of individuals tested." He had previously (Wiener, 1939) mentioned three cases of anti-M and had given references to two of them. The first had been reported, without details being given, by Wolff and Jonnson (1933, p. 84), the second by Friedenreich (1937), and another case, which may be the third one referred to by Wiener, has been described by Moureau and Lambert (1939a, 1939b).

Details of the Case

Recently, as a result of testing, against the red cells of potential donors, the serum of a woman (M. W.) who might have needed a transfusion in connexion with parturition, an antibody, apparently anti-M, has been discovered. No transfusion was given. M. W. was 28 years of age and pregnant for the fourth time. Her blood group was ON and she was Rh-positive. Friedenreich's case was that of an infant aged 2½ months, of group ON, whilst Moureau and Lambert's case was that of a man of group A,BN aged 35. Friedenreich intended to find out what became of the anti-M as the child grew up, but it died of an epidemic disease when 9 months old.

Serum obtained from M. W. four months after her confinement was tested against the red cells of 20 persons belonging to group O. Equal volumes of serum and cell suspension—about 5% whole blood, as judged by eye—were mixed in 2 in. by 1/4 in. precipitin tubes; readings were made after the tubes had stood at room temperature for two hours. Undoubted and clear-cut agglutination was found in 14 of the mixtures; in some the reactions were seen by the naked eye, in others by using a microscope (see Taylor, Race, Prior, and Ikin, 1942). The 14 lots of cells which were agglutinated all contained the agglutininogen M; 5 were OM and 9 OMN. On the whole the reactions given by the homozygous M cells were stronger than those given by the heterozygous MN cells. The 6 donors whose cells did not react belonged to group ON, and so lacked the antigen M. When the reactions given by a known and an unknown antibody and the same panel of red cells are identical the odds in favour of the two antibodies being the same can easily be calculated. The probability that the apparent identity of the two antibodies is due entirely to chance is given by the formula $\frac{a! b!}{n!}$,* where n is the number in the panel

and a and b the numbers of positive and negative reactors. Applying the present figures, we get $\frac{14! 6!}{20!}$, or $\frac{1}{38,760}$, as the probability that the identity of the results is due merely to chance; in other words, the odds in favour of the antibody in M. W.'s serum being anti-M are 38,759 to 1. After absorption of the serum in the cold with OM cells the reaction, both in the cold and at room temperature, disappeared, while absorption with ON cells did not remove the antibody.

Table showing Titration of Serum of M. W.

Temperature	Serum Dilution	Cells			M. W.
		OM	OMN	ON	
2° C.	1/1	V	++	—	—
	1/2	V	w	—	—
	1/4	++	—	—	—
	1/8	—	—	—	—
Room temp.	1/1	V	(+)	—	—
	1/2	++	—	—	—
	1/4	—	—	—	—
37° C.	1/1	—	—	—	—

No reaction is scored as negative without a microscopical examination; reactions weaker than V were determined with a microscope.

C=Clumps of cells in clear surrounding fluid visible to naked eye.

V=Somewhat weaker reaction, with clumps distinctly visible to naked eye, although surrounding fluid is not clear.

++=Very big clumps under microscope: +=not quite such big clumps; (+)=less than ++.

w=Definite weak reaction in which there is a uniform distribution of very small clumps of about 6 to 8 cells.

Titration of the antibody in M. W.'s serum, detailed in the Table, showed that it was most active in the cold, less active at room temperature, and undetectable at 37° C.; the homozygous M reacted better than the heterozygous MN cells.

* We are indebted to R. A. Fisher for this formula. (6!= "factorial six" = 6×5×4×3×2×1=720.)

This iso-agglutinin anti-M, like those described by Friedenreich and by Moureau and Lambert, had some of the characteristics of a cold agglutinin.

Both Friedenreich, and Moureau and Lambert, examined the relatives of their patients, but found no evidence that the occurrence of the iso-agglutinin anti-M was familial. M. W.'s father is dead and her mother and one sister are OMN; a second sister belongs to group ON, but anti-M has not been discovered in her serum. The husband of M. W. is OM and all their children will therefore be OMN. It might be suggested that the anti-M in M. W.'s serum resulted from the stimulus provided by the antigen M, present in the cells of all her foetuses, but there is no evidence to support this possibility. Her four pregnancies were: 1935, female, 6 lb., alive and well; 1937, male, 6 lb., alive and well; 1939, miscarriage, 3/12; 1941, female, premature, alive and well. No child has shown any signs of erythroblastosis foetalis. The anti-M was not the result of a previous transfusion, for none had been given.

Summary and Conclusions

Iso-agglutinin anti-M has been found in the serum of a woman as the result of tests made to obtain a suitable blood transfusion donor for her.

Although the occurrence of iso-agglutinin anti-M must be exceedingly rare, the case here reported shows that its presence may interfere with the selection of a suitable blood transfusion donor for a person in whose serum this antibody appears.

REFERENCES

- Friedenreich, V. (1937). *Z. Immunforsch.*, **91**, 485.
 Moureau, P., and Lambert, J. (1939a). *C. r. Soc. Biol.*, Paris, **131**, 148.
 — (1939b). *Ibid.*, **131**, 819.
 Taylor, G. L., Race, R. R., Prior, Aileen M., and Ikin, E. W. (1942). *J. Path. Bact.*, **54**, 81.
 Wiener, A. S. (1939). *Blood Groups and Blood Transfusion*, 2nd ed., p. 153, Baillière, Tindall and Cox, London.
 — (1941). *J. Immunol.*, **41**, 181.
 Wolff, E., and Jonnson, B. (1933). *Dtsch. Z. gerichtl. Med.*, **22**, 65.

FURTHER DATA CONCERNING HUMAN FERTILITY

BY

G. PUGH SMITH, B.Sc., Ph.D.

University College of South Wales and Monmouthshire, Cardiff

Recent contributions to knowledge concerning the period of ovulation and successful fertilization in the human female (Weinstock, 1934) have thrown some doubt upon the validity of Knaus's theory of the relation between the dates of ovulation and onset of menstruation, and upon the deductions which may be made concerning the existence and duration of a pre-menstrual "safe period." Data quoted by Pryde (1941) and by Fleck, Snedeker, and Rock (1940), however, tend, within limits, to substantiate Knaus's views. Further data given below support the following hypotheses: (i) if fertilization does not occur menstruation follows approximately 15 days after ovulation; (ii) within limits there is a "safe" or infertile period a few days before the onset of the next menstrual cycle; (iii) an average "safe period" can be predicted with fair accuracy by a sufficiently extended study of the individual's menstrual periodicity.

The Present Investigation

The data concern all the acts of uncontraceptive intercourse during 31 menstrual cycles after which pregnancy did not occur and one cycle which was followed, as intended, by pregnancy. Pregnancy intended in cycles 30 and 31 was not fulfilled owing to the intermittent absence of one partner. There were no other acts in which contraceptive methods were used. An accurate record was kept of the dates and duration of each cycle, and the dates on which intercourse took place. A table was drawn up with vertical columns for the individual days of a cycle, starting with the first day of menstruation, data for successive cycles being recorded horizontally (see Chart). As each cycle was completed the last day was marked, and also

the hypothetical day of ovulation, assuming it to be 15 days before the first day of the next cycle. A box was drawn round the supposed fertile period of each cycle, assuming it to be 3 days before and 1 day after the hypothetical day of ovulation: it was assumed that the maximum period for which spermatozoa were able to withstand the body temperature of 98.4° F. and still remain active enough to penetrate the ovum was 72 hours, and that the viability of the ovum after shedding was up to 48 hours. On these premisses the safe period for a 28-day cycle ran from the 16th day onwards. However, owing to variation in cycle length this assumption could not be applied as a generalization to all cycles. Therefore, before attempting uncontraceptive intercourse the variation in length of the menstrual cycle of the same partner was ascertained by recording the lengths of 21 successive cycles (Chart and Table I). It was decided that in her case, if Knaus's theory

TABLE I.—Duration of Cycles

Period	Duration (Days)													Total No. of Cycles
	25	26	27	28	29	30	31	32	33	34	35	36	37	
1937-8	1	1	2	9	1	4	2	0	0	1	0	0	0	21
1938-41	0	0	4	10	8	4	1	2	1	0	0	0	1	31
Total	1	1	6	19	9	8	3	2	1	1	0	0	1	52

was correct, and in spite of one longer cycle on June 27, 1937, a "safe period" would be assumed to run from the 20th day to the end of any cycle, and that intercourse before this and later than the 9th day would invite fertilization. Guided by this assumption, during a further 29 cycles sexual activity was largely avoided between the 9th and 20th days. On certain occasions this practice was deliberately discarded. As pre-

When predicting the fertile period of a given individual the most convenient way is to count from the beginning of a cycle. If, however, the dates of ovulation and onset of the following menses are more closely related than the date of the preceding menses is to ovulation, then, taking variation of cycle length into account, it is difficult to generalize by indicating the "safe period" in terms of the beginning of the cycle. When the data are arranged as tabulated by Pryde—i.e., assuming the fertile period always to occur from the 10th to 15th day of a cycle (Table II)—it will be seen that in the non-fertile cycles 1 to 31

TABLE II.—Distribution of Acts of Intercourse without Contraception, shown according to Date from Beginning of each Menstrual Cycle (cf. Pryde, 1941)

Day of Cycle	Total No. of Uncontraceptive Acts	
	Non-fertile Cycles 1-31	Fertile Cycle 32
1	0	0
2	0	0
3	0	0
4	0	0
5	0	0
6	0	0
7	0	0
8	4	0
9	2	1
10	3	1
11	1	0
12	1	0
13	1	1
14	0	2
15	1	1
16	0	1
17	0	0
18	1	0
19	5	0
20	16	0
21	11	0
22	16	0
23	12	0
24	10	0
25	8	0
26	8	0
27	12	0
28	8	0
29	6	0
30	4	0
31	1	0
32	1	0
33	1	0
34	0	0
35	0	0
36	0	0
37	0	0

there was intercourse on some of the days of this very period, although it happens that in cycle 32, which was followed by pregnancy, there was intercourse on all days of the fertile period except the 12th.

Time Relation between Menstruation and Ovulation

However, in considering the period of fertility in the light of Knaus's views—i.e., the relation between the onset of menstruation and the number of days prior to it when ovulation occurs—it is more appropriate, in arranging the data, to relate the date of intercourse to the date of onset of the following cycle (Table III).

The data in the Chart and Table III show that in this particular case during 31 cycles there was a period of infertility up to a maximum of 13 days before the onset of the next menstrual cycle. The Chart and Table II show that the assumption that this infertile period ran from at least the 20th day of any cycle was fairly well justified. In view of the longer cycle beginning on March 23, 1940, the 21st day onwards was temporarily resorted to as being safer for uncontraceptive intercourse, although the unexpected abnormally long cycle beginning on August 19, 1940, would suggest that the 25th day was more appropriate. The occurrence of such a long cycle after a succession of shorter ones may explain the failure of some predictions of infertile periods (Fleck *et al.*). In spite of this "escape," however, in the case cited, the 20th day was again assumed to be the beginning of the infertile period. It is unfortunate that there is no record whether any ailment (cold, etc.) occurred during the early part of the cycle beginning on August 19, 1940, that might be considered a possible factor in the postponement of ovulation.

Chart showing distribution of uncontraceptive acts of intercourse throughout 32 menstrual cycles, the variation in length of which and of 21 other cycles is illustrated. The narrower assumed limits of the fertile period in each cycle are also shown.

viously stated, sexual activity in cycles 30 and 31 was intended to fall within the hypothetical fertile period, but this arrangement was not fulfilled. In cycle 32, however, pregnancy ensued. The details are shown graphically in the Chart.

From Table II it is clear that in the 32nd (fertile) cycle fertilization occurred between the 9th and 16th days.

The foregoing conclusions depend upon the assumption that, throughout, the spermatozoa were capable of fertilizing. There was a long period of abstinence from regular sexual activity

TABLE III.—*Distribution of Acts of Uncontraceptive Intercourse shown on Days before the Onset of the Next Cycle*

Days before Next Cycle started	Total No. of Uncontraceptive Acts	
	Non-fertile Cycles 1-29, 31	Non-fertile Cycle 30
25	1	
24	0	
23	0	
22	3	
21	2	1
20	0	0
19	1	1
Assumed fertile period (narrower limits)	0	1
	1	1
	0	1
	0	0
	0	1
18	3	0
17	3	0
16	4	0
15	16	0
14	9	0
13	14	0
12	11	0
11	9	1
10	11	1
9	9	1
8	11	1
7	9	1
6	10	1
5	11	0
4	6	0
3		
2		
1		
Menstruation begins		

between the onset of menstruation and the 20th day of each cycle. Both partners were young and healthy, and in a good state of nutritional well-being.

Summary

Data are given showing the variation of 52 menstrual cycles in the same individual, and the relation between an assumed fertile period and the beginning and end of each cycle.

Ovulation is assumed to occur 15 days before the onset of the following menses.

Records of uncontraceptive intercourse during 31 infertile cycles show that there were occasions when intercourse took place as much as 13 days before the beginning of the next cycle without ensuing pregnancy. Intercourse was most frequent up to 10 days before the next cycle without pregnancy resulting.

Intercourse which took place on the 9th, 10th, and 13th to 16th days after the beginning of a cycle was followed by pregnancy.

It is concluded that prediction of the narrower limits of the fertile period of an individual can only be made by counting back from the beginning of the next cycle.

Only the wider limits of the fertile period may be predicted by counting from the beginning of the same cycle, requiring a knowledge of the variation of menstrual periodicity.

REFERENCES

- Fleck, S., Snedeker, E. F., and Rock, J. (1940). *New Engl. J. Med.*, **223**, 1005 (cf. *British Medical Journal*, 1941, **2**, 23).
 Pryde, J. (1941). *British Medical Journal*, **1**, 12.
 Weinstock, F. (1934). *Zbl. Gynäk.*, **58**, 2947.

W. M. Fowler and Adelaide P. Barer (*J. Amer. med. Ass.*, 1942, **115**, 421), investigating the rate of regeneration of haemoglobin in blood donors, found that the average drop in blood haemoglobin was 2.3 g. after the removal of 555 c.cm. of blood, and that the average time needed to replace this amount of haemoglobin was 49.6 days. Longer recovery periods were associated with a steeper fall in haemoglobin and could not be correlated with initial blood haemoglobin values. Hb was regenerated in man at the rate of 0.049 g. per 100 c.cm. of blood a day, and in women at the rate of 0.040 g. The administration of 1 g. of iron and ammonium citrates a day increased the daily haemoglobin regeneration by 49% and shortened the recovery period from 49.6 to 35.2 days. This was noticed during the first period, but the effect after subsequent blood donations became progressively less. If the haemoglobin of the donor is not regularly estimated the authors consider that three months should be allowed between donations.

Medical Memoranda

Scabies in an Army Unit

It has been held that blankets and clothing play an important part in the spread of scabies in the Army. Mellanby (1941a), on the other hand, from recent experiments with volunteers and other considerations, believed that fomites are unimportant in the transmission of scabies, and that many cases are acquired on leave, from wife or child.

The following is an account of 39 cases seen in one unit during 7 months. Of these, 36 were carefully investigated in an attempt to find out how the disease was acquired. The number of cases is small, but the series is thought to be interesting in that the conditions in the unit remained unchanged during the period and the circumstances were such that men rarely slept out except when they returned home on privilege leave. Week-end leave did not complicate the picture.

THE INVESTIGATION

Our methods of control consisted of monthly skin inspections of the whole unit, inspection of each man when he returned from leave, and the immediate hospital treatment of each case when detected, together with disinfection of bedding and clothing. When a man reported sick with scabies he was questioned as to possible contact with other cases both within and outside his unit, as to the date when he last returned from leave, whether he was married or single, about children, and as to the whereabouts of his home. Little evidence was obtained of spread within the unit by means of blankets. In only 2 cases was there any connexion with another case within the unit (i.e., sleeping in the same hut or guard-room). In several cases it was evident that scabies had been present for at least 14 days before being detected, and yet skin inspection of other men of the hut failed to disclose further cases. The cases occurred at an even rate throughout the 7 months; there were no little epidemics confined to one hut or one company such as readily occur in pediculosis, which is undoubtedly spread by fomites.

Direct evidence of scabies acquired on leave was difficult to obtain. To contract scabies is considered by the men to be a disgrace, and as they are not willing to admit that their families could have the disease, great tact is necessary in questioning them. In 5 instances, however, clear evidence that there was scabies at home was obtained. It was found that out of the 36 cases 14 (39%) developed the condition within a week, 2 (5.5%) within 2 weeks, and 5 (14%) within 3 weeks of returning from leave. Thus 58.5% developed scabies within 3 weeks of returning. The leave rate during this time was about 6.4% a week, so in a normal group of men only 19% could have been expected to return from leave within 3 weeks. If Mellanby's views are correct a higher proportion of married men in the series was to be expected: actually it was found that 74% were married. In a control group of men from the unit only 51% were married. The towns where the men had been on leave were those of the industrial North and Midlands. No particular town was found to be associated with an undue proportion of these cases.

Mellanby (1941b) estimated the incidence of scabies in the general population as about 25 per 1,000. In the period under review there were 39 cases, and 1,700 men went on leave and were in contact with their homes. If 60% of cases are due to infection from home then a rough approximation of a scabies incidence in the general population of 16 per 1,000 is arrived at. If it is believed that a higher proportion than 60% are infected at home, then the figures rise to 23 per 1,000. When, therefore, the incidence of scabies in the unit is compared with Mellanby's figures for the general population it is not inconsistent to hold the view that the majority of cases were infected on leave.

CONCLUSION

Consideration of the cases of scabies occurring in an Army unit over a period of 7 months suggested that the majority of these men were infected from their homes while on leave. It would seem that blankets and clothes do not play a large part in transmission, and that fairly prolonged and intimate contact with another case is necessary to acquire the disease. The disease cannot be reduced much further in the Army at home until the problem of civilian scabies is vigorously tackled.

P. N. COLEMAN,
Captain, R.A.M.C.

REFERENCES

- Mellanby, K. (1941a). *British Medical Journal*, **2**, 405.
 — (1941b). *Med. Off.*, **66**, 141.