6	50·5	1·0	Apyrexia.
D.A.	60·6	10 am.	98·4°F	3390	1/890	29·3	20·2	50	·5	Quartan.
		4 pm.	104·4°F	6560	1/462	12·4	27·6	58·6	1·4	Height of attack.
B.L.	73·3	2·30 pm	98·6°F	3280	1/1117	22·2	23·1	54·4	·5	Subtertian.
		8 p.m.	103°F	7520	1/487	16·4	18·2	64·6	·8	No rigor.
S.L.D.	80	9 am.	98·4°F	3740	1/1069	21·2	18·4	60	·4	Quartan.
		2 p.m.	102·6°F	4340	1/961	10·5	11·4	77·7	·4	Shivering.
		3 p.m.	104°F	5900	1/677	11·8	11·5	76·2	·5	Marked "
		4 p.m.	103·8°F	3820	1/1047	17	12·9	69·8	·3	Temperature falling.
		9 a.m.	98·2°F	3670	1/1089	22·6	20·1	56·5	·8	Apyrexia.
S.F.	65	3 pm.	98·6°F	2290	1/1419	24·6	23·6	50·4	1·4	Double quartan.
		8 p.m.	103·2°F	2170	1/1497	12·8	18·9	67·8	·5	
		8.50 p.m.	104·2°F	8643	1/376	13·1	17·4	68·9	·6	Slight rigor.
		10 a.m.	98·2°F	2340	1/1397	22·8	22·5	53	1·7	

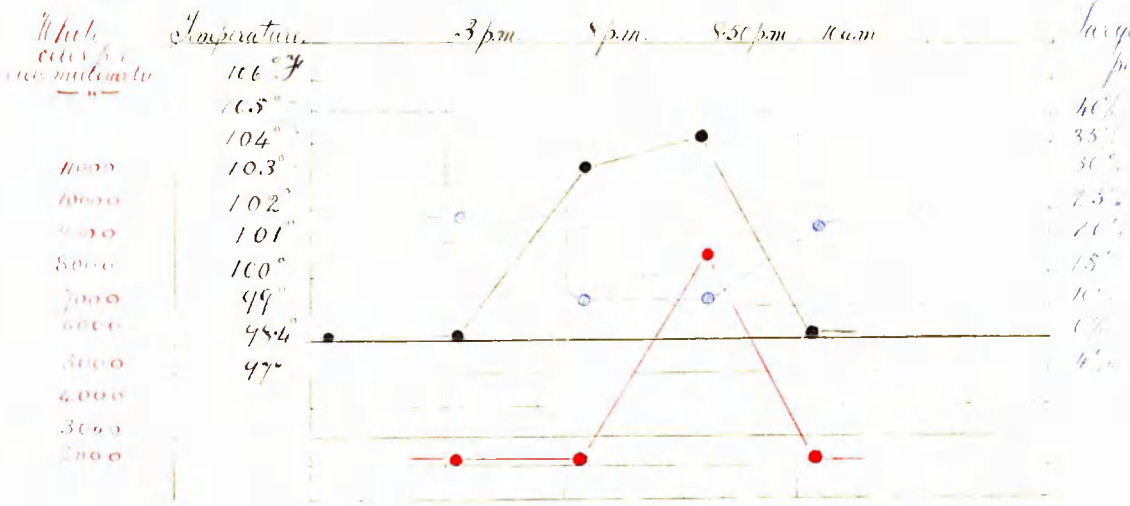
The points to be noticed above are :— a fall in the abnormally big percentage of large mononuclear cells, and a corresponding rise in the percentage of polymorphonuclears, with the onset of pyrexia. This is most marked during the shivering when the temperature

is highest and the actual white count is rising, but may become evident before leucocytosis has developed. With the falling temperature and white count, the percentage of large mononuclear cells rises again to almost its former apyretic height, and the polymorphonuclear cells correspondingly decrease.

The sequence of events can be graphically shewn in chart form as below.

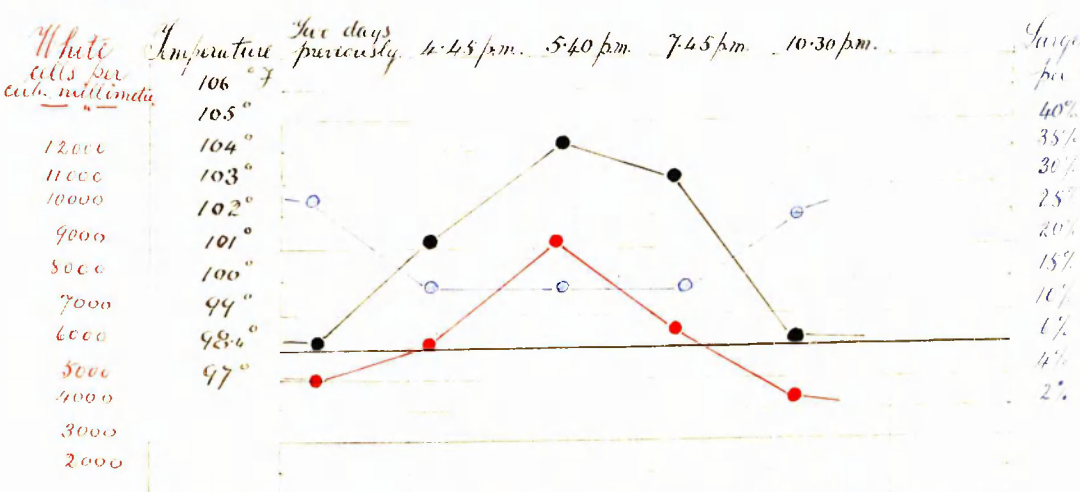
Double Quartan.

N. F.



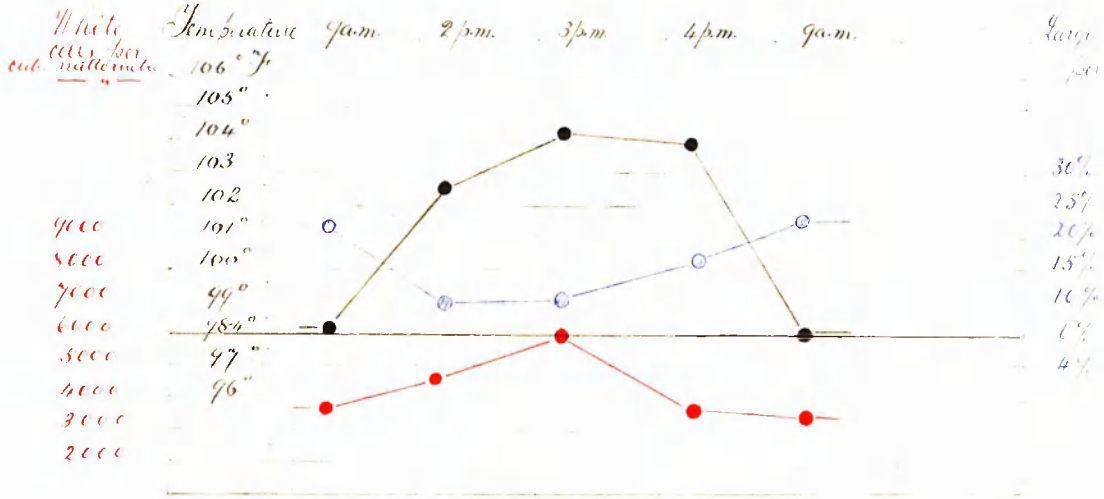
Quartan

N. L. G.



Quarton.

S. F. L.



Regarding the effect of pyrexia on the absolute increase of large mononuclear cells, this depends on the preservation or not of the relative increase and also on the presence or absence of leucocytosis.

If, with leucocytosis, the relative mononuclear reduction is slight, naturally there is great absolute increase. If with leucocytosis there occurs considerable relative reduction, the one condition neutralizes the other and the absolute number of large mononuclear cells remains about the same, or may possibly be diminished.

Thus taking the five cases lately considered on page .

	Temperature.	Large Mononuc. per mm.³	Normal number for case	
A.B.C.	98.4° F	1392	253 - 634	Absolute increase in apyrexia. Then, before white count rises,
	101°	876	288 - 721	the relative count falls, and the absolute increase disappears.
	104°	1293	" "	Rise in actual white count restores matters.
	103°	899	" "	Actual count falls,
	98.6°	1155	" "	great relative rise restores absolute increase.
L.C.F.	98.4° F	993	241 — 603	The slight absolute increase present is kept at par by the
	104.4° F	813	" "	same, by relative fall and actual rise.

	Temperature	Large clear-nucleus per m.m.^{3}	Normal number for case.	
B.K.	98.4°F	728	293 – 732	No increase: then, the relative reduction being
	103°F	1233	" "	slight leucocytosis gives an absolute increase.
S.L.D.	98.6°F	792	320 – 800	No absolute increase.
	102.6°	453	" "	Still less: (relative fall before actual rise).
	104°	696	" "	feeble actual rise.
	103.8°	649	" "	" " "
	98.4°	829	" "	fall in actual, and rise in relative count.
S.J.	98.4°F	563	260 – 649	No increase.
	103.2°	277	" "	Relative fall before white count rises.
	104.2°	869	" "	Slight abs. increase due to actual rise.
	98.4°	533	" "	return to 'status quo'.

Conclusions.

regarding differential white counts in postmalarial anaemia.

(1). The most striking feature is the relative increase of large mononuclear and transitional cells, as a rule reaching to 20% of all varieties, and occasionally rising higher, even to 40%.

(2). During apyrexia, (when leucopenia is present), this change is constant and most marked.

(3). This increase may persist, though usually to a less degree, when pyrexia and leucocytosis are present, but as a rule at such times it disappears temporarily, to return again with apyrexia and leucopenia.

(4). It is also to be found in the blood for a long time after the fever has

ceased, and may persist (with leucopenia), when the red cells and haemoglobin are normal.

(5). The relative increase is often so marked as to constitute, even when the leucopenia is great, a distinct absolute increase of large mononuclear cells per cubic millimetre. This absolute increase may in pyrexia become more marked, remain unaffected, or disappear.

(6). The polymorphonuclear cells are generally proportionately reduced in percentage as the large mononuclear cells are increased: and vice versa.

(7). The lymphocytes are little affected relatively, being only occasionally slightly reduced.

(8). The eosinophile cells are almost invariably diminished.

(9). A true polymorphonuclear leucocytosis does not occur in uncomplicated postmalarial anaemia.

White Count in the presence of complications.

When a complication occurs in postmalarial anaemia which ordinarily produces leucocytosis, the actual white count is characteristic of the complicating disease. In addition, the differential white counts fail to shew malarial peculiarities, and the result is a leucocytosis with normal percentages of all varieties, or with excess of polymorphonuclear cells — a true polymorphonuclear leucocytosis.

For example:-

Double tertian malaria complicated by acute nephritis.

Age	Red Cells %	Haemogl. %	White cells.	W.C. / R.C.	Organisms	Large Mononuclears	Lympho cytes.	Polymorph-onuclears	Eosinophs.	
8	78	60	6000	1/650	Yes.	31.9	28.4	39.1	.6	Apyretic. No nephritis.
	84	75	10,000	1/422	No.	17.4	24.6	56.3	1.7	9 days later.
	80	72	15,500	1/258	No.	10.6	25.2	61.8	2.4	8 days later.

In this case, as the result of treatment fever had stopped, and all organisms had disappeared from the peripheral circulation. Then suddenly pain in the

back set in accompanied by facial oedema. The urine became very scanty and contained blood and albumin in great quantity, and epithelial casts. The counts shew the occurrence of leucocytosis, and the relative fall of the large mononuclear cells.

Quartan case complicated by acute nephritis.

Age.	Red cells%	Haem%	White cells	W.C / R.C.	Orgms.	Large Mon.	Lympho-cytes	Polymorph nuclears	Eosins.	
17	58	44	5400	1/537	Yes.	29·7	23·6	45·4	1·3	2/9/4.
	56	40	7000	1/400	Yes.	11	18·5	69·9	·6	Onset of Nephritis. 7/9/4.
	66	52	10,800	1/299	No.	13·7	27·7	56·8	1·8	15/9/4.
	80	70	8900	1/450	"	16·4	20	63·2	·4	25/9/4.
	84·6	70	7780	1/543	"	28·1	23·5	46·7	1·7	7/10/4 recovery.

Here with the onset of nephritis, the leucopenia is changed to leucocytosis, and the large mononuclear count falls relatively. On the disappearance of the nephritis the blood becomes characteristic of malarial infection once more.

Subtertian case complicated by empyema.

Age.	Red cells%	Haem%	White cells.	W.C / R.C.	Organisms	LARGE MON. NUCLEAR	Lympho-cytes.	Polymorphonuclears	Eosinophils	
13.	46·3	38	10,185	1/227	Yes.	12·6	16·5	70·4	·5	Day of admission
	57·2	50	10,300	1/287	No	19·8	19	61·1	·1	3 days later (after operation).
	52·4	42	17,450	1/50	No	6·8	8·1	84·9	·2	8 days later.

A case of chronic malaria: attacks frequent during the three months preceding admission. On admission:— marked cachexia: general oedema and ascites. Spleen huge, liver enlarged, and fluid in left pleural cavity. This fluid on aspiration proved to be pus, and two portions of ribs were removed to ensure proper drainage. Temporary improvement resulted, as seen above, with a striking relative mononuclear increase. A few days later however patient died of general peritonitis. (The leucocytosis due to this is seen in the third count).

Chapter V.

(a). Abnormal White Cells etc.

In malarial blood the polymorphonuclear cells, the lymphocytes, and the eosinophiles, present the appearances and variations seen normally. It may be added however that malarial pigment is found occasionally in the first mentioned variety.

Our interest lies in the large mononuclear cells. The large majority of these present the same appearance as those met with in smaller amounts in normal blood. The average size is increased however. These cells take an active part in phagocytosis, and are frequently seen containing malarial pigment either scattered throughout the protoplasm or lying in little masses. In almost every blood-film examined great numbers of large mononuclear cells were seen in an advanced state of degeneration, the protoplasm being ragged and vacuolated, and hardly taking up the stains.

On two occasions karyokinesis was observed in large mononuclear cells, shewing that cell multiplication was going on in the peripheral circulation.

In several cases, large mononuclear cells whose protoplasm and nucleus stained a deep reddish purple with eosin and haematoxylin were observed in small numbers. These seem identical with those of similar appearance described by Bastianelli.

Myelocytes. These were rarely found, in very small amounts, and only in severe cases. Almost always the cells were of large size and with neutrophile granules, on one occasion only a specimen of large eosinophile myelocyte being seen. Their presence was noted in 9 out of 70 cases. All these were subtertian in nature, six being very young, and four having marked leucocytosis. The percentages lay between ·1% and ·7%.

(b). Summary of Pathological Signs, in 70 cases.

Enlargement of the Spleen was fairly constant. The degree of enlargement varied from slight to enormous. The largest spleens were found in bad cachectic cases.

In 3 cases, the Splenic mass extended into the pelvis.

In 12 " " " to below the umbilicus.

In 22 the enlargement was marked, although not to the umbilicus.

The liver was occasionally moderately enlarged. In 2 cases the vertical dulness was increased 4" in the nipple line.

Slight jaundice was present in 3 cases.

Subcutaneous oedema occurred in 11 cases, in 2 of which ascites was also present. Albuminuria occurred in 11 cases sometimes accompanied by oedema. (In the 2 cases of ascites there was no albuminuria). Nephritis occurred twice.

Systolic heart murmurs with maximum intensity over the base, were heard in 5 cases.

Chapter VI.
Notes on Diagnosis.

In the majority of cases the diagnosis of postmalarial anaemia or, more broadly expressed, of malarial infection recent or actually present, is not very difficult. In benign infections occurring in a district where attacks are common, the diagnosis is usually easy, and quickly confirmed by treatment.

The finding of the malarial organism in a patients blood is of course conclusive evidence; and, if after careful search organisms

cannot be found, (often the result of taking quinine), the discovery of pigmented leucocytes justifies the diagnosis of malaria.
The greatest difficulty arises in severe cases of subtertian fever where neither organisms nor pigmented leucocytes can be found, the temperature is remittent, and no shivering occurs.
The disease most commonly confused with malaria is typhoid fever. Thus, as above said, in subtertian fever no organisms may be seen and no pigmented leucocytes; there may be no shivering and the temperature may be only slightly remittent. The spleen is generally enlarged to some extent, and there may be diarrhoea and vomiting.
On examining the blood in any such doubtful case, one gets great assistance from the leucocytes. The actual counts per cubic millimetre are only helpful in limiting the diagnosis, as leucopenia may be present in both typhoid fever and malaria; but the differential counts separate the diseases from each other unmistakeably. The abnormally large percentage of large mononuclear cells in malarial blood is the distinctive feature of value, the presence of a large percentage varying from 20% to 40% excluding typhoid fever at once.
It is true that in typhoid fever, especially in the later weeks, as the general condition becomes weaker and the white count falls, a relative increase in mononuclear elements may occur, but never to the degree found in postmalarial anaemia.
Thayer, in his study of typhoid blood includes the following table, representing averages of the percentages of the white cells in the different weeks of the disease: (Cabot page 206).

Averages of differential counts in typhoid. (Thayer).

	No. of Counts.	Polymorphonuc's %	Small Mononuc's %	Large Mononuclear %	Eosinophiles %
1st week of fever.	12	74	13	12	·5
2nd "	39	71	14	13	·8
3rd "	34	66	21	11	·3
4th "	19	65	20	14	·4
5th "	8	62	18	19	·3
6th "	4	58	22	13	6·0

The large mononuclear cells are not greatly increased here at any time, and least of all in the first weeks when the question of diagnosis might occur. The polymorphonuclear cells appear fairly normal in percentage, and there is an occasional diminution of lymphocytes and eosinophiles. One must remember that the above figures are averages, but then is a great contrast between them and the malarial averages on page 37.

According to Stephens and Christophers, "it is not going too far, to say that typhoid and malaria can be readily distinguished by the leucocyte count." (though these writers make a relative increase of lymphocytes in typhoid blood, an important point of contrast).

Among other diseases which might possibly be confused with post-malarial anaemia is so-called Splenic Anaemia. This though comparatively uncommon, might, occurring in a malarial district, be mistaken for malarial cachexia. Both conditions have large spleen; both may have severe anaemia with the blood tending to the chlorotic type, and leucopenia is common to both.

Here again however the peculiarities of the malarial relative count exclude Splenic anaemia.

The severe anaemia accompanying rickets, or hereditary syphilis of infants, might possibly at times be attributed to malaria

where that disease is prevalent. The frequency of leucocytosis with relative increase of lymphocytes in these diseases, along with the associated symptoms, afford a sufficient contrast to malarial features.

Acute inflammatory conditions accompanied by pigour, (e.g. pyelitis) may cause symptoms similar to those of a malarial attack. (I have examined a patient, sent home as a good case of subtertian fever, and found he was suffering from an empyema). The inflammatory leucocytosis present in such cases excludes uncomplicated malaria at once.

Finally, a disease may be mentioned as possibly resembling malarial infection in its relative white counts; namely trypanosomiasis. Daniels says that in trypanosomiasis the increase of large mononuclear cells "appears to be constant"; while Stephens and Christophers say; "It has been found in one case, but if confirmed can but slightly affect the value of the counts in malaria as a diagnostic means, for the clinical features of trypanosomiasis as far as are known are extremely characteristic."

Conclusions.

(1). The absence of the characteristic leucocytic features of malarial blood in any given case, can be said to exclude malaria from the diagnosis.

(2). If in any case in apyrexia, a leucopenia with relative increase of large mononuclear cells to 15% or upwards be not present, then the case is not one of uncomplicated post malarial anaemia. Or, to state it differently,

(3). An increase of large mononuclear and transitional cells to 20% or more in any suspected case in apyrexia, warrants the diagnosis of malarial infection, to the exclusion of all others.

(4). If this increase occur during pyrexia, with or without

leucocytosis, the diagnosis of malaria can be even more positively made.

(3). If however during pyrexia, no marked increase of large mononuclear and transitional cells is found, one cannot affirm that the case is not malarial.

(Stephens and Christophers found an increase to beyond 15%, proof of actual or recent infection, while with a value of 20% they could almost always find an organism or two, or pigmented leucocyte; a value of over 20% implying actual infection at the time of Examination).

Notes on a case of Postmalarial anaemia, indistinguishable from pernicious anaemia.

As before stated, (page 8), Bignami and Dionisi mention cases of very pernicious malaria, where the blood is similar in all respects to that of a typical case of pernicious anaemia. The following case is of interest, the condition of the blood being evidently the result of malarial infection of long duration.

cf. G. M. aet 58, miner,

had suffered every summer for several years from severe malaria, accompanied by marked shivering. At intervals after large doses of quinine, the fever would disappear and patient would be able to return to work: he always felt tired however, and far from well. Four months prior to examination, after some months of freedom from fever, the attacks started again, and in spite of vigorous treatment by his doctor he failed to improve, and had to take to bed. There he had remained three months, when he was carried to the Rio Tinto hospital.

On Admission, patient was greatly emaciated, and extremely anaemic in appearance, his face being a blanched yellow grey.

while his lips were almost of the same colour. Considerable oedema of the feet and ankles was present.
Spleen was moderately enlarged. Liver dulness normal. A soft V.S. murmur was audible all over the praecordia, but with greatest intensity at the base. No albuminuria present.

The following counts shew the progress of his condition while in hospital. Patient's last definite attack of fever had occurred two or three weeks previously. No malarial organisms were found at any time.

Date.	Red Cells %	Haemoglº %	Col. Index.	White Cells. p.c.mm.	Large Monons.	Lympho-cytes	Polymorphs.	Eosinos	
15/1/5.	18·6	25	1·3	2807	6·8	40·4	51·2	1·6	4 normoblasts, 3 megaloblasts in 1200 white cells.
20/1/5.	17·4	22	1·3	2100					Poikilocytes. Polychromia.
25/1/5	17·2	22	1·3	2500	13·6	39·7	44·7	1·0	5 Megs. 2 Normos. per 1000 Whites.
31/1/5	16·35	20	1·3	3500	2·6	50·1	47·3	—	59 megals. 85 normoblasts in whole large film.
7/2/5	24	40	1·6	2600	·4	48	51·5	·5	7 Normos. 1 Megs. per 1000 Wh.
14/2/5	37	45	1·2	3250	2·4	35·4	60·2	2·0	2 normoblasts per 1000 W.C.
21/2/5	40	50	1·2	3000	1·4	30·3	46·9	1·4	1 normoblast " "
29/2/5	45	56	1·2	4000	2·9	22·6	72·6	·9	no nucleated red cells.
8/3/5	37	52	1·4	4500	2·3	25·1	71·6	1·0	relapse.
14/3/5	35	45	1·3	3700	4·1	40·4	54·1	1·4	

To all appearances this is a case of pernicious anaemia. But the history of malaria almost up to the time of admission, is beyond all doubt, the patient having been under the frequent and competent care of Dr Rafael Sancha of Zalamea, who supplied the history in all its details. Whether the anaemia was of the same type from the beginning, or only latterly took on the

characteristics of pernicious anaemia, it is impossible to say definitely. For this reason the case has been inserted here, instead of in the general tables.

Notes on Prognosis. Chapter VII.

The prognosis of malarial anaemia is more or less the prognosis of the malarial fever causing it. If the fever is mild and of short duration, so then is the resulting anaemia. On the other hand, when fever has continued for a long time and cachexia developed, recovery may be slow; and there is a certain risk of patient becoming a victim by reason of his weakened resistance, to intercurrent disease, or to some disease the result of secondary cachectic changes in the various organs.

The prognosis however is usually good, being better in benign infections than subtertian.

In Quartans. There is no direct risk to life, this form of fever never taking on pernicious symptoms, and the anaemia never becoming extreme. Cachexia may be marked, but good recovery is the rule under systematic treatment. Quartan cases however not infrequently shew a tendency to relapse, attacks of fever with reappearance of organisms occurring after patient has considerably improved and shewn signs of being free from infection.

In Benign Tertians. The same remarks hold good, except that while the anaemia is more rapidly produced, there is a speedier response to quinine and less tendency to relapse.

Subtertians. The prognosis is scarcely so good. The infection is of severer type, and the extreme anaemia which may result in pernicious cases is of grave import in itself. Fortunately such cases are not common, and the large majority make good recoveries

under treatment. The prognosis for adults is much better than for children. The mortality in 68 cases here reported was as follows:- 24 quartans - no deaths.

10 benign tertians - one death, (cause not reported).

34 subtertians - 6 deaths, viz.

3 — infants with very pernicious attacks.

1 — a girl, 10 years old, who died with diarhoea, ascites, and oedema, in a very cachectic state.

1 — a woman; pernicious attack with cerebral symptoms.

1 — a boy, aet. 13, who died of complicating empyema and general peritonitis.

Chapter VIII
Notes on Treatment.

In all cases the system employed was, first to rid the blood of malarial organisms if these were present, and then to assist new blood formation. When a patient was actually infected and suffering from continuing attacks of fever, aperient medicine was given some hours before the expected paroxysm, usually in the form of $MgSO_4$ and Na_2SO_4, aa ℥ii in solution. Then 2½ to 3 hours before the attack quinine sulphate in doses of grs X to grs XXX, or more, was given. This was always prescribed in solution, (℥ss containing grs X). This quinine treatment was continued, (only on the days when an attack was expected, or possible), for a varying time, according to the case and the result.

When organisms had completely disappeared from the blood, the solution was discontinued and Arsenic, iron, and quinine given regularly each day, sometimes in solution, but

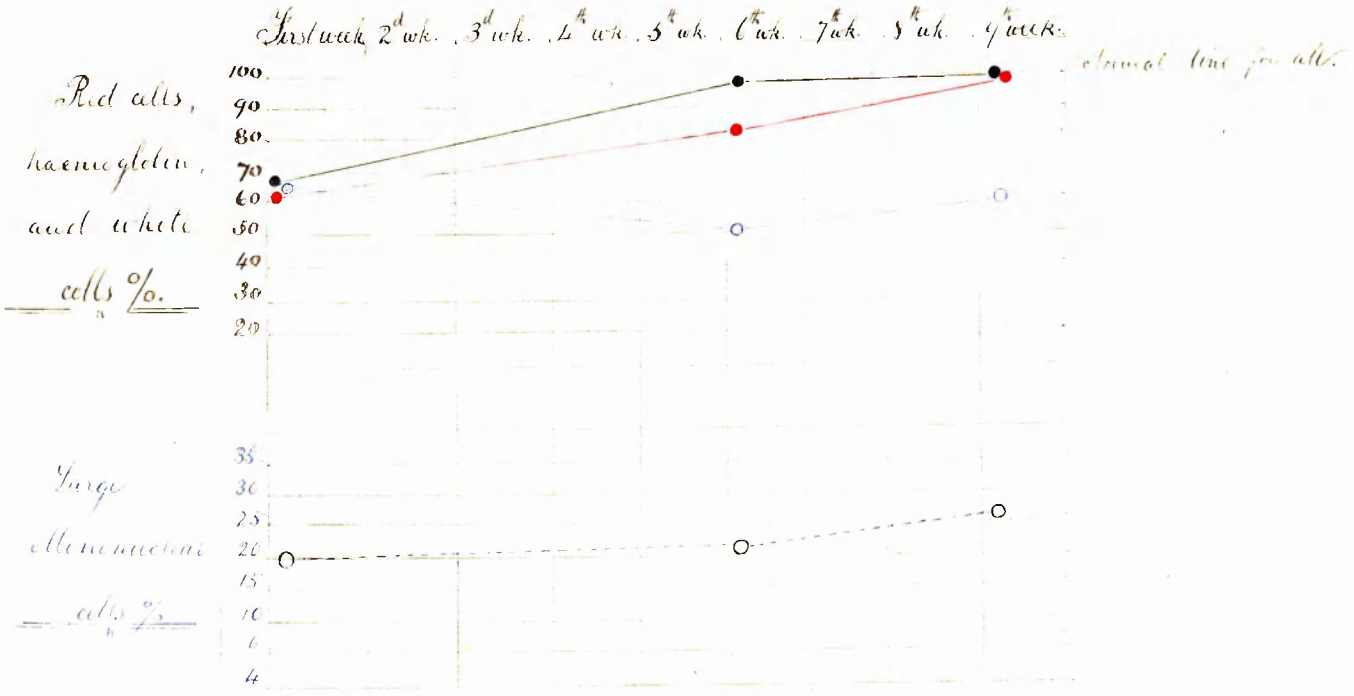
usually in pill form. A favourite pill at Rio Tinto was "Esanopheles" pill, containing

Hydrochloride of quinine, ·10 grammes.
Citrate of iron and quinine, ·03 gms.
Arsenious acid ·001 gms.
Extract of Gentian ·8 gms.

One pill was given thrice daily, gradually increasing till eight or nine daily were being taken. The results obtained were good. Relapses occured frequently however, through the patients failing to return for more medicine

In conclusion a few cases are given in chart form, illustrating at a glance the blood story of each.

(1). F. Guerito. aet 29. Quartan.

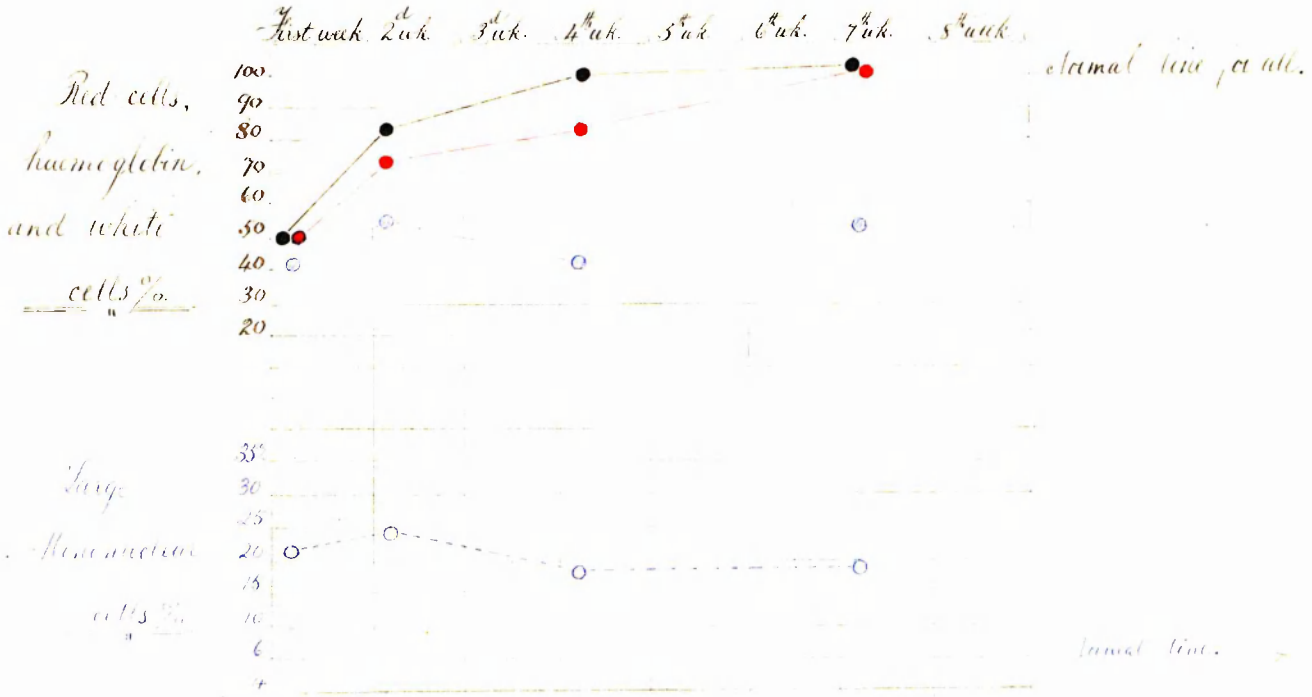


Black = Red cells.

Red = Haemoglobin.

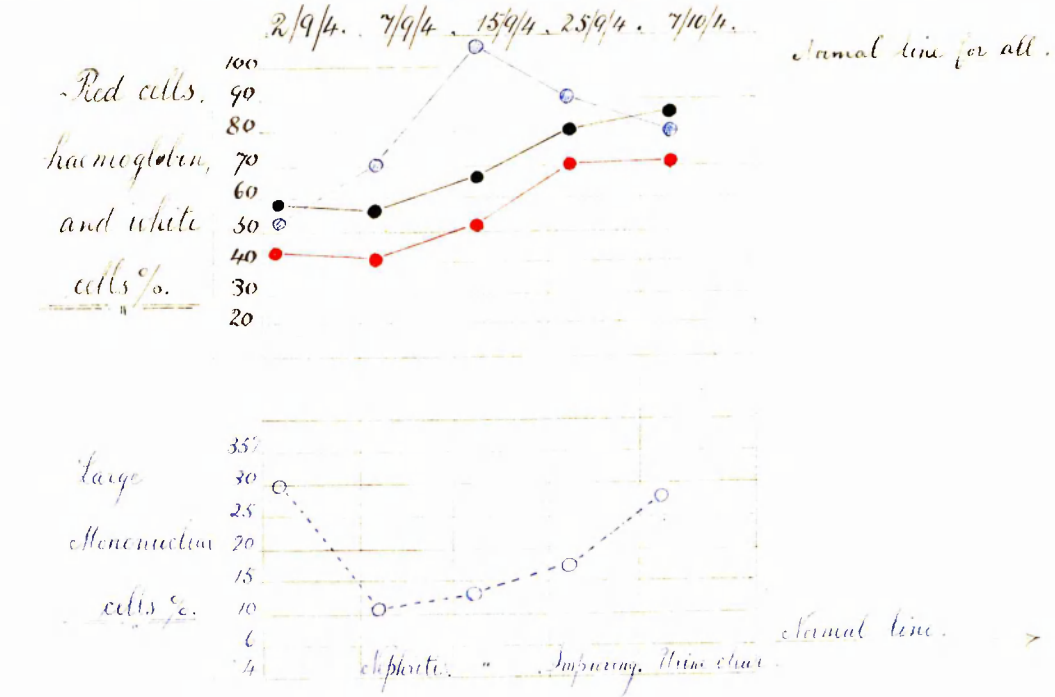
Blue = White cells.

(2). J. G. Vasquez. act 38. Quartan.



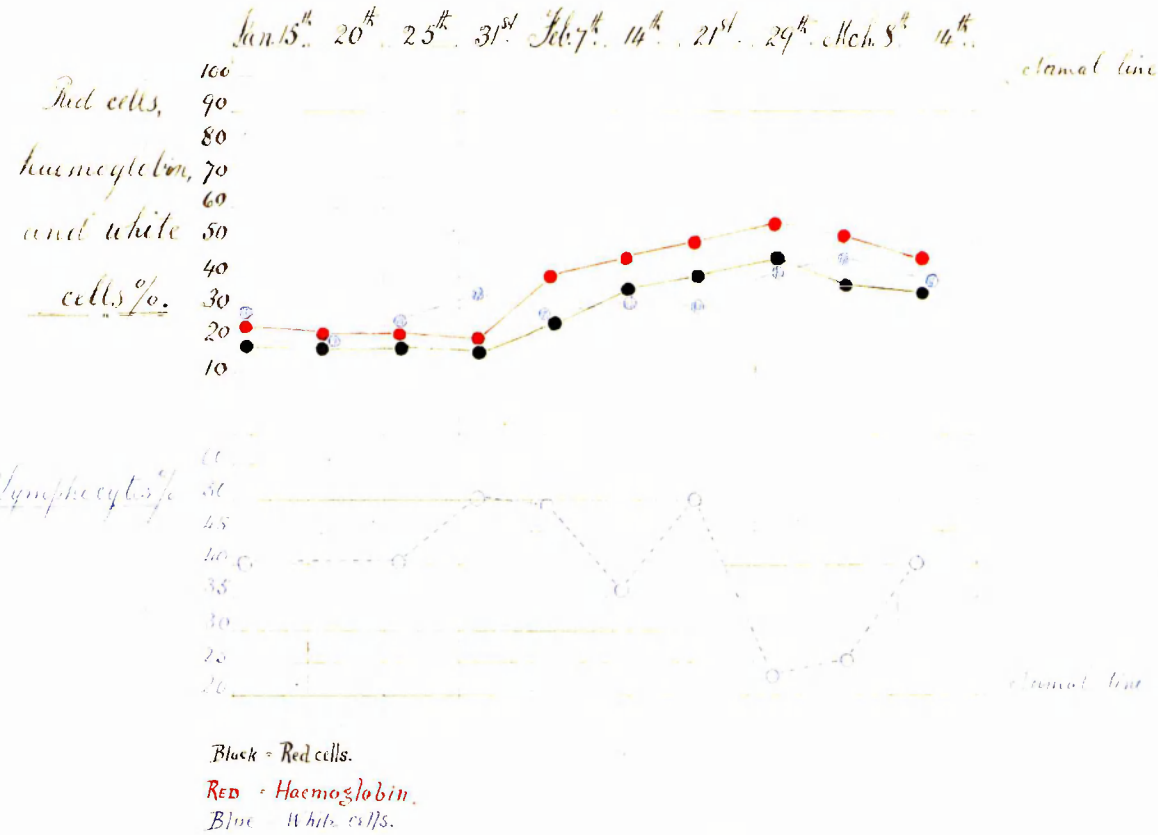
Black = Red cells.
Red = Haemoglobin.
Blue = White cells.

(3). Quartan: complicated by Black Cachexia. (page 45).



Black = Red cells.
RED = Haemoglobin.
Blue = White cells.

(4). c/A. G. Menton. Pernicious anaemia following subtertian fever. (page 31).



The End.