Fifth Day.—Phenergan, one tablet at 6 a.m., 12 noon, 5 p.m., and 10 p.m.; anthisan, one tablet at 10 a.m., 2 p.m., and 8 p.m.

Tenth Day.—Phenergan, two tablets at 6 a.m. and 10 p.m., and one tablet at 12 noon, 4 p.m., and 7 p.m.

The drugs were given in this manner in an effort to avoid, if possible, any feeling of drowsiness and also to make use of the minimum efficient dosage. It was found necessary to prescribe 5 mg. of amphetamine sulphate each morning when the dosage reached seven phenergan tablets per day; this counteracted the drowsiness very effectively.

By the end of the third day of treatment her condition had improved considerably, and by the fifth day all vomiting had ceased. The nausea gradually decreased and finally disappeared completely by the eighth day. She remained absolutely symptom-free until she was discharged from hospital on the nineteenth day, looking and feeling a "different woman." Thereafter the dosage was gradually decreased until a maintenance dose of three tablets a day was reached. This was discontinued after a period of three weeks; the symptoms did not recur, and at the time of writing this patient is approaching the end of her second trimester of pregnancy.

Commentary

The treatment of nausea and vomiting of pregnancy still constitutes a major problem in antenatal care. It is well recognized that spontaneous relief of symptoms may be expected by the end of the first trimester of pregnancy, and the majority of patients resign themselves to awaiting this happy outcome. Most cases, fortunately, are of mild degree and do not appear to require any special treatment. When treatment is necessary simple dietary measures usually suffice to give adequate relief. In many cases, however, despite such treatment, the annoying symptoms persist and render life miserable even if they do not constitute a potential danger to it. Such being the case, there is a need for a simple and safe method of treatment which will relieve the symptoms in those patients who do not find dietary measures sufficient.

The results of the investigation into the use of anthisan and phenergan in this condition suggest that the anti-histamine drugs may offer just such a form of therapy. The majority of patients who received treatment with these drugs had already been treated along the usual lines, and, even allowing for the fact that some of these patients could have expected eventual relief without further treatment, it is difficult not to be impressed with the results obtained. At any rate, the success of this method has made it desirable to carry the investigation further with a series of patients treated in various other ways.

I am indebted to Messrs. May and Baker, Ltd., for supplies of anthisan and phenergan, and to the medical advisory staff of that firm for their advice and assistance.

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ANAEMIA OF PREGNANCY IN GLASGOW AND DISTRICT

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The importance of anaemia as a complication of pregnancy seems to have diminished in recent years in many parts of the British Isles. For instance, Fullerton, Mair, and Unsworth (1944) found that in Aberdeen only 3.9% of pregnant women of the hospital class suffered from anaemia, and comparison with previous surveys in that area indicates a rapid diminution in the number of cases since 1935 (Davidson, Fullerton, and Campbell, 1935). Similar observations have been made in Edinburgh (Davidson, Donaldson, Dyar, Lindsay, and McSorley, 1942; Davidson, Donaldson, Lindsay, and Roscoe, 1944).

It is therefore surprising to find that in Glasgow anaemia is one of the commonest complications of pregnancy and among the most serious. Unfortunately no previous investigation has been made in this area, and it is therefore impossible to assess progress.

The following attempt to survey the present position on Clydeside and to discover the cause of this high incidence of anaemia is based on the investigation of 4,595 patients at the antenatal clinic of the Glasgow Royal Maternity and Women's Hospital during 1947 and the latter half of 1946.

Methods

These were the standard procedures adopted by most haematological departments. Venous blood, withdrawn without constriction, was collected in heparinized tubes from every patient attending the antenatal clinic, and all investigations were carried out within six hours. Haemoglobin estimations were made by the Sahli method, 65% on this scale being equivalent to 70% Haldane, or 10.36 g.%. The haemoglobinometers were standardized at regular intervals against blood of known oxygen capacity. Pipettes requiring no correction factor were used.

Most authors consider 70% Haldane to be the lowest normal value during pregnancy. Roscoe and Donaldson (1946) have suggested that this lower limit varies with the patient's age, and that pregnant women in younger age groups are in an anaemic state at haemoglobin levels which come within the range of normality for older women. In view of this we have classified our patients into three groups: those with haemoglobin readings falling within the range 60–65% Sahli were classified "low normals"; those with readings between 50 and 60% were considered moderately anaemic; and those with readings below 50% were regarded as severely anaemic.

Classification of Patients

We found that 17.6% of all patients were anaemic at their first visit to the antenatal clinic. In addition a further 2.5% seen early in pregnancy became anaemic at some later date in pregnancy. These latter patients were in the "low normal" group originally. This gives a high incidence of 20.1%. Owing to the natural curve of haemoglobin values occurring in pregnancy certain corrections

were necessary before we arrived at this figure: these will be discussed later. The majority were cases of moderate anaemia, but approximately 5% of all patients had a severe anaemia with haemoglobin readings below 50% Sahli (8 g.%).

Since the numbers were so great and the majority of patients appeared at the clinic for the first time just before term it was impossible to investigate each case fully. Accordingly 140 were chosen for investigation in some detail over an average period of 2.2 months, and in no case less than one month. The average duration of pregnancy at first attendance was 5.6 months, with a range of from three to eight months. All anaemic patients were treated empirically with iron, and according to their response to that treatment these 140 patients were eventually classified into three groups: (A) 112 (80%) patients who showed satisfactory progress; (B) 26 (18.6%) patients who maintained their original haemoglobin level but failed to improve; and (C) two (1.4%) patients who deteriorated.

FIG. 1.—Whole of Group A. Monthly haemoglobin increments of 112 cases treated with iron as out-patients.

The results of treatment in this group are shown in Fig. 1. It will be seen that the increase in haemoglobin was greatest in the first month of treatment, and that the rate of increase diminished slightly in succeeding months. Seventy-seven of these patients were only moderately anaemic, and a graph of their monthly increments (Fig. 2) shows practically no curve. On the other hand, the remaining 35 severely anaemic patients showed a very steep curve of haemoglobin increments (Fig. 3), a rise of 10.8% being recorded in the first month, 5.4% in the second month, and 3.8% during the third month. Both curves (Figs. 2 and 3) are atypical when compared with non-pregnant cases, in which the rate of haemoglobin regeneration is said to be inversely proportional to the haemoglobin level (Whitby and Britton, 1946).

FIG. 2.—Cases of moderate anaemia in Group A. Monthly haemoglobin increments of 77 cases treated with iron as out-patients.

FIG. 3.—Cases of severe anaemia in Group A. Monthly haemoglobin increments of 35 cases treated with iron as out-patients.

FIG. 4.—Cases of moderate "pure" anaemia in Group A. Monthly haemoglobin increments of 41 cases treated with iron as out-patients.

FIG. 5.—Cases of severe "pure" anaemia in Group A. Monthly haemoglobin increments of 21 cases treated with iron as out-patients.

FIG. 6.—Group A cases of moderate anaemia with gastro-intestinal upset. Monthly haemoglobin increments of 22 cases treated with iron as out-patients.

FIG. 7.—Cases of severe anaemia with gastro-intestinal upset. Monthly haemoglobin increments of 14 cases in Group A treated with iron as out-patients.

A further subdivision of these cases could be made on clinical grounds. Of the total, 62 were cases of "pure" anaemia—i.e., no other complication existed. Forty-one of these were of moderate degree, and their response is shown in Fig. 4; it was almost the same as in Fig. 2. The remaining 21 were cases of severe anaemia (Fig. 5), and these showed monthly increases which were inversely proportional to the haemoglobin level. In other words, the response of pregnant patients with uncomplicated severe iron-deficiency anaemia is the same as that shown by anaemic non-pregnant patients.

Of the remaining 50, 36 had a mild gastro-intestinal disorder: 22 of these were cases of moderate anaemia, and the curve of haemoglobin increments was similar to that of all moderate anaemias (Fig. 6); 14 were severely anaemic, the curve in their case being very steep (Fig. 7). A rise of 12.9% was recorded in the first month, but thereafter the response was only slight. It would therefore seem that a mild gastro-intestinal disturbance has little effect on the course of a moderate anaemia, but that in severe anaemia it seriously interferes with the response to treatment. Since the initial response in these cases was satisfactory it is unlikely that the gastro-intestinal disturbance

produced its effect directly by interfering with the absorption of iron. It is possible that it interfered with the utilization of iron, or it may have produced deficiencies of other haematinic factors.

The remaining 14 patients suffered from mild infections or high blood pressure, but the numbers in each group were too small to allow any further subdivision. The response to treatment did not appear to be affected. Most were cases of moderate anaemia.

While assessing the response to treatment of these 112 patients who improved it was noted that 20 showed a

FIG. 8.—Monthly haemoglobin increments of 20 out-patients in Group A who showed a delayed response to iron therapy.

refractory to iron therapy unless treatment has been continued for more than one month.

Group B

Although at first sight all of these 26 cases might be considered refractory, closer investigation suggests possible reasons for this apparent refractoriness in some. Thirteen of these patients received iron therapy for just over one month, and in view of the delayed response noted above it is not justifiable to consider them resistant to treatment. Two others developed severe infections necessitating confinement to bed for several weeks—an ample cause for their resistance (Pepper, 1927; Wintrobe, 1942; Saifi and Vaughan, 1944; Cartwright *et al.*, 1946). Another four were uncooperative, one patient improving after admission to hospital. Two patients had initial haemoglobin values of 55 and 57%. Although neither showed an increase of more than 5% in two months this was sufficient to bring them into the low normal range, and they might be incapable of further response. Only the remaining five cases of this group could be definitely regarded as resistant.

Group C

Of the two patients who deteriorated, one developed diarrhoea and vomiting in the ninth month, deteriorating thereafter. The other patient received iron for two months, during which time the haemoglobin fell 8%. She was admitted to hospital one week before term and given iron in large doses, but failed to respond although the blood picture was microcytic and hypochromic.

The first patient can scarcely be considered resistant to treatment in view of the complicating intestinal disorder. Out of the total of 140 cases of anaemia, therefore, six were definitely resistant.

Discussion

Although the survey covers a period in which many economical and social changes occurred it will be seen from Table I that there were only slight variations in the inci-

TABLE I.—Incidence of Anaemia

Year	Severe Anaemias	Moderate Anaemias	Low Normals	Normals
1946	4%	17%	29%	50%
1947	4.8%	17.8%	24.5%	52.9%

dence of anaemia during 1946 and 1947. One out of every 20 to 25 patients attending the clinic was severely anaemic. It is interesting to note, however, that the average monthly haemoglobin readings for each of these years showed a tendency to rise in summer and fall in winter, but no correlation could be found between the incidence of severe anaemia and this seasonal variation. With the exception of a temporary rise during the Christmas season, when the numbers attending the clinic fell, this variation was quite regular, and it was also interesting to note that whereas the peak haemoglobin reading was in August, 1946, it was again reached in May, 1947, and fell rapidly thereafter.

From Table II it seems that age is significant only in severe anaemia. Parity is of no apparent importance.

TABLE II.—Effect of Age and Parity

	Age in Years	Standard Deviation	Parity	Standard Deviation
Normals	26.8	3.237	2.1	1.698
Moderate	28.3	3.5	3.5	3.5
Average severe	30.7	2.812	3.6	2.810

Low Normal Series

In an attempt to elucidate the aetiology of anaemia of pregnancy a study of 85 patients whose haemoglobin values fell within the range of 60–65% was undertaken. These were followed from the fifth month of pregnancy onwards. They formed three groups.

Group I consisted of 44 patients who maintained their haemoglobin level throughout, sometimes increasing it towards term.

Group II consisted of 16 patients who showed an initial fall in haemoglobin but later improved. In none of these was the fall below 58%, and they could not be considered anaemic. Similar monthly variations in the haemoglobin values of normal patients have been noted by many authors (Meyer-Wedell, 1943; Roscoe and Donaldson, 1946; Kühnel, 1927; McGeorge, 1935; Boycott, 1936; Oberst and Plass, 1936; Thomson, Hirsheimer, Gibson, and Evans, 1938; Dieckmann, 1933). The maximum fall recorded in these patients was 4%, and these variations provide criteria for estimating the progress of any particular patient. It follows that in any patient of the "low normal" group a fall of less than 5% at any subsequent examination should not be considered significant. Doubt may be felt about the justification for this statement, since the original haemoglobin levels varied from patient to patient, and the stage of pregnancy on their first appearance at the antenatal clinic varied similarly. Statistical examination, however, showed that neither of these factors affected the validity of this conclusion.

Group III consisted of 25 patients who became anaemic. Incidentally, it was found in this group that if the haemoglobin fell below 58% Sahli the fall was progressive thereafter. Treatment was withheld until the haemoglobin fell below 55%.

A study of these three groups established certain facts relating to the onset of anaemia. Age and parity were of no significance. No difference in regard to these factors could be detected between those who maintained their haemoglobin level and those who became anaemic. Also,

since only a small percentage of "low normals" in any age group developed anaemia, pregnancy itself is not a cause of anaemia. Anaemia usually appears during the latter part of pregnancy, when foetal storage of iron is greatest. Maternal storage, however, is highest in early pregnancy, and it follows that anaemia of the later months may be related to the state of health earlier in pregnancy.

Investigation showed that 48% (12 cases) of those who became anaemic suffered from a gastro-intestinal upset in the early months, compared with 33% of those who maintained their haemoglobin level. Further, these 12 cases developed anaemia at the seventh month, whereas the remaining 13 with no such history did not become anaemic until the eighth month. Two conclusions may therefore be drawn. First, mild disorders of this nature in the early months are not a cause of anaemia later in pregnancy, although they probably hasten the onset. Secondly, the fact that the majority of those who deteriorated were healthy during the earlier months suggests that there was a relative deficiency of iron or other factors before pregnancy.

In order to test this hypothesis small groups of "low normal" patients were given dietary supplements. Twenty-five patients five months pregnant were given iron for several months. Twenty-five others received vitamin C, 150 mg. daily for one month, then 50 mg. daily till term. A similar group were given dietary advice on the type of food they should take and the best methods of preparing it. In addition, most received $\frac{1}{2}$ lb. (227 g.) of liver each week for a period of not less than one month. Finally, one group received 3 dr. (11.6 g.) of "marmite" daily for one month. By that time most of them complained of nausea. All patients who deteriorated were given iron. The results of the test are shown in Table III, the control

TABLE III.—Results of Therapy in the Low Normal Group

Group	Improved	No Change	Deteriorated	Av. Rise in Hb After 1 Month of Iron Therapy
Control ..	4.7%	65.9%	29.4%	6.3%
Iron ..	40%	52%	8%	—
Vitamin C ..	16%	72%	12%	9%
Diet ..	32%	52%	16%	13%
Marmite ..	—	80%	20%	11%

group of 85 patients being used as a standard for comparison. From this it will be seen that iron therapy produced the best results but did not prevent the onset of anaemia in all cases. Vitamin C maintained the existing level of haemoglobin in a greater number of cases but was not so effective as iron in preventing deterioration. Its value may lie in its reducing power, thus improving the absorption of iron (McFarlane, 1936; Powell, 1944). Patients receiving special diet or marmite showed an increase in the incidence of deterioration, although not so high as in the control group. It is interesting to note the response to iron therapy of those who deteriorated in these groups. The steep rise in haemoglobin in those who had previously received special diet or marmite suggests that the rate of haemoglobin regeneration was enhanced by the diet, and that a small number of these patients had a deficiency of haematinic factors other than iron.

Summary and Conclusions

The results of the present survey show a high incidence of anaemia—namely, 17.6%—in pregnant women at their first attendance at the antenatal clinic of the Glasgow Royal Maternity and Women's Hospital. Reference to the group of low normals, however, shows that 29.4% of these patients ultimately become anaemic and a further 18.8% had readings

below 60% Sahli at one time during pregnancy, though they did not develop anaemia. It is obvious that of the women attending the clinic those with haemoglobin readings below 60% at their first visit, diagnosed as anaemia, will not include the 29.4% of low normals who ultimately become anaemic, but may include the 18.8% whose haemoglobin reading is temporarily diminished. Correction for these figures gives an amended incidence of 20.1%—i.e., 20.1% of all patients seen for the first time at the clinic are or will become anaemic.

Direct comparison with other reports is difficult, but it is interesting to note that repeat surveys in other parts of Scotland show a diminished incidence of anaemia in patients attending antenatal clinics.

The reason for this high incidence on Clydeside is not apparent. The greatest emphasis has hitherto been laid on dietary iron intake. Coons (1932) estimated the daily iron requirements of the pregnant woman as 14.7 mg. Ohlson and Daum (1935) and the National Research Council, U.S.A. (1947), agree with his figure. McCance and Widdowson (1946), however, put the level as high as 20 mg. per day. Diet in the British Isles has become fairly standardized in recent years and it is therefore difficult to understand why anaemia of pregnancy should be so common in Glasgow. We have recently undertaken a dietary survey of cases of anaemia, and although to date we have examined only 16 patients the results emphasize the problem. The average daily iron intake of these patients was 16.67 mg., which is above the standard in America. It seems likely that social habits and environment may prove more important than iron intake as factors inducing anaemia in the pregnant woman.

Several points arise out of the investigation of cases of anaemia and of patients with "low normal" readings. These are best summarized as follows:

1. Thirty per cent. of all women with haemoglobin readings in the range 60–65% Sahli become anaemic if untreated.
2. Iron is the best form of preventive therapy, but an adequate intake of vitamins B and C should be maintained.
3. In these patients 58% Sahli (9.28 g. %) seems to be a critical level. Below this figure progressive anaemia develops.
4. In estimating progress a fall of less than 5% is not significant in any individual patient.
5. Pregnancy is not a cause of anaemia, and age and parity play no part in its onset.
6. Mild gastro-intestinal disorders in the early months hasten the onset of anaemia but are not responsible for it.
7. Those patients who develop anaemia are probably cases of deficient iron storage, and the defect arises before pregnancy.
8. In established cases of uncomplicated severe anaemia the response to iron therapy is similar to that obtained in non-pregnant cases. Moderate anaemias show a regular response which does not vary with the haemoglobin level.
9. When the anaemia is complicated by a gastro-intestinal disturbance there is no difference in response to treatment provided the anaemia is of moderate degree. When the anaemia is severe the response, initially good, practically ceases.
10. In 17.8% of cases the response to iron by mouth may be delayed for as long as one month.
11. An unsatisfactory response was obtained in 20% of cases, but reasons for this could be found in all but six cases, or 4.5%.

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ACUTE MASTOIDITIS IN CHILDREN TREATED WITH PENICILLIN AND SULPHADIAZINE

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It has been said that penicillin places a premium on good surgery, but is no substitute for it. While not preparing to dispute the former, the series of 17 cases recorded below would largely appear to disprove the latter.

It has been the practice at one ear-and-throat clinic at the Children's Hospital to treat as out-patients large numbers of cases of mastoiditis, early or subacute, by the extensive use of the sulphonamides and penicillin in the form of an oil emulsion, reserving for admission those cases which hitherto had appeared to demand immediate operation. While the possible risks attached to this procedure laid it open to criticism, the difficulties of obtaining adequate facilities for in-patient treatment within this or any other hospital in the vicinity were so great that it was considered a justifiable expedient.

The results, however, were so satisfactory that it was resolved to apply this method of treatment to those cases of mastoiditis which by all previous standards demanded immediate operation. The cases in this series, seen within a period of three months, are consecutive ones in which there could be no shadow of doubt of a clinical diagnosis of acute mastoiditis, and were treated by conservative methods. Cases were selected on admission and none was excluded on the grounds of its severity. Only those in which the disease had progressed so far as to produce, in addition to systemic disturbances, tenderness, swelling, oedema, and in some cases a fluctuating abscess over the mastoid process were included in the series. All showed, to a greater or lesser degree, the typical forwards and downwards displacement of the ear so well shown in the accompanying photographs. This, coupled with the appearance of the drum and meatus, left no doubt of the diagnosis nor, by the usual standards, of the necessity for operation. X-ray examinations were made only in the later cases in the series, and bacteriological examinations not at all. The latter is unfortunate, because it may be that the prevalent invading organisms at the time the cases were admitted were particularly penicillin- or sulphonamide-sensitive. All cases originally selected are recorded. A

careful watch was kept throughout for signs of intracranial complications, but none occurred.

Treatment

On admission to hospital the following routine treatment was adopted: *Myringotomy* was performed in those cases in which the drum was intact and distended. *Intramuscular penicillin* was given in watery solution, 50,000 units six-hourly, in most cases. In the more severe cases 100,000 units were given six-hourly, and in one case 50,000 units three-hourly. *Sulphonamides* were given either four- or six-hourly, according to convenience in dosage, up to a total dose varying from 10 g. in infants to 30 g. in children of 10 years and over. No sulphonamide was given in one case in which there was acute glomerulonephritis. Sulphadiazine was used in most cases; and mist. sulphonamide co. (consisting of sulphadiazine 37%, sulphathiazole 37%, and sulphamerazine 26%) in younger children. Great attention was paid to a large fluid intake.

Local treatment consisted in careful cleaning of the meatus thrice daily and instillation of penicillin aural drops, 10,000 units per ml. As most of the children were drawn from the working-class districts of the city, one of the most important factors in the recovery of these cases was undoubtedly the excellent nursing care and attention to general health which they received.

The following is a summary of the notes of one of the most striking cases.

Case 1

Admitted April 13, 1948, aged 4 years, under the care of one of us (A. J. M.). Five weeks previously this child developed measles with otalgia and bilateral otorrhoea. The left otorrhoea ceased four weeks later, but the right otorrhoea had continued and right otalgia had been severe for the last three days. A right post-aural swelling was noticed three days before admission. It had since become worse.

On examination the child looked pale and ill. Temperature 100° F. (37.8° C.). From the right ear came a profuse muco-purulent discharge, the exact source of which was obscured by deep meatal oedema. There was considerable diffuse periostitis over the mastoid process, which was extremely tender. The pinna was pushed down, forwards, and outwards (see Fig. 1). The left drum was wrinkled but without active inflammation. Treatment consisted of systemic penicillin, mist. sulphonamide co., and penicillin aural drops.

FIG. 1.—Photograph of Case 1 taken on admission.

FIG. 2.—Condition of Case 1 ten days after admission.