Causes and Consequences of Menstrual Variation

A Community Study

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SUMMARY

Women have a lower haemoglobin concentration than men, either because of hormonal influences or because they are marginally iron deficient. If there is iron deficiency, menstrual blood loss is likely to be largely responsible. The literature is reviewed and discussed. The evidence is inconclusive and little is known about menstrual blood loss apart from the very wide range that may occur in apparently normal women.

A population study of menstrual blood loss and haemoglobin concentration was carried out in a Northumbrian mining village. 94 per cent (348) of the non-pregnant women between 17 and 45 years of age co-operated. Menstrual blood losses were measured for two consecutive periods. Haemoglobin, haematocrit, serum iron, iron binding capacity and fibrin degradation products were estimated from venous blood samples. A medical history was taken in each case, and a gynaecological examination was performed on the married women. Endometrial biopsy was attempted, but was successful in only a small proportion of cases.

The results confirmed the wide range of blood loss and the positively skewed distribution curve previously reported by other workers. There was a significant decrease in menstrual loss in women taking an oral contraceptive and a significant increase in those with an intra uterine contraceptive device. There was a positive correlation between menstrual loss and parity, but not with age. Within broad parity groups the women who had had heavy babies had larger menstrual losses than those

with lighter babies; and menstrual loss may be related to stature, tall women lose more than short women.

Blood loss of over 45 ml per period is associated with significant changes in all the haematological indices measured, and a marked rise in the prevalence of anaemia (Hb <12 g/100 ml). This implies that many women are unable to tolerate losing blood equivalent to more than 1.4 ml per day.

Rises in the concentration of serum fibrin degradation products (F.D.P.) indicate pathological fibrinolysis. In this population there was no correlation between menstrual loss and F.D.P. concentration. Endometrial biopsy in 45 subjects did not show any histological pattern associated with either heavy or scanty blood loss. The gynaecological signs and symptoms discovered in the population were discussed.

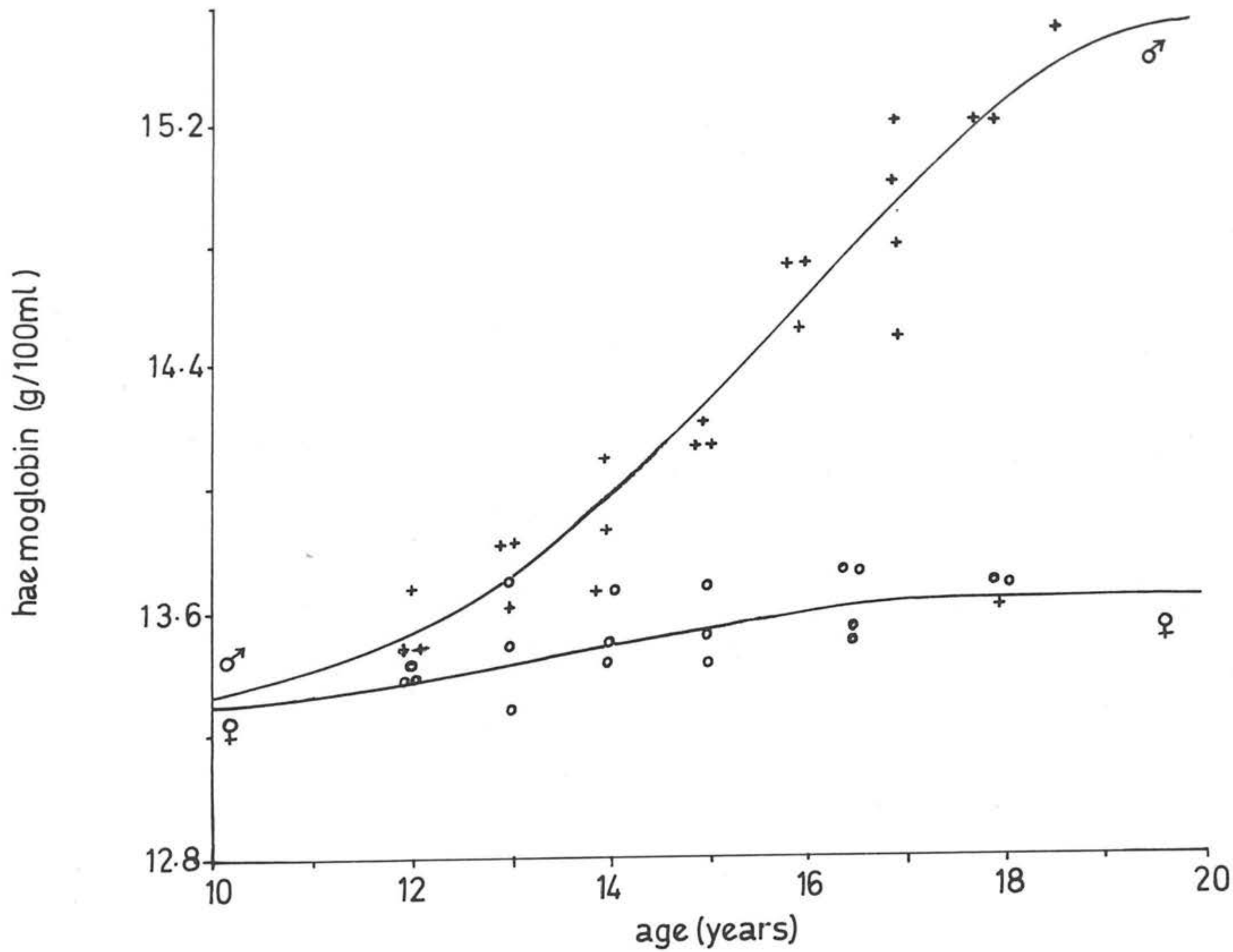
Menstrual blood loss was thought to be associated with uterine size and blood flow. Although contradictory features remain, iron balance in women appears to be precarious.

CHAPTER 1

Introduction

The average haemoglobin concentration in women during the reproductive years is consistently about 12 per cent lower than in men. This has been shown in a large number of studies. Though the absolute values may not be strictly comparable because of differences in method of haemoglobin estimation and in selection of population, the validity of observed male/female differences is not thereby diminished. For example, Davidson et al (1943) found that the mean male haemoglobin concentration was 102.8 per cent (Haldane) and the mean female concentration was 91.7 per cent, in a group of factory workers, nurses, maids and students. Because of different methods and subjects, this study cannot be directly compared with a recent population survey in one of the Orkney Islands (Gourlay et al, 1970) which showed a mean haemoglobin of 15.2 g/100 ml (cyanmethaemoglobin read on an EEL haemoglobinmeter) in men, and 13.4 g/100 ml in women. Dacie (1954) gave a mean haemoglobin level for men of 15.8g/100 ml and of 14.0 g/100 ml for women, in England. Snell (1950) in a Japanese population, in which parasite infestation and tubercle were rife, found that mean values for men and women were 14.1 g/100 ml and 12.4 g/100 ml respectively. Similar sex differences have been found by many other workers (Price Jones, 1931; Osgood et al, 1931; Jenkins and Don, 1933; Wintrobe, 1933; Whitby, 1951; Berry et al, 1952; Verloop et al, 1959; Davies et al, 1967; Natvig and Vellar, 1967).

Haemoglobin levels in adolescent boys and girls

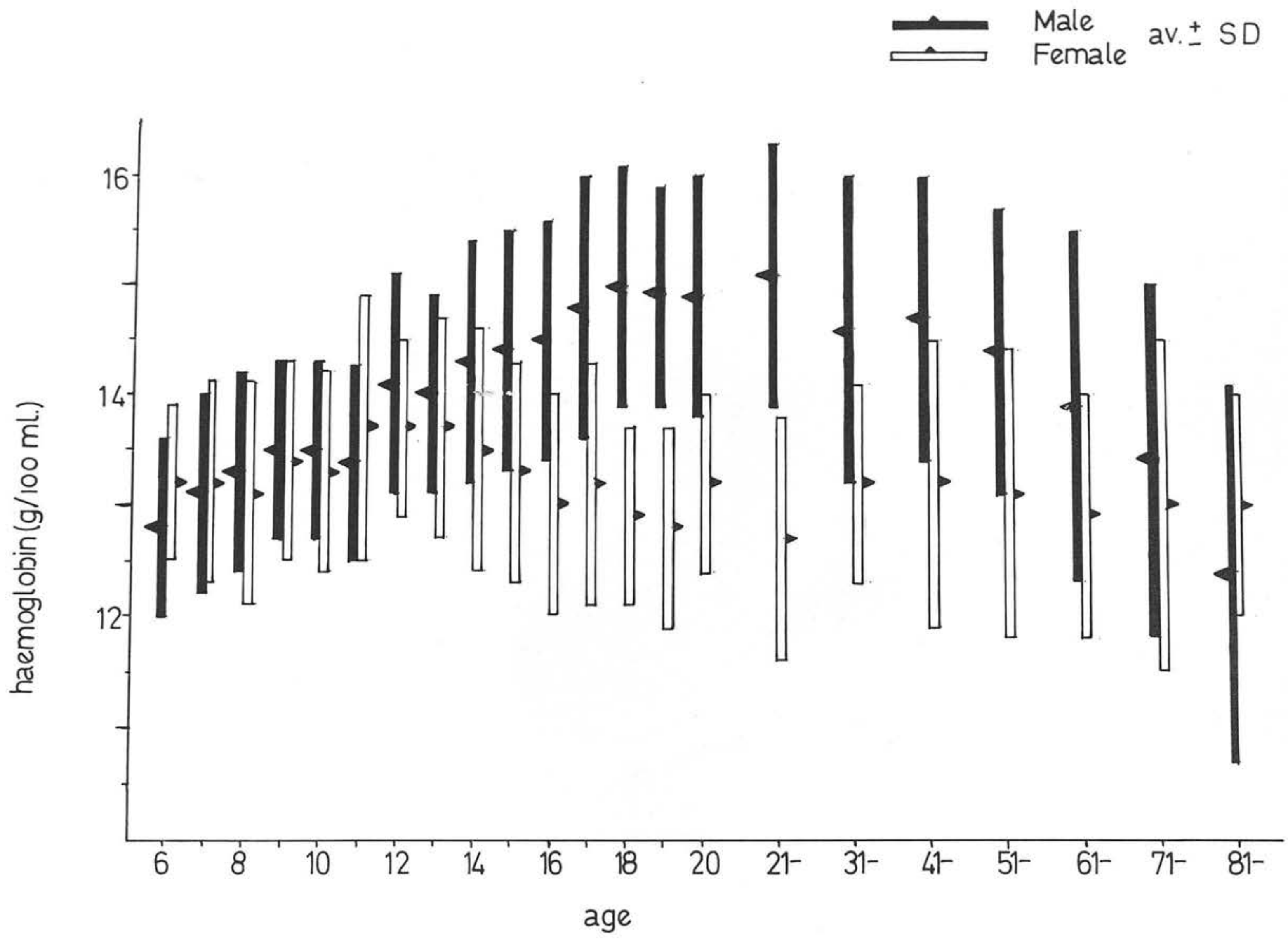


(from De Wijn and Rusbach 1961)

FIGURE 1

There is not as much information about sex differences in haemoglobin values before puberty. Mugrage and Andresen (1936) and de Wijn and Rusbach (1961) have shown that the sex difference in haemoglobin concentration does not appear before about 13 years of age. During adolescence, the haemoglobin values in boys rise in parallel with the appearance of secondary sex characteristics, and the development of an adult physique. Figure I (from de Wijn and Rusbach, 1961) shows the development of the sex difference in haemoglobin values in adolescence. In girls the haemoglobin concentration appears to remain at about the prepubertal level, although there is disagreement as to its exact behaviour. Hawkins et al (1954) showed a gradual decline in haemoglobin concentration from 13.7 g/100 ml at 13 years, to 12.8 g/100 ml at 19 years. But Mugrage and Andresen (1938) and de Wijn and Rusbach (1961) failed to show this trend. Elwood et al (1964) found that the mean haemoglobin level in premenarchial adolescent girls was significantly higher than that of post-menarchial girls of the same age by 0.33 g/100 ml, but, they pointed out, no account was taken of the phase of the cycle at which the blood samples were obtained, so that this difference might be artificial. (Duckles and Elvehjem (1937) and Leichsenring et al (1941) found that the maximum mean fluctuation of haemoglobin during the menstrual cycle was 0.94 and 0.19 g/100 ml respectively.)

In old age, there is a suggestion that the sex difference diminishes, mainly by a gradual fall in the haemoglobin concentration of aging men. Olbrich (1947) showed a mean haemoglobin concentration of 13.9 g/100 ml in 41 men aged 61 to



(from Hawkins et al 1954)

FIGURE 2

88 years, and 13.2 g/100 ml in 47 women aged 64 to 98 years all living in the same old people's home. Hobson and Blackburn (1953) and Semmence (1959) showed mean differences of 0.6 g/100 ml and 0.8 g/100 ml respectively. Semmence also found that over the age of 74 years there was no significant sex difference in haemoglobin levels. Indeed in a large population survey in Nova Scotia, Hawkins et al (1954) found that a group of 33 elderly women over 81 years had a mean haemoglobin concentration of 13.0 g/100 ml, whereas 28 men of a similar age had a mean concentration of 12.4 g/100 ml. The Nova Scotia study included 2,372 subjects from 6 to 98 years of age, and Figure 2 shows the trend of haemoglobin values with age and sex in that population.

The sex differential during the reproductive years must be maintained either by some essentially male/female difference, or by the iron depletion that menstruation and child bearing produce in women; or the difference may be a result of both effects.

<u>Endocrine Influence.</u> There is strong evidence that the sex difference in haemoglobin concentration is mainly an endocrine effect. In Figure I, p. 4, de Wijn and Rusbach show that haemoglobin levels in males parallel the increasing androgenic activity in puberty, and in the elderly male the haemoglobin begins to fall progressively by decades over the age of 50 years (Hawkins et al, 1954; Kilpatrick, 1961; Gourlay et al, 1970). The sex differential is virtually abolished in extreme old age when male sex hormone levels are declining (Migeon et al, 1957). McCullagh and Jones (1941 and 1942) have shown that administration

of methyltestosterone will increase the haemoglobin concentration and red cell mass in eunuchs. Conversely, there is some evidence that oestrogens may slow erythropoesis. Women regain their previous haemoglobin levels after blood donation slightly more slowly than men do (Fowler and Barer, 1942). The haemoglobin concentration in female rats is increased after oophorectomy and subsequent administration of oestradiol lowers it (Steinglass et al, 1941). Valquist (1950) noted that a group of women under 45 years of age, who had undergone hysterectomy with conservation of the ovaries, had haemoglobin levels comparable to those of a similar group of intact women who were menstruating. The concept that androgens confer a positive "maleness" on males, and that a female is a non-male being, has its parallel in the development of primary and secondary sex characteristics.

If this endocrine factor is indeed a major one in maintaining the male and female haemoglobins at their respective levels, one might expect to find confirmatory evidence from the animal kingdom. But unfortunately the information available is meagre and unconvincing. Anderson and Gee (1958) found higher haemoglobin concentrations in male than in female beagles. Afonsky (1955) could find no sex difference in dogs, and drew attention to the marked variation in haemoglobin levels from dog to dog, and sample to sample in the same dog. Rosahn et al (1934) found that buck rabbits had a mean haemoglobin concentration of 72 per cent and that virgin does from the same litter had a mean level of 67 per cent, but this was not confirmed by Wintrobe et al (1935). Two studies on cats (Landsberg, 1940; Windle et al, 1940) gave mean male and female values of 10.75 g/100 ml and 10.32 g/100 ml; and 12.2 g/100 ml and 12.0 g/100 ml respectively. In pigs (unpublished data of F.E. Hytten) there does appear to be a sex difference with values of 14.1 g/100 ml in boars and 12.1 g/100 ml in sows.

<u>Iron Depletion.</u> The alternative hypothesis, that women have lower haemoglobin concentrations then men because they are existing on the fringes of iron deficiency, has been tacitly assumed in much of the literature. Adult men and women form two distinct populations statistically with respect to their haemoglobin distributions, although there is a considerable overlap between the two (Garry et al, 1954). Elwood (1968) has commented on the marked negative skew on the female distribution curve and this has been attributed to anaemia being prevalent in the reproductive period (Witts, 1969). But closer examination of population surveys that compare haemoglobin concentrations of men and women, shows that in men also there may be a negatively skewed distribution (MRC, 1945). More recent surveys, however (Natvig and Vellar, 1967; Gourlay et al, 1970), have shown male and female populations in the 15-50 age group where haemoglobins have an almost normal distribution curve.

If iron deficiency is producing the lower haemoglobin concentration of women, then one might expect a fall in haemoglobin to occur shortly after the menarche, and to be gradually progressive until the menopause. In fact, as has been mentioned already (p. 4) there is conflicting evidence about the behaviour of haemoglobin concentration in adolescent girls. There is also some confusion about haemoglobin levels during female reproductive life. Davidson and Fullerton (1938) and MRC (1945) both showed a gradual fall during the child bearing years. But Elwood (1964) found a slight rise until 54 years of age, and Hawkins et al (1954) (figure 2, p. 5) showed no change in mean haemoglobin concentration between 31 and 60 years. The iron depleting effect of pregnancy is also questionable. The MRC (1945) report showed that parous women had slightly lower haemoglobin concentrations than nulliparous women. Berry and coworkers (1952) failed to confirm this in every respect, but did show that women with four or more pregnancies had a lower mean haemoglobin concentration than those with three or fewer pregnancies. Sunderman et al (1953), in a review of the literature found the evidence for an association between haemoglobin and parity was conflicting.

The administration of iron to groups of women, with a subsequent increase in haemoglobin concentration has been given as evidence of iron deficiency in large sections of the female population. Natvig and Vellar (1967) showed that a three month course of iron, 60 mg daily, administered to 268 normal urban women with haemoglobin concentrations in excess of 12 g/100 ml, raised the mean value from 13.9 g/100 ml to 14.2 g/100 ml, and narrowed the area of scatter, and that this did not occur in men.

However, Fowler and Barer (1941) showed that if the haemoglobin levels continued to be checked regularly for six, instead of three months - a study carried out on a group of mildly anaemic but otherwise healthy young adults of both sexes - the haemoglobin levels of all rose initially for 10-12 weeks, and then fell over the subsequent three months - back to the original level in one group (which they postulated had a "low normal" haemoglobin) and to a level half way between the original and highest haemoglobin value in the second group (which presumably had "a mild anaemia"). This fall occurred whether or not the subjects were still taking their oral iron. There is, therefore, some reason to believe that iron in therapeutic doses may have an erythropoietic effect, irrespective of the presence or absence of "anaemia". But Yudkin (1944) would seem to disagree with this, as he found that a group of recruits just about to enter the WAAF had a mean haemoglobin concentration of 94.8 per cent and that girls who had been in the service for periods from six months to four years had a mean concentration of 102.5 per cent. Yudkin attributed the difference to the WAAF diet which at that time was said to contain 35 mg iron a day, mainly because of the iron cooking utensils. In 1936 Widdowson carried out weighed diet surveys on 63 men and women from the middle classes and compared their diets with six poor unemployed men and women. Both groups of women had poorer diets than their husbands; and the wives of the unemployed men had considerably poorer diets than the wealthier middle class women. Fullerton (1936) found that women of the poorest social classes in Aberdeen had the following mean haemoglobin concentrations:-

Age-years	Mean haemoglobin*	
15-19	83%	(11.45 g/100 ml)
20-24	84%	(11.64 g/100 ml)
25-29	83%	(11.45 g/100 ml)
30-34	81%	(11.18 g/100 ml)
35-39	80%	(10.99 g/100 ml)
40-44	76%	(10.49 g/100 ml)
45-54	85%	(11.82 g/100 ml)
55-64	89%	(12.10 g/100 ml)
65+	89%	(12.10 g/100 ml)

*100% = 13.8 g/100 ml

The work of Davidson et al (1943) shows that diet is probably an important factor, at least during growth. 95 per cent of children attending a fee-paying private school in Edinburgh had a haemoglobin concentration above 11 g/100 ml (80 per cent Haldane), whereas only 60 per cent of the children attending a municipal school were above this level. Both groups of children were aged between 5 and 12 years, so the sex difference would not be apparent, and menstruation would hardly be involved.

In 1937-39 the average iron intake per person per day in England varied from 12.0 mg in households with one child to 7.9 mg in households with six children (Rowett Research Institute 1955). Since the war the National Food Survey Committee has published annual reports on average food consumption, based on weighed surveys of food going in to the household. In 1968 the average iron consumption of the housewife per day, by age and social class, was as follows:-

Age-Years	Social Classes I and II	Social Classes III, IV and V
<25	12.7 mg	12.8 mg
25-34	11.7 mg	12.1 mg
35-44	12.4 mg	13.3 mg
45-54	14.9 mg	15.0 mg
55-64	16.1 mg	15.4 mg

All the iron intakes are over the recommended dietary allowances and the social class difference has disappeared. There is no recent information available about variation in haemoglobin concentration by social class.

There is, however, data on the South African Bantu who are known to have a diet with a very high iron content, which may often exceed 100 mg/day (Walker and Arvidsson, 1953). The iron comes from the iron cooking utensils and also from the native beer. Presumably the women both eat and drink less than the men, but even so, their diets are probably very rich in iron. Walker (1966) has shown that although the haemoglobin concentration is high compared with other underprivileged peoples, the sex difference remains. He found that 50 urban Bantu women had a mean haemoglobin concentration of 13.5 g/100 ml, and that urban males had a mean haemoglobin concentration between 15 and 16 g/100 ml.

The Bantu, of course, are likely to have diets deficient in other essentials that are necessary to maintain the optimum iron balance, and it may be unreasonable to dismiss the influence of diet in reducing the male/female difference in haemoglobin concentration from this evidence alone.

There might be proof of a mild state of iron deficiency if it could be shown that the iron stores in women were depleted, although there is controversy about the availability for erythropoesis of iron in the tissues, and over its quantitative assessment. The problem of assessing the iron stores can be approached in several ways (Beutler, 1957). The serum iron level may give a somewhat indirect indication of the amount of iron available in the stores because it represents iron being conveyed from the point of absorption to the stores, and from the stores to the sites of utilization; presumably, therefore, deficient iron stores would eventually be reflected in low levels of serum iron. But in women, there is a considerable hormonal control of serum iron concentrations, with a fluctuation ranging from ± 20 per cent of the mean, depending on the stage of the menstrual cycle (Zilva and Patson, 1966), so that the significance of a single serum iron value may be very difficult to interpret.

Studies with radio isotopes of iron are also unhelpful when trying to evaluate the iron stores, as injected iron appears to be used immediately in the production of red cells, 70-100 per cent of a dose appearing in the red cells within a few days

(Dubach et al, 1946). After the destruction of the first generation of red cells, the radio isotope is not uniformly incorporated into the iron stores, but is largely recycled into the production of further red cells. Similar rates of incorporation into red cells have been found in groups of anaemic (Bothwell et al, 1956) and non-anaemic subjects (Dubach et al, 1946).

A more direct assessment of iron stores, by examination of bone marrow is only slightly more satisfactory. The method was first intorduced by Rath and Finch in 1948, when they attempted to assess quantitatively on an arbitrary scale of 0 to 6+, the amount of haemosiderin in the reticulo endothelial cells of aspirated samples of bone marrow. But, as the specimens so obtained are necessarily small, and the iron granules irregularly distributed in the marrow (Fielding, 1965), interpretation of the numbers of observed iron granules may be misleading in border-line cases, although results may be more satisfactory in cases of severe iron deficiency anaemia, and in diseases associated with over-storage of iron, such as haemochromatosis. Douglas and Dacie (1953) pointed out that red cell precursors containing iron granules in the cytoplasm (sideroblasts) were more commonly present in the bone marrow of normal individuals than of anaemic patients. But Bainton and Finch (1964) found that even in very experienced hands there might be a 20 per cent counting error on any given slide, and that there was little or no correlation between the sideroblast count and the marrow haemosiderin.

This method of evaluating the iron stores, therefore, seems at best to be crude, subjective and qualitative.

In 1965 Fielding described a method of measuring chelatable body iron, which he implied might be directly associated with the "available" compartment of the total iron stores in the body. The sites of chelation are unknown, but haem iron is not involved (Wohler, 1962). Fielding thought that the different pools that go to make the total body iron may have different chelatable susceptibilities, related to the degree of their availability for haem synthesis. If this is so, then his differential ferrioxamine test would be a more physiological method of assessing iron stores, than any way of trying to measure total stores. Fielding et al (1965) assessed the chelatable body iron in groups of healthy male and female volunteers, and found a considerable overlap, but 33 per cent of the women had values below the male range and in the range for patients with iron deficiency anaemia. But there is no reason to suppose that if serum iron is affected by fluctuating hormone levels, and haemoglobin concentrations are influenced by androgens and oestrogens, iron stores may not also be influenced by the sex steroids.

It does, therefore, begin to appear that there is a hormonally-determined difference between the sexes in iron metabolism, and in haemoglobin levels, but that, in addition, some women may be verging on iron deficiency. The extent to which these two factors influence the haemoglobin concentration in women is not clear, but menstruation is likely to be a major source of iron depletion.

Menstrual Blood Loss

The quantitative assessment of menstruation has interested authors since the days of Hippocrates. Barer and Fowler (1936) reviewed the literature and found studies that differed widely in method - from the weighing of menstrual blood to enumerating the numbers of used sanitary towels. Not surprisingly, the results varied considerably, from 26-52 cc (Hoppe-Seyler) to 20 oz or "several pounds" (Hippocrates and Magendie respectively, both quoted by Novak, 1931). Since 1936, however, there have been some 17 papers on the subject, which sought to establish the normal menstrual loss in adult women. The results, methods of estimation and types of women studied are given in table form (Table 1). It will be noted that only two studies have attempted to present a representative population selected at random. Hallberg et al (1966b) picked at random urban women stratified by age; and Elwood et al (1968) selected 44 women at random from a population stratified by haemoglobin. Other studies have picked students, nurses, hospital employees and patients. The results are usually presented as millilitres of blood, obtained from estimation of iron and conversion to the equivalent volume of blood derived from the current haemoglobin status of the patient. It has been argued (Elwood et al, 1968) that the iron loss is more important from a nutritional point of view. But a normal woman losing 100 ml blood per period will lose much more iron

TABLE 1

Previous Studies on Menstrual Loss

	Author	No.	Age Years	Method of estimation	Mean loss	Range	Remarks
1	Barer and Fowler, 1936	100	15-43	Chemical determination of iron	50.55 ml blood	6.55-178.69 ml blood	Hospital employees with Hb > 10.2g%. Menstruation considered normal
2	Leverton and Roberts, 1937	4	21-27	Chemical determination of iron	34.24 ml blood	26.48-50.78 ml blood	Students
3	Moore, Minnich and Welch, 1939	14	-	Haemoglobin determination	-	9-41 ml blood	Students
4	Arens, 1945	51	15-23	Chemical determination of iron	58.9 ml blood	11.7-157.8 ml blood	Hb > 10.4 g /100 ml
5	Schlapphoff and Johnston, 1949	6	13-14	Chemical determination of iron	17.62 mg iron	6.12-50.11 mg iron	Healthy subjects
6	Millis, 1951	14	21-27	Chemical determination of iron	21.8 mg iron (48.2 ml blood)	3.5 -66.8 mg iron (13-126 ml blood)	Healthy nursing students. Menstruation considered normal
7	Baldwin, Whalley and Pritchard, 1961	21	-	Radio isotope technique (^{59}Fe)	25 ml blood	10-55 ml blood	Healthy nurses and technicians, menstruation considered normal

	Author	No.	Age	Method of estimation	Mean loss	Range	Remarks
8	Hagedorn, Kiely, Tauxe and Owen, 1961	12		Radio isotope technique (^{51}Cr)	27 ml blood	6-50 ml blood	Healthy subjects. In 15 iron deficient subjects loss was 103-579 ml
9	Rankin, Veall, Huntsman and Liddell, 1962	20	-	Radio isotope technique (^{51}Cr)	-	9.3-970. ml blood	Patients complaining of menorrhagia
10	Apte and Venkatachalam, 1963	13	-	Chemical determination of iron	37 ml blood	20-62 ml blood	Healthy, adult, non-anaemic subjects
11	Hallberg and Nilsson, 1964	12	21-23	Haemoglobin determination	28 ml blood	9.1-55.8 ml blood	Healthy, non-anaemic nurses, 12 periods measured in each subject
12	Hytten, Cheyne and Klopper, 1964	38	21-38	Chemical determination of iron	25 ml blood	7-70 ml blood	15 healthy nulliparous midwives; 23 healthy parous women
13	Price, Forsyth, Cohn and Cronkite, 1962	7	24-46	Radio isotope technique (^{59}Fe). Whole body counting	-	33-552 ml blood	6 of the 7 women complained of menorrhagia
14	Jacobs and Butler, 1965	(17	21-40	Radio isotope technique (^{51}Cr)	34.7 ml blood	3-87 ml blood	Healthy midwives with Hb > 12 g/100 ml
		(14		" " "	85.5 ml blood	21-183	Subjects with iron deficiency

	Author	No.	Age	Method of estimation	Mean loss	Range	Remarks
15	Hallberg, Hogdahl, Nilsson and Rybo, 1966a	137	16-52	Haemoglobin determination	34 ml blood	1.6-199.7 ml blood	Factory workers
16	Hallberg, Hogdahl, Nilsson and Rybo, 1966b	476	15-50	Haemoglobin determination	43.4 ml blood	-	Random selection in age groups, of women living in Gothenberg
17	Elwood, Rees and Thomas, 1968	44	20-39	Dry ashing process	12.17 mg iron	-	Random selection of women stratified by haemoglobin level and treated with iron before measuring menstrual losses

than an anaemic woman losing the same volume of blood. On the other hand, there is a suggestion that in clinical iron deficiency anaemia there may be a protective mechanism which reduces the menstrual flow (Jacobs and Butler, 1965), although this is disputed, Taymor and coworkers (1964) having advanced the theory that menstruation is increased in anaemia. The opinion of Taymor and his colleagues was based on the subjective impressions of the patients without any measurements of menstrual loss, a procedure which has been shown to be unreliable (Rankin et al, 1962; Hytten et al, 1964). In attempting to assess the normal range of menstrual loss, particularly interesting are the numerically large studies of Barer and Fowler (1936) (100 women), Arens (1945) (51 women), Hytten et al (1964) (38 women), Hallberg et al (1966a and b) (137 and 476 women), and Elwood et al (1968) (44 women). Barer and Fowler studied hospital employees with haemoglobin levels above 10.2 g/100 ml, 66 per cent were anaemic by generally accepted standards today (haemoglobin below 12 g/100 ml). This is rather a high anaemia rate, and if menstruation does cause iron deficiency, perhaps their mean menstrual blood loss of 50.55 ml might be on the high side too. Similarly, Arens studied a group of 51 girls aged 15-23 years, with haemoglobin concentrations above 10.4 g/100 ml; they had the same order of blood loss of 58.9 ml per period. Hytten et al (1964) studied a group of women more representative of the reproductive years, ranging in age from 21-38 years - omitting the adolescent and menopausal groups - and their mean menstrual loss was 25 ml. Elwood et al (1968) with 44 women over a similar age range, produced almost identical results. Hallberg's two papers (1966a and b) have stemmed from the largest studies of 137 and 476 women respectively. He picked his groups between the ages of 15 and 50 years, at the extremes of which there might be expected to be women with a changing pattern of menstruation which, although physiological, is not "normal" with reference to the established pattern of most of their reproductive lives. The mean menstrual blood loss in his series was 34 ml and 43.4 ml respectively.

Although different workers have reported different mean results, all have shown that there may be a very wide variation in menstrual loss from woman to woman. Most agree that there is relatively little individual variation in loss from period to period in any given subject (Leverton and Roberts, 1937; Millis, 1951; Apte and Venkatachalam, 1963; Hytten et al, 1964; Hallberg and Nilsson, 1964). Other authors, however, reported considerable variation between measured periods in the same subject, even though these differences were not noticed subjectively (Barer and Fowler, 1936; Arens, 1945; Baldwin et al, 1961). But there is virtually no explanation of why there should be such a wide range of menstrual losses. There is no definite evidence to suggest that either parity or age is associated with changes in the volume of blood loss. Barer and Fowler (1936) noted that 11 nulliparous married women had a mean loss of 36.7 ml and 13 parous married women a mean loss of 48.2 ml. Hallberg et al (1966a) found that highly parous young women under 25 years had a significantly higher menstrual loss than the rest of their age group. From this finding he inferred that there might be an association between recent delivery and heavy menstrual loss. Parity appeared to exert no influence in other age groups, and was not mentioned in his population study in Gothenberg (1966b). Elwood et al found no effect of either parity or age on menstrual loss. But Hallberg and Nilsson found that age had a statistically significant effect on both extremes of the reproductive years (1966b).

Age (years)	15	23	30	40	45	50
No. of subjects	95	77	89	92	86	37
Mean loss per period (ml)	33.8	38.9	49.0	44.5	42.7	62.4

<--------- 44.9 ml --------->

The 15 year old group lost significantly less blood than the four age groups between 23 and 45 years, and the 50 year old group lost significantly more. But one must have doubts about the "normality" of a group of 37 women aged 50 who were still menstruating. No pelvic examinations were made and Hallberg's series may have included some cases of menorrhagia of pathological origin.

There is some evidence to suggest that certain women complaining of menorrhagia may have a demonstrable abnormality in the fibrinolytic system (Nilsson and Bjorkman, 1965; Basu, 1970). Rybo (1966) has shown that endometrial plasminogen activators are increased pre-menstrually in women with losses of over 80 ml per period, interfering perhaps with normal haemostatic mechanisms (Astrup, 1956).

Hallberg et al (1966b) has shown that the distribution curve of menstrual losses has a marked positive skew and that there is a correlation between menstrual loss and haemoglobin concentration, with menstrual losses of over 80 ml per period being associated with a 67 per cent incidence of haemoglobin concentrations below 12 g /100 ml. This finding of a correlation between menstruation and haemoglobin is evidence in favour of the theory that the iron balance of some women may become negative due to recurrent loss of blood at menstruation. But this finding is unconfirmed, and the causes of variation of menstrual blood loss are virtually unknown. It is the purpose of this study to examine these problems in a population.

CHAPTER 2

General Procedure

The survey was undertaken in Broomhill, a small coastal mining community in Northumberland, about 25 miles north of Newcastle upon Tyne. The area was about three miles in diameter, and included a council estate, Coal Board and privately owned houses and several farms. The local pits had been closed, but extensive opencast coal mining was being carried out, and pits were still being worked about ten miles away. High unemployment was leading to considerable migration, especially in the younger age groups. Yet, although the area was depressed, even by north east standards, there did not appear to be gross poverty. Nearly all the houses had television sets, and in a few of the Coal Board houses there was colour television. The children appeared well fed and most were well clothed. Many families had cars, and although there was great variation in cleanliness and quality of furnishing within the houses, this appeared to depend more on the individual than on the type of job of the husband. Supplementary and unemployment benefits are probably sufficient to prevent the appalling poverty that was prevalent between the wars.

One group medical practice had a virtual monopoly in the area - this was verified by comparing the names on the electoral roll with the practice files, a task that was greatly facilitated by the locally-born practice secretary and receptionist. The names of all women born between 1925 and 1952 were obtained from the files. The intention was to study these women between

Coal Board Houses

Private Houses

Private Houses

October 1969 and May 1970 when they were aged from 17 to 45 years. These ages were chosen because by 17 most girls would have established a regular pattern of menstruation and by 45 only a few women would have reached the menopause.

The women were contacted initially by a letter over the general practitioner's signature, announcing that a survey on anaemia in women was to be carried out in the district, and that a personal visit would be made by the investigator to ask for co-operation. These letters were sent out in batches of 20-25 every week and each person so contacted was visited within the week. At this first visit the possible association between menstruation and anaemia was explained and each woman was asked to collect her used sanitary towels and tampons for two consecutive periods. Although the use of tampons ensures the most complete collection of menstrual blood, it was thought that co-operation would be more likely if the women were not asked to alter their normal habits to use tampons, if they did not already do so, but the importance of a complete collection of the blood lost was stressed. If co-operation was obtained at that initial visit the woman was given a black polythene bag in which to collect the used towels, two packets of sanitary towels and a stamped addressed postcard to be returned to the investigator after the next period. The expected date of that period was also noted, so that if the postcard did not arrive, the woman concerned could be visited, and the reason discovered. On receipt of the postcard, a second visit was made, and at that time a medical history was obtained, with special reference to other possible sources of blood loss; drug therapy including iron, aspirin and oral contraceptives in the previous year; and gynaecological history. A blood specimen of about 25 ml was taken from an antecubital vein for estimation of haemoglobin, packed cell volume, serum iron, iron binding capacity and fibrin/fibrinogen degradation products. The date that the period started was noted, and the woman was asked to give an estimate of the completeness of collection of menstrual blood. Her answers were recorded as "Complete", "Almost Complete" or "Incomplete". The last category included cases where a tampon or sanitary towel had been thrown away in error, or, more usually, where underclothes or sheets were stained, or clots were reported to have been lost down the lavatory. The woman was given another supply of polythene bag, sanitary towels and postcard, this last to be mailed at the end of the second period when the final home visit was made. The date of the second period was again noted, and the collection classified according to the woman's estimate of completeness. She was also asked after both periods whether the blood loss was normal for her, or lighter or heavier than normal. Usually, a second blood sample for haemoglobin estimation was obtained after the second period, but in some cases where the woman had previously fainted, or had objected strongly to venepuncture, the procedure was omitted. At this visit also the married women were given appointments to attend the general practitioner's surgery for a brief medical and gynaecological examination. As far as possible the appointments were given for a day during the third or fourth week of the woman's menstrual cycle, although occasionally this proved impractical as examinations were only carried out once a week on Wednesdays.

At the examination in the surgery, a specimen of urine was obtained and tested for sugar and protein. Height, weight (in underclothes but without shoes) and blood pressure were measured. At this point the gynaecological examination with cervical smear was explained in greater detail, especially to the nulliparous, the parous women being, of course, familiar with the procedure at the post natal clinic. (After the survey had been completed the relevance of height and weight became apparent from a preliminary analysis of the clinical data and so, in September 1970, the unmarried women and married women who had refused examination were visited at home and height was measured with a steel tape and weight was measured on portable scales.)

Permission to carry out an endometrial biopsy was sought of the parous women, and in those who gave permission the biopsy was carried out with a sterile Sharman curette and with the examiner gowned, masked and gloved. Especial care was taken to abandon the procedure if the patient showed signs of discomfort, as it was thought that the high degree of co-operation would diminish if rumours of pain were to spread in the close knit community. In the event, out of 231 women who were asked to provide a biopsy specimen, 87% agreed to undergo curettage, but adequate material for interpretation was only obtained from 20% (41) of these.

TABLE 2

Husband's Occupation	*S-E. Group	Survey: Broomhill		1961 Census: Amble District	1961 Census: Northumberland
Professional and Managerial	1-4 and 13	16	(5.5%)	12%	13.2%
Other white collar workers	5 and 6	29	(10%)	5.7%	15.2%
(Miners	7-10	101)	(69%)	63.9%	61.3%
(Skilled and semi-skilled (manual workers		101)			
Unskilled manual workers	11	36	(12.7%)	16.4%	9.7%
Others, including unemployed		7	(2.7%)	-	-
		290	(99.9%)	(98%)	(99.4%)

*Registrar General's Socio-economic classification.

Population studied

Of 507 women born between 1925 and 1952 listed in the practice files, 348 were eventually included in the survey. 136 names on the list were excluded for the following reasons:-

Moved from the district	85
Pregnant or within four months of delivery by May 1970	44
Could not be contacted	3
Severe psychiatric or mental defect	3
Dead	1
	136

The list was compiled in August 1969 and the last group contacted in March 1970, so that the migration of 85 women spanned eight months, and indeed, four more women left during the time that they were participating in the survey. Of the remaining 371 cases, 23 refused to co-operate; the success rate was therefore 93.8%.

The socio-economic status of the women co-operating in the survey was classified by their husbands' employment (Table 2). Compared with the Registrar General's findings in the 1961 census for the larger district of Amble of which Broomhill forms part, and for Northumberland as a whole, there were relatively fewer women whose husbands were professional or managerial, and a relative excess of skilled and semi-skilled workers.

Seven women were divorced or widowed, and fifty-one were unmarried. These women were classified separately according to their own jobs (Table 3). As a comparison, the previous or present occupations of the married women are shown in the second column. There were more professional and managerial, and clerical workers among those fifty-eight single women than among the married women and relatively fewer in the service trades.

Details of the types of job included in the categories listed in Tables 2 and 3 are given in the Appendix 2.

Table 4 shows the distribution by age and parity of the surveyed population. There are relatively few younger women below 30, and this is largely because of unemployment and the outward migration of the young.

TABLE 3

Occupations of single, divorced and widowed women			*Occupations of Married Women	
Professional and Managerial	7	(12%)	22	(7.5%)
Clerical	15	(25.8%)	45	(15.5%)
Distributive Trades	15	(25.8%)	87	(30%)
Service Trades	8	(13.8%)	78	(26.8%)
Factory Workers	11	(19%)	44	(15.1%)
Unemployed	2	(3.4%)	14	(4.8%)
	58	(99.8%)	290	(99.7%)

*Current or previous occupation.

TABLE 4

Distribution of the cases studied by age and parity: and of cases who refused to co-operate by age.

Parity ↓ / Age (Years) →	17-19	20-24	25-29	30-34	35-39	40-44	Total
0	25	20	7	3	5	1	61
1	3	18	7	11	9	8	56
2	0	9	21	30	26	20	106
3	0	5	12	17	9	20	63
4+	0	1	5	13	19	24	62
Co-operating Total	28	53	52	74	68	73	348
Refusals	4	3	2	4	2	8	23
TOTAL	32	56	54	78	70	81	371

TABLE 5

No measured menstrual loss

Hysterectomy	6
Oligomenorrhoea	6
Menopausal	3
Post partum amenorrhoea	5
Total	20

Only one period measured

Amenorrhoea associated with oral contraceptive	4
Pregnant after 1st period	1
Oligomenorrhoea	9
Metrorrhagia	1
Left the district after 1st period	4
Persistent defaulter	5
Total	24

CHAPTER 3

Menstrual Loss

It has been reported that there is little variation from period to period in the same individual (Hallberg et al, 1964, 1966a; Hytten et al, 1964). In 1964 Hallberg and coworkers measured losses in twelve consecutive periods in twelve nurses, showing mean losses ranging from 9.6 to 55.8 ml per period, and although in the text they point out that there is only a small standard error of the mean of the twelve losses in each woman, the standard deviations indicate a variation of about 30 per cent from period to period in the same women ($\pm$ 1 S.D.). Where the mean loss is fairly low, this does not connote any great variation in absolute terms, but with a large menstrual loss, the absolute loss during one period may easily differ by 20 ml or more from that during another period. It was therefore decided in this current survey that the measured mean blood loss of two periods would be more representative of the usual menstrual pattern than one measured period.

Comparison of menstrual losses during two consecutive periods

Of the 348 women taking part in the survey, 20 were amenorrhoeic, and 24 could be measured during one menstrual period only. The reasons are given in Table 5. In 304 cases two menstrual periods were measured. Table 6 shows the difference in volume between two periods. The correlation coefficient (r) was 0.82. In 82 per cent (250) of these cases, the variation between period I and period II was less than 20 ml, and in 54

TABLE 6

Difference in blood loss between two menstrual periods

Difference between periods (ml blood)	0-	5-	10-	15-	20-	25-	30-	35-	40-	45-	50+	Total
Number	116	67	44	23	17	12	7	2	1	5	10	304
Percentage	38.2	22.0	14.5	7.6	5.6	3.9	2.3	0.7	0.3	1.6	3.3	100.0

Correlation coefficient (r) of blood loss in Period I and Period II = 0.82

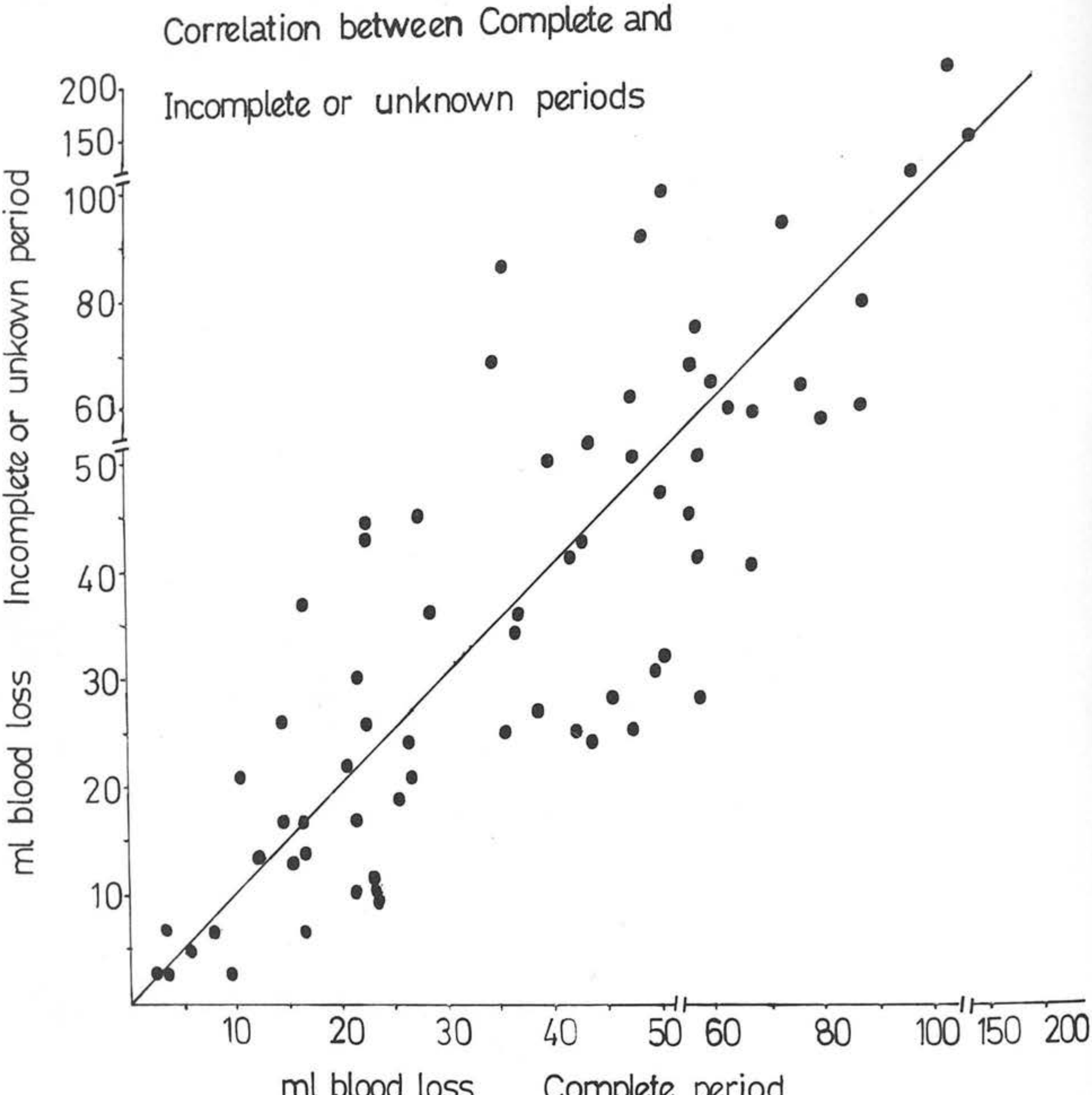

Correlation between Complete and
Incomplete or unknown periods
Incomplete or unkown period
ml blood loss
200
150
100
80
60
50
40
30
20
10
10
20
30
40
50
60
80
100
150
200
ml blood loss Complete period

FIGURE 3

cases (18 per cent), it was greater than 20 ml. Such large variations might be due to faulty collection of one period, but in these 54 cases only 12 women reported that one or both periods were "incomplete" and in 9 the "incomplete" period was larger than the "complete" period.

In the whole series, there were 71 cases in which one period was reported as being "complete" or "almost complete" and the other as being "incomplete" or "not stated". Figure 3 shows that the "incomplete" or "not stated" period was smaller than the "complete" period only 38 times. Since there is no evidence that variation between pairs was influenced by completeness of collection, as reported by subjects, it was decided to use all the data, and to average the two periods where available, as giving the best estimate of the loss experienced by each woman.

Subjective impressions of women about menstrual loss

Hytten and coworkers (1964) have previously shown that women are notoriously inaccurate in their subjective impressions of menstrual loss, and this has been confirmed in this study. As well as being asked whether each period that they collected was representative of their usual loss, each woman was asked to judge whether her periods in general were light, normal or heavy. It is apparent from the range of menstrual loss in each category (Table 7) that an individual woman may be a very poor judge of her own menstrual loss and that complaints of menorrhagia should not always be taken at their face value.

TABLE 7

Subjective assessment of menstrual loss

	No.	Mean loss (ml)	Range (ml)
Amenorrhoea	20		
Not stated	34		
"Variable loss"	2		
Light periods	63	17.5	(0.3-93.0)
Normal periods	175	37.6	(1.0-170.0)
Heavy periods	54	62.8	(7.0-280.0)
	348		

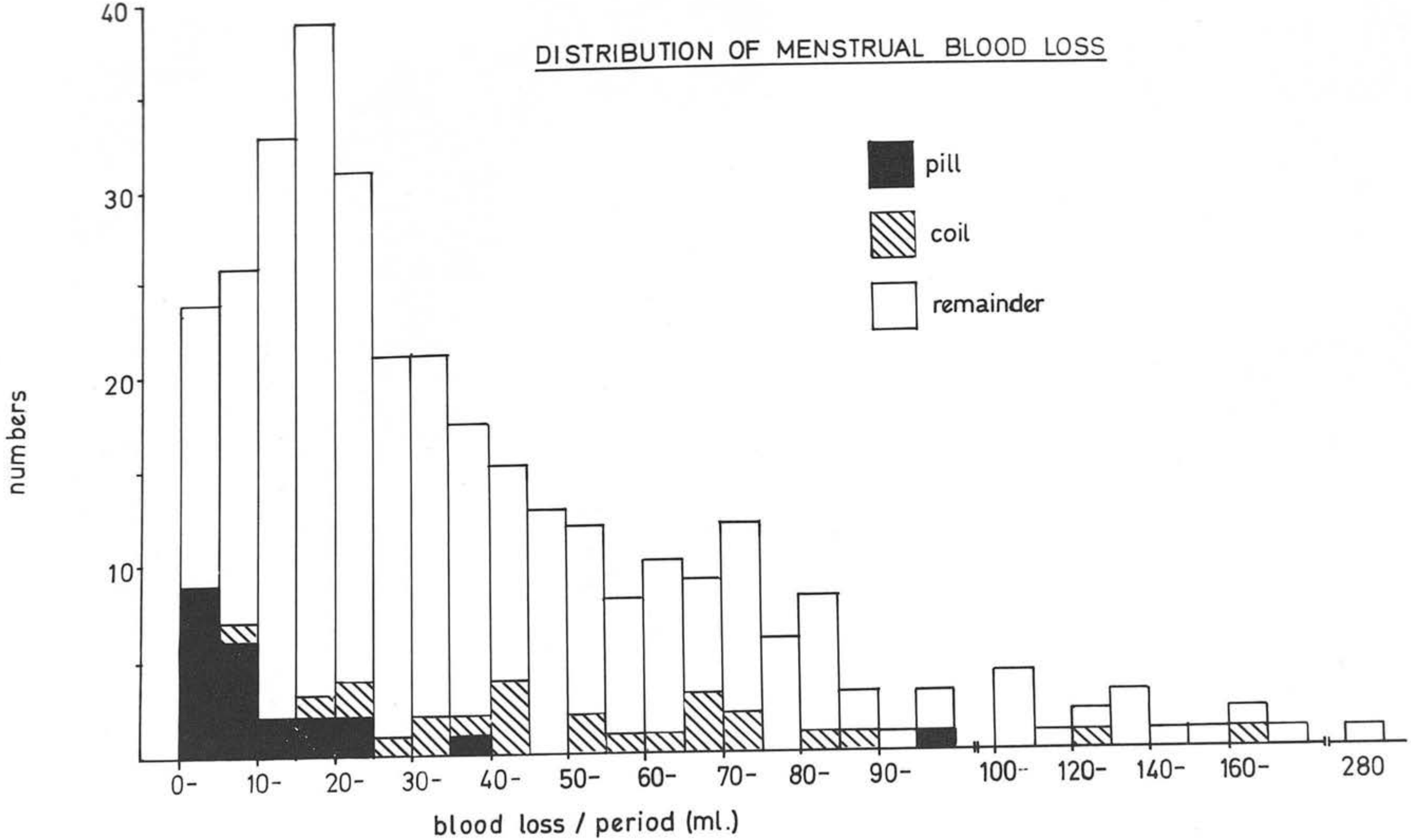

DISTRIBUTION OF MENSTRUAL BLOOD LOSS
pill
coil
remainder
numbers
40
30
20
10
0-
10-
20-
30-
40-
50-
60-
70-
80-
90-
100-
120-
140-
160-
280
blood loss / period (ml.)

FIGURE 4

TABLE 8

Distribution of menstrual blood loss (ml per period), and influence on menstrual loss of oral contraceptive (Pill) and intra uterine device (Coil).

Mean loss	Pill	Coil	Remainder	Total Number
0-	9		15	24
5-	6	1	19	26
10-	2		31	33
15-	2	1	36	39
20-	2	2	27	31
25-		1	20	21
30-		2	19	21
35-	1	1	15	17
40-		4	11	15
45-			13	13
50-		2	10	12
55-		1	7	8
60-		1	9	10
65-		3	6	9
70-		2	10	12
75-			6	6
80-		1	7	8
85-		1	2	3
90-			1	1
95-	1		2	3
100-			4	4
110-			1	1
120-		1	1	2
130-			3	3
140-			1	1
150-			1	1
160-		1	1	2
170-			1	1
250+			1	1
Total	23	25	280	328
Mean loss	12.7	56.3	37.9	37.5
S.D.	20.4	35.2	33.9	34.2

Pill v Coil $p < 0.001$
Pill v Rest $p < 0.001$
Coil v Rest $p < 0.05$

However, it is interesting to note that the mean loss in each of these three groups corresponds to the descriptions.

Distribution of menstrual loss

Figure 4 and the final column of Table 8 shows the distribution of menstrual loss in the population studied. The range of loss was very large - from 0.1 ml to 280 ml at either extreme - and the distribution showed a marked positive skew. Because of this, the mean value is an unhelpful figure, except for purposes of comparison with other studies. In this population the mean blood loss per period was 37.5 ml. (See Table 1, following p.15.)

Factors influencing menstrual loss

Contraception. In the group studied, 23 women were taking an oral contraceptive, and 25 had an intra uterine device. Table 8 shows the distribution of menstrual loss in these two groups compared with the remaining population of 280 who used neither method of contraception. The significant differences in mean loss of the two contraceptive groups confirms subjective impressions reported by women using an oral contraceptive or an intra uterine device, and the indirect evidence of the haematological sequelae (Zadeh et al, 1967) of these methods of contraception. All further analyses of factors influencing menstrual loss are based on the 280 women who were not using these contraceptive measures.

Iron therapy

It has been stated that menstrual loss is decreased when a woman is iron deficient, and that correction of anaemia leads to increased loss. (Jacobs and Butler, 1965.) In the 280

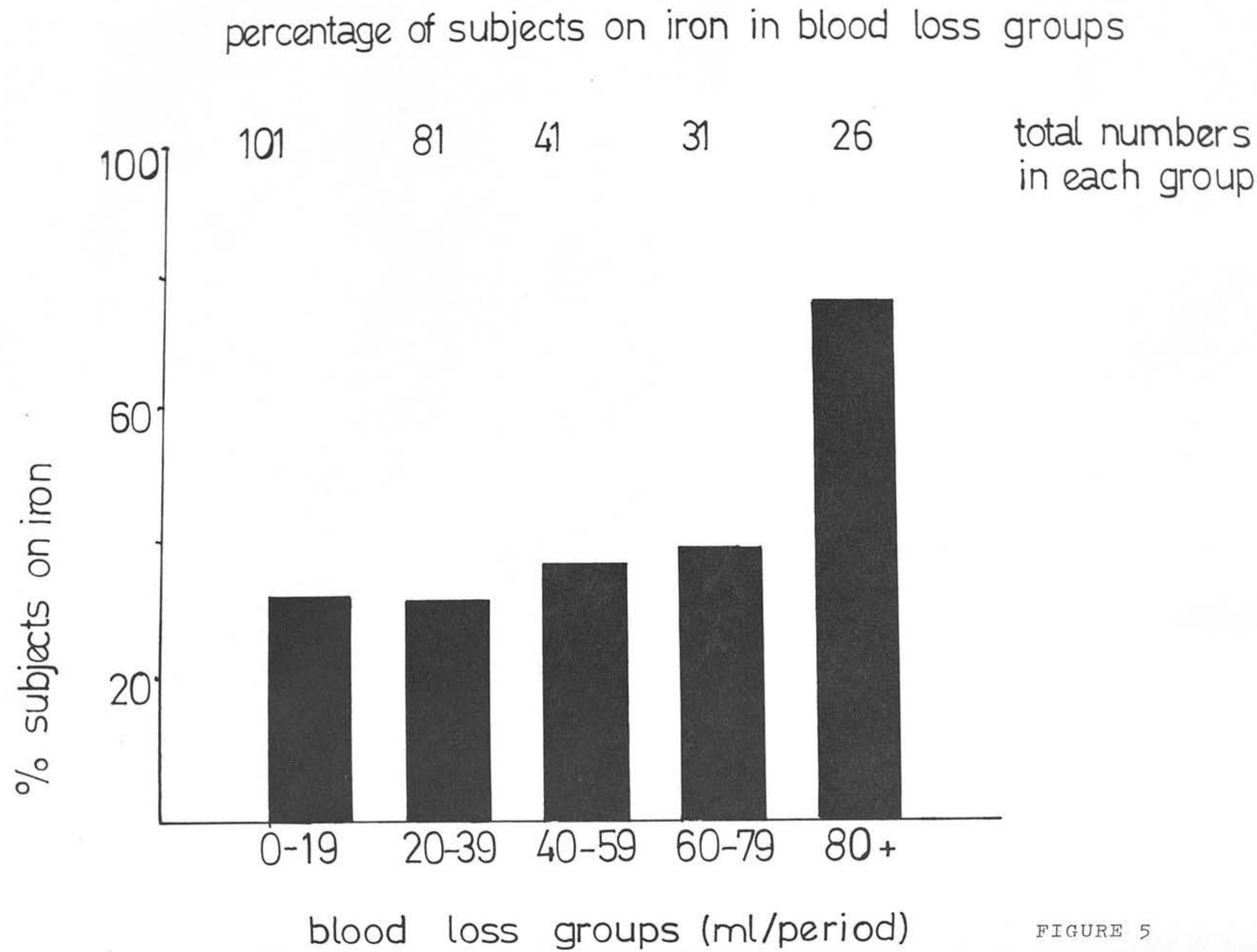
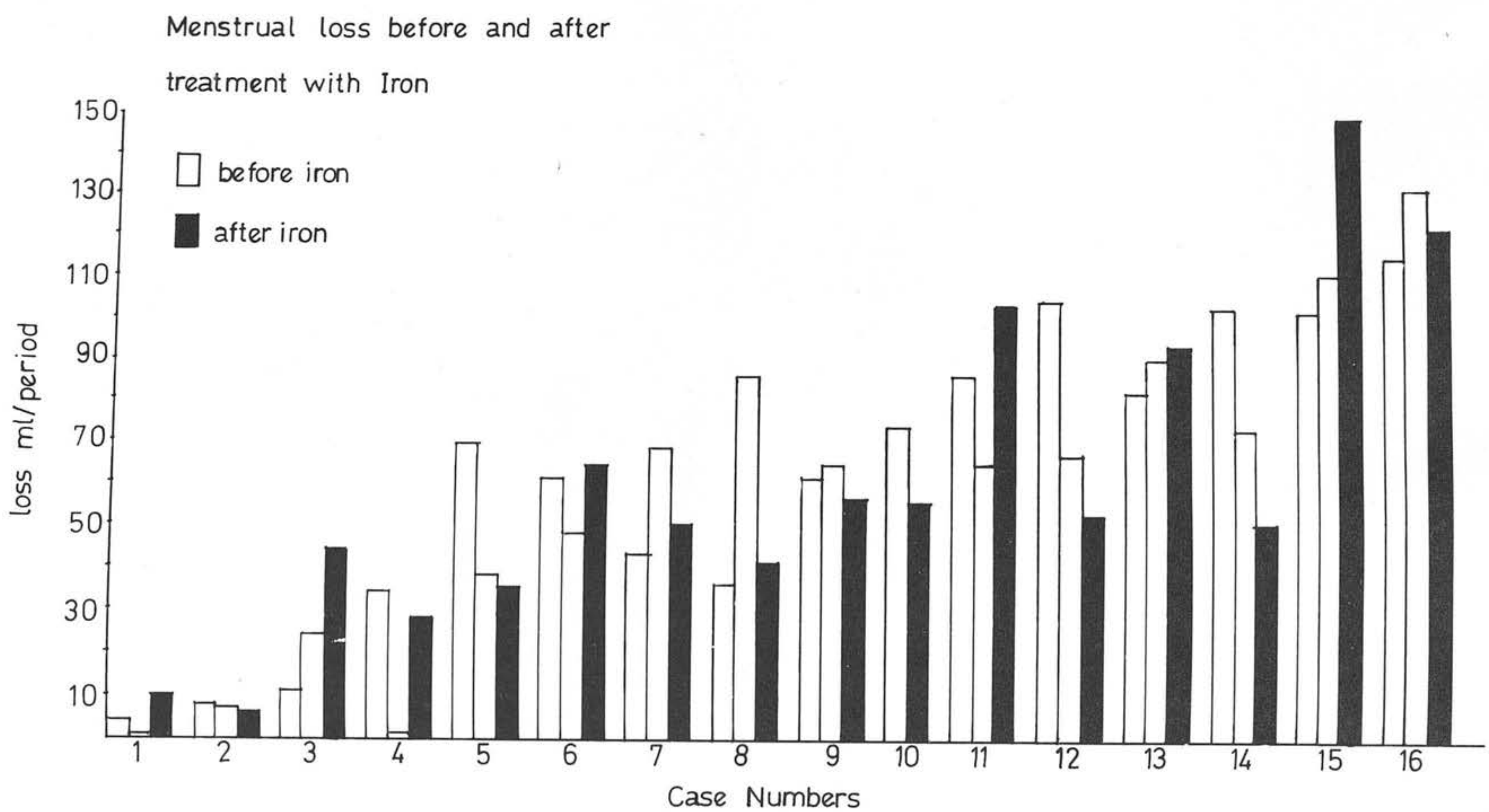

percentage of subjects on iron in blood loss groups
101
81
41
31
26
total numbers in each group
100
60
20
% subjects on iron
0-19
20-39
40-59
60-79
80+
blood loss groups (ml/period)

FIGURE 5

menstruating women who used neither an oral contraceptive nor an intra uterine device, 101 gave a history of having had some form of supplementary iron in the previous year. This usually had been prescribed by the general practitioner, but in a minority of instances it was self-prescribed and the diagnosis of anaemia by no means always preceded prescription. Figure 5 shows the proportion of women in each menstrual loss group who had had oral iron in the previous year. More women with heavy losses had taken iron, and conversely, fewer women with light losses had taken iron. However, it is not legitimate to infer from this that the administration of iron leads to heavier menstrual loss, as there may well have been some selection of women with heavy losses, for iron therapy. In order to clarify the situation, the first 20 women found to have a haemoglobin of less than 12 g per 100 ml, were asked to co-operate further by collecting menstrual blood lost at a third period after a six week course of iron (525 mg ferrous sulphate daily, equivalent to 105 mg iron). Four women defaulted, and 16 completed this part of the investigation. The results are presented in Table 9 and Figure 6. A check was kept on the consumption of iron by asking to see the bottle and counting the remaining tablets. In only one instance (Case 9), 12 tablets were left untaken. Case 2 was taking an oral contraceptive, and Case 10 had an intra uterine device. It is interesting to note that Cases 1, 2 and 15, who had initial serum iron values above 80 μg per cent, did not show any change in haemoglobin concentration after taking oral iron, and presumably



Menstrual loss before and after
treatment with Iron
before iron
after iron
loss ml/period
150
130
110
90
70
50
30
10
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
Case Numbers

FIGURE 6

TABLE 9

Menstrual losses and haematological indices before and after iron therapy

		BEFORE TREATMENT					AFTER TREATMENT			
Case No.	Age years	Hb gm %	PCV %	S.Iron µg %	Loss ml blood	Mean	Hb gm %	PCV %	S.Iron µg %	ml blood loss
1	19	11.1	36	88	4 0.5	2	11.0	35	82	10
2	30	11.9	38	132	8.1 7.0	7.5	11.3	37	108	6
*3	36	10.9	38	29	11 24	17.5	13.9	45	55	44
4	17	11.7	36	59	34 1	17.5	12.4	39	109	28
*5	18	10.9	37	18	69 38	53.5	13.1	40	60	35
6	31	11.3	38	73	61 48	54.5	12.0	39	101	64
*7	28	11.3	39	47	43 68	55.5	13.9	45	-	50
*8	19	11.4	36	33	36 85	60.5	14.2	45	76	41
9	38	11.7	38	76	61 64	62.5	12.6	39	208	56
10	25	10.8	36	-	- 73	73	11.7	37	77	55
11	22	11.1	33	32	84.5 64	74	12.2	-	49	102
*12	29	11.2	36	23	103 66	84.5	13.2	42	71	52
*13	42	9.2	33	30	81 89	85	13.5	42	107	92
*14	44	9.7	33	21	101 72	86.5	13.0	41	96	50
15	33	11.6	37	96	100 109	104.5	11.8	37	55	147
*16	38	10.9	36	38	113 130	121.5	13.5	42	51	120

*Iron deficiency anaemia

TABLE 10

Mean menstrual loss by parity
(excluding pill and coil)

Parity	No.	Mean loss ml	S.D.
0	58	26.3	19.6
1	46	34.3	31.6
2	88	38.3	30.1
3	45	46.9	48.6
4+	43	47.1	36.6
	280		

Trend with parity is significant ($p < 0.01$)

TABLE 11

Menstrual loss and parity
(all losses over 80 ml called 80 ml)

Parity	No.	Mean loss ml	S.D.	% with losses over 45 ml
0	58	26.2	19.4	17.3
1	46	32.1	24.7	30.4
2	88	35.5	22.9	32.9
3	45	40.0	27.7	40.0
4+	43	41.3	25.4	38.4

they were either in the "low normal" group in the distribution of haemoglobin values in the population, or their aneamia was not iron deficient in type. It was decided arbitrarily that if there was an improvement in haemoglobin concentration of 2 g. per 100 ml after a course of iron, and if the initial serum iron values were below 80 ug per cent, then an initial diagnosis of iron deficiency anaemia was reasonable. Five cases, 4, 6, 9, 10 and 11, did not show this substantial improvement in haemoglobin concentration, although the first three had a marked improvement in serum iron. Eight cases, in retrospect were probably truly iron deficient (Cases 3, 5, 7, 8, 12, 13, 14 and 16) and in these no consistent change in menstrual loss could be discerned in the third period. Iron therapy and correction of anaemia was not a source of variation of menstrual loss in this group of women.

Age and Parity

The influence of age and parity on menstrual loss has not been altogether clear in the past, as already discussed on p.17 of the introduction. In this study, increasing parity gave rise to a significantly increasing trend in mean menstrual loss per period ($p < 0.01$) (Table 10). In order to minimise the effect of a few very high menstrual losses on the mean values, Table 11 and subsequent Tables show the mean values recalculated with all menstrual losses over 80 ml, called 80 ml.

The population could be divided into three approximately equal menstrual loss groups. 122 women lost less than 20 ml per

TABLE 12

Mean menstrual loss (ml blood) by age and parity

Age	No.	Para 0 menstrual loss (ml)	No.	Para 1+2 menstrual loss (ml)	No.	Para 3+ menstrual loss (ml)	No.	Total menstrual loss (ml)
17-19	25	26.6	3	35.0	-	-	28	27.5
20-24	18	26.8	21	37.9	4	40.4	43	33.5
25-29	6	12.2	21	43.7	7	50.3	34	39.5
30-34	3	22.4	36	33.8	22	34.7	61	33.6
35-39	5	42.5	31	38.6	21	47.5	57	42.2
40-44	1	25.5	22	32.4	34	54.7	57	45.6
Total	58	26.3	134	36.9	88	47.0	280	37.9

period, 105 lost between 20 and 44 ml, and 101 lost 45 ml or over. In any group of women, therefore, about a third might be expected to fall into each of these three menstrual loss groups. In the following Tables the proportion of women having a heavy loss (over 45 ml per period) has been used to show if the group under consideration has a higher or lower loss than expected.

At first sight (final column Table 12) there does appear to be a correlation between age and menstrual loss, but this is a parity effect, and when age is considered within parity groups there is no consistent trend with age.

Height

Height and weight were measured in 300 women. Of the 280 menstruating women who were not using oral or intra uterine contraception, 254 were measured. Height ranged from 144 cm to 177 cm ($56\frac{1}{2}$-$69\frac{1}{2}$ inches) and weight from 38 kg to 100 kg (84-220 lb). This gave a rather low correlation between weight and height ($r = 0.31$) with a large number of women overweight. The correlation between weight and height of 4,995 women of all ages, was given as 0.34 in 1957 (Joint Clothing Council Ltd.). It was suggested that chronic anxiety over their husbands' dangerous jobs might lead miners' wives to overeat. The mean height of miners' wives was 161.5 cm (63.5 inches), and of the rest was 160.9 cm (63.3 inches), whereas the mean weight of miners' wives was 64.2 kg (141.2 lb) and of the rest was 60.6 kg (133.3 lb), giving a correlation coefficient of 0.19 in miners' wives and 0.36 in the rest.

TABLE 13

Mean menstrual blood loss (ml per period), by height (cm).
Excluding Pill and Coil.
All values over 80 ml called 80 ml.

Parity →		0			1		
		No.	Mean loss± S.D.	% with loss of 45+ ml	No.	Mean loss±S.D.	% with loss of 45+ ml
Height cm	<160	15	23.72±15.47	13.3	14	23.92±20.96	15.4
	160-	8	23.92±20.96	16.7	14	37.78±26.90	35.7
	165+	9	32.24±24.44	22.2	15	31.40±24.18	33.3

Parity →		2+			All parities		
Height cm	<160	64	32.24±24.44	26.6	93	29.62±22.87	22.6
	160-	63	40.58±25.19	41.2	95	37.59±25.51	35.8
	165+	42	43.63±25.35	45.2	66	38.46±24.89	39.4

Overall Blood loss x height $r = 0.19$

($p < 0.01$)

There was no correlation between weight and menstrual loss, but when the effect of height was considered, there was a significant increase in menstrual loss with increasing height ($p < 0.01$) (Table 13). Any parity-height interaction within the multiparous group (Table 13) would tend to work in the opposite direction as 60 per cent of the short women had 3 or more children, whereas only 40 per cent of the tall had 3 or more children.

A similar trend may be seen within parity groups, but the numbers are too small to reach significance in the nulliparous women and women with one child. However, in all parities, the proportion of women who fall into the heavy loss category of 45+ ml per period, increased with increasing height.

Baby weight

Birth weight and maternal height are related. (Thomson et al, 1968).Birth weights of infants were obtained from the women in the course of taking a medical history. These birth weights were subsequently checked against discharge letters from maternity hospitals, and district midwives' records where available. It was decided that the average baby weight for each women would be the most useful way of characterising her reproductive performance as far as fetal growth was concerned. Women with one baby were examined separately from the multiparous women, again and in Table 14, it can be seen that menstrual loss increased significantly with increasing birth weight in multiparous women ($p < 0.01$).

When the height effect is allowed for, the correlation of

TABLE 14

Mean menstrual loss (ml per period) by average baby weight (Kg).
Excluding Pill and Coil.
All values over 80 ml called 80 ml.

Parity		1			2+		
		No.	Mean loss±S.D.	% with loss of 45+ ml	No.	Mean loss±S.D.	% with loss of 45+ ml
Av.birth Wt.Kg	<3	13	28.43±26.57	15.4	31	30.33±23.03	25.8
	3-	16	Δ29.11±21.68	20.0	82	*34.83±23.07	28.0
	3.5+	17	Δ37.68±26.35	47.1	63	*46.11±25.99	50.8

Parity		All parities		
		No.	Mean loss±S.D.	% with loss of 45+ ml
Av.birth Wt.Kg	<3	44	29.77±23.83	25.0
	3-	98	33.90±22.84	24.5
	3.5+	80	44.33±26.14	50.0

Δ Not significant. * $p < 0.01$.

birth weight with menstrual loss in all parities remains significant ($r = .24$: $p < .01$). But when the effect of birth weight is eliminated, the correlation between height and menstrual loss just fails to achieve statistical significance ($r = .13$) at the 5 per cent level.

CHAPTER 4

Haematological Indices

Distribution of haemoglobin in the population and comparison with other studies

There have been four recent surveys of the haemoglobin of a total population or of a group selected at random from the population. The mean haemoglobin concentration, range and prevalence of anaemia are given, and compared with the results of this study in the tabulation below:-

Place	Numbers &	Age Years	Haemoglobin g/100 ml Mean	Range	% < 12 g/ 100 ml	Reference
Orkney	289 women	15-75+	13.4	7-17	11.4	Gourlay et at, 1970
S.Wales	920 women	20-64	13.3	7-18	10.4	Elwood et al, 1967
Belfast	213 women	21-75	Not reported	8.8-15	14.6	Elwood, 1964
Wensley-dale	230 women	15-75	12.7		20.8	Kilpatrick 1961
Broom-hill	348 women	17-45	13.1	7-16.6	13.2	Present survey

Effect of supplementary iron on haemoglobin

In the whole population, 125 women gave a history of having had some form of supplementary iron in the previous year, whereas 223 had had no iron. The haemoglobin distributions of these two groups are shown in the second and third columns of Table 15. The main difference to be seen in the group who had

TABLE 15

Comparison of distribution of haemoglobin in subjects taking iron and those not

G Hb/100 ml	Total	%	No Iron No.	No Iron %	Iron No.	Iron %
<8.5	1	.29	1	.45		
8.5	1	.29	1	.45		
9.0	3	.86	3	1.35		
9.5	4	1.15	3	1.35	1	.8
10.0	1	.29	1	.45		
10.5	7	2.01	6	2.69	1	.8
11.0	15	4.31	10	4.48	5	4.0
11.5	14	4.02	9	4.03	5	4.0
12.0	42	12.07	26	11.66	16	12.8
12.5	43	12.36	28	12.55	15	12.0
13.0	72	20.69	42	18.83	30	24.0
13.5	67	19.25	40	17.94	27	21.6
14.0	44	12.64	31	13.90	13	10.4
14.5	18	5.17	13	5.83	5	4.0
15.0	7	2.01	3	1.35	4	3.2
15.5	5	1.45	4	1.70	1	.8
16.0	2	.57	0		2	1.6
16.5	2	.57	2	.90		
Total	348	100.00	223	100.00	125	100.00
Mean Hb	13.12±1.24		13.07±1.33		13.21±1.07	
% with Hb <12 gm	13.2% (46)		15.2% (34)		9.6% (12)	

Haemoglobin distributions in subjects taking iron in the previous year and those not

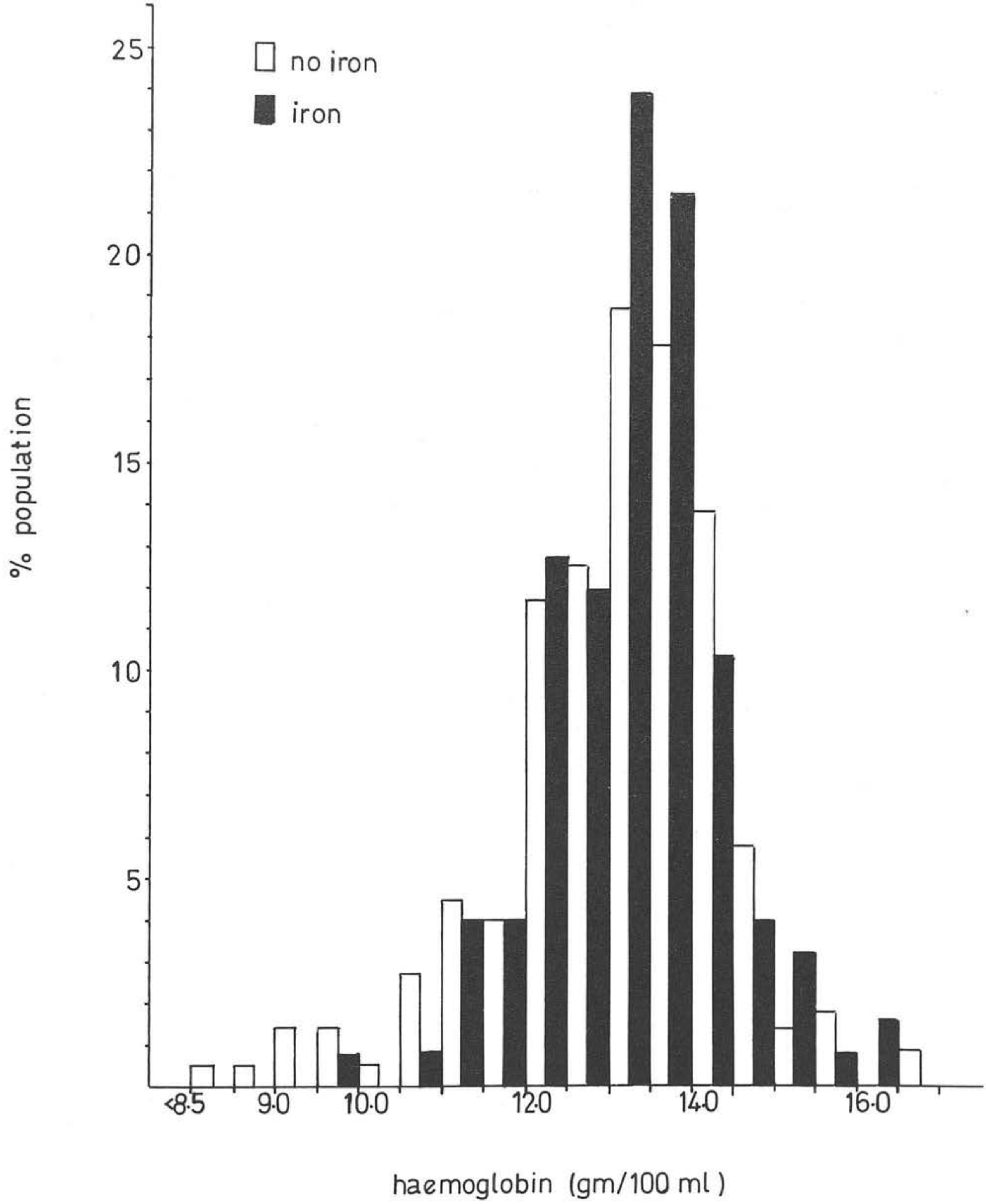


FIGURE 7

TABLE 16

(g/100ml) Mean haemoglobin concentration by menstrual loss in three groups of iron takers (Pill and Coil excluded)

Menstrual loss	Light -20 ml	Medium 20- ml	Heavy 45+ ml
Iron taken			
(A) Current and -3 months	12.96 (10)	12.80 (8)	13.04 (14)
(B) 4-6 months	13.86 (7)	13.43 (3)	13.65 (8)
(C) 7-12 months	13.61 (15)	13.55 (16)	12.34 (20)

iron is that the range of haemoglobin values is reduced, with only 9.6 per cent having a concentration lower than 12 g/100 ml, compared with the "no iron" group who had a low haemoglobin rate of 15.2 per cent. The modal value of the two groups is the same, there is no general shift to the right in the group who took iron (Figure 7). Generally, the iron had been prescribed by the family doctor and usually because of complaints of fatigue or menorrhagia, or because of pregnancy. Haemoglobin was not usually estimated before iron therapy began. In 19 instances the iron was self-prescribed in a proprietary tonic which contained small amounts only. The women were divided into three groups:

(A) Current or recent (1-3 months) therapeutic course of iron;

(B) an intermediate group who had had a therapeutic course of iron 4-6 months previously;

(C) a group who had therapeutic doses of iron over 6 months previously.

Group (C) included all those who had taken a self-prescribed iron containing tonic at any time during the previous year. Table 16 shows the mean haemoglobin concentrations for a given menstrual loss in these three groups of iron takers. Group (A) showed very similar haemoglobin concentrations in all three menstrual loss categories, as did group (B), but in all three menstrual loss categories, group (B) had a higher mean haemoglobin than group (A). In group (C), the haemoglobin concentrations show a falling trend

TABLE 17

Relationship of menstrual loss and haemoglobin concentration in 101 women taking iron and 179 taking no iron, in the previous year (Subjects on oral contraceptive and with coil and those with amenorrhoea shown separately)

Menstrual loss/ period	No Iron				Iron			
	No.	Mean Hb g/100 ml	% <12 g / 100 ml	Mean loss	No.	Mean Hb g/100 ml	% <12 g / 100 ml	Mean loss
Amenorrhoea	10	14.27		-	10	13.97		-
Pill	17	13.78		15.53 ml	6	13.55		9.00 ml
Coil	17	13.01		55.56 ml	8	12.71		61.75 ml

Menstrual loss/ period	No Iron				Iron			
	No.	Mean Hb * g/100 ml	% <12 g / 100 ml	Mean loss	No.	Mean Hb * g/100 ml	% <12 g / 100 ml	Mean loss
Light -20 ml	69	13.23	10.1 (7)	11.13 ml	32	13.46	6.2 (2)	13.18 ml
Medium 20- ml	65	13.19	7.7 (5)	29.94 ml	27	13.31	3.7 (1)	30.44 ml
Heavy 45- ml	45	12.13	42.4 (19)	69.52 ml	42	12.82	16.7 (7)	84.31 ml

*p < 0.01 (No Iron) *p < .05 (Iron)

with rising blood loss similar to the group who had taken no iron at all (Table 17).

Relationship of haemoglobin to menstrual loss

There is a significant trend of falling haemoglobin with increasing menstrual loss ($p < 0.01$ in women with no iron: and $p < 0.05$ in women who had taken iron)(Table 17). Here the population is divided into the same two groups of all iron takers and non-iron takers; and within these two groups the women with amenorrhoea and those using oral or intra uterine contraception are considered separately. The women who had no period during the time of the survey had a higher mean haemoglobin concentration than that of the women in the menstruating groups ($p < 0.02$ no iron: $p > .05$ not significant, on iron). The women using either the pill or the coil had had, in some instances, only been using them for a short time, but even so, the mean haemoglobin concentration of women using a coil was significantly lower than the mean haemoglobin concentration of women taking an oral contraceptive ($p < .05$ no iron: $p > .05$ not significant, on iron). Of the remaining 280 women those with heavy losses (over 45 ml per period) had much lower haemoglobin levels, and much higher "anaemia rates" (< 12 g/100 ml) than those with light or medium losses. This is highly significant in the "no iron" group ($p < 0.001$) and just fails to reach significance in the "iron" group. The anaemia rate in the heavy loss group, rises from 10.1 per cent to 42.4 per cent in the no iron group, and from 6.2 per cent to 16.7 per cent in the iron group.

TABLE 18

	PCV per cent			MCHC per cent			Serum Iron µg per cent			Iron binding capacity µg per cent		
	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.
NO IRON												
Amenorrhoea	7	43.14	3.18	7	33.16	1.19	10	97.20	21.52	10	352.90	38.73
Pill	17	42.38	2.33	17	32.49	1.29	17	123.76	41.35	17	424.88	81.39
Coil	16	40.66	2.55	16	31.86	1.12	16	74.69	32.65	16	392.31	78.77
Av. loss per period												
Light -20 ml	68	41.15	3.53	68	32.09	1.48	65	93.03	34.16	64	384.20	63.25
Medium 20- ml	63	40.87	2.59	63	32.18	1.22	64	89.90	32.75	63	370.75	59.92
Heavy 45+ ml	43	38.52	3.23	43	31.22	1.74	44	53.57	28.90	44	422.70	70.29
IRON												
Amenorrhoea	5	42.00	2.24	5	33.08	2.08	10	97.60	32.87	10	316.50	34.73
Pill	3	42.67	1.53	3	33.32	3.22	5	104.40	42.38	5	469.00	66.57
Coil	7	39.14	1.84	7	32.45	2.60	8	59.94	24.25	8	361.94	62.28
Av. loss per period												
Light -20 ml	28	41.27	2.63	28	32.42	1.33	31	85.00	34.59	30	341.80	40.29
Medium 20- ml	25	41.42	3.56	25	32.13	1.36	27	92.22	35.18	27	363.96	54.27
Heavy 45+ ml	39	40.09	2.47	39	31.85	1.19	41	84.12	43.00	41	387.02	57.67

Haematological and Serum Iron values in different menstrual loss groups

Pill, coil and amenorrhoea considered separately

Relationship of other haematological indices to menstrual loss

In Table 18 the other haematological indices are shown. If the no iron group is considered first, it can be seen that the trend of falling haemoglobin with heavy menstrual loss is repeated with the haematocrit ($p < 0.001$), mean corpuscular haemoglobin concentration ($p < 0.002$) and serum iron ($p < 0.001$). Iron binding capacity is significantly increased with heavy menstrual loss ($p < 0.001$). As has been previously reported (Burton, 1967; Mardell and Zilva, 1967) serum iron concentration was found to be significantly increased in women taking the pill compared with other menstruating women (p at least < 0.005). There was no significant difference between the mean serum iron concentration of women on the pill and women with amenorrhoea. The iron binding capacity was significantly raised in women taking the pill, when compared with the amenorrhoeic group and those losing less than 45 ml per period (p at least < 0.05). There was no significant difference when compared with women using the coil and those with heavy menstrual losses. The blood picture of the group of women who had taken iron in the previous year showed similar trends to the ones described above, but in some instances the changes are reduced and the picture more blurred.

Serum Iron

The mean serum iron concentration in this population was 79.82 μg per 100 ml (range 15-215 μg per 100 ml). There is a well known diurnal variation in serum iron concentrations which

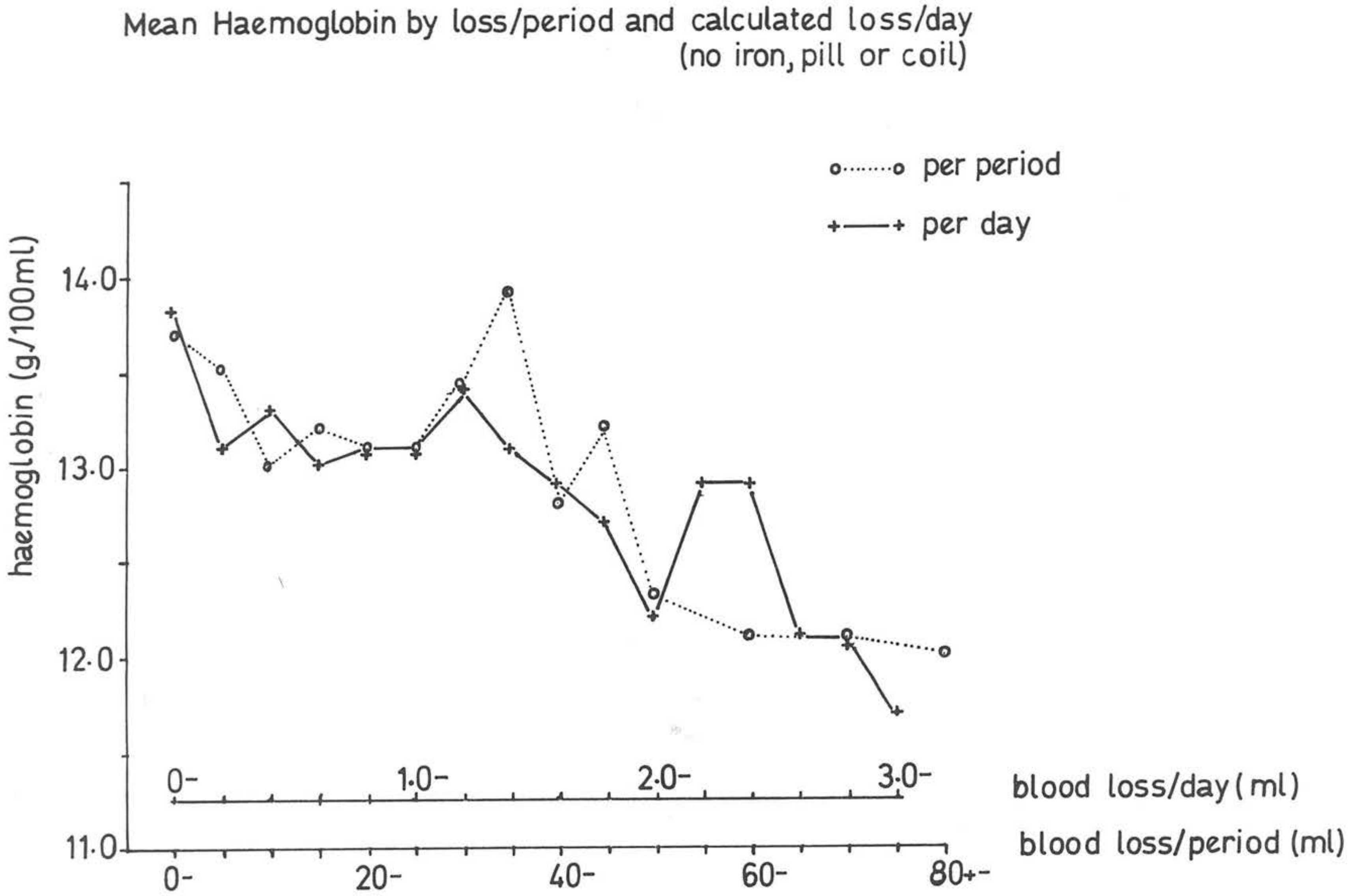

Mean Haemoglobin by loss/period and calculated loss/day
(no iron, pill or coil)
per period
per day
haemoglobin (g/100ml)
14·0
13·0
12·0
11·0
0
1·0
2·0
3·0
blood loss/day (ml)
0
20
40
60
80+
blood loss/period (ml)

FIGURE 8

may be as much as 50 per cent (Hamilton et al, 1950), and there may also be a day to day variation in the same individual (Ramsay, 1957). The blood specimens in this survey were all taken at about the same stage of the menstrual cycle, so that the cyclical variations described by Zilva and Patson (1966) should be eliminated, but the subjects were seen at any time during the day from 9 a.m. to 9 p.m. so that the diurnal fluctuations are involved. De Vries et al (1968) gave a mean serum iron concentration of 157 μg/100 ml (79-212 μg/100 ml) in 16 women below 50 years of age. Verloop and coworkers (1959) gave a mean of 120 μg/100 ml and a normal range of 68-172 μg/100 ml (mean ± 2 standard deviations) in 20 healthy young women. Both these studies give higher mean values than that found in the present survey.

Blood loss and cycle length

It was thought that variations in the length of the menstrual cycle might influence the total amount of blood lost over a length of time, and hence influence the haemoglobin concentration. A "blood loss per day" (loss per period ÷ cycle length in days) was therefore calculated for the group who had not taken iron and who used neither the pill nor the coil (179 women). The majority, 138, had a cycle of 28±4 days; 14 women had a shorter cycle, and 27 had a longer cycle. As Figure 8 shows, the fall in mean haemoglobin concentration appears to start with a loss equivalent to about 1.4 ml blood per day, which is about 40 ml per period in a 28 day cycle. Because most women have a regular

TABLE 19

Mean haemoglobin by age.
Women with amenorrhoea,
pill and coil excluded.

Age	No Iron			Iron		
	No.	Mean Hb± S.D. g/100 ml	% < 12 g	No.	Mean Hb±S.D. g/100ml	% < 12 g
17-19	18	12.98±1.35	27.8 (5)	10	12.90±0.69	10.0 (1)
20-24	26	13.24±0.91	7.7 (2)	17	12.87±0.87	5.9 (1)
25-29	21	13.07±1.23	19.0 (4)	13	13.35±0.81	7.7 (1)
30-34	41	12.89±0.99	12.2 (5)	20	12.95±1.38	15.0 (3)
35-39	40	13.11± 1.52	20.0 (8)	17	13.24±1.08	11.8 (2)
40-44	33	12.46±1.73	21.2 (7)	24	13.48±0.96	4.1 (1)
Total	179	12.94±1.34	17.3 (31)	101	13.16±1.03	8.9 (9)

cycle of about 28 to 30 days, measurements of blood, or iron loss, per period is sufficient in a large group of women; but when iron loss is being assessed in an individual, a calculation of "loss per day" may be more informative if she has an unusually short or long menstrual cycle.

Possible depletion effect of age and parity on haemoglobin

If menstruation and child bearing gradually deplete body iron stores, then one might expect to see a trend of falling haemoglobin concentration with age or parity. Table 19 shows mean haemoglobin concentration, and prevalence of low haemoglobin by age. In the "no iron" group, there is a suggestion of a falling haemoglobin with age, from 20-44 years. The trend of the incidence of anaemia is not so consistent. The 17-19 year old group have a comparatively low mean haemoglobin concentration and a high anaemia rate. One might speculate that the twin stresses of growth and menstruation are responsible, and that when growth is no longer an important factor, in the twenties, haemoglobin concentration improves. As age is related to increasing parity, and increasing parity has been shown to lead to heavier menstrual losses, the trend of falling haemoglobin with age is not surprising.

Possibly there is an element of depletion to be seen when the haemoglobin concentration is considered within given blood loss groups in different parities (Table 20). If the nulliparous group are ignored (they are largely the 17-19 year olds who have already been shown to have low haemoglobin concentrations, there

TABLE 20

Parity and mean haemoglobin in menstrual loss groups
(Patients on pill, with intra uterine device
and amenorrhoea excluded)

NO IRON								
Menstrual loss →	-20 ml		20- ml		45+ ml		Total	
Parity ↓	No.	Mean Hb g/100ml	No.	Mean Hb g/100ml	No.	Mean Hb g/100ml	No.	Mean Hb±S.D. g/100ml
0	19	13.31	18	13.16	3	11.73	40	13.12±1.02
1	13	13.58	6	13.45	8	12.33	27	13.18±1.31
2	17	13.38	21	13.16	17	12.20	55	12.94±1.41
3+	20	12.77	20	13.14	17	12.05	57	12.70±1.48
IRON								
Menstrual loss →	-20 ml		20- ml		45+ ml		Total	
Parity ↓	No.	Mean Hb g/100ml	No.	Mean Hb g/100ml	No.	Mean Hb g/100ml	No.	Mean Hb±S.D. g/100ml
0	7	13.14	4	13.15	7	12.70	18	12.86±0.84
1	7	13.63	7	12.87	10	12.99	24	13.19±1.22
2	10	13.59	10	13.72	9	12.72	29	13.32±1.13
3+	7	13.19	7	13.36	16	13.01	30	13.13±0.87

is a trend of falling haemoglobin for the same blood loss with increasing parity. The numbers in each cell and the changes in haemoglobin are too small to achieve statistical significance, but the consistency of the trend is perhaps suggestive of an iron depletion effect influencing haemoglobin concentration.

Other Blood Loss

Each woman was questioned about other sources of blood loss and, according to her answer, was placed in one of three groups; those who had no other blood loss; those who gave a history of other significant blood loss, such as blood donation, bleeding haemorrhoids, recent operation or dental clearance; and women who claimed that they bruised very easily, as it was thought that capillary fragility might conceivably be associated with heavy menstrual loss. Details of the numbers in each group are given in Table 21. Of the 65 women who gave a history of bruising very easily, 24.6 per cent had menstrual losses over 45 ml per period, about the expected proportion. There was no demonstrable association between bruising and the volume of menstrual loss (Table 22). When the 54 women who had other significant blood losses were considered within menstrual loss groups, there was no evidence that their mean haemoglobin concentration was materially influenced. (Table 23)

Aspirin

Aspirin taken regularly is associated with gastro-intestinal bleeding (Croft and Wood, 1967). In this survey the women were specifically questioned about their use of analgesics which

TABLE 21

Other blood loss
(Excluding Pill, coil and amenorrhoea)

	No Iron	Iron	Total
No other loss	112	49	161
Bruises easily	40	25	65
(Significant loss (6-12 months previously	20	22	42
(Significant loss up to (6 months previously	7	5	12
	179	101	280

TABLE 22

Other blood loss and proportion with heavy menstruation

	No.	% with menstrual loss > 45 ml/period	
No other loss	161	29.2	(47)
Bruises easily	65	24.6	(16)
(Significant loss 6-12 (months previously (Significant loss up to (6 months previously	54	44.4	(24)
	280		

TABLE 23

Other losses

54 women with a history of other blood loss.
Mean Hb in menstrual loss groups.

	Light -20 ml	Medium 20- ml	Heavy 45+ ml
NO IRON Mean Hb g/100 ml	(8) 13.15	(11) 13.40	(8) 12.51
IRON Mean Hb g/100 ml	(6) 13.54	(5) 12.06	(16) 12.89

contain aspirin. In the whole surveyed population, only 5 women admitted taking aspirin daily, 31 took aspirin once or twice a week, 177 once or twice a month, and 135 did not use an analgesic which contained aspirin. In neither the small "daily" nor "weekly" group was there any suggestion of unexpectedly low haemoglobin values individually or as a group. The 5 women who took aspirin daily had a mean haemoglobin concentration of 13.34 g/100 ml, and the 31 who took aspirin once or twice a week had a mean haemoglobin concentration of 13.01 g/100 ml.

CHAPTER 5

Fibrin Degradation Products

Fibrin degradation products (F.D.P.) are peptide fragments produced by the proteolytic action of plasmin on fibrin. These peptides are of varying molecular weight, with two large fractions D (molecular weight 80,000) and E (molecular weight 30,000) which have marked antigenic properties, a characteristic made use of in measuring circulating levels of F.D.P.

F.D.Ps. were measured by Dr. Tony Clarkson (see Appendix IV) in 331 of the 348 individuals studied; the mean concentration for the whole group was 12.09 μg/ml S.D.$\pm$ 6.54. The samples were assayed in three batches to reduce error. The range of F.D.P. values in this study gave a mean concentration that was about 50 per cent higher than that previously reported in normal individuals (Das et al, 1967), but the method used in this study is a haemagglutination inhibition immunoassay of tanned human red cells, as opposed to sheep's red cells, and has been found to be more sensitive (Das and Hoch, personal communication).

F.D.Ps. were not related to menstrual loss. There was no significant difference between the different menstrual groups, the women with amenorrhoea, or those with a coil. There was a higher mean concentration in women on the pill, but this is produced by two women who had very high values of 37.6 μg/ml and 45.1 μg/ml (Table 24).

Other Studies on fibrinolysis and menstruation

Hallberg et al (1966b) attempted to define the upper limit

TABLE 24

F.D.P. by menstrual loss

	No.	Mean F.D.P. µg/100 ml	S.D.
Amenorrhoea	18	11.51	4.12
Pill	23	15.78	9.92
Coil	21	10.21	5.88
Light -20 ml	93	11.45	6.17
Medium 20- ml	90	12.46	6.71
Heavy 45+ ml	86	12.21	6.07
45- ml	61	11.87	5.90
80+ ml	25	12.83	6.33
Total	331	12.09	6.54

of normal menstrual blood loss as above the 95th percentile value in the women who had normal haematology and who thought of their menses as normal. This value, 76.4 ml blood, very nearly coincided with the amount of menstrual blood loss (80 ml) that produced anaemia in significant numbers of his whole study population. This blood loss was much heavier than the 45+ ml loss that was associated with a significant rise in the anaemia rate in this survey. But Rybo, one of Hallberg's coauthors, found that in subjects with a measured menstrual loss of more than 80 ml per period, there was an increase in endometrial plasminogen activators (Rybo, 1966); local fibrinolysis therefore may interfere with normal haemostatic mechanisms (Astrup, 1956) to produce a pathologically heavy menstrual loss. Nilsson and Bjorkman (1965) found that patients complaining of menorrhagia acknowledged a symptomatic improvement after treatment with epsilon amino caproic acid - an inhibitor of plasminogen activation - and that there was an accompanying increase in haemoglobin concentration, indirect evidence of a lighter menstrual loss. In none of their patients was there any evidence of increased fibrinolytic activity or coagulation failure in the systemic circulation.

Since 1966 it has been possible to measure the concentration of circulating F.D.Ps., widely regarded as a measure of fibrinolytic activity in vivo (Merskey et al, 1966; Das et al, 1967). In 1970 Basu found that women who complained of menorrhagia had a significantly higher mean concentration of circulating F.D.Ps. (24 μg/ml) than women attending a gynaecological clinic for other reason, or than a group of healthy controls (9.9 μg/ml).

Discussion This finding of Basu's was rather surprising because in certain renal diseases local fibrinolysis is known to occur and there may be very high F.D.P. concentrations in the urine while there is no evidence of raised F.D.P. in the systemic circulation (Coleman et al, 1969; Clarkson, personal communication). Basu also found that the serum F.D.P. levels fluctuated throughout the menstrual cycle, and were highest during and immediately after menstruation. In this current survey, the blood samples were taken shortly after menstruation, and any abnormality associated with high blood loss should have been noticed. There are several reasons why this discrepancy between Basu's results and these might have arisen. Possibly the lack of correlation between menstrual loss and F.D.P. in this study may imply that a "normal" group of uncomplaining menstruating women is different from the women who complain of menorrhagia even though the volume of blood loss may be the same. The women who complain may have had a sudden change in menstruation, with pathological fibrinolysis inducing a sudden increase in blood loss. And a population whose menses had not changed recently and therefore who were uncomplaining, would not show evidence of fibrinolysis. However, the most probable explanation for the differences between the present findings and those of Basu, lies in the immunoassay technique itself. The immunoassay measures both Fragment D and Fragment E, and the result is a sum of the two. Different batches of antisera prepared in rabbits against the same human fibrinogen may contain different amounts of anti-D and anti-E, so it is hardly surprising that different studies may give different results (Nussenzweig et al. 1961). The situation may be clarified when Fragments D and E can be measured separately.

TABLE 25

Case No.	Age Years	Blood loss ml	Cycle days	Day of Biopsy	Pathology Report
66	42	5.2	21-23	18	Mild glandular hyperplasia
341	36	9.0	26	15	Proliferative phase
308	39	15.5	33	27	Proliferative phase
58	31	30.5	35	28	Proliferative phase
54	33	55.0	30	19	Proliferative phase
136	40	110.5	25	24	Glandular hyperplasia
211	23	130.5	27	20	Proliferative phase
26	42	132.0	36	30	Mild glandular hyperplasia
251	41	30.5*	28	18	Proliferative phase
56	37	15.0*	26	19	Proliferative phase
95	34	2.95Δ	28	23	Secretory phase
44	30	7.55Δ	28	22	Probably decidua

* Coil

Δ Pill

CHAPTER 6

Endometrial Biopsy

During the gynaecological examination of the married women, all the parous women were asked if endometrial biopsy might be performed. Seven women refused, and in the remainder, the procedure was abandoned if pain or discomfort was felt while attempting to pass the uterine sound through the cervical canal. Biopsy was carried out in 82 women. In 37, the material was too scanty to interpret on microscopy, and in 45 sufficient endometrial tissue was obtained. The biopsies were carried out in the second half of the menstrual cycle, and 33 (73.3 per cent) specimens showed the expected secretory phase endometrium. But in 12 women the glands and stroma showed an unexpected pattern; these are listed in Table 25. Three of the women in their forties (Cases 26, 136 and 66) showed a glandular hyperplasia, that, in two women, was associated with a very heavy loss of over 100 ml in the previous two periods, and a loss of 5 ml in the previous periods of Case 66. All three had had a history of regular cycles. Seven other women, including two with an intra uterine device, had proliferative phase endometrium in the second half of the cycle, implying that that cycle at least was anovular. Cases 95 and 44, both on an oral contraceptive, are included for interest. One showed definite signs of ovulation, and the other showed decidual changes which, in the opinion of the pathologist (Dr. R. Schade) were not the pseudo-decidual reactions associated with the pill. This second patient was troubled with intermittent bleeding in the cycle following biopsy - a complaint she had not had in the previous three years on the pill. Both of these women were intelligent and appeared to be quite certain that they had not forgotten to take the pill.

It may be unwise to infer that the period following biopsy would have a similar blood loss or even that the cycle length would be the same as the previous two measured periods, and to lay too much stress on the fact that anovular cycles and glandular hyperplasia may not necessarily be associated with heavy menstrual loss. How often apparently normal menstrual cycles are anovular is unknown. Sturgis (1966) remarks that "transient or sometimes prolonged episodes of anovulatory bleeding ..... frequently occur in otherwise normal or healthy women". But he does not define "frequently" or discuss how this was discovered. In this series 10 out of 45 women (22.2 per cent) showed an anovular pattern. Unfortunately, one can do no more than report this fact, as the evidence does not allow one to suggest that one period in five may be anovular.

CHAPTER 7

Gynaecology in the Community

In the course of the survey a picture of minor gynaecological problems in the community became gradually apparent. Though not directly relevant to the main theme of the thesis, the material is of socio-medical interest, particularly as no other community survey of gynaecological signs and symptoms seems to have been published. The following chapter gives some information on the problems encountered.

Interview

All the women participating in the survey were questioned about gynaecological symptoms when the history was taken at the second interview (Appendix I). These questions were put to them directly, and they were not asked to volunteer complaints as in a conventional medical history. Most of the women, if asked whether they had any complaints would have replied negatively. The symptoms elicited, therefore, may well have been less severe or annoying than those experienced by women presenting themselves at a clinic. However, they do combine to give a picture of discomfort or inconvenience that seems to be accepted by large numbers of women.

Examination

Of the 348 women in the survey, the nulliparous unmarried women were not asked to come to the surgery for examination, nor were any of the women who had previously undergone hysterectomy. A few women were unable to come, because they had left the

TABLE 26

Numbers Examined

Subjects examined	231	
Subjects refusing examination	51	282
Not asked:		
Single and nulliparous	49	
Hysterectomy	6	
Unable to come	11	
TOTAL	348	

TABLE 27

51 subjects refusing examination by age and parity

Parity -> Age - years ↓	0	1	2	3	4+	Total	%	Total at risk
17-19	-	2	-	-	-	2	3.9	2
20-24	-	4	1	2	1	8	15.7	32
25-29	-	4	3	3	1	11	21.6	47
30-34	-	2	1	2	2	7	13.7	71
35-39	-	1	2	1	4	8	15.7	63
40-44	-	2	1	6	6	15	29.4	67
Total	-	15	8	14	14	51	100.0	
%		29.4	15.7	27.4	27.4			
Total at risk	12	53	96	61	60			282

TABLE 28

231 subjects examined by age and parity

Parity -> Age - years ↓	0	1	2	3	4+	Total	%	Total at risk
17-19	-	-	-	-	-	-	-	2
20-24	1	13	7	3	-	24	10.4	32
25-29	4	2	17	9	4	36	15.6	47
30-34	2	9	28	14	11	64	27.7	71
35-39	4	8	20	9	14	55	23.8	63
40-44	1	6	16	12	17	52	22.5	67
Total	12	38	88	47	46	231		
%	5.2	16.5	38.1	20.3	19.9	100.0		
Total at risk	12	53	96	61	60			282

TABLE 29

Symptoms in 49 single nulliparous women

	No.	%
Dysmenorrhoea	29	59
Discharge with/without pruritus	5	10
Urinary (History of recurrent UTI)	3	6
Amenorrhoea/oligomenorrhoea	4	8
No symptoms	15	30

TABLE 30

Women with multiple symptoms by age and parity

Parity → Age - years ↓	0	1	2	3	4+	Total with multiple symptoms	% of survey group	Total in survey group
17-19	3	1	-	-	-	4	14.3%	28
20-24	3	7	3	2	1	16	30.2%	53
25-29	2	1	4	9	2	18	46.1%	52
30-34	1	4	8	6	6	25	33.8%	74
35-39	1	2	12	3	7	25	36.8%	68
40-44	-	1	5	7	9	22	30.1%	73
Total	10	16	32	27	25	110		
% of survey group	16.4%	28.5%	30.2%	42.9%	40.3%	31.6%		
Total in survey group	61	56	106	63	62			348

district, or were in hospital, or were newly pregnant (Table 26).

Table 27 shows the distribution by age and parity of the 51 women (17.7 per cent of the 282) asked to come for examination, but refusing. Table 28 shows a similar distribution of the women who were examined.

Symptoms

1. The single, nulliparous women. In these 49 women, who just gave a history, and on whom no examination was carried out, the commonest complaint was of dysmenorrhoea. Very often this was no more than mild lower abdominal pain readily amenable to analgesics. Some girls described mood changes and headaches associated with dysmenorrhoea. In only one girl did the pain appear to be acute enough to cause regular days off work. None of the girls was asked about sexual experience as the interviews were often conducted in the presence of other members of the family, so no inferences can be drawn about discharge and pruritus and recurrent urinary tract infections. (Table 29) 15 girls had no symptoms and only 5 had two symptoms.

2. Women with multiple complaints. It was decided to examine the number of complaints of each woman initially, to see if one could characterise the types of women with multiple symptoms. Table 30 shows that increasing parity is associated with an increase in the percentage of women with multiple complaints. Only 10 per cent of the unmarried girls had two symptoms and this rose to 16.4 per cent after marriage. 30 per cent of the women with one or two children had two or more

symptoms and with three or more children, 40 per cent had multiple symptoms. The problems seemed to be particularly acute for the younger highly parous woman.

When these women were considered by husbands' employment (Table 31) only the numbers of miners' wives and the skilled manual workers' wives were large enough to allow reasonable comment. 44 per cent of all miners' wives had multiple symptoms compared with only 33 per cent of the skilled manual workers' wives. One may, perhaps, infer that anxiety and stress have a part to play in the production of gynaecological symptoms.

3. Types of symptoms. The types of symptoms were grouped into seven categories:-

Dysmenorrhoea

Menstrual

Discharge with or without pruritus

Vaginal laxity: stress incontinence; feeling of something coming down

Urinary: urge incontinence and recurrent urinary tract infection (UTI)

Non-menstrual bleeding: intermenstrual and post coital bleeding

Sexual: dyspareunia and loss of libido

Dysmenorrhoea

A woman was counted as having some dysmenorrhoea if she had to take some analgesic for perimenstrual discomfort. This is not an altogether satisfactory criterion as it probably depends

TABLE 31

Women with multiple symptoms by husband's employment*

Husband's employment	No.	% of survey group	Total married women in survey
Professional and Managerial	6	37.5	16
Other White Collar	7	24.1	29
Skilled Manual	33	33.0	101
Miners	44	44.0	101
Manual unskilled	10	27.8	36
Unemployed	4	57.1	7

*6 women unmarried

TABLE 32

Women complaining of dysmenorrhoea by parity

Parity	No.	% of survey group	Total in survey
0	33	54.1	61
1	20	35.9	56
2	38	35.8	106
3	25	39.7	63
4+	20	32.2	62
Total	136	39.1	348

more on the woman's tolerance level rather than on the degree of pain, but it is some measure of the degree of discomfort which cannot be assessed in any objective way.

There were only 10 women in all who appeared to have disabling pain that caused loss of work. 136 out of 348 (39.1 per cent) had some degree of dysmenorrhoea. Over 50 per cent of the nulliparous complained of this symptom, and in all other parity groups the numbers fell to about 35 per cent (Table 32). This might be a true improvement, as clinical impressions have suggested in the past, or perhaps a relatively minor discomfort may become submerged by the other symptoms that seem to increase after childbearing.

Menstruation

28 women complained of irregularity of menstruation, of these 7 did not menstruate at all during the survey and were included in the amenorrhoea category. 9 only menstruated once, and in 12 women two periods were measured during the survey. By age, 10.7 per cent of the youngest age group had irregular periods, and thereafter periods seemed to become more regular until the forties when 11 per cent of that age group had irregular menstruation (Table 33).

Only 3 women in the whole group persistently complained of menorrhagia. One had complained to her general practitioner and was waiting to see a consultant gynaecologist, she was aged 40 and losing 280 ml during a prolonged period. The second, aged 39, was losing 170 ml per period and was on the point of consulting her family doctor, and the third, aged 44, was losing 86 ml

TABLE 33

Women complaining of irregular periods by age

Age Years	No.	% of survey group	Total in survey
17-19	3	10.7	28
20-24	5	9.4	53
25-29	5	9.4	52
30-34	4	5.4	74
35-39	3	4.4	68
40-44	8	11.0	73
Total	28	8.0	348

TABLE 34

Symptoms of vaginal laxity by parity

Parity	No.	% of survey group	Total in survey
0	-	-	61
1	2	3.6	56
2	14	13.2	106
3	14	22.2	63
4+	15	24.2	62
Total	45	12.9	348

per period and had no intention of seeking medical help. Each of the three graphically described clotting and flooding, a complaint which was not given by any of the women who thought that their periods were heavy.

Discharge

101 women complained of discharge with or without pruritus (29 per cent); 30 women were not examined. In 27 there was no detectable pelvic abnormality, and in the remaining 44 there was some minor abnormality that might reasonably be associated with an excess discharge.

Vaginal laxity

45 women complained of stress incontinence and (or) the feeling of "something coming down". This was notably associated with parity (Table 34). 33 women were examined, and only 11 had obvious vaginal laxity that could clinically be associated with the symptoms.

Urinary

11 women (3 per cent) had urge incontinence and 17 (5 per cent) had a history of recurrent urinary tract infection (defined as two or more bacteriologically proven episodes with symptoms). The 17 women were equally distributed in all parity groups (including nulliparous). Kass (1962) in his study of adult women in Jamaica quotes an incidence of asymptomatic bacteruria of 4 per cent in a non-pregnant population.

Non-menstrual bleeding

35 women complained of intermenstrual and (or) post coital

TABLE 35

Symptoms of dyspareunia and loss of libido, by parity

Parity	No.	% of survey group	Total married women in survey
0	2		12
1+2	13	8.4	162
3+4	16	13.6	125
Total	31	10.4	299

TABLE 36

Women examined, by parity - showing those with clinical gynaecological signs

Parity	Total No. examined	No. with signs	
0	12	3	(25%)
1	38	13	(34.1%)
2	89	38	(42.7%)
3	46	23	(50.0%)
4+	46	29	(63.0%)
	231	106	(45.9%)

bleeding. 8 refused examination, and in the remaining 27, 14 had an erosion, cervical polyp or infected discharge that might be held responsible. Just over half of the remaining 13 with no obvious abnormality used either an oral contraceptive or intra uterine device.

Sexually related complaints

31 women complained of dyspareunia and (or) loss of libido. 21 of these women were examined and in 4 there was some physical abnormality which might be implicated. 2 women had pelvic adhesions following previous surgery, one had a retroverted uterus and one nulliparous girl had vaginismus. These symptoms may in part be due to fear of further pregnancy because it increased with increasing parity (Table 35). On the other hand, it is possible that repeated pregnancies leave a gaping introitus that may be drier, and the problem may be one of failure of lubrication.

Signs

231 women were examined of whom 106 (46 per cent) had some abnormality. Most of these were of a relatively trivial nature. The incidence of signs appeared to be associated with increasing parity (Table 36).

About a quarter of these women had no symptoms at all and of the rest, a further quarter had signs and symptoms that did not match. Two women had malignant cells in the cervical smear and subsequently proceeded to cone biopsy. The types of clinical

TABLE 37

Women with vaginal laxity, by parity and previous average baby weight

Av. Baby Wt. → / Parity ↓	-3,000 g	3,000 g -	3,500 g +	Total
1+2	1	2	4	7
3+4	0	7	9	15
Total	1	9	13	23

abnormality are described under five headings:-

Cervical conditions: erosion, polyp

Vaginal laxity: cystocoele, urethrocoele, rectocoele, enterocoele

Fibroids

Cystic ovary

Miscellaneous

Cervical

By far the commonest minor abnormality was a cervical erosion. An erosion or polyp was seen in 72 cases (31.1 per cent). Only half of these were associated with complaints of discharge, or intermenstrual or post coital bleeding. One of the women who had malignant cells in the cervical smear had an erosion, but the other had a normal looking cervix.

Vaginal laxity

There were 23 women who had some clinically obvious vaginal laxity. This was definitely parity-associated (Table 37) and the average birth weight of the previous children also appeared to influence this sign. 15 women had laxity of the anterior vaginal wall, and in 11 this was associated with symptoms of stress incontinence (in the section on symptoms, it was noted that 45 women in all complained of some degree of stress incontinence).

Fibroids

Only 5 women had palpable fibroids. The youngest was 34 and all had three or more children. 4 had a menstrual loss over

45 ml blood per period (heavy loss) (range 46-83 ml per period) and the other woman had a menstrual loss of 32 ml per period.

Cystic Ovaries

Only 4 women were found to have a unilateral cystic ovary and none was larger in size than a golf ball. Three were under 25 years and one was 38.

Miscellaneous

There were 23 miscellaneous minor abnormalities which included retroverted uteri, purulent discharges, transverse lacerations of the cervix, and three women with previous pelvic surgery who had adhesions tethered round an appendage.

Contraception

In comparing the signs and symptoms of the two small groups of women using one of the modern methods of contraception (Table 38), it is surprising that six women (25 per cent) using an oral contraceptive still complained of dysmenorrhoea. A third of the women with an intra uterine device had menstrual discomfort, a clinically recognised complication. If symptomatology can be taken as an index of satisfaction with the contraceptive method, about the same number in each group had no complaints. The survey was undertaken at a time when there was a lot of newspaper publicity about the hazards of oral contraception and I had the impression that some of the women were openly worried about the possible risks they were running. The other interesting point arising from comparison of the two groups is the raised incidence

TABLE 38

Signs and symptoms in women using the oral contraceptive or an intra uterine device

Oral contraceptive		Intra uterine device
24 women - 7 had no complaints		26 women - 6 had no complaints
<u>Symptoms</u>		
Dysmenorrhoea	6	9
Discharge	10	9
Vaginal laxity	1	2
Urinary	2	3
Non-menstrual bleeding	4	8
Sexual	2	2
5 refused examination		3 refused examination
19 women		23 women
<u>Signs</u>		
Cervical	7	8
Vaginal laxity	-	1
Fibroid	-	-
Cystic Ovary	1	-
Miscellaneous	4	2
No signs - 7 women		No signs - 12 women

of intermenstrual or post coital bleeding. There was an overall incidence of intermenstrual or post coital bleeding of 11.7 per cent in the married population, in the group on an oral contraceptive there were 4 women (17.7 per cent), about the same incidence, but with the intra uterine device 8 (30.8 per cent) had intermenstrual or post coital bleeding (these differences are not statistically significant because of small numbers). Apart from this one symptom, the other signs and symptoms were remarkably similar in both groups.

Conclusion

It proved virtually impossible to relate the signs and symptoms in any meaningful way. It was quite striking that frequently a long series of complaints did not appear to be related to any organic abnormality and the impression that gynaecology and female psychology are closely linked, was reinforced.

	Signs	No Signs
Symptoms	82	87
No Symptoms	24	38

Similar numbers, in the group who were examined, had symptoms whether they had a clinical abnormality or not, and also the uncomplaining group (far fewer in number) were distributed between those who had an abnormality or not.

In this chapter, I have accepted the symptoms at their face value and have tried to draw a picture of endemic pathology in the community which is often totally unrelated to chronic discomfort or inconvenience that women undergo - or think they undergo - with varying degrees of fortitude. The trauma of childbirth certainly seems to be implicated in the aetiology of the minor abnormalities found.

CHAPTER 8

Discussion

Sources of Variation of Menstrual Blood Loss

Menstrual blood loss has been shown to increase with increasing parity. Menstrual loss may be, in part at least, controlled by uterine size, as the weight of uteri, obtained from hysterectomy specimens increases with increasing parity (Woessner and Brewer, 1963). It is not clear whether this increase in weight is a result of an increased thickness of the uterine wall alone, or there is an accompanying enlargement of the cavity, giving a larger endometrial area from which to bleed. This may be the reason for the suggestive trend of increasing menstrual loss with increasing height, taller people presumably having larger uteri than smaller people. Woessner and Brewer also found that increasing parity altered the proportions of collagen and elastin in the connective tissue. After six pregnancies the amount of collagen in the uterus had doubled, but the elastin had increased five-fold. Elastin is deposited around blood vessels and they implied that increasing amounts of elastin were deposited around the same number of blood vessels in the myometrium. There was no suggestion that an increase in vascularity was represented by the elevated levels of elastin. But Jansson (1969) found that the blood flow, shown by the clearance rate of ^{133}Xenon, was greater in a parous uterus than in a nulliparous uterus, and the theory that uterine vascularity must influence menstrual loss seems plausible. This would perhaps help to explain the strange observation that the birth weight of previous infants influenced subsequent maternal menstruation. It seems a little naive to postulate that size is the connecting factor in this case - a uterus that has produced a heavy baby remains larger than a uterus that carried a small baby. But the theory of uterine vascularity seems more reasonable, a good blood flow is the common factor underlying both babies of heavy birth weight and relatively heavy menstruation. A large prospective study of blood loss and the birth weight of subsequent children might clarify the situation.

The discovery of these factors which influence menstrual flow does not explain the range of menstrual loss which remains large in every category that was considered. The attempts to reduce the range by discovering an "end point" of normal menstrual loss failed. The concentration of serum fibrin degradation products gave no indication that there might be a pathological degree of fibrinolysis associated with very heavy menstrual loss. The endometrial biopsies succeeded in too small a group to draw any conclusions about anovular menstruation or glandular hyperplasia producing heavy blood loss. And the pelvic examinations revealed no more than 5 women who had fibroids, an acknowledged cause of menorrhagia, and even they had relatively unremarkable blood losses.

Iron Deficiency

On the basis of the evidence presented in this survey, it does appear that a menstrual blood loss of 45 ml or over produces a fall in all the haematological indices measured. This is equivalent to about 0.7 mg iron a day, which is even lower than Hallberg's finding of about 1.5 mg iron a day (80 ml per period). This implies that women have startlingly low iron resources. Most premenopausal women will eat a diet which contains between 11.7 mg and 13.3 mg of iron a day (National Food Survey Committee 1968) and it is usually calculated that 10 per cent of dietary iron is absorbed. One can therefore construct a type of balance sheet:-

Iron losses per day		Iron intake per day	
Menstruation	0.7 mg	Absorbed	1.17-1.33 mg
Loss in sweat, urine and faeces (approx.)	0.5-1.0 mg		
Total	1.2-1.7 mg		

And deduce from this that women's iron metabolism is very nearly overstretched. The fact that haemoglobin does not fall progressively from the menarche to the menopause may be because most women do not have menstrual losses of over 45 ml, and that, perhaps, those that had, in this survey, had not always had such large losses. Supplementary iron in the previous year certainly improved the haemoglobin concentration, and it was rather surprising that about 30 per cent of the surveyed population had had such iron. If this proportion is representative of all women, and not just those in one general practice, it perhaps is one reason why iron balance arithmetic is sometimes contradictory in large groups of women.

This work confirms the impression of Hallberg et al (1966b) that many women may be iron depleted, and that this is reflected in small changes in haemoglobin concentration. But our finding that the situation may be even more finely balanced than Hallberg suggested (and instead of menstrual losses of 80 ml or more producing depletion, the critical blood loss that a woman can tolerate may be as low as 45 ml per month) seems, in biological terms, to fly in the face of commonsense. It is possible that the role of plasma volume deserves closer examination. Oestrogens appear to increase plasma volume but not red cell mass (Cruickshank, 1970). No one has shown whether there is an association between high menstrual blood loss in normal women, and a slightly raised oestrogen level, which might lead to a fall in haemoglobin concentration through a dilution effect rather than a true reduction in red cell mass. The problem could be investigated in another way by measuring the menstrual losses over 6-12 months in a group of women newly fitted with an intra uterine device - increasing blood loss without, presumably, influencing hormone excretion - and watching for serial changes in haemoglobin concentration in response to heavier periods.

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APPENDIX I

HISTORY AND EXAMINATION

Date:	Name:		Complete Incomplete Refusal		Preg. Left Other
Address:					
			Birth No:	Serial No:	
Employment:	SC	SEC	Age:	Para:	
Husband's Employment:		SC	SEC		

Past Medical History:

Habitual Medication:

Blood Transfusion	No	Yes	When	Amount, Reason	
Blood Donation	No	Yes	Last Date	How Often	
Nose Bleeds	No	Yes			
Haemorrhoids	No	Yes	Do they bleed	No	Yes
Indigestion	No	Yes			
Haematemesis	No	Yes	When		
Melaena	No	Yes	When		
Other Bleeding	No	Yes			

(Haemorrhagic Diathesis, Dental Extraction)

Operation (Nature, dates)

Accidents (Nature, dates)

Medication in Past Year

Taken? No Yes

Analgesics? No Yes Type

Daily ½ week ½ month

Less Often

Name: No:

<u>Contraception</u>

Loop No Yes When inserted

Pill No Yes Type Dates

<u>Menarche</u> (Accurate Approx:)

<u>Periods regular</u> No Yes

<u>Always thus?</u> No Yes

Change? When?

<u>Cycle</u> Minimum: Maximum:

<u>Days bleeding</u> Minimum: Maximum:

Heavier Lighter Same

<u>Pattern of Flow</u>

<u>Patient's Assessment</u> Heavy Medium Scanty

<u>No. Packets used</u>

<u>Intermenstrual Bleeding</u> No Yes When

<u>Postcoital Bleeding</u> No Yes When

<u>Dysmenorrhoea</u> No Yes

<u>Dyspareunia</u> No Yes

<u>Discharge</u> No Yes

Pruritus No Yes

<u>Mict. Symptoms</u> No Yes

Details

<u>P.O.H.</u>

Year	Place	Pregnancy	Gest.	Del.	Sex	B.Wt.

Name: No:

Date:

Examination

Urine	Alb.	Sugar:	
Height		Weight	
B.P.			
V.E.	Vulva Vagina Cervix		
	Uterus		
	Adnexae		
Smear Taken	No	Yes	Result:
Endometrial Biopsy	(1)	No	Yes
	(2)	No	Yes

Lab. Reports

Date of Spec.	Hb.	PCV	S.Fe	IBC	%Sat.	Blood loss	Fe loss
1)							
2)							

Notes on Collections

F.D.P.

Tissue Activator

Classification of Employment

APPENDIX II

A. HUSBANDS

1. Professional and Managerial (PM)

Civil Engineer
Factory Owner
Farmer
Manager - Car Hire
- Colliery
- Co-op
- Plant
Mental Nurse (R.M.N.)
Shop Owner
Teacher
Teacher in Training

2. Other White Collar (OWC)

Betting Shop Owner
Cashier
Clerk
Club Steward
Inspector - Electrical
- Insurance
Manager - Bar
- Store
Money Collector
N.C.O. Forces
Police Constable
- Sergeant
Security Officer
Surveyor

3. Miners (M)

Underground
Coal Face
Coal Face Filler
Miner - Open Cast
- Temp. unemployed
- Surface
Driller
Pumper
Weighman

4. <u>Skilled Manual (SM)</u>

Aerial Rigger
Air Defence Operator
Army Bandsman
Blacksmith
Bricklayer
Brick setter
Builder's foreman
Building worker
 (father's business)
Butcher
Coal Merchant
Cook
Driver - Ambulance
 - Bus, Coach
 - Dumper, Excavator
 - Lorry
 - N.C.B.
 - Open Cast
 - Van
Electrician
Fireman
Fitter
Garage Foreman
Joiner Foreman
Joiner
Mechanic
Motor Engineer
Painter
Plate Layer
Plumber
Pipe Layer
Radar Fitter
Radio Technician
Upholsterer
Welder
Welding Inspector

5. <u>Manual unskilled (MUS)</u>

Barman
Bath Attendant
Coal Merchant's employee
Dairyman
Driver - tractor
Fencing Contractor
Fisherman
Labourer - builder's
 - farm
 - road
Odd job man
School Caretaker
Storekeeper
Waiter
Workshopman N.C.B.
Inspects fabrics for floors

6. <u>Unemployed (U)</u>

Permanently unemployed
 because of disability
 or illness

B. WOMEN

1. Professional and Managerial (PM)

Analyst
Chiropodist - training
Dispenser
Domestic Science Teacher
Graduate (unemployed)
Librarian
Pupil Nurse
R.M.N.
Shop Owner
S.R.N.
S.E.N.
Teacher
Teacher in training
Laboratory Technician

2. Clerical (C)

Bank Clerk
Bar Manager's Wife
Cashier
Cash Collector
Clerkess
Comptometer
Club Stewardess
P.O. Counter Clerk
Policewoman
Receptionist
Shop Buyer
Shorthand Typist
Secretary
Secretary - training
Storewoman
Schoolgirl - Grammar
Wages Clerk

3. Distributive (D)

Bus Conductress
Hairdresser
Milk Round
Paper Delivery
Shop Assistant
Snack Bar Assistant (Cafe)

4. Service and Domestic (S)

Auxiliary Nurse
Bus Cleaner
Batwoman
Cake Decorator
Canteen Worker
Caretaker
Char
Cleaner
Cook
Domestic
Home Help
Kitchen Worker
Lollipop Woman
Nanny
Nursery Nurse
School Auxiliary
School Meals - Assistant
- Supervisor
Ward Maid
Waitress

5. Factory and Agricultural (F)

Factory worker
Fishing Tackle Maker
Fly Tier
Forestry Worker
Invisible Mender
Land Army (Farm Worker)
Laundress
Machinist
Tailoring/Dressmaker

6. No previous Occupation (NPO)

APPENDIX III

DATA

The data on each patient is given in the following tables.

Number — Each patient was given a number in alphabetical order. An asterisk marks the unmarried women.

Age — The age is that at which she took part in the survey.

Parity — The first figure is the number of pregnancies that continued beyond the 28th week of pregnancy, and the second figure gives the number of pregnancies that terminated before the 28th week.

Occupation — Indicates the husband's occupation. Where there is an asterisk the occupation of a woman who has no husband is given.

Husband's Occupation		Woman's Occupation	
PM	Professional and Managerial	PM	Professional and Managerial
OWC	Other White Collar	C	Clerical
SM	Skilled Manual	D	Distributive
M	Miner	S	Service
MUS	Manual - unskilled	F	Factory and agricultural
U	Unemployed	NPO	No previous occupation

The types of jobs in each category are given in Appendix II.

Height — The height of the subject is given in centimetres.

Weight — The weight of the subject is given in kilograms.

Average baby weight — The mean weight of all babies previously born to that woman.

<u>Haemoglobin</u> Is the average of two specimens taken after each period and is given as gm/100 ml blood.

<u>Packed Cell Volume</u> Is an average, where two values are available, and is expressed as a percentage.

<u>Serum Iron</u> is expressed as μg/100 ml.

<u>Iron Binding Capacity</u> is also expressed as μg/100 ml.

<u>Fibrin/Fibrinogen Degradation Products</u> expressed as μg/ml.

<u>Menstrual loss</u> of period 1 and period 2 given as ml blood. In the 16 women who participated in collecting a 3rd period after a course of iron, the results of haematology and menstrual loss are shown immediately below.

<u>Cycle</u> The length in days observed between period 1 and period 2. Where only one period was collected, the cycle length stated by the patient, is given.

<u>The final column</u> contains other coded information about each patient. The key to the code is given below.

A1 Aspirin 1-2 month

A2 Aspirin 1-2 week

A3 Aspirin 1-2 day

Fe1 Iron up to 3 months ago

Fe2 Iron 4-6 months ago

Fe3 Iron 6-12 months ago

X Bruises easily

Y Other small blood loss (bleeding haemorrhoids, epistaxis etc.) - or larger loss over 6/12 ago.

Z Large loss less than 6/12 ago (operation, blood donation).

Signs

B Abnormal discharge

D Erosion

E Polyp

G Cystocoele/ urethrocoele

H Rectocoele/ enterocoele

J Cervical descent

K Retroversion

L Fibroid

M Ovarian Cyst

N Adhesions/ tender appendage

Q Scarred or lacerated cervix

O Not examined (single, left, etc.)

OR Not examined - refused or defaulted

P Pill

C Coil

Symptoms

1 Dysmenorrhoea

2 Discharge

3 Pruritus

4 Stress incontinence

5 Urge incontinence

6 Recurrent urinary tract infection

7 "Something coming down"

8 Intermenstrual bleeding

9 Post coital bleeding

10 Irregular periods

11 Dyspareunia

12 Loss of libido

13 Infertility

14 Menorrhagia

No.	Age years	Parity	Occ.	Ht. cm	Wt. kg	Av. Baby Wt. Kg	Hb G/100ml	PCV per cent	S.Fe ug/100ml	IBC ug/100ml	FDP ug/ml	Blood loss ml 1	Blood loss ml 2	Cycle days	
1	41	5+0	SM	164.8	67.59	3.30	12.2	38	112	398	7.9	87	113	56	A1.X.10,2.OR.
2	44	5+1	U	155.6	66.45	3.57	7.8	27	15	489	10.6	11	12	31	A1.OR.
3	29	2+0	PM	158.8	64.51	2.99	13.6	42	105	491	22.6	26	15	28	Y.1,4.
*4	25	0+0	PM*	-	-	-	13.2	40	121	354	3.7	22	23	27	A1.X.O.
5	21	0+1	OWC	157.5	53.98	-	13.7	43	115	346	15.0	41	37	23	A2.1,2,3,6,10,11.B.
6	39	1+0	M	169.6	95.71	4.48	12.2	39	23	417	15.0	166	174	31	A1.Y.4,14.G,H.
7	40	3+0	SM	162.6	58.29	3.26	12.0	39	53	480	18.5	61	82	25	
8	36	2+0	OWC	165.1	70.76	3.22	13.5	41	122	368	15.8	38	46	21	A1.D.
9	32	2+0	SM	157.5	66.68	2.93	13.9	45	111	348	12.4	22	21	25	A1.Fe3.2.D.
10	36	1+0	OWC	165.1	81.42	4.54	15.5	43	88	-	5.6	7	10	28	A1.X.2.
11	32	3+0	SM	-	-	-	12.7	39	83	365	21.1	-	-	-	A1.Hysterectomy.1,4.O.
12	42	4+0	SM	155.6	54.88	3.56	12.9	40	103	278	5.6	2	5	24	2,4.G,J,K.
13	41	0+0	SM	157.5	46.27	-	13.6	43	57	411	4.3	22	29	24	A1.Fe1.X.
14	40	2+0	SM	161.3	67.81	3.59	13.2	41	71	379	7.4	47	51	27	A1.2,3,6,8.G,D.
15	34	1+1	M	160.7	70.53	3.86	12.9	40	79	390	12.4	26	27	26	A1.Y.2.OR.
16	26	2+0	PM	163.2	51.26	3.30	13.9	45	99	425	15.8	28	26	30	A1.Fe3.1.Q,K.
17	31	2+0	SM	160.7	53.52	4.24	11.3	38	73	415	17.4	61	48	28	)Case No.6-iron trial.
							12.0	39	101	296		64			)1,D.
18	30	2+0	MUS	155.6	57.15	3.47	14.2	43	99	290	6.6	32	36	24	A1.Fe2.
19	33	3+0	M	157.5	61.23	3.29	12.7	42	83	343	10.6	135	18	26	A1.Fe1.X.
20	28	2+1	SM	153.7	56.25	3.30	14.6	-	125	323	7.5	17	20	29	A1.Fe2.Y.
21	37	6+0	M	160.7	49.89	2.69	13.3	-	118	347	22.6	17	25	26	A1.Fe1.
22	23	2+0	M	162.6	49.89	3.30	12.7	37	98	330	5.3	47	41	29	Fe3.1.
23	42	2+0	M	167.6	49.89	-	15.8	-	144	315	14.9	-	-	-	A2.Fe3.X.10.
24	25	3+0	M	-	-	3.29	14.9	45	140	394	10.6	9	-	28	P.X.2,3,8.OR.
25	41	2+0	M	156.2	62.82	2.88	13.1	42	80	302	7.5	15	14	28	A1.Fe1.D.
26	42	6+0	M	160.0	62.40	3.86	12.1	39	44	403	15.8	118	146	35	Fe3.8.H.
27	27	5+0	MUS	156.9	81.65	3.50	13.1	42	103	483	-	57	81	27	C.A1.Y.2,3.
28	30	5+2	MUS	149.9	45.81	3.21	11.6	39	34	548	3.3	42	43	34	C.K.
29	23	1+0	M	162.6	87.32	2.18	13.6	40	92	307	5.0	17	20	26	Fe2.1,2,6.

No.	Age-years	Parity	Occ.	Ht. cm	Wt. Kg	Av. Baby Wt. Kg	Hb g/100ml	PCV percent	S.Fe μg/100ml	IBC μg/100ml	FDP μg/100ml	Blood loss ml 1	Blood loss ml 2	Cycle days	
*30	19	1+0	F*	-	-	2.69	15.2	44	76	476	22.6	76	85	29	A2.1.0.
31	32	2+2	SM	-	-	2.10	13.7	-	128	440	12.4	22	12	28	P.Fe1.X.Y.1,2,3,11.OR
32	30	2+1	SM	161.3	56.25	3.74	12.6	41	107	531	6.2	23	20	25	A1.1.D,K.
33	37	2+0	M	157.5	65.32	3.26	14.1	42	115	295	15.5	14	17	28	2,3,4.D.
34	30	2+0	M	174.0	64.41	3.35	11.2	36	53	382	15.0	126	75	26	A1.Fe3.2,3.D,K.
35	26	3+0	M	163.8	48.99	3.88	11.5	37	74	296	11.3	56	68	38	A2.1,2.OR
36	44	4+1	M	167.6	61.69	3.53	13.8	39	61	316	19.8	41	65	29	A1.Fe1.X,Y.H.
37	31	4+0	M	158.1	53.52	3.25	13.0	40	89	378	10.6	16	16		Fe3.X.9,11.
38	42	3+0	OWC	161.3	57.15	3.29	9.9	-	-	-	15.8	21	-	42	A1.4,10.OR
*39	18	0+0	D*	160.7	44.45	-	11.9	40	63	315	18.5	4	10	36	Fe1.Z.10.0
40	25	3+0	SM	167.0	57.15	3.08	10.8	36	-	-	7.9	73	-	28	)Case No.10-Iron Trial
							11.7	37	77	351		55+			)C.Z.1,2.D
41	35	3+0	MUS	170.2	68.49	3.43	12.6	42	22	388	18.5	30.8	33	30	Fe3.X.D.
42	22	1+0	M	164.5	81.87	3.69	12.3	41	46	376	15.8	64	61	29	A3.X.1,9,11.OR
43	31	3+1	SM	167.6	61.69	3.45	14.0	42	55	282	15.0	59	52	30	A1.Fe1.Z.3,11.OR
44	30	3+1	OWC	158.1	61.23	3.10	11.9	38	132	497	45.1	8.1+	7,0	28	)Case No.2-Iron Trial
							11.3	37	108	321		6			)P.A1.D.
45	25	3+0	M	163.2	69.40	3.37	12.8	41	38	368	13.2	136	110	33	C.A1.Fe2.8,9.D
46	37	0+0	SM	160.0	61.69	-	13.5	42	75	385	7.5	14	22	33	A1.Fe3.2.13.
47	33	4+0	M	157.5	55.34	3.27	13.3	43	93	347	5.6	36	36	28	A2.
48	21	3+1	M	160.0	88.90	3.16	13.8	39	64	376	4.0	26	24	38	C.Fe2.OR
49	23	3+0	M	167.6	56.70	3.67	12.5	39	123	305	9.4	17	12	31	A1.Fe1.X.3.OR
50	23	3+0	M	166.4	83.91	3.53	13.8	45	62	350	3.8	7	6	29	A1.1,9,11.
51	27	5+1	SM	158.8	59.42	3.47	12.9	42	102	406	14.9	25	36	28	C.A1.Y.1,2,10.K
52	22	1+0	MUS	152.4	53.52	3.16	13.8	41	71	426	5.6	13	5	26	Fe3.A2.X.3.
53	30	1+0	MUS	157.5	72.12	3.52	14.0	44	100	429	4.6	0.2	13.0	28	P.A3.1.N
54	33	3+0	M	156.2	41.28	3.71	13.2	42	41	386	10.6	58	52	31	A1.2.D.
55	26	1+0	M	156.9	-	3.97	13.3	42	-	-	7.5	18	6	73	Fe1.A1.8.0.
56	37	4+0	PM	163.8	80.74	3.49	13.7	41	41	283	9.2	15	15	26	A1.Y.2,8.
57	32	2+0	SM	166.4	74.39	4.06	13.3	42	63	447	15.0	89	78	31	Fe3.Z.X.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
58	31	2+1	OWC	156.2	55.34	3.49	13.1	42	152	392	7.9	21	40	35	A1.1,10.
59	36	1+0	SM	163.8	57.04	3.01	14.8	46	106	329	1.6	4.9	6	28	
*60	17	0+0	D*	156.2	50.35	-	12.2	39	98	321	4.6	9	42	27	A1.X.10.0
61	37	5+0	OWC	164.5	62.14	3.74	13.8	42	158	360	21.1	31	22	24	1.
62	21	1+1	SM	162.6	58.97	3.35	16.2	44	-	-	-	8	6	27	P.Fe2.Y.2.M.
*63	17	0+0	D*	156.9	47.63	-	12.3	39	80	413	9.2	29	31	31	X.1.0.
64	43	4+1	M	154.9	54.09	3.18	12.3	40	-	-	21.1	51	42	25	Y.2,9.D,K,L.
65	31	1+0	SM	152.4	75.30	3.01	13.2	44	62	348	18.5	42	43	28	A1.D.
66	42	3+0	OWC	151.1	56.70	3.08	12.6	41	89	478	13.2	5.4	5	22	A1.Y.2,3,4,5.K.
67	42	2+0	SM	161.3	73.03	3.13	14.3	41	99	320	19.8	12	15	24	Fe2.5.
68	42	1+0	M	163.2	62.60	3.06	12.3	39	136	443	21.1	67	75	26	Fe3.E.
69	38	1+0	MUS	161.3	43.09	3.18	14.0	41	60	520	18.8	7	-	29	P.1.Q.
70	41	7+0	SM	148.6	45.38	2.60	13.3	42	114	456	3.3	13	20	23	A2.2.D.
71	42	4+0	SM	-	-	3.46	13.8	44	113	424	13.2	-	-	-	A1.2,4,11,12. Hysterectomy 0
*72	17	0+0	F*	-	-	-	12.1	40	153	519	6.2	78	80	27	Fe1.1.0.
73	25	3+0	SM	151.1	48.99	3.47	12.1	39	68	300	18.5	88	59	29	Fe1.A1.X.3,8.D.
74	26	0+0	SM	157.5	49.44	-	13.1	42	158	365	15.8	9	11	33	Fe3.A1.X,Y.10.
75	22	1+0	M	156.9	48.31	2.89	14.5	-	129	275	7.4	24	-	34	OR.
76	44	3+1	M	161.9	60.78	3.48	13.1	41	96	437	13.2	15	-	46	X.10.OR
77	40	3+0	M	170.8	65.32	3.09	14.1	41	44	335	18.5	34	44	26	1.
78	25	1+0	M	162.6	46.72	3.50	13.5	42	53	-	1.9	6	14	31	Fe1.X.OR
79	38	4+1	M	168.9	79.83	3.64	13.0	40	121	318	15.0	47	37	25	C.Y.2,3.G.
80	26	3+0	SM	163.8	56.25	2.99	14.3	43	29	330	9.2	48	41	43	Fe3.A1.1,10.D.
81	39	1+0	M	168.9	59.42	3.54	13.4	43	97	467	14.9	42	48	26	Fe1.A1.Y.1,2,9,11.D.
82	35	2+0	MUS	-	-	3.86	14.9	46	111	317	10.6	42	41	25	A2.X.1,2,3,11.0
*83	18	0+0	D*	154.3	58.97	-	14.0	41	120	334	22.6	42	31	35	A1.0.
84	23	4+0	M	-	-	-	15.3	42	116	300	21.1	-	-		P.Fe3.3,6.OR. Amenorrhoea-Lactating
85	42	3+0	M	160.0	93.67	3.46	14.9	46	105	393	7.9	31	29	23	Y.1,2.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
86	31	2+0	M	162.6	46.15	2.70	13.4	49	92	343	14.9	10	13	26	Al.2.
87	40	2+0	M	152.4	62.14	3.26	14.2	45	66	360	12.4	6	9	18	1,4.
88	36	3+0	M	158.8	58.06	2.64	14.5	43	41	246	-	16	13	29	Fe2.X.1.D,K.
89	28	2+0	PM	165.1	64.41	3.39	14.3	44	149	442	18.8	20	20	31	1.
90	41	2+0	PM	161.3	54.43	2.59	14.2	43	101	354	10.6	38	30	24	Al.D.
91	42	1+0	M	161.9	57.61	2.35	9.2	33	30	467	7.5	81	89	28	)Case No.13-Iron Trial
							13.5	42	107	364		92			)X.
92	40	3+1	MUS	157.5	73.48	3.17	12.7	39	141	495	26.3	18	7	25	Al.1.D.
93	37	3+0	SM	161.3	65.32	4.18	13.7	43	174	300	15.0	98	108	32	Fe3.Al.Y.
94	40	2+0	M	149.9	38.78	2.24	12.1	41	59	485	26.3	8	4	30	1.D.
95	34	3+0	SM	172.7	82.55	3.87	13.0	40	150	337	37.6	2.9	3	30	P.Al.Y.2,3.
96	39	2+1	M	165.1	67.13	3.23	14.2	-	62	363	12.4	2	-	-	Fe2.Al.4,5,10.
97	35	2+1	SM	175.5	63.50	2.73	12.6	41	100	444	4.0	10	24	24	Al.Y.K.
*98	17	0+0	C*	166.4	68.27	-	13.6	44	75	332	13.6	24	10	34	Fe1.Al.Y.O.
99	30	5+0	SM	161.3	47.63	4.05	12.2	41	110	419	13.2	25	48	35	Fe1.1,2,3,9,10,11,12. D,K,N.
100	26	3+0	MUS	165.1	-	3.26	11.4	-	41	579	9.4	1	-	-	P.Fe2.Y.X.6,2,10.OR.
101	39	2+0	PM	165.1	61.69	3.15	9.4	33	18	418	6.6	59	64	29	Al.X.2,3,4.D,Q.
102	37	5+0	SM	169.6	67.58	3.27	10.5	36	53	519	6.2	140	127	28	Al.2,12.D,K.
*103	18	0+0	F*	161.3	54.66	-	13.7	44	96	437	-	15	17	21	Al.1.O.
104	34	2+0	PM	167.6	58.06	4.45	12.2	39	49	442	15.0	35	19	30	Al.1.
105	42	5+0	OWC	157.5	48.08	2.72	13.4	44	141	276	18.8	23	43	23	Al.X.1,2.OR.
106	40	2+1	SM	152.4	62.60	3.67	14.4	46	106	343	-	14	17	28	Fe3.X.
107	40	4+1	M	157.5	63.96	2.52	12.8	41	73	276	7.5	26	23	29	Al.Y.4.
*108	21	0+0	C*	162.6	56.93	-	12.5	37	60	343	31.7	29	23	33	A2.6.O.
109	42	1+0	SM	158.8	50.46	3.97	14.2	44	45	383	10.6	81	65	24	Fe2.Al.
110	37	0+0	M	161.3	77.56	-	13.9	45	138	349	9.9	83	79	24	Fe2.Al.1.
111	38	2+0	OWC	163.2	51.94	2.55	14.6	44	110	389	7.9	0.2	0.5	28	P.Al.X.1,8.O.
112	44	6+2	OWC	157.5	59.87	-	14.0	43	117	395	18.5	-	-	-	Fe3.Y.4,7.G,H. Menopausal

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
113	19	1+0	SM	168.3	63.50	3.35	13.0	41	35	395	15.8	14	21	29	1.OR
*114	20	0+0	D*	-	-	-	15.6	-	93	333	15.8	-	-	-	A1.10.O.
115	34	3+0	SM	168.9	54.43	3.72	13.1	44	56	429	4.0	73	71	28	A1.1,8.D,Q,K.Grade IV Cervical Smear
116	30	2+0	PM	166.4	58.06	3.29	13.2	42	85	406	-	79	86	26	C.A1.1,8,9.
117	43	6+0	OWC	172.7	67.13	4.20	14.3	44	111	326	8.7	50	58	24	C.A1.1.
118	30	6+0	M	161.3	63.50	3.61	13.1	40	52	307	9.2	33	82	30	Fe3.Y.X.2,4.Q,K.
119	24	3+0	MUS	153.7	52.62	2.64	11.0	36	28	418	10.6	96	51	27	A1.X.1,11.N.
120	29	4+0	M	158.1	97.52	2.31	16.6	49	57	388	22.6	1	0.4	31	X.3,4.OR.
121	30	3+0	OWC	160.0	72.57	4.05	14.0	44	114	367	5.6	24	46	23	A3.X.1.G.
122	29	0+0	PM	161.3	56.25	-	12.3	39	75	366	10.6	15	7	36	Z.1.
123	25	3+0	SM	158.8	60.33	3.91	14.6	45	137	395	5.0	2	1	29	P.A2.X.2.
124	39	4+2	MUS	154.9	60.78	3.53	13.1	43	113	477	21.1	8	13	28	P.Fe2.A1.2,3,4.B.
125	37	3+0	SM	167.6	58.51	3.57	13.9	40	171	343	18.5	25	11	29	Fe3.A1.2.D.
126	32	1+0	OWC	166.4	48.99	3.35	12.7	39	112	450	11.3	18	15	27	2,3,9.D.
127	41	2+0	M	166.4	70.76	4.65	14.0	45	74	-	10.6	28	46	24	A1.2,3,5.D.
128	31	2+0	SM	163.8	53.52	4.06	13.5	41	78	416	14.9	5	11	26	A1.1.D.
129	35	2+2	M	163.8	63.50	2.86	12.9	42	154	475	18.8	16	5	28	A1.4,11.D,H,K.
130	43	5+0	M	156.2	48.99	3.19	14.2	45	84	377	7.9	31	46	45	A3.2,3,4,8,10.B,H,K.
131	21	1+0	M	163.8	52.62	3.35	13.1	38	118	336	9.4	30	29	25	Fe2.A1.X.
132	35	2+0	SM	161.3	82.55	3.86	13.9	45	60	459	6.6	76	66	24	A1.Y.1.
133	40	6+1	SM	158.8	66.22	2.69	14.2	39	103	295	7.5	41	58	27	1,4.D.
134	24	1+0	SM	165.7	53.52	3.83	14.1	45	88	390	7.9	18	17	30	3.
*135	18	0+0	PM*	165.1	54.43	-	12.4	39	78	370	15.0	58	43	35	Fe3.Y.1.O.
136	40	4+1	M	155.6	45.81	2.13	12.4	40	93	392	22.6	104	117	23	Fe3.
*137	22	0+0	C*	171.5	62.14	-	13.5	43	138	403	3.1	35	-	72	Fe3.A1.X.1.O.
138	34	2+1	MUS	161.3	59.87	4.01	13.1	43	133	362	-	14	13	26	A1.2.D.
139	24	3+0	SM	160.0	57.15	2.92	12.2	40	70	424	15.8	67	67	25	Fe3.
140	38	3+1	M	153.7	61.69	3.89	11.7	39	69	363	12.4	17	17	34	4,5,8,9.G,M.
141	40	2+1	M	169.6	71.67	3.06	12.6	40	113	277	4.0	27	21	22	A2.O.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
*142	18	0+0	F*	156.9	49.21	-	13.3	40	79	288	37.6	26	16	27	A1.X.1,2.0.
*143	21	0+0	C*	158.1	47.17	-	13.4	42	59	320	15.8	23	17	31	A1.1.0.
144	38	2+0	MUS	160.0	51.71	3.40	11.3	38	23	438	21.1	64	51	26	Fe3.A1.X.1,8.
145	43	3+0	C*	163.8	50.35	3.55	8.6	29	17	398	5.3	18	17	28	A2.1.
146	38	5+1	MUS	-	-	3.38	12.5	40	80	413	-	34	-	25	1.0.
147	43	3+0	U	143.5	46.72	4.42	14.0	44	117	362	4.0	30	17	26	C.Y.1,2.
148	38	4+1	SM	173.3	61.69	3.06	13.1	42	44	413	14.9	33	16	26	A3.1,6.
149	25	2+0	S*	162.6	64.41	3.11	11.5	-	88	419	10.6	169	145	40	Fe3.X.
150	28	3+0	M	165.2	63.50	3.18	13.9	-	138	431	31.7	87	71	32	Fe2.A1.8,9,11.D.
151	33	3+1	M	160.0	60.10	3.74	12.0	40	64	498	7.5	69	58	25	C.A1.Y.8.
*152	17	0+0	NPO*	158.1	55.34	-	12.4	39	122	332	11.3	44	54	27	Fe1.A1.1.0.
153	22	1+0	M	156.9	90.26	3.26	13.4	40	58	422	13.2	20	15	32	A1.X.4,11.OR.
154	37	2+1	M	170.2	61.69	3.36	11.7	36	40	348	18.8	50	40	25	Fe2.Y.2,3.D.
*155	23	0+0	D*	-	-	-	12.9	39	51	393	5.3	49	45	24	2,3,6.0.
156	35	2+2	M	160.0	70.99	3.64	14.2	43	92	300	15.8	7	4	26	Fe3.X.2,3,7.OR.
157	23	2+0	SM	-	-	2.83	11.3	36	25	333	10.6	19	-	28	Fe2.A1.1,2,3.0.
158	31	5+0	M	161.3	81.65	3.31	14.5	43	93	489	4.6	1	1	27	P.A1.X.2,3.D.
*159	22	0+0	D*	163.8	54.20	-	13.5	40	57	384	7.9	30	22	28	A1.1.0.
160	33	2+0	MUS	163.2	78.02	3.52	9.8	34	20	464	6.6	41	49	25	A2.X.2,3.D.
161	33	2+0	PM	165.1	63.50	3.46	12.9	40	113	287	10.6	68	35	30	A1.
*162	21	0+0	D*	-	-	-	14.0	42	71	322	13.2	41	9	30	A1.1.0.
163	43	3+0	S*	165.7	58.06	3.65	13.3	45	31	421	22.6	202	126	28	Fe1.A2.4.D.
164	38	4+0	SM	157.5	61.69	3.47	13.1	38	60	353	15.0	4	17	30	A1.X.1.OR.
165	42	7+1	SM	149.9	43.54	2.35	12.9	38	46	421	5.0	39	27	31	Fe3.4.OR.
*166	18	0+0	PM*	167.0	70.76	-	11.2	35	45	424	10.6	21	21	27	A1.1.0.
*167	18	0+0	D*	165.7	60.78	-	10.9	37	18	434	5.6	69	38	26	)Case No.5-Iron Trial
							13.1	40	60	321	-	35			)A1.X.1.0.
168	40	3+0	MUS	150.5	57.61	3.55	14.5	44	117	401	14.9	10	12	17	Fe2.Y.X.
*169	17	0+0	F*	154.3	48.08	-	14.1	42	78	453	5.6	21	11	28	X.1.0.
170	27	4+1	MUS	154.9	49.33	2.83	12.2	41	104	358	15.0	0.75	1	27	P.1.B.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
171	26	2+0	MUS	-	-	-	14.2	-	73	334	7.9	-	-	-	10.OR.
172	41	3+0	SM	154.9	56.45	3.65	13.2	39	58	303	5.6	30	28	28	X.1,2,3,4.
173	33	2+0	OWC	170.2	58.06	3.06	12.5	41	63	338	9.2	52	53	29	A2.2.
174	29	4+0	M	152.4	70.76	3.37	12.6	41	93	364	5.3	73	88	30	Fe3.Al.
175	36	2+0	SM	-	-	2.60	14.9	-	103	440	15.0	47	-	25	Al.X.2,3.OR.
176	39	4+0	MUS	163.8	61.23	3.27	12.1	38	34	338	3.8	238	100	28	C.E.
177	29	1+0	SM	170.2	61.35	3.74	13.8	44	160	387	8.7	21	27	28	Fel.OR.
*178	22	0+0	D*	165.1	100.92	-	12.8	38	85	411	21.1	27	27	25	Al.1.O.
179	27	2+0	MUS	160.7	61.23	3.27	12.6	39	52	358	15.0	101	91	30	Fe2.Al.OR.
180	36	0+0	OWC	167.0	55.79	-	10.9	38	29	458	13.2	11	24	26	)Case No.3-Iron Trial
							13.9	45	55	385	-	44	-	-	)Al.D.
181	30	3+0	M	158.8	57.15	3.47	13.1	41	120	290	4.7	1	6	28	1,2,4.OR.
182	35	3+0	M	167.6	57.61	3.44	13.6	43	69	333	15.0	10	6	28	1,2,3,6.
183	36	1+1	SM	170.2	77.11	2.83	13.9	42	24	313	15.8	58	48	29	Al.
184	26	2+0	SM	167.6	72.57	3.63	13.1	42	70	427	30.1	82	104	26	D.
185	36	5+0	SM	-	-	3.24	13.7	41	80	278	10.6	32	-	28	1,2,3.OR.
186	36	4+1	PM	160.0	57.15	3.11	14.4	44	155	327	5.3	24	21	28	Al.2.
187	40	4+0	MUS	164.5	67.58	3.35	13.8	43	134	396	7.9	36	29	24	1,5.L.
188	37	1+0	MUS	154.9	70.76	2.61	15.1	48	65	376	29.8	7	9	26	Fe3.Al.X.6.
189	35	2+0	SM	163.8	70.87	3.46	14.8	45	110	368	9.9	53	44	24	Al.1,3.D.
190	35	6+0	SM	156.2	52.16	3.30	12.7	39	26	342	22.6	61	40	32	C.Fel.Y.1,2,3,4,5,11,12.
191	41	2+0	SM	153.0	68.95	3.32	13.4	43	156	363	12.5	17	8	23	Z.
*192	17	0+0	C*	-	-	-	13.9	-	140	347	9.9	13	-	49	Fe3.X.1.O.
193	27	3+1	SM	162.6	59.87	3.30	13.9	43	92	498	18.8	18	28	28	P.D.
194	40	3+0	M	160.7	77.11	4.01	15.2	-	53	349	7.5	280	-	-	Fel.10,14,1,2,3,4.O.
195	26	1+0	SM	-	-	2.95	13.6	-	135	340	9.9	-	-	-	Amenorrhoea.Lactating.
															OR.
196	23	1+0	SM	160.0	63.50	3.06	15.3	46	137	437	18.5	32	44	28	P.Al.X.D.
197	40	1+1	SM	165.1	57.15	4.08	12.4	39	113	317	7.5	9	9	25	
198	24	1+0	U	165.1	47.17	3.15	13.5	-	88	405	10.6	0.5	1	28	P.Fe3.Al.2,8.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
199	32	2+0	M	166.4	90.72	3.56	16.3	47	129	473	15.0	28	37	26	Fe3.A2.X.1,2,3.
200	36	6+0	M	154.9	68.95	3.54	13.2	40	37	397	5.3	63	84	24	A1.X.2.D.
*201	20	0+0	NPO*	-	-	-	12.6	41	121	345	9.2	-	-	-	10.0.
202	20	2+1	SM	161.9	73.94	3.73	14.2	43	76	356	15.0	4	3	42	X.OR.
203	37	3+0	MUS	155.6	54.43	3.03	13.2	42	-	-	-	2.7	3	29	A2.1.
204	28	2+0	MUS	163.8	60.78	3.67	11.3	39	47	422	15.0	43	68	25	)Case No.7-Iron Trial
							13.9	45	-	-	-	50	-	-	)A1.X.2,3.
205	29	1+0	M	164.5	69.85	4.06	11.2	36	23	483	5.3	103	66	27	)Case No.12-Iron Trial
							13.2	42	71	408	-	52	-	-	)A2.1.D.
206	26	2+0	SM	158.8	75.75	3.74	13.0	-	45	439	22.6	74	64	32	C.A1.1.
207	23	1+0	SM	167.6	65.32	2.81	13.1	41	95	402	14.5	30	33	23	Fe3.A1.
208	35	0+0	MUS	158.8	65.54	-	13.6	42	-	-	-	16	10	26	A2.Y.
209	40	3+0	OWC	153.0	59.87	3.22	13.0	41	64	413	6.6	8.5	28	29	Fe3.OR.
210	30	4+0	U	168.9	73.48	3.60	13.2	42	76	332	8.7	35	35	29	Fe3.A1.X.1.OR.
211	23	2+0	OWC	170.8	48.53	3.50	13.8	41	134	352	7.9	174	87	27	Fe2.A1.D.
212	34	1+0	S*	161.3	48.53	2.78	13.5	39	126	342	9.9	4	4	29	2.
*213	19	1+0	C*	159.4	51.94	3.43	13.6	-	72	283	15.8	7	-	28	Fe3.1,2.OR.
214	38	2+0	SM	165.7	68.04	4.28	10.9	36	38	497	10.6	113	130	28	)Case No.16-Iron Trial
							13.5	42	51	300	-	120	-	-	)1.
215	40	6+1	SM	168.9	88.90	3.52	13.0	42	-	-	-	143	55	28	Fe3.A2.Z.2,3.G,D.
216	32	5+0	MUS	160.0	42.18	2.42	12.6	40	88	322	13.2	0.3	-	-	A1.1,3,10.OR.
*217	30	0+0	PM*	160.7	53.98	-	13.6	42	94	408	3.8	43	25	26	1.
218	27	1+0	M	165.7	60.33	3.52	14.0	41	120	349	3.7	10	18	34	A1.X.1.
*219	18	0+0	PM*	-	-	-	12.6	39	60	415	7.9	9	7	34	1,2.
220	29	0+0	MUS	165.1	63.50	-	13.6	42	150	344	5.3	9	11	24	A1.Y.1,2,3,13.
*221	20	0+0	C*	160.7	60.55	-	12.3	40	74	384	-	35	22	28	0.
222	44	4+0	SM	162.6	63.96	3.80	9.7	33	21	541	15.0	101	72	24	)Case No.14-Iron Trial
							13.0	41	96	331	-	50	-	-	)A1.X.1,14.OR.
223	39	2+1	MS	160.0	54.88	3.80	12.0	37	45	421	15.0	34	37	23	Fe3.A1.X.
*224	40	2+0	F*	159.2	62.14	3.06	13.1	42	34	454	15.0	26	41	26	Fe3.A2.5.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
225	29	3+0	SM	149.9	44.91	2.93	13.1	-	47	361	18.5	89	53	26	A1.Y.1,3,11.
226	28	2+0	PM	167.6	64.64	3.18	12.8	40	128	252	11.3	15	12	29	O.
227	29	2+0	MUS	154.9	41.73	2.76	12.1	40	215	603	21.0	23	24	29	P.A1.Z.D.
228	35	4+0	M	166.4	78.02	3.40	12.4	39	58	411	9.9	44	38	28	X.1,2,3,4,7.G.
*229	17	0+0	D*	160.7	52.39	-	14.6	44	97	391	2.5	157	315	25	A1.1.O.
230	33	3+1	SM	160.7	81.65	3.36	12.4	38	61	348	22.6	45	28	28	A1.Y.
231	23	1+1	M	163.8	58.06	2.95	13.0	40	90	288	21.1	20	22	39	Fe2.A1.Y.2,3,6.
232	41	4+0	M	166.4	68.95	2.90	11.6	39	90	337	13.2	54	84	28	C.Fe1.X.Y.D.
233	42	3+1	SM	162.6	73.48	3.29	11.3	37	58	411	10.6	71	82	36	Fe3.2,3,4,7.D,G,L.
234	39	2+0	M	162.6	67.13	3.57	10.4	35	24	484	10.6	85	34	22	A1.1.
235	33	1+0	SM	156.2	53.52	4.08	13.3	42	133	350	2.0	14	13	27	A1.
236	34	3+0	OWC	160.0	62.60	-	14.2	45	130	333	11.3	5	1	28	P.Y.1.
237	44	3+0	OWC	-	-	4.01	15.0	47	117	353	7.9	58	13	35	Fe3.8.OR.
*238	20	0+0	C*	-	-	-	13.6	43	107	352	5.3	19	18	26	O.
239	33	0+1	OWC	158.8	53.18	-	13.8	44	-	-	10.6	0.1	-	-	X.1,6,10.N.
240	32	1+0	M	153.7	64.41	2.49	13.8	42	89	411	11.3	5.5	4.7	28	A1.1,3.
241	39	2+0	OWC	162.6	58.06	3.03	14.6	46	57	337	9.2	10	10	29	1.
242	40	2+0	PM	166.4	74.84	4.31	12.6	39	72	437	12.4	91	48	30	Fe1.A2.Y.4.H.
243	34	2+0	M	156.2	54.88	3.76	13.4	43	57	360	9.2	36	37	28	Fe1.A1.2.
244	22	1+1	SM	165.1	50.80	2.98	12.2	40	93	535	12.4	7	1	41	2,3.
245	44	1+0	SM	-	-	3.18	15.8	48	74	401	13.2	-	-	-	Menopause.2.OR.
246	26	2+0	SM	151.8	47.63	3.21	13.2	41	125	339	15.8	37	17	28	Fe3.
*247	21	0+0	D*	-	-	-	13.9	42	89	330	9.2	26	20	30	A2.Y.1.O.
248	34	2+0	M	163.8	58.06	3.02	13.5	41	47	406	10.6	18	22	22	Y.X.1,2,3.
249	22	2+0	MUS	153.7	64.41	2.52	11.1	33	32	380	4.0	845	64	66	)Case No.11-Iron Trial
							12.2	-	49	374	-	102	-	-	)A1.2,3,10.D.
250	21	1+0	SM	159.4	52.62	3.12	14.0	43	121	355	9.9	93	31	31	Fe2.6,8.M.
251	41	6+0	M	154.9	49.89	3.31	15.1	45	59	314	7.9	32	29	29	C.H.
252	34	2+0	M	161.3	62.60	2.47	13.2	41	87	355	3.8	31	22	25	A1.X.2,3.
253	27	2+1	SM	160.0	49.89	2.57	12.4	41	146	407	11.3	9.5	7.5	26	A1.1.D.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
254	36	2+0	MUS	163.8	98.88	3.09	12.2	39	38	519	7.9	47	71	28	A2.1,2.H.
255	41	2+0	MUS	-	-	2.41	14.0	40	127	354	11.3	-	-	-	Hysterectomy.Al.X.O.
256	26	2+0	SM	161.3	54.88	3.29	13.6	43	86	363	5.0	58	74	27	1,2,3.D.
257	28	2+0	SM	-	-	-	12.7	39	86	289	9.2	-	-	-	Post partum.
															Amenorrhoea.
															C.Fe2.Y.2,3.OR.
258	38	4+1	M	158.1	74.39	3.87	11.7	38	76	435	13.2	61	64	29	)Case No.9-Iron Trial
							12.6	39	208	305	-	56	-	-	)Al.Y.H.
259	43	2+0	M	156.9	54.88	3.35	12.8	-	79	342	7.4	-	-	-	1,2,3,10.H,E.
260	44	5+2	M	161.3	67.13	3.31	14.2	43	78	322	6.6	56	22	17	C.Al.X.1.
261	23	2+0	M	172.7	55.34	3.49	13.0	40	113	343	10.6	5	94	43	Fe3.2.
262	27	2+0	SM	153.7	70.76	3.22	13.2	42	128	444	4.6	45	28	27	Al.1.D.
*263	18	0+0	D*	160.7	60.78	-	13.7	40	123	428	9.4	16	-	60	1.10.0.
264	34	3+0	U	165.7	92.08	3.36	14.2	44	75	387	12.4	93	74	21	Fe2.Y.1,11.L.
265	37	6+0	M	163.2	74.39	3.71	12.1	39	51	443	10.6	141	147	29	Fel.X.9.OR.
*266	19	0+0	S*	171.5	69.85	-	11.1	36	88	323	7.5	4	0.5	28	)Case No.1-Iron Trial
							11.0	35	82	272	-	10	-	-	)Al.X.1.O.
*267	29	0+0	C*	157.5	80.06	-	13.8	42	54	349	10.6	19.5	13	26	Z.O.
268	25	3+0	SM	170.8	57.15	3.52	13.5	42	64	313	30.1	16	13	24	Al.2,3,4.D.1.
269	44	1+0	SM	165.1	58.06	3.15	13.6	42	44	346	10.6	66	68	25	Fe3.1.
*270	18	0+0	C*	-	-	-	14.4	42	96	336	9.2	22	17	24	1,2,3.O.
*271	23	0+0	C*	-	-	-	13.5	43	96	325	18.8	27	32	25	Fe3.O.
272	27	1+0	SM	158.1	49.89	2.95	13.0	-	85	338	6.2	3	10	21	C.Fel.X,Y.1,2,3,9,11.OR.
*273	17	0+0	C*	-	-	-	11.7	36	59	513	10.6	34	1	41	)Case No.4-Iron Trial
							12.4	39	109	340	-	28	-	-	)Al.O.
*274	20	0+0	C*	-	-	-	13.3	40	77	302	7.4	44	36	28	O.
275	27	2+1	SM	162.6	65.32	3.81	13.2	42	193	362	4.7	99	52	28	Fel.1,11.
276	31	2+0	SM	157.5	45.70	3.65	13.4	44	174	419	5.6	24	44	35	1,8.
277	33	2+3	PM	158.8	51.70	4.03	11.6	37	96	546	7.5	100	109	27	)Case No.15-Iron Trial
							11.8	37	55	324	-	147	-	-	)Fel.Al.1,2,3,9.D.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S.Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
*278	19	0+0	F*	160.7	51.70	-	13.2	40	41	338	-	14	12	31	Fe1.A1.X.O.
279	34	3+0	SM	158.8	64.18	3.85	13.1	42	76	308	18.5	53	78	23	Fe3.A3.Y.4.G.
280	27	2+0	OWC	160.0	44.91	3.26	12.6	42	34	505	12.6	103	75	26	C.Fe2.A1.D.
281	37	1+0	SM	151.1	63.50	3.43	12.2	39	114	561	9.9	19.6	26	28	A1.1.OR.
*282	20	0+0	F*	154.9	49.89	-	10.8	36	17	351	5.3	53	51	27	Fe3.A1.X.Y.O.
283	36	6+6	U	161.9	74.39	4.05	13.4	43	83	463	4.3	40	68	24	Fe1.1.L.
284	40	4+0	M	152.4	76.66	3.46	12.8	40	70	350	13.2	69	84	30	A1.Y.2,4,5,7,11.G.
285	41	3+0	MUS	-	-	-	13.3	-	52	281	7.5	-	-	-	Fe3.A2.10.OR.
286	40	2+0	SM	165.1	82.10	3.16	13.6	43	98	307	15.0	9	16	25	Fe3.A1.4.D,E.
287	32	2+0	MUS	172.7	63.50	4.28	13.6	43	49	265	2.3	44	23	27	A1.Y.6.
288	35	2+0	SM	163.8	68.95	3.46	14.4	43	91	353	7.4	25	27	24	X.Y.
289	31	4+0	M	155.6	53.98	3.46	12.3	39	28	375	12.4	15	29	27	A2.2,3.D.
290	37	2+0	PM	160.0	52.6	3.18	12.1	39	48	382	21.1	41	48	30	C.X.9.
291	39	3+0	OWC	156.9	61.69	3.55	13.9	41	50	456	9.9	146	46	21	P.A1.Y.D.
292	44	2+0	SM	166.4	57.15	4.37	11.5	36	125	413	2.5	7	22	25	
293	40	3+0	M	154.3	48.31	4.01	10.6	33	25	405	8.7	63	77	42	A1.X.8,10.OR.
294	39	3+0	M	157.5	71.21	4.27	12.7	40	71	464	12.4	54	79	26	A1.X.1,2,3,4,7,11.OR.
*295	21	0+0	D*	-	-	-	13.8	41	-	-	-	11	-	26	1.O.
296	32	3+0	SM	162.6	85.39	2.55	12.4	38	40	488	-	26	23	30	C.A2.6.D.
297	30	4+0	M	162.6	61.69	3.47	13.3	40	89	338	1.7	16	18	26	A1.Y.1,4.
298	37	2+0	OWC	161.3	63.96	3.33	12.8	40	104	362	15.0	8.1	34	49	A1.Y.10.
299	34	3+1	MUS	162.6	74.39	3.77	12.1	39	65	329	2.5	19	18	28	Fe3.A1.X.Y.4.
300	32	0+0	SM	160.0	54.32	-	12.0	36	108	317	15.8	34	32	25	Fe1.Y.1.
301	23	2+0	M	167.6	55.79	2.69	12.3	38	111	346	2.6	48	50	33	Fe3.X,Y.1,2,3.
302	32	2+0	M	-	-	3.03	9.4	34	30	437	15.0	40	-	26	A1.11.O.
303	42	3+2	SM	158.8	53.07	3.11	13.2	43	75	470	9.9	15.7	20	38	11.
*304	19	0+0	PM*	-	-	-	11.4	36	33	492	22.6	36	85	21	)Case No.8-Iron Trial
							14.2	45	76	351	-	41	-	-	)A1.Z.1.O.
305	44	3+0	M	-	-	-	15.7	46	121	338	-	-	-	-	Hysterectomy.A2.Z.X.4.O.
306	34	1+0	SM	-	-	3.91	13.9	43	152	347	5.3	11	19	28	1.OR.

No.	Age	Parity	Occ.	Ht.	Wt.	Av. Baby Wt.	Hb	PCV	S. Fe	IBC	FDP	Blood loss 1	Blood loss 2	Cycle	
307	40	1+0	SM	158.8	50.80	3.23	13.6	-	101	362	18.8	27	22	21	Fe3.Y.1,11.
308	39	2+0	SM	157.5	63.50	2.71	16.6	50	131	344	9.2	7	24	33	Al.1,2,3,4,7,8,9.
309	39	5+0	M	-	-	-	13.2	-	69	312	12.4	-	-	-	Fe3.Y.10.OR.
310	24	1+0	OWC	168.9	78.47	3.49	13.9	44	88	327	22.6	24	16	27	A2.X.2.D.
311	31	5+2	M	160.7	78.02	3.20	13.9	-	112	351	18.5	51	30	28	X.2,3,4,11.G.
312	33	5+0	M	158.8	55.79	3.40	13.4	42	111	464	22.6	13	9	28	Al.11.
313	43	2+0	M	158.8	54.43	3.18	14.5	45	115	241	12.4	29	15	32	Fel.X.1.
314	22	1+0	M	172.7	56.25	3.54	12.7	40	29	386	10.6	65	62	27	Al.Z.1.
315	31	2+0	M	163.8	51.71	2.88	12.1	35	26	318	18.8	14	23	28	Fel.Al.X.1,3,6.
316	27	2+0	M	157.5	47.63	3.16	11.3	36	84	406	2.3	36	30	35	Al.X.8.D.
317	32	1+0	M	160.0	63.96	4.00	11.9	39	107	378	2.0	45	56	26	1,2,11.N.
318	38	1+0	OWC	160.7	67.58	3.18	14.0	42	73	353	18.5	58	29	27	
319	23	2+0	M	162.6	52.16	3.01	13.1	36	75	331	7.5	111	4	20	C.Fe3.X.Y.6.8.
320	33	4+0	SM	168.9	53.98	3.35	11.5	37	51	453	15.8	40	48	44	Al.2.3.Grade IV Smear
321	30	1+6	SM	162.6	57.15	2.83	9.6	32	97	325	-	24	29	26	Fel.Z.
322	31	2+0	SM	160.7	82.55	3.76	13.9	43	76	350	9.2	13	29	28	Al.X.2,4.D,G.
323	26	0+0	PM	156.2	51.14	-	12.7	42	150	275	6.6	10	3	30	P.Al.Y.2,3.11.
*324	20	0+0	F*	161.3	48.76	-	14.4	-	126	380	10.6	5	1	22	Al.X.O.
325	21	2+0	M	170.8	59.87	3.96	13.4	41	152	444	21.1	11	22	22	P.Fe3.Al.8.
326	40	4+0	M	-	-	-	14.1	42	123	355	4.6	-	-	-	Menopause.Al.X.OR.
*327	18	0+0	D*	161.9	54.66	-	14.3	42	84	391	18.5	14	38	28	A2.1.O.
*328	27	0+0	S*	164.5	-	-	13.5	41	39	329	10.6	4	3	27	O.
329	40	1+0	M	-	-	2.95	14.3	-	60	295	9.9	-	-	-	Post Partum. Amenorrhoea. Fe3.X.OR.
330	20	0+0	MUS	-	-	-	13.6	41	94	292	12.4	11	-	-	Al.1,2,3,10.O.
331	41	2+0	M	-	-	3.40	14.0	43	86	283	10.6	-	-	-	Hysterectomy.X.4.O.
*332	19	0+0	F*	161.3	49.9	-	13.1	39	32	356	12.4	67	57	24	Fel.1.O.
333	33	3+0	U	154.3	46.27	3.16	13.3	44	139	334	7.9	5	7	25	Al.X.1,2.
334	21	1+0	SM	153.0	67.13	1.99	14.8	44	115	371	13.2	1.0	0.5	30	P.D.

No.			Occ.	Ht.	Wt.	Av. Baby Wt.	Hb			IBC	FDP	Blood loss 1	Blood loss 2		
335	27	2+1	M	158.1	70.76	3.08	12.6	41	87	425	21.1	28	24	28	Al.Y.X.
336	32	2+1	OWC	170.8	70.76	3.57	13.0	41	113	364	5.3	32	51	23	C.Z.4.
337	33	2+0	SM	163.8	85.27	2.45	13.0	41	113	440	18.8	18	17	36	Al.D.
*338	18	0+0	F*	157.5	51.03	-	12.8	40	81	348	15.8	2	2	28	Fe3.Al.X.O.
339	35	3+0	OWC	162.6	82.55	3.91	11.0	38	27	533	10.6	75	75	26	
340	34	1+0	SM	153.0	46.72	2.64	13.7	41	102	367	22.6	14	14	32	Fel.Al.1,3.
341	36	2+1	M	157.5	73.48	3.05	13.8	42	56	345	15.0	10	8	26	1,2,4,11.D.
342	32	2+0	SM	141.6	45.59	3.02	12.1	42	37	617	15.8	58	68	27	
*343	23	0+0	C*	-	-	-	13.3	42	88	393	5.6	26	15	27	Al.O.
*344	38	0+0	PM*	160.7	58.51	-	12.2	39	69	404	7.9	85	81	28	Fe3.X.Z.2,3,6.O.
345	31	2+0	SM	155.6	43.54	2.49	13.6	41	189	442	18.8	17	8	26	P.Al.
346	20	1+0	SM	-	-	3.63	12.6	37	152	414	21.1	46	-	29	Fe2.Y.1,2,3,0.
347	38	2+0	M	-	-	-	14.9	45	76	293	10.6	-	-	-	Hysterectomy.Fel.X.Y. 2.3.O.
348	41	2+1	M	167.6	84.82	3.09	14.1	42	81	398	15.8	14	22	28	Fe3.A2.X.1,11.OR.

APPENDIX IV

Laboratory Methods

For practical reasons blood specimens had to be taken at various times of day, and the subjects had not rested. But all specimens were collected at about the same stage of the menstrual cycle - within a few days of the end of the period. The samples collected on one day were taken to the laboratory in the evening for estimation the following morning, so that there was a delay of less than 24 hours.

Haemoglobin and packed cell volume

0.5 ml of blood was collected in a lithium heparin tube. The haemoglobin was estimated in grams of haemoglobin per 100 ml blood, as cyanmethaemoglobin in a Unicam SP 60 Spectrophotometer. The standard calibration curve was prepared with Acuglobin standards (Orthodiagnostics) and checked monthly. Packed cell volumes were measured as percentages after centrifuging for 5 minutes in a Hawksley microhaematocrit. Unfortunately the centrifuge broke down towards the end of the survey, and the PCV of 27 subjects was not obtained.

Serum Iron and Iron binding capacity

20 ml blood was withdrawn into plastic syringes, and transferred to iron free glass universal containers; serum iron estimations were carried out with the Boehringer test combination by the method of Trinder (1956). This technique was also used for estimating iron binding capacity. Excess iron was added in the form of ferric chloride, followed by the

absorption of the unbound iron by magnesium carbonate. The estimations were not carried out on 10 subjects either because the blood had haemolysed by the time it had reached the laboratory, or because it was difficult to obtain 20 ml of blood from poor veins.

<u>Menstrual Blood Loss</u> (Cheyne and Shepherd, 1970.)

Clean portions of the pads were cut away, and the blood-stained part of the pads and tampons were soaked overnight in a measured volume of distilled water, and then wrung out until free of visible blood. Iron in samples of the wash was measured by atomic absorption spectrophotometry and its equivalent as blood calculated from haematological data. A Unicam SP 90 Spectrophotometer fitted with an Fe hollow cathode lamp was programmed to wavelength 248 nm. Slit width was 1.2 mm, burner height was 10 mm, scale expansion x 2, fuel (acetylene) ± 1 l/min, and air 5.0 l/min.

A calibration curve was plotted with working standards prepared from a stock solution. The stock solution was made up by dissolving 0.1 gm pure Fe metal in 40 ml glass distilled water containing 10 ml AR hydrochloric acid. Complete solution was achieved by gentle heating, after which the solution was cooled, transferred to a volumetric flask and diluted to 100 ml in volume. Dilution of this stock solution gave working standards containing from 0.5 to 10 mg Fe per 100 ml. Zero value on the spectrophotometer was obtained by using distilled water in which 12 unused sanitary towels had been soaked overnight.

Efficiency of wash procedure

Venous blood of known haemoglobin concentration was distributed onto clean sanitary towels in amounts varying from 5.0 ml to 40.0 ml. After being allowed to dry for 7 days at room temperature, iron was estimated by the method described above. In seven lots of sanitary towels with known amounts of blood the average ratio of "calculated blood" to "known blood" was 101% and the largest discrepancy was 12%.

Recovery of added iron

A standard iron solution was used to prepare specimens containing 0.6 to 1.5 mgs Fe per 100 ml. These were added to 4 samples of washes in which the iron content had already been estimated. Recovery of added iron was from 97.5% to 105%.

Reproducibility

The reproducibility of 2 samples from a given wash and the variation of duplicate estimations of the same sample were studied in 6 washes.

Wash No.	Estimate No.	Sample A Fe mg/100 ml	Sample B Fe mg/100 ml
1	1	1.75	1.65
	2	1.90	1.87
	Mean	1.825	1.750
2	1	2.70	2.65
	2	2.55	2.55
	Mean	2.625	2.600
3	1	1.15	1.15
	2	1.15	1.15
	Mean	1.150	1.150
4	1	4.65	4.65
	2	4.60	4.60
	Mean	4.625	4.625
5	1	0.40	0.45
	2	0.50	0.40
	Mean	0.450	0.425
6	1	1.70	1.70
	2	1.65	1.65
	Mean	1.675	1.675

The standard deviation between duplicate estimations from a given sample is 0.1 mg Fe/100 ml. The largest difference encountered was 0.2 mg Fe/100 ml.

The standard deviation of differences between Sample A and B from the same wash was 0.029 mg Fe/100 ml.

Fibrin degradation products

Collection and storage of specimens

5 ml of blood were added to a non-siliconised glass test tube containing 0.1 ml of Trasylol (500 Kallikrein inactivator units, Bayer Ltd.) and incubated in a water bath at 37^{o}C for 4 hours. The serum was removed following centrifugation at

3,400 r.p.m. for 10 minutes and stored at -20°C until the end of the survey when all the samples were assayed together under a code that was not broken until results for all samples were obtained.

Tanned Human Red Cell Haemagglutination Inhibition Assay

Preparation of Human Red Cells

(a) Buffers

Phosphate Buffered Saline pH8.

9 volumes 0.15 M Na Cl (8.767 g per litre).

1 volume 0.15 M Na_2HPO_4 (21.295 g per litre).

5 volumes Distilled water.

pH adjusted to 8 with HCl or NaOH.

Citrate Buffer pH6.4

0.35 volume 0.15 M $Na_2HPO_4.2H_2O$ (26.70 g per litre).

0.65 volume 0.15 M KH_2PO_4 (20.4135 g per litre).

1 volume 0.1 M trisodium citrate (29.41 g per litre).

(b) Diluting fluid

Citrate Buffer

Sodium Azide 1 mg per ml (preservative)

Bovine serum albumin 2% (stabilizer)

(c) One unit of packed group O Rh-ve human cells washed three times in twenty times their volume of 0.15 M sodium chloride. Centrifuge for 4 minutes.

(d) <u>Fixation</u>

Measure PCV of cells after centrifuging for 5 minutes.

Place tubes of packed cells in iced water.

Make 1% solution of gluteraldehyde (Koch Light Laboratories) in phosphate buffered saline.

Then make 2% suspension of cells in 1% gluteraldehyde solution.

The fixing cells are kept in iced water for thirty minutes mixing frequently.

(e) Wash cells three times in 0.15 M sodium chloride.

(f) Wash cells three times in distilled water.

(g) Wash cells three times in phosphate buffered saline.

(h) Measure PCV.

(i) Make 2% cell suspension in phosphate buffered saline.

(j) <u>Tanning</u>

Mix equal parts of 2% cell suspension with 1 in 40,000 tannic acid.

Incubate mixture at 56°C for 30-60 minutes, mixing every 10 minutes.

Wash three times in phosphate buffered saline.

(k) <u>Coating</u>

Wash once in citrate buffer and resuspend cells in citrate buffer.

Make up fibrinogen solution 15 μg per ml. (Kabi)

Measure PCV of resuspended cells and add equal volumes of suspended cells to fibrinogen solution. Mix thoroughly and incubate at 37°C for 30 minutes.

Wash three times in citrate buffer.

Measure PCV.

(1) Storage

Make 10% suspension of cells in diluting fluid and store in universal containers.

Dilute to 2.5% for use. (Method of Das and Hoch, to be published.)

F.D.P. Assay. Microtitre Method

Thaw stored specimen in water bath at 37°C.

Add 0.1 ml thrombin (100 units/ml in 0.9% saline) to 1 ml serum.

Incubate at 37°C for half an hour to remove any residual fibrin.

Centrifuge at 3,400 rpm for 5 minutes at 4°C.

Separate serum from any deposit at the bottom of the tube.

Microtitre plates (Cooke Engineering Co.) were prepared.

Three concentrations of human fibrinogen (Kabi Pharmaceuticals Ltd.) 1.25, 2.5 and 5.0 µg/ml were included in each run. The concentration of clottable protein in these standards was estimated many times by the method of Ratnoff and Menzie (1951), and mean values calculated, based on these, the sensitivity of the immuno assay was 0.4-0.6 µg/ml. Also included in each run were two control serums, the value of which ranged from 7.4-7.7 µg/ml.

The positive control consisted of 1 drop diluting fluid and 1 drop 1 in 5,000 antiserum. The negative control consisted of

2 drops diluting fluid.

Each serum to be tested was assayed at 1 in 5,000 and 1 in 10,000 concentration of antiserum. (Hoechst Pharmaceuticals Ltd.) and a system of alternate doubling dilutions beginning at 1 in 2 and 1 in 3 was used.

The incubation period of the antigen-antibody reaction was 24 hours at $4^{o}C$.

1 drop of freshly washed 2.5% suspension of sensitised human red cells was added to each cup of the plate, mixed well and incubated at $4^{o}C$ overnight.

The results were recorded using the fibrinogen and control serum end points as a guide and the results (dilution x sensitivity) were expressed as F.D.P. µg/ml serum.

(Microtitre method of Merskey et al 1966, with modifications by Woodfield et al 1968 and Das 1970.)