ON CERTAIN CYCLICAL CHANGES OBSERVED IN THE BLOOD PICTURES OF CASES OF UNTREATED ANÆMIA COMPLICATING PREGNANCY IN TEA ESTATE COOLIES*

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Introduction.—In a paper on anæmia in tea garden labour forces, Napier (1937) stated, in support of a plea for the early administration of iron to pregnant women, that 'there is some evidence that these microcytic anæmias become macrocytic during the later months of pregnancy'. The evidence mentioned was not stated in that paper and a search of the scanty literature dealing with the subject has failed to reveal, either a repetition of the statement, or any evidence on which such a statement could be based†.

Now this statement is not only of academic interest, nor is it of interest purely as a basis on which to initiate prophylactic measures. If such a change from microcytic to macrocytic anæmia does in fact occur, a knowledge of the time of its occurrence and the character of the change would be more than likely to provide some evidence of an epidemiological nature on which an hypothesis as to the reasons for the change could be based. I therefore felt that evidence of a positive nature should be searched for, hoping that, if the statement were proved to be true, the epidemiological evidence would also emerge on analysis and our search for the true cause of the deadly macrocytic type of anæmia would take another step forward.

I therefore set myself the task of examining, at monthly intervals during their pregnancy, such anæmic women, spotted by near-by garden assistant medical officers, as were found to be in the early stages of pregnancy. The examinations carried out were as follows :—

(1) A full clinical examination,
(2) examination of the urine for albumin and sugar,
(3) examination of the stools for helminthic ova,
(4) estimation of hæmoglobin with the Sahli instrument,
(5) red and white cell counts,
(6) estimation of cell volume percentage of the blood using Napier's technique,
(7) calculation of the usual mean corpuscular values,
(8) examination of a stained blood film.

Fuller details regarding technique have been given in a series of papers dealing with other investigations into problems of anæmia which I hope will appear in the *Indian Journal of Medical Research*.

The series of cases on which this paper is based was dealt with during the latter half of 1938 and was in the nature of a try-out for a more ambitious programme on the same lines projected for 1939. I was engaged at the time on another series of pregnant anæmics so that I was only able to spare the time to examine fifteen women and, from the point of view of its conception, the experiment was a failure.

Six of the cases had passed the twenty-eighth week of pregnancy before their first examination (though that did not matter much because none of the six ever showed any tendency to a true macrocytic anæmia); more important, the three cases which did suffer from a true macrocytic anæmia with megaloblasts in the stained films and a high mean corpuscular hæmoglobin (MCH) were macrocytic when first examined at 20, 22 and 25 weeks. None of the remaining cases showed any permanent change from true microcytic to true macrocytic anæmia, or *vice-versa*. Evidence in support of the suggested transformation was, therefore, completely lacking and, from that point of view, we are in the same position as before.

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[† The statement was based on the observation that amongst 100 labourers, male and female (early pregnancy not excluded), there were only 5 cases of 'hyperchromic anæmia' (Napier and Das Gupta, *I. J. M. R.*, **24,** 855), whereas amongst pregnant women of the same population the incidence of 'hyperchromic anæmia' was about 33 per cent (Napier and Bilimoria, *I. J. M. R.*, **25,** 529). In the latter series hypochromic anæmia predominated markedly in the early months of pregnancy, whereas in the last trimester about 50 per cent were hypochromic. In both series, though emphasis was laid on hæmoglobin content rather than size, the words 'macrocytic' and 'microcytic' could be substituted for 'hyperchromic' and 'hypochromic', respectively, without altering the truth of these observations.

Such evidence, though not conclusive, carries more weight than the negative findings in the six essentially hypochromic cases reported in the present paper. The subject is still open for further investigation.—L. E. N.]

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and letting us have two references and our thanks are also due to Dr. B. N. Mukherjee, Clinical Pathologist, Medical College Hospitals, for helping us in the collection of the material and to the Superintendent, Medical College Hospitals, Calcutta, for supplying us with the records.

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Some observations of interest did emerge, however, and form the basis of the present communication.

The observations reported

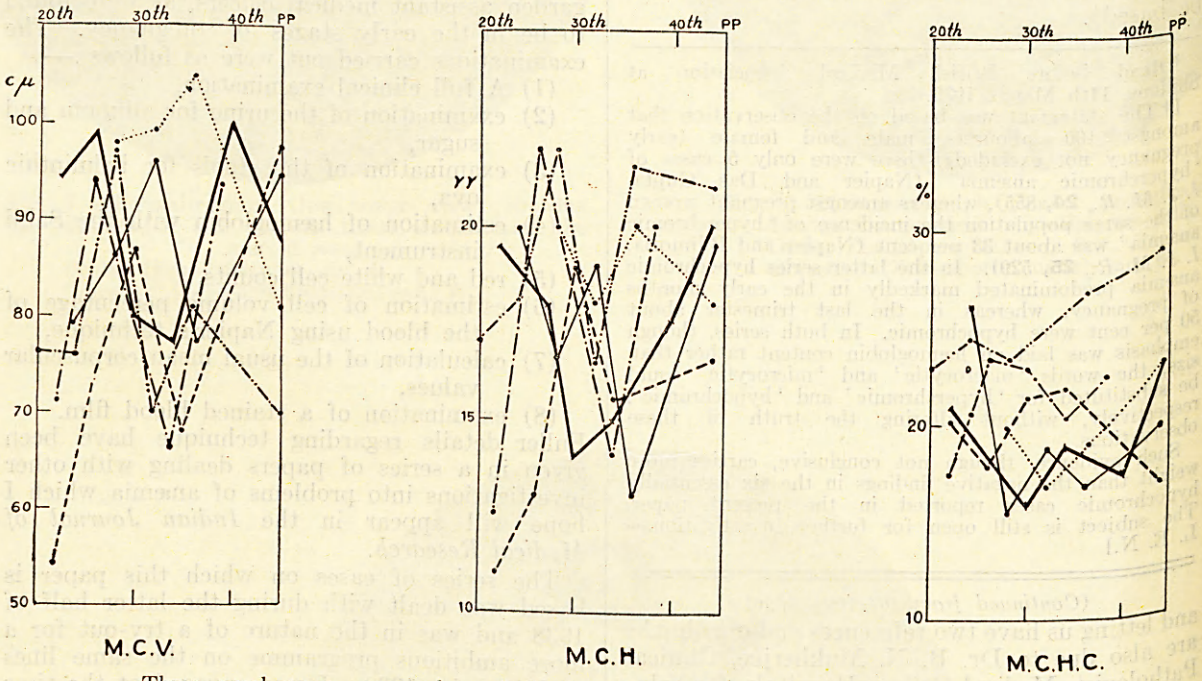
Of the fifteen women examined, six fulfilled three main conditions :—

(1) They were examined at intervals of at least four weeks on at least three occasions before delivery,
(2) they did not deliver until full-term,
(3) none of them received any anti-anæmic treatment of any description.

During the progress of the investigation it became obvious that changes were taking place in the blood pictures of these women without any apparent reason and that, taking individual cases, the changes were not always in the same direction. I was, at first, afraid that these changes might be merely an indication of faulty technique and would therefore throw suspicion on other observations. But, as these changes occurred in all the cases it seemed more probable that they were real and might be periodic in nature. I therefore plotted the usual mean corpuscular values in each case against duration of pregnancy in weeks and found that in the majority of cases the curves were of the same general form. The similarities were sufficiently marked to render it almost inconceivable that the variations were due to errors of technique. It therefore behoved one to examine these variations in detail to see if any other cause suggested itself.

Examination of the diagrams, which show mean corpuscular volume (MCV), mean corpuscular hæmoglobin (MCH), and mean corpuscular hæmoglobin concentration values plotted, in each case, against duration of pregnancy in weeks, shows that the variations recorded do not occur at exactly the same time in each case though a fair time relation does exist, but that for each mean corpuscular value the majority of the cases show the same type of curve. This particularly applies to the central portion of the curves—that covering the period between the 28th and 36th weeks of pregnancy.

Curves of mean corpuscular volume.—The central portion of five of the curves is of 'V' formation with the low point occurring somewhere between the 28th and 36th weeks of pregnancy. In three cases both the high points are well marked. In one the first examination was too late to catch the first high point and in another, one examination was missed so that the second high point, though suggested by the subsequent post-partum examination, was missed. The remaining curve is of reverse 'V' formation, having a high point at the 32nd week and low points at the 28th and 36th weeks. In the majority of cases, then, there was a tendency for the cells to be normocytic about the 28th and 36th weeks of pregnancy with a tendency to microcytosis during the intervening period.



Three usual mean corpuscular values plotted against duration of pregnancy in weeks.

Curves of mean corpuscular hæmoglobin.—Here again, the central portion of five of the curves is of 'V' formation and, again, the low point occurs between the 28th and 36th weeks. In one case, as before, the second high point was missed but is suggested and in the sixth case, as before, the curve during the critical period is a reversed 'V' with the high point at the 32nd week. This is the same case which showed a reversed curve for MCV. We may say that there is a tendency, in the majority of cases in

this series, to marked hypochromicity during the period between the 28th and 36th weeks and that round about the 28th and 36th weeks the anæmia tends to be less hypochromic.

Curves of mean corpuscular hæmoglobin concentration.—This set of curves is rather more complex. Three of them show the 'V' form during the critical period: one shows a steady rise, and the other two, one of which is the case whose other curves were reversed, show a reversed 'V' form. In other words, the degree of saturation of the red cells with hæmoglobin is also variable but its variations do not appear to be subject to a definite law.

Discussion

I have shown that, in the only six cases of anæmia complicating pregnancy which were untreated and fulfilled all the conditions laid down earlier in this paper, variations have occurred in the three main mean corpuscular values. As regards volume and hæmoglobin content, all except one case varied in the same manner and, approximately, at the same time. In the remaining case the variations took place at the same time but were in the opposite directions. With regard to corpuscular saturation the variations were irregular.

Now, what is the explanation of this difference? I suggest that the irregularity of the variations in corpuscular saturation is due to the rapidity with which the alterations in volume and hæmoglobin content are taking place. The blood, in other words, is in an unstable condition during the latter half of pregnancy.

What is the cause of this instability? We know that the rate of growth of the fœtus *in utero* varies with the duration of pregnancy. The figures given by Bourne (1932) and by Jellett and Nadill (1930) for fœtal measurements and weight at various stages of pregnancy show that growth is very rapid between the 28th and 32nd weeks and slows down enormously between the 32nd and 36th weeks. I have not, however, been able to discover in the literature available to me any information as to the nutritional needs of the fœtus. I suggest that, *pari passu* with the varying rate of fœtal growth, these needs may conceivably also vary from time to time. In that case, even if the mother's intake of iron, calcium and the vitamin-B complex remained at a steady level, increased fœtal calls for certain substances at certain times might render the intake deficient in one or more particulars. If the views of those workers who support the theory that these anæmias are nutritional in origin are correct, such variations in the effective intake of certain essential blood-forming substances would be sufficient to account for the hæmatological changes described above.

In any event, whatever may be the cause, I feel that attention should be drawn to the occurrence of these variations owing to their

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EXPERIMENTAL MALARIA INFECTIONS IN TWO RACES OF *A. STEPHENSI**

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and

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This brief note reports some comparative experimental tests of two races of *A. stephensi* Liston, 1901, as to their susceptibility to infection with *P. falciparum* Welch, 1897. The mosquitoes used were: (1) *A. stephensi* (type) and (2) *A. stephensi mysorensis*, as described by Sweet and Rao (1937). Those of the type form were obtained from larvæ in our laboratory colony which was started with larvæ from some wells in Madras City. Those of the form *mysorensis* were obtained from larvæ collected for us by one (B.A.R.) of the authorities whose work led to the separation of this form from the type (Sweet and Rao, 1937) and brought by us from Bangalore to Madras. We did not ourselves make a differential diagnosis.

We fed the mosquitoes in three lots, both races in each lot feeding at the same time on the same carrier and having the same treatment thereafter. In lots 1 and 2 the donor was a girl of 4 years having for the first lot 6 and for the second lot 4 crescents per 100 leucocytes. The donor in lot 3 was a girl of 9 years having 3 crescents per 100 leucocytes at the time the mosquitoes were applied. In lot 2, some mosquitoes

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bearing on the interpretation of the results of treatment of anæmia. All these six cases received no treatment whatsoever yet their blood pictures underwent great changes. Had they been receiving treatment one would have been tempted to claim that the changes were the result of whatever specific treatment had immediately preceded them. To my mind there is a danger in attempting to classify anæmias on a basis of response to treatment when our knowledge of their underlying pathology is so scanty.

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