PUERPERAL SEPSIS.

AN INVESTIGATION INTO THE

ETIOLOGY, PROPHYLAXIS AND TREATMENT,

WITH A NOTE ON THE RELATIONSHIP OF

POLYMORPHO-NUCLEAR LEUCOCYTOSIS

TO THE CONDITION.

Thesis submitted for the

M.D. Glasgow

by

William Simpson, M.B.Ch.B. 1923.

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INTRODUCTION.

Puerperal sepsis is a disease which must command the serious attention of the medical profession to-day owing to the immediate and ultimate morbidity and mortality which it produces amongst parturient women. Despite the intense scientific and clinical research to which the condition has been subjected, its incidence does not show a satisfactory or encouraging diminution.

Its conception as a disease of bacterial origin was first suggested by Semmelweis and has now been fully demonstrated.

It is universally agreed that sepsis arising in the puerperium is due to breaches of continuity of the mucous membrane lining the vagina, cervix, or uterus, or of the skin covering the vulva, with subsequent invasion by pathogenic organisms, and is therefore a special type of wound infection.

The organisms may be introduced from without or may have been in the genital tract during pregnancy. In the latter case, they reach the uterus via the lochia, which is/

is rich in bacteria-feeding matter. If the patient's powers of resistance are low, no matter in what way the organisms gain entrance, the possibility of infection is increased.

A wide variety of organisms, especially the pyogenic, coliform and typhoid groups, has been found in the lesions produced, and will be referred to later.

The results of bacteriological investigation reveal that the local and general conditions found in puerperal infections depend on the modus operandi of the causative organisms. The activities of these occur along two definite lines, depending on whether they are saprophytes or parasites. The former remain localised at a particular site, usually some retained products of pregnancy,and elaborate toxins. Concurrently the saprophytic action of the organisms on the tissues leads to the production of ptomaines, which, with the toxins, are absorbed by the blood and lead to systemic intoxication or sapraemia.

The latter multiply at the site of invasion, and with their toxins penetrate into the underlying tissues, enter the lymph and blood streams, and thus cause septicaemia. Clinically, these two conditions, sapraemia and septicaemia, are not definitely distinguishable and may be combined in one case. Sometimes one is predominant, sometimes the other. Each may be due to the same type of organism, as in the case of/

of streptococci, which, although essentially parasitic, are facultative saprophytes, or , there may be a superposition of a parasitic infection on an existing saprophytic one.

It is highly probable that in the severe and fatal cases the organisms gain entrance during or soon after the process of parturition, when the patient's vitality is low and the natural measures for the protection of the patient are often extremely deficient.

As the direct result of increased knowledge and improved methods of prevention and treatment based thereon, especially pre-natal control of pregnant women and detailed attention to sterilisation during parturition and the puerperium, the incidence of puerperal infection in properly conducted lying-in hospitals has been substantially reduced, and the mortality from it, lowered almost to vanishing point. Outside these institutions, however, parturient women have not shared in the benefit, and upwards of 40 per cent of the total puerperal mortality is still caused by septic diseases, from which, on the average, more than 2000 women die every year in England and Wales.

Since puerperal infection is almost eliminated if proper precautions are taken, its development is per se strongly suggestive of the neglect of modern methods during pregnancy/

pregnancy and parturition. It is proposed to show subsequently how the occurrence of puerperal infection can be anticipated, permitting therefore the institution of preventive measures.

Nevertheless, failure to appreciably reduce maternal mortality is almost inevitable so long as midwives supervise 50-75 per cent of all pregnancies, and the general public remain indifferent to routine pre-natal work. Because, then, the general practitioner is very often compelled to undertake the treatment of obstetrical difficulties in emergency without adequate assistance and often under grossly unsuitable conditions, or, the case is admitted to hospital after unsuccessful treatment at home, sometimes in extremis, or at least, in circumstances highly "suspect", and which, in spite of the resources of hospital technique and equipment, may completely discount the value of otherwise safe and effective treatment. In broad terms, the rule appears to be, with regard to women who suffer from puerperal infection, that if they are not left to work out their own fate as best they may in their own homes, they are sent into Poor Law Hospitals where the provision for effectual treatment is either inadequate or non-existent.

The mortality percentage of cases of puerperal sepsis is/

is uncertain; but ten is probably not far wide of the mark. At this rate, there will be in England and Wales every year an average of something like twenty-thousand cases of puerperal infection. The mortality varies with the organism and with the country. For example, in a series of 50 cases of streptococcal origin published by Whitridge Williams the mortality was 4%, and in a series of 100 cases due to the same organism published by the American Gynaecological Society the mortality was 30%.

The disease has been made notifiable and there are the strongest possible reasons for the community to provide effective means of isolation and treatment. Parturition is almost inevitably accompanied by wounds of the genital canal - the placental site is itself in the nature of an abrasion - and the patient's vitality becomes lowered, thereby providing the necessary conditions for infection by organisms, which may assume an alarming virulence and meet with little resistance.

In the following thesis the writer proposes to review the existing knowledge of the etiology and clinical manifestations of puerperal sepsis and, with a view to prophlaxis, to describe experiments which indicate a method of recognising cases where puerperal sepsis is likely to arise, and a line of/

of treatment, in addition to that already existing, should infection occur.

It is further proposed to make a brief survey of the history of Puerperal Sepsis, since the writer considers, that the facts of history support the conclusions he will attempt to formulate.

The experiments were carried out in the Glasgow Royal Maternity and Women's Hospital, and the treatment has been applied in general practice. The conditions relating to obstetrics in general practice were also observed.

Historical Outline.

The occurrence of puerperal sepsis after parturition is essentially abnormal, therefore it is fair to presume that its incidence was proportionately less the more the conditions of human life resembled those of animal life. This presumption is based on the hypothesis that civilisation entails an increasing displacement of the natural by the artificial. Therefore, the inherent protective properties of the body weaken proportionately to the use made of them, and since the influence of civilisation makes for a decreased use of these, they deteriorate in accordance with the laws of evolution. Hence, puerperal sepsis is only found in civilised communities, and until measures were taken to control it, increased as they advanced.

It is quite unknown among races living primitive lives, and, among these, does not occur where obstetric surgery is practised by the white man under conditions much less hygienic than those in the poorer quarters of the cities of Great Britain.

In so far as the darkness enveloping medical history/

history before the nineteenth century can be penetrated, the facts relating to puerperal sepsis support these statements, which assist in substantiating the conclusion drawn from the experiments to be described in this thesis.

Thus, each succeeding civilisation following that of Greece contains, in its medical literature, record of an increasing amount of what can only be interpreted as puerperal infection, particularly in the realm of practical midwifery, with the passage of time and the consequent more widespread departure of human existence from strictly natural influences. This is borne out by the writings of Hippocrates of Greece, Galen of Rome, Philumenos and Paulos Aeginetes of the Byzantine Empire, and Ambrose Paré, Vesalius, Rösslin and Rueff of the Renaissance period.

Up to the early part of the nineteenth century, therefore, puerperal sepsis had been gradually increasing to such an extent that many institutions were threatened with closure, and actually several did cease their activities. This continued until the discovery made in Vienna in 1847 by the great obstetrician, Ignaz Philipp Semmelweis, a Hungarian, born in Budapest in 1818.

At that time, in the midwifery department associated with the University of Vienna, there was a midwives' clinic/

clinic and a students' clinic. The wards in the former were not so large nor so airy as those in the latter, yet the mortality in the fine wards where the students were instructed was extremely high. It ranged from 1 in 9·16 to 1 in 3·92, whilst in the midwives' clinic the range was from 1 in 91·66 to 1 in 34·37. The student was instructed on the dead body of some female, and each patient in his clinic was examined by at least five different persons. The midwife pupil was instructed on the leather phantom and not upon the dead body, yet each patient was examined as frequently or even more so than in the students' clinic.

Thus, by purely deductive reason, Dr. Semmelweis, who was then assistant physician in the students' clinic, clearly enunciated the conclusion that the reason for the disparity in the mortality statistics between the two clinics was to be found in the "hands of the medical men in attendance contaminated with cadaveric poisons," that is the members of the staff and students, who diligently attended autopsies in the adjacent mortuary.

Therefore, Semmelweis put all students in quarantine for a day after attending an autopsy, and directed all who worked in the students' midwifery clinic to wash their hands in a "solution of chlorine prior to and after every examination" made on the living subject.

The/

The result of these precautionary measures was that the number of deaths at once fell to seven per month, or the usual average in the midwives' clinic.

This demonstration that washing the hands in a chlorine solution greatly reduced puerperal sepsis, was the first attempt to prevent its onset to be followed by encouraging results, and took place long before Lord Lister, incited by Pasteur's experiments, demonstrated the value of antiseptic lotions in surgical practice.

The work of Dr. Semmelweis was demonstrated in this country at a meeting of the Royal Medical and Chirurgical Society on November 28th, 1848, in a paper entitled, "On the causes of the Endemic Puerperal Fever of Vienna," communicated by Dr. Murphy and prepared by Charles Henry Felix Routh, M.D., who worked with Semmelweis during the period of his discovery. Dr. Routh was unable to read the paper himself as he did not become a Fellow of the Society until the following year. Thus, Routh was the pioneer in this country in the use of antiseptic principles in midwifery.

The views propounded by this paper aroused tremendous controversy among the prominent obstetricians of the time, and were regarded with profound scepticism and ultimately/

ultimately temporarily refused acceptance. Two of the many reasons for this amazing unbelief in what later proved to be an epoch-making discovery were - (1) that the conception of puerperal sepsis as a specific fever (introduced by Sir James Y. Simpson in 1842) was generally accepted and therefore could not be influenced by the method suggested; and (2) the occurrence of puerperal sepsis among cases in charge of midwives who had not taken any part in autopsies.

The findings of Dr. Semmelweis, who died insane in 1865, were published in his great work "Die Aetiologie der Belgriff und die Prophylaxis des Kindbettfiebers" in 1861, which ranks as one of the greatest monographs in medicine. His methods were practised by Michaelis of Kiel with marked success soon after his discovery, but even this failed to interest the great number of European obstetricians who were antagonistic to his views.

After the publication of Semmelweis' work in 1861, however, the value of his theories began to be recognised. These theories were practised with encouraging degrees of success, which prompted many workers to investigate the causes of this serious complication of a physiological process. The recognition of bacteria as pathogenic agents opened up new fields of research in puerperal sepsis, with the/

the result that, on the recovery of certain organisms from the uteri of fatal cases, the suggestion of its being a specific fever was finally refuted. The condition is often referred to, even now, as "Puerperal Fever."

From this time up to the present, research into the problems of puerperal sepsis can be separated into three distinct phases:-

I. 1863 - 1900. Investigation of the flora of the vagina, and of the causal organisms in puerperal infection.

II. 1900 - 1910. Determination of the relationship of the streptococcus to puerperal sepsis.

III. 1910 - 1926. Attempts to reduce the incidence and efforts to determine the predisposing conditions of puerperal sepsis.

I. The Period between 1863 and 1900 was characterised by (1) investigation of the flora of the genital tract at all periods in the life of the nulliparous, parous, and puerperal woman, and (2) attempts to define the causal organisms in puerperal infection.

In 1863 Mehrhofer recovered streptococci from the/

the uterus of a woman suffering from puerperal sepsis.

In 1869 Coze recovered streptococci from the blood of a fatal case and suggested that the occurrence of general symptoms was due to invasion of the blood by the causal agent.

In 1879 Pasteur, in the course of his bacteriological investigation, isolated streptococci on several occasions from the lochial discharges of physiological and pathological puerperia, and the uteri of fatal cases of puerperal infection.

About this time it began to be appreciated that although microscopic examination of specimens and secretions revealed the presence of many organisms, accurate information could only be obtained by cultural methods. With secretions it was essential that removal be effected without contamination from the vulva, and therefore the method probably least open to objection and now generally used, namely, the introduction of a tube into the vagina after separating the labia and before inserting a platinum loop to collect the secretion, was adopted by Krönig and Menge.

During the next ten years, 1880 - 1890, these two, also Gonner, Winter and others, found many bacilli and cocci in the vaginal secretion. These were mostly anaerobic in type/

type and not pathogenic to animals.

In 1889, notification of Puerperal Sepsis was made compulsory under the Notification of Infectious Diseases Act, and constituted an important step towards more complete control of the condition.

In 1892 Döderlein published his classical paper, based upon the examination of the vaginal secretion of 195 pregnant women. He described two forms of secretion as existing in pregnancy. He found that in the normal condition the vaginal secretion is scanty, white in colour, and cheesy in consistence, containing epitheleal cells and leucocytes, it is intensely acid in reaction and is characterised by the presence of long anaerobic bacilli. These organisms appear to produce lactic acid and to exert a bactericidal influence on pyogenic bacteria introduced from without. In the other type, considered by him to be pathological, the secretion is profuse, yellowish-white in colour, containing many leucocytes and epitheleal débris, it is only slightly acid in reaction and contains a large number of micro-organisms of various kinds, including streptococci, (which were present in ten per cent. of his cases.)

The long anaerobic bacillus described by him has become known as Döderlein's bacillus. His interpretation of/

of its function was received with much difference of opinion, and led, during the next few years, to further observations.

These showed that, whilst the acid vaginal secretion is unfavourable to the growth of organisms, the bacillus of Döderlein itself only plays a subordinate part, and that although the two forms of secretion undoubtedly exist, it is of little practical value to distinguish between them. The men, of whose researchs these are the main conclusions, were Stroganoff, Dubendorfer, Bergholm, Burghardt, Vahle and Stolze.

II. From 1900 - 1910 research was directed principally towards determining the relationship of the streptococcus to puerperal sepsis. This was a natural result of the trend of events towards the end of the nineteenth century. The prevalence of streptococci in puerperal infections, combined with contradictory reports from reliable observers, was noticed. Reference to the results published, relevant to this period of the history of puerperal sepsis, proves this.

The/

The six observers last mentioned found streptococci present in a proportion varying from 15 to 20%. Bumm and Sigwart in 1904 were able to cultivate streptococci in 30 to 50% of women examined during pregnancy, the secretion being obtained by the use of a speculum. Krönig, in a series of 167 cases, was unable to demonstrate the presence of streptococci and concluded that the vaginal secretion should be regarded as free from pyogenic organisms, with the exception of the gonococcus which was occasionally present, as also were a number of anaerobic organisms, including an anaerobic streptococcus, which was not however pathogenic to animals. Whitridge Williams and Bergland have published a series of observations which tended to show that, if sufficient precautions are taken to avoid vulvar contamination, no pyogenic organism would be found in the vagina during pregnancy.

Following upon the publishing of these reports, which occurred between 1900 and 1906, Bergholm, Bohne, Stähler and Winter carried out experiments to show that the widely different results of other workers were attributable, partly to the absence of any uniform method of removing the secretion, and partly also to the different culture media which had been adopted.

The/

The conclusions formulated by them were that those who used alkaline agar only rarely discovered streptococci, but if the agar were combined with a slightly reducing substance such as grape-sugar, streptococci were found in a considerable proportion of cases, the secretion being obtained without any probability of vulvar contamination.

The reasons that the part played by the streptococcus was the correct avenue along which investigation should be pursued are easily discernible.

Streptococci were found to be not infrequently present in the vaginal and uterine secretions after delivery in cases pursuing a normal course. They were found in the slighter forms of infection, which are clinically regarded as being of sapraemic origin. It was, therefore, of great importance to determine whether the streptococci found in severe forms of infection were essentially different from the saprophytic types of the organism or not. Also the remarkable variations in the infective power of streptococci raised the possibility of there being various types in existence and led to many attempts to classify them, with the object of bringing their morphological and cultural features into relation to their pathogenic powers.

Efforts/

Efforts were made to detect specific differences between varieties of streptococci according to the length of their chains, their mode of growth, and staining reactions, their power of agglutination and their virulence for animals. None of these features was found to be constant.

Natvig, Zangemeister and Meissl carried out experiments to show that all facultative anaerobic streptococci were essentially of one stock; Schab investigated this question and stated that it was impossible to distinguish between streptococci existing as saprophytes in the lochial discharge, and those causing puerperal infection.

About 1906 great stress was laid upon the haemolytic power of streptococci, as an indication of their virulence, and of the presence of infection.

The observations of Bordet in 1897 and of Marmorek in 1902 showed that many streptococci possess a haemolytic power. Schlesinger in 1903 conducted a series of experiments with the object of determining the significance of haemolysis, with inconclusive results. Schottmüller in 1906 published the results of observations made over several years, and claimed that the haemolytic power is proportional to the virulence of the organism, and that the presence of a haemolytic streptococcus clearly indicates a pathogenic type/

type of the organism.

This led Lea and Sidebotham, of Manchester, to carry out examinations of the lochial secretion of 58 cases between the second and ninth day after delivery, and, in a paper, read before the Obstetrical and Gynaecological section of the Royal Society of Medicine, they concluded that the presence of haemolytic streptococci in the vaginal or uterine secretion can not in itself be regarded as an indication of the existence of infection.

In the following year, 1910, the late Arnold W. W. Lea, M.D., B.S., F.R.C.S., published his great work "Puerperal Infection", described by the reviewers of the time as "the first monograph on this subject."

It is regarded as the last word on the causal agents of puerperal sepsis, and the treatment it advocates is more or less that adopted to-day, allowing for the various modifications practised by the different schools of Obstetrics.

It will be seen from the foregoing that approximately fifty years (1863-1910) were required to discover definitely the factors of causation of infection during the puerperium. Despite this knowledge and the improved methods of treatment, combined with the greater scope for their/

their practice, the incidence and mortality of puerperal sepsis has diminshed very little.

III. 1910 - 1926. It is obvious that a clear line of demarcation between various phases in the elucidation of the mysteries of puerperal sepsis does not exist. The divisions in this section indicate approximately the periods devoted to particular lines of investigation.

The next sixteen years were characterised by attempts to reduce the incidence and efforts to determine the predisposing conditions of puerperal sepsis.

According to Eden, the maternal mortality from childbirth increased between 1911 and 1920; he points out that this increase was due to the factor of infection, as death from other causes actually showed a decrease.

Reference to the statistics of Howard and Eichel prove that in America, childbirth was more dangerous in 1921 than in 1916.

In properly conducted lying-in hospitals the condition has been reduced very considerably, but outside these institutions its incidence has shown very little alteration./

alteration. Consequently, research during the last decade has been directed towards ascertaining the conditions which predispose to the occurrence of infection.

These efforts have not been attended with much success, in so far as decreased incidence of the condition is concerned, but increased ante-natal control has had a salutary effect especially in preventing the development of the more serious forms of infection.

The position to-day is that puerperal sepsis is found relatively least in rural communities, and, while in large urban areas, where a considerable proportion of deliveries are conducted in hospitals under trained specialists, a greater amount is found, it is greatest in medium-sized and small towns.

An important contribution was made on the subject by George Geddes, M.D., of Lancashire, who expounded his "Industrial Accident Theory" in 1924.

He states that puerperal sepsis is entirely due to the introduction of septic material, notably the streptococcus, into the genital tract by the medical attendant. He shows how many cases of infection have been preceded by the attendance of the practitioner upon a patient with a septic wound, this being a common occurence in large industrial areas like Lancashire/

Another method of overcoming the scourge, which is receiving much attention just now, and one of whose principal advocates is Professor J. M. Munro Kerr, is that all confinements should be conducted in hospitals, or houses prepared for the purpose, or if this is not practicable, the services of an obstetrician should be within the reach of all women approaching term.

In 1925, legislation with regard to the notification of puerperal pyrexia as distinct from puerperal sepsis was introduced, all puerperal women with increased temperatures after the third day being involved. This is a further attempt to suppress infection as early as possible.

This concludes a brief historical account of puerperal sepsis, giving the chief discoveries in connection with the condition in chronological sequence and indicates the enormous amount of work done to probe the mysteries of this grave complication of the puerperium.

Despite the detailed attention given to the condition, its incidence shows only a comparatively slight reduction, and reveals the necessity for more complete understanding of the factors of prevention.

ETIOLOGY AND PATHOLOGICAL ANATOMY.

It is proposed to separate this section into four parts:-

I Causal Agents.

II Predisposing Factors.

III Sources of Infection.

IV Pathological Anatomy.

I Causal Agents.

It has now been proved beyond all question, as described in the historical outline, that the exhibition of any degree of puerperal sepsis is due to bacterial activity.

The Bacteriology associated with the Genital Tract in Health.

The Vagina.

The vaginal canal of the new-born infant is usually sterile for a few days after birth. From then, all manner of undifferentiated organisms, staphylococcus pyogenes, both aureus and albus, and bacilli coli communis, may be found. During adolescent and adult life, organisms, some harmless, others of a pyogenic nature of more or less virulence/

virulence, frequently gain entrance.

The dangers attendant on this are counteracted by the action of Döderlein's bacillus; the lactic acid produced by it inhibits and destroys pyogenic organisms.

The occurrence of menstruation is said to establish a potential danger of infection, as, during the menstrual period, part of the menstrual blood lies in the vagina before being discharged, patches of uterine mucous membrane are shed, the cervical canal is more patent, and the normal acid secretion of the vagina is temporarily weakened or even rendered neutral by the alkalinity of the blood discharged from the uterus. Yet, despite all these opportunities for the activities of organisms which have been shown to be present, infection only occurs in very isolated cases.

I attribute this freedom from infection to the abnormal amount of blood present in the pelvis during menstruation, which means that there are large quantities of polymorphonuclear leucocytes in the affected area. These leucocytes in the presence of opsonins elaborated in the blood plasma exert a bactericidal effect on any organisms whose activities, in the suitable conditions, might have a pathogenic effect.

I propose to adduce evidence in support of this in the part dealing with Predisposing Factors.

During/

During pregnancy there is a tendency for the vaginal secretion to become weaker in acidity, which increases the risk of infection at and after parturition.

The vaginal secretion in healthy women during pregnancy has been the subject of an enormous amount of research, with the object of determining its bacterial content. The following is a list of the organisms which have been found, including the name of the workers responsible:-

a) Facultative anaerobic streptococci.

Döderlein, Bohne, Stähler, Winkler, Bumm.

b) Facultative anaerobic diplo-streptococci.

Natvig.

c) Anaerobic streptococci.

Krönig, Menge.

d) Staphylococci. (albus)

e) Coliform Bacilli.

Bensis, Kottmann, Walthard.

Thus, organisms indistinguishable from pyogenic types may exist in the vagina of healthy pregnant women.

During the first twenty-four hours of a normal puerperium, there are relatively few organisms in the vagina. This is apparently the result of the cleansing process which occurs/

occurs as the result of the act of parturition, also, the presence of fresh blood, and therefore fresh supplies of the bactericidal polymorpho-nuclear leucocytes, I consider, exerts some influence.

After the second day, large numbers of organisms may be cultivated from the lochia. The bacillus of Doderlein is not found, and the alkaline secretion favours rapid multiplication of any organisms existing in the vagina before delivery.

The Cervix.

The cervical canal in pregnancy is occupied by a plug of firm clear mucus, which effectually closes the uterine cavity. The secretion of the cervical glands contains abundant polymorpho-nuclear leucocytes, which exert a definite bactericidal influence.

The Uterus.

All observers agree that the cavity of the uterus is free from organisms during normal pregnancy, as of course it is in the healthy nullipara.

The bacteria present in the uterine cavity during the normal puerperium have been investigated by numerous observers with widely different results.

The/

The following list shows this clearly:-

Döderlein, Wintermitz von Ott, Czerinewski	70-80% of cases - sterile 7% - pyogenic organisms. remainder - anaerobic saprophytes.
Franz	pyogenic organisms in every case after the 5th day.
Burghardt, Wonnser, Stähle, Vogel	20-50% pyogenic organisms after the 3rd day.
Krönig	Streptococci and staphylococci often present after 3rd day, disappearing after 7th day - afebrile cases.

Hellendahl	demonstrated that organisms ascend from the vagina along blood clots present in the upper part of the vaginal and cervical canals.
Bumm Sigwort	50-75% cases - streptococci after the 3rd day.
Leo	17·6% streptococci.
Stolz	80% cases - organisms on the 4th day. 36·9% cases - streptococci.
Mansfield	60% cases - orgnaisms. 22·5% cases - streptococci.
Little	92% cases - sterile on the 1st day. 62% cases - sterile on the 3rd day. 1 case - streptococcus.

In this series, the secretion was taken from the upper part of the uterus, with precautions to prevent contamination from the vagina.

Nicholson Evans	suggested that the variability of results was due to faulty technique

By using a vaginal speculum and a glass tube inserted into the uterine cavity, they found organisms in a few cases only.

Allowing for the disparity between the figures of those who took strict precautions to prevent contamination by the vaginal lockia and those whose methods are open to suspicion, it/

it would seem that in the majority of cases the uterus is sterile.

It must be concluded from this brief review that organisms, many with pathogenic power and closely resembling those in puerperal infection, exist in the female genital tract from a few days after birth.

Considered in the light of potentiality, and bearing in mind the gradual loss of the bactericidal action of the acid vaginal secretion in pregnancy, it is a matter of wonder that there are not a great many more cases of puerperal infection.

The extent of puerperal infection in this country can be seen from an examination of the Registrar-General's statistics of Births and the notifications of puerperal sepsis. These show that on the average 6% of puerperal women suffer from puerperal sepsis, and it is an accepted fact that all cases are not reported. This result testifies to the value of research on puerperal sepsis but the actual number of women infected (roughly 20,000 annually in England and Wales) and the havoc wrought in them, shows that all the links/

links in the chain for shackling the condition have not yet been forged, and warrant continued investigation taking place.

Obstetric text books attribute immunity from puerperal sepsis to sufficient "resistance" on the part of the patient to overcome the causal agents. I consider that a proper understanding of the factors which form the defences of the body against infection will make for a diminution in the incidence of puerperal sepsis, and theoretically, its elimination.

Physiology teaches us that the basis of defence against infection is the leucocyte, and I will record the results of observations later to show that the onset of puerperal sepsis is predisposed to by an absence of the leucocytosis associated with pregnancy.

The Organisms Associated with Puerperal Sepsis.

These may be divided into two groups:-

(1) Cocci.

micrococcus pyogenes tenuis
micrococcus pyogenes tetragenus
diplococcus intracellularis meningitidis
Pneumococcus Fränkel
staphylococcus cereus albus

staphylococcus cereus flavus
staphylococcus pyogenes albus
staphylococcus pyogenes albus epidermidis
staphylococcus pyogenes citreus
staphylococcus pyogenes aureus
streptococcus pyogenes longus
streptococcus pyogenes brevis
streptococcus pyogenes conglomeratus
streptococcus pyogenes conglomeratus anginosus
gonococcus

(2) Bacilli.

Bacillus pyocyaneus
Bacillus aerogenes encapsulatus
Bacillus lactis aerogenes
Bacillus pyogenes foetidus
Pneumobacillus Friedländer
Bacillus coli communis
Bacillus diphtheriae (Klebs Loeffler)
Bacillus tuberculosis
Bacillus of soft sore (Duprey)
Bacillus Typhosus
Bacillus tetanus
Bacillus oedematosus
Bacillus proteus vulgaris
Bacillus funduliformis
Bacillus radiiformis

Observations show that in about 50% of cases, streptococci are found generally in association with any of the others named. After streptococci, staphylococci are most frequently cultivated from cases of puerperal sepsis. The anaerobic organisms found in the condition tend to increase the virulence of any pyogenic organisms present.

II. Predisposing Factors.

It is proposed to classify the predisposing factors of puerperal sepsis thus:-

Principal Factors.

A. Breaches of Continuity in the Genital Tract.

B. Deficiency of Polymorpho-nuclear Leucocytes.

Accessory Factors. include any condition in the patient, or her environment which causes diminution of the polymorpho-nuclear leucocytes.

Principal Factors.

A. The relationship of breaches of continuity in the genital tract to puerperal sepsis will be discussed under circumstantial sources of infection. It is generally agreed that without a wound in the parturient canal, infection does not occur, therefore such wounding is one of the principal predisposing factors.

B. While I was resident physician in the wards of Dr. J. B. Mackenzie Anderson in the Glasgow Royal Infirmary (April to October 1923) I gained considerable experience, under his direction, in the enumeration of the cells, estimation of the amount of haemoglobin, and the microscopical examination of the blood.

During/

During this time, the variation in numbers of the white cells of the blood in acute inflammatory conditions was borne in upon me.

It is an accepted fact in medicine that one of the reactions of any foci of inflammation is a leucocytosis.

I observed that the rate of resolution in these cases varied directly with the departure from the normal in the number of leucocytes, thus, the greater the increase the quicker the recovery, the nearer the number was to the normal the slower the recovery. Conversely the presence of a leucopenia denoted that resolution would be slow, tending towards chronicity in local inflammatory conditions, and a fatal termination in those of a general nature. These manifestations were most marked in cases of acute lobar pneumonia. Further it was clear that the relationship between inflammation and leucocytosis was not simply a direct one, in that a low leucocytosis may mean either a slight (or perhaps chronic) infection, with good resistance, or a very severe infection with poor resistance.

Conversely, a severe infection may show itself (as in lobar pneumonia) either by a high leucocytosis (with good resistance) or a leucopaenia (as in the aged).

The publicity given in the medical journals about that/

that time to puerperal sepsis, combined with my interest in obstetrics, raised the possibility in my mind that, since puerperal sepsis was an inflammatory condition, and would therefore react in the usual way on the leucocytes, a study of their behaviour in pregnancy and puerperal infection might yield useful results.

The opportunity to do this came when I was appointed Indoor House Surgeon in the Glasgow Royal Maternity and Women's Hospital, and I have continued my investigations during the last two and a half years in general practice.

As a result of this, I desire to state now that, in my opinion, deficiency in the numbers of polymorphonuclear neutrophil leucocytes in a pregnant, parturient or puerperal woman is the fundamental predisposing factor determining the occurrence of puerperal infection.

When I consider the eminence of many of the workers on the subject of puerperal sepsis, it is with a degree of diffidence that I attempt to expound the views I hold. The work I have done, however, combined with the literature on the subject I have read, convinces me profoundly that I can suggest a means of controlling still further the occurrence of the condition. I am therefore glad to have the opportunity of submitting my work to men of more mature experience and/

and wider knowledge.

Enumeration of the leucocytes of pregnant and puerperal women was made. The polymorpho-nuclear neutrophil leucocyte, which forms 70% of the white cells, was the type which underwent changes in numbers, therefore the word "leucocyte" is used to indicate that particular form.

The instrument used for making the counts was the Thoma-Zeiss haemocytometer, and the blood, removed from the lobe of the ear, was diluted with a 1% solution of glacial acetic acid coloured by adding a small quantity of gentian violet. This solution dissolves the red cells and stains the nuclei of the white.

The results of these experiments are separated into three classes:-

(a) Enumeration of leucocytes in normal pregnancy.

(b) " " " according to environment and mode of life.

(c) " " " in puerperal sepsis.

(a) Enumeration of leucocytes in normal pregnancy.

The following list shows the leucocyte content of the blood of twenty females whose pregnancy, parturition and puerperium pursued a normal course. Twelve of these cases (9 to 20)/

(9 to 20) were delivered by forceps under anaesthesia.

The results are shown to the nearest thousand for the sake of definition; the patients concerned did not come to me until the second or third month of the pregnancy, therefore it was not possible to ascertain the number of leucocytes at the beginning of it. The counts were arranged to be made at four weekly intervals, so that seven to ten days elapsed between the last one in pregnancy and the first one in the puerperium.

As I wish to draw attention to the effect of social position on the leucocyte content of the blood, I have indicated the occupation of the wife or husband. In the district in which I practise, fifty per cent. of the community are engaged in the heavy woollen industry (cloth, shoddy, blankets,) and the remainder in agriculture or coal-mining.

(See Table I over leaf.)

Enumeration of Leucocytes at intervals in 20 Cases of Pregnancy and Puerperium.

Phase	Pregnancy							Parturition	Puerperium			
Month	3	4	5	6	7	8	9	Day	2	5	10	occupation of woman or husband
No. in Series 1	5	6	6	7	8	10	11		12	9	8	textile operative
2		6	6	7	8	12	12		13	10	8	wife of do
3		6	6	6	7	7	8		10	9	7	do.
4		5	5	5	6	7	8		10	9	8	do.
5		6	7	7	8	8	10		12	10	7	do.
6		8	8	8	10	11	13		14	12	10	wife of farm labourer
7		6	7	7	7	7	8		9	6	5	wife of clerk
8		6	6	6	5	7	10		11	9	7	wife of miner
9		5	5	5	5	7	8		10	11	9	wife of bank-manager
10		6	6	6	7	8	8		10	11	8	textile operative
11		6	7	7	7	7	9		12	11	9	wife of miner
12		6	6	6	6	7	8		12	12	9	wife of text.oper.
13		5	6	5	5	7	9		11	10	8	wife of clerk
14		4	4	5	6	8	8		11	10	9	wife of millowner
15		6	6	6	6	6	8		10	11	8	wife of farm lab.
16		5	5	6	5	7	8		11	12	9	wife of school master.
17		6	6	6	7	8	9		12	11	10	wife of text.oper.
18		5	5	5	5	7	9		13	12	9	wife of millowner
19		6	6	5	6	8	9		14	13	8	text. operative.
20		5	5	5	6	8	8		10	10	9	wife of colliery manager.

TABLE I.

It will be seen from these figures that no leucocytosis was observed until the end of the eighth month of pregnancy; that this leucocytosis had become definitely more marked by the second day of the puerperium; that by ninth day it had approached the normal amount; that the leucocytosis in forceps deliveries persisted longer in the puerperium than in spontaneous deliveries, and occasionally actually increased during the first few days of the puerperium; that those women who lead "sheltered lives" (wives of mill-owners, colliery-managers and bank managers in this case) had lower leucocyte counts than those women whose lives were cast in rougher moulds (wives of miners, farm labourers and textile operatives.) Twelve cases in this series (9 to 20) were delivered under anaesthesia and I did not find that the anaesthetic, whether long, deep, badly taken, or in its after effects, had any effect on the number of leucocytes.

Dr. L. Colebrook of London stated at a meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine on December 3rd, 1925, that during pregnancy, labour and the puerperium "the killing power of the blood was not reduced." I venture to express the opinion/

opinion, based on examinations of the blood of pregnant women, that its bactericidal power is actually increased in a normal pregnancy.

(b) Enumeration of Leucocytes according to environment and mode of life.

The number of leucocytes in the blood seems to vary with the conditions of life in the individual. A woman who works hard, who is seldom without a minor injury of some sort - abrasion on the hands, bruises, received nearly always under conditions liable to permit the entrance of pyogenic organisms to the body, - who lives in confined spaces in districts where the elements of hygiene are not practised, has a greater leucocyte count than the woman who lives in comfort and is protected from almost all physical hardship by the conveniences of modern civilisation.

The leucocytes of the blood are the means whereby the body is protected from the development of diseased conditions after organisms have gained entrance. In the case of the former woman, her defensive mechanism is constantly carrying out its inherent function of protection, and consequently, in accordance with the axiom that stimulation of protoplasm leads to its hypertrophy, it becomes stronger/

stronger and more efficient. That is, the leucocytes increase in number, the more their sefvices are required. Whereas, in the latter, the powers of protection are required to a much less extent, and since the converse of the biological fact stated above is true, they become less effective. That is, the leucocytes decrease in number.

That this response by the leucocytes in the blood to stimulation or, in other words, irritation by pathogenic (including pyogenic) organisms from infected matter or polluted atmosphere, does in fact occur, will be seen to a certain extent from an examination of the social position and the intiial leucocyte count of each patient in Table I. The accompanying figures reveal this more clearly.

Enumeration of polymorpho-nuclear leucocytes in the blood of ten female agricultural workers.

1.	9,000	per	cubic	millimetre	of	blood.
8.	8,000	"	"	"	"	"
3.	8,000	"	"	"	"	"
4.	8,000	"	"	"	"	"
5.	8,000	"	"	"	"	"
6.	8,000	"	"	"	"	"
7.	8,000	"	"	"	"	"
8.	7,000	"	"	"	"	"
9.	7,000	"	"	"	"	"
10.	7,000	"	"	"	"	"

TABLE II.

These ten women live typically rural lives associated with fresh moorland air, plain wholesome food, and generally a rough mode of living. They suffer exposure to all kinds of weather and their domestic lives are not associated with much physical comfort. Yet, they are remarkably free from disease, and since they are comstantly being exposed to the possibility of it, it must be concluded that their powers of resistance, the leucocytes, are able to meet the demands made on them. The counts show that the number of leucocytes is above the mormal, but is normal to these women, and, I contend, to the class they represent, for, they were chosen at random from women in farms in the West Riding of Yorkshire, who were found to be in good physical condition at the time the blood was taken.

Enumeration of the polymorpho-nuclear leucoytes in the blood of ten female textile workers.

1.	7,000	per	cubic	millimetre	of	blood.
2.	7,000	"	"	"	"	"
3.	6,000	"	"	"	"	"
4.	6,000	"	"	"	"	"
5.	6,000	"	"	"	"	"
6.	6,000	"	"	"	"	"
7.	6,000	"	"	"	"	"
8.	6,000	"	"	"	"	"
9.	6,000	"	"	"	"	"
10.	6,000	"	"	"	"	"

TABLE III.

These women work in the heavy woollen mills of the district. The hygienic conditions under which textile operatives work are as good as is possible in the presence of machinery, oil and cloth in various stages of its manufacture. In my capacity of Certifying Factory Surgeon I visit these mills, and see that the conditions of workplaces conform to Home Office standards. Nevertheless, it is obvious that no factory atmosphere is entirely free from pollution. Further, the home conditions of these women are generally unsatisfactory - small houses, large families - and consequently the maintenance of good health in women of this class depends on proper protection from disease, whose activities their mode of life tends to promote.

The figures reveal that the number of polmorpho-nuclear leucocytes was above normal which shows the reaction of environment on the individual in regard to defensive properties.

Enumeration of the polymorpho-nuclear leucocytes in the blood of five "sheltered women".

1.	4,000	per	cubic	millimetre	of	blood.	Wife	of	mill	owner.
2.	4,000	"	"	"	"	"	"	"	"	"
3.	4,000	"	"	"	"	"	"	"	bank	manager.
4.	5,000	"	"	"	"	"	"	"	"	accountant.
5.	3,000	"	"	"	"	"	"	"	Headmaster.	

TABLE IV.

The term "sheltered" is used to indicate a woman who lives in a home made physically comfortable in every way. The heating of the house is ample, often excessive; the atmosphere is healthy; the household work is carried on by servants; and the mistress is suitably clothed to counteract the dangerous effects of cold or damp weather.

The inference from these figures, which shows that the "leucocyte content" were slightly below normal, is that the extra corporeal protection of these women leads to a weakening of intra-corporeal protection, that is, to a diminution of the number of leucocytes in the blood.

Incidentally it is my experience that this type of woman develops inflammatory condition of the respiratory passages on much less exposure to cold than the one in a lower social grade.

It will be seen from these records that the number of leucocytes in, and therefore the bactericidal power of, the blood varies with the mode of life, and since these are the protective elements of the body, it is reasonable to assume that variation in their number will affect the development of any morbid condition with which the body comes into contact. For example, women of/

of the "sheltered" class are not affected to the same extent by puerperal sepsis as their less fortunate sisters, because of the aseptic and antiseptic precautions taken by their medical attendants together with the proper environment. It is, however, an acknowledged fact that when infection does arise, more stringent measures are required for its arrest.

Therefore, I contend that it is logical to assume that this is due to a normal deficiency in the number of leucocytes in the blood, for the reason just stated and also that investigation in all other directions, except the part played by the leucocyte, has not so far yielded a satisfactory explanation.

(c) Enumeration of the leucocytes in puerperal sepsis.

It is necessary to point out that in the Glasgow Royal Maternity and Women's Hospital it was only possible to make examinations of the blood after labour had begun, as patients were not admitted until then, unless a complication of pregnancy had arisen, when of course earlier examination took place.

During the last three years I have conducted ninety confinements, none of which developed puerperal pyrexia. If the leucocyte count was less than 5,000 per cubic/

cubic millimetre of blood at the sixth month, the treatment to be described later was carried out. This was necessary in forty-seven cases, and I am convinced that the freedom from infection was largely due to the information gained from blood examination and thereafter the exercise of special care.

Puerperal sepsis is of infrequent occurrence in the Glasgow Royal Maternity and Women's Hospital and in the great majority of cases is due to infection before admission. In cases where it arose without a history of operative interference before admission, the number of leucocytes was found constantly to be low. The records of their enumeration affords a striking contrast to those of a normal puerperium.

(See over leaf for Table V.)

Enumeration of Leucocytes in 10 Cases with Increased Temperature and Pulse Rate after the Third Day of the Puerperium.

On admission	4th Day	Temp.	Pulse	10th Day	Temp.	Pulse	Remarks
4,000*	4,000	100·4°F	98	6,000	98·2°F	68	M‡ Forceps applied before admission.
3,000	2,000	99·2	85	3,000	98·4	73	M normal Delivery, Home conditions poor.
5,000	4,000	99·8	87	5,000	97·8	64	M normal Delivery, Home conditions poor.
3,000	3,000	99·8	89	4,000	98	68	M normal Delivery, Home conditions poor.
2,000	2,000	100·6	115	4,000	98·6	83	P c.v - 3 inches. Forceps delivery. Several examinations outside.
4,000	3,000	99·4	81	5,000	98·2	71	P Home conditions good. General Health poor.
4,000	4,000	99·6	84	6,000	98·4	69	P Worked as tailoress till 7 days before labour.
3,000	2,000	99·8	90	5,000	98·6	78	M Failed Forceps outside
5,000	4,000	100·2	95	5,000	98·2	75	M Delivered in ambulance.
4,000	3,000	99·6	86	5,000	97·8	69	M Home conditions poor.

TABLE V.

* ‡ per c. mm. blood
M = multipara
P = primipara

The outstanding feature of these observations is the small number of leucocytes at the end of pregnancy when compared with the usual number found just before labour as shown in Table I. All the women except one came from the poorer districts of Glasgow, where sanitary conditions are usually deplorable and the fundamental rules of hygiene are flagrantly ignored - overcrowding, bad ventilation, vitiated atmosphere. These factors combined with an insufficiency of proper food lead to a lowering of the vitality, and when, to an already lowered constitution, is added the strain of pregnancy, any infection to which the patient may be exposed meets with little resistance. Seven of the cases were multiparae in whose cases there is more work to do and probably little chance to recover from the effects of former pregnancies.

In spite of the poverty in leucocytes, these patients had become normal or almost so by the tenth day, as the result of the institution of therapeutic measures whereby the patient's strength was conserved, and no claims made on her energy, which was utilised solely in counteracting the effect of the invading organisms and which was increased by good food and healthy atmosphere.

I wish to draw attention to one case in particular which I think shows the value of the leucocyte and how its presence, in sufficient numbers, will overcome infection by the most virulent of organisms.

A/

A patient was admitted to the Glasgow Maternity Hospital at 5.30 a.m. forceps having been applied unsuccessfully three times outside. There were three large lacerations in the vaginal wall, each of which would have admitted two fingers, the cervix was only three-quarters dilated and torn, and the patient was in an exhausted condition. The presentation was a transverse one and a hand protruded from the vagina. While preparations were being made for the operation of decapitation, I estimated the number of lencocytes in the blood, and found there were 15,000 per cubic millimetre of blood. I was allowed to carry out the operative measures under competent supervision, and know that the parts involved were subjected to considerable pressure before the body and finally the head were removed. The operation was interrupted once owing to signs of collapse in the patient.

Two days later the patient's temperature was 99.6° F., after which it gradually became normal. On account of the treatment the patient had received outside, a swab was taken from the cervix and examined bacteriologically. Haemolytic streptococci were isolated.

On the fourth day after operation the leucocytes numbered 18,000 p.c. m.m; on the tenth day 12,000 p.c. m.m. The patient was able to leave the hospital thirty-seven days after the operation, and a leucocyte count made the day before discharge showed that there were 7000 p.c.m.m blood.

I interpret the marked leucocytosis in this woman, who/

who was strong and well-nourished, as a striking response to infection by virulent organisms.

These results of my own observations I offer as indicating that the leucocyte is a determining factor in the onset of puerperal sepsis. I would repeat that I am convinced that a deficiency in the number of leucocytes is the primary predisposing factor in infection.

I would add to this experimental evidence, facts of a supplementary nature. History shows that puerperal sepsis was a rare occurrence until civilisation began with its consequent softening effects and increased artificial protection from dangerous external influences. Infection is unknown among savage tribes where immunity from disease is dependent solely on factors within the individual which are strengthened by constant contact with potential morbidity.

In cases of puerperal sepsis where the infection is limited to the uterus and is not excessively virulent, a barrier of leucocytes is established beyond the infected area, and prevents further extension of the disease. This protective barrier becomes proportionately less the more acute the case is, until in very severe cases it is entirely absent.

I contend that this occurrence gives considerable support/

support to the view that the numerical strength of the leucocytes is the determining factor in the development of puerperal sepsis, and shows how essential it is that a woman approaching term should be well protected from the development of infection, by having the leucocytosis which is normal at the end of pregnancy.

The formation of this protective barrier is generally said to depend on the resistance of the patient and the virulence of the invading organism. I suggest that leucocytosis is the chief factor of resistance and if it has commenced before parturition the patient is in a position to withstand infection. The virulence of the organisms then becomes of secondary importance since the patient has had time in which to prepare herself, and it is physiologically true that the greater the stimulation the body receives the greater its response will be, provided always of course, that the power of the patient to increase her leucocytes exists before the end of pregnancy.

Accessory Factors.

There are certain conditions which contribute to the possibility of infection in the puerperium in so far as they tend to produce a lowering of the general health and in so doing lead to a lack of response by the leucocytes when infection occurs.

These/

These conditions are:-

1. Overwork.

2. Insufficient quantities of proper food.

3. Insanitary environment and vitiated atmosphere.

4. Debilitating diseases - such as tuberculosis, cancer, syphilio and diabetes. In these conditions the resources of the body are utilised in reparative processes and if there be added pregnancy, the introduction of organisms produces a mild, and sometimes no reaction, favouring the development of puerperal sepsis.

5. The Toxaemias of pregnancy, especially eclampsia and the vomiting of pregnancy. As in (4) the resources of the patient are directed towards combating the toxaemia. In most forms of anaemia except pernicious anaemia, the white cells of the blood are not markedly affected. There is agreement amongst observers that puerperal infection does not often occur when anaemia and pregnancy are associated.

6. Haemorrhage leads to a loss of leucocytes, and in as much as it produces a weakening of the vital functions, the regenerative powers of the body, including therefore the blood-forming tissues, are retarded.

7. Any of the products of pregnancy which, after labour, remain in the uterus predispose to infection by forming a suitable nidus for the activity of saprophytic organisms. Pabulum is provided in plenty and ideal conditions exist for anaerobic/

anaerobic bacteria.

III. Sources of Infection.

I propose to divide the sources of infection in two groups:-

(1) Endogenous (a) Circumstantial

(b) Incidental

(2) Exogenous

(1) Endogenous.

(a) Circumstantial sources.

The genital canal is situated admirably for the activities of organisms during, and in the days following, parturition. Tears and bruises occur in the cervix and vagina; the lochia act as pabulum and their alkalinity favour bacterial growth; the placental site is an abrased surface and the dilated blood vessels and lymphatics offer abundant scope for the absorption of toxins and organisms; the vulva is an area rich in organisms and the bowel a most septic canal.

The late Dr. A. W. W. Lea of Manchester in his "Puerperal Infection" states that 96% of all labours result in wounds or abrasions, and, since the placental site is essentially/

essentially a wound, then logically all labours produce breaches in the continuity of the surface of the genital tract with a consequent liability to infection.

It has been shown that organisms capable of producing puerperal infection often exist in the genital tract before labour, and their presence during and after labour provides opportunity for the expression of their pathogenic activity. It is therefore of paramount importance that there be sufficient leucocytes in the blood to overcome bacterial invasion.

In 1925, the London Committee's Report and that of the North of England in connection with the Ministry of Health's enquiry into the prevalence of puerperal sepsis, stated that very few cases of puerperal sepsis were due to auto-infection. The cases concerned in their reports, however, were hospital ones, and the hygienic environment of a hospital, as regards bodily comfort and food, conduces to increased "resistance" (synonymous in this thesis with an increased number of leucocytes) to infection by the body, as described in "Predisposing Factors". I do not infer that "auto-infection" occurs oftener outside institutions, indeed puerperal infection is extremely rare in women who have precipitate labours with no interference whatever, but I contend/

contend that since the great majority of puerperal infections now occur outside, it is only by investigating conditions there that success will be found.

(b) Incidental sources.

If a puerperal woman be suffering from any inflammatory or septic condition, she may accidentally be the means of bringing organisms into the genital tract, and so set up infection there. The organisms introduced in this way possess a high degree of virulence, since the infedtions they produce are of a severe nature. This depends upon the bacteriological fact proved by Pasteur, that passage through the human body increases the virulence of the bacteria.

Examples of the pathological conditions which form an incidental source of puerperal infection are:-

Vulvitis		Urethritis	Intestinal Infection
Bartholinitis		Cystitis	from the rectum.
Eczema Furunculosis	) of vulva	Pyelitis	Ulcerated haemorrhoids. Fissure in ano.
Cutaneous infection -		septic wounds otitis media infective oral and nasal conditions.	fissure of nipple. abscess of breast

(2) Exogenous.

Into this group fall all cases where the infection has been introduced from outside the patient. In this connection the most common source is the hands of the attendant contaminated with infected material. This is possible by the attendance of doctors or nurses on cases of septic wounds, erysipelas, diphtheria or scarlet fever, and other infectious diseases, while attending puerperal women.

Other sources are instruments, vaginal douches and baths, which have been used without employing rigid aseptic precautions.

In brief, therefore, the onset of puerperal sepsis is due to the infection of wounds in the genital tract, generally during labour and the puerperium, by organisms usually introduced from without.

IV. Pathological Anatomy.

A survey of the manifestations of puerperal sepsis is deemed necessary, in that it emphasises the powerful influence and, in the opinion of the writer, the tremendous possibilities for prophylaxis, which the polymorpho-nuclear leucocyte possesses.

All/

All the forms of puerperal infection are associated with a degree of toxaemia or septicaemia. Septicaemia has been defined by Hamilton as "A class of diseases induced primarily by putrefactive liquids in which different organisms are appropriated by different hosts and live upon the hosts".

Lea defines puerperal infection as "The general term applied to all infective conditions which arise from the entrance of organisms into wounds of the genital tract in connection with labour or the puerperium. It is essentially wound poisoning or wound infection, and is strictly comparable to surgical wound fever."

The term "puerperal fever" has been, and even now is, loosely applied to infective processes occurring after delivery. It is not a disease sui generis and its retention is undesirable, because it suggests the existence of a specific fever in puerperal women, which has been abundantly proved to be entirely fallacious.

The morbid conditions of puerperal infection can be arranged in three groups of increasing severity:-

(1) Localised inflammation, usually at the site of infection.

(2) Inflammation extending through lymphatic or vascular channels, or by direct continuity.

(3) Generalised infection.

(1) Localised inflammation, generally at the site of infection.

The perineum, vulva, vagina and cervix may be bruised and lacerated during the course of parturition, and under circumstances already discussed in the part devoted to predisposing factors, this may result in the formation of congested and inflamed areas. Sometimes a yellow fibrinous exudate forms over these wounds, and, rarely, extends over the surface of the area under consideration giving rise to the suspicion of diphtheria. The term "exfoliative" is often applied to this development, for example exfoliative vaginitis.

The most characteristic vaginal lesion is the formation of the so-called puerperal ulcer on the posterior wall.

Puerperal infection generally commences as a septic inflammation of the uterine mucous membrane, abrasions of its surface, including the placental site, acting as starting points for the infecting organisms. When pieces of placenta, membrane or blood clot have been allowed to remain in the uterus a suitable nidus is formed with abundant pabulum for bacterial development. Whatever the lesion in the endometrium may be, its presence is synonymous with potential septicaemia.

(2) Inflammation extending through the lymphatic or vascular channels or by direct continuity.

The conditions in the preceding group may cause, by extension along adjacent channels or direct continuity, any or all of the following conditions:-

Condition.	Possible local sequelae.
i) Vulvar lymphangitis	Phlegmon vulvae.
ii) Gangrenous vaginitis	Paravaginitis.
iii) Lymphatic metritis	(Thrombophlebitic metritis (Dissecting metritis (Abscess of the uterus
iv) Salpingitis	(Pyosalpinx (Oophoritis (Abscess of the ovary
v) Pelvic cellulitis	Local or diffuse
vi) Peritonitis	Local or diffuse
vii) Metrophlebitic thrombosis	Phlegmasia alba dolens.

This formidable list is, even to the most casual, ample justification of the vital necessity for the prevention of puerperal infection.

(3) Generalised Infection.

The onset of systemic complications and the form which they take depends entirely on the mode of activity of the causal organisms. The organisms associated with puerperal sepsis have already been indicated, and the ways by which they produce their various results have been described in the introduction.

It/

It is proposed therefore to represent the production of puerperal sepsis including generalised infection diagrammatically, showing the results of bacterial activity and classifying the organisms according to the methods they adopt:—

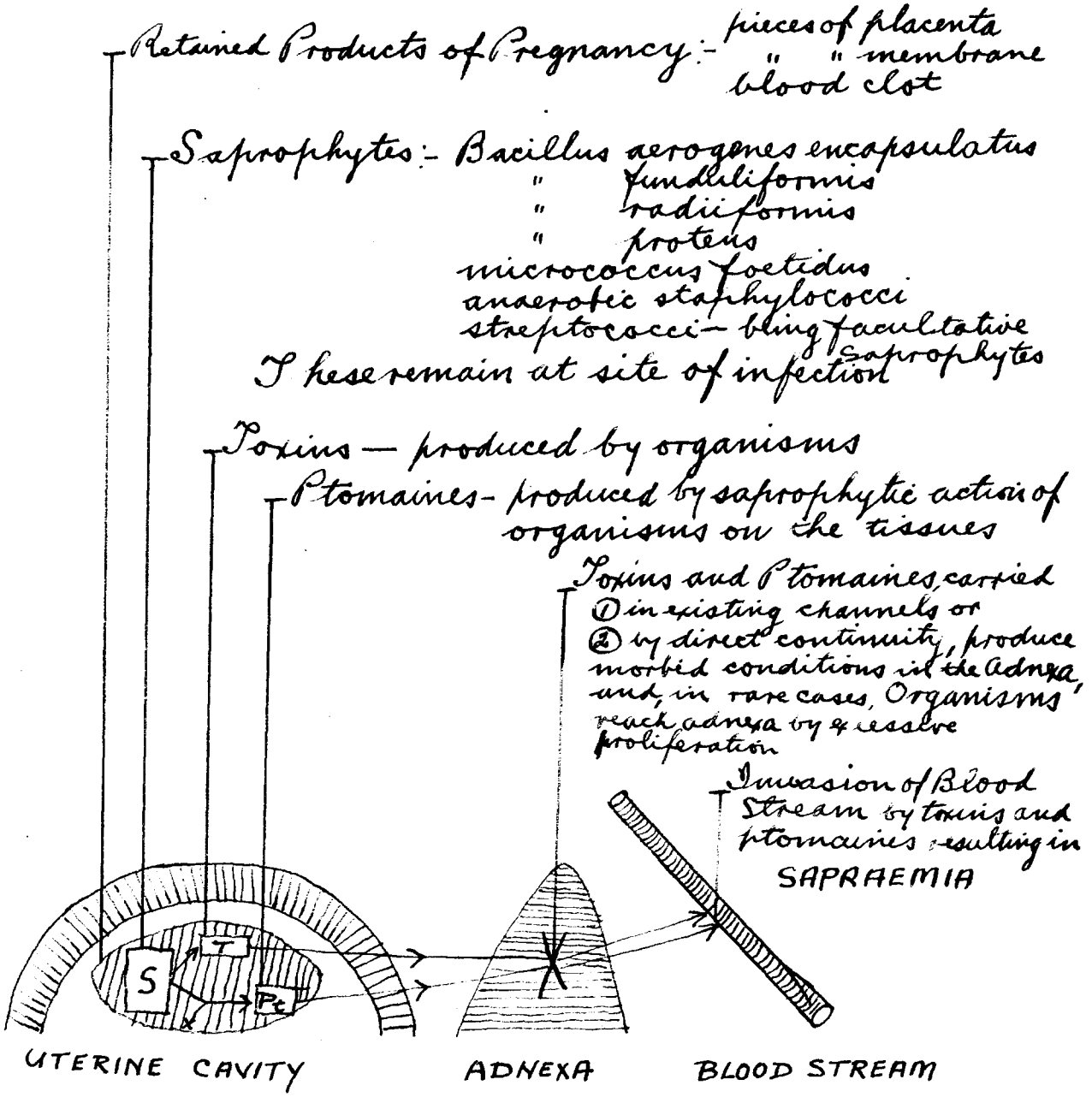

FIG I: DIAGRAM ILLUSTRATING SAPRAEMIA

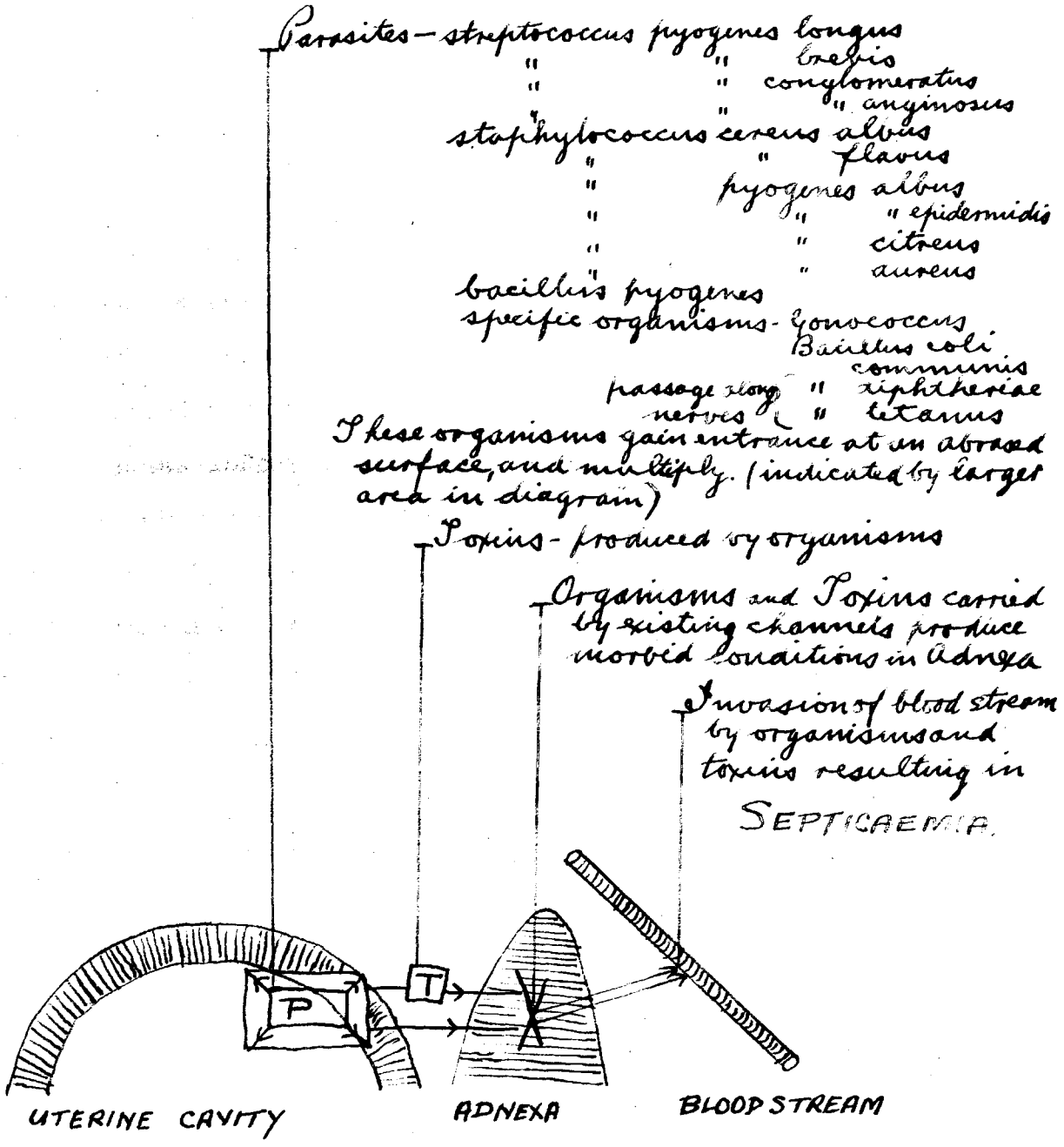

FIG II : DIAGRAM ILLUSTRATING SEPTICAEMIA

It will be seen from these diagrams that sapraemia occurs by invasion of the blood stream by the products of bacterial activity, while the organisms remain at the site of infection, and are only found elsewhere by reason of excessive reproduction.

The development of septicaemia requires the presence in the blood stream of the organisms and their products. In severe cases infected thrombi enter the blood and set up pyaemia, characterised in addition to the symptoms of septicaemia by metastatic abscesses in various parts of the body. In rare cases the only evidence of puerperal sepsis is the sudden onset of septicaemia with little or no local reaction.

Thus, the initial and subsequent development of puerperal sepsis constitute a series of inflammatory conditions, which, ipso facto, means that hyperaemia is an outstanding feature.

According to Sir William MacEwen, all the elements of the blood take part in the hyperaemia associated with inflammation, but the reaction is more marked in the case of the white cells.

I have shown that those who are constantly surrounded by factors of potential morbidity have a higher normal "leucocyte count"/

"leucocyte count" than those who live "sheltered lives", and I contend, therefore, that the leucocyte is the unit of resistance to infection.

I submit, then, that it is reasonable to assume that treatment designed to promote leucocytosis, and described later, will prevent - and if infection has begun, markedly, if not completely, arrest - the pathological sequence just described.

Prophylaxis and Treatment.

Prophylaxis.

Prophylaxis is becoming increasingly regarded as the true aim of the science of medicine. It is right that this should be, since, no matter how complete treatment of a pathological condition may be, the strain entailed by the efforts of the body to overcome the disease might predispose to subsequent morbidity.

The methods employed for the prevention of puerperal sepsis may be divided into two groups:- (1) External (2) Internal.

(1) External methods.

This group includes those measures whose object is to/

to prevent bacteria being brought into contact with the genital tract during and after parturition, and, if they are already there, taking steps to remove or destroy them. Thus, rigid application of the principles of asepsis and antisepsis is involved.

These measures have resulted, in lying-in hospitals, to such a diminution in the number of cases of puerperal sepsis as to make the condition approach vanishing point. It is my experience, short as it has so far been, that puerperal sepsis in institutions occurs only under two interdependent conditions, the second being the deciding one. The first of these is, when the patient has been admitted during or shortly after labour, and secondly, when the number of her leucocytes has been such as to suggest that her condition has prevented the production of the leucocytosis which is usual in a normal pregnancy.

The external methods of prevention include the thorough cleansing of the hands of the accoucheur and the use of sterilised rubber gloves. All instruments which may be used in operative interference must be thoroughly sterilised. Professor I. Munro Kerr's dictum on the point admits of no argument "No condemnation is too strong regarding neglect/

neglect to sterilise all instruments before use, especially as this can so easily be done by simple boiling."

The vulva and mucous membrane of the lower vagina must be thoroughly cleansed, as failure to do this may result in the introduction of organisms varying in type from the simple saphrophyte to the most virulent parasite.

(2) Internal methods.

This group is concerned with efforts to prevent puerperal infection by stimulating the patient to increase her normal powers of resistance.

This is effected to a degree, and in many cases sufficiently, by giving the patient opportunity to breathe pure air, partake of ample nourishing food and obtain plenty of rest.

These conditions are achieved in lying-in hospitals and result in the conservation of energy and the strengthening of the patient's powers of resistance. The latter is brought about by the production of, or the increasing of an already existing, leucocytosis. Therefore, in the event of infection during the puerperium, the patient is able to react efficiently to the stimulation and overcome the invading organisms and their products.

Under our present social conditions, it is impossible, in/

in the majority of cases, to provide hospital conditions outside. It is, therefore, of extreme importance to discover and employ means of controlling puerperal infection to the extent that it is controlled in institutions.

As described in the previous section, I have pursued a line of investigation hitherto unexplored, as far as I am able to discover, with the object of finding out how puerperal sepsis can be prevented. I have come to the conclusion that by securing a definite leucocytosis in all pregnant women and paying attention to the external methods of prophylaxis, infection can be avoided. The desired leucocytosis occurs normally in many cases as shown in Table I of the previous section. When it fails to arise, then measures must be instituted to attain this object.

I propose to describe the methods I have used to produce a leucocytosis in pregnant women when it seemed that therewas little alteration in the number of leucocytes as the pregnancy advanced.

I would explain that I impressed upon my patients, wherever pregnancy was a likely contingency, to inform me as soon as possible. I then carried out frequent enumeration of the leucocytes for the purposes of this thesis.

I therefore consider that it will be clearer if I describe the routine method I have evolved, as the work done/

done for the purposes of investigation is in excess of that required to ensure the safety of the patient.

At the middle of the sixth month of pregnancy the number of leucocytes in the patient's blood is ascertained. Knowledge of the patient's normal "leucocyte content" is thus obtained. If it is found to be less than the average number for a female, 5000 - 6000 p.c. mm blood, then steps are taken to increase it. Another enumeration is made at the middle of the ninth month. If the number is less than the normal plus one third of the normal, treatment to increase the number of leucocytes is begun. In the cases where it was necessary to begin treatment in the sixth month, I always found that a considerable leucocytosis had occurred by the middle of the ninth month of pregnancy.

The treatment I have adopted and will now describe was carried out by me in 47 cases in a series of 90 pregnancies. The puerperia of the 90 patients pursued normal courses, more than two-thirds required delivery by forceps, one was a face presentation, one an occipito - posterior presentation requiring rotation, and one required internal version.

The treatment whether required at the sixth or ninth month/

month is as follows:- Arrangements are made for the patient to be the sole occupant of the bedroom at night. In many of the cottage houses in this district there are two bedrooms, one small, the other large. The large one usually contains two double beds and sometimes one single bed. It was therefore sometimes difficult to secure isolation of the patient at night, but in all cases, despite the inconvenience to the household, it was achieved by explaining the possible dangers of non-compliance. The atmosphere of the room is kept fresh by adequate ventilation. During the day the patient takes a walk, in open spaces - public parks, in the country. Attention is paid to the diet to ensure that there are no irregularities. It should consist mainly of porridge, milk, eggs, fish, and red meat once a day. The patient is advised to lie down for one hour after each meal - two hours after the midday meal.

The following mixture is given:-

R/	Ammonia Benzoatis	gr X
	Magnesii Sulphatis	gr XXX
	Spiriti chloroformi	m X
	Aquam camphoram	Ad 3T
	Signetur.	

Two tablespoonsfuls night and morning. When the treatment is commenced at the sixth month the mixture is stopped every third week.

Ammonium/

Ammonium Benzoate is given because of its effect in greatly increasing the polymorpho-nuclear leucocytes in the blood. It stimulates and disinfects the urinary mucous membrane and therefore facilitates the increased work of the kidneys produced by pregnancy. It is excreted in the urine as hippuric acid by combining, in the kidneys, with glycocoll, whose source is unknown.

Magnesium sulphate has a mild effect in promoting leucocyte formation. By exerting its saline action on the intestine, it stimulates the circulation and assists in the elimination of toxic matter.

Spirit of chloroform acts as a flavouring agent and aqua camphorae positively influences the increase of leucocytes in a small degree.

This treatment, I repeat, was carried out in 47 cases and resulted in a marked increase in the leucocytes in the blood and the puerperia followed normal courses, despite the fact that in many cases the mode of life and environment of the patients did not conduce to a healthy existence, and the patient was surrounded by potential sources of infection.

I contend that by the application of these external and internal methods of prophylaxis against puerperal sepsis the risk of its development will be eliminated.

I/

I base these statements on the results of personal investigation and application of the methods described.

It might be argued that the practical application of this theory, namely the enumeration of polymorphonuclear leucocytes is impossible for several reasons. For example some general practitioners do not posses a microscope, and most do not possess a haemocytometer. Moreover, skill in enumeration of blood cells and confidence in one's results is only obtained by constant practice; and it will be agreed that only a relatively small proportion of the medical profession count the cell elements of the blood after graduation.

Nevertheless, other diagnostic methods with similar difficulties can be used by the general practitioner - Wassermann reaction, examination of sputa, and swabs from the throats of diphtheria suspects.

The collection of the blood is a matter of no difficulty, and once it is mixed with the diluting fluid, the actual enumeration of the cells can be delayed at least 48 hours, provided both ends of the tube are covered by rubber caps.

Treatment.

Since leaving the Maternity Hospital, Glasgow, I have/

have had no opportunity of studying the treatment of puerperal sepsis except for occasional visits to the Leeds Maternity Hospital on the personal invitation of Mr. Carlton Oldfield, F.R.C.S., Professor of Obstetrics and Gynaecology, Leeds University.

If I were called upon to treat the condition I should follow the teaching received as a student and house-surgeon.

I, therefore, venture to feel that I am not in a position to discuss the treatment of puerperal sepsis in this thesis, except to make a suggestion.

Since the production of a leucocytosis has been successful in preventing the onset of puerperal sepsis in the cases which have come under my observation, I would suggest that the administration of the mixture employed by me might assist in arresting the infection, provided that the toxaemia produced by the infection had not paralysed the leucoblastic elements of the bone marrow, which would interfere with the supply of polymorpho-nuclear leucocytes.

Conclusions.

Up to the middle of the nineteenth century, puerperal sepsis increased in prevalence as civilisation advanced.

Those unaffected by civilisation are exposed to many dangerous stimuli which results in an increase in the natural powers of protection. It was suggested by Metchinkoff that phagocytes, which name he gave to leucocytes, were the essential agents in bacterial destruction, and with several modifications, such as the action of opsonins and the theory of phylaxis suggested by Sir Almoth Wright, this view is still held. Therefore, it is reasonable to conclude that the polymorpho-nuclear leucocyte is the unit of resistance to infection. Under the influence of civilisation, however, the body is protected from outside influences and this protection results in a weakening of resistance. Further, the number of polymorpho-nuclear leucocytes in the blood of a woman, as shown in Tables II, III, IV, increases the more the conditions of her life are removed from the protective influences of civilisation./

civilisation.

Consequently, any efforts to prevent puerperal infection, the disease at present under discussion, must aim at increasing the polymorpho-nuclear leucocytes of the blood.

Upon the observations recorded in this thesis I base the conclusion that an absence of leucocytosis in a pregnant woman is the principal factor predisposing to puerperal sepsis, for the presence of leucocytes in sufficient number leads to the suppression of bacterial activity. An absence of leucocytosis may mean either that the leucocytes remain unaltered in number, or, in cases of low vitality, the production of a leucopenia.

Infection during the puerperium in the slightest degree is a serious pathological manifestation because of its tremendous potentiality.

It is most definitely amenable to prophylactic measures because the chief factor leading to its inception is the condition of the patient.

The condition of the patient which makes puerperal sepsis possible, if the causal agents are present, is a deficiency of neutrophil polymorpho-nuclear leucocytes. It is desirable to know the normal "leucocyte content" of a pregnant woman's blood. Enumeration of the white cells up to/

to the sixth month supplies this information.

The precautions adopted in lying-in hospitals have reduced puerperal sepsis to vanishing point. Conditions outside these institutions are vastly different, and it is here that puerperal sepsis causes an enormous amount of morbidity and suffering. In order that a parturient woman be protected from infection during the puerperium it is essential that her polymorph-nuclear leucocytes equal in number at the end of pregnancy the normal plus one third of the normal.

It is necessary that a leucocytosis exist at the end of pregnancy, for, should the conditions for infection in the puerperium be present, the infective process will develop rapidly since it meets with no resistance. Any attempt to produce a leucocytosis then will fail, owing to the paralysing effect of the toxins on the leucoblastic action of the bone-marrow.

The principles of antisepsis and asepsis must, of course, be conscientiously applied, but if lacerations of the genital tract occur and organisms are introduced, the existence of a leucocytosis provides a further line of defence against infection.

If the symbiosis represented by pregnancy does not result/

result in a leucocytosis per se, then the application of the treatment suggested in this thesis will ensure one at the end of pregnancy, thereby providing sufficient resistance to overcome any infection, should it arise.

Finally I would venture to express the opinion, that an absence of leucocytosis during the last two months of pregnancy is synonymous with the appearance of the results of infection during the puerperium. The three essentials for infection are site, agent and opportunity. In parturition, the site is always present in as much as breach of continuity of surface is unavoidable; outside maternity hospitals it is almost impossible to completely exclude the agent; the opportunity is represented by the lack of resistance of the patient, and it is attention to this that will ultimately lead to the complete elimination of puerperal sepsis.

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