lowered productivity, students become mentally duller, the suicide rate is higher and untold marital unhappiness and domestic discord have resulted from premenstrual outbursts of temper and irritability.

The cost of progesterone therapy is high, but when this charge is weighed against the price in terms of human misery, suffering and injustice it is seen as a justifiable expense opening up a new vista of Medicine.

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[*December* 15, 1954]

DISCUSSION ON ANÆMIA IN GENERAL PRACTICE

Dr. D. G. French:

My contribution is a brief account of the incidence of the different forms of anæmia among 5,000 patients during the past eleven years.

Iron-deficiency anæmia is overwhelmingly the commonest form; it is difficult to give a true estimate of the prevalence of the condition, probably about 80 cases per year, of which half are associated with pregnancy. Next in order of frequency, and forming about 1% of the total has been the macrocytic, pernicious type of anæmia, and in the period under review there have been 13 cases. Anæmias less commonly encountered are shown in Table I.

TABLE I.—THE LESS COMMON FORMS OF ANÆMIA.

Chronic myeloid leukæmia	2
Acute lymphatic leukæmia	1
Banti's disease	1
Aplastic anæmia	1
Eosinophilic syndrome	1
Hypersplenic panhæmatopenia	1
Acholuric jaundice	1
Tropical sprue	1
Non-tropical sprue	1
Total cases	10

In addition, there are in the practice 4 cases of hæmophilia, 3 of them being brothers.

The conditions shown in Table I occur so infrequently that the chance occurrence of any one of them can almost be ignored, but as a group the incidence is very similar to that of pernicious anæmia.

(a) Investigation of the Anæmia

The first examination of the blood which takes about 1 hour involves hæmoglobin estimation, erythrocyte and leucocyte counts, and the preparation of a blood film which is stained and used for a general examination of the character and distribution of the cells and for a differential count of 200 leucocytes.

The reticulocyte count has an essential place in hæmatology. Mistakes in diagnosis do occur, and the failure of treatment to produce a reticulocytosis will probably be the first indication of this. If the reticulocyte count is not checked, it may be several weeks before one becomes certain that no real improvement is taking place, whereas failure to obtain a reticulocyte response in three or four days should cause one to re-examine the blood and to re-consider the diagnosis.

Diagnosis.—The diagnosis may be completed gradually over a period of days and by means of the methods mentioned one should be able to label the anæmia, and if it is due to iron deficiency, the cause of this should nearly always be evident.

In iron-deficiency anæmia, there is a colour-index of less than 1; the hæmoglobin level is reduced to varying degree but the erythrocyte count, which may be reduced, is more often than not within normal limits.

Anæmias with a colour-index greater than unity, in which the presumptive diagnosis is megaloblastic anæmia, should be sent to hospital for further investigation, and the diagnosis will usually be confirmed; but keep one at home and try to treat it, and you may be sure that it will turn out to be something unusual, and by that time the treatment will have rendered the diagnosis virtually impossible.

Quite commonly borderline cases are encountered with a fairly severe degree of anæmia in which the erythrocyte count and the hæmoglobin level are proportionately reduced and in which the colour-index remains close to 1. These nearly always prove to be iron-deficiency anæmia or anæmia due to depressed blood formation, rather than pernicious anæmia, and in the differentiation of these the stained film can be very useful. In such cases the outlook has been uniformly bad due to some underlying condition. In these doubtful cases, one is justified in starting treatment with iron as no interference is caused thereby, and the progress can be checked by daily reticulocyte counts: but the casual use of liver extract or vitamin B_{12} is absolutely contraindicated, as this quickly converts a megaloblastic marrow to a normoblastic one, and it may be impossible to establish the diagnosis afterwards for some months. That, of course, is the danger and the menace of the blunderbuss preparations.

Reliance on the colour-index is a source of error when there is a combination of pernicious anæmia with iron deficiency, in which the colour-index is less than 1; but if the progress of the case is carefully watched it soon becomes apparent that the diagnosis requires reconsideration. Though such cases are extremely rare this also serves as a reminder that established cases of pernicious anæmia can become iron deficient and benefit from occasional iron therapy.

When one of the rare forms of anæmia is encountered, it may not be possible to establish the true diagnosis owing to sheer lack of familiarity, but they are fairly readily differentiated from iron-deficiency anæmia. Many are associated with considerable enlargement of the spleen which is not a feature of iron-deficiency anæmia; and if the similarity of the peripheral blood picture causes a mistake to be made, the error will soon be apparent when the case fails to respond to treatment, and no harm is done.

(*b*) *Investigation for the Cause of the Anæmia*

Iron-deficiency anæmia can never be regarded as a diagnosis; it is at best a physical sign. Take the history carefully, remembering the possibility of tuberculosis at any age; of peptic ulcer in young and middle-aged people of both sexes; of hæmorrhage following parturition, miscarriage or oft-repeated pregnancies, or of menorrhagia with or without pelvic tumour in women of child-bearing age; and of cancer somewhere, especially gastro-intestinal, in men and women over the age of 45. In the last group other common causes are rheumatoid arthritis, peptic ulcer and piles, though the patient's diagnosis of piles may in fact conceal a carcinoma of the rectum.

Idiopathic hypochromic anæmia which has recently been described in young males, and nutritional hypochromic anæmia in the aged are rare conditions, and in each the diagnosis must be reached by a process of careful exclusion.

Examination of the patient.—Some indication of the probable cause of the anæmia may have been obtained already; if not, one must conduct an examination which will include all the systems, remembering chest X-rays, also examination of hair, skin, glands, joints, and frequently also pelvic and rectal examinations. When the diagnosis is still obscure, the stool must be examined for occult blood. If there is still no indication of the probable cause of the anæmia there is no point in sending the case into hospital *at this stage.*

Treatment of the anæmia should now be started and the results checked by frequent blood examinations. I consider that the diagnosis of idiopathic hypochromic anæmia of young males, and of chronic nutritional hypochromic anæmia in the aged, should only be applied *in retrospect* to cases which have been examined and treated in this way, which have remained well after treatment and which in the fullness of time have been shown to have no serious underlying disease.

When an apparently uncomplicated iron-deficiency anæmia is effectively treated, (*a*) one must be able to demonstrate a reticulocytosis; and (*b*) the increase in the hæmoglobin level should then follow a definite pattern; if it fails to do so, the diagnosis is not completely correct, the most probable cause being some complicating factor which has not been found, and the ætiology must be re-considered. One must be perfectly satisfied in every case of iron-deficiency anæmia that the cause has been found.

Treatment of Iron-deficiency Anæmias

Oral iron therapy.—About 14% of the administered dose of ferrous sulphate is absorbed and utilized, compared with 1·5% of ferri et ammon. cit.

We have been urged to prescribe ferrous gluconate; and, more recently, ferrous succinate.

Perhaps one might add here that the general practitioner might ignore the possible ætiological significance of deficiency of the trace elements, but he should be alert to the occasional occurrence of subthyroid states.

When a patient responds satisfactorily to oral iron therapy, there is an interval of about nine days before any increase in the hæmoglobin level can be measured. After this, there is a steady return to normality at the rate of about 1% per day. The treatment of a fairly severe degree of anæmia must therefore be continued for about two months, and I do not think that the choice of preparation makes much difference. Fig. 1, which was prepared from observations made on recent cases treated with ferrous succinate, indicates the normal response to oral iron therapy.

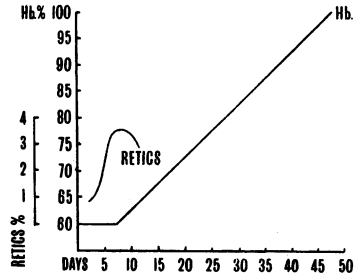

FIG. 1.—The normal response to oral iron therapy. This figure was constructed from observations made on four cases treated with ferrous succinate.

The disadvantages of oral iron therapy are that it is uncertain, because one cannot be sure that the patient is taking it regularly, and absorption is variable, especially in pregnancy where I have found the results quite unpredictable; it may not be well tolerated; and its action is a little slower than intravenous therapy, which in certain circumstances is important, for example, in late pregnancy. In general terms, the hæmoglobin level increases at rather less than 1% per day with oral iron, and at rather more than 1% per day with intravenous iron.

Intravenous iron therapy.—I use intravenous iron therapy for the majority of severe anæmias with hæmoglobin levels below 60% on account of its rapid effects, for all cases of hypochromic anæmia of pregnancy since prolonged experience of oral iron in these cases had been so disappointing, for the small minority of cases which fail to respond to oral iron therapy, and in all cases in which any part of the diagnosis is in doubt.

In 1948 I began to use Ferrevenin in the treatment of 2 cases of iron-deficiency anæmia of pregnancy, and I believe that these were the first 2 pregnant women ever to have intravenous iron therapy (French, 1948).

Administration.—In the administration of intravenous iron preparations the dangers of perivascular infiltration are very real. In my experience thrombophlebitis is extremely rare, and it probably results from failure to keep the point of the needle within the lumen of the vein, with the result that some of the material is injected into the wall of the vein, under the intima. I have tried on so many occasions to test the truth of this assertion that it has become practically a rule with me to use the same place in the vein for every injection, and I have seen no harm result. At the end of a course of injections, I can usually demonstrate the series of prick marks in the antecubital fossa in an area that could be covered by the end of a cigarette.

The injections must be given slowly; there is no doubt that the reactions which sometimes occur are to some extent related to the speed of giving the injection. The more common reaction usually appears within five minutes of the injection; the patient becomes hot, flushed and alarmed; there may be headache, a constricting pain in the chest, and, most constantly, a really severe colicky pain in the renal areas. The attack usually passes off in about twenty minutes, after which the patient feels shivery and cold. The second type of reaction resembles a vaso-vagal attack and comes on almost at once; if there is an interval the reaction is usually milder. This reaction, characterized by collapse of the patient, is more alarming and requires immediate action.

Speaking generally, one may expect to encounter a reaction when the injection is given quickly, but if the treatment is given intensively, as in some of my cases, the speed of the

injections may be gradually increased until the later ones, from about the eighth, may be given at nearly twice the speed of the earlier ones. And here is a strange thing: if there is a break for a few days in the treatment, the next injection must be given at the original rate or a reaction will occur.

It is recommended that the first dose should be 2·5 ml.; if there is no reaction, subsequent doses may be increased to 5 ml., and then to 10 ml., and it is not advised to increase the dose beyond this level.

The makers state that subsequent doses may be given at intervals, the total required quantity having been calculated from the hæmoglobin level. I prefer to give the injections daily; sometimes it suits me to give them night and morning; and I had one remarkable case in which I administered large doses three times a day.

Results of intravenous iron therapy.—Intensive treatment produces dramatic results. Subjective improvement is evident almost from the first injection, and is probably related to the raised serum iron levels.

The first objective change shown by the methods used is the appearance in the peripheral blood of increasing numbers of reticulocytes, and there is a significant increase in the reticulocyte count on the third day, though my most intensively treated case had a significant reticulocytosis forty hours after the start of treatment. The reticulocyte peak usually occurs about the fifth day, but it may be delayed until the eighth day, and is most commonly about 8 to 10%, though the actual magnitude of the increase appears to have little clinical significance.

The interval between the start of treatment and the first undoubted and significant increase in the hæmoglobin level varies from five to nine days; thereafter there is a steady return to normality which is reached about five weeks later, depending to some extent upon the original starting level. The first significant increase in the erythrocyte count is observed about ten days after starting treatment, and this returns to normal more rapidly than the hæmoglobin level; in fact there is frequently a period about four weeks after the start of treatment during which counts between 5,000,000 and 6,000,000 are not uncommon, and this would seem to indicate that the formation of new erythrocytes was taking place at a rate in excess of the destruction and removal of effete cells (Fig. 2).

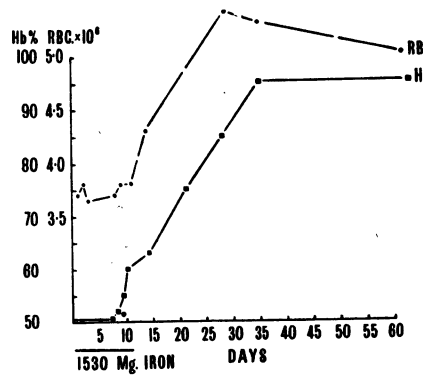

FIG. 2.—The normal response to intravenous iron therapy administered daily. Abnormally high erythrocyte counts are commonly observed four or five weeks after the start of treatment, as production proceeds at a greater rate than destruction.

Failures.—In the beginning, cases were encountered in which the results did not quite come up to expectation; for example, in cases in which the anæmia was due to repeated hæmorrhage and in which the hæmorrhage continued during treatment. And later it was noticed that the anæmia associated with rheumatoid arthritis did not respond fully. But there was a residue of apparently healthy persons in whom physical examination was completely negative, whose blood condition did not return to normality.

The following is a brief outline of 5 such cases. 2 were young people aged about 19; about three years later mass miniature radiography revealed that they had pulmonary tuberculosis with cavitation. Another was a woman of 55, and three months later she developed intestinal obstruction due to an annular scirrhous carcinoma of the colon. A man of 63 developed a perforation of the gall-bladder nine months later; he was operated upon but died. Another man of 59 developed retention of urine a year later, and was found to have an inoperable carcinoma of the prostate.

In the light of these and similar experiences, I now take the view that iron-deficiency anæmia in an apparently healthy person, which fails to respond fully to intravenous iron therapy in correct dosage, has some undiscovered serious cause for which an intensive search must be made. In actual practice, one can be sure in about three weeks that the hæmoglobin curve is lagging behind the normal expectation and that something is wrong. I have described this in greater detail elsewhere (French, 1953).

The hypochromic anæmia of pregnancy.—During pregnancy a physiological hydræmia occurs, and this causes a reduction in the erythrocyte count and hæmoglobin level when estimated by ordinary methods. Now, when iron deficiency is superimposed on these physiologically reduced levels, a major difficulty becomes apparent. The hydræmia is not constant either from patient to patient, or in the same patient for the duration of the pregnancy. Is there, then, a critical hæmoglobin level at which one can differentiate between a physiological anæmia and one due to iron deficiency?

With the introduction of Ferrivenin, much of the earlier difficulty was solved. It became evident that oral iron therapy during pregnancy is unsatisfactory and the results unpredictable.

The next step was one which had held me up on more than one occasion in the days of oral iron therapy. This objective was to obtain a clear picture of the fluctuations which occur in the erythrocyte counts and the hæmoglobin level during pregnancy and the puerperium in the known absence of iron deficiency; in other words, to create an ideal of normality which would be a standard against which future cases could be judged. Without this, what is meant by anæmia in pregnancy? Yet, so far as I am aware, this approach to the subject is unique.

To obtain this information, I selected 5 perfectly healthy young primiparæ, who had no evidence of anæmia so far as I could ascertain, and who lived in perfectly satisfactory home conditions. They were all given injections of intravenous iron in amounts calculated purely from their hæmoglobin levels, without reference to the fact that they were pregnant. This treatment produced no change in the blood pictures, and in no case was there a reticulocytosis. I then felt justified in assuming that these women were not iron-deficient, and went on to make frequent observations on their blood during pregnancy and the puerperium. Fig. 3 is the record of one of these cases. The means of the observations of all 5 cases are shown in Fig. 4.

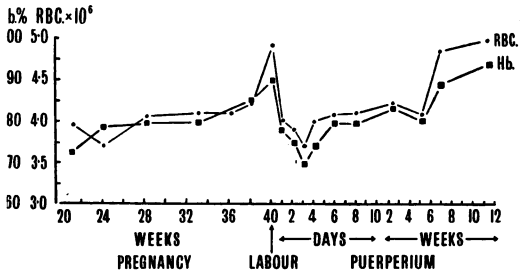

FIG. 3.—Normal fluctuations in the erythrocyte counts and hæmoglobin levels during pregnancy and the puerperium in healthy primipara, in the absence of iron deficiency.

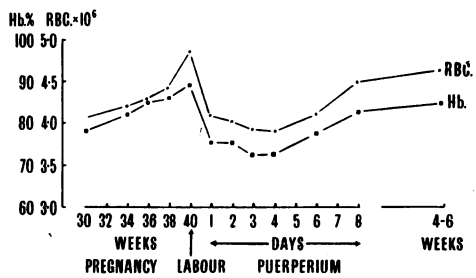

FIG. 4.—Similar to Fig. 3, but representing the means of observations on five non-anæmic primiparæ.

The significant points in Fig. 4 are these:

(1) There is a reduction in the erythrocyte count and hæmoglobin level during the greater part of pregnancy, and this is physiological.

(2) As would be expected, this is uninfluenced by iron therapy.

(3) The lowest values are found between the 20th and 30th week (in one of these cases, a hæmoglobin level of 65% was observed on three occasions during this period); there is then a very gradual rise until about the 35th week, after which the increase in both values is rapid and continues until the onset of labour when values closely approximating to normal non-pregnant levels are observed.

(4) After labour, there is a rapid fall in both values on the first day of the puerperium; this fall continues more gradually for a further two or three days, when values similar to the lowest pregnancy levels are reached; thereafter there is a steady return to normality which is reached in six to eight weeks.

(5) The two curves remain close together, which indicates that the colour index remains close to unity.

In addition to the injections of intravenous iron and the checking of the results by reticulocyte counts, the results of 146 hæmoglobin estimations and 127 erythrocyte counts are incorporated in Fig. 4.

It is made clear by Fig. 4 that a statement of the hæmoglobin level is only of value when the stage of pregnancy is indicated. And also that it is patently fallacious to judge the efficacy of any form of therapy when hæmoglobin estimations made during the last month of pregnancy or the first month of the puerperium are included. When the hæmoglobin level is the only criterion adopted, as it so often is, it could equally well be argued that any outlandish form of therapy is a cure for anæmia, as the hæmoglobin level is subject to a very considerable physiological increase during these periods without any treatment whatsoever. Similarly, any efforts to raise the hæmoglobin level during the early months of pregnancy in the face of a developing hydræmia must surely account for some of the so-called failures.

Treatment of the hypochromic anæmia of pregnancy.—Finally, I wish to show the results of intravenous iron therapy in the hypochromic anæmia of pregnancy, in two typical cases.

The findings shown in Fig. 5 relate to a primipara aged 21 years, who was 27 weeks preg-

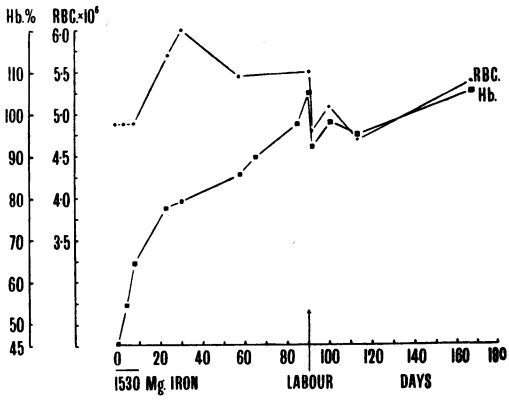

FIG. 5.—The hypochromic anæmia of pregnancy treated with intravenous iron.

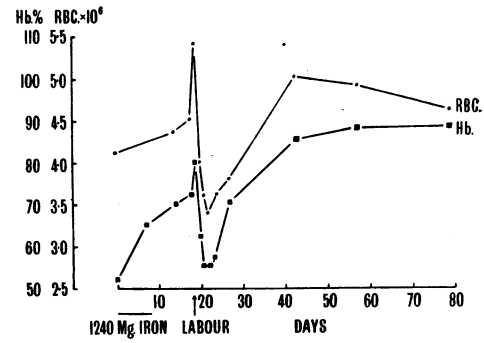

FIG. 6.—Hypochromic anæmia of pregnancy treated with intravenous iron. Differs from Fig. 5 in that treatment was started very late in pregnancy.

nant. The findings were: R.B.C. 4,900,000; Hb 45% (Sahli); colour-index 0·46. The low colour-index is represented on the figure by the wide separation between the curves representing the erythrocyte counts and the hæmoglobin levels. She was treated by the intravenous administration of the equivalent of 1,530 mg. of elemental iron, spread over ten days. Thirty-two days after the start of treatment, when she was 31 weeks pregnant, the erythrocyte count was 6,000,000. The hæmoglobin level increased rapidly, and thirty days after the start of treatment was 80%. The colour-index returned to normality more slowly over a period of eighty days.

The next case (Fig. 6) was a multipara, 37 weeks pregnant. The findings were: R.B.C. 4,100,000; Hb 52% (Sahli); colour-index 0·63. She received the equivalent of 1,240 mg. elemental iron by intravenous injection during the next seven days. The rate of improvement was rapid, and in the early puerperium, thirty days after the start of treatment, blood levels within physiological limits had been attained. The day before the onset of labour, the findings were: R.B.C. 4,500,000; Hb 72%; colour-index 0·80; these levels, achieved in eighteen days, are almost physiological.

Speaking generally, the hæmoglobin level in pregnancy is restored to within normal physiological limits by means of intravenous iron therapy within five weeks. The colour-index returns to unity more slowly, as it depends to some extent upon the rate of removal of "anæmic" effete erythrocytes, cells which must be included in a count but which contain very little hæmoglobin. For this reason, the colour-index, which is so valuable in diagnosis, lags too far behind to have a similar value as a criterion for the effectiveness of treatment.

I have mentioned that a hæmoglobin level of 65% (Sahli) was observed on several occasions in one of my non-anæmic cases. Attempts are constantly being made to fix some arbitrary hæmoglobin level as a standard for anæmia in pregnancy, and I am convinced that this cannot be done. The fluctuations due to hydræmia are such that any chosen hæmoglobin

level down to 65% will be observed at two periods in pregnancy: once during the early months when values are falling, and again during the last month when values are rising; and no single hæmoglobin level can indicate the presence of anæmia at all stages of pregnancy. In all these physiological fluctuations, the colour-index remains fairly stable, and should be far more extensively used than hæmoglobin levels as a guide to the presence or absence of iron-deficiency anæmia in pregnancy.

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Dr. M. C. G. Israëls:

Iron-deficiency anæmia can nearly always be dealt with by the practitioner himself; patients need only come to hospital if the cause of their anæmia is in doubt, particularly if malignancy is suspected as the cause of the anæmia.

So I will confine myself to considering how the other anæmias are best managed in practice.

The patient will have had a blood count and I am taking it for granted that physical examination has excluded such things as grossly enlarged spleen, enlarged lymph gland masses, abdominal tumours.

If the colour-index is less than 1·0, iron-deficiency anæmia is the answer. If it is about 1·0, the conditions in Table I are those to be considered. Iron-deficiency anæmia with

TABLE I.—COLOUR-INDEX ABOUT 1·0

Iron-deficiency anæmia
Malignancy (alimentary tract especially)
Reticuloses (including Hodgkin's disease)
Uræmia

TABLE II.—COLOUR-INDEX OVER 1·0

Pernicious anæmia
Leukæmia, aleukæmic forms
Acquired hæmolytic anæmia
Sprue, and non-tropical steatorrhœa
Aplastic anæmia

body fluid dilution, as for example in pregnancy, can present with a C.I. about 1·0. But the possibility of other causes is much more likely with a normochromic anæmia and they should be excluded. To do this, out-patient hospital investigation is necessary. Alimentary tract malignancy can be very difficult to demonstrate, especially tumours affecting the fundus of the stomach. The reticuloses are liable to be deceiving when the mediastinal glands or the abdominal glands are the only areas affected. Uræmia can be astonishingly silent, and the first sign may be anæmia perhaps with some epistaxis. The prognosis is always bad in patients who present with anæmia as a first sign of kidney failure.

If the colour-index is over 1·0 quite a different set of conditions must be thought of (Table II). Pernicious anæmia is the most obvious. But it is bad practice to give liver, vitamin B_{12}, or any similar compound to patients merely because they have a hyperchromic anæmia. The other diseases in this list need quite different treatment, and giving the wrong treatment to a patient with hyperchromic anæmia may greatly confuse the diagnosis because a very important piece of information in the differential diagnosis of this group is the state of the bone-marrow. In pernicious anæmia the marrow is megaloblastic; in leukæmia the marrow shows large numbers of abnormal and primitive leucocytes even though these are not to be found in the peripheral blood. In acquired hæmolytic anæmia the marrow is normoblastic, and in sprue the marrow will be megaloblastic in patients with hyperchromic anæmia. In aplastic anæmia the marrow may be very hypocellular with mostly lymphocytes, or it may show some erythroblasts, mostly mature normoblasts.

When no treatment has been given, megaloblasts and normoblasts are quite distinct from typical cases but exhibition of B_{12} or folic acid or liver, alone or in mixtures, causes megaloblasts to change over to normoblasts. In relatively early cases of pernicious anæmia and quite a few of steatorrhœa, there may only be partial megaloblastic changes in the nuclei of the erythroblasts. These transitional megaloblasts are more easily covered up by treatment.

So, unless there are very good reasons, any suspected pernicious anæmia patient should be sent for marrow examination before treatment is given. After all, the patient is being condemned to life-long treatment, and it is surely worth while having the diagnosis firmly established.

If the patient will not go to the hospital or laboratory, then a sore tongue with a lemon-yellow colour, flatulent indigestion and paræsthesiæ, in the absence of significant enlargement of the spleen or lymph glands, or abdominal mass, can be taken as a clinical picture of pernicious anæmia, and treatment with cyanocobalamin can be given. But if the patient does not respond, the trail has been muddled.

It is for this reason that both Dr. French and I are so insistent that no one should use the hæmatinic mixtures that are so powerfully advertised. If patients need more than one hæmatinic, they should be prescribed separately.

In the differential diagnosis of hyperchromic anæmia the diagnosis of leukæmia turns almost entirely on the examination of the bone-marrow.

Acquired hæmolytic anæmia is more difficult. Patients often present a lemon-yellow pallor. The spleen is often, but not always, much enlarged. In the blood a persistent reticulocytosis is present, significant if no treatment has been given, and the marrow is normoblastic throughout. The Coombs antiglobulin test is nearly always positive and is a valuable confirmation of the diagnosis.

Sprue and steatorrhœa are very likely to be the cause of hyperchromic anæmia in young adults, an age when pernicious anæmia is very rare. If severely anæmic, a true megaloblastic marrow can be found. But free HCl is usually present in the gastric juice. A properly carried out fat balance shows less than 90% absorption with a 70-gram fat diet. These patients respond to folic acid, rarely to vitamin B_{12}. They need control of the fat and starch in their diet.

Aplastic anæmia is obvious enough when a young woman appears bleeding from mucous membranes with depression of all the elements of the blood. But there are less severe grades that can be very deceiving and they occur most often on the older age groups, 50 and upwards. They often show a hyperchromic blood picture. The marrow is less cellular than usual; there is depression and relative maturity of the erythroblasts and granulocytes; there are no megaloblasts. These patients will not respond to hæmatinics, and only blood transfusion does them any good. But they are worth trying to treat this way on an out-patient basis as useful life can often be prolonged for many years.

Table III shows a summary of the treatment of the different forms of hyperchromic anæmia,

TABLE III.—TREATMENT OF HYPERCHROMIC ANÆMIAS

Disease	Treatment
Pernicious anæmia	Vitamin B_{12} (cyanocobalamin)
Leukæmia, subleukæmia	Cortisone
Acquired hæmolytic anæmia	Cortisone or splenectomy
Sprue, steatorrhœa	Folic acid and diet
Megaloblastic anæmia of pregnancy	Folic acid
Aplastic anæmia	Blood transfusion

and it will be seen how important it is to get the diagnosis right before the start of treatment.

Anæmia of Pregnancy

Here I shall consider only the megaloblastic anæmia of pregnancy. Regular bone-marrow examination of patients whose anæmia does not respond to parenteral iron treatment has shown that some degree of megaloblastic anæmia is much more frequent than was suspected. But megaloblastic anæmia of pregnancy is still much less common than the occurrence of a high colour-index in pregnancy would lead us to expect. In fact, no reliance can be placed on the colour-index in pregnancy; this is because of the serious changes in the balance between red cell mass and plasma volume. A high colour-index often occurs when this dilution disturbance is present, and it does not mean a megaloblastic anæmia, which implies an anæmia with hæmoglobin less than 9 grams/100 ml. (70%) that will not respond to parenteral iron. There may be other significant clinical signs, like sore tongue. The diagnosis is settled by examination of the bone-marrow. It is typical of the condition that many erythroblasts are the so-called "transitional" megaloblasts. These patients can be very ill with unpleasant mouth lesions and grave anæmia.

Folic acid is the correct treatment and for quick results it can be given intravenously in a dose of 100 mg. A daily oral dose of 20 mg. should be continued throughout the pregnancy and for one month afterwards. Such patients should come to hospital for investigations as soon as it is clear that they are becoming anæmic and do not respond to simple measures.

If Dr. French's figures are typical, general practitioners do not see hyperchromic anæmia very often. All the more reason for sending them for proper investigation as soon as possible, and for sending them untreated. If the patient has had some treatment, then it is essential to inform the hospital physician exactly what has been given. With this policy, management of the hyperchromic anæmias should be a source of satisfaction rather than of frustration to the practitioner.