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C-Reactive protein in malaria

LOTFALI HAGHIGHI

From the Department of Microbiology, Medical School, Pahlavi University, Shiraz, Iran

SYNOPSIS C-Reactive protein has not been studied in malaria so far but with the reappearance of malaria in the southern part of Iran there is now an opportunity to study the behaviour of C-reactive protein in malaria. One hundred and sixty-two patients suffering from malaria have been so tested. Of those patients, 85·2% showed a positive result and among them more than 50% had a strongly positive reaction. It may be concluded that malaria is one of the outstanding diseases in which the C-reactive protein test is positive. Those patients who were examined for C-reactive protein in the first two days of the disease showed a negative result.

The presence of C-reactive protein in the blood serum of patients with acute inflammatory disease was first demonstrated by Tillett and Francis (1930). Subsequently, these authors as well as others reported on the relationship of C-reactive protein to the erythrocyte sedimentation rate (Anderson and McCarty, 1950; Dawson, 1957; Russo, Romeo, and De Lieto Vollaro, 1965; Tiagi, Tyagi, and Jain, 1965). This substance is so called because it forms a precipitate with the somatic C-polysaccharide fraction of the Pneumococcus. Although it was discovered in the sera of patients in the acute phase of pneumococcal pneumonia (Tillett and Francis, 1930), it is no longer considered specific for pneumococcal infections.

C-Reactive protein is not normally present in human serum but appears in the blood in response to a variety of inflammatory or tissue-destroying diseases, such as rheumatic fever (Anderson and McCarty, 1950; Dawson, 1957; Kwapiński and Snyder, 1962; and Tiagi *et al*, 1965), acute myocardial infarction (Kroop and Shackman, 1954), tuberculosis (Lozovan, 1964; Haghighi and Doust, 1966), pneumonia (Tillett and Francis, 1930), typhoid fever (Lapszewicz, 1963; Russo *et al*, 1965), leukaemia (Hyde and Garb, 1965), bronchial asthma (Prasad, Venkitasubramanian, and Viswanathan, 1965), and in pregnancy with and without heart disease (Sharma and Bhatia, 1965). The significance of finding this abnormal protein has also been demonstrated in the detection of cancer and certain chronic diseases (Carpenter, Heiskell, and Aldrich, 1966). In certain other illnesses, *eg*, syphilis (Daguet, 1960; Bonelli, Armuzzi, and Tomasini, 1962), and in some eye diseases (Somani, Arora, and Agarawal, 1965) it plays no significant role.

Although the presence of C-reactive protein is found not to be specific, its disappearance from the blood serum is correlated with treatment, so the effect of some new drugs can now be studied in certain diseases, including malaria, with the C-reactive protein test (Kwapiński and Snyder, 1962; Haghighi and Doust, 1966).

MATERIALS AND METHODS

Blood specimens were obtained from all patients who were suspected of suffering from malaria and examined both for the presence of parasites in the thin smears and for the detection of C-reactive protein in those cases in which malaria parasites were present. All smears were stained by Giemsa as recommended by Shute and Maryon (1966).

C-Reactive protein antiserum was prepared from polystyrene latex and serum hyperimmune to C-reactive protein[1] was used.

Sera from 162 patients were inactivated at 56°C for 30 minutes. The test was performed with both undiluted and serum diluted 1 : 5 with buffer diluent. If clumping was present with 1 : 5 diluted serum, quantitative serial dilutions were performed and the highest dilution giving a positive reaction was accepted as the final result. Positive tests were classified as positive as follows: undiluted, weakly positive; 1 : 5, positive; 1 : 10 and advanced dilution, strongly positive.

One hundred and fourteen patients (about 74%) in this study were between 18 and 30 years of age (Table I); the youngest was 6 years old and the oldest 74. Thirteen patients were female.

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[1]Hyland Laboratory, Los Angeles, California.

TABLE I

AGE INCIDENCE

	Age Group (yr)						
	Less than 10	*10-17*	*18-20*	*21-25*	*26-30*	*31-31*	*More than 70*
Number of cases	3	12	33	46	35	25	8
Percentage	1·8	7·4	20·4	28·4	21·7	15·4	4·9

One hundred and fifty-eight patients were suffering from vivax and four from falciparum malarias.

The average number of parasites was about one per high-power field with the minimum of one per 20 and a maximum of seven parasites in each high-power field. Additionally, three smears showed about one malaria parasite per 100 high-power fields. Of these three patients, two were suffering from falciparum and one from vivax malaria.

The duration between the first attack of the disease and obtaining the blood specimen is recorded in Table II

TABLE II

TIME BETWEEN FIRST ATTACK AND OBTAINING BLOOD SPECIMEN

Duration between First Attack and Obtaining Specimen	*No. of Patients*
1-2 days	6 (3·7%)
3-7 days	71 (43·8%)
Second week	67 (41·3%)
Third week	15 (9·2%)
More than three weeks	3 (1·8%)

RESULTS

The results of the C-reactive protein test and the degree to which these tests were positive are shown in Tables III and IV.

The relationship between the number of parasites in each high-power field and the degree of positivity is shown in Figure 1. Figure 2 represents the relationship between the percentage of positive results and duration of the disease.

The prozone phenomenon was observed in the sera of four patients.

DISCUSSION

As Table III indicates, about 85·2% of patients suffering from malaria gave a positive result with the C-reactive protein test and more than 50% of these positive cases showed a strongly positive reaction (Table IV). So we can conclude that malaria is outstanding in giving a positive reaction to the C-reactive protein test and the quantity of C-reactive protein in sera of cases of this disease is very high in more than half.

TABLE IV

DEGREE OF POSITIVITY OF C-REACTIVE PROTEIN TEST

Total No. of Positive Tests	*Weakly Positive*	*Positive*	*Strongly Positive*
138	8(5·8%)	50(36·2%)	80(58%)

It would be interesting to find the reason for the negative result that appears in 14·8% of cases of malaria.

Although most of the patients were male, sex does not appear to have been a relevant factor in determining whether C-reactive protein will be positive.

Age does not seem to influence the result. Although most of our patients were between 18 and 30 years of age, we obtained for the same age both positive and negative results.

The number of parasites per high-power field was interesting, because, as Fig. 1 shows, a higher number of parasites gives more chance of highly positive results, but it should be mentioned that we had patients harbouring large numbers of parasites and a negative C-reactive protein test. A few cases with about four or five parasites in each high-power field also had a negative C-reactive protein test.

The first two days of the disease are important, because, as Fig. 2 shows, at the beginning of the disease the result of the C-reactive protein test is negative. We had six patients during this period of their illness and all of them gave a negative result so we cannot accept the classical opinion that is based upon the appearance of C-reactive protein in the first hours of the conditions in which C-reactive

TABLE III

RESULTS OF C-REACTIVE PROTEIN TEST IN 162 PATIENTS

Total No. of Patients	*Negative*	*Weakly Positive*	*Positive*	*Strongly Positive*		
		Undiluted	*At 1/5*	*At 1/10*	*At 1/20*	*At 1/40*
162	24 (14·8%)	8 (4·9%)	50 (30·8%)	44 (27·1%)	21 (12·9%)	15 (9·2%)

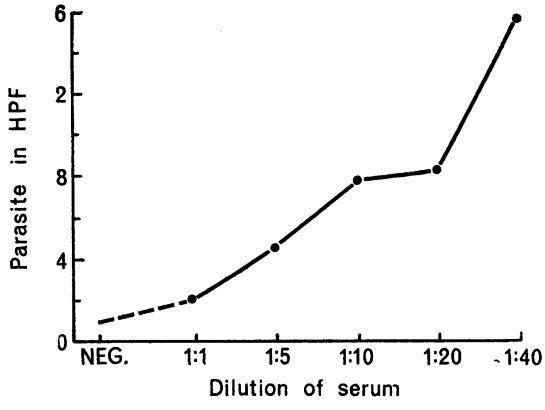

FIG. 1 *The relationship between the number of parasites with the degree of positivity in C-reactive protein tests.*

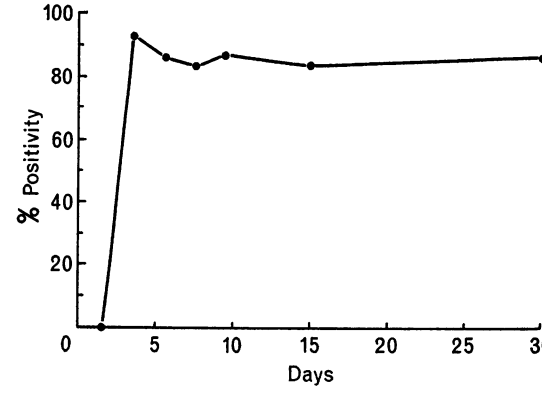

FIG. 2 *The relationship between the percentage of positive C-reactive protein tests with duration of disease.*

protein is found, *eg*, rheumatic fever (Bennett, 1964). However, after the first two days of the illness the duration does not seem to play an important role, because we had negative results in patients ill for three days as well as in those with a longer period of illness. Duration of the disease also does not seem to have any correlation with the degree of positivity.

Among four patients who had falciparum malaria, two gave a negative result so the incidence of positive results in cases of this type of malaria apparently is less than in vivax malaria. As the number of patients with falciparum malaria is not large enough we cannot draw definite conclusions.

No follow-up data are available on our patients as most of them had come from distant places to Shiraz for medical care, returning to their homes after improvement. It would be of interest to investigate the relationship between the results of the C-reactive protein test and complete recovery from malaria, using this test as an index of success in therapy as is customary in certain other illnesses.

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