on both the volume and nature of the fluid to be used. Some regimens leave out colloid infusions altogether and emphasize the replacement of sodium and the correction of acidosis.⁵ The diversity of opinions is confusing and we chose to stick to one regimen and modify it according to our basic knowledge of fluid replacement and the clinical state of the patients, which was assessed by frequent ward rounds. The management of the fluid requirements demands intensive care and we found that the time spent on ward rounds calculating fluid balance and adjusting the fluid regimen paid considerable dividends in the overall management of the patients. In most cases a urinary output greater than 2 litres a day was achieved and there were no serious biochemical disturbances.

In the local treatment of burns the application of antibacterial agents has been shown to have clear advantages in limiting infection.¹ Our experience with silver sulphadiazine has confirmed other reports of its effectiveness and lack of toxicity. After their transfer to other centres we had encouraging reports on the progress of the patients treated initially with silver sulphadiazine. We were particularly struck by the absence of infection and odour of the burns.

All three patients admitted with asphyxia had a relatively normal PCO_2 though they were deeply cyanosed. We were unfortunately unable to estimate PO_2 at the time of the disaster, but it can be assumed that it was very low in each case. A rising PCO_2 , however, supported the clinical assessment of the need for I.P.P.R. Endotracheal intubation should be avoided unless indicated by the retention of secretions or the necessity for

I.P.P.R. since it is particularly prone to produce tracheal ulceration in cases of asphyxia. There remains considerable controversy regarding the use of steroids in these patients. In our opinion the serious degree of bronchospasm that occurred made the use of steroids mandatory. We did not use them locally as an aerosol, but there is some evidence that this may be beneficial and perhaps avoid the need for systemic steroids.

We found diazepam carefully titrated by intravenous injection to be useful and safe for controlling restlessness, which can further aggravate respiratory distress. The use of carbenicillin by inhalation using an ultrasonic nebulizer as well as intravenously was very effective in the patient with pseudomonas infection.

We thank every member of the hospital staff and the many volunteers who worked so hard to help the victims of the disaster. We are also indebted to Miss A. Lees for preparation of the typescript.

References

- ¹ Fox, C. L. jun., *Annals of the New York Academy of Sciences*, 1968, **150**, 823.
- ² Fox, C. L., jun., *Archives of Surgery*, 1968, **96**, 184.
- ³ Lowbury, E. J., et al., *Journal of Clinical Pathology*, 1962, **15**, 339.
- ⁴ Lowbury, E. J., et al., *Lancet*, 1971, **2**, 1105.
- ⁵ Settle, J. A. D., personal communication, 1973.

Hospital Topics

Anaemia of Pregnancy: The Changing Postwar Pattern

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Summary

A population survey covering over a quarter of a century has shown clearly the improvement in haemoglobin levels in women attending antenatal clinics at the Glasgow Royal Maternity Hospital. Various influences have helped to bring this about, foremost among these being routine early prophylaxis with combined iron and folate supplements. Indeed, a time-space relationship between changes in prophylactic therapy, rates of improvement, and the incidence of megaloblastic anaemia can be shown. The women at risk are still essentially the same except for a new group of young, unmarried girls, who must be watched.

In our view the withdrawal of routine prophylactic therapy in pregnancy would be a retrograde step.

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Introduction

Records of anaemia in women attending the antenatal clinic at this hospital have been kept since the mid-1940s. Over the years the average booking haemoglobin level has risen appreciably though not always consistently. Periods of more-rapid improvement have occurred and it was felt that it might be interesting to analyse these changes more closely to see how far they could be related to altered social habits and standards and to discover to what extent improved medical care and treatment had played their part.

Methods

Haemoglobin readings were made on venous samples until 1970, when preliminary capillary testing was introduced to have results immediately available to the obstetrician. Patients with haemoglobin values below 10 g/dl, and from 1973 all those with values below 11 g/dl, had blood sent to the laboratory for a full count.

Methods of haemoglobin estimation were strictly controlled. In 1946-7 a Sahli haemoglobinometer standardized with acid haematin was in use. By 1957 the ammonia method for oxy-haemoglobin had replaced this and the results were read in a photoelectric colorimeter standardized against a whole blood

commercial standard. The cyanmethaemoglobin method replaced this in 1965, daily standards with Drabkin's solution being put through. In 1970, with the introduction of capillary blood testing, a reversion to the oxyhaemoglobin ammonia method was made because of the time factor. To maintain strict control of the results a range of blood specimens of known haemoglobin value standardized in the laboratory were put through daily. Finally, in 1972, to avoid mouth pipetting break-off tubes (Harshaw) were introduced. These were found to be reliable and have the added advantage of speed, each test per patient taking a mean of $66.5 \pm \text{S.E. } 16.2$ seconds (range 45-135 seconds; $n = 74$).¹

Results

In 1946, when the first records were prepared, a haemoglobin reading of 10 g/dl was accepted as normal for a pregnant woman; below this anaemia was recognized. Classification has therefore centred on the 10 g/dl level, and though few people today would accept this as normal the older grouping has been retained for comparison purposes.

Patients were divided into three main groups according to whether their booking haemoglobin was below 10 g/dl (group 1), from 10 to 11.9 g/dl (group 2), or 12 g/dl or over (group 3), and the percentage distributions calculated yearly. The incidence of megaloblastic anaemias (group 4) was expressed as a percentage of the total number of hospital deliveries for each year. Initially only frank megaloblastic anaemias were recorded but from 1965 minor grades of this condition showing hypersegmentation of polymorphs were included. The criteria of Chanarin *et al.*² were used in the diagnosis.

In the 10 years between the first two surveys, 1946-7 and 1957-8, only a slight reduction in group 1 occurred (fig. 1). Thereafter surveys were made yearly and trends became easier to recognize. Two distinct periods of rapid improvement stood out, 1960-4 and 1968-72. During the first of these the proportion

FIG. 1—Percentage yearly distribution of groups during 1946-73. For definition of groups see Results. Group 2 is omitted for simplicity.

of group 1 patients fell from 14.4% to 6.0% while the proportion of group 3 patients rose from 32% to 40%. Over the next four years little change of any significance occurred in any of the groups, but from 1968 steady improvement developed during which the proportion of group 1 patients fell from 7.8% to 0.6% and the proportion of group 3 patients rose to 79.2%. The figures for 1973 did not show this sustained improvement, with group 1 at 1.2% and group 3 at 71.8%.

Over the years the predelivery haemoglobin values also improved. These figures were more difficult to obtain as they are not recorded separately. Sampling had therefore to be

adopted and we decided to compare the booking and preterm levels (36-40 weeks) of the first 100 patients delivered in 1951, 1961, and 1971, cases with bleeding being omitted. Unfortunately the results for 1951 were incomplete as only anaemic patients were followed up regularly at that time. The mean booking haemoglobin level in 1961 was 10.99 g/dl as compared with 12.15 g/dl in 1971. The 1961 values, however, improved significantly ($P < 0.001$) during the antenatal period and reached a preterm level of 11.73 g/dl; this was only slightly lower than the mean preterm level (11.99 g/dl) recorded in 1971, which had shown no significant change (fig. 2).

Postnatal clinic figures for haemoglobin became available in 1972, but since only 60% of patients return to this clinic the findings are selective. The mean haemoglobin value was 13.5 g/dl, and only 0.8% of values were below 12.0 g/dl.

Megaloblastic anaemias (group 4) were less regularly recorded (fig. 1). Initially, when diagnosis depended on the presence of megaloblasts in the marrow or buffy coat, the incidence was below 1%, but in 1965, when minor grades showing polymorph hypersegmentation were included, the incidence rose sharply, reaching 10.8% in 1968. Thereafter it fell slowly to 6.7% in 1972 but rose to 12.2% in 1973 when all patients with haemoglobin readings below 11 g/dl were screened. Analysis of the 1972 cases showed that the diagnosis had been made antenatally in 71.5% of patients; of these 29.1% were defaulters, 18.0% had received antenatal care elsewhere, and 17.5% had megaloblastic anaemia in a previous pregnancy and developed it again despite folate prophylaxis (300-500 μg daily). Compared with the hospital population in 1972 there was a significant difference in the overall distribution of social class grading ($P < 0.001$) owing to a reduction in classes I and II (15.1% to 7.6%) and an increase in classes IV and V (33.6% to 48.2%). Only two patients in class I developed megaloblastic anaemia, and one of these had β -thalassaemia minor.

The frequency of high parity (four or more) was significantly greater ($P < 0.05$), as was the illegitimate birth rate ($P < 0.01$); 84.6% of these births were in girls and young women (average age 20.2 years; range 15-22 years), a trend which stands out in sharp contrast to megaloblastic anaemias in general, where there was a significant increase in the anaemia in women over 40 years ($P < 0.01$).

Complications usually associated with megaloblastic anaemia were present but neither urinary tract infection (11.9%) nor haemorrhage (9.3%) was significantly more common. Rarer complications included β -thalassaemia minor (two cases), Hodgkin's disease (1), and sarcoidosis (1). There were four Pakistani women, two of whom had hookworm infestation.

Discussion

Most women nowadays begin pregnancy with a satisfactory haemoglobin level and maintain this despite persistent fetal demands and increasing blood volume. Looking back over the years it is clear that improvement results from a variety of factors. One, more apparent than real so far as anaemia is concerned, is the earlier timing of the booking visit before haemodilution noticeably influences levels. In 1951 few patients reported before 16 weeks' gestation; by 1971 37.9% had reported by that time and 19% were seen before the 20th week. Even more important is the fact that prophylactic therapy is started earlier and adequate stores are built up. In 1951 less than 1% of patients were receiving iron when they first reported; by 1961 this figure had reached 50% and by 1971 87%. In most cases the initial prescriptions were given by the patients' general practitioners, and in this respect it is worth noting the recent warning about the teratogenic effect of iron given in the first 56 days of pregnancy.³

With adequate antenatal care most patients should remain in positive balance, though complications such as third-stage haemorrhage may well reverse this. Fortunately most deliveries

FIG. 2—Booking and preterm haemoglobin values in 1961 and 1971 in first 100 patients delivered in those years.

now take place in hospital, where haemorrhage is assessed and treated, but as a further measure we should like to see improved follow-up at the postnatal clinic, for the legacy of a persisting negative balance could be a low booking haemoglobin level in the next pregnancy. It is heartening, therefore, to note that booking levels as a whole are rising, though the 1973 results were less promising.

The interrupted pattern of improvement shown in fig. 1 is intriguing. None of the factors so far considered seem to be involved. All were too gradual in onset to produce such a dramatic effect, and in looking for an alternative agent it seemed to us that only changes in treatment could offer an explanation.

In the early years, with the limited number of staff available, only patients with haemoglobin levels below 10 g/dl were followed up and treated. Inevitably improvement remained variable and slow. From 1959 onward haemoglobin levels in all patients were checked at intervals throughout pregnancy and those with values below 12 g/dl were given iron. It could be said that the first period of rapid improvement was initiated then, though its effect was not confirmed till 1962. One would, however, expect a lag in time before booking haemoglobin levels could rise as a result of corrected balance in an earlier pregnancy.

By 1965 no further improvement was occurring with this regimen. Milder forms of megaloblastic anaemia were actually increasing (group 4), and though some of this could be related to improved methods of diagnosis the remainder were in all probability unmasked by iron therapy.^{4,5} Trials with varying amounts of iron and folic acid were instituted in 1966 and routine iron and folate prophylaxis was adopted the following year. The second period of steady improvement seemed to date from then, allowance again being made for a latent period of two years; group 1 cases showed a significant downward trend by 1970, reaching a record low of 0.6% in 1972, with a slight rise to 1.2% in 1973. For the first time group 3 cases began to show a significant increase. In the four-year period following the introduction of routine iron and folate prophylaxis patients with haemoglobin values over 12 g/dl more than doubled, reaching a maximum of 79.2% in 1972. The 1973 figures were less satisfactory (71.8%) though still well above the pre-folate era. Thus combined iron and folate prophylaxis has had its effect at all haemoglobin levels, a finding which supports the hypothesis that minor degrees of folic acid deficiency, like iron deficiency, exist in apparently non-anaemic subjects.⁶

Folate prophylaxis also had its effect in reducing the number of megaloblastic anaemias. Owing to the method of recording and the fact that preventive measures affect the current pregnancy improvement was more obvious by 1969 and the incidence continued to fall, reaching levels around 6.7% in 1971 and 1972. The rise in 1973 appeared to be due to expansion of the screening procedure to include all women with haemoglobin levels below 11 g/dl.

Thus there was a time-space relationship between changes in prophylactic therapy, booking levels, and the decline in megaloblastic anaemia, and while other measures such as earlier bookings or earlier institution of treatment may have influenced levels generally clearly they could not have had this specific effect. Nor did there appear to be any significant change in the type of patients which could account for it. The 1972 review of megaloblastic anaemias showed that despite the institution of family planning clinics high parity was still an important factor in the development of the anaemia and a large number of women were over 40 and belonged to social classes IV and V. Many were also defaulters. The only new feature in the group was the larger number of young, unmarried girls.

According to Hall,⁷ in areas such as the United Kingdom, where most pregnant women do not suffer from iron deficiency, it is doubtful whether iron should be routinely prescribed, and in developed countries she feels that the practice of routine folic acid prophylaxis is not justified. As an alternative she suggests screening all patients with haemoglobin values below 12 g/dl in early pregnancy and 11 g/dl in the last trimester. If these recommendations were to be applied to Glasgow women at present on routine iron and folic acid therapy 30% would have to be screened initially and at intervals thereafter. Eventually this figure would drop to 14% preterm (fig 2, 1971 preterm levels). Nevertheless, it represents a heavy work load. Fully automated counting could probably cope with this but polymorph nuclear segmentation counts, on which the diagnosis of megaloblastic change depends, require trained staff and time.

With the present system, in which prophylaxis is given, screening can be safely limited to patients with haemoglobin readings below 11 g/dl, but should it be withdrawn not only would numbers requiring screening have to be increased immediately but there would be the added risk that trends in reverse of those shown in fig. 1 might develop. In our opinion this would be a retrograde step. Indeed, taking prevailing economic conditions into consideration and the fact that the 1973 levels were less promising it seems advisable to err on the side of caution.

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References

- 1 Brown, A., M.Sc. thesis, Health Research Unit, University of Strathclyde, 1973.
- 2 Chanarin, I., Rothman, D., and Berry, V., *British Medical Journal*, 1965, 1, 480.
- 3 Nelson, M. N., and Forfar, J. O., *British Medical Journal*, 1971, 1, 523.
- 4 Scott, J. M., *Journal of Obstetrics and Gynaecology of the British Empire*, 1954, 61, 646.
- 5 McKenzie, A., and Abbott, J., *British Medical Journal*, 1960, 2, 1114.
- 6 Chanarin, I., and England, J. M., *British Medical Journal*, 1972, 1, 651.
- 7 Hall, M. H., *British Medical Journal*, 1974, 1, 661.