Conclusions

1. Anaemia due to iron deficiency is of very frequent occurrence in women of the poor classes in Aberdeen.
2. The iron deficiency is due to a combination of factors, of which a diet poor in iron and loss of iron during reproductive life are of great importance.
3. Evidence has been presented to show that in the group of 1,534 adult women investigated menstruation constitutes an iron loss at least as great as that due to pregnancy and lactation.
4. A quantitative study of the loss of iron due to menstruation and pregnancy has made it clear that the diets of poor women are very frequently inadequate to compensate for the iron demands of reproductive life.

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The Archives of the Academy of Sciences of the U.S.S.R. in Leningrad have received the first batch of papers belonging to the late Professor I. P. Pavlov. The papers, which were presented to the Academy by Pavlov's widow, comprise some 2,500 letters from scientists in Russia and foreign countries. Most of them relate to the years following the revolution. Among those received before the revolution are several from Metchnikov.

ANAEMIA AND TOXAEMIA OF
PREGNANCY*

BY

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AND

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The aetiology of toxæmia of pregnancy is at the present time so much under discussion that it is of interest to review any possible bearing that anaemia may have on either its aetiology or its development. It is also of value to consider the relationship of anaemia to the clinical and to certain biochemical findings in patients with well-established toxæmia.

Recent Literature

The references in the literature dealing with the haematological findings are singularly lacking. The majority of writers, however, agree that the anaemia, if present, is in this country of the hypochromic or microcytic type. This anaemia is probably a deficiency state due to lack of iron, and therefore improvement takes place when iron therapy is instituted. In India there is an entirely different state of affairs, as the anaemia is of the hyperchromic or macrocytic type, and is due to some deficiency in the vitamin B complex in the diet. Only occasional cases of macrocytic anaemia are seen in this country, therefore in this paper we shall confine ourselves to the consideration of the hypochromic (microcytic) type of anaemia.

O'Sullivan, in his investigations of pregnant women with albuminuria, either due to toxæmia or associated with urinary infections, found that in the former or toxic group fifteen patients out of nineteen suffered from hypochromic anaemia. In the "pyelitis" group twenty-one out of thirty-two patients who were given iron in addition to the usual treatment for the albuminuria, either of toxic or infective origin, looked and felt better after iron treatment. This improvement was also shown by a diminution in the amount of albumin present and by the rise of the haemoglobin content of the blood and the red cell count. On the other hand, Boycott, in his investigations on anaemia associated with pregnancy, did not find any connexion between anaemia and toxæmia.

A consideration of toxæmia in patients in whom there is pre-existing renal disease such as chronic nephritis led Whitby and Britton to form the opinion that anaemia of the hypochromic type is almost always associated with chronic nephritis. In these patients there is probably a disordered or diminished blood production, and it is not known whether this is due to a nutritional deficiency or to a toxic disorder. The haemoglobin value is usually about 60 per cent. or less if the disease is progressive. Robscheit-Robbins and Whipple, in their recent publication, suggest that anaemia in infective and toxic states in animals is due to a disturbance of the internal metabolism inhibiting the haemoglobin-building powers of the body, and not to a defective absorption or defective formation. They believe that this same factor is often of importance in human disease. Moore, in his series of haemoglobin percentages and blood count estimations amongst pregnant women, found that the lowest average readings occurred in the group of patients suffering from chronic nephritis complicating pregnancy. Stieglitz found that the presence of renal disease hindered the treatment of anaemia in pregnant women, and advised that energetic measures should be taken to combat this anaemia.

* Read in opening a discussion in the Section of Obstetrics and Gynaecology at the Annual Meeting of the British Medical Association, Oxford, 1936.

Present Investigation

Our contribution to this discussion consists of a clinical and biochemical study of a group of patients attending the ante-natal clinic of the Royal Free Hospital, who were subsequently confined in the obstetrical wards of the hospital.

The majority of our patients were young primigravidae, with ages varying from 18 to 30 years. They were more or less of the same financial status. The average income per head per week was 15s. to 17s. 6d., and only in a few patients did the weekly income fall below 12s. per head. The only factor taken into consideration in the selection of the patients was accessibility to the hospital. These patients were divided into two groups:

- (1) Patients treated with iron as a routine throughout their pregnancy. (Blaud's pill, 30 grains t.d.s.)
- (2) Controls not so treated with iron.

Patients were placed alternately into the iron-treated or non-iron-treated groups, but some of the control series became anaemic (haemoglobin dropping to below 65 per cent.) so that iron treatment had to be started. These cases were eliminated from the present series, and their results will be discussed separately later. All patients were given the same advice with regard to diet and personal hygiene.

Routine Treatment

The diet was a general one containing "protective foodstuffs," and consisting of fresh meat or fish once daily, eggs, butter, an unlimited amount of fresh fruit and vegetables, and a pint of milk daily. Milk was obtained for needy cases through the municipal authorities. The patients were asked to write down a record of their diet for three days prior to each ante-natal visit. At the clinic the dietetic discrepancies were criticized and the shortcomings explained to the patient. The majority of patients were interested in their diet and co-operated with us by bringing truthful records of their dietary, and by adhering to our instructions so far as was financially possible.

At each visit to the clinic the usual routine examination of blood pressure and urine was made, and the presence or absence of toxic symptoms and signs, such as oedema, headaches, nausea, vomiting or heartburn, cramps in limbs, and visual disorders were noted. Haemoglobin percentage, blood urea, blood uric acid, serum carotene, and van den Bergh estimations were also performed as a routine at each visit.

We have analysed and compared the clinical and pathological evidence of toxæmia in our iron-treated and non-treated groups. We had only one case with toxic albuminuria having a blood pressure above 150 mm. Hg, and there were six other patients who showed some clinical toxic symptoms.

Toxic Cases

In our iron-treated and non-treated groups seven patients only had any degree of toxæmia: one patient in the iron-treated group of thirty-five cases; six patients in the control group of thirty-four cases. Of these seven patients three were suffering from a mild to moderate degree of toxæmia, and required admission before delivery for the following reasons:

- (1) On account of albuminuria with a systolic blood pressure of 160/90 mm. Hg.
- (2) On account of an extensive urticarial rash associated with a blood pressure reading of 146/92 mm. Hg.
- (3) On account of excessive vomiting at term with some oedema but no albuminuria.

The case with raised blood pressure and albuminuria was induced at thirty-nine weeks' gestation by rupture of the mem-

branes; the case with the toxic rash was induced medically at term; in the third labour commenced spontaneously at term. The remaining four cases were treated as out-patients.

This small number does not give us much scope for the study of the possible clinical and biochemical findings present during the development of toxæmia. We have therefore drawn up a further series of cases of established toxæmia admitted to the maternity department for in-patient treatment prior to confinement during the same period that our own cases were being investigated. In the general group of in-patient cases sixty-five, or 5.8 per cent. of the total number of deliveries, were toxæmic; these can be subdivided into two groups:

(1) Pregnancy toxæmia (including 2 cases of eclampsia)	61	cases
(2) Toxæmia with pre-existing renal disease	4	"
Total	65	"

All of these patients were suffering from a moderate or severe degree of toxæmia, and required in-patient treatment before confinement. Surgical induction of premature labour was performed in seventeen cases, drug induction in two cases; Caesarean hysterectomy was necessary in one case for severe ante-partum haemorrhage. The remaining forty-five cases were allowed to go into labour spontaneously. Three of the cases were emergency admissions and had not been attended to at the Royal Free Hospital ante-natal clinic.

In this series of toxic in-patients twenty-nine had haemoglobin estimations prior to delivery, and the following table gives the results:

HAEMOGLOBIN (HALDANE METHOD)

Haemoglobin Content:	50-59%	60-69%	70-79%	80-89%	90% +	Total
Cases of toxæmia ...	1	3	12	9	2	27
Cases of toxæmia and chronic nephritis	1	—	—	—	1	2
Total ...	2	3	12	9	3	29

Haemoglobin Investigations

In all patients in our iron-treated and non-treated groups the haemoglobin percentage was estimated by Sahli's method, using a neoplan haemometer for comparison, at monthly intervals.

Toxic Cases.—In toxic cases of these iron-treated and non-iron-treated groups we found that in six patients, who were controls, the haemoglobin fell to between 70 and 79 per cent. before toxic symptoms and signs became apparent. In the only toxic case amongst those given iron by mouth the haemoglobin rose from 77 per cent. in early pregnancy to 93 per cent. at term. This patient showed mild toxic symptoms, such as headaches, vomiting, and cramps, throughout pregnancy.

Non-toxic Cases.—The haemoglobin variations found were a rise of 17 per cent. in iron-treated cases and a fall of 8 per cent. in the untreated cases. This rise in haemoglobin percentage was proportionate to the length of iron administration. The iron-treated cases certainly showed a clinical improvement and appeared to be more free from minor infections, such as colds, etc., than the untreated group. This agrees with the findings of Strauss and Castle. Chart I shows the haemoglobin variation in the treated and untreated groups of non-toxic cases.

On analysis of their financial position it was found that there were no really poor patients. In working out the financial status the total income coming into the home was noted, the out-going expenses of rent were deducted, and the remainder divided by the number of dependants.

The result gives the available purchasing power for food, clothes, and fuel per head. An arbitrary dividing line was taken at 17s. 6d. per head per week. Out of seven toxic cases four patients were poor. The incomes of three were

CHART I.—Average haemoglobin variations in the course of pregnancy in three groups of non-toxic cases: a normal group and an anaemic group treated with iron; and a normal untreated control group.

raised one month prior to a raised blood urea. This confirms the findings of most workers that uric acid is a more sensitive indication of impending toxæmia than urea.

CHART II.—Blood urea variations in non-toxic cases.

Gastric Analysis

In 1932 Strauss and Castle made gastric analyses in twenty-four women during pregnancy, and showed that 75 per cent. did not secrete normal amounts of free hydrochloric acid during more than half the period and, excluding three patients who had a persistent achlorhydria, 80 per cent. of these patients secreted a higher concentration of free hydrochloric acid after delivery than during pregnancy. In further papers Strauss and Castle correlated this relative gastric hypo-acidity with the hypochromic anaemia occurring in the latter half of pregnancy, and demonstrated that this anaemia may be completely relieved by the administration of iron in large doses. In

1934 the findings of Davis and Shelley were in accord with those of Castle and Strauss. They demonstrated a definite reduction in acidity during the last two months of pregnancy. This reduction was only temporary, and was replaced by a return to normal soon after delivery.

In our groups of iron-treated and control patients histamine test meals were performed approximately at the twentieth and thirtieth week of pregnancy, and repeated on the eighth and tenth day of the puerperium. The patient reported to the laboratory fasting, a Ryle tube was passed, and the resting juice withdrawn. Histamine acid phosphate 0.3 mg. was injected and the stomach emptied at ten-minute intervals for a period of one hour. The volume of each sample was measured and the free and total acid estimated by titration against N/10 or N/100 sodium hydroxide, using Topfer's reagent as an indicator. The figures quoted below are those of the total

CHARTS III and IV.—Average variations in percentages of free HCl determined by histamine test meals in two groups of cases: A represents the average of twenty-five summer pregnancies, B twenty-five winter pregnancies. Note the rise in A and the fall in B.

CHART V.—Seasonal variations in gastric secretion. Average results of the total gastric output of free hydrochloric acid in histamine test meals performed each month irrespective of the stage of pregnancy on iron-treated and untreated patients.

amount of free acid, expressed in terms of c.cm. of N/10 acid, produced after the injection of histamine, and also the highest percentage of free acid found in any one of the ten-minute samples.

A study of the first twenty-five cases of our iron-treated and non-iron-treated patients showed that there was in the majority a marked rise in the free hydrochloric acid secretion during the later part of pregnancy. The investigation began during the first quarter of the year and the patients were delivered in the summer and early autumn, so that our test meal performed at the thirty-sixth week of pregnancy came during the middle third of the year. On

continuing the series we found that this rise was not maintained when the patients reached the thirtieth week of pregnancy during the autumn and winter months. These cases showed the drop in later pregnancy found by previous workers (Charts III and IV). The variation led us to analyse our results from a seasonal point of view.

Chart V shows the average total gastric output of free hydrochloric acid in histamine test meals performed each month irrespective of the term of pregnancy, and represents the average results for iron-treated and non-treated patients.

patients as many of these patients were too ill on admission. A few had test meals performed within fourteen days of delivery, and these all fell within the normal limits. In our iron-treated and non-iron-treated groups of patients who developed toxæmia the gastric secretions all fell within normal limits at the twentieth or thirtieth week of pregnancy; it is felt, therefore, that little evidence as to the aetiology of toxæmia may be obtainable from this study of gastric secretion, as the gastric examinations were made eight to ten weeks before toxic symptoms developed.

CHART VI.—Seasonal variations. Total free acid output in cubic centimetres of N/10 acid.

CHART VII.—Seasonal variations. Highest percentage free hydrochloric acid.

The seasonal variation giving a rise in the curve in the summer months is obtained whether the highest percentage of free hydrochloric acid or the total free acid output is plotted. This was found to be the case in the untreated as well as in the iron-treated patients.

Further cases are being investigated, and the series will be published in full shortly. It is possible that the lower gastric secretion in autumn and winter months may be due to intercurrent infections such as colds. Up to date we cannot correlate the gastric secretion with haemoglobin values. In fact, contrary to the findings of Strauss and Castle, we found in certain of the cases a fall in the haemoglobin level associated with a rise in gastric secretion; but in view of the numerous factors affecting both the haemoglobin level and the gastric secretions, further work is essential before any dogmatic statement can be made on the interrelationship of these two variants. Histamine test meals were not performed during the ante-natal period in the general series of toxic

Sugar-tolerance Tests

Sugar-tolerance tests were only done on our iron-treated and non-iron-treated patients at the twentieth and thirtieth weeks of pregnancy, and repeated after confinement at the tenth to fourteenth day. On each occasion a fasting blood sugar was estimated, 100 grams of glucose were given and the blood sugar recorded at half-hourly intervals for two and a half hours. Specimens of urine were passed at one hour and two hours, and were tested for sugar. The results are differentiated into those patients who leaked sugar after 100 grams of glucose and those in whom there was no leak.

In 31.4 per cent. of the series there was no sugar leak, but in 68.6 per cent. a leak was found. The results obtained in both groups are within the normal variations. In toxic patients of these groups the average curves fell well within the normal limit except in the post-confinement curve, where the fall was more delayed. In the three more toxic patients of this series the sugar curves were

more markedly raised about the time of incidence of the toxæmia and in the post-partum period. These results, though few in number, serve to emphasize that the occurrence of a raised blood sugar curve at any stage of pregnancy is of importance. Dietetic treatment by meals with the carbohydrate content evenly spaced can then be instituted to avoid miscarriage or premature birth.

Conclusion

The scope of this paper has been limited to the effect of anaemia as an aetiological factor in the development of toxæmia. The haemoglobin curve appeared to follow the duration of pregnancy: in the untreated cases the haemoglobin dropped persistently, whereas in the iron-treated group it rose. There was no seasonal variation in the haemoglobin curve.

Although some workers have failed to show that there is any connexion between anaemia and toxæmia without pre-existing renal disease, in our small series of cases the incidence of toxæmic signs or symptoms is much lower in our iron-treated series than in the controls. In other

words, when the haemoglobin value is kept up in the region of 90 per cent. the incidence of toxæmia is lowered.

We should like to take this opportunity of thanking Professor Amy Fleming for permission to investigate these patients; Professor Robert A. Webb in whose department the work was carried out; the Medical Research Council for a grant allotted to us for this investigation; Miss M. B. Harford, B.Sc., A.I.C., for her technical assistance with the biochemical investigations; and to Mr. Luck for producing the charts.

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MILD RADIUM THERAPY*

BY

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My reasons for presenting a paper on treatment by radium emanation, called indifferently mild radium therapy, radon therapy, emanotherapy, may be briefly stated. Here we have a therapeutic agent which has been used empirically for ages, scientifically for thirty or forty years, and yet is very little known in this country, although now employed abroad in many ways, such as in the form of compresses, sprays, subcutaneous injections, baths, inhalation, drinking-water, etc. Once looked upon by the medical profession with distrust, this form of treatment has now a definite place in physical therapy, and as Bickel of the Charité, Berlin, said:

"Twenty years' experience of radium emanation therapy has now established the method as a recognized form of medical treatment, and it is likely to be used more extensively in the future."

It is a therapeutic agent now modernized and scientifically used. It was blessed by no less an authority than d'Arsonval in a communication to the Académie des Sciences (June 13th, 1932), after an experience with the gas of over five years. It is being used in no fewer than twenty hospitals in Paris, and also extensively in many countries besides France, notably, Germany, Italy, Czechoslovakia, Spain, Portugal, and the U.S.A., and it is to bring before the medical profession of England this form of therapy, and to have it used in our hospitals as it is being used on the Continent and to induce our spas to add it to their armamentarium, that this paper is presented.

Another reason is to clear the widespread error that radon was dangerous. It is still confused in the minds of many people with radium. Radium and radium emanation are not the same; on the contrary, they are distinctly different, but still too many people, even in the profession, impute to the beneficent qualities of emanation

the dangerous properties of radium itself. Radium emanation cannot possibly be dangerous; it is essentially innocuous, and even its opponents, who can hardly be considered authorities on the subject, sometimes admit it may be beneficial.

Alleged Dangers of Radium Emanation

At the outset perhaps it would be as well to recount the origin of the legend of the dangers of radium emanation which gave rise to the well-nigh universal impression that radium gas is dangerous. It is not dangerous. It is from radium and radium salts the danger comes, as the following cases, which are so often quoted, go to prove.

During the years 1917 to 1924 an accumulative total of 800 girls were employed in a factory in New Jersey, U.S.A., painting the dials of watches and clocks with luminous paint. This paint contained phosphorescent zinc sulphide, activated by means of small amounts of radium and its congener, mesothorium. Several of the girls employed developed a very resistant infection of the jaw, with buccal lesions and marked anaemia, and later they died of carcinoma.

It is important to note that it was only the girls who had worked steadily in this painting for from one to two or more years who showed effects of radium poisoning.¹ In these factories the radium paint was mixed with acacia, which was thinned out with distilled water, and given to each girl in a porcelain crucible. It was the habit of most of these girls to point the tip of the camel-hair brush used in painting with their lips, so that a more accurate work could be performed. The material for the painting was sticky and adhered to gums and teeth, and was difficult to expectorate; one girl stated it was gritty, and she always swallowed it, as doubtless did the rest of the girls. The report showed that in six months anything from 360 micrograms to over 5 milligrams of radioactive substance might have been swallowed.

The other case so often quoted, which must be mentioned only in order that the danger of radium emanation may be refuted, is that of a gentleman of Pittsburg, who drank thrice daily, for a considerable period, a solution of soluble radium and mesothorium in an endeavour to rejuvenate himself and improve his golf. He developed carcinoma and died.

So these cases, arising as they do from radium itself or radium salts, have nothing whatsoever to do with mild radium therapy.

* Read in opening a discussion in the Section of Physical Medicine at the Annual Meeting of the British Medical Association, Oxford, 1935.