I hope what I have said about the Aberdeen report will show that, although it adds little to our knowledge of the causes of maternal mortality, it is yet of great interest and does a great deal to indicate the direction along which further inquiries may usefully proceed. We do not know what are the intentions of the Ministry of Health with regard to the English report; we may get a series of reports from different centres, or we may have to await the preparation of a national report. The work will occupy many years, and I am sure we shall be prepared to do everything we can to assist the investigators in their tremendous task, realizing how urgently necessary it is in the national interest to reduce our terrible wastage of maternal life.

A Study

OF

THE BACTERICIDAL POWER OF THE BLOOD DURING PREGNANCY AND THE PUERPERIUM, AND ITS RELATIONSHIP TO THE DEVELOPMENT AND COURSE OF PUERPERAL INFECTION.*

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THE introduction of pyogenic organisms into the reproductive tract, with or without trauma as an important contributory agency, is recognized as the commonest and most important factor in the causation of puerperal infection. While this is so, the anomalous nature of its incidence is a commonplace attribute of this disease; the occasional appearance of infection in a case in which delivery has been spontaneous and even free from examination, and on the other hand its failure to develop where trauma and manipulation have made its occurrence probable, constitute a paradox with which everyone engaged in midwifery practice is familiar.

A partial explanation of this phenomenon was suggested by those workers who investigated the cervical and vaginal flora during pregnancy and attempted to relate the occasional unexpected development of sepsis to a pre-existing infective condition of the genital passages. The recent observations of Burt-White and Armstrong,¹ however, would appear to call into question the validity of the conclusions offered by previous observers. Burt-White and Armstrong examined the cervical flora in 55 pregnant women; in 40 per cent. of these cases streptococci of different types were isolated, but in only one did the strain present the characters of the *Streptococcus pyogenes*, the common cause of puerperal fever; they report, moreover, 15 cases of pregnant women whose cervixes harboured haemolytic streptococci, including *Streptococcus pyogenes*, and in none did sepsis occur. These workers conclude that "the presence of the haemolytic streptococcus in the reproductive tract does not necessarily give rise to sepsis in the puerperium," and state further that their results appear "to support definitely an exogenous origin for infection in puerperal sepsis, while leaving unexplained those rare cases of sepsis in which there has been no manipulation during pregnancy or labour." A similar conclusion is suggested by a study of the epidemics of puerperal sepsis with which hospitals in pre-Listerian days were ravaged, and Young² instances in this connexion the long intervals of freedom from fatal sepsis in support of the view that, as compared with trauma and contagion, autogenous infection must at best play a minor part in the etiology of the disease.

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Bacteriological and clinical evidence seems accordingly to warrant the inference that puerperal sepsis can rarely be explained on the basis of an endogenous infection. It appeared to us possible, however, that the occurrence of sepsis in cases in which there has been a minimum of interference might be related to an abnormally low degree of resistance on the part of the individual; a variation in susceptibility of this nature would readily explain the capricious distribution of puerperal sepsis—for example, in the lying-in wards of a maternity hospital.

To test the validity of this hypothesis it was decided to examine the bactericidal and bacteriostatic* power of the blood in a large series of pregnant and parturient women. Coincidentally with this larger investigation the skin sensitiveness to streptococcal toxin was examined in a small number of those women in whom at the same time the bactericidal power of the blood was tested. The toxin employed in the test of skin sensitiveness was isolated from a culture of a haemolytic streptococcus found in the blood of a woman suffering from puerperal sepsis and was prepared by the method described by Lash and Kaplan.³

For two reasons it was decided not to persevere with the examination of skin sensitiveness as a method of determining individual susceptibility to infection. In the first place, in those cases in which this reaction was tested no relationship was observed between the type of reaction and the incidence of pyrexia in the puerperium. Of the 49 women tested, 10 were toxin-sensitive, while 39 did not react; among the positive reactors the puerperium was morbid in two cases, in one of which delivery was effected by forceps; of the non-reactors six women, one of whom was delivered by forceps, experienced morbid puerperia. The inconsistent character of these results is disappointing in view of the observations of Burt-White,⁴ who found a morbidity rate of 30 per cent. in women who reacted positively to streptococcal toxin. It should be mentioned, however, that Burt-White employed scarlatina toxin and that his investigation was on a scale considerably larger than that here reported. In those cases in which the two tests above referred to were carried out it was found that one had no relationship to the other, the bactericidal power of the blood being in point of fact higher as a rule in those cases in which the skin reaction was positive than in those in which it was negative.

In the second place, although a negative skin reaction of the type referred to may indicate that the patient possesses antitoxic substances to streptococcal toxin, it is probably not in the same sense a measure of resistance on the part of the individual to the important locally invasive as distinct from the toxin-producing property of the organism, a property which, from anatomical considerations, is of special importance in puerperal sepsis. In the expectation that such resistance to organismal invasion might possibly be related to the bactericidal activity of the blood, we decided to employ this test in our investigation, and were influenced further in our choice by its non-specific character (see Table II), and its applicability, therefore, to forms of infection other than streptococcal.

The method employed in the examination of bactericidal and bacteriostatic power was that described by Wright, Colebrook, and Storer,⁵ and consists essentially in mixing whole blood with a known quantity of bacteria on "slide cells," the bactericidal power being gauged by the number of colonies which develop after incubation for twenty-four hours.

One disadvantage of this method may be mentioned: in an investigation of this kind a very large number of individual observations is required to provide the necessary data. This is so in the first place because of the technical impossibility of preparing for the purposes of a series of tests, carried out at different times, inocula each of exactly the same uniform density, with the result that a direct comparison is possible only between units of a group each member of which has been tested with the same inoculum, and not between units of different groups in

* The term "bacteriostatic" implies inhibition of bacterial growth. Wright⁵ has interpreted the results obtained by the method which he originally described as due to a "bactericidal" action; it seems possible that growth inhibition may also be an important factor, but while recognizing this we have in this paper employed the term "bactericidal," as originally used by Wright.

which different inocula may have been employed.* Furthermore, as the subjoined table shows, after blood has been drawn off it loses, at first slowly, then more rapidly, its bactericidal property.

Blood was withdrawn from the same individual at the same time each day on four successive days; on the fourth day all the samples were tested together, approximately 80 organisms being implanted in each sample.

TABLE I.

The number of colonies which grew in—				
Blood tested as soon as withdrawn	...	...	...	= 5
Blood kept for one day	...	...	...	= 18
Blood kept for two days	...	...	...	= 38
Blood kept for three days	...	...	...	= 68

Because of this deterioration in the bactericidal power of the blood on keeping it is possible only to compare the results in a group of samples of blood withdrawn at approximately the same time. Each group has to be investigated at once and considered individually. In practice it was found convenient to examine at one time a group of six samples of blood all withdrawn simultaneously and all tested with one inoculum of uniform density.

Before presenting the results of our investigation two further preliminary observations may be made: (1) Little or no variation has been observed in the bactericidal power of the blood of a healthy individual from hour to hour, or from day to day; this finding is not in keeping with the observation of Alston⁷ that a diurnal variation in bactericidal activity occurs. (2) In the majority of our observations a twenty-four-hour broth culture of *Staphylococcus aureus*, dilution 1 in 5,000, was employed; the non-specific character of the test, however, is illustrated in Table II.

TABLE II.

Patient.	Twenty-four-hours broth culture <i>Staph. aureus</i> , dilution 1 in 5,000: viable organisms introduced estimated to be 88.					Streptococcus (haemolytic type), dilution 1 in 5,000: viable organisms introduced estimated to be 176.				
	Slide Cells.				Average No. of Colonies.	Slide Cells.				Average No. of Colonies.
	(1)	(2)	(3)	(4)		(1)	(2)	(3)	(4)	
1	18:	17:	16:	13	15	30:	42:	35:	32:	35
2	25:	24:	20:	26:	21	43:	64:	65:	67:	61
3	25:	30:	21:	24:	25	47:	70:	53:	65:	59
4	34:	25:	34:	34:	32	74:	87:	61:	65:	72

In all, the bactericidal power of the blood of 396 individuals was examined; as each sample of blood was incubated with organisms in four separate "slide cells," and each of these four subdivisions individually examined, a total of approximately 1,600 clinical experiments was performed.

The first series of experiments was undertaken to determine whether or not such individual variation in bactericidal activity as might exist could be related to the incidence of pyrexia in the puerperium. This series comprised 229 healthy individuals, all of whom experienced spontaneous, uncomplicated labours, blood being withdrawn at or about the time of delivery. There were in this group 17 women who subsequently experienced febrile puerperia due to pelvic infection. An analysis of these cases shows that in 14 of them the degree of bactericidal power in the patient who subsequently developed sepsis was lower than the average bactericidal power of the other members of the respective groups, while in 3 cases it was higher. These findings appear to us of such importance that we include a short summary of the cases herewith.

Brief Notes of 17 Women who, subsequent to Delivery, Experienced Morbid Puerperia.

Case 30.—Spontaneous delivery; mild sepsis; one vaginal examination; blood withdrawn 5 hours after delivery; colonies = 82; average number of colonies in group = 54.

Case 14.—Spontaneous delivery; severe sepsis; blood withdrawn 6 hours before delivery; colonies = 90; average number of colonies in group = 55.

Case 3.—Spontaneous delivery; mild sepsis; blood withdrawn 24 hours after delivery; colonies = 22; average number of colonies per group = 17.

Case 27.—Spontaneous delivery, mild sepsis, blood withdrawn one hour after delivery; colonies = 2; average number of colonies in group = 6.

Case 54.—Spontaneous delivery; one vaginal examination; severe sepsis; blood withdrawn 6 hours before delivery; colonies = 27; average number of colonies in group = 6.

Case 50.—Spontaneous delivery; one vaginal examination; mild sepsis; blood withdrawn 6 hours before delivery; colonies = 50; average = 24.

Case 93.—Spontaneous delivery; one vaginal examination, died from acute streptococcal septicaemia 7 days after delivery; blood withdrawn 10 hours after delivery; colonies = 60; average = 19.

Case 175.—Spontaneous delivery; mild sepsis; blood withdrawn 7 days before labour; colonies = 12; average = 5.

Case 145.—Spontaneous delivery; two vaginal examinations; mild sepsis; blood withdrawn one hour after delivery; colonies = 3; average = 6.

Case 129.—Spontaneous delivery; one vaginal examination; mild sepsis; blood withdrawn one hour before delivery; colonies = 12; average = 5.

Case 121.—Spontaneous delivery; one vaginal examination; mild sepsis; blood withdrawn at onset of labour; colonies = 7; average = 3.

Case 100.—Spontaneous delivery; one vaginal examination; died of acute streptococcal septicaemia; blood withdrawn 20 hours after delivery; colonies = 10; average = 17.

Case 224.—Spontaneous delivery; no vaginal examination; mild sepsis; blood withdrawn 10 hours after delivery; colonies = 21; average = 17.

Case 193.—Spontaneous delivery; three vaginal examinations; severe sepsis; blood withdrawn 5 days before labour; colonies = 52; average = 37.

Case 357.—Spontaneous delivery; four vaginal examinations; mild sepsis; blood withdrawn one week before labour; colonies = 113; average = 70.

Case 297.—Spontaneous delivery; three vaginal examinations; severe sepsis; blood withdrawn at onset of labour; colonies = 14; average = 5.

Case 248.—Spontaneous delivery; three vaginal examinations; mild sepsis; blood withdrawn 12 hours after delivery; colonies = 70; average = 45.

A further investigation, complementary to that just described, was concerned with cases in which labour had been seriously complicated and in which, from the amount of interference and extent of trauma, it appeared probable that serious sepsis would develop. Twelve such cases were investigated, each potentially septic case being as far as practicable grouped along with women who had experienced normal labours, the latter constituting a control by which the degree of bactericidal power might be compared. In each of the twelve cases referred to the blood in one of the four "slide cells" was not inoculated, so that should the blood already contain organisms their presence might in this way be detected and a source of fallacy be excluded. In none of the twelve cases examined, however, was any organismal growth obtained in the "slide cells" which were left unimplanted as described.

In eight of the twelve groups investigated the bactericidal power of the potentially septic case was above the average of that of the other members of the respective groups; all of these patients recovered, and in two cases (*vide infra*, Cases 313 and 201) in which there had been extensive trauma and contamination the puerperium was afebrile. In one case no difference was noted in the degree of bactericidal power of the "suspect" as compared with the others; this patient recovered. In three cases the bactericidal power of the potentially septic patients was lower than the average; two of these patients died.

Short Notes on the 12 Cases referred to above.

Case 49.—Labour 60 hours; numerous vaginal examinations; difficult forceps delivery; mild sepsis; recovery; blood withdrawn 9 hours before delivery; colonies = 10; average = 30.

Case 215.—Labour 28 hours; numerous vaginal examinations; difficult forceps delivery; traumatic post-partum haemorrhage; primary cervical repair; mild sepsis; recovery; blood withdrawn 2 hours before delivery; colonies = 6; average = 35.

Case 94.—Labour 36 hours; numerous vaginal examinations; difficult forceps delivery; mild sepsis; recovery; blood withdrawn 12 hours after delivery; colonies = 8; average = 19.

Case 318.—Labour 28 hours; unsuccessful forceps outside; craniotomy; extensive laceration; severe sepsis; recovery; blood withdrawn 2 hours before delivery; colonies = 2; average = 13.

Case 320.—Labour 55 hours; numerous vaginal examinations; forceps delivery; mild sepsis; recovery; blood withdrawn 2 hours before delivery; colonies = 2; average = 13.

Case 313.—Labour 28 hours; unsuccessful forceps outside; forceps delivery; extensive laceration; normal puerperium; blood withdrawn 12 hours after delivery; colonies—no growth; average = 14.

Case 164.—Shoulder presentation; early rupture of membranes; labour 60 hours; ineffectual attempts to deliver outside; Caesarean hysterectomy; clinically very bad prognosis; cellulitis; recovery; blood withdrawn immediately before operation; colonies = 5; average = 16.

Case 201.—Labour 20 hours; unsuccessful forceps outside; spontaneous delivery in hospital; extensive laceration; normal puerperium; blood withdrawn 36 hours after delivery; colonies = 33; average = 49.

Case 81.—Labour 40 hours; unsuccessful forceps outside; spontaneous delivery in hospital; normal puerperium; blood withdrawn 21 hours after delivery; colonies = 22; average = 22.

Case 23.—Labour 31 hours; unsuccessful forceps outside; forceps delivery; severe sepsis; recovery; blood withdrawn 18 hours after delivery; colonies = 16; average = 12.

Case 289.—Labour 14 hours; unsuccessful forceps outside; craniotomy; death from streptococcal septicaemia 14 days after delivery; blood withdrawn 60 hours after delivery; colonies = 32; average = 10.

Case 92.—Difficult forceps delivery outside; post-partum eclampsia; death from streptococcal septicaemia 4 days after delivery; blood withdrawn 30 hours after delivery; colonies = 32; average = 7.

There were in these two series of observations, comprising a total of 29 cases, 7 cases (Nos. 3 and 100 in the first series, and the last five cases in the second) in which blood was withdrawn for examination more than twelve hours after delivery; the findings in these cases must on that account be interpreted with caution as representing the primary degree of haemo-bactericidal power possessed by the individual. With these exceptions, however, the investigation was made either before delivery or so soon afterwards as probably to anticipate any serious modification in antibacterial activity which might result from the introduction of infection. The data obtained appear to show with considerable conclusiveness that the degree of resisting power to infection, as measured in this way, has an important influence on the subsequent development and course of puerperal sepsis.

The variation in degree of antibacterial power which the above investigation disclosed led naturally to an effort to determine the factors on which this variability might depend. The next series of experiments accordingly was undertaken to determine (1) whether or not the degree of bactericidal power varied as between pregnant and non-pregnant individuals; (2) whether the bactericidal power during pregnancy was within limits constant or was influenced by the stage of gestation reached; and (3) the influence on bactericidal power of multiparity as compared with nulliparity or primiparity, and of such conditions as albuminuria, prolonged labour, instrumental delivery, and severe blood loss.

I. A COMPARISON OF THE BACTERICIDAL POWER OF THE BLOOD IN PREGNANT AND NON-PREGNANT INDIVIDUALS* (see Chart 1).

A series of observations was made in which the blood of healthy non-pregnant individuals was compared with that of women at or about the sixth month of pregnancy, at the

CHART 1.

* The possibility that pregnancy might confer an enhanced degree of bactericidal power was suggested by a chance observation that in one of a group of six women investigated in the ante-natal out-patient department of the Royal Maternity Hospital the bactericidal power of the blood was markedly lower than that of the other women whose blood was tested at the same time; subsequent examination showed that in this individual the abdominal enlargement was due to an ovarian tumour and not to pregnancy.

end of the eighth month of pregnancy, at the time of delivery, and at ten days, at six weeks, and at twelve weeks after delivery. The following results were obtained:

A. Comparison of Non-pregnant Women and Women at or about the Sixth Month of Pregnancy.—Three groups of cases were investigated, each containing three non-pregnant and three pregnant individuals. In each of the three groups the average bactericidal power of the pregnant exceeded that of the non-pregnant women. The combined ratio, pregnant to non-pregnant, expressed in terms of the colonies which formed after incubation, was approximately as 74 to 100. The method of calculation is shown in the following table.

TABLE III.

Case	Group I.	Group II.	Group III.
	Average No. of Colonies.	Average No. of Colonies.	Average No. of Colonies.
1	Pregnant ... 8	38	27
2	" ... 6	28	17
3	" ... 5	30	25
	60	80	82
4	Non-pregnant ... 7	32	18
5	" ... 10	40	31
6	" ... 14	38	28
	100	100	100

$$\text{Combined group ratio, pregnant to non-pregnant} = \frac{60}{100} + \frac{80}{100} + \frac{82}{100} = \frac{74}{100}$$

As the number of organisms introduced was not constant for each group this figure represents an approximate and qualitative rather than an exact mathematical ratio.

B. Comparison of Non-pregnant Women and Women at End of the Eighth Month of Pregnancy.—Six groups of cases were investigated, each group containing two or more non-pregnant and two or more pregnant individuals. In four groups the average bactericidal power of the pregnant exceeded that of the non-pregnant; in one group no difference was found, and in one group the bactericidal power of the non-pregnant women was the higher. The combined ratio, pregnant to non-pregnant, expressed in terms of colonies, was approximately as 69 to 100.

*C. Comparison of Non-pregnant Women and Women in Labour or Shortly after Delivery at Term.**—Seven groups of cases were investigated, each group containing two or more pregnant and two or more non-pregnant individuals. In six groups the average bactericidal power of the parturient individuals exceeded that of the non-pregnant, while in one group no appreciable difference was found. The combined ratio, parturient to non-pregnant, expressed in terms of colonies, was approximately as 46 to 100.

D. Comparison of Non-pregnant Women and Women Ten Days after Delivery at Term.—Four groups of cases were investigated. In two groups the bactericidal power of the puerperal women exceeded that of the non-pregnant, while in two groups the reverse obtained. In none of the four groups was the difference marked, the combined ratio, puerperal to non-pregnant, expressed in terms of colonies, being approximately as 110 to 100.

E. Comparison of Non-pregnant Women and Women Six Weeks after Delivery.—Three groups of cases were investigated. In all three groups the bactericidal power of the late puerperal individuals slightly exceeded that of the others. The combined ratio, late puerperal to non-pregnant, expressed in terms of colonies, was approximately as 89 to 100.

F. Comparison of Non-pregnant Women and Women Twelve Weeks after Delivery.—In three groups of cases investigated no appreciable difference was observed in the bactericidal power of the one as compared with the other.

II. THE BACTERICIDAL POWER OF THE BLOOD AT DIFFERENT STAGES OF PREGNANCY (see Chart 2).

A complementary series of observations was made in which the blood of healthy parturient women, in labour or immediately after delivery, was compared with that of non-pregnant women and of women at or about the sixth month of pregnancy, the end of the eighth month, and at ten days, at six weeks, and at twelve weeks after delivery.

A. Comparison of Women at Full Term and Non-pregnant Women.—This group has already been considered (*vide supra*, C).

* So far as our observations go, the effect of spontaneous uncomplicated labour on bactericidal activity is inconsiderable. The bactericidal power of fifteen healthy women at the commencement of labour was contrasted with that of a similar number at its conclusion; it was found that at the commencement of labour colonies were more numerous in eight and less numerous in six than at the time of delivery, while in one case no difference was observed. There is thus apparently a slight increase in bactericidal activity at the time of delivery as compared with the onset of labour, but the difference is not pronounced.

B. Comparison of Women at Full Term and at the Sixth Month of Pregnancy.—Three groups of cases were investigated, each containing three women at full term and three at or about the sixth month of pregnancy. In each of the three groups the bactericidal power of the former exceeded that of the latter. The combined ratio, expressed in terms of colonies, six months to full term, was approximately 160 to 100.

CHART 2.

C. Comparison of Women at Full Term and at End of Eighth Month of Pregnancy.—Seven groups of cases were investigated. In each of the seven groups the bactericidal power at full term exceeded that at the end of the eighth month; the combined ratio, expressed in terms of colonies, eighth month to full term, being approximately as 150 to 100.

D. Comparison of Women at Full Term and at the Tenth Day after Delivery.—Five groups of cases were investigated. In three groups the bactericidal power of the blood of women at full term considerably exceeded that of women ten days after delivery, while in two groups no appreciable difference was observed. The combined ratio, expressed in terms of colonies, ten days post partum to full term, was approximately as 184 to 100.

E. Comparison of Women at Full Term and at the Sixth Week after Delivery.—Three groups of cases were investigated. In two groups the bactericidal power at full term exceeded that of the late puerperium, while in one no appreciable difference was observed. The combined ratio, expressed in terms of colonies, six weeks post partum to full term, was as 143 to 100.

F. Comparison of Blood of Women at Full Term and at the Twelfth Week after Delivery.—Three groups of cases were investigated. The combined ratio, expressed in terms of colonies, twelve weeks post partum to full term, was as 175 to 100.

So far it is evident that in both pregnant and non-pregnant individuals there is considerable variation in the degree of bactericidal activity which the individual possesses. This variation is more marked during pregnancy and has a definite relationship to the period of gestation which has been reached. There appears to be a gradual increase in bactericidal activity as pregnancy advances which reaches its maximum at or about the full term of pregnancy. After labour there is a rapid decline in bactericidal power, the curve (see Charts 1 and 2) falling sharply, so that about the tenth day of the puerperium it reaches the non-pregnant level; thereafter there is a further temporary increase, which has disappeared by the twelfth week after parturition. In contrast to the views expressed by Bonney,⁸ Douglas,⁹ and others, a woman at the time of delivery appears to possess a degree of resisting power to infection considerably in excess of that of the non-pregnant individual. During the days which immediately follow delivery there is, however, a relative "negative phase" which may have an important application in the light of the serious character which a puerperal infection is liable to assume.

III. THE INFLUENCE ON BACTERICIDAL POWER OF PARITY AND OF SUCH CONDITIONS AS ALBUMINURIA, PROLONGED LABOUR, INSTRUMENTAL DELIVERY, AND SEVERE LOSS OF BLOOD.

1. Parity.—So far as our observations go, there appears to be no difference in the degree of bactericidal power possessed by the parous as compared with the nulliparous non-pregnant individual; nor have we found any difference in this respect between the primigravida and the multigravida woman. In thirty-six groups of cases which were investigated it was found that the colonies which formed in the blood of primi-

gravidae were more numerous than those in the blood of multigravidae in ten groups and less numerous in eleven, while in fifteen groups no appreciable difference was observed. The more frequent occurrence of sepsis in primiparae than in multiparae is probably to be explained by the greater difficulty which generally attends a first labour rather than by any difference in resisting power to infection which the one class possesses as compared with the other.

2. Albuminuria.—The increased liability to infection which appears clinically to be associated with albuminuria and eclampsia prompted an investigation into the influence which this complication of pregnancy might exert on the bactericidal activity of the individual. In sixteen groups of cases the blood of a patient suffering from albuminuria or eclampsia was compared with that of healthy women advanced to the same stage of pregnancy; in eleven cases the bactericidal power of the albuminuric individual was below and in four cases above that of the others, while in one case no difference was observed. It would appear, accordingly, that albuminuric toxæmia tends to depress the resisting power to infection as measured in this way.

3. Duration of Labour.—In thirty groups of cases the bactericidal power of the blood was investigated in relation to the duration of labour, blood being withdrawn for examination at or about the time of delivery. For the purposes of analysis cases of difficult instrumental delivery were excluded. In each group the average duration of labour in the six cases making up the group was ascertained: the blood of those in whom the duration of labour exceeded the average was then compared with that of those in whom it was shorter than the average. In nineteen groups the bactericidal power was poorer in those women who had relatively long labours, in six groups the reverse obtained, while in the remaining five groups no appreciable difference was observed.

4. Instrumental Delivery.—In twelve groups of cases an attempt was made to determine the effect of instrumental delivery on the bactericidal power of the blood. Each group contained one or more cases in which the patient had been delivered by forceps, and in addition, for purposes of comparison, two or more cases in which delivery had been spontaneous. So far as was practicable blood was withdrawn within a few hours of delivery so as to minimize any modification in the bactericidal activity of the blood which might result from the introduction of infection. In ten of the twelve groups analysed it was found that the bactericidal power of those women who had been delivered by forceps was poorer than that of those delivered spontaneously, while in the remaining two groups this finding was reversed.

The above analysis of the effect of prolonged labour and of instrumental delivery (3 and 4) does not take into account the influence of such associated factors as fatigue, anaesthesia, or incidental obstetric complications, the effect of which it is difficult to appraise. It is illogical, accordingly, to interpret the findings just quoted as indicating that the resisting power to infection is necessarily affected either by the number of hours which a woman may pass in labour or by the forceps operation as such. All that seems reasonable to assume is that, apart from any question of the introduction of infection, a labour which is short and spontaneous will in general tend to react less injuriously on bactericidal activity than one which is tedious and instrumental.

5. Severe Blood Loss.—The number of cases in which it was possible to estimate the effect of severe blood loss on bactericidal power was restricted by the difficulty of excluding extraneous and, for the purposes of analysis, confusing factors in such conditions as ante-partum and post-partum haemorrhage, in which measures employed for the control of bleeding may of themselves modify bactericidal activity. So far, however, as an analysis has been possible it has conveyed the impression that with severe loss of blood a lowering of bactericidal power occurs.

RELATIONSHIP OF BACTERICIDAL ACTIVITY TO THE BLOOD ELEMENTS AND IN PARTICULAR TO THE LEUCOCYTE COUNT.

The observations of Payer,¹⁰ Dietrich,¹¹ and others have shown that during pregnancy an increasing leucocytosis occurs, which reaches its maximum at the time of delivery and thereafter rapidly subsides. It was decided, accordingly, to examine the extent to which the modification in antibacterial activity which we have described could be related to the changes which occur in the blood elements, and in particular to the numerical increase in the white cells.

In this part of our investigation two lines of inquiry were followed. In the first place a series of observations was made of the blood picture of healthy women at the same stages of pregnancy and the puerperium as those at which the bactericidal power of the blood had been examined, so that a broad comparison might be made of the changes which take place in the blood elements and those which concurrently affect bactericidal activity as the result of pregnancy. In the second place, in a series of cases the bactericidal activity of the blood and the blood picture were simultaneously studied and directly compared. It may be said at once that no relationship was found to exist between the degree of bactericidal power and the number of red blood cells, the percentage of haemoglobin, or the colour index.

I. The leucocyte count was examined in 84 cases, observations being made at each of the following seven periods of pregnancy and the puerperium: during the sixth month of pregnancy; at the end of the eighth month; at or near the commencement of labour; shortly after the completion of delivery; and at ten days, at six weeks, and at twelve weeks after delivery. The series does not include any case in which infective conditions or other complications might have altered the blood picture. The findings are summarized in the following table and represented graphically in Chart 3.

TABLE IV.

Stage of Pregnancy or Puerperium.	No. of Cases Examined.	Average Leucocyte Count.
During sixth month ...	9	8,200
End of eighth month ...	13	9,100
Commencement of labour ...	15	10,200
Within twelve hours of delivery ...	17	16,600
Ten days after labour ...	14	9,200
Six weeks after labour ...	10	7,800
Three months after labour ...	8	8,000

CHART 3.

A comparison of Charts 1 and 3, which represent respectively the average degree of bactericidal activity and of leucocytosis at the same periods of pregnancy and the puerperium, shows a broad qualitative similarity between the two curves, to which reference will presently be made.

II. Forty-five cases were studied in which the bactericidal power of the blood and the leucocytic count were simultaneously examined. Each of these cases formed one of a group of three or more healthy women of the same period of pregnancy whose bactericidal power was known and served as a control for purposes of comparison. The result of this investigation may be summarized as follows:

(1) Leucocyte count under 6,000; number of cases studied=9. In 5 of these cases the bactericidal power was below and in 4 cases above the group average. In terms of the colonies which formed, the average bactericidal power, compared to that of the other women in the respective groups, was approximately as 120 to 100.

(2) Leucocyte count 6,000 to 8,000; number of cases studied=12. In 6 of these the bactericidal power was slightly above and in 6 slightly below the group average. In terms of colonies the ratio, as above, was approximately as 114 to 100.

(3) Leucocyte count 8,000 to 10,000; number of cases studied=14. In 8 of these the bactericidal power exceeded, while in 6 it was less than, the group average. In terms of colonies the ratio, as above, was approximately as 94 to 100.

(4) Leucocyte count above 10,000. Number of cases studied=8. In 5 of these the bactericidal power exceeded the group average, while in 3 the reverse obtained. In terms of colonies the ratio, as above, was approximately as 85 to 100.

These findings, taken in conjunction with the observations represented in Charts 1 and 3, disclose a broad parallelism between the degree of bactericidal activity and

the leucocyte count, and suggest that the increase which occurs in the former during pregnancy may be related to a similar increase in the latter. The reservation which is implied has been prompted by the observation that such relationship as exists is inconsistent in character. Whereas with a low leucocyte count we have usually found a similarly low degree of bactericidal activity, a white count above the average is not so uniformly accompanied by a corresponding increase in bactericidal power. This applies more particularly to cases of infection, but has frequently been noted in the absence of any apparent disturbance of health. It is illustrated particularly in the rapidly increasing leucocytosis which occurs during labour without any corresponding accentuation in bactericidal activity. Furthermore in groups of cases in which both have been examined simultaneously it has occasionally been found that no relationship obtained between the one and the other. This is illustrated in Table V, which comprises a group of four healthy pregnant women of whom the individual with the lowest white cell count was found to possess the highest degree of bactericidal activity.

TABLE V.

Case.	Leucocyte count.	Colonies.
368	10,000	47
370	9,000	76
371	9,700	54
373	7,000	24

It would appear probable, therefore, that the accentuation of the antibacterial activity of the blood which occurs during pregnancy can only partially be explained by the simultaneous increase in the leucocyte count, and is attributable to factors other than, or in addition to, a mere numerical increase in white cells. What precisely these factors are, and by what means they can be stimulated so as to increase resistance to infection, must be left for further research to determine.

CONCLUSIONS.

The conclusions suggested by the investigation which we have made may be summarized as follows:

1. There is considerable individual variation in resisting power to infection as determined by Wright's "slide-cell" method of estimating the degree of bactericidal power of the blood.

2. This variation is more marked in the pregnant than in the non-pregnant individual, and appears to bear a definite relationship to the development and course of puerperal infection.

3. There is during pregnancy a gradual increase in the bactericidal activity of the blood, which reaches its maximum at or about the time of delivery and thereafter rapidly subsides. The bactericidal power of the blood at the full term of pregnancy considerably exceeds that of the non-pregnant individual.

4. The antibacterial activity of the blood does not materially differ in the nulliparous as compared with the multiparous pregnant or non-pregnant individual. This property, however, appears within limits to be depressed by the albuminuria of pregnancy, prolonged labour, instrumental delivery, and severe blood loss.

5. While there is a broad parallelism between variations in the bactericidal activity of the blood and the leucocyte count, the relationship is not a constant one, and the increase in bactericidal power which occurs during pregnancy is probably due to factors other than, or in addition to, a mere numerical increase in white cells.

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