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on

"THE INTENSIVE TREATMENT OF PUERPERAL SEPSIS."

Presented by

MARGARET WYLIE THOMAS, M.B., Ch.B. (Glas.).

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THE INTENSIVE TREATMENT OF PUERPERAL SEPSIS.

The Scottish Departmental Committee, in a report published in 1924 and dealing with the question of Puerperal Mortality and Morbidity, made the following statement:- "The evidence which we have received is unanimous on the essential point that the present maternal mortality of Scotland is reducible." This conclusion was arrived at by the general experience that the main cause of maternal death was a puerperal infection; and were corroborative evidence required, it could be found in the number of investigations which have been made during the past decade in the hope that by a diminution of the incidence of this disease the above claim might in some measure be realized.

Attention has been directed chiefly to its etiology and prevention, and it is wise that these should form the main lines of inquiry. It has to be remembered, however, that while these investigations are being carried out, and theories are being propounded, every week brings into hospital more and more women demanding treatment for a disease, which is to a large extent a preventable one. It does not require a long association with patients suffering from this disease to be appalled by its utter tragedy. Every death is a calamity in the face of which one does not pause to affix guilt, but rather to reflect whether another of the many suggested methods of treatment might have been the means of saving the life of the patient.

The death rate from Puerperal Infection is alarming; but what of its morbidity? Many women who survive are burdened with after effects which sap their strength and undermine their happiness, and it has been stated that 70% of all patients in gynaecological wards can trace their illness to a puerperal source. The effects of this disease are indeed far reaching and the

necessity of finding a reliable method of treatment is urgent.

A consideration of the question of treatment divides itself naturally into two main aspects - the local lesion and the generalized infection or toxæmia. If Puerperal Infection is - as Fothergill ⁽¹⁾ states - just the same as ordinary wound infection, early treatment of the seat of disease would at first sight appear indicated; and such has been the ambition of medical men since the full significance of the condition was realized. The list of methods which have found favour is long and varied, and illustrates the changing theories concerning the disease. The idea of contagion first voiced by Holmes, ¹⁸¹² and later by Gordon, found expression fifty years later in the Listerian methods of Semelweiss, who, in 1847, by the free use of antiseptics, greatly reduced the mortality and prevalence of the disease. A few years later, the belief that all cases followed on retention of placental debris or blood clot prompted the free use of curetage. Lea ⁽²⁾ writing prior to 1910, favoured intra-uterine treatment in all but the most virulent infections, sometimes substituting for the curette a brushlike scraping instrument - the "ecouvillon." Shear ⁽³⁾ Fitzgibbon and Biggar ⁽⁴⁾ ten years later strongly opposed such methods. Geddes, ⁽⁵⁾ however, in 1926 advocated the early use of curetage, claiming that if all cases were thus treated at the outset, few would develop into the more serious types of the disease. In this he was supported by Benoit, ⁽⁶⁾ Whitehouse, ⁽⁷⁾ Delmans, ⁽⁸⁾ Becker, ⁽⁹⁾ and many others, but as strongly opposed by Williams, ⁽¹⁰⁾ Luker, ⁽¹¹⁾ Sigwart, ⁽¹²⁾ Halladay, ⁽¹³⁾ Van Dongen ⁽¹⁴⁾ and Gordon ⁽¹⁵⁾, Those who had experience of Puerperal Sepsis when it first became a notifiable disease, can still remember vividly the horrors of routine curetage and its pyæmic sequelæ.

With further research, the acid reaction of the vaginal secretions became the focus of attention and the importance of Doderlein's Bacillus Acidophilus was realized. The introduction of lactic acid cultures into the vagina soon became the rational treatment of the disease. Cherie, ⁽¹⁶⁾ writing in 1924, speaks favourably of this method. Concurrently there were other investigators who

plead for more heroic treatment. Baldwin (17) advocated panhysterectomy; Munro Kerr, (18) vaginal hysterectomy; (19) while Blair Bell, (20) and Bonney, both recorded favourable results, in severe cases, from tying and removing the thrombosed vessels of the parametrium. In the wake of these militant methods came the ideas of "masterly inactivity." Even in 1925, Williams, (21) described his ideas on treatment in the line "feed them well and give them fresh air;" while in the same year Russell, (22) epitomized his practice as "nursing and looking out for pus," This conservative method regarded the patient simply as an ill woman; and rest in bed, freedom from examination, and minimal disturbance of mind and body were its main essentials.

Once more, however, we are being assailed by the advocates of local interference. The introduction of glycerine (23) into the uterus - first described by Hobbs, has its enthusiasts in all countries, and the technique of this treatment frequently includes intra uterine douching a relic of the days when curetage held the field. Lymph drainage and lavage à retro have thus assumed much importance.

In the treatment of the general infection there is to be found even greater cause for bewilderment. Previous to, and indeed for the most part during the era of curetage, no specific remedies were employed to combat the toxæmic or septicæmic state. Liberal diet, fresh air and the free use of stimulants were the main bulwarks of the general treatment. When the value of vaccines in other diseases became known, many observers found them of benefit in all stages of Puerperal Infection. Among (24) these were Kerr, (25) Jordan, (26) Daels, (27) and Western, who recommended the use of autogenous vaccines in the early stages of the disease. Chomé (28) and Lequeux (29) on the contrary considered them to be dangerous in the acute forms of sepsis. Koehler, (30) doubted their value at all times, and considered that any effect was simply a foreign protein reaction.

Intravenous medication with antiseptic substances was the next line of experimental investigation. Many and varied have been the substances used by those who advocate this type of treatment. Fitzgibbon (4) favours colloidal iodine. Dudgeon (31) recommends perchloride of mercury, (11) while Kiehae (32) combines this with arphenamine. Luker favours quinine bi-hydrochloride, Whitehouse (7) .4% acriflavine, Gastelum (33) .3% magnesium sulphate, and Gracie (34) eusol in 50 c.c. doses. Schumann (35) amongst others advocates mercurochrome, while Scholtem (36) uses colloidal Silver and Copper. These colloidal preparations (37) have also given successful results in the hands of Ramsay. (38) Gow, (30) writes favourably of Witte's peptone solution. Kochler (39) after a very wide survey of all other intravenous medicaments finds most benefit with Pregl's iodine solution. Philip (40) writing in 1925 records an unsuccessful attempt to sterilize the blood by means of inhalations of narcylyene gas. Finally there are the findings of Polak and Piper (41) who tried intravenous therapy extensively and abandoned it as being quite ineffective. It is interesting, however, to note that as early as 1870 Tyler Smith (41) recorded a case which he treated successfully with intravenous ammonia.

It is a tribute to the ineffective character of the foregoing methods, that there were at the same time advocates of a form of treatment which aimed at the production of an inflammatory reaction. Lea (2) and Jordan (25) in 1910 both remarked on the improvement which always resulted if a circumscribed infective focus formed in the course of the disease, and this was the basis of the fixation treatment favoured by many - notably, Irens, (42) Carles, (43) Portaccoeli, (44) Poux, (45) Rascol, (46) and Pery. (47) Abscess of fixation (30) thus became a frequently accepted practice. Kochler, however, strongly opposed this method.

At present attention is being directed towards the treatment of the disease by an appropriate serum. Organic preparations of arsenic are also favoured by many; while vitamins - eminently successful in various other conditions - are finding their adherents.

This multiplicity of treatment, both local and general, is indeed confusing. Medical knowledge has advanced so rapidly within the past few years that one is apt to mistake novelty for worth; and in our advocacy of what is new, and what may be moreover theoretically sound procedure, we are in danger of forgetting much of what the older methods had to recommend them.

There are types of treatment for which high claims are made. In the hands of other observers these have yielded results, which - if universally obtained - would rob the disease of many of its terrors. This investigation was undertaken to test these methods critically, and to compare them in their application and results with a less militant routine previously followed. All the patients were notified cases of Puerperal Fever, treated in the wards of Belvidere Hospital; and 800 came under review. Of this number 600 were personally treated and supervised by myself during the period April, 1929 - January, 1931. The additional 200, who form part of the necessary control series, were under the care of my predecessors who have allowed me to utilize their clinical records for this purpose. The complete investigation of so many patients has revealed many interesting and instructive details apart from those of treatment, but their inclusion would make this work cumbersome and I have reserved them for separate publication. The following analysis therefore is concerned primarily with treatment, especially with reference to the several methods which are elsewhere advocated.

At the outset it is essential to define the standards by which results of treatment are to be interpreted. There is, in the first instance, a personal estimate which may be confirmed by

obvious clinical findings. On the contrary, there is frequently definite response without manifest signs, although the patient may affirm betterment. The benefits of treatment also, do not cease with saving life. Its effects on the febrile period, on the whole duration of illness and on the liability to complications, are also of paramount importance. Standards vary with the same observer and between different observers, and are thus valueless unless based on something more than a personal estimate, however impartial that may be. In the following investigation I have used four definite standards for comparison, and a few other factors have been considered in the course of the discussion.

In this report it is proposed to describe fully the types of case dealt with, discussing them from the clinical and bacteriological aspects. The methods of treatment will then be stated in detail and their results critically reviewed. A statistical analysis follows - each treatment being compared in its application and judged in the light of definite criteria. It will then be apparent whether the personal estimate in any way corresponds with the statistical results which have been thus obtained; and finally it may be possible to discover which method of treatment is in the highest degree satisfactory and dependable.

C A S E S.

THE CASES.

It is obvious that if methods of treatment are to be compared they must be examined with regard to their effect on similar lesions and on their associated constitutional disturbances. Although such a system of grouping is essentially superficial it has been found convenient to classify the cases under review into four main categories, in accordance with the extent and distribution of the disease. Thus in each group there will be several methods of treatment available for contrast and criticism.

The system of classification is as follows:-

- Group 1 Infections limited to perinaeum, vagina and cervix.
- Group 2 Infections within the uterus - in addition to or without gross infection of the lower parts of the tract.
- Group 3 Infections spreading outwith the uterus.
- Group 4 Infections which are invading the blood stream.

It should be noted that this grouping refers to the conditions found on admission to hospital, when the question of treatment is most urgent. Many women develop complications which would justify their later inclusion in other groups, but the original lesion is the more important for the purpose of this analysis.

In the majority of cases the infection resulted from full time confinement. Premature Birth accounted for another small proportion. In the remainder- amounting to almost one quarter of the whole series - sepsis followed abortion or miscarriage. In order that repetition may be avoided, it has been thought advisable to consider the small group of premature births with, the full time cases, and the miscarriages with the abortions. The term "Post Abortum Sepsis" as ^{it} is used in the following discussion therefore includes abortions and miscarriages. The clinical features of these latter cases, and to a greater extent the problems of their treatment, differ from those of the full-time pregnancies. I have therefore considered them separately throughout the whole investigation. Table 1 gives an analysis of the total cases in accordance with the above grouping.

TABLE 1.

Showing types of cases in relation to grouping.

	Full Time	Premature Births	Miscarriage	Abortion	All Pregnancies
Group 1	69	7	5	31	112
" 2	237	12	26	73	348
" 3	176	11	12	29	228
" 4	91	1	10	7	112
All Severities	573	34	53	140	800

The relative proportions of each type of pregnancy in the whole series are shown in Table 2.

Table 2.

Table - showing cases in whole series in relation to type of pregnancy.

Duration of Pregnancy.	Number of Cases.	Total Cases In Full Time and Post Abortum Groups.	Percentage of Each in Group.
Full Time Birth	573)	607 =	75.9 %
Premature Birth	34)		
Miscarriage	53)	193 =	24.1 %
Abortion	140)		

A more detailed examination of the groups will be helpful in the later discussions.

Group 1. LESIONS LIMITED TO PERINAEUM AND CERVIX.

Of the total cases 112 i.e. 14% were of this type. This number is made up as shown in Table 3.

Table 3.

Table showing cases in Group 1 in relation to type of pregnancy.

Duration of Pregnancy	Number of Cases	Total Cases in Full Time and Post Abortum Groups.	Percentage of Each in Group.
Full Time Birth	69)	76	67.8 %
Premature Birth	7)		
Miscarriage	5)	36	32.2 %
Abortion	31)		

The proportions therefore differ from those for the whole series, Post Abortum cases being slightly increased.

The lesion here may consist of a sloughing perineal laceration with or without bruising of the vaginal walls. If there is any infection of the lower parts of the genital tract, the uterus does not involute well; and a frequent finding on admission is therefore perineal tear with subinvolution. This is the mildest type. More often the cervix also is oedematous, bruised, or frankly lacerated and will be found covered with slough and membranous exudate, but it is important to realize that there may be gross cervical damage without perineal or vaginal injury. Usually when the cervix is lacerated the cervical canal is open and the os internum may admit a finger. There need not however be gross uterine infection, even when the cervix is markedly involved.

Clinical Features. These patients are rarely ill. The temperature is, if at all, very slightly elevated, and the pulse rate is in many cases unaffected. The symptoms may indeed be nil. If there are extensive lacerations such as complete perineal tear or injuries radiating from the cervix to the vaginal vault, local discomfort or pain may be noted, but such symptoms are remarkably few even in the worst degrees. Bruising round the urethral orifice occasionally results in painful frequent micturition, and retention of urine sometimes ensues. The purulent character of the lechia is however the main source of complaint throughout this group.

The cases of Post Abortum Sepsis are mostly the result of delayed emptying of the uterus, and rarely show any lesion apart from slight subinvolution of this organ. It is unusual to find gross laceration of the parturient canal or perineum although in criminal cases small cervical tears are sometimes produced. Erosions of the cervix, and vaginitis are however common, and the lechia is usually prolonged, excessive, and seropurulent in character.

The symptoms here are practically always nil. Slight back-ache may be complained of and the temperature rarely rises beyond subfebrile levels.

COMPLICATIONS. A small proportion of women in this group develop complications while in hospital. Pelvic cellulitis is the most common, and this is always in relation to cervical or vaginal damage, the spread of infection being by way of the lymphatics and not via the body of the uterus, which still remains uninfected. Occasionally the condition progresses to abscess formation although the sepsis is still entirely outwith the uterus. Phlegmasia Alba Dolens is also an occasional complication, and may be related to a similar cervical or vaginal source. Where the vaginal and perineal lacerations are extensive, erysipelalous inflammation of the surrounding skin is a frequent sequel. Post Abortum sepsis of this group usually runs a mild uncomplicated course; and the prognosis in all types is good.

Group 2. INFECTIONS WITHIN THE UTERUS.

This group comprises 348 patients i.e. 43.5% of the series. The proportions are found in Table 4.

Table 4.

Table showing number of cases in Group 2 in relation to type of pregnancy.

Duration of Pregnancy.	Number of Cases .	Total Cases in Full Time & Post Abortum Groups.	Percentage of Each in Group.
Full Time Birth	237)	249	71.6
Premature Birth	12)		
Miscarriage	26)	99	28.4
Abortion	73)		

Post Abortum sepsis is thus a little less frequent in this group, although still in advance of the percentage for the whole series.

This is the large group of intrauterine sepsis, and the main lesion is Septic Endometritis. The number of patients in whom a purulent discharge is found issuing from the os internum is itself large; but there are many other occasions where the discharge is scanty, thick, and not obvious at a first or single examination. Many cases of septic endometritis follow on the retention of small pieces of membrane or blood clot which have undergone putrefaction and gangrenous change. When infection has entered the uterus in this way, one of the main factors determining its further course is the degree of drainage obtained. Failure of drainage results from a variety of extra uterine and uterine causes. Among the former are pressure of a loaded rectum, a distended bladder or other pelvic tumour. The uterine causes include malpositions, spasm of the os, or actual blocking of the cervical canal by blood clot, membrane, placental debris, sloughs, ^{or} oedematous swelling of the tissues. In these circumstances the lochia may practically cease, and if the uterus is not much enlarged the sepsis within it is in danger of being overlooked, with later disastrous results. Although septic endometritis frequently occurs therefore in combination with laceration and sloughing of the parturient canal, - and is then an obvious feature of the case, the presence of little or no discharge, and the absence of local sepsis in perinaeum vagina or cervix, must never be taken as evidence that there is no sepsis within the uterus itself. Frequently one finds marked toxæmia, but no clinical signs of sepsis apart from slight enlargement of the uterus. Yet on manipulation of the womb large quantities of pus will drain from it, and there will be immediate relief from general symptoms. The uterus has been nothing less than a closed abscess cavity from which toxic absorption proceeded apace. The number of such cases is certainly equal to those where septic endometritis occurs as part of a gross infection involving the remainder of the tract.

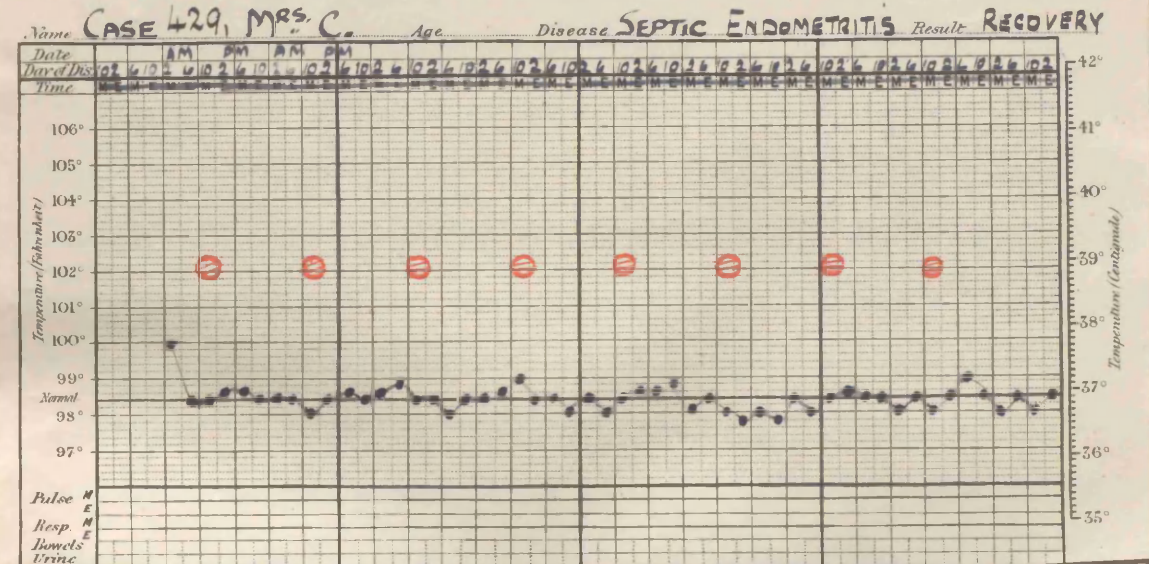
A few women in this group have slight inflammation

of one or both Fallopian Tubes or a very mild degree of induration in the pelvic cellular tissue - usually in association with a cervical or vaginal laceration. But the chief lesion is the sepsis within the uterus itself.

The Symptoms vary greatly. Fever is rarely absent.

The accompanying temperature chart was however provided by a woman (case 429) afebrile throughout, although her main lesion was severe septic endometritis.

⊖ = INTRA UTERINE DRAINAGE OF PUS



There have been several such. If there is a free exit from the uterus there may be very little toxic absorption and few symptoms; but should drainage be impeded backache, headache, abdominal pain, sickness, and the general signs of toxæmia become manifest - sometimes to a very high degree. Frequently at this stage, the uterus can be palpated as a large tender mass reaching almost to the umbilicus; but backward displacements may obscure this sign. With regard to failure of involution, due consideration must be given to the duration of the puerperium, and the uterine enlargement interpreted accordingly. Many women also have on admission marked distension of the urinary bladder which makes the uterine enlargement more apparent than real. The womb is however always palpable in cases of this group, and in the majority definite tenderness may be elicited. The changes in the lochia have already been noted.

The Post Abortum cases usually result from the retention of septic products within the uterus. In practically all these were still present on admission to hospital, and it was not unusual to

find foul putrid material still firmly adherent to the endometrium. It would be little short of miraculous if the uterus escaped infection under such conditions. Intra uterine sepsis in varying degree was therefore the rule.

The clinical features vary a little from those obtained in the full time cases. Such gross uterine enlargement is not as a rule met with, and the lochia is rarely so profuse. Blockage of the cervical canal by small pieces of placenta is however relatively more common in the post abortum cases, and frequently the removal of such an obstruction is followed by an outpouring of very foul pus - the multiplicity of organisms usually present in decaying organic matter contributing in great measure to this. The Symptoms also are mainly sapraemic and on the whole more insistent than in the full time cases. Headache, sickness, backache, are rarely absent and there is a distinct general feeling of ill-being which contrasts strongly with the euphoria of the toxic states. The temperature is usually high and the pulse rapid, but neither of these may show much departure from the normal even in the presence of much sepsis, so long as drainage is adequate.

COMPLICATIONS.

The most frequent complication is pelvic spread of the infection, and although this may occur when the cervix and vagina, are intact, it is seen at its fullest extent if there are sloughing lacerations of these parts. The cellular tissue, Fallopian Tubes, and even the perⁱitoneum may thus become involved. In this series eight women developed pelvic abscess, and in one other fatal peritonitis supervened. Phlegmasia Alba Dolens is also an occasional complication, signs of spread to the cellular tissue being usually apparent before the veins become implicated and the leg swells. Secondary septicaemia is also liable to occur if the infection is of a virulent character. Five women of the series developed this complication. A few gave evidence of subacute

nephritis and in two cases Pyelitis was noted. Bronchitis and Broncho Pneumonia are not infrequent complications, and other incidents such as sore throat, otitis media and mastitis are notable; but these are not strictly complications of the local condition, and in the later analysis have not been classed as such.

PROGNOSIS. This is on the whole good. Well established septic endometritis acts in much the same way as an abscess of fixation, and spread to vital tissues rarely occurs. Peritonitis and Secondary Septicemia provide most of the fatal cases, and these are comparatively rare after admission to hospital. Intercurrent Pneumonia, especially if Lobar in type, may also prove fatal.

Group 3. INFECTIONS SPREADING OUTWITH THE UTERUS.

This includes 228 patients i.e. 28.5% of the whole series.

The relative proportions of the group are given in Table 5.

Table 5.

Table showing cases in Group 3 in relation to type of pregnancy.

Duration of Pregnancy.	Number of Cases.	Total Cases in Full Time and Post Abortum Groups.	Percentage of Each in Group.
Full Time Birth	176)	187	82
Premature Birth	11)		
Miscarriage	12)	41	18
Abortion	29)		

The diminishing percentage of Post Abortum cases is noteworthy.

The outstanding feature of this group is the spreading tendency of the infection. The uterus and parturient canal may be grossly or minimally involved, but the fact that the infection

is not remaining limited to these regions becomes the urgent matter. This spread may be directly into the Fallopian Tubes or outwards to the connective tissue of the broad ligament, so that pelvic cellulitis and lymphangitis result. If the pelvic veins become involved in the latter instance, localized or spreading thrombophlebitis occurs, and this may assume septic characters. From tubes and cellular tissue the pelvic peritoneum is readily infected, and by continuity general peritonitis supervenes. Many spreading infections become localized early, in the Fallopian Tubes or parametrium; others - probably more virulent - advance rapidly to the peritoneal surface. When localization occurs abscess formation is liable to follow. The group includes patients admitted in all of these stages of pelvic infection.

The Clinical Features vary very much within the group.

Tubal Infections if recent and acute, are usually accompanied by severe pain of a colicky type, and by marked local tenderness with muscle guarding on the affected side. Sickness may occur, the pulse is rapid, and the temperature high. Slight early inflammation may be suspected if there is tenderness in one or other lateral fornix without palpable swelling, and in many instances the condition progresses no further than this. It is only when the inflammation has been active for days or even weeks, that tubal swellings may be detected on bimanual or abdominal examination. Later when definite pyosalpinx has developed many adhesions are usually present and a firm mass will be easily palpable. The pulse rate is usually slightly increased, but subfebrile or even afebrile temperatures are the rule at this stage, and the patient may be quite symptomless.

Pelvic Cellulitis usually begins with severe pain, diffuse, over the lower abdomen; and while it is spreading and active, pain is an outstanding feature. The temperature is elevated, the pulse rate high, sickness may be frequent, and the woman looks ill. Definite tenderness and muscular rigidity may be present on the

affected side even in the absence of peritoneal involvement. It is possible, however, that there is slight transient peritoneal irritation in these cases. A little resistance and tenderness of the fornices may be all that can be determined at this stage and the diagnosis is often difficult. As the acute condition subsided the symptoms usually disappear, and even when the pelvis is filled by an indurated stony mass there may be little indication of its presence previous to vaginal or abdominal examination. A few patients at this stage do however complain of backache; and flatulence, chronic constipation, dysuria, or frequency of micturition are of frequent occurrence. Bimanual examination will then reveal a hard brawny mass continuous with the uterus in one or several directions, sometimes masking the fundus completely, at other times pushing it aside into the fornices. Tenderness is rarely acute even when abscess formation has occurred, and there may be no toxic signs at this stage. Occasionally patients are admitted with pelvic abscess already developed, but this is typically a complication of the group and will be discussed under that heading. In the severe spreading infection tubal involvement may occur concurrently with cellulitis, and doubtless the large masses palpable in many cases are composed of the inflamed uterine adnexa ~~and~~, and indurated cellular tissues.

Phlebitis. Inflammation of the pelvic veins may occur in addition to cellulitis or salpingitis, but in many cases it is the only lesion discoverable and in this event is a late manifestation of the disease. In a strict analysis these latter are examples of spreading uterine infection, but the disease is so attenuated that there is rarely any local sepsis when the patient is admitted to hospital. These are cases of Phlegmasia Alba Dolens occurring in the third week of the puerperium. Here the gravity of the condition is rather due to

the mechanical factors of venous obstruction and clot formation, then the result of septic absorption from diseased areas; and since they require no special treatment these patients have been excluded from the present survey.

When Phlebitis develops concurrently with uterine infection and cellulitis, it is apt to assume a very grave form, spreading through all the ramifications of the pelvic veins in addition to those of the legs, and ultimately involving the larger vessels of the abdomen. Post mortem examination revealed two cases where thrombus formation extended up the Inferior Vena Cava to the heart, and lesser degrees were common. Pyaemia frequently produces the fatal issue, however, before the thrombus formation has reached these greater limits, and it is only when the clot is aseptic that such extension is possible. These pyaemic cases are included in the group of blood infections. In the absence of Pyaemia the symptoms are those of the uterine and para uterine infection which is concurrent, and apart from moderate oedema of one or both lower limbs there may be no special indication that the veins are affected. It is to be noticed that this oedema is rarely severe, usually painless, and differs in these and many other ways from the typical Phlegmasia Alba Dolens to which reference has already been made.

Peritonitis. Inflammation of the pelvic peritoneum is a frequent occurrence. The pulse is rapid, the temperature elevated, sickness and flatulence are troublesome and the patient feels ill. The chief complaint is of severe pain across the lower abdomen, and examination reveals varying degrees of tenderness and rigidity below the umbilicus. Vaginal examination is restricted by pain, but a boggy swelling of the fornices may be determined. Local sepsis may be severe. Many cases of pelvic peritonitis however show little evidence of intra uterine activity, and it is presumed that here the virulence of the infecting organism carried it rapidly through the confines of the uterus

before any defence could occur.

Generalized Peritonitis. is a further stage of the above condition, although in fulminant cases it may develop without any previous indications of localization to the pelvic area, and occasionally patients in the first or second day of their puerperium were found to have peritonitis already well established. The outstanding clinical features are the constant distressing sickness and the severe abdominal pain. The abdomen is at first rigid, and tenderness is extreme; but both of these features are of short duration and soon give place to distention without hyperaesthesia, and even without pain. Women admitted at this later stage may thus give little indication of peritonitis although the abdominal cavity contains much purulent material. Many observers have noted this, among whom (48) Nuthall, writes "Clinically it is characterized by a Peculiar Absence of the Local Pain, Tenderness, and rigidity of other forms and the patient is much more ill than the symptoms seem to indicate." Williams, (10) remarks that the discovery post mortem of diffuse peritonitis may come as a surprise, since abdominal symptoms are often slight or even absent; and Hauch (18) confirms this. Kerr, on the contrary, regards the clinical features of puerperal peritonitis as perfectly obvious and characteristic. Much however depends on the patient and on the virulence of the infecting organism.

The Post Abortum Cases of this group usually present extensive pelvic infection. Most of these are women who for weeks or months have been harbouring dead disintegrating material within the uterus, and who in addition are debilitated by continuous or recurring haemorrhage. In one third of these cases such foul products were still present on admission to hospital. If the abortion has been criminally induced there is an additional source for organismal infection, and it is not

surprising that very wide spread sepsis results. The cellular tissue does not become affected so readily as in the full time cases, but any involvement is severe and frequently of a gangrenous character. Salpingitis is however common, in many cases bi-lateral, and an adhesive type of pelvic peritonitis may be concomitant. Even at this stage septic putrefying products may still be present within the uterus. General peritonitis following abortion is usually of a very virulent nature and rapidly terminates in death.

The Clinical Features. are analagous to those found in full time cases. Intense pelvic pain is usually present in the acute stages when the Fallopian Tubes are becoming involved, especially if there is perisalpingitis and the over lying peritoneum is affected. In the gangrenous types where massive pelvic infection is the rule, pain may be extreme and commonly radiates through the sacral foramina to the lumbar region and to the thighs. The general symptoms are very acute and the patients seem much more ill than the other cases - a condition partly accountable to the sapraemic element.

COMPLICATIONS.

Further extension of the pelvic sepsis frequently occurs. Thus a unilateral cellulitis or salpingitis may become bilateral, the peritoneum may be involved, and a general peritonitis result.

Abscess may develop centrally in a large pelvic mass or even when cellulitis is not extensive. It is possible that in many instances the purulent material is never evacuated but becomes encapsulated and perhaps later is absorbed. Usually however a pelvic abscess tracks towards an external surface; and it may do so in several directions.

(a) In the first place it may extend upwards and outwards towards the iliac fossa. As such it may gradually form

an obvious swelling above the inguinal ligament chiefly in its inner half. The infection frequently subsides behind as it passes upwards; and it is the rule in these cases to find the fornix on the affected side empty and freely palpable,

(b) Secondly, it may burrow backwards into the hollow of the sacrum. Its usual course is then through the sacral foramina or sacro-sciatic notch, and gradually it appears as an oedematous infiltration which may become a fluctuant swelling over or lateral to the sacral spine. Spread in this direction is accompanied by very severe pain radiating round the lumbar region and into the buttocks and thighs, and this is of diagnostic significance for days or weeks before the external swelling appears. Rupture into the rectum occasionally occurs in these cases of backward spread. This happened in two cases of the series, and was preceded by days of acute pain which was instantly and permanently relieved when rupture occurred.

(c) Finally and less frequently extension may occur downwards into the Pouch of Douglas, rupturing into the vaginal vault. This is surprisingly rare and was noted in only one patient.

It is of importance that all these directions are extra-peritoneal. Rupture into the peritoneal cavity appears to be unusual, and the series includes no patients where such an occurrence could be diagnosed with surety.

Thrombophlebitis is a frequent complication of this group, if the infection is active and spreading. One or several veins may become involved; and although primarily sterile—the clot may be infected, with pyaemic sequela.

Secondary Septicaemia results if a vein is implicated in a pelvic abscess. Its wall softens, and if it does not actually

rupture it at least becomes easily permeable to the infecting organisms which thus readily gain access to the blood stream. This inoculation may be continuous or it may occur on one occasion only; but if the bactericidal powers are low the effects are especially disastrous.

Bronchitis, Broncho Pneumonia, Cystitis, Pyelitis, and Nephritis readily develop and are to be related chiefly to the lowered vitality incident on such extensive infection.

PROGNOSIS.

The death rate for the group is relatively high, and prognosis should therefore be guarded in all but the very mild localized types. Peritonitis and Secondary Septicaemia usually provide the fatal issue, and while the infection is active and spreading these are mainly to be feared. It should be noted however that patients frequently survive an acute peritoneal infection yet succumb in the later chronic stages; and the prognosis must therefore be made carefully even if few symptoms remain. Thrombophlebitis is also responsible for several fatalities in this group. Here death may result from pyaemia of an acute or chronic type; but there are a few patients who recover from the active stage, become afebrile and apparently improve, yet gradually exhibit signs of progressive venous obstruction which ends fatally when the heart itself becomes implicated. Pneumonia may also cause death.

The morbidity rate is high. Few cases of spreading pelvic infection ever completely recover; and many women leave hospital with chronic salpingitis, cellulitis or even peritonitis. This is specially true of post abortum infections, which once they invade the pelvis may rarely be persuaded to leave it.

Group 4. INFECTIONS INVADING THE BLOOD STREAM.

In this group there are 112 patients i.e. 14% of the whole series. The relative proportions are illustrated below.

Table 6.

Table showing cases in Group 4 in relation to type of pregnancy.

Duration of Pregnancy	Number of Cases.	Total Cases in Full Time and Post Abortum Groups.	Percentage of Each in Group.
Full Time Birth	91)	95	84.8
Premature Birth	4)		
Miscarriage	10)	17	15.2
Abortion	7)		

The proportion of post abortum sepsis in this, as in the preceding group, is thus definitely below that for the complete series. On the whole, therefore, this type of sepsis assumed a less grave form than in the full time cases.

The patients in this group were all clinically Septicaemic on admission to hospital. Blood examination was made in each case, and repeated if no organismal growth was obtained. Of the series, fourteen gave repeated negative results; but they have been included because they showed unmistakable signs of blood infection, and of their number, nine ended fatally. A few patients appeared Septicaemic, but repeated blood culture did not reveal the presence of a generalized infection, and the subsequent clinical features decided the issue against Septicaemia. These have been relegated to other groups and discussed therein.

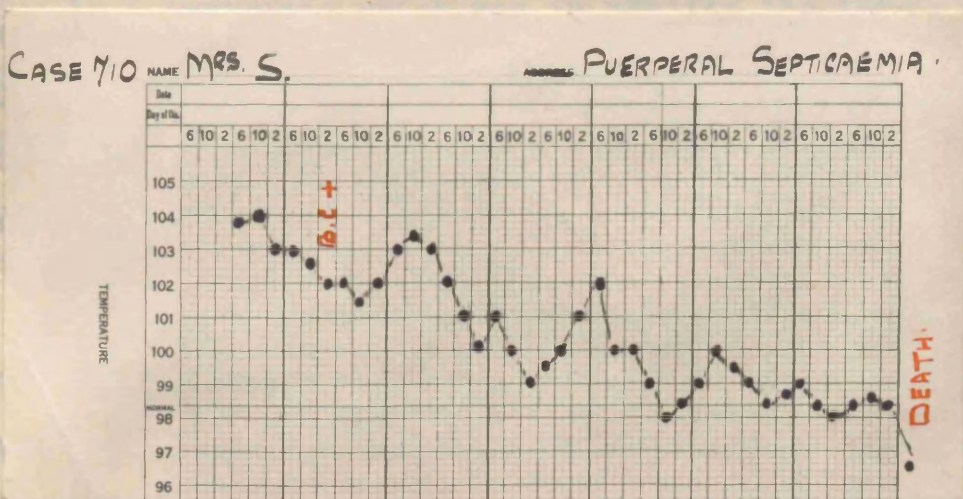
It must be realised that many patients otherwise belonging to the preceding groups are also septicaemic; but if the infecting organisms have invaded the blood stream, this must be considered as the salient feature and the local lesion - no matter how severe - becomes of minor importance. A considerable proportion have, however, very little evidence of local sepsis. There may be no lacerations, the uterus slightly, if at all, enlarged, the lochia scanty and serous, and there may be no appreciable signs or symptoms of pelvic inflammation; yet the patient is

In typical Septicaemia the patient looks ill but seriously ill and a blood examination will reveal the presence of generalized infection. This is the group of Primary persistent feature. Thorpe, (49) this as a very Septicaemia described by Brindeau, and it is doubtless constant symptom, altered only by peritonitis or impending the result of massive infection by way of the placental sinuses death; but there are few cases where even the latter is of during or soon after labour. Secondary Septicaemia occurs much effect, and until practically unconscious a septicaemic as a relapse about the fifth or seventh day of the puerperium, patient will frequently affirm that she is improving. Saugh usually after septic endometritis, parauterine infection, and Benschheim have also drawn attention to the euphoria and phlebitis have already become manifest and an acute spread- of puerperal septicaemia, and consider it as a valuable aid to ing infection has been established. Pyaemia - which is an inter- diagnose. mittent blood infection - is a still later development and follows on pelvic phlebitis occurring alone or as part of a larger suppurating pelvic focus.

Clinical Features.

Puerperal Septicaemia entails

is a marked acetone odour from the breath. There may be fleeting a serious clinical picture which is almost unmistakable. At joint pains, or slight cough and some dyspnoea without apparent the outset there is a long marked rigor, followed in most cases cause for same - "dyspnoea sine materia" described by Brindeau. by a continuous high elevation of temperature. Febrile Mild delirium is frequent and there may be periods of mental temperatures are however by no means constant and in profound confusion accompanied in many cases by hallucination of both septicaemia the patient may be quite afebrile. High elevations - visual and auditory nature. Even in the early stages the liver especially if remittent - are found in the less severe infections, may be appreciably enlarged, and in most cases there is a slight and may in these assume prognostic significance to a limited icteric tinge which (5) extent. Geddes, among others, has remarked on this. Figure 2 is the temperature chart of a Group 4 patient (case 710) - palpable unless in prostrated cases. Although the temperature whose temperature fell by lysis during the seven days which is usually high the skin feels cold and clammy and sweaty eruptions may appear. Venipunctoid sores developed in several fatal



In typical Septicaemia the patient looks ill but feels well, and even when she is moribund euphoria is a persistent feature. Thorpe, ⁽⁵⁰⁾ regards this as a very constant symptom, altered only by peritonitis or impending death; but there are few cases where even the latter is of much effect, and until practically unconscious a septicaemic patient will frequently affirm that she is improving. Haugh ⁽⁵¹⁾ and Ronsheim ⁽⁵²⁾ have also drawn attention to the euphoria of puerperal septicaemia, and consider it as a valuable aid to diagnosis.

Frequently there is distressing effortless vomiting or an ineffective sickness. The tongue becomes dry and thickly furred, the lips fissured and crusted, the mouth dirty, and there is a marked acetone odour from the breath. There may be fleeting joint pains, or slight cough and some dyspnoea without apparent cause for same - "dyspnoea sine materia" described by Brindaeu. ⁽⁴⁹⁾ Mild delirium is frequent and there may be periods of mental confusion accompanied in many cases by hallucination of both visual and auditory nature. Even in the early stages the liver may be appreciably enlarged, and in most cases there is a slight icteric tinge which may deepen to definite jaundice before death. Splenic enlargement is constant but the organ is soft and rarely palpable unless in protracted cases. Although the temperature is usually high the skin feels cold and clammy and sweaty eruptions may appear. Pemphigoid sores developed in several fatal instances of this series. The abdomen is usually soft and freely palpable without pain or tenderness, even when extensive pelvic inflammation is present. Diarrhoea is, however, a frequent symptom.

The changes in the pulse are most important, and are dependable from the prognostic stand point. While the pulse remains full and strong there may be some hope of recovery; but the typical pulse of virulent septicaemia is rapid and feeble, and when it appears a fatal issue is almost definitely assured.

Pyæmic cases are rarely as ill. The temperature is remittent, and rigors are frequent; but between these there may be periods of hours or even days when the patient is afebrile, the pulse slow and strong, and the condition on the whole is satisfactory. Foci of infection may develop in bone, joints, glands or skin, and the appearance of these may mark the onset of recovery.

Post Abortum Septicaemia differs very little from the full time infection. These women are, however, if possible more ill, and euphoria is frequently absent. Intrauterine and pelvic sepsis are usually active and septic retained products may still be present. There is thus a concomitant local and general infection. Abdominal and lumbar pain may be almost constant; peritonitis is in many cases active; the woman is mentally acute and aware of her condition; and this combination of circumstances makes the disease a particularly distressing one.

COMPLICATIONS.

Broncho-Pneumonia is frequent and may obscure the puerperal origin of the illness. The local signs of infection are often few or absent, and a blood examination may be necessary to decide the diagnosis. Several patients of this type were notified as puerperal pyrexia, and there can be no doubt that previous to the adoption of this regulation many maternal deaths were certified as due to a pneumonia which was in reality the terminal feature of a septicaemic infection. Recently Solomons (53) when discussing this question, decided that the occurrence of pneumonia nullified the value of statistics about sepsis for the majority of cases certified.

Peritonitis and Septicaemia are occasionally concurrent, and these are in most instances virulent fatal infections. The peritoneal involvement may not be apparent, however, and is

frequently unsuspected until discovered at post mortem examination. There are also a few cases where signs of general peritonitis develop, and thereafter death rapidly ensues.

Many of the more protracted types develop septic arthritis or patchy cellulitis of the limbs, and in three instances panophthalmitis occurred probably as a result of thrombosis in the ocular vessels. These surgical incidents are, however, quite overshadowed by the Septicaemic condition.

PROGNOSIS. Many septicaemic cases die within a few hours or days from the onset, but others live for a week or more, and there are a few who eventually recover. The primary cases are almost invariably fatal, and it is in the Secondary group that the occasional recovery occurs. This is important in that if given adequate treatment on the first indication of sepsis, these might be saved from later blood infection. Frequently, however, patients are kept under observation at home until septicaemia develops; and when they are admitted to hospital they are moribund. Nothing is more difficult than the diagnosis of Puerperal Septicaemia in its early stages; but although every grave infection is not necessarily accompanied by blood invasion, it is wiser to regard this as present until repeated negative blood culture or the clinical course, ^{has} decided the issue.

The prognosis in pyaemia is much more hopeful and is influenced to a large extent by the intervals and by the degree of recovery between each inoculation from the infective source. On the whole, each day of survival gives a better prognosis, but there are many who drift into a chronic pyaemic state which terminates in death.

Post Abortum Septicaemia is probably least hopeful of all the blood infections. The multiplicity of the infecting organisms, and the concomitant sapraemia, may be responsible for

this; and in practice this type of infection is almost irrecoverable.

There are a few other clinical types which do not naturally accord with the preceding arrangement, but are of some interest in the discussion of treatment: and to these brief reference may be made.

LATE CASES.

Occasionally patients do not come into hospital until several weeks after their confinement. The puerperal infection may be then more or less quiescent, and little beyond general treatment necessary or possible. Cases of Phlegmasia Alba Dolens are of this type, and in others chronic pelvic cellulitis, salpinge-oophoritis, or chronic subinvolution may be the only lesion. Suppurative mastitis sometimes necessitates removal to hospital late in the puerperium, and this may be accompanied by mild pelvic sepsis which does not accord with any special system of treatment. Occasionally however late cases of this nature present acute lesions such as Secondary Septicaemia or Peritonitis, and these have been included in their appropriate groups. On the whole the treatment of these late cases is of special type and does not lend itself to statistical analysis; but in so far as they illustrate various factors, reference will be made to them in the later discussion.

PUERPERAL INSANITIES.

Since the commencement of the pyrexia regulations, patients of this type have been admitted to puerperal fever wards in increasing numbers, and they present special problems of diagnosis, prognosis and treatment. All degrees of nervous change are found, varying from a mild instability which makes the patient excitable, hysterical and emotional, to the fully established manic or depressive insanity. In most cases a definite toxic focus can be found, and this is probably the

factor which determines the onset. This series includes ten cases where septicaemia was responsible for severe manic insanity. Frequently, however, the woman is naturally of an excitable disposition.

The mild types usually recover as the puerperal infection subsides, since this is the outstanding feature of the illness. The septicaemic types rarely recover, even when the blood infection does not produce a fatal issue; and these women frequently become so uncontrollable that removal to observation hospitals is later indicated.

The definite insanities present a different problem. Here the mental state is the urgent feature, and the puerperal infection mild and secondary. Little treatment is possible in these cases, and they have, therefore, been excluded from the present survey.

BACTERIOLOGY.

BACTERIOLOGY.

The bacteriological investigation of Puerperal Fever has assumed paramount importance in the study of its etiology, but it is also of interest when attempts are made to rationalise the treatment of the disease. A review of the findings in these patients may therefore prove of some value. There were four main lines of inquiry -

1. Cultivation of organisms from the cervix and, where possible from the endometrium.
2. Cultivation of organisms from the blood.
3. Examination of material from secondary suppurative processes during life and at post mortem.
4. Tests for cutaneous sensitiveness.

TECHNIQUE.1. Cultivation of Organisms from Cervix & Endometrium.

This phase of the inquiry was carried out in all cases on admission, and in 237 of these prior to dismissal.

The examination was conducted in the operating theatre, or in bed if such movement were contraindicated, as in very ill patients and cases of thrombo phlebitis where embolism was to be feared. With the legs in lithotomy position and after thorough cleansing of the perinaeum and external parts, speculae were introduced into the vagina and the cervix manipulated into view. A smear of the cervical canal could then be taken on a simple sterile swab of cotton wool, and at the laboratory a peptone broth medium of P.H. value 7.4 was innoculated with this material.

If purulent discharge issued from the uterus or from lacerations in the vaginal vault, additional smears were taken and cultures made.

Various methods of taking cervical smears, have been recommended by different authors. Marbais uses a platinum loop.
(2)
Lea - in his treatise on the subject, describes an elaborate

technique evolved by Doderlein and Little; whereas Berkeley
 (20)
 and Bonney advocate a much simpler method. More recent
 communications, however, recommend the procedure above described;
 and in particular it is the routine method at Aberdeen and in
 many other research centres where the disease is being investigated.

Many writers advocate the taking of smears from the
 endometrium, the swab stick being passed well within the os uteri
 for this purpose. This is a procedure which should, however, be
 avoided. Frequently although the endometrium is healthy the
 cervical canal contains sloughing or purulent material, which may
 be carried upwards when the smear is taken. If, on the contrary,
 the cervical canal is first irrigated thoroughly with antiseptic
 solution, there is scant possibility of a positive culture being
 obtained; and in any case it is difficult to be sure that the
 organisms found are really uterine and not merely added from the
 cervix when the swab is passing through it. When the os internum
 is widely open and the cervical canal is gaping, intra uterine
 smears may be taken with comparative safety; but there are few
 occasions where the procedure is reliable or justifiable, and
 cervical smears give in most cases all the information required.

After incubation at 37 C. for twenty-four hours the
 broth culture was examined for organismal growth. Its appearance
 usually gave some indication of its contents. With pure growth of
 Streptococci the medium remained clear and a fine sediment consisting
 of the organisms gathered at the apex of the tube. Pneumococci,
 Staphylococci, and Coliform organisms rendered the broth turbid,
 and, in the last of these, foul smelling due to gas formation.
 Combinations of organisms gave varied results, and with scanty
 Streptococci the medium might appear unaltered.

Microscopic examination was conducted in the usual way,
 Gram's method of staining being found most useful. If the culture
 proved sterile it was returned to the incubator and re-examined
 twenty-four hours later, and should this again prove negative a second,

and if necessary, a third smear was taken. No patient of the series gave persistent negative findings. The few cultures primarily sterile were obtained almost entirely from cases with extensive sloughing lacerations from which abundant growth might have been expected. The organisms were doubtless protected on the under aspect of the sloughs, and did not become accessible until the dead epithelium had separated and the underlying granulating surface was exposed. Thus patients who appeared free of streptococci frequently gave proof of them after a few days in hospital.

Cervical smears prior to dismissal were taken in the same way and similarly examined.

2. Cultivation of Organisms from the Blood.

Blood cultures were taken from all patients who appeared ill on admission and from those who developed septicaemic symptoms while in hospital. For various periods routine blood examination was made on all but the very mild cases; but in no instance was a positive result obtained in a patient who did not appear ill enough to have been examined in any case. The practice was therefore abandoned as being unnecessary, and the blood cultures were made only from those patients in whom septicaemia was suspected. For this purpose 5-10 c.c. of blood were removed from an accessible vein and 20-25 c.c. of a broth medium immediately inoculated with this. Strict aseptic precautions with regard to overlying skin were observed during the procedure. Peptone broth of P.H. value 7.4 was again found to give most satisfactory results, especially if care were taken to bring it to body heat before the blood was added, and to maintain it at this temperature during transference to the laboratory. After twenty-four to forty-eight hours' incubation the culture was examined for organismal growth. Its appearance was at this stage to some extent distinctive. If haemolytic streptococci were present the medium was black and fluid, the blood being haemolysed. Pneumococci, however,

frequently produced a similar appearance, and it was not therefore entirely diagnostic. A brownish turbid fluid frequently denoted a staphylococcic or bacillus coli infection, and in the latter case foul smelling gas was usually present above the medium. In the absence of growth, the blood clotted and remain suspended in the clear straw coloured broth.

Microscopic examination was made as with the cervical cultures, great care being taken to avoid contamination of the medium so that further incubation could be given if no organisms were found. Repeat cultures were made in all negative cases where the clinical picture still suggested a blood infection.

3. Examination of Material from Secondary Suppurative Processes.

Purulent effusions and discharges were treated in the same way/mears being taken and broth medium inoculated. Occasionally death occurred before blood examination was possible or any bacteriological examination could be made, Post mortem examination was obtained in most of these cases, organisms being cultivated from the endometrium, cervix, and from any purulent effusions found. Where possible also the splenic pulp was examined for organismal infection. For this purpose a few drops of blood were aspirated from it with a fine pipette and inoculated into the usual broth medium. A preliminary searing of its surface with a hot knife obviated any risk of contamination from a peritoneal source. The finding of organisms within the splenic pulp was of course absolute evidence of blood infection.

4. Tests for Cutaneous Sensitiveness.

These were undertaken to discover whether any relationship existed between the toxins of puerperal and scarlet fever organisms; and in how many women the puerperal infection was

caused by the scarlet fever type of streptococcus or by one closely allied to it. The test was performed strictly in accordance with the accepted method of Dick testing, .2 c.c. of diluted toxin being injected intradermally on the forearm. Two toxin solutions were employed. The scarlet fever toxin was that usually supplied for the ordinary Dick test. The puerperal toxin was derived from organisms obtained by blood culture from a previous patient, and was prepared by the method of Lash and Kaplan⁽⁵⁵⁾, dilutions of $\frac{1}{100}$ and $\frac{1}{250}$ being employed.

The test was made as soon as possible after admission, different toxin being chosen for each arm. In order to avoid multiplicity of injections, the usual control solutions were dispensed with, these being not absolutely essential in a comparative examination of this nature. The areolae were measured at twenty-four and forty-eight intervals thereafter, and any general reaction noted.

RESULTS OF BACTERIOLOGICAL EXAMINATIONS.

1. Cervical and Uterine Smears.

The organisms found fall into six categories-

1. Streptococci alone.
2. Streptococci in combination with other organisms.
3. Staphylococci alone.
4. Pneumococci alone.
5. Bacillus coli alone.
6. Other organisms alone or in combination with staphylococci, pneumococci or bacillus coli. These include diphtheroids, diplo-bacilli and various unclassified Gram positive diplococci. The gonococcus was found alone in three cases.

In the series of Full Time and Premature Births, the findings are as shown in Table 7.

TABLE 7.

Table shewing organisms found in cervical smears of Full Time Cases.

Type of Case.	No. of Cases	Strep.	Strep. + others	Staph.	Pneum.	B. Coli	Other Orgs.
Group I	76	23	7	20	11	10	5
Group II	249	103	25	48	25	30	18
Group III	187	68	21	31	30	20	17
Group IV	95	45	30	4	7	6	3
<u>All Cases</u>	607	239	83	103	73	66	43
Rate per cent.		39.3	13.7	16.9	12.0	10.9	7.2

Streptococcal infections thus account for 53% of this series.

In the Post Abortum Cases the results are somewhat similar.

TABLE 8.

Table shewing organisms found in cervical smears of Post Abortum Cases.

Type of Case.	No. of Cases	Strep.	Strep. + others	Staph.	Pneum.	B. Coli	Other Orgs.
Group I	36	8	4	11	1	9	3
Group II	99	34	13	10	13	22	7
Group III	41	16	18	4	1	2	-
Group IV	17	9	6	-	2	-	-
<u>All Cases</u>	193	67	41	25	17	33	10
Rate per cent.		34.8	21.2	13.0	8.7	17.1	5.2

Streptococcal infections are here present in a slightly higher percentage - 56% - of the series, but the difference is so slight as to be of accidental occurrence. The higher proportion of coliform infections in these cases is of some importance, in that many are the result of criminal interference, which takes little heed of surgical asepsis, and organisms from the rectum are thus readily introduced. Of the complete series of 800 cases, therefore, 54.5% are the result of streptococcal invasion. This figure is in agreement with the findings of most recent workers, among whom are:-

Abrahams ^{56(a)} who found 52.5% in a series of 120 cases.

Foularton ^{56(b)} " " 46.2% " " " 54 "

Napier ^{56(c)} " " 53% " " " 500 "

Whitridge Williams ⁽¹⁰⁾, however, discovered only 29.2% of streptococcal infections in a series amounting to 226 severe cases of the disease.

An analysis of the preceding tables, as given in Table 9, reveals the following relationship between the frequency of streptococcal infections and the severity of the disease.

TABLE 9.

Table shewing relation between Streptococcal Infections and Severity of Disease.

Group	Percentage of <u>Full Time Cases</u> with Streptococcal Infections.	Percentage of <u>Post Abortum Cases</u> with Streptococcal Infections.
I	39.9	35.3
II	52.3	47.7
III	47.9	82.9
IV	78.9	88.2

The slight decrease in frequency seen in the Full Time Cases of Group III may be related to the fact that when the parametrium is invaded the streptococci in many cases disappear from the surface tissues. Repeated cultures from cervical smears may then reveal only the secondary organisms such as bacillus coli, diphtheroids, or other saprophytes. Frequently also the cervical or uterine lesions may be practically healed at this stage, and streptococci cannot be cultivated from them.

The high proportion of streptococcal infections in Group III abortions is also of note. Here, as already described, there is still active intra-uterine sepsis even when the pelvic tissues are extensively invaded; and the streptococci are thus readily found in cervical cultures.

FATAL CASES.

The whole series includes 132 fatal infections, and Table 10 shows the incidence of the various organisms in these cases.

TABLE 10.

Table shewing organisms in cervical smears of fatal cases.

Organisms.	Strep.	Strep. + others	Staph.	Pneum.	B.Coli.	Others
No. of Cases	59	38	2	9	11	4
Rate %	73.5		1.5	6.8	8.3	3

The high incidence of cases in which the streptococcus was the dominating feature is again noteworthy.

Examination on Dismissal.

With regard to the 237 cases which were examined prior to dismissal, it was found that 45 of these - or 19% - still showed streptococci in the cultures taken from the cervix. This will be found of interest in the later discussion of treatment.

2. Examination of Blood Cultures.Full Time Cases.

In this respect 174 patients come under review, and Table 11 gives a summary of the results obtained in them.

TABLE 11.

Table shewing results of blood culture in Full Time Cases.

	No. of Cultures.	Strep.	Staph.	Pneum.	B.Coli.	No growth
Group I	6	-	-	-	-	6
Group II	30	1	-	1	-	28
Group III	43	11	2	-	-	30
Group IV	95	70	-	7	5	13
<u>All Cases</u>	174	82	2	8	5	77
Rate per cent.		47.2	1.1	4.7	2.8	44.2

Thus of 97 cases which gave a positive blood culture, 84.5% were streptococcal in character; while in the group as a whole the blood culture was positive in 55.8% of cases, and of this number the streptococcus was the causal agent in 47.2%.

Post Abortum Cases.

Here 32 patients are analysed, as shown in Table 12.

TABLE 12.

Table shewing results of blood culture in Post Abortum Cases.

	No. of Cultures.	Strep.	Staph.	Pneum.	B.Coli.	No Growth Other Organisms
Group I	-	-	-	-	-	-
Group II	3	2	-	-	-	1
Group III	12	6	-	-	-	6
Group IV	17	9	-	3	-	5
<u>All Cases</u>	32	17	-	3	-	12
Rate per cent.		52.5	-	10.0	-	37.5

In this series 20 gave evidence of a blood infection, which was streptococcal in 85%. In the total cases in the group the percentage of streptococcal infections was thus 52.5, and in only 10% was infection traced to other organisms.

The total number of positive blood cultures was therefore 117, and of these 84.7% were due to the *Streptococcus Haemolyticus*. In his recent investigation, Smith⁽⁵⁴⁾ found 88%, and various workers have had corresponding results.

Fatal Cases.

In 127 of these, blood examination was carried out, or at post mortem splenic pulp examined. The findings are as shewn.

TABLE 13.

Table shewing organisms in blood cultures of fatal cases.

Organisms.	Strep.	Staph.	Pneum.	B.Coli.	No growth
No. of Cases	87	1	7	4	18
Rate %	76.2	.8	5.5	3.2	14.3

It will be noted that 99 fatal infections gave proof of blood invasion. These amounted to 77.9% of the cases so examined, and among this number 76.2% were found to be of the streptococcal type.

3. Examination of Material from Suppurative Foci or at Post Mortem.

Such foci include pyaemic infections of joints, muscle and skin; peritoneal effusions found at abdominal operation; and pus from parametric and mammary abscesses. In all 89 cultures were made, and the results are shown in Table 14 below.

TABLE 14.

Table shewing organisms in secondary suppurative foci, etc.

Organisms.	Strep.	Staph.	Pneum.	B.Coli.	Diptheroids.	Other Saprophytes.
No. of Cases	79	3	2	3	1	1

Of the cases so examined, therefore, 88.7% revealed the presence of streptococci. This is in agreement with most workers.

3. The results appeared very inconsistent and haphazard. Many women recovering from severe streptococcal infections gave marked local reactions, while in several patients who suffered from mild sepsis - apparently not due to this organism - no reaction was obtained.

4. Only five women were sensitive to the scarlet fever toxin, and as a means of comparison it was therefore valueless.

CONCLUSIONS.

The first real proof of the relationship between streptococcal and puerperal infection was afforded by Pasteur, when in 1879 before the Academie de Medecine in Paris he demonstrated their presence in the blood of patients suffering from the disease. Even among the earlier observers therefore, *Streptococcus Pyogenes* came to be regarded as the most frequent cause of this infection, and the chief agent in determining death. More recently Fitzgibbon and Biggar, Williams, Benians, Luker, Dafoe, and Eden, have shown that haemolytic streptococci are the organisms mainly concerned both in localized sepsis and in septicaemia, and in 1925 Colebrooke, concluded that 90% of cases were due to this organism. Within the past few years, however, others have cast doubt on such an assertion. Schwarz and Beickmann, in 1927 described a technique by which anaerobic streptococci might be isolated; and claimed that these were equally as potent as the aerobic variety; and several months ago Colebrooke, adduced results which appeared to confirm such views. Smith, however, refutes them. The present investigation includes 14.3% of fatal cases whose blood appears sterile when cultured by aerobic methods, and it is possible that a few of these women may have been examples of the anaerobic

infections of which Schwarz writes. But the figures do prove conclusively that aerobic streptococcal infection is by far the most potent cause of death.

It must be admitted that there is a great variety of organisms in the genital tract during the puerperum, and that puerperal sepsis is not necessarily associated with streptococcal infection. Serious forms of the disease are, however, definitely associated with these organisms. The greater the severity of the disease, the higher is the incidence of this type of infection. Of the fatal cases in this series 73.5% were found to have streptococci in the cervix or uterus, and in 76.2% the blood contained the same organism. If serious morbidity and death from puerperal sepsis is to be avoided, therefore, concentration on the streptococcus is essential. Thus treatment of the disease - in the large majority of cases-would appear to be centred round those remedies which have a specific action on the streptococcus.

TREATMENT.

T R E A T M E N T.General Considerations.

Before the relative merits of different forms of treatment can be discussed, it is important to realize the many benefits which hospitalization in itself affords—a factor frequently overlooked by those who advocate remedies.

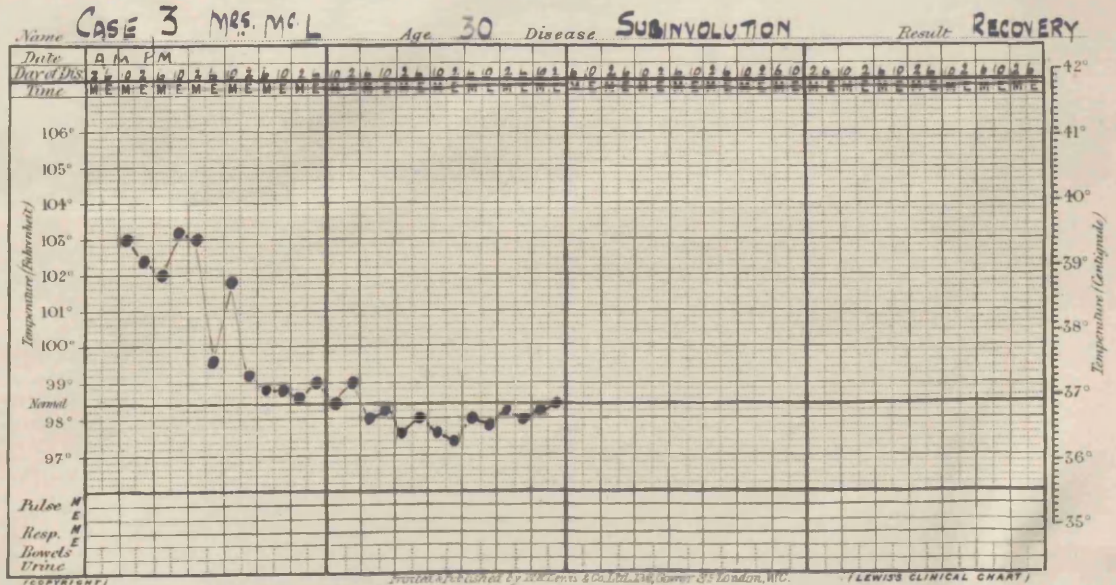
Admission to a hospital ward entails in the first place freedom from the worries and from the actual presence of home and family; but scarcely less important is the comfort and cleanliness of the hospital bed, and the essential cleansing of the patient herself in a way which is in most cases impossible in her home conditions. The following routine was observed in all cases of the series. On admission each was bathed in bed, and the pubic hair shaved; the bladder was emptied by catheter, and the bowel by emema. Thereafter the perinaeum and vulva were swabbed carefully every four hours— or oftener in cases of profuse foul discharge— fresh pads being supplied on each occasion. This procedure was carried out by an experienced senior nurse who wore a sterile gown and rubber gloves, the latter being changed between each patient. Sterile wool soaked in lysol solution was used, fresh lotion and basin being provided at each bed. The dangers of contagion were thus avoided, and all severities of infection could be nursed in the same ward without ill effects. Most of the patients had lesser degrees of albuminuria, probably the result of the febrile condition, although in some cases dating from the later months of pregnancy; and part of the ward routine was the administration of a diuretic mixture to all febrile patients, until the temperature had settled and the urine was clear of albumen. The diet was restricted in early stages, but was rapidly increased as the fever diminished

and the toxæmia disappeared. An abundance of fruit and fruit juice was, however, allowed at all times. Impairment of appetite is- it should be noted - rather an unusual finding, even in highly febrile and toxic patients suffering from this disease.

It would be difficult to over estimate the value of the routine above described. Many cases respond to this hospitalization in a remarkable way, and it is doubtless a factor of importance in determining the total effect of other methods of treatment. Under this regime alone, the temperature may subside and the toxæmia rapidly disappear. This is illustrated by the following patients.

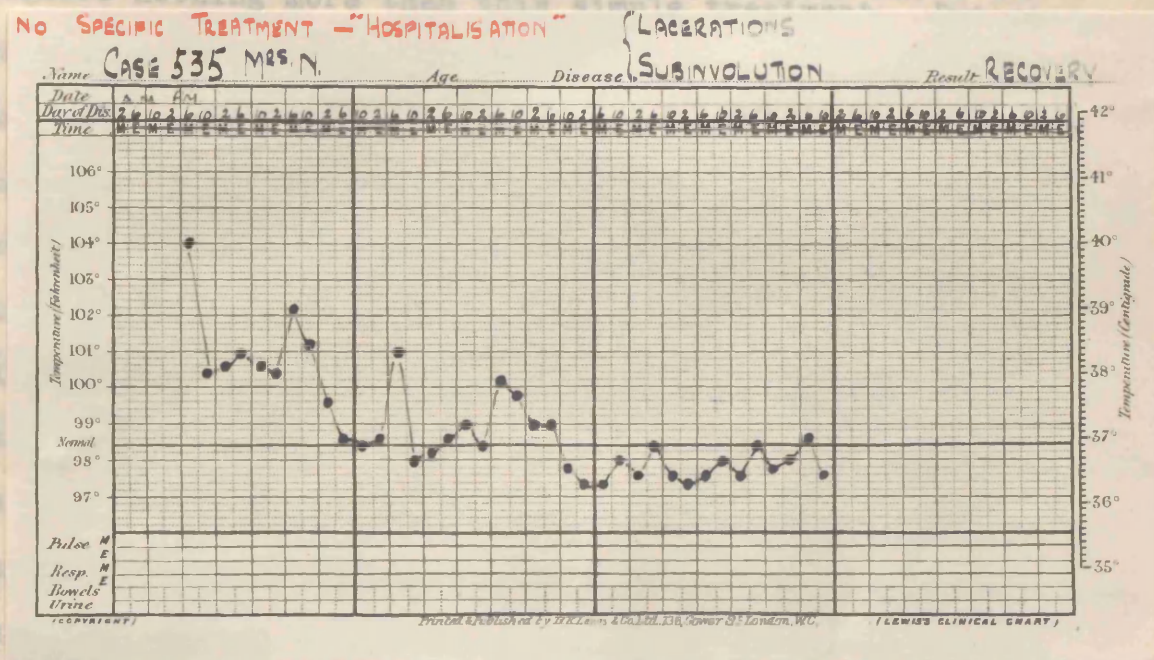
Case 3 was admitted moderately ill on the second day of the fever. No special treatment was given. The temperature fell rapidly, and there was a marked general improvement during the first three days in hospital. There were no complications. Her chart is subjoined - figure 3.

NO SPECIFIC TREATMENT — "HOSPITALISATION"



Case 535 is somewhat similar. This woman had a full time pregnancy ten days before admission, but did not become febrile until the seventh day of her puerperium. She appeared moderately ill, and the local lesion was a healing laceration with subinvolution of the uterus. Her temperature

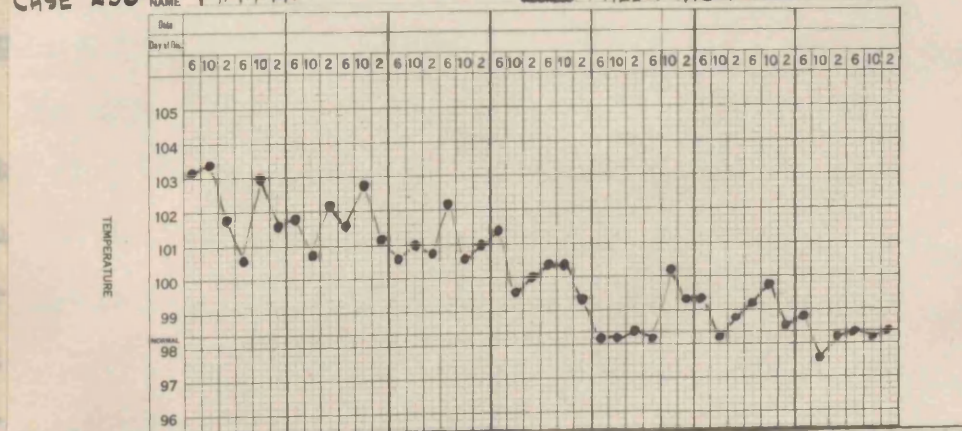
chart shows the gradual but definite improvement which occurred in the absence of any specific treatment -



Case 236 shows a less dramatic result. This girl was admitted sharply ill with pelvic cellulitis and early Phlegmasia Alba Dolens. No treatment was given. Her temperature slowly subsided and the general condition improved concurrently; and by the end of the first week she had become permanently afebrile. No complications were noted and the convalescence was uneventful.

NO SPECIFIC TREATMENT - "HOSPITALISATION"

CASE 236. NAME M. M.A. PHLEGMASIA ALBA DOLENS.



It was by no means rare to admit a patient in the evening highly febrile and looking ill, and to find her afebrile in the morning endowed with new life and anxious to

be home again, after one night's regime in hospital. These are in most cases mild or early infections, and many require nothing more than this simple treatment. But among them there are a few potentially of a severe type whom hospitalization saves from more serious illness. Herein lies the chief advantage of early notification. In the whole series the average duration of illness before admission to hospital was 4.4 days. This is a great improvement on the nine days reported by Reid ⁽⁶²⁾ two years ago, but there is still room for betterment. Theoretically, all patients should be admitted in the first or second day of fever, but in the whole series only 98 were in this category. Many women whose infection proved fatal had been treated in the unsuitable circumstances of their own homes for several days prior to admission. In the fatal cases the average duration of illness before admission was 4.9 days: but there were many who had been febrile much longer than that, and early hospitalization might have averted this fatal issue.

The actual remedies which have been advocated in the treatment of Puerperal Sepsis are legion, and to a few of these reference has already been made. At the outset they may be classified into two main categories. The first of these is the Conservative, and the second the Intensive method. The former, as its name implies, is inactive and non-specific. Here the patient is conserved in every way. Suitable diet and bed routine are enforced, and apart from a preliminary examination for diagnostic purposes, no local interference is made, unless outstanding pelvic symptoms supervene. No specific remedies are directed against the infection; and the only indication that the illness is puerperal in origin, may be given by the fact that the woman is nursed in Fowler's position and routine doses of Ergot and Quinine are prescribed for her.

The Intensive method is, on the contrary, active and militant. By it, the local lesion is thoroughly investigated and attempts are made to promote rapid and complete healing. If the infection has become general, attempts are made to sterilize the blood and to prevent further inoculation from the pelvic focus. No avenue of attack against the infection is left unexplored. It might indeed be said that the Conservative method is concerned mainly with the patient, whereas the Intensive is engrossed with the organism which is attacking her.

The remedies which will now be discussed are those which form the basis of the investigations, and are to a large extent of the intensive type. Several are directed against the local lesion, and others against the general infection.

LOCAL TREATMENT.

The aim of this is to combat the disease at its source, to limit its spread and prevent toxic absorption, and to promote healing of the perineal, vaginal, uterine, and adnexal lesions. The methods under review are;-

1. ERGOT ADMINISTRATION.
2. ROUTINE SWABBING OF PERINAEUM, VAGINA AND CERVIX WITH ANTISEPTIC SOLUTION.
3. ICHTHYOL DISINFECTION OF VAGINA AND CERVIX.
4. VAGINAL DOUCHING.
5. UTERINE DRAINAGE.
6. INTRAUTERINE DOUCHING.
7. INTRAUTERINE GLYCERINE INJECTIONS.

Several of these methods are mainly adjuvant and may be discussed with brevity.

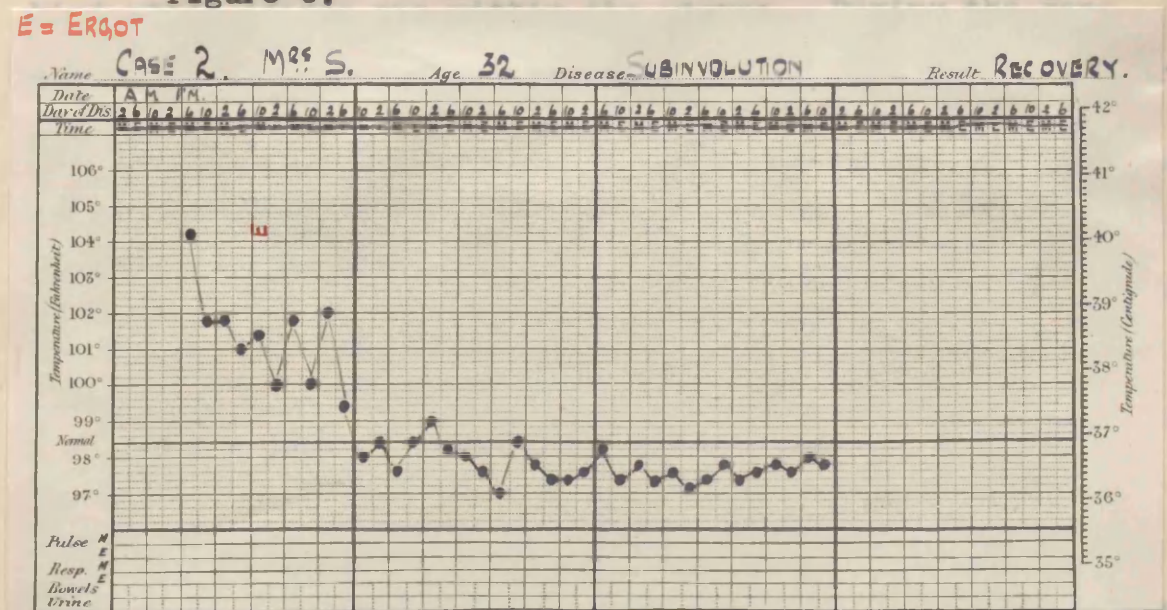
1. ERGOT ADMINISTRATION.

This method of conservative treatment was utilized in 269 patients. Although taken orally Ergot is said to have a focal action and since Mediaeval times it has held

great repute as a uterine stimulant. In adequate doses when the uterus is healthy, it is of value as a temporary measure to control haemorrhage and to expel any retained blood or membrane from it. Whether this action still occurs when the endometrium is diseased and the uterine wall saturated with toxins, is indeed doubtful. The mild cases of Group 1 where the uterus is merely subinvolved, congested and oedematus may receive some benefit, and theoretically Ergot should be of value; but in all other groups its colour and taste have a mental effect which far outstrips any local action, and this is its only value in their treatment.

Figure 6 is the temperature chart of a Group 1 case treated only by this means. The temperature rapidly subsided, and there were no complications; but this woman had urinary retention on admission, and much of the general improvement may have been due to the relief of this.

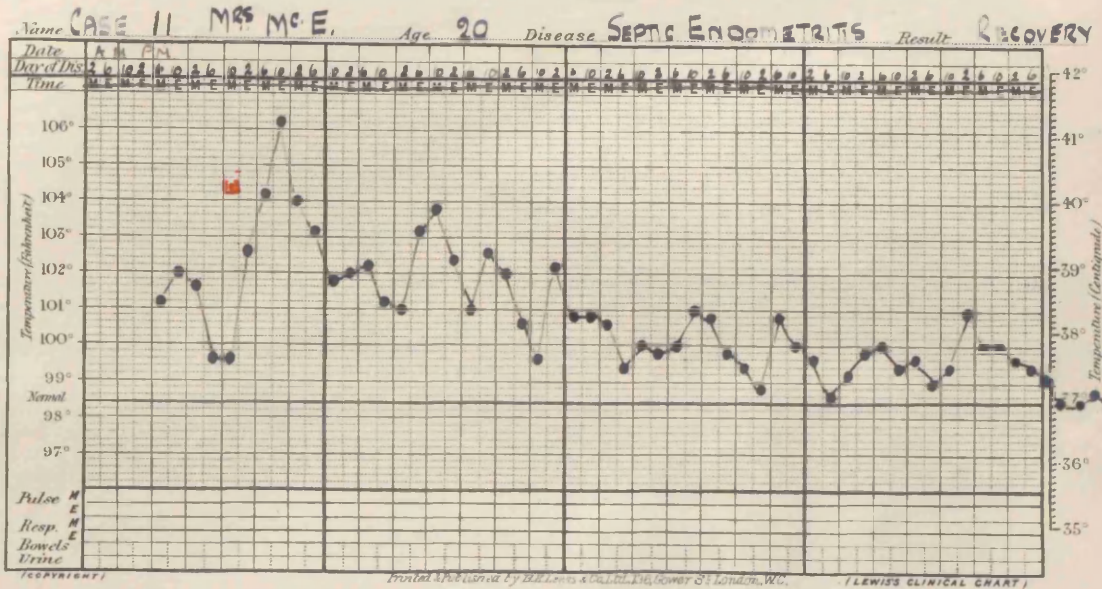
Figure 6.



Patients of any other group make little or no progress if this is the only line of treatment. Figure 7 shows the lack of reaction in a Group 2 case who received this remedy alone. This woman had no other lesion when a moderate degree of septic endometritis, but she was still febrile and ill after ten days in hospital.

Figure 7.

E = ERGOT



Ergot is of little value as a means of local treatment once sepsis has been established. Geddes suggests that it be given in all cases to appease the patient and her relatives; and in this he is probably very near the truth of the matter. (64) Hobbs affirms that in 50% of cases treatment of this kind still leaves pus within the uterus. During the convalescent period if there is still a blood stained lochia Ergot may be given with more hope of effect, but even then there is little appreciable result; and it is concluded, therefore, that even if sepsis is minimal, its administration does not appear to have any material effect on the progress of the disease.

2. ROUTINE SWABBING of PERINAEUM, VAGINA AND CEVIX.

Simple swabbing of the perinaeum, vagina and cervix, apart from the routine cleansing of the external surface which forms part of the ward regime, is probably sufficient for the local treatment of very mild cases. Women who have a scanty vaginal discharge due to chronic vaginitis, healing lacerations, or cervicitis need only be kept clean locally; and swabbing of these parts with sterile wool soaked in an antiseptic solution such as lysol, may be all that is necessary. This can be carried out with the patient in bed, but more complete

inspection of the infected area will be obtained if she is taken into theatre for the purpose. In badly lacerated patients, burrowing abscesses often form in the pelvic cellular tissue, and thorough daily cleansing of the vagina is the most effective treatment.

Again, in the severe infections, where there is marked toxæmia or septicaemia; in cases complicated by Pneumonia; and in others where the peritoneum is involved, movement from bed would prejudice the recovery, and simple local cleansing must be employed although the main sepsis is intrauterine.

The effects of this procedure were sometimes very satisfactory. It was a fairly common occurrence to find a patient whose sole lesions consisted of a stitched perinaeal tear, slight vaginal bruizing with slough formation, and a mild cervicitis with perhaps superficial laceration of the lips. Behind the repaired perinaeum there was in most cases a collection of foul retained purulent lochia. Removal of the stitches allowed the edges of the wound to separate, and the discharge,—escaping freely—could not subsequently become locked in the vagina again. Perinaeum, vagina, and cervix were thereafter swabbed carefully and the patient was returned to bed. By the following day, the temperature was in many of these cases normal or showing indications of settling, and the local inflammation was already subsiding. Every day thereafter the parts were notably cleaner, and within five or six days the wounds were healthy, granulating, and requiring no further treatment. This rapidity of healing was indeed remarkable in view of the situation of the lesions in such close association with anus and urethra; and if adopted from the outset of fever, a simple procedure such as this would in many cases obviate hospital treatment in the later stages.

3. ICHTHYOL DISINFECTION OF VAGINA AND CERVIX.

When applied to a mucous membrane ichthyol produces congestion and local leucocytosis of the surrounding tissues, and for this reason tampons soaked in ichthyol-glycerin solution have been found to have a definite value in chronic sepsis of the vagina and cervix. An attempt was made to utilize the drug in a similar way, during the subacute stages of the disease, when, although the cervical os was closed, a fairly profuse vaginal discharge was still present. Painful inflammation resulted, however, even in low dilutions; and accordingly the procedure was abandoned.

The field of ichthyol treatment is definitely limited, therefore, to the period of late convalescence. Tampons moistened with a 10% solution of ichthyol in sterile glycerin, if inserted into the posterior fornix every second or third day, in many cases caused marked diminution in a discharge of vaginal or cervical origin, which proved resistant to other treatment; and at this stage no untoward effects were noted. Frequently when otherwise fit for dismissal patients still showed streptococci in smears from the cervix; and in these cases ichthyol treatment was followed until negative cultures were obtained. Along such lines ichthyol may prove of value, but in the presence of active sepsis this drug is definitely to be avoided.

4. VAGINAL DOUCHING.

Douching of the vaginal canal with warm solutions of antiseptic substances is a form of local treatment which is not confined to the hospital ward, but is frequently practiced in the patient's own home. Lysol in varying dilutions; Perchloride of mercury in 1.1000 - 1.5000 solution; and Biniodide of Mercury in 1.2000 - 1.4000 solution, are the substances in most repute. Douches of this nature are said to serve the double functions of cleansing and antiseptis, and of stimulating chronic lesions so that an active healing results.

In hospital, the douching fluid is contained in a large sterile vessel which is connected by a rubber tube to a terminal glass nozzle. When the latter is in place in the vagina, the solution flows in by gravity with a force determined by the height of the container above the level of the patient's buttocks; and the returning fluid drains into a bedpan or other utensil. In general practice the antiseptic solution is usually poured from a jug over the perinaeum and into the vagina, the patient's buttocks being at the edge of the bed and the legs held apart for this purpose.

Until recent years the procedure of douching the vagina and uterus appears to have been much favoured by general practitioners, and by those responsible for the treatment of septic cases; and there are still many who advocate its use. Frequently patients were found to have been douched regularly from soon after their confinement until admission to hospital, and this was probably the worst line of treatment which could have been pursued. The risk of spreading infections upwards in this way is great, even under hospital conditions, with asepsis at its best; and women treated by douching in their own homes were very often found to have wide spread pelvic inflammation or even Septicaemia, when admitted to hospital. A large proportion of the most severe infections in this series, had been so treated; and three cases of virulent and fatal septicaemia admitted to hospital within a period of seven days, each gave a history of daily vaginal douching since the onset of fever 2-5 days after the confinement. All three were found to have foul gaping lacerations of perinaeum, vagina and cervix, and the os internum was widely dilated. A free entrance was thus provided for the douching fluid and for the organisms, which were thus washed up into the uterus rather than out at the vagina. The ill effects of promiscuous douching are not however entirely due to the fact that infection may be carried

upwards if too much force is used. The heat of the douche and the sodden surfaces which it leaves, both tend to promote spread of any active sepsis in and around the vagina.

CONTRAINDICATIONS.

The following types of patient appear definitely unsuited for this method of local treatment.

1. Women recently confined and in whom therefore the cervical canal and os internum may still be patent.
2. Women with wide lacerations of the parturient canal.
3. Cases of established intrauterine sepsis.
4. Cases of active or subacute pelvic infection - especially where there is the slightest evidence of even a mild pelvic peritonitis.
5. Cases of established septicaemia, even, when there is no apparent activity in the local lesion.
6. Women with retained products either full time or post abortum, whether or not these appear to be infected.

In all of these the effect of vaginal douching may be to spread the infection, render it more active, and inoculate the blood; especially if the treatment is conducted by a person of limited experience, and in the difficult situation of a private dwelling. There may be a few cases of benefit, but once sepsis has become established - and who can say when first that occurs? - the practice should be rigorously condemned.

An outstanding example of these evil effects is provided by case 591 - an unmarried girl of 21 years who suffered from Post Abortum Sepsis, criminally induced. It appears that the foetus had been dead for several weeks but was not expelled. On account of moderate vaginal haemorrhage medical advice became necessary, and the products were removed manually by a consultant

gynaecologist in the patient's own home. A vaginal and uterine douche was thereafter given. Twelve hours later signs of spreading pelvic infection were apparent, and the following day she was admitted to hospital, moribund. Post Mortem examination 24 hours later confirmed the presence of general peritonitis. The uterus was in a state of gangrenous endometritis and its wall contained multiple confluent abscesses. At the placental site the uterus was so thin as to be, in effect, absent. This girl was apparently healthy and at her employment on the day of her haemorrhage; and doubtless her douche, instead of washing away the septic products - as was intended - merely served to advance the infection, and hastened if not caused her untimely end.

It is not surprising therefore that the practice of douching has been deplored recently by many writers. Madill, (63) addressing the Royal Society of Medicine in Ireland only two months ago, stated that the one advance in the active treatment of Puerperal Sepsis was the cessation of douching and curetage; an expression of opinion which was strongly supported by Roulette (63) on the same occasion. Other writers such as Davidson (53) and Solomons have also recently condemned it.

INDICATIONS.

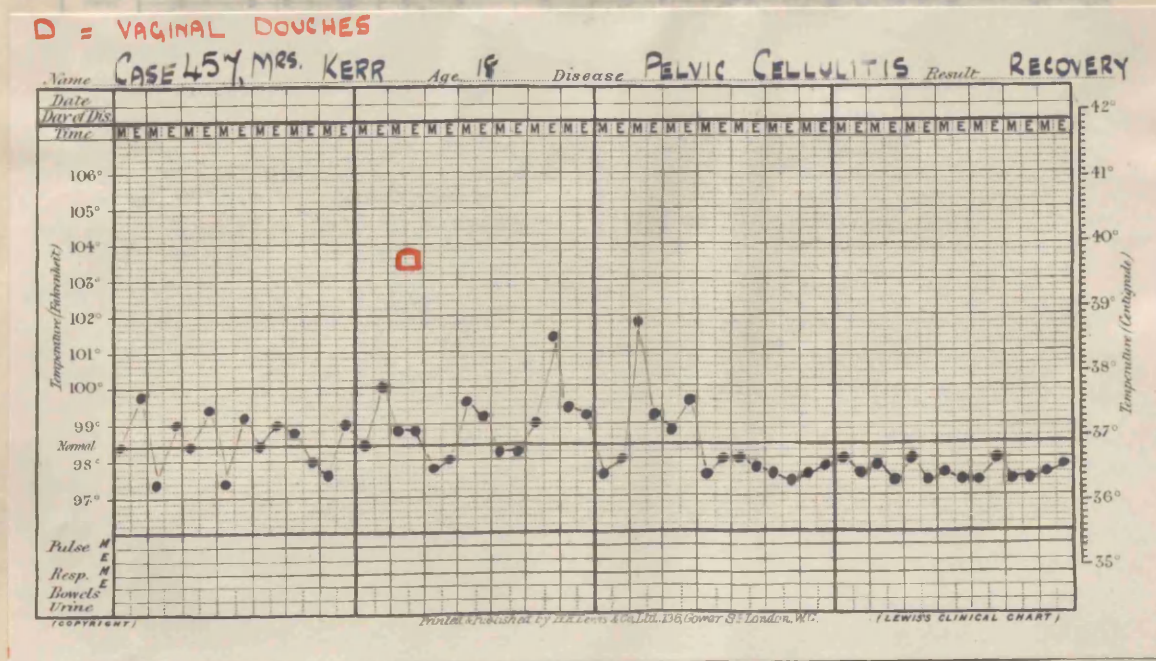
There are, however, a few instances where vaginal douching may have beneficial effects. Patients who have chronic cervicitis, subinvolution, established chronic pelvic cellulitis, or a tubal infection which is inactive and of long standing, find douches comforting; and in some cases good results such as lessening of the discharge or subsidence of an inflammatory swelling may be obtained. For this purpose warm isotonic saline solution is quite as effective as any antiseptic which is sufficiently dilute to be nonirritating. Three effects of such douches on a parametric or other

inflammatory pelvic swelling, may be noted.

The symptoms which were caused by it will also vanish.

1. Resolution after Reaction.

In this type of reaction the swelling may increase in size and tenderness, and there may be general signs of toxic absorption such as malaise, headache, elevation of temperature, and increase of pulse rate. This initial reaction may be somewhat alarming and suggests that harm has been done; but after a few days the general symptoms disappear, tenderness diminishes, and the original swelling gives indications of resolution. Case 457 was of this type. This woman was admitted as Puerperal Scarlet Fever. Twelve weeks later she was still subfebrile, and a large indurated mass of cellulitis was found filling the left side of the pelvis. Douches were followed by further elevation of temperature and by acute tenderness and enlargement of the inflammatory swelling. By the end of a week, however, the patient was for the first time definitely and permanently afebrile; and the mass was no longer palpable from the abdomen. When she was allowed up a fortnight later there were no traces of parametritis even on bimanual examination. Figure 8 illustrates this reaction.

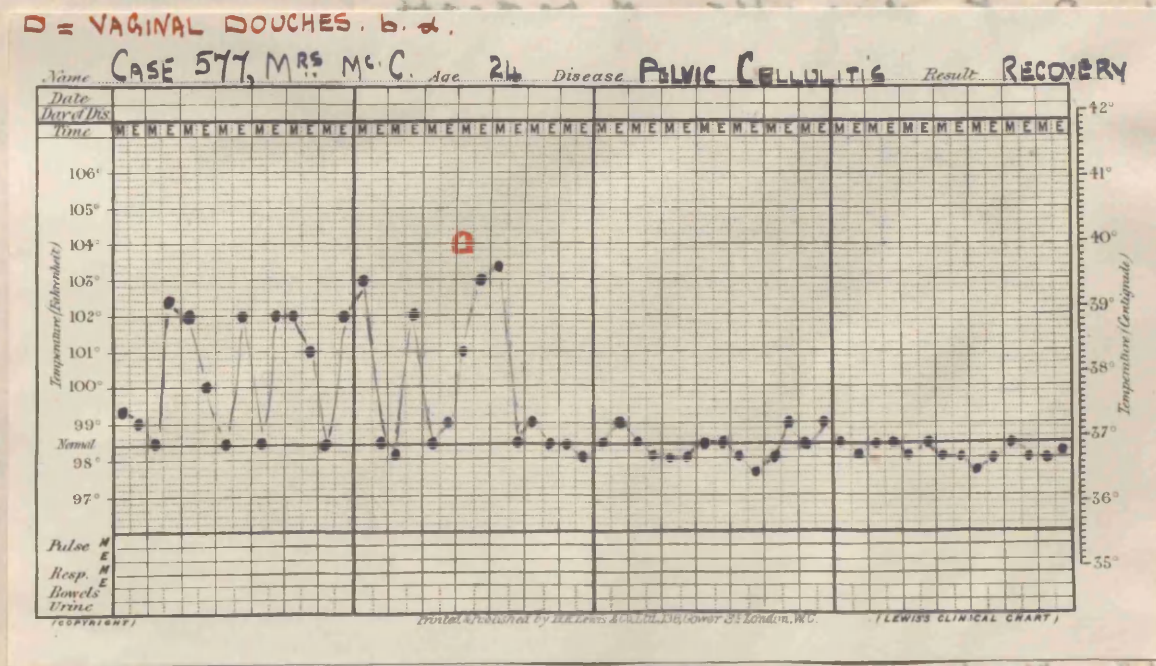


2. Resolution Without Acute Reaction.

In this case there is no apparent increase in local activity. After several douches have been given any previous temperature gradually subsides, the inflammatory swelling disappears, and

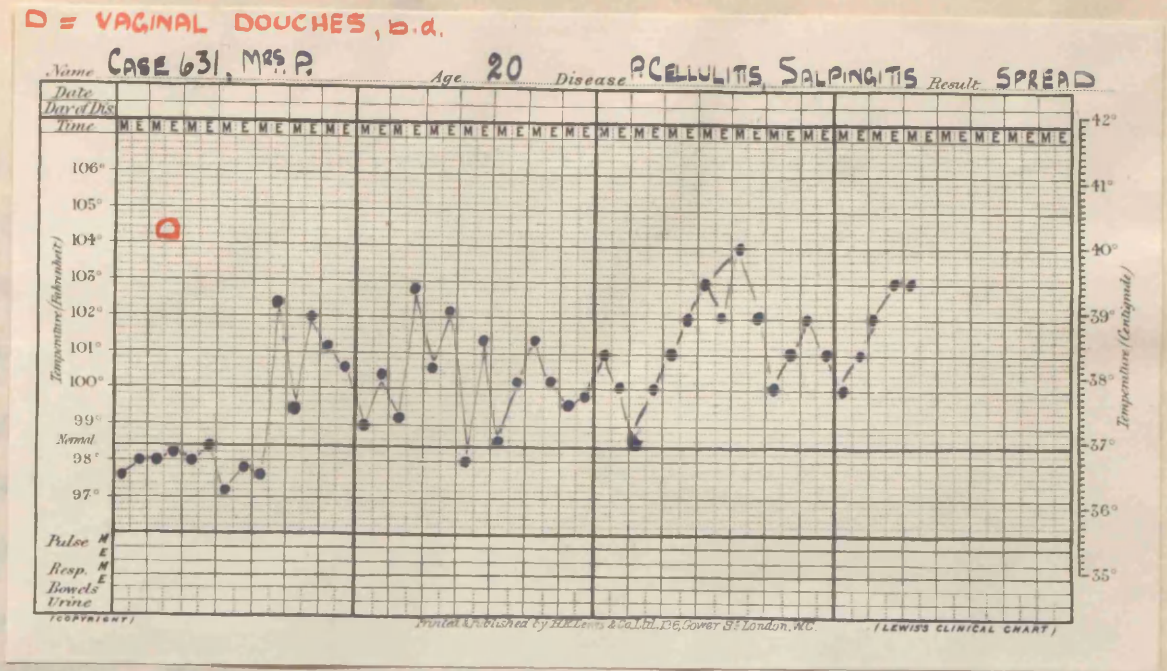
the symptoms which were caused by it will also vanish. This was the result in case 577 where there had been extensive bilateral pelvic cellulitis of nine weeks duration. This woman was subfebrile and complained bitterly of pain chiefly in association with micturition - doubtless due to implication of bladder and urethra in the inflammatory process. No other treatment having been of any avail, douches were tried and with almost immediate effect. Pain ceased, temperature subsided, and pelvic mass slowly disappeared. Within a month of the onset of this treatment she was dismissed well, with very little indication of her previous pelvic swelling.

Figure 9.



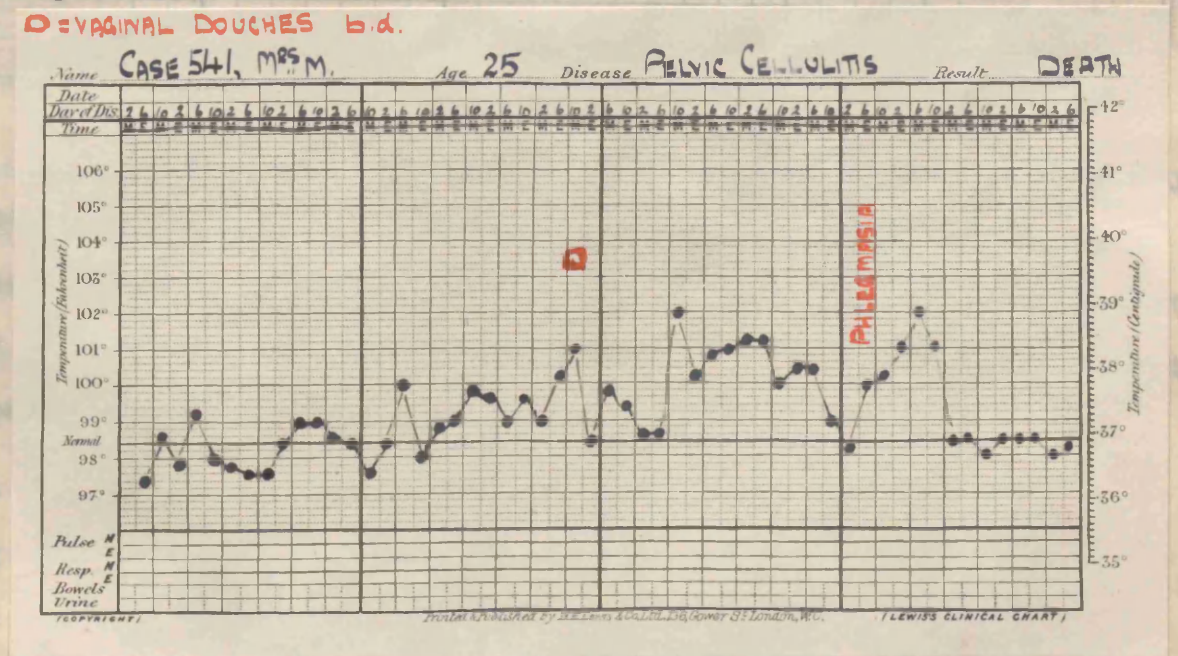
3. Acute Reaction, Causing Extension of the Disease.

Here the douches have a deleterious effect, and are followed by increased activity of the pelvic lesion. Case 631 illustrates this unfortunate occurrence. In this patient there was a left sided pelvic cellulitis of five months' duration, presumably inactive. After several douches the temperature became sharply elevated, general symptoms supervened, and the whole pelvis was soon filled by a tender inflammatory mass which originated in the primary focus. Her temperature chart is shown (figure 10)



Case 541 is of similar type. On this occasion, douches were followed by a spreading thrombophlebitis which ended in death two months later. *This woman had an old standing unilateral cellulitis, and was practically afebrile; but there was slight elevation of temperature, after several vaginal douches had been given. Two days later oedema of the left ankle became apparent, and the treatment was stopped. But the phlebitis continued until the pelvic and abdominal veins were completely blocked by thrombus formation. Ascites followed and death resulted from mechanical obstruction to veins, not on account of pyaemia or any other septic process.

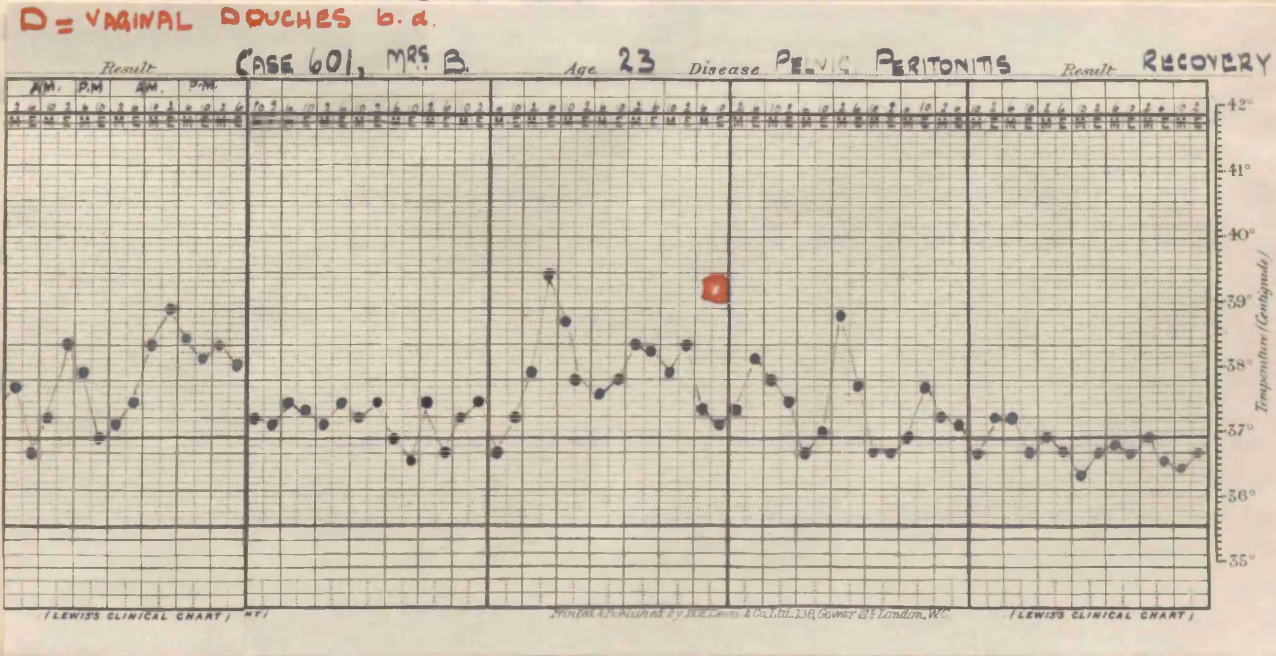
Figure 11.



After this fatal termination, attributed in the main to injudicious douching, this form of treatment was for a short

time discontinued. Excellent results were however later obtained in case 601, the lesions in this patient being chronic pelvic cellulitis and chronic peritonitis. This woman had been very ill on admission, and gave definite indications of peritoneal infection. After six weeks, however, the condition had subsided into a chronic, febrile state characterised by moderate distension, flatulence, spasms of colicky abdominal pain, and a firm resistant lower abdomen. Within three days of the onset of douches she was comparatively free from pain, flatulence disappeared, and the abdomen gradually became soft and freely palpable. No elevation of temperature and no signs of an acute reaction were noted.

Figure 12.



In spite of this and a few other instances of apparently great benefit, it seems, however, safer to avoid douching as a dangerous form of local treatment. It is on the whole too uncertain for promiscuous use, and should be reserved for occasional selected cases under hospital supervision.

5. UTERINE DRAINAGE.

The frequency with which drainage from the uterus is impeded or completely prevented, has been already noted in the consideration of Group 2 cases. Hobbs⁽⁶⁴⁾ believes that "after

/"after pains" are not physiological but pathological, being always the result of obstruction in the cervical canal; and he maintains that failure of drainage, whether due to uterine or extrauterine causes, is the starting point of all puerperal infections. In his brochure on the subject, he deploras the fact that every day one sees surgeons watching intently the spread of infection to tubes and peritoneum, and making no attempt to deal initially with the intrauterine sepsis which is the source of the trouble, and which in most cases may be traced to a simple lack of adequate drainage. This may be the view of an extremist but it is a sound working principle.

One of the fundamental rules of surgery is that pus must be allowed free exit. There are several methods of obtaining drainage from a septic uterus.

1. Adoption of Fowler's position - if there is no mechanical blockage of the os internum.
2. Removal of obstructions - whether these be due to inspissated pus, blood clot, placental debris, or malpositions.
3. Catheterization of the uterus.

Fowler's Position.

The use of this position marked a great advance in the nursing of puerperal fever patients. When a healthy woman is allowed to lie flat in bed after her confinement, the heavy uterus, - ill supported by its lax stretched ligaments, - tends to fall backwards into the pelvis. This causes acute flexion of the cervix at its junction with the uterus, while at the same time the uterine veins become twisted and the whole organ further congested. Drainage from its walls and cavity becomes more and more impeded, and the end result is the retroflexed or retroverted subinvolted uterus deplored by gynaecologists. If, however, the uterus is infected, its wall toneless, and the pelvic tissues stretched and torn after a difficult labour, this same sequence of

events will have much greater effect. The uterus is not only subinvolted and retroflexed; it is for all practical purposes an abscess and a potent source of pelvic infection.

There is no doubt that the adoption of the Fowler position early in the puerperium will in many cases prevent the assumption of retroflexion, and will promote free drainage from the uterus; but it must be stated at once that when retroflexion has occurred or the cervical canal is blocked by a wedge of placenta or blood clot, no amount of this attitude will avail to remove such obstruction.

In the true Fowler position the patient sits upright supported by pillows behind and by a firm cross pillow below the level of the hips. This extreme position has many disadvantages. If the pelvic supports are lax, the uterus tends to sink downwards, and varying degrees of prolapse are produced. Further stretching then occurs, and gradually there is so much loss of tone that the position becomes irrecoverable. The full Fowler position also is liable to increase the natural ante-⁽³⁾version of the uterus, with effects similar to those of the backward displacements which it is aimed to avoid. Shear has remarked on this frequent result and on this account recommends a lateral posture. Finally, the position is difficult to maintain and involves considerable strain on patients who are already too ill to withstand it.

For these reasons, the medium course of elevating the head of the bed on a trestle, was adopted; and in practice this proved excellent. The height could be regulated, and this position, was much more comfortable than the true Fowler position, which was reserved for occasional cases of spreading peritonitis where the erect posture was more urgent. Even in these patients, however, the disadvantages of the position nullified its advantages; and in most cases it was found that

if the bed were simply elevated to the highest rung of the trestle, the results were more satisfactory.

The placing of all patients in this modified Fowler position was a matter of ward routine, and was begun immediately after admission to hospital. Cases of Phlegmasia Alba Dolens were however nursed on a level bed with the leg raised; and a few collapsed or moribund patients were similarly treated. Many women who had been free of discharge for several days prior to admission, were found to have profuse purulent lochia after a few hours in this elevated position. While this may have been due in part to the emptying of bowel and bladder - any extrauterine causes of obstruction being thus removed; - there is little doubt that the Fowler's position was an important factor. This is a matter of interest to general practitioners who are treating the disease at its onset, and who by insisting on the early adoption of the position, might appreciably affect the course of the illness.

Removal of Obstructions.

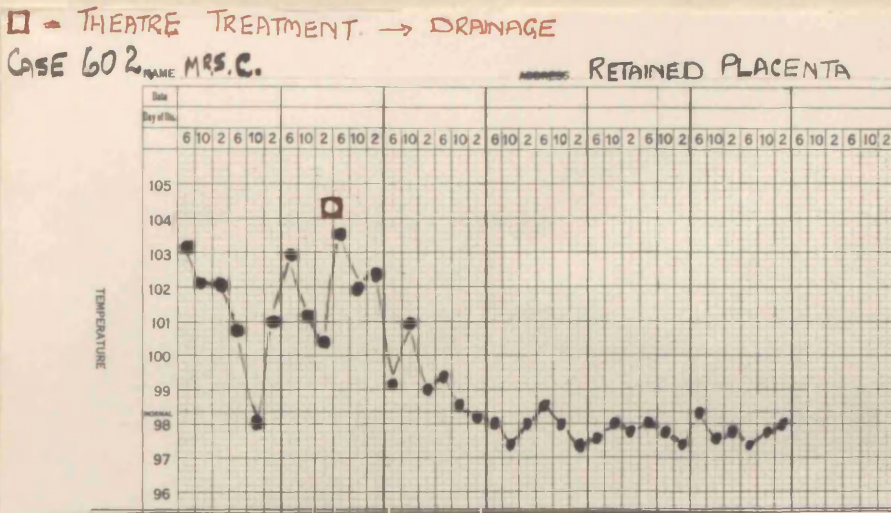
The frequent occurrence of mechanical obstruction of the cervical canal is alarming. Malposition of the uterus accounted for many cases of this series- backward and forward displacements about equally. Occasionally small fragments of placenta were found wedged in the cervix or lower uterine segment; and less frequently oedematous sloughing of the cervical canal was found to be the cause of blockage. Spasm of the os internum was present in a fair number of cases. These are of course, examples of gross obstruction. There are many more instances of partial blockage leading to incomplete drainage.

In cases of fully established septic endometritis removal of the obstruction was often attended by almost immediate and very gratifying results. This was carried out in theatre with complete aseptic precautions, malpositions being corrected

manually and obstructing debris removed by swabbing or with forceps. Frequently such a procedure was followed by a profuse discharge of very foul pus, or a small quantity of thick old-standing lochia would escape from the uterus: and this might occur on one occasion only. Malposition and cervical spasm tended to recur, however, to some extent, and the complete establishment of drainage in many cases entailed several daily treatments. Usually a smaller amount of pus escaped on each occasion. The temperature occasionally settled by crisis after the first drainage, but more commonly it subsided by lysis during the period of treatment. Cases where the obstruction was due to placental debris or blood clot were usually in the first category. Examples of both types might be multiplied.

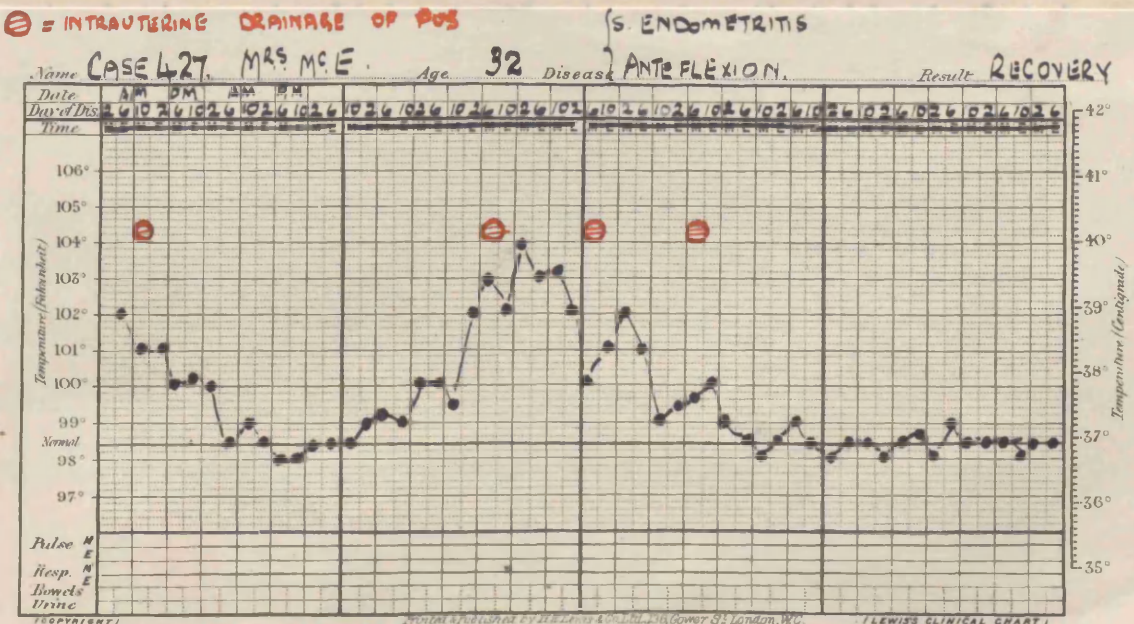
In the first group is case 602, whose temperature chart is appended. This woman was admitted from a Maternity institution a fortnight after her confinement therein. She had been highly febrile for at least a week, and on admission appeared acutely ill. The uterus was palpable as a tender abdominal mass extending almost midway to the umbilicus, and there was no lochia. No local examination was made on the day after admission, as the woman appeared too ill to withstand much movement; but in theatre the following day she was found to have a small piece of placenta firmly wedged in the cervical canal, and the uterus above this was large, tense, and tender. When this obstruction was removed, a profuse foul discharge escaped from the cervical os. Within 24 hours the patient was afebrile, and had an uninterrupted convalescence thereafter. Her temperature chart, Figure 13, illustrates the subsidence of the toxæmic manifestations.

Figure 13.

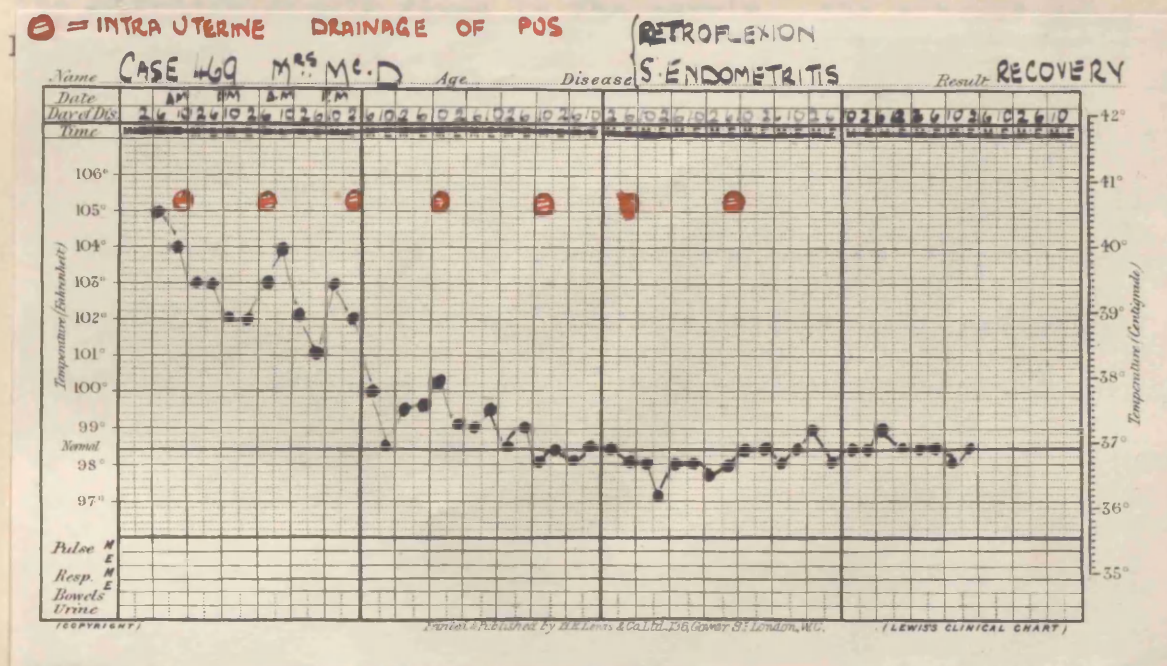


Case 427 differed slightly from the above. In this instance intrauterine pus and an acutely anteflexed uterus were found on the day after admission; but as the patient was very excitable and almost maniacal, theatre treatment was not continued. Although the temperature fell after the first examination she gradually became febrile again during the next few days, and on the fourth day of admission the patient looked very ill indeed. A further examination was then made and this revealed anteflexion with failure of drainage, about 3 oz. of pus escaping whenever the displacement was corrected. The toxæmia diminished rapidly thereafter, and as far as the local lesion was concerned only two more treatments were found necessary. Her chart is shown in figure 14.

Figure 14.



Case 469 was of the type requiring frequent corrections. This woman was admitted sharply ill with septic endometritis and a retroverted obstructed uterus. This malposition recurred after each correction, but always to a lesser degree. By the end of a week the uterus was firmly involuting in good position and permanent drainage had become established. During this period her temperature gradually subsided as shown in figure 15.



The frequency of these obstructions is sufficient to warrant the complete examination of all patients soon after admission, even those who appear so ill as to deserve a little delay in handling. In such patients the examination must be made with extreme care; and if the uterus is moved, such manipulations should be gentle in order that blood clot in nearby veins may not be dislodged or localized infection disseminated. The importance of establishing primary drainage in this way cannot be overestimated, and it would be well if on the first elevation of temperature a careful bimanual examination were always made with this object in view. In many patients the fever would progress no further than a day or two, and of the cases cited at least one would not have required transference to hospital.

Catheterization of the Uterus.

Drainage of the uterus by catheter becomes advisable when the uterus is fixed in malposition, where cervical spasm is persistent, and in cases where complete emptying cannot be obtained by the means above described. This is a procedure which has its greatest exponent in Remington Hobbs ⁽⁶⁴⁾. Although for its performance it requires neither elaborate technique nor appliances, it is a method of local treatment which should be restricted to the hospital theatre.

The Technique used was as follows. With the patient in lithotomy position the external genitalia were thoroughly swabbed with sterile wool soaked in lysol solution, and the vagina was thereafter cleansed in a similar manner. Anterior and posterior specula were then introduced by an assistant, and the cervix gently brought into view. The cervix and cervical canal were thoroughly cleansed by means of pledgets of wool moistened with lysol solution. Often this clearing of the canal was followed by a free discharge of pus from the cervical os, and in any case an ordinary rubber catheter with a terminal eye (about size 8) could be safely introduced. If the uterus contained pus this was drained off through the catheter into a bucket or other utensil.

The advocate of catheter drainage insists on the fact that it must be continuous if it is to be effective. He therefore leaves the catheter with, ⁱⁿ the uterus, fixing it by means of light packing in the vagina; and he contends that cervical spasm and malposition cannot then recur. This method is contraindicated for the following reasons:-

1. The catheter rarely remains in position. It should be remembered that the uterus is a mobile organ, and most patients are themselves fairly active even when ill. Every movement of bowel or bladder affects the position of the uterus, and of the vagina, and of the catheter which has been left protruding into

the uterine cavity. Bruising of the endometrium is thus liable to occur at the one end, and contamination of the catheter at the other; and usually within an hour or two the latter is found out of the uterus entirely.

2. If the pus is thick the catheter soon becomes blocked and useless. The terminal eye is after all a fairly small aperture.

3. If the vagina is packed tightly enough to keep the catheter firmly fixed in the cervix, the other discharges are impeded, and the patient is soon in a worse condition than before. Packing - no matter how loosely - has always proved detrimental in this disease.

4. It has been found that daily catheterization is just as effective and is much safer than the continuous method. Even if spasms and malpositions recur after the first few treatments, the complete drainage effected on each occasion is usually sufficient for that day and the natural drainage soon becomes established.

The leaving of any instrument - no matter how soft - to move about blindly within a septic devitalized uterus, is a procedure which has proved to be quite unjustifiable. The condition of the uterine wall in most patients who go to post mortem, is sufficient to show what the ill effects of such treatment might well be. Catheterization of the uterus in cases of Septic Endometritis with imperfect drainage ought therefore to be a daily procedure rather than a continuous one.

Several observations may be made with regard to this treatment. In the first place the introduction of the catheter is very easy and seldom requires any manoeuvring. Very few patients ever complain of pain during the cleansing process or when the catheter is inserted, and no anaesthetic is required. A minority do feel the treatment painful; but these are women who have extensive lacerations into the pelvic cellular tissue; and usually after a few days the procedure becomes comparatively

painless. It should be noted also that the appearance of the vagina and cervix must never be taken as an indication of the condition of the uterine cavity. As previously described, many cases of septic endometritis are accompanied by very little external inflammation, and often a small firm cervix has locked within the uterus some foul retained blood and clot which forms an excellent medium for organismal growth. The findings were in this respect rather in contradiction to the usual teaching that the cervix will not contract firmly until the uterine cavity is empty. This series includes numerous examples of full time and Post Abortum Sepsis where the cervix was small, firm, and the os closed, yet the uterus contained appreciable amounts of dead and decomposing material.

Finally it must be realized that just as in those cases where manual correction is alone employed, the number of treatments which are required will vary with each patient. In a few instances catheterization on one or two occasions may be all that is necessary, while in others daily drainage for a week or more may be required. These prolonged cases are undoubtedly examples of well established Septic Endometritis; whereas those recovering in a day or two are probably incipient cases where retained blood or clot has decomposed and the uterine wall itself is fairly healthy.

Simple drainage from the uterus may be the only local treatment necessary; but usually more is desirable to promote healing of the inflamed endometrium and prevent further spread of the septic process. This additional treatment may take the form of intrauterine irrigations or the injection of sterile glycerin into the uterine cavity, or a combination of these procedures. In this investigation most of the patients who were given uterine drainage by catheter also received glycerin injections; and in a few, irrigations were also employed.

6. Uterine Irrigation.

Irrigation of the uterus in cases of Septic Endometritis is practised by Hobbs and by many others, various fluids being used for the purpose. Hobbs (64) recommends normal saline while Morris (65) advocates hypertonic saline. ~~Carrel~~, Dakin Solution has been employed by other observers, among whom are Whitehouse (7) and Canney (65). It must be admitted that when catheterization reveals a profuse foul uterine discharge, especially if this is thick and does not drain well, there is a strong temptation to irrigate the cavity and thereby remove more pus and organisms than the simply process of drainage could ever accomplish. In addition if an efficient antiseptic solution were used the double effect of douche and antisepsis might be obtained. In the cases under review 24 patients received uterine irrigations as adjuvant local treatment.

Technique.

The procedure consisted in affixing a rubber connecting tube between the catheter - which was already in place within the uterus - and a glass funnel containing irrigating fluid at body temperature. By adjusting the height of the funnel the force and rate of flow could be regulated, a level slightly above that of the patient's buttocks allowing a very gentle stream. The returning fluid escaped from the cervix round the sides of the catheter. At the outset thick pus was usually washed out, but gradually the return became clear, about one pint being usually sufficient for this purpose.

It may be imagined that such a procedure is very comforting to the patient, and most of its recipients express themselves as much relieved by it. But it is at all times a dangerous procedure on account of the dissemination, which may be produced. If the fluid is allowed to run in from a high level and therefore with much force it tends to open up

the gland orifices, thus allowing the infecting organisms to penetrate into the deeper layers of the mucosa. Thence the uterine sinuses are readily involved, especially if - as in many patients who go to post mortem - there are large placental vessels still patent close to the endometrium. Even when irrigation is performed very gently and with the fullest precautions, there are a few women in whom subsequent shivering or even well marked rigors are noted.

Much might be accomplished with a suitable irrigating fluid. In this investigation normal saline was used - as Hobbs recommends. Such a fluid has the advantage of being non-irritating, whereas hypertonic saline is liable to produce superficial necrosis of the already unhealthy endometrium. Other antiseptic solutions have this same disadvantage. The evils of vaginal douching are indeed repeated in the intrauterine method, but to a much higher degree; and it is a procedure which while undoubtedly beneficial in many cases is in others fraught with danger. It should therefore be reserved for a few patients only.

7. Intra Uterine Glycerin Injections.

Since its discovery by Scheele in 1779, glycerin has found extensive use in medical practice. Modern research however is revealing many other applications hitherto undreamed; and in particular Hobbs and his co-workers have demonstrated its value in the treatment of sepsis in the uterus and adnexa.

The therapeutic value of glycerin has been attributed mainly to its physiological action as a lymphagogue, which, by setting up drainage, results in a washing away of bacteria from the surface and from the deeper layers of the inflamed tissue. In this connection Douvier ⁽⁶⁶⁾ writes as follows. "It is conceivable that this drainage may be utilised to produce a lavage à retro of the mucusae and of the diseased cutaneous surfaces, and to contribute to their detersion. This lavage is

evidently much more efficacious than superficial lavages which never penetrate the mucosae and which produce merely a surface action. It is evident," he concludes, "that for medicinal applications one should avoid toxic or irritating substances, or these liable to destroy the tissues. Osmotic drainage can be used in a very general manner for all mucous membranes and for the treatments of infected wounds."

(67)

Compton has proved, however, that the action of glycerin is not merely due to osmosis, but that there is in addition a definite bactericidal effect. In strong concentrations, or in the pure state, this effect is very marked, although in weaker dilutions glycerin is inhibitant and antiseptic rather than bactericidal. It is found that Streptococci succumb readily when exposed to the action of glycerin, whereas staphylococci are more resistant. Bacillus Coli will remain in association with pure glycerin for two hours before the bactericidal effect comes into play, although long before this, it has been inhibited. It is this antiseptic rather than bactericidal effect which is obtained when the various bacterial types met with in the genital tract are so tested.

When determining the value of any antiseptic substance of this nature, it is important to discover the extent of its toxicity to the tissue cells with which it will come into contact. As Ene (68) aptly remarks, "There is a class of antiseptics cheap to make, dear to buy, and strong to smell, which in dilutions of sufficient strength are too irritating to be applied with propriety to either the exterior or interior surfaces of the human body. In dilutions weak enough to be comparatively harmless their use gives a sense of false security and satisfaction, probably accounted for by their odour and certainly not warranted by their effect." These antiseptics

are indeed more toxic to tissue cells than to the organisms which they set out to combat. It appears however that glycerin is probably unique in the opposite respect. If applied to surface epithelium glycerin does produce a mild irritation due to abstraction of fluid from its cells, but no untoward effect such as necrosis or sloughing has ever been found to follow its intrauterine use. It has been proved experimentally that leucocytes - which may be taken as an example of typical tissue cells - can support a much higher concentration of glycerin than can staphylococci, and these are probably the most resistant type of micro-organism. Glycerin is thus claimed by many as vastly superior to most other antiseptics for general surgical use, and in particular for application to the uterine surfaces.

Other writers on the contrary deny this antiseptic property, and suggest that some unexplained biochemical factor is responsible for the good results obtained by its use. Recently Kyle ⁽⁶⁹⁾ maintained that unless in pure solution glycerin has no effective hygroscopic power, and even in pure solutions manifests this property with extreme slowness. This writer suggests that the increased flow of serum in the lymph drainage, may in reality be due to irritation of the exposed surface by the pure glycerin.

Many recent workers however claim that the application of glycerin to the treatment of Puerperal Sepsis is of most dramatic and far reaching importance, and in the present investigation a serious attempt was made to test fully the truth of the above statement.

The Glycerin Treatment will be discussed in the following sequence.

- A. Type of case chosen.
- B. Technique employed.
- C. Contraindications to the treatment.

D. Advantages of the treatment.

E. Estimate of the results.

A. Type of Case Chosen.

Of the total series, 402 patients received this type of local treatment. When the method was first adopted the procedure followed was that advocated by Hobbs⁽⁶⁴⁾ - who is its greatest exponent - and all patients received it no matter how severe their illness. It was soon apparent however, that it was a treatment almost entirely unsuited for Group 4 patients, and that cases of virulent spreading infection were often rendered more ill by it. As far as possible therefore the treatment was reserved for patients in the first three groups, with certain reservations however in the third.

B. Technique.

This was in every way similar to the method employed at St. Mary Abbots' Hospital where glycerin treatment has reached the apex of its fame. There, however, the injections are given on several occasions during the day, whereas in the present series only one daily treatment was given. Quite apart from the fact that such an intensive method requires special arrangements with regard to medical and nursing staff, it was found that one glycerin injection each day was all to which most patients would consent, - no matter how painless the procedure.

Catheterization of the uterus formed the first stage of the treatment. Hobbs recommends fixation of the cervix with volsella during this procedure; but this proved quite unnecessary so long as the cervix was sufficiently brought into view by the vaginal specula; and in all cases if the internal os was open the catheter passed easily through. If the puerperium had not advanced far, and if there were much local sepsis, the catheter passed up into the uterus for

about six inches and could be felt impinging on the fundus. In this event it was withdrawn a little. Occasionally the os appeared firmly closed, but yielded to light pressure with the tip of the catheter, especially if this were lubricated with a little glycerin. Intra-uterine pus, if present, was allowed to drain completely through the catheter, and in a few very foul cases the uterus was gently irrigated with saline solution. In these instances the catheter was then removed, and another inserted well within the uterus. The glycerin was then injected slowly and without force from an ordinary glycerin syringe, which was slipped on to the open end of the catheter. Pure glycerin was used for this purpose, complete sterilization in an autoclave having been of course effected.

The amount of glycerin used varied with the size of the uterus, and this depended both on the degree of sepsis and on the stage of the puerperium. In full time cases recently delivered 30 c.c. or more were frequently required; whereas in Post Abortum Sepsis, or at later stages of the puerperium, 10 c.c. or even 5 c.c. would fill the uterus. In the former type, daily diminution in size of the uterus was most noticeable, the amount of glycerin required becoming less at each injection, until finally, about 5 c.c. only could be injected, and even that ^{the amount} partially escaped round the sides of the catheter. By the following day, or soon thereafter, the cervical os would be firmly closed, and the glycerin treatment therefore ceased. In cases where there was much intra-uterine sepsis, this gradual diminution in size was not apparent for a day or two, and indeed involution appeared to be at a standstill in many instances. After a few injections, however, involution became established and less glycerin was required; and this was obvious even in grossly septic cases.

The number of injections varied with the individual response. Cases of established septic endometritis occasionally

required as many as fifteen daily treatments. Simple infections where the sepsis was mainly in the perineum vagina and cervix required from two to six injections. In this series of 402 women, 2,069 daily treatments were given. This gives an average of 5.6 injections per patient. A few of these however received only one or two injections, the treatment being discontinued for various reasons; and if these are discounted the average rises to 6.9 per patient. Many however received ten or twelve injections and one woman received twenty-five daily treatments. As a general rule the injections were continued so long as the cervix admitted the catheter; and for a few days thereafter the vagina was irrigated with glycerin or swabbed with lysol solution. A week after cessation of local treatment a re-examination was made and glycerin given if the cervix admitted a catheter again - a proceeding rarely necessary.

Frequently on the second or third day of treatment a profuse thin purulent discharge drained through the catheter, although at the outset such had been absent or scanty. This was evidence of the hygroscopic action which forms the basis of the whole treatment, and it usually coincided with distinct improvement in the general condition. Colebrook⁽⁶⁵⁾ and his colleagues have made mention of this phenomenon, and regard it as of definitely favourable omen.

C. Contraindications.

The lesions which many patients present make it difficult to stand aside and do nothing, and there is no doubt that as a means of local treatment glycerin has much to recommend it. There are however definite contraindications to its use in all cases, and it is important that these limitations be at the outset clearly defined. Apart from the type of patient who is found to have the os internum firmly closed, the uterus well involuted, and the septic process established

in the adnexa or surrounding parts; there are many who are locally suited for the glycerin treatment yet must be denied it. These may be grouped as follows:-

(1) Cases of marked toxæmia or definite septicaemia.

Glycerin treatment cannot adequately be carried out in bed, and very ill patients cannot withstand the requisite manipulation which movement to theatre demands. A toxic woman becomes greatly exhausted by the lithotomy position, after even 5-10 minutes maintenance of it, which the glycerin treatment requires. Apart from the fact that surgical asepsis is difficult to achieve when the patient is in bed, it is impossible to introduce specula accurately while she is in the recumbent position; and the cervix cannot therefore be brought into view sufficiently for cleansing and for introduction of the catheter. If, however, she is turned round so that her buttocks are at the edge of the bed and her legs held in lithotomy position, the amount of movement necessary and the resulting exhaustion are often so great as to be unjustifiable. On this account glycerin treatment must frequently be denied to the severest cases of local sepsis, although these are the patients who most require it and who might be expected to benefit in the highest degree from it. Septicaemic cases especially are excluded from this treatment, in spite of the fact that they continue to absorb toxins and organisms from the intr^auterine focus of infection. The latter course must be considered as the lesser evil, since no matter how gently such patients are treated the excitement and strain produced are dangerous to them. Cases complicated by Pneumonia also are for similar reasons unsuited for local treatment by this means although Hobbs maintains that if care is taken no ill results will ensue. Several such patients treated in this way at the commencement of the investigation gave definite evidence of resulting cardiac failure and further spread of the Pneumonic condition; and the procedure appeared therefore inadvisable even when the pulmonary lesion was of the simpler

broncho pneumonic type.

(2) Cases of active spreading pelvic infections.

When the main sepsis is extra uterine the necessary manipulations - both general and local - have a definite tendency to cause further extension of the infective process. Cases complicated by Peritonitis are thus in the highest degree unsuited for glycerin treatment. Even a mild pelvic effusion definitely contraindicates it, and there are many such cases. The assumption of the horizontal attitude, or elevation of the buttocks as frequently happens when the patient is placed in lithotomy position, can only result in spread of the infection upwards to the general peritoneal cavity; and since the recovery rate from pelvic peritonitis is so much higher than that from the general type, it is essential that everything should be done to limit the infection to the pelvic area. These patients also present toxic symptoms - frequently severe - and there can be no doubt therefore that on both of these accounts the glycerin treatment should not be pursued.

(3) Cases of Phlegmasia Alba Dolens.

As already described this condition arises typically late in the puerperium when the uterus is fairly well involuted and the cervical os is firmly closed; but there are a few cases where swelling of the legs occurs early in the illness. These women are usually sharply ill and have severe local sepsis, but the risks of embolism are great and it is unwise to move them in any way. The glycerin treatment must therefore be avoided.

(4) Cases complicated by Insanity.

The excitement of daily treatment in theatre is apt to set up a manic phase in these women, even when the mental condition is of a mild type. There are occasions when this risk must be accepted and local treatment pursued, and case 427 was in

this category. Reference to this woman has already been made in the discussion on uterine drainage. Although an anteflexed septic uterus had been discovered, glycerin treatment was contraindicated by her mental state. After several days, however, she was highly febrile, and looked very toxic; and it was then decided to explore the uterus. This decision was justified by the fact that the uterus was again found anteflexed and distended with pus; and after several daily treatments the temperature became definitely and permanently normal.

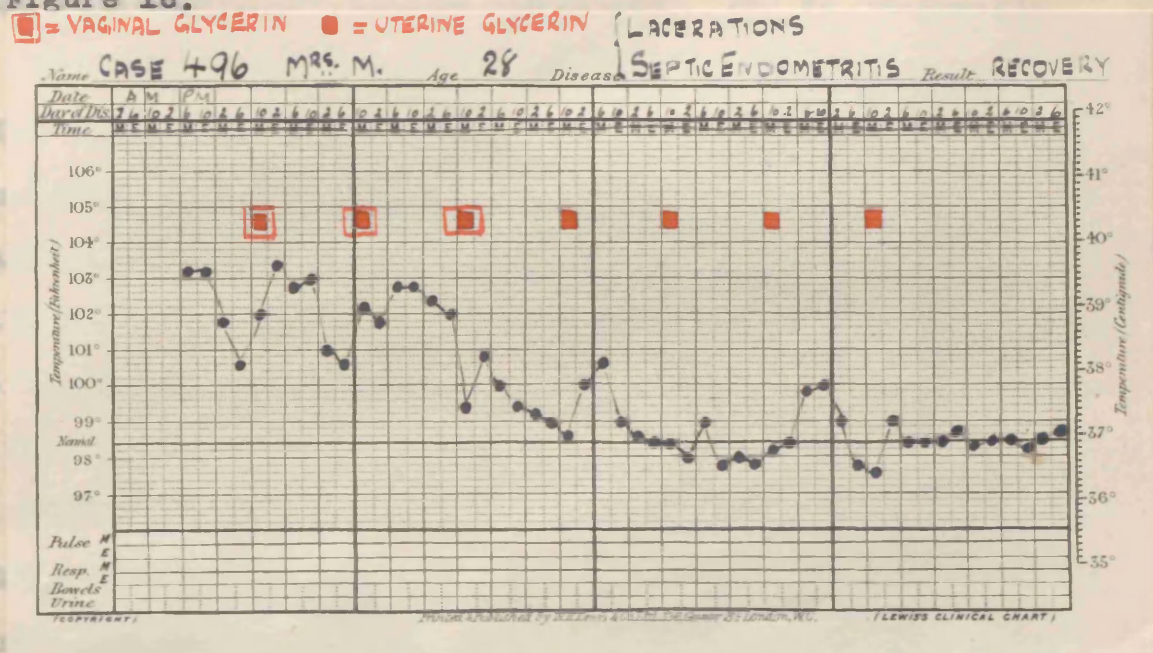
There are many similar cases where, however, the patient is so wildly maniacal that local treatment with glycerin is absolutely impossible.

(5) Cases presenting very foul infections of the lower parts of the tract.

Even after thorough cleansing, the vagina and cervix are occasionally so septic that it is unwise to pass a catheter into the uterus. The cervix was frequently discovered to be a gangrenous sloughing mass in which the os was not readily discovered, and the vagina was in many cases so badly lacerated that the cervix could not be manipulated into view, quite apart from the painfulness of the procedure. In these cases daily swabbing of the vagina and cervix may be the only local treatment possible, and by such means simple drainage from the uterus may be maintained. Glycerin might be injected into the posterior fornix; but it is wise to delay intra-uterine treatment until the sloughs have separated and the granulations are appearing, unless there is certain evidence that the uterus already contains pus. Figure 16 is the temperature chart of such a patient. This woman, had gross perinaeal, vaginal and cervical lesions, and the uterus itself did not appear greatly infected. It was not until the fourth daily treatment that catheterization of the uterus was considered free of danger; and although there was a slight elevation of temperature after that injection, subsequent

treatment produced a very satisfactory local and general result.

Figure 16.



The main limitations of the glycerin treatment therefore are that women who are very ill, and especially Septicaemic cases, are debarred from it; that the presence of active spreading infections, of Peritonitis, and of Phlebitis make it a dangerous proceeding; and that for obvious reasons the group of insanities cannot be treated in this way. A further factor might be noted at this juncture. This method of local treatment is quite impossible in the absence of adequate nursing assistance. It is desirable that these nurses should be familiar with the disease and with its complications, and should thoroughly understand the theory of the procedure. In the absence of complete asepsis it is a dangerous form of treatment, and only those who will conscientiously take the necessary care with regard to this should be employed. The importance of posture and of gentleness in moving the patients between bed and operating theatre must be realized by them, or the whole advantages of the treatment are at once nullified.

D. Advantages of the Treatment.

In spite of the contraindications above cited, there are many patients to whom glycerin treatment might be applied,

and there are several distinct advantages which result from its pursuance in these cases. These are briefly as follows.

(1) Daily inspection.

The local condition is examined daily in a way which is unlikely under the ordinary methods of treatment. The amount and type of the discharge, the localization of the sepsis or its tendency to spread, the development of erysipelalous lesions round the perinaeum, and many other facts are noted early and treated accordingly.

(2) Thorough Cleansing.

The daily swabbing of the perinaeum, vagina and cervix promotes rapid healing. Sloughs and inspissated pus blocking the cervix are removed, and free uterine drainage is thus promoted. An abscess of any other region would be dressed daily; why not a foul sloughing vagina, or a gangrenous cervix? Lochia has a marked tendency to gather in the posterior fornix, especially in primiparae, where the perinaeum is firm; and by this thorough daily cleansing, the locking up of discharge in the vagina for more than twenty-four hours is also avoided.

(3) Drainage.

There is no doubt that glycerin does promote drainage from the oedematous congested uterus, and in addition the daily catheterization completely removes any pus or blood which may collect between the treatments. The cervical canal is also kept clear and the internal os open, so that the maximum of spontaneous drainage may take place in the intervals. Even if the glycerin acts simply as a douche it is a non-absorbable, and non-irritating, and particularly safe one, and more to be recommended than any irrigating fluids yet devised. The procedure also is distinctly comforting to the patients, and they frequently request its repetition.

(4) Separation of Placenta.

Hobbs lays great emphasis on the value of glycerin as a substitute for digital curettage; and he recommends its use as a douche in all cases where placental fragments or membrane are retained, or even when the whole placenta is within the uterus. He claims that the glycerin not only washes away any loose debris, but by its hygroscopic and stimulating action causes the uterus to contract and expel its contents. It is difficult to understand how one injection of glycerin can, as Hobbs affirms, result in the expulsion of a whole placenta; and even in respect of smaller debris it proved of little value. Frequently after repeated injections the drainage became very profuse, and increasing amounts of blood appeared in it; and this was related to partial separation of placental fragments. No amount of glycerin however caused these to be expelled, and in all cases of this nature digital exploration of the uterus became necessary. Very minute pieces of membrane or placenta may have been detached and disintegrated; but anything larger than a hazel nut usually remained fixed to some part of the uterine wall, and more than glycerin was necessary to remove it.

The real advantage of the glycerin treatment in these cases is that usually by the time intrauterine interference becomes necessary the cavity of the uterus is much less septic and the procedure has lost many of its dangers. Case 355 was of this type. This was an example of Post Abortum Sepsis in whom a large placental fragment was retained. On admission the woman looked very toxic; but as the lechia was extremely foul, it was considered inadvisable to explore the uterus digitally. After four daily injections of glycerin however, the placenta began to loosen and haemorrhage was so profuse that interference became necessary. Although this resulted in the removal of very foul gangrenous material, there were no

Table 15.

Table showing relation between treatment and persistence of organisms.

Treatment.	Glycerin.	Conservative.
No. of Cases	169	68
No. of Positive Smears	11	44
Rate % of Positive Smears	6.5	64.7

Thus 6.5% of the cases treated with glycerin still harboured the causitive organisms; whereas 64.7 % of those receiving no local treatment were found potentially infective.

This is striking proof of the efficacy of the regime, if not of the glycerin which forms its basis.

E. Estimate of the Results.

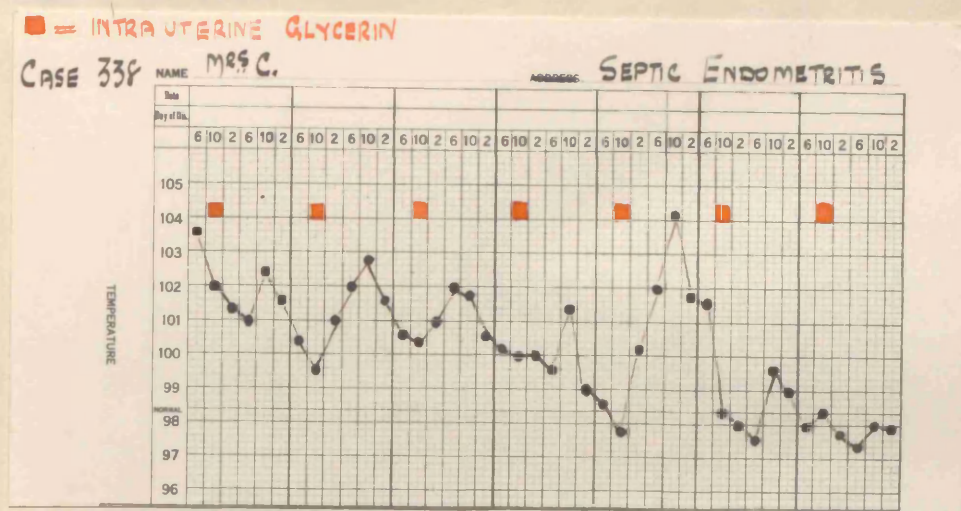
In estimating the value of this treatment for which so much is claimed, full account must be taken of any other remedies which the patient coincidentally receives. Hospitalization is at work in all cases, and this factor may therefore be discounted. There are, however, forms of general treatment which are given to all but the mildest infections. Statistical evidence with regard to its benefits is thus difficult to adduce, and will be reserved for a later section. A personal estimate is however of some value.

Group 1 Cases. A few women in this group are suitable for glycerin treatment and appear to be helped by it, but most of these patients are in no need of intensive local treatment. Usually the internal os is closed, and routine swabbing in bed or theatre is all that may be necessary. The possibility of carrying organisms upwards into an uninfected uterus must always be considered, and where there are foul vaginal or cervical lacerations the risk is scarcely justifiable. It appears that other factors being equal, just as good local healing is obtained by less extreme measures.

Group 2 Cases. Treatment along such lines seems to be the most rational for women of this type. The benefits which accrue are not entirely due to the glycerin, but to everything which the whole regime implies. The great need of this group is for adequate drainage, and the glycerin treatment ensures this to an extent unapproached by any other local treatment or by the conservative methods. As noted above, Hobbs claims that in the absence of local treatment 50% of cases still harbour pus within the uterus; and it is alarming to realize in how many patients of this series the organ was found functioning as an abscess, a condition undetected and untreated under the conservative regime. Daily uterine injections in women of this group frequently gave gratifying results, even when it was the only treatment pursued. Tœxæmia definitely diminished, and there was a gradual subsidence of temperature. This type of reaction is typical, and alone glycerin gives no immediate results. Sudden improvement such as a temperature crisis is not due to glycerin, but more probably to the relief of a mechanical obstruction in cases where the endometrium itself is fairly healthy.

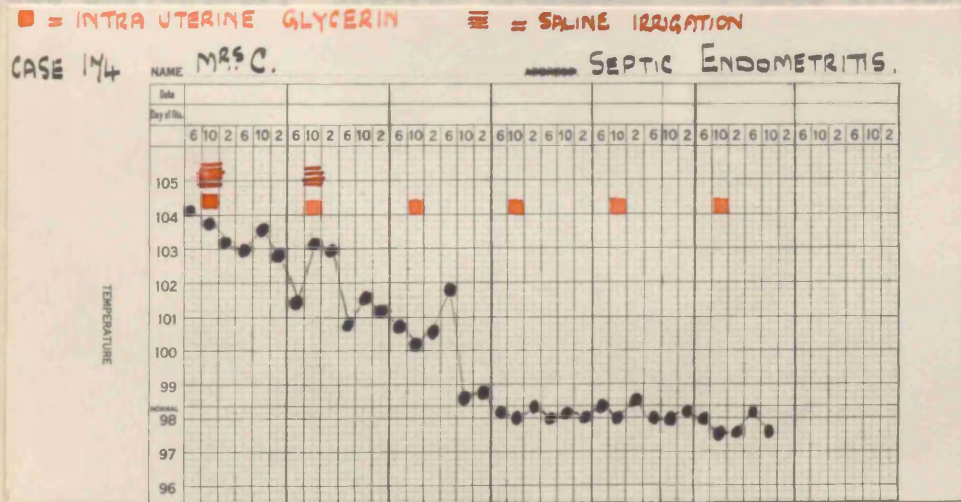
Case 338 illustrates this gradual response. This woman was on admission very acutely ill, and on examination a condition of severe septic endometritis was discovered. Glycerin treatment was instituted and this was followed by slow improvement in the general and local condition, so that by the end of a week no further local treatment was necessary and the convalescence proceeded normally thereafter. As her chart shows (figure 18) there was a temporary relapse of temperature on the fifth day; but this was the result of breast engorgement and responded to the usual treatment. Apart from this the gradual subsidence of temperature is noteworthy.

Figure 18.



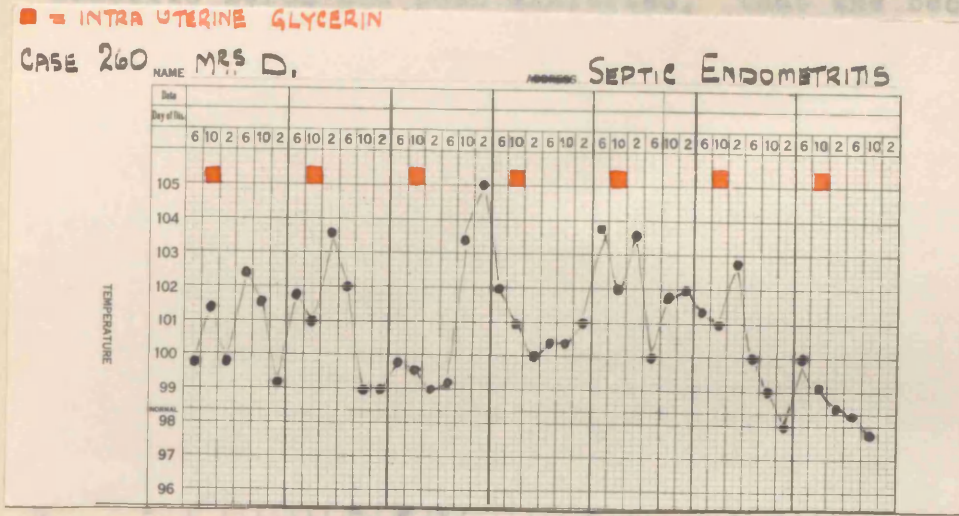
Case 174 shows a more rapid response. On this occasion intracavitary irrigation with normal saline solution was also practised on the first two days of treatment, and no ill results were obtained from this procedure.

Figure 19 (a).



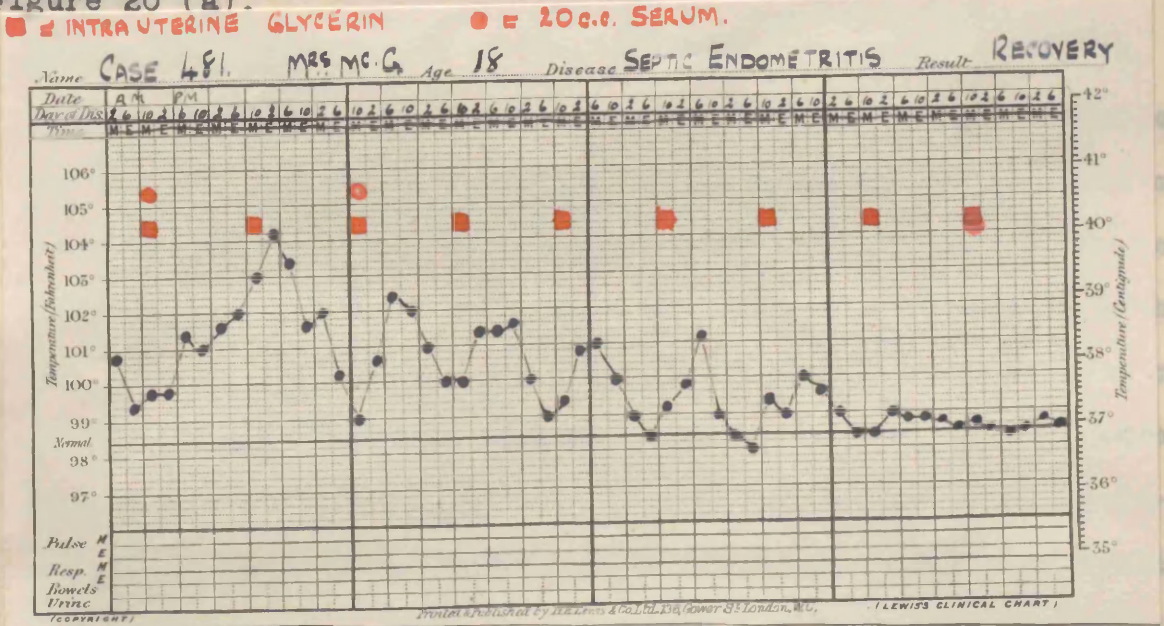
An indefinite effect - almost amounting to absence of response - was noted in Case 260. This woman had very active septic endometritis of streptococcal origin and her temperature during the first week varied in a most haphazard manner despite daily local treatment.

Figure 19 (b).



Case 481 is again more gradual in her response. This woman had typical Group 2 lesions, but was so toxic that glycerin treatment was almost contraindicated. Under this regime however she made an uninterrupted recovery, and her convalescence was uneventful. General treatment was also pursued in this case - as her chart indicates - but no signs of betterment were noted as a result of it.

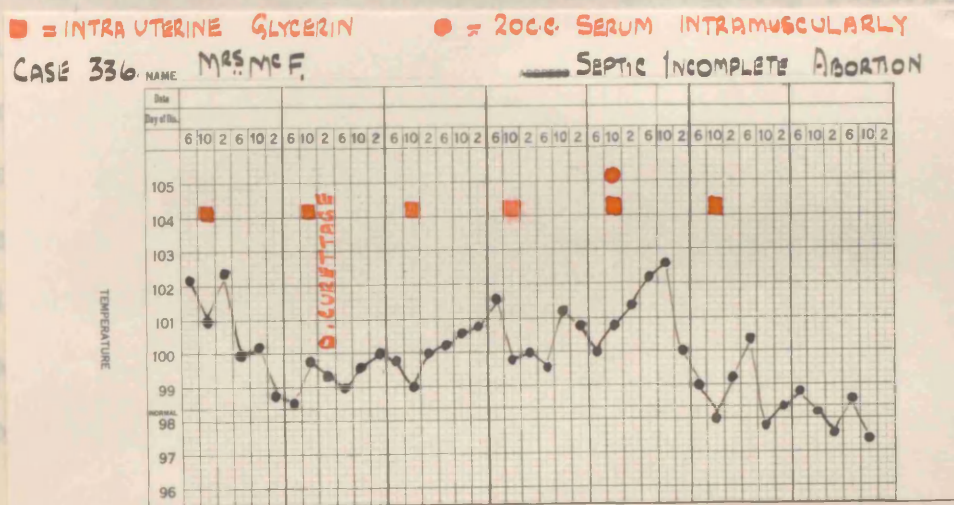
Figure 20 (a).



Case 336 was a typical Group 2 patient who did not apparently benefit greatly from intrauterine treatments of this nature. As her chart (figure 20 b) shows fever increased in spite of the injections, and it was only after general treatment with

specific serum had been exhibited, that she became permanently afebrile.

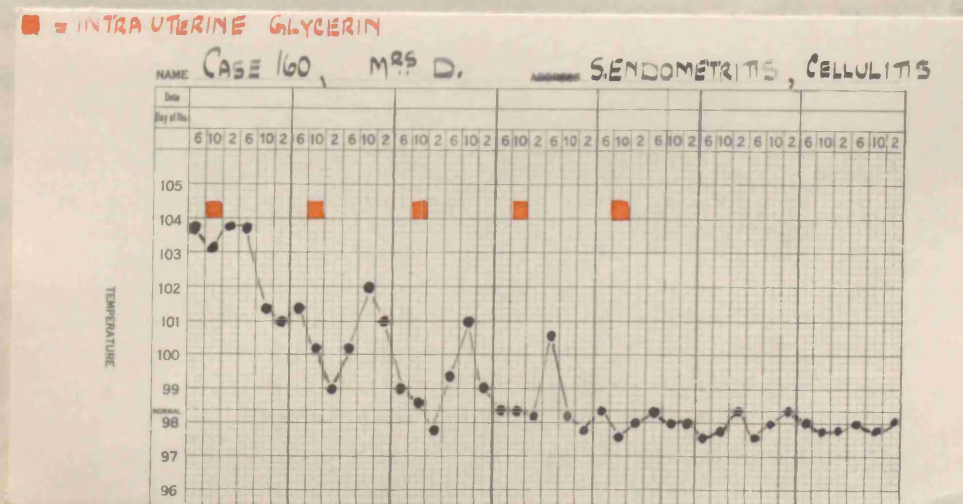
Figure 20 (b).



may be dislodged, with septicaemic or pyaemic results. Vaginal examinations, unless absolutely necessary for diagnosis or treatment, should be definitely restricted if there is active pelvic sepsis, and for this reason many cases of Group 3 are quite unsuited for local treatment by this or any other method. Even if glycerin treatment is carried out, however, in specially chosen cases, it does not appear to exert any favourable influence on the pelvic or adnexal lesions, which, clinically at least, merely run their ordinary course.

The following five patients have been selected to show the varying effects of glycerin within this group. Case 160 showed no deleterious results. This woman had moderate septic endometritis and left sided cellulitis; and on admission she looked ill. Five glycerin injections were made and during this period the temperature gradually subsided. The general condition showed corresponding improvement, and convalescence was uneventful. she was afebrile and

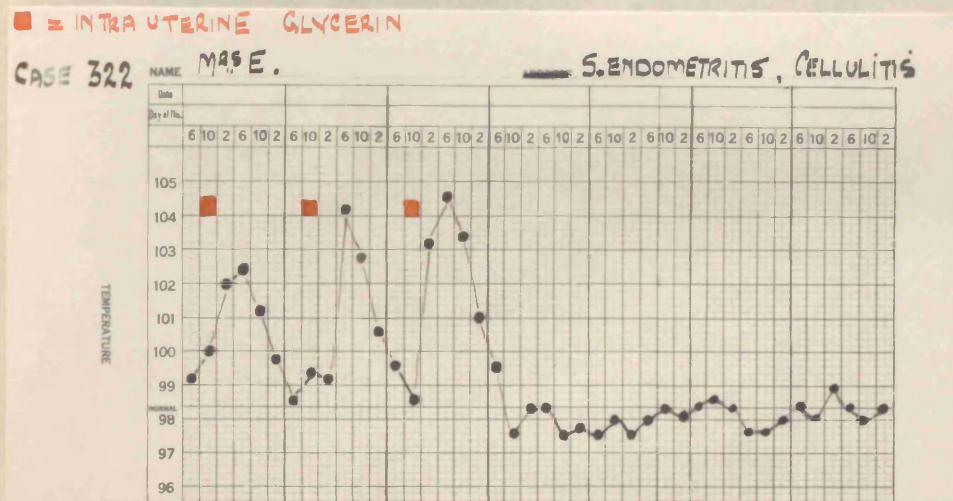
Figure 21.



Case 322 shows an exactly opposite reaction. This woman had septic endometritis and slight unilateral pelvic cellulitis. After each glycerin injection her temperature became sharply elevated, rigor occurred, and she appeared ill.

The treatment was thus stopped and no further general symptoms were noted. Her chart (figure 22) shows the definite response to withdrawal of treatment.

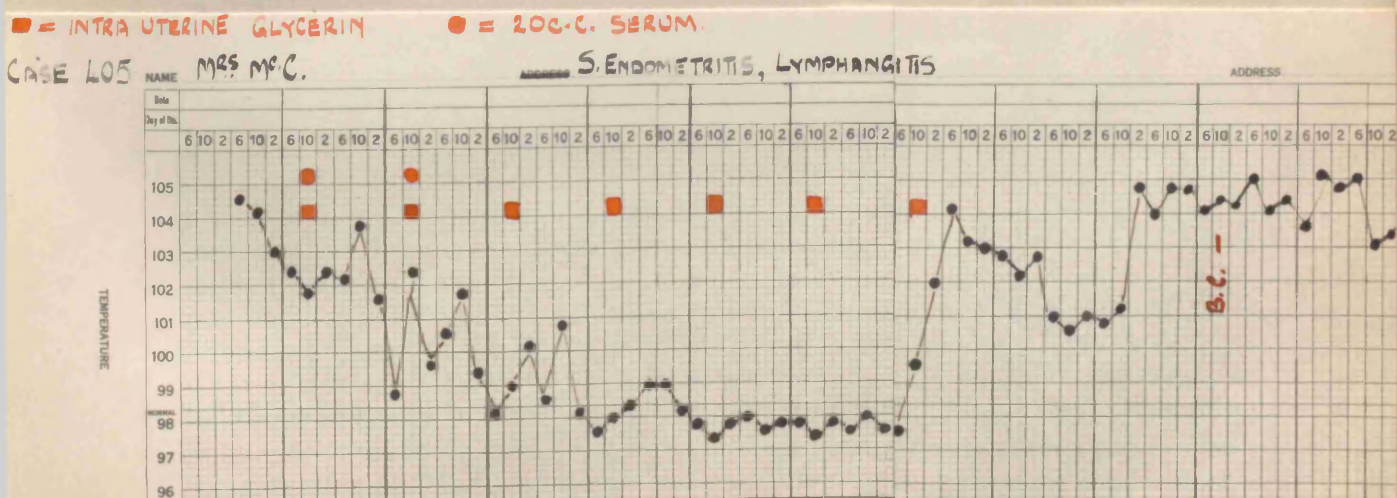
Figure 22.



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with the
glycerin

Case 405 illustrates an apparent good effect from glycerin, which was however nullified by later happenings. This woman was acutely ill on admission but responded quickly to local and general treatment. Within four days she was afebrile and symptomless, but on the eighth day of admission she again became highly febrile and for several weeks thereafter she was clinically septicaemic. It was felt that in this case the glycerin had definitely spread an already established, but mild, lymphangitis.

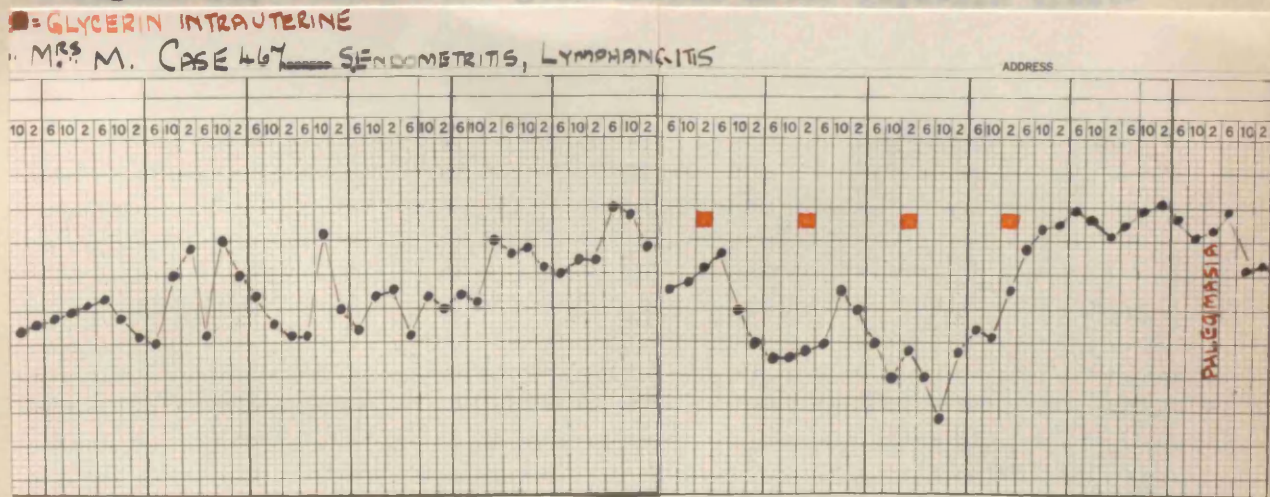
Figure 23.



local treatment was carried out and the temperature remained

permanently settled. Her chart (figure 25) shows these
 Case 467. This woman also showed apparent improvement,
 later counteracted by complications. On this occasion
 glycerin treatment was not initiated until the end of
 the first week in hospital. Profuse intrauterine pus
 was found, and the release of this on three successive
 days brought the temperature for the first time down to
 normal levels. The fourth treatment was however followed
 by relapse of temperature, and two days later bilateral
 Phlegmasia Alba Dolens was apparent. In view of the
 previous serious condition of this patient-although clinically
 there had been no signs of pelvic infection outwith the
 uterus,- it is difficult to be sure whether the glycerin
 was actually responsible for her relapse.

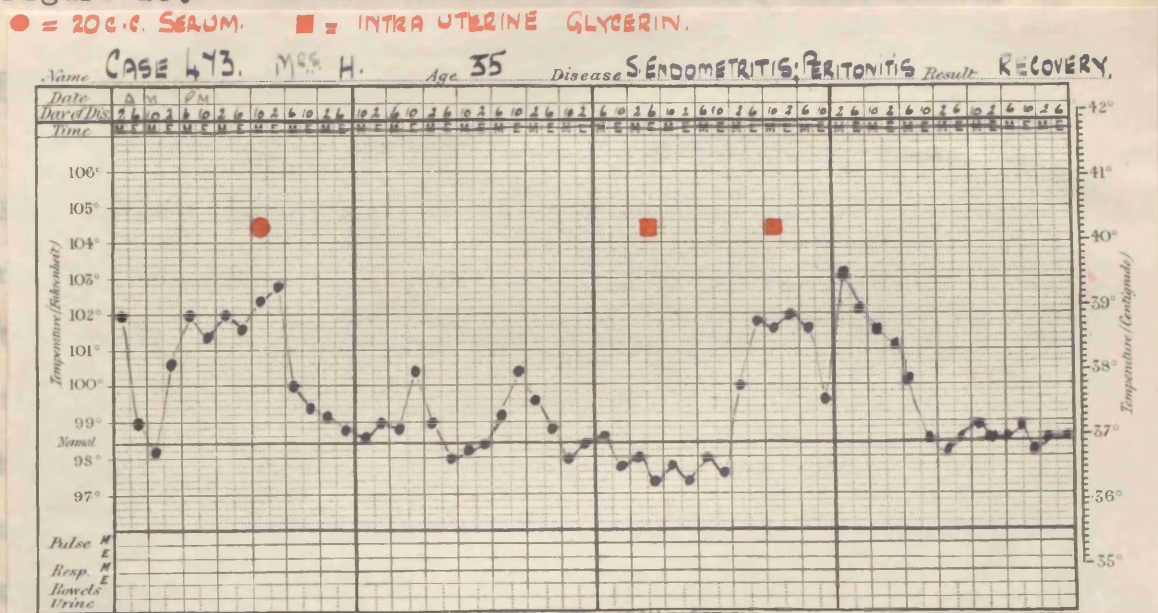
Figure 24.



Case 473 was, however, definitely harmed by local treat-
 ment. This woman when admitted was very ill and gave
 definite indications of pelvic peritonitis. She improved
 rapidly however with general and postural treatment, and
 within five days she was afebrile and symptomless. Examination
 in theatre was then conducted, intrauterine pus found, and
 glycerin given. Twelve hours later she complained of headache
 and shivering, and her temperature was again elevated. Intra-
 uterine pus had been profuse, however, so another treatment
 was given. This was again followed by fever. No further
 local treatment was carried out and the temperature remained

permanently settled. Her chart (figure 25) shows these reactions.

Figure 25.



There were also in this group several women with pelvic peritonitis which became generalized after glycerin treatment, and terminated fatally. These were virulent infections which might have proved fatal in any case, but the risks entailed were not justifiable. A certain familiarity may be achieved in judging which cases of the group may with safety be given local treatment with glycerin; but it is a facility which is sometimes dearly bought.

Group 4 Cases. The women in this group appear definitely unsuited for glycerin treatment. The exact extent of the local sepsis is difficult to estimate, and the septicaemic condition may be arising from abscesses in the very wall of the uterus or in the veins beside it. Even the gentlest local handling could scarcely avoid disturbing these and innoculating the blood afresh with microorganisms. A few women of this series became rapidly more ill, and several potentially septicaemic became definitely so while glycerin treatment was being carried out. Incidental reference is made to several of these in the later discussion of general treatment.

These patients should be moved as rarely and as gently as is compatible with efficient nursing. The general strength

must be conserved and increased, and the local lesion, no matter how active should be rigorously left alone.

Post Abortum Cases.

The foregoing discussion applies chiefly to the Full Time cases, and little more need now be said with regard to the Post Abortum group. It should be remembered that here the uterus and its cavity are much smaller than the full time puerperal organ. Glycerin treatment may however be pursued. In Group 1 it is unnecessary and inapplicable since the uterus is usually very small, firm, and the os closed.

Cases falling into the category of Group 2 showed a marked response to this method of treatment. Glycerin acts in these cases as an aid to drainage and as a means of loosening placental fragments, membrane, or blood clot from the uterine wall. Although it rarely causes the complete expulsion of these, it creates a cleaner atmosphere within the uterus, and inhibits the development of septic complications should manual removal become necessary.

With regard to Group 3, glycerin is even more definitely contraindicated than in the full time cases of the same group, and this may be related to the greater tendency for massive pelvic infection in the Post Abortum cases.

Lastly, in Group 4, as in the full time series local glycerin treatment is definitely to be avoided.

GENERAL TREATMENT.

The general methods adopted in the treatment of puerperal infection have for their aim the neutralization of the toxæmic and septicaemic manifestations. They assume increasing importance in the stages between the localised types of the disease and those severer forms where there is evidence of an absorption of inflammatory products; and they become the all-important factor in the fully established septicaemic type, where the general infection constitutes the major problem.

Apart from the specific forms of general treatment which will be later discussed, there are ordinary principles to which brief reference must first be made.

Stimulants.

Throughout the investigation cardiac stimulants were prescribed freely, both as an emergency and as a routine measure; Digitalis, Pituitrin, and Strychnine being the drugs usually employed. The second of these - Pituitrin - has also a stimulant effect on the uterus and bowel, and is valuable in cases of hæmorrhage and in Peritonitis where intestinal paresis is imminent. Recently this drug has been divided into two components - pitressin, which has mainly a cardiac effect, and pitocin, which acts chiefly on uterus and bowel. Both of these were used extensively without much difference of effect being noted; and since in this disease the combined action was often required, the older complete form was in the main favoured.

Alcohol has a definite value, whether for occasional or routine use. One of the important factors which determine recovery is the "will to live;" and in the depressed type of patient whisky or brandy may prove beneficial if given for brief/

brief periods. In the protracted anaemic cases Port is also useful, while Champagne is invaluable in Septicaemia and Peritonitis where frequent distressing sickness is the outstanding symptom. Often this stimulant is retained in the stomach when all else is vomited, and by its use the patient may be saved for a few days until the acute condition subsides. Kustner⁽⁷⁰⁾ believes that alcohol should be given in large doses as a specific form of treatment, in the belief that the toxic effect of the alcohol is destructive to bacteria in the blood and in the local lesion. On this account he advocates complete intoxication of the patient; but such heroic measures have not appeared advisable.

Hypnotics.

The value of sleep as a therapeutic measure cannot be over-estimated, and the improvement in the patient's condition after a satisfactory rest was often noteworthy. Unless strongly contra-indicated, therefore, for other reasons, 1/6th gr. of morphia was given as a routine treatment on the first night in hospital. Nепenthe in 20-25 minim doses was reserved for ordinary use, and in albuminuric or pulmonary cases chloral syrup in two drachm doses was frequently employed.

Morphia is also invaluable in cases where there is much pain, and especially where there is peritoneal involvement. The conservative treatment of this complication would be impracticable without the free administration of morphia in the acute stages.

Patients exhibiting mental symptoms or undue nervous excitement were a continual source of worry. Chloral and bromide mixtures, even in large doses, were frequently quite ineffective, luminal was of little value, and paraldehyde/

paraldehyde readily lost its effect if repeated at short intervals. It was therefore necessary in many cases to have recourse to morphia and hyoscine, while in the more severe forms chloroform anaesthesia was frequently the only means of control.

Tonics.

Many women presented severe degrees of anaemia. Puerperal anaemia has a double origin in haemorrhage and sepsis, and although secondary in type, frequently assumes pernicious features. Liver - either fresh or in extract form - was occasionally of benefit; while others improved rapidly after hypodermic injections of iron solutions - Cacodylate of Iron with Strychnine being a preparation which appeared to have some value. Organic preparations of arsenic were also used in a few cases with good results. Oral administration of iron salts with or without small quantities of arsenic appeared equally as effective as any of the hypodermic methods; but in practice these tonic substances were of most use in the absence of definite anaemia, and frequently patients suffering from marked degrees of anaemia showed so little response to treatment that they were eventually dismissed from hospital in an almost chlorotic state.

Specific general remedies are of three main types:-

- I. Those which aim at killing the causative organisms or neutralizing their toxins, e.g., quinine, anti-toxic serum, arsenical preparations, and mercurochrome;
- II. A second group designed to raise the resistance of the/

the body against infection, e.g., vaccines, and vitamins.

III. Lastly, a group of substances which have a diluting effect on the infection, e.g., salines.

In the present investigation all of these were tested, with the exception of vaccines; and they will now come under review in the following sequence:-

1. QUININE.
2. SERUM.
3. ARSENIC.
4. MERCUROCHROME.
5. SALINES.
6. VITAMINES.

1. QUININE.

This drug has long enjoyed much repute as a uterine stimulant and as a general antiseptic to the blood and tissues. It has an undoubted value in Malaria and other protozoal infections, where it appears to exercise a definite antiseptic effect on the blood stream; and for many years it has been used extensively both as a prophylactic and a cure for Puerperal Sepsis. Alone or in combination with ergot it forms the main bulwark of the conservative treatment, and for this purpose is given orally in doses of 10-15 grains at intervals of four hours during the febrile period. If, as frequently happens, the temperature is for days or weeks unsettled, signs of poisoning may be manifest, and administration of the drug must be discontinued.

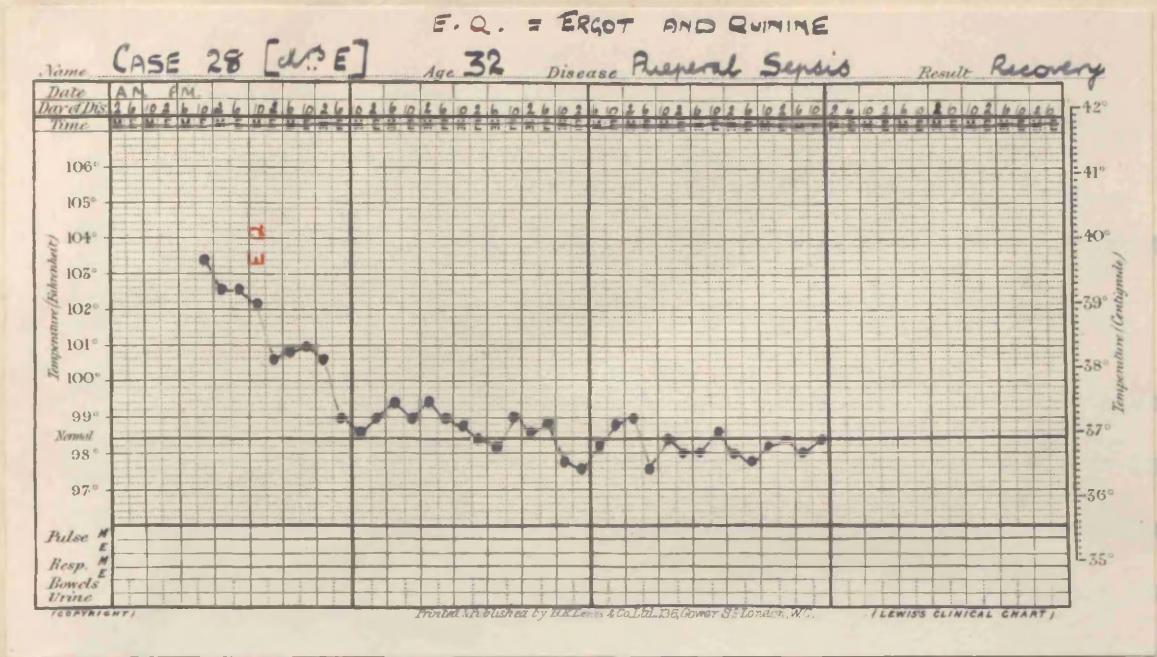
Quinine/

Quinine is also available for intramuscular or subcutaneous injection, the bi-hydrochloride being usually employed. In the present series this route was avoided. Experience of its action was, however, provided by three patients so treated in other hospitals and admitted still febrile and ill, days or weeks later. Two of these presented deep sloughing indurated sores at the site of injection, and the third complained for several months of agonizing pain resulting from dosage with this drug. This was not a hysterical phenomenon, as the same woman later received five other intramuscular injections without complaint.

This phase of the investigation deals with 75 patients who received Ergot and Quinine as their only specific treatment, and the following observations may be made with regard to its results.

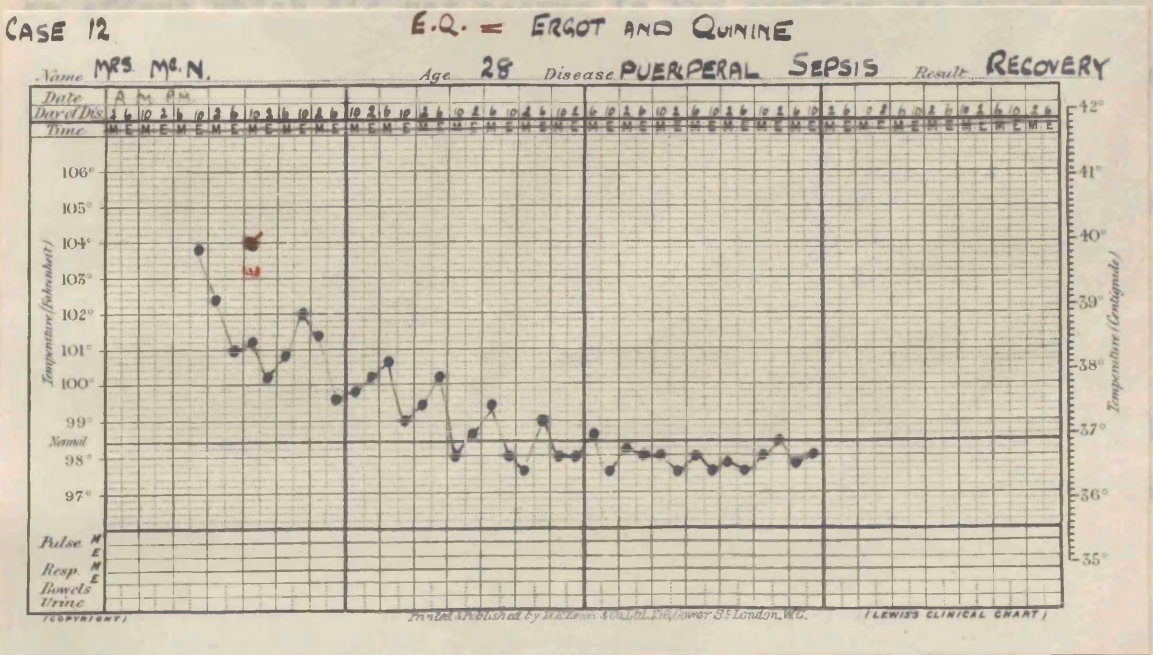
(1) Sometimes in mild cases there is an apparent fall in temperature after quinine has been taken, but in almost every instance this improvement can be traced to other more likely causes. Case 28 was of this type. This woman was admitted febrile and moderately ill. In the theatre the following day the uterus was found to be retroflexed and obstructed by reason of a distended bladder. When this condition was relieved and drainage established the temperature gradually subsided. Ergot and Quinine were administered from the day after admission, but it seemed that their exhibition merely coincided with the improvement in the local and general condition. The accompanying chart illustrates also that her temperature was practically normal before the drugs could have exercised any real effect.

Figure 26.



Case 12 was an example of mild septic endometritis treated also by this means. The uterus was in good position and there was no other obstruction to drainage; and her temperature chart figure²⁷ reveals a gradual subsidence by lysis which may have been due to the ergot and quinine, but which is also typical of drainage alone.

Figure 27.



(2) In cases of established sepsis quinine appears to have little value even when given in toxic doses. It was difficult to pursue this test very far since, when it was apparent that the drugs were having no effect, that, in fact, the patient was becoming steadily more ill in spite of them, remedies of more established value were quickly prescribed.

Reference/

Reference will be made later, however, to a patient who developed fatal Septicaemia although she appeared only moderately ill on admission, and received ergot and quinine from the outset.

(3) The profundity of established puerperal toxæmia makes it almost impossible that quinine could ever have any real value as a method of general treatment. Prophylactically it may be of some use; yet it is difficult to reconcile such an action with the frequent occurrence of Post Abortum Sepsis in patients who have admittedly been swallowing large quantities of the drug, and whose blood might conceivably be saturated with it. Most medical men prescribe quinine on the first onset of temperature following a confinement, and cases admitted to hospital are presumably those who have not benefited from this treatment. It seems unlikely, therefore, that further dosage, once sepsis has become established, can have an effect which did not accrue in the earlier stages of the illness. If given before or at the onset of a rigor, quinine does not prevent it; but it may have a slight inhibitory action, and this appears to be its chief value in this group of cases.

(4) Although it is generally believed that quinine stimulates uterine contractions and may thus produce drainage and promote involution, it is difficult to understand how the drug can have any real effect on a uterus whose musculature is saturated with toxins, and more so if in addition the cervix is also mechanically obstructed as the result of malposition or placental debris.

It may be concluded, therefore, that in established sepsis any good effects obtained by the use of this drug may in most cases be ascribed to the concomitant treatment, whether this be specific or non-specific, or merely hospitalization.

The/

The mental effects of all forms of oral medicine are, of course, important, and for this reason quinine may be employed as the sole treatment in the mildest forms of the disease. But in definitely septic cases its therapeutic value cannot be other than minimal.

2. SERUM ADMINISTRATION

Specific sera are utilized for their antitoxic and anti-bacterial effects. The striking and far-reaching results obtained by the exhibition of antitoxic serum in Diphtheria have resulted in the advocacy of a similar mode of treatment in many allied conditions, and serum treatment of Scarlet Fever, Erysipelas, and of Plague, has thus become everyday knowledge. It is believed that if the patient be provided with antibodies in this way, these will neutralize the general infection, or at least reduce it to such a level as to make it a negligible factor. Not only so, but the antibodies in the circulating blood and lymph will come into contact with the micro-organisms and toxins at the seat of disease, and will have a curative effect on the local lesion. Thus with a diminished or absent toxæmia and a less virulent focus of infection, the patient may himself combat successfully the remainder of the disease.

Theoretically, if serum is to be effective it must contain antibodies in respect of the organism with which the patient is infected. Most of the severe cases of Puerperal Sepsis result from infection with a hæmolytic streptococcus. Scarlet Fever, Erysipelas, and various pyogenic conditions are caused by a similar organism; but recent research has failed to discover any method, serological or otherwise, by which the hæmolytic streptococci may be grouped into varieties/

varieties causing any of the above types of disease. It appears, in fact, that Scarlet Fever itself may be caused by a variety of haemolytic streptococci, and that Puerperal Fever may occasionally be the result of infection by the same organisms.

Working with Scarlet Fever, Erysipelas, and Puerperal Fever toxins, and with convalescent sera and antitoxins, Ferry and Fisher⁽⁷¹⁾ found that in low dilutions of the serum there was more or less cross neutralization of the toxin by the serum; but that in high dilutions the sera neutralized only their homologous toxins. If these results are to be accepted, it is evident that to get the fullest advantage from antitoxic treatment the special antitoxin should be employed. Smith,⁽⁷²⁾ on the contrary, maintains that in streptococcal infections an antitoxic serum, whether prepared for Scarlet Fever, Erysipelas, or Puerperal Fever strains, will help to combat the exotoxic action of either of these organisms. That is to say, the exotoxins will be neutralized by any monovalent antitoxin. In this the haemolytic streptococci are considered as analogous to the diphtheritic group of organisms, since here also an antitoxin specific for one variety will have a direct counter effect on the exotoxins of all the others in the group.

Probably neither view is quite the correct one. There is no clinical support for the theory that "any monovalent antitoxin" will be of use. Scarlet fever antitoxin in most cases neutralizes (wholly or partially) puerperal fever toxin, because the haemolytic streptococci producing these diseases are very closely allied, and may indeed be occasionally identical. But erysipelas antitoxin is not so related. The true explanation of the value of Scarletinal antitoxin in allied conditions lies in the fact that the causative streptococcus—more than all other varieties—stimulates/

stimulates the formation of antibodies. The curative serum is thus very potent. Streptococci obtained from Erysipelas or Puerperal Fever patients have, on the contrary, very little power to cause antibody formation, and consequently the serum is a poor antitoxic agent. Serum produced from scarlet fever streptococci, therefore, although not absolutely specific or homologous, may be more effective than a Puerperal Fever serum which is specific and homologous, but which is poor in antibodies. If, however, the puerperal infection is due to a Scarlet Fever streptococcus, the antiserum is absolutely specific against it.

Many other factors are at work, and it is not only a matter of subtraction or neutralization - no organic process is so simple. The avidity of toxin for antitoxin probably plays an important part in determining serum effect, and there are many factors which might produce variations in this.

To be of perfect value, however, serum must also be antibacterial. Smith⁽⁷²⁾ has shown that antitoxic serum, however potent it may be in neutralizing toxins, has little value in eradicating the organisms once tissue invasion has occurred, and that for this purpose a type (serological) of specific, antibacterial serum will be required. It has been claimed that Scarletinal antitoxic serum has also this antibacterial property. This will, however, be in respect only of the homologous organism; and only in patients definitely infected with the Scarlet Fever type of streptococcus can any clinical manifestations of such an action be expected. Recent research,⁽⁷³⁾ however, has shown that serum in no way increases the bacteriocidal powers of the blood, even against such organisms.

Apart from the serum prepared against the Erysipelas streptococcus, there are available three types of anti-streptococcal/

anti-streptococcal serum - Puerperal, Multivalent Streptococcal, and Scarletinal - and all three have been advocated as specific general remedies in the treatment of Puerperal Fever. In the present investigation 395 patients received serum. Of these 40 were given the puerperal and multivalent types, but the results obtained were disappointing except in occasional cases of no great severity. The Scarletinal antiserum was for the above reasons selected for use in this experimental inquiry, and may be discussed under the following headings:-

- (1) Technique and Dosage.
- (2) Prophylactic Effect.
- (3) Antitoxic Effect.
- (4) Antibacterial Effect.
- (5) Serum Anaphylaxis.

(1) Technique and Dosage.

Serum may be given subcutaneously, intramuscularly, or intravenously. The first of these, the subcutaneous, has the obvious disadvantages of being more slowly absorbed, more painful in administration, and further, more liable to become, at a later date, the seat of abscess formation than either of the other routes. The intramuscular method, on the other hand, does not present these disadvantages, and has been chosen, therefore, for routine use. Here the serum is injected into the buttock or into the external muscles of the thigh, strict aseptic precautions being observed during this procedure, and the area massaged lightly thereafter to facilitate absorption. When given in this way the serum enters the blood stream slowly, and it is about 4-6 hours before it is in sufficient concentration to produce any/

any noticeable clinical effects.

The intravenous route, therefore, becomes more rational when dealing with cases of great toxæmia or with frank septicaemia where rapidity of effect is desirable. For this purpose the median basilic or other arm veins are usually available, although some difficulty may be experienced in the case of collapsed or very obese patients. In this latter group of cases one of the larger veins in the leg is usually available.

Dosage.

Much controversy has raged round this question. Some observers claim that if serum is to have any effect it must be given in very large doses, although all do not go so far as Hamm⁽⁷⁴⁾ who declares that an adequate dose of serum cannot be less than half a litre. The daily administration of 100-200 c.c. is recommended by many, while there are others of opposing views who claim that two unit doses - 20 c.c. - are quite sufficient not only to neutralize the toxins of the blood, but to provide the patient with sufficient antitoxin for protection against further inoculation from the infective focus.

With regard to dosage, it must be realized at the outset that there are three separate objectives in serum administration. There is first of all the prophylactic use recommended for non-septic cases, and for the patients of Group I who shew little evidence of streptococcal toxæmia. For this purpose 10-20 c.c. will be sufficient. The second objective aims at combating toxæmia in the severe and moderately ill cases where the infection is still local and blood culture negative; that is, in Group II and Group III infections. In these cases the effect is purely antitoxic, and is directed against the circulating toxins which have been/

been absorbed from the local lesion. For this purpose 20 c.c. may be given initially, and subsequent dosage regulated by the original response and by the clinical findings. It was found that no effect was obtained beyond a dosage of 80 c.c. in these cases, and that in many cases much less was required.

The third objective aims at utilizing the antitoxic and antibacterial powers of the serum in established Septicaemias, i.e., in Group IV cases. For this purpose 100-150 c.c. may be employed. It appeared that nothing was to be gained by dosage beyond this amount; and that if the serum was of any value its effect was, in most cases, obtained with much smaller quantities.

Since all puerperal infections are not streptococcal in origin, it might be thought advisable to discover which type of infection is present before using serum for its curative effect. Such findings must, however, be accepted with some reservations. Most severe cases are the result of streptococcal infection, although-as previously indicated-the causative organisms frequently migrate to the deeper layers of the mucosa, and may not be detected until the lesions are healing. Thus it is unwise to place much faith in a negative finding, until repeated cultures from the cervix have failed to demonstrate this organism. Meanwhile much valuable time for treatment might be lost. It is advisable, therefore, to regard all infections as streptococcal, and at the outset treat them accordingly.

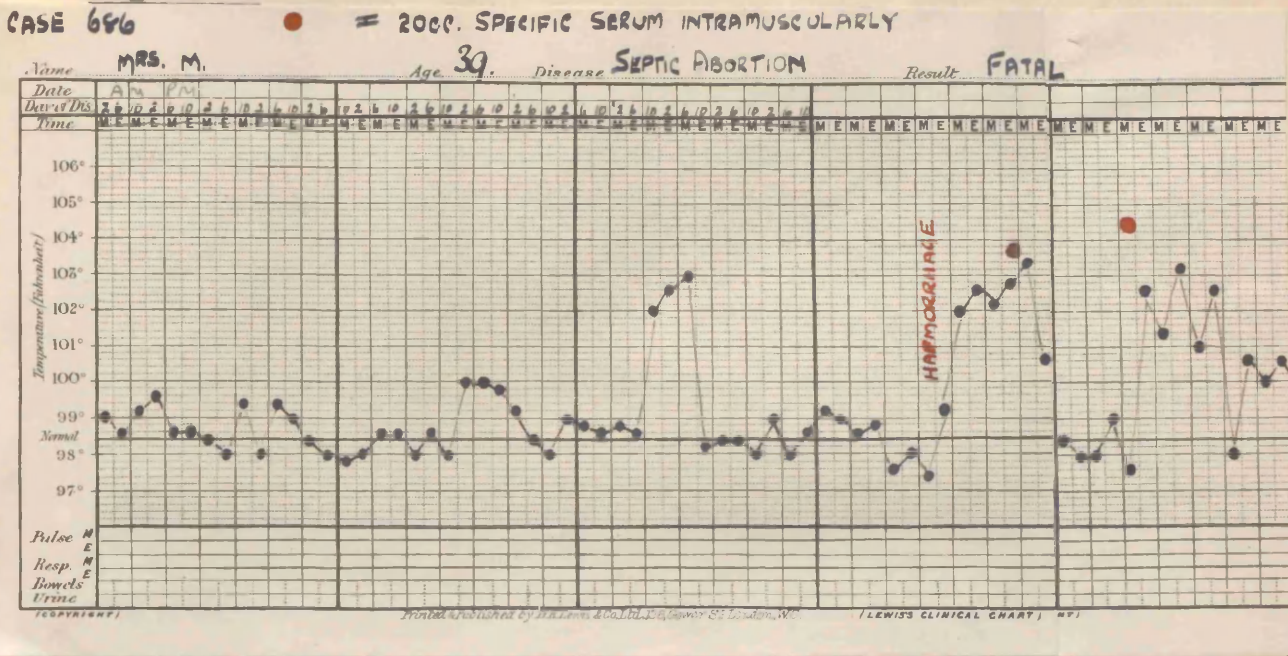
Prophylactic Effect of Serum.

Undoubtedly there is a wide and useful field for serum in this connection. Non-septic cases, if protected in this way, may be safely treated in puerperal fever wards without sepsis arising, and the value of a prophylactic dose of serum in such cases cannot be over-estimated. A few women/

women - notably cases of incomplete or threatened abortion - were from time to time admitted, and on examination no indications of sepsis were found. These were protected with serum. Similarly, any mildly septic cases requiring intra-uterine manipulation, if given a prophylactic dose of serum, remained free of complications; whereas in a few women-not so protected-signs of awakened infection became evident.

Case 686 showed this unfortunate effect. This woman was admitted as complete septic abortion, and appeared very moderately ill. Streptococci were cultured from the cervix, but no serum was given, and she continued subfebrile for about a week. At the end of this time there was a brisk uterine haemorrhage which necessitated immediate intra-uterine interference; and on the following day there was a long rigor followed by sharp elevation of temperature. 20 c.c. of serum were given at this juncture, and the temperature fell to normal again. Two days later, however, the temperature again rose; and on this occasion the serum produced little or no effect. Thereafter the temperature was remittent and unaffected by any treatment, and clinical and bacteriological signs of streptococcal septicaemia were soon manifest. This patient died. There is no doubt that her septicaemia resulted from an intra-uterine infection which was spread on the occasion of the haemorrhage which made digital interference necessary. A prophylactic dose of serum on admission, or at the date of the haemorrhage, might have saved her from the later toxæmia and septicaemia, if the marked benefit which resulted from the first dose be taken as any indication of the type of her infection.

Figure 28.



action on the local lesion. There are few instances where it is possible to measure such local benefit, but the general bodily effect may be reasonably gauged by reference to the following factors:-

Temperature. There may be crisis or rapid lysis after serum injection, an occurrence which is unusual in untreated cases.

Pulse. A fall in pulse rate, or increase in its quality, may be noted. That is to say, the pulse becomes slow and full in contrast to the rapid, thin pulse of a streptococcal toxæmia.

Facies. There is not infrequently a disappearance of labial tremor, and of the sunken ashen expression typical of toxæmia. The mucosæ become a healthy pink, and the characteristic listlessness is replaced by an appearance of alertness.

Skin. There is also a noteworthy change in the character of the skin, which instead of being hot and fiery becomes cool and moist.

Other Signs. Disappearance of sickness and of tremor of limbs; and return of appetite, may occur pari passu with the above changes. It is of importance that patients who benefit frequently will state voluntarily that they "feel quite different," and may occasionally time the onset of this betterment within a few hours of the serum injection. These signs of benefit may indeed be complete within 8-12 hours of the treatment, although the first indications of improvement may be noted much earlier than this.

In Groups II and III, 260 women received serum for its antitoxic effect. The injection was intramuscular in the majority of cases, but in a few very toxic patients the intravenous/

intravenous method was employed. Three types of reaction were noted:-

Type 1. Rapid, definite, and permanent improvement.

Type 2. Indefinite improvement, gradual, sometimes questionable.

Type 3. No obvious reaction.

Type 1. A small series of patients benefited remarkably from the administration of specific serum. In all of these there was marked toxæmia; but while each had definite uterine sepsis, in none was para-uterine infection far advanced. All were cases of Streptococcal infection.

The almost immediate benefit which resulted in these patients cannot adequately be described. Case 730 was of this type. This woman had been ill for a week before admission, and presented a septicaemic appearance. The uterus was enlarged and tender, but there was no gross pelvic sepsis. An hour after admission a blood culture was made and 30 c.c. of serum injected intravenously. As her chart shows (Figure 29) she was afebrile within 4 hours. Her pulse was by this time full and firm, sickness and tremor had ceased, and she was quite altered in appearance. The blood culture proved negative, and doubtless the case was one of powerful toxæmia rather than septicaemia.

CASE 730 ○ = 30 cc. SPECIFIC SERUM WITH SALINE INTRAVENOUSLY
 Name M.S.C. Age 29. Disease PUERPERAL SEPSIS Result RECOVERY

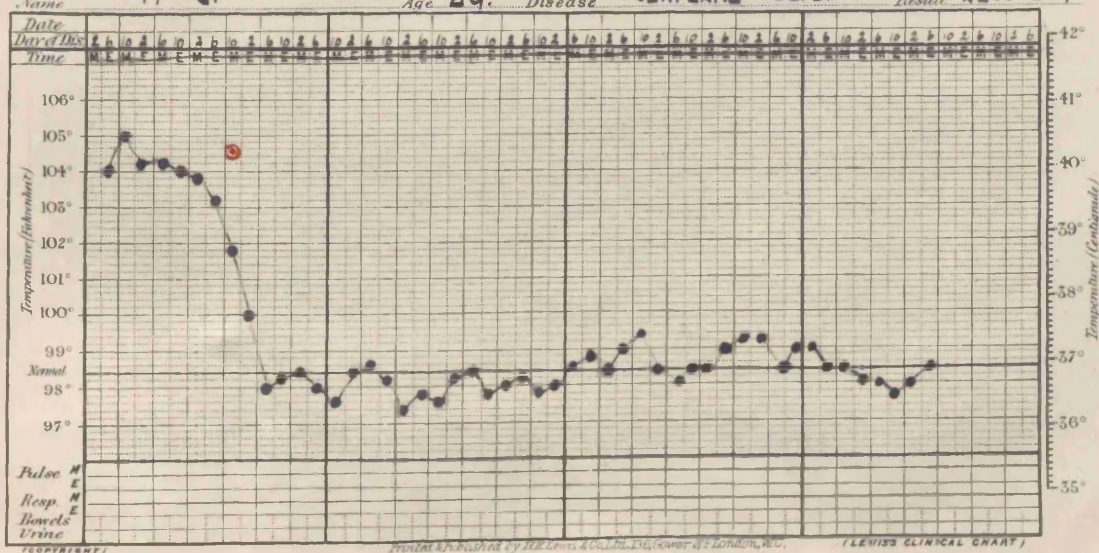
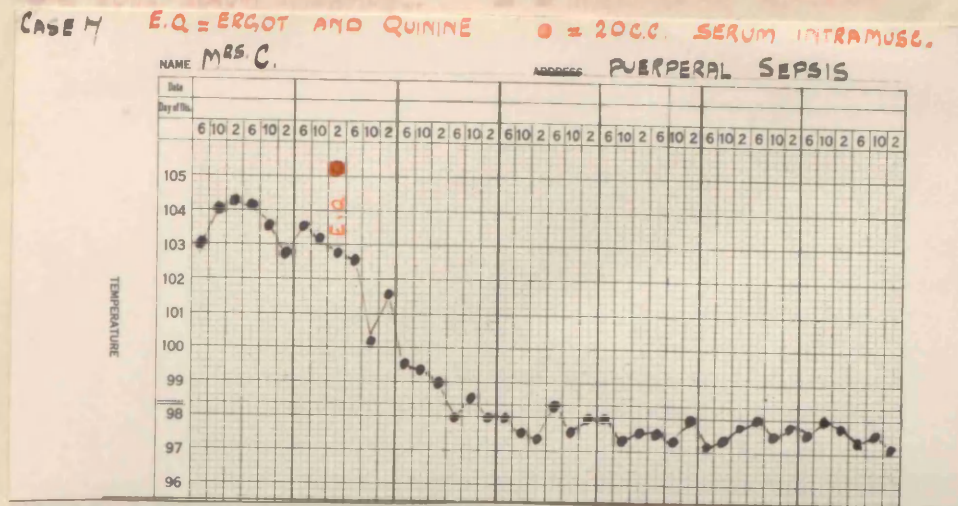


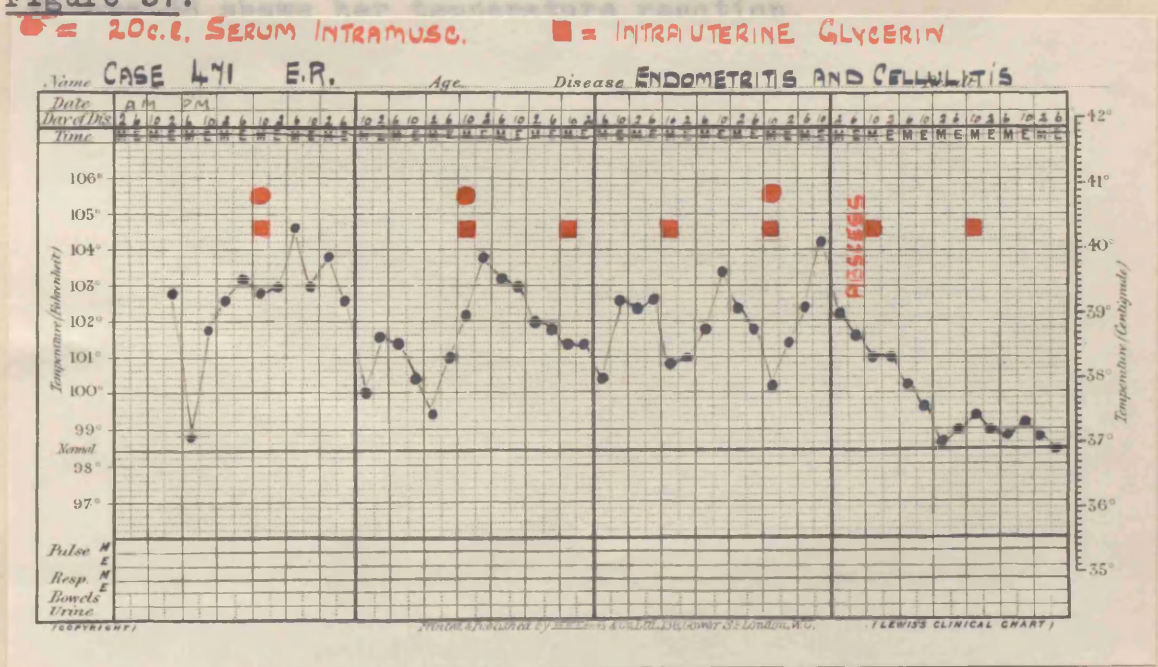
Figure 34.



It might be suggested that several of the above mentioned patients really benefited from hospitalization, and that the rapid improvement in their condition was not due to the serum which they received. Such a possibility is admissible, but may be discounted in these cases, since the women were too acutely ill to improve so suddenly and permanently merely as the result of hospital regime, and in a few instances had been in the ward for at least one day prior to the initiation of the specific treatment. It is extremely unlikely, however, that hospitalization was responsible for the results obtained in Case 342. This woman had typical Group II lesions with an additional marked toxæmia, and was highly febrile from admission. Daily glycerin injections were given, but the temperature steadily mounted and the general condition deteriorated; and on the third day 20 c.c. of serum were injected. This did not result in much fall of temperature, but the toxæmia definitely lessened; and a further similar dose was given. On this occasion the patient became rapidly afebrile, and with the exception of a very slight elevation the following day, remained permanently normal thereafter. This excellent result is shown in the figure 35

Case 471 was somewhat similar, and was again an example of profound toxæmia combined with a very extensive local infection, streptococcal in origin. Three intramuscular injections of 20 c.c. were given, and each was followed by a gradual but temporary fall in temperature. As her chart shews, however, (Figure 37) the fever was remittent in any case; and there was no corresponding clinical improvement as a result of this treatment. The toxæmia in fact persisted until several days later when a large abscess of the left buttock was incised; and the opening of this removed all general symptoms. The effect of serum on this girl was really minimal.

Figure 37.

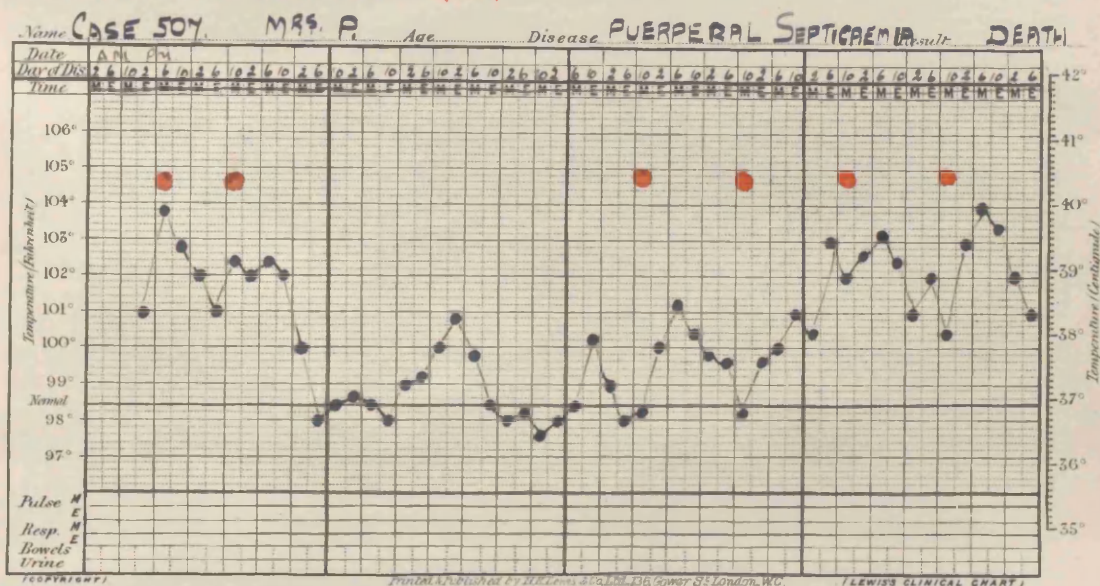


Case 507 gave interesting results. This woman was confined in her own home where there were also three other children with undiagnosed Scarlet Fever. She became fevered nine days later, and when admitted on the following day a bright punctate rash was noted. Serum was given twice within the first twenty-four hours, with good effect, and the temperature appeared to settle to subfebrile levels. Two days later, however, she again appeared ill, and very active ulcerative stomatitis developed. Further injections of serum were then made, but without effect, and signs of Septicaemia/

Septicaemia rapidly appeared. Blood culture revealed the presence of haemolytic streptococci and this patient ultimately died. If, as might be expected, this puerperal infection was due to a Scarlet Fever type of organism, it seems remarkable that, apart from the early effect, the serum was of such little avail. Her initial toxæmia was sufficiently countered, but the serum proved valueless to prevent septicaemia or to kill the organisms themselves once they had invaded the blood stream. It is possible, however, that the serum was not homologous, since, as it appeared, the original Scarlet Fever infection of her children had presented atypical features, and in no case had the rash been distinctive. Figure 38 shows her temperature reaction.

Figure 38.

● = 20c.c. SERUM INTRAMUSCULARLY



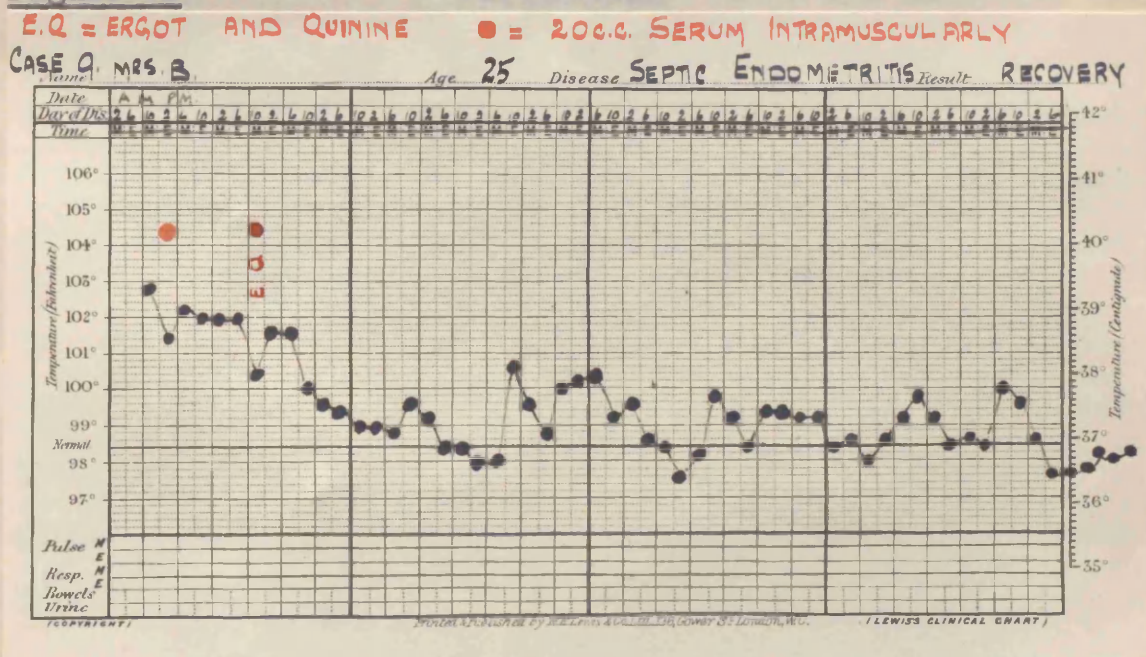
Type 3. No obvious reaction.

The majority of the cases so treated gave this unsatisfactory result. In them serum, even in large repeated doses, produced no apparent diminution in toxæmia, temperature, or pulse rate. The whole infection either progressed - sometimes to a fatal issue - or slowly recovered, either spontaneously or aided by local treatment. Some of these patients were definitely examples of streptococcal infection, but many presented/

presented mixed organisms such as streptococci, bacillus coli or pneumococci, and in these a specific antitoxic reaction was not to be expected.

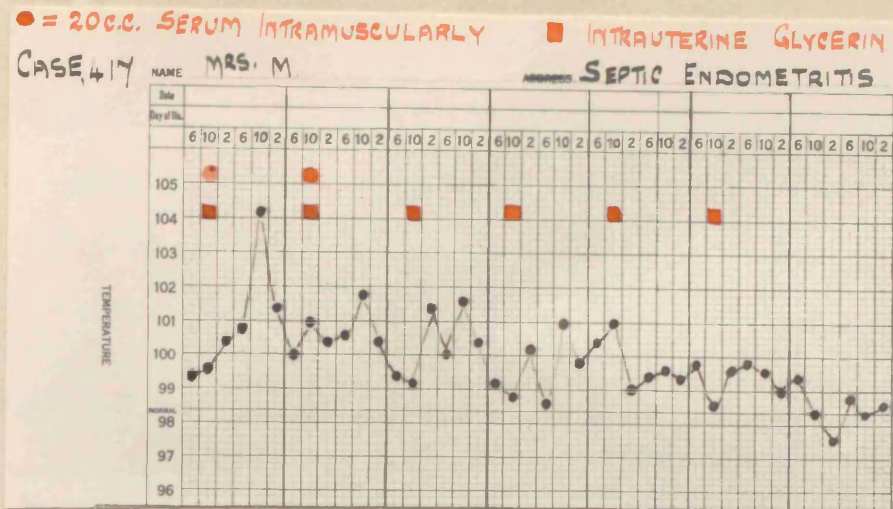
Case 9 was of the latter order. This patient looked extremely ill and had foul local lesions which were in the main due to coliform infection. Intramuscular injections of serum were given on the first and second days, without apparent effect. Uterine drainage was well established, however, and she gradually made a complete recovery, with local cleansing in bed as the only active treatment. Figure 39 shews her irregular course during the first ten days in hospital. Ergot and Quinine were also given orally in this case.

Figure 39.



Case 417 was an example of streptococcal infection showing somewhat similar lesions to the above. This patient made a gradual recovery under local treatment with glycerin, and the two injections of serum which she received at the outset were apparently valueless.

Figure 40.



Examples of this lack of effect might be multiplied.

CONCLUSIONS.

A consideration of the foregoing results would appear to lead to the following conclusions with regard to the anti-toxic value of serum in this disease.

(1) Some very toxic patients receive immediate and lasting benefit, even with moderate dosage. In this series such were all cases of Streptococcal infection, and it is possible that the serum happened to have been produced from a homologous organism.

(2) There are a few who shew slight improvement which may be temporary or permanent. In some of these, concomitant factors may be responsible, but in others the serum seemed to be the determinant. Larger dosage might probably produce the dramatic results obtained in the preceding series, although the patients do not appear more toxic or otherwise in need of this extra amount.

(3) There is a large group of patients whose general condition is in no way influenced by the exhibition of serum.

Many/

Many of these are the result of infection by streptococci, but a few give no proof of these organisms, and in these the serum has simply a prophylactic value.

(4) In the patients who benefit, serum produces a definite antitoxic reaction similar to that obtained in Diphtheria. A few writers, notably Kochler⁽⁷⁴⁾ and Bécart,⁽⁷⁶⁾ are opposed to this view. The former maintains that any effects obtained by the use of serum are simply due to the production of a leucocytosis, which could be brought about much more easily by other means. Lemel has, however, shewn recently that serum produces a leucopenia. Bécart also writes, "Serum is of no avail. It gives no palpable results, but always produces seric reactions which are sometimes very impressive, but at the least useless."

The results above recorded do not appear entirely "useless." Another writer⁽⁷⁷⁾ maintains that any examples of improvement after serum administration cannot be attributed to larger dosage or earlier administration, but only to the presence of a less grave form of infection. There is some corroboration for this statement. Dosage and early administration are important, in that a small early injection will be prophylactic rather than curative; but the results also prove that even in later cases of severe toxæmia serum is of value so long as it is or nearly approaches to "type." This is probably the real answer to the varying effects of serum administration in these toxic cases, where presumably the results should be most outstanding.

Antibacterial Effect.

The problems of Septicaemia differ markedly from those of the more simple toxic state; and the necessity for finding an adequate method of treatment for this large group of/

of infections justifies a special discussion with regard to serum and its effects on them. It will be agreed that if serum is to be of specific value at this stage of the disease it must, in the first instance, possess antibacterial power in respect of the causative organisms. In addition, it must be given in sufficient quantity not only to neutralize toxins and kill streptococci already in the blood, but to fortify it and prevent further inoculation from the active focus of infection; and on this account it should come into close association with blood and lymph in all parts of the body.

Of the 112 patients in this group, 83 received serum. In a series of 34 of these only one small intramuscular dose was given and the real treatment of the Septicaemia depended on conservative routine. Of the remainder, 12 were treated with glycerin locally, and repeated intramuscular doses of serum supplied the general remedy. The remaining 37 received serum alone, usually in repeated doses, and always by the intravenous route.

The results of a single intramuscular injection of serum in patients with established septicaemia appear absolutely nil, and need not be further discussed; while in the combined effect of glycerin and serum it is difficult to assess the true value of either factor. Cases treated by the intravenous route, and receiving no concomitant local applications, are of greatest value as a means of testing the efficacy of serum in this connection. This method of serum administration seems most rational in blood infections, and numbers Whitehouse, ⁽⁷⁾ Roulland, ⁽⁷⁷⁾ Murray, ⁽⁷⁸⁾ ~~Bolesher~~ ⁽⁷⁹⁾, and many others among its advocates. Luker, ⁽¹¹⁾ who is otherwise strongly in support of serum treatment, avoids the intravenous route, however, as being not devoid of risk; and there are many who are in agreement with this view.

The Technique employed in the present series was very simple, and the procedure occupied little more than a few minutes. The initial dose was always 20 c.c. and was injected slowly into an arm vein from an ordinary record syringe. In about half of the cases isotonic saline solution was also given, and it was found more satisfactory, and less fatiguing to the patient, to inject this very slowly from a large syringe rather than to trust to the usual method of gravity. About 140 c.c. of saline was the amount commonly used. It was sometimes found advantageous to give the patient ten grains of quinine hydrochloride and a stimulating drink immediately after the injection had been made, since occasionally rigors were mitigated by this procedure; and for the same purpose radiant heat frequently proved useful.

The first dose of intravenous serum was in almost all cases given after blood had been withdrawn for culture, and while the needle was still in place within the vein. By the following day the result of this culture was usually determined, and this, considered with the clinical condition, determined further dosage. If streptococci had been found in it, the intravenous injections were continued daily in the same amount until four or five doses had been given, when the issue of the case was usually apparent and signs of improvement noted in those who were benefiting by them. Many patients, however, improved remarkably after the first injection, and if the blood culture proved negative no further injection, or only an intramuscular dose, was given. These were examples of pure toxæmia, and it is patients of this type who are responsible for most of the dramatic results obtained by intravenous serum medication. They have been relegated to the previous groups and already considered.

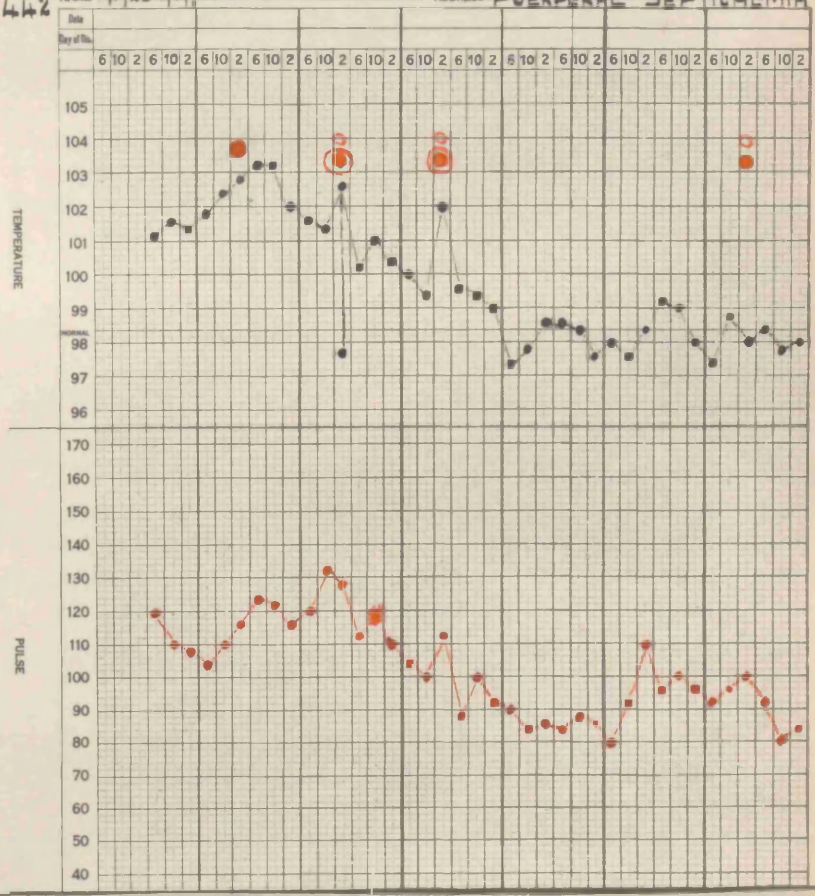
Response to Treatment.

The effect of serum when given in this way was almost constant, occurring in all but absolutely moribund patients. At varying intervals after the injection - sometimes almost immediately, and at others two or three hours later - a severe rigor usually developed. This has been attributed by some writers to the setting free of endotoxins from the circulating bacteria, as a result of the bactericidal action of the serum on them. Others maintain that the rigor is a form of protein shock, since serum contains so much foreign material and since a similar reaction follows the injection of normal horse serum which has not any such specific properties. This is the opinion held by Burt-White⁽⁸⁰⁾ and his colleagues. Probably the latter view is the correct one, in as much as rigors always occurred in cases which proved to be simple toxæmias without circulating bacteria from which endotoxins could be freed; whereas patients who were very ill, and whose blood yielded abundant streptococci, frequently failed to shew this reaction. Non-development of a rigor proved, in fact, to be rather an ominous feature of prognosis. It should be noted, however, that the degree of reaction diminished with each subsequent injection, and on the fourth or fifth occasion little rigor might occur.

During such a reaction the temperature rose - frequently to hyperpyrexial levels, - and remained elevated for three or four hours. At this stage the patient looked and felt ill. The pulse became rapid and feeble, faintness and sickness were complained of, perspiration was profuse, dyspnoea insistent, and a clammy cyanosed appearance developed. In favourable cases this was followed by rapid subsidence of temperature to normal or subnormal levels, and the pulse became correspondingly slower and fuller. At this stage the patient/

although the bacterial part was still present - if not active. In a few of these, if further serum was administered, a permanent result was obtained. This is shown by Case 442 who was given 20 c.c. of serum intramuscularly, on admission, without apparent effect. On the following day blood culture was taken and a similar dose given intravenously, this being followed by pseudo-crisis and by marked improvement in the general condition. After 24 hours, however, the temperature was again high, although - as her chart reveals - her pulse was still less frequent. Blood culture had by this time proved positive, so a further injection was given, on this occasion with permanent results. No complications developed, and the patient was dismissed from hospital well, within 38 days of her admission.

Figure 42. ● = 20cc. SERUM INTRAMUSC. ○ = 20cc. SERUM INTRAVENOUS. ○ = SALINE
 NAME Mrs. M. ADDRESS PUERPERAL SEPTICAEMIA
 CASE 442



Case 688 provided like results. Two intravenous injections were here given without permanent effect, although toxæmia definitely diminished. After a third dose, however, the temperature subsided by rapid lysis, the pulse became slow/

but gradual improvement. Severe rigors followed the first two injections, although later doses produced little of this effect. In this case Phlegmasia Alba Dolens developed a few days after cessation of treatment.

Figure 45.

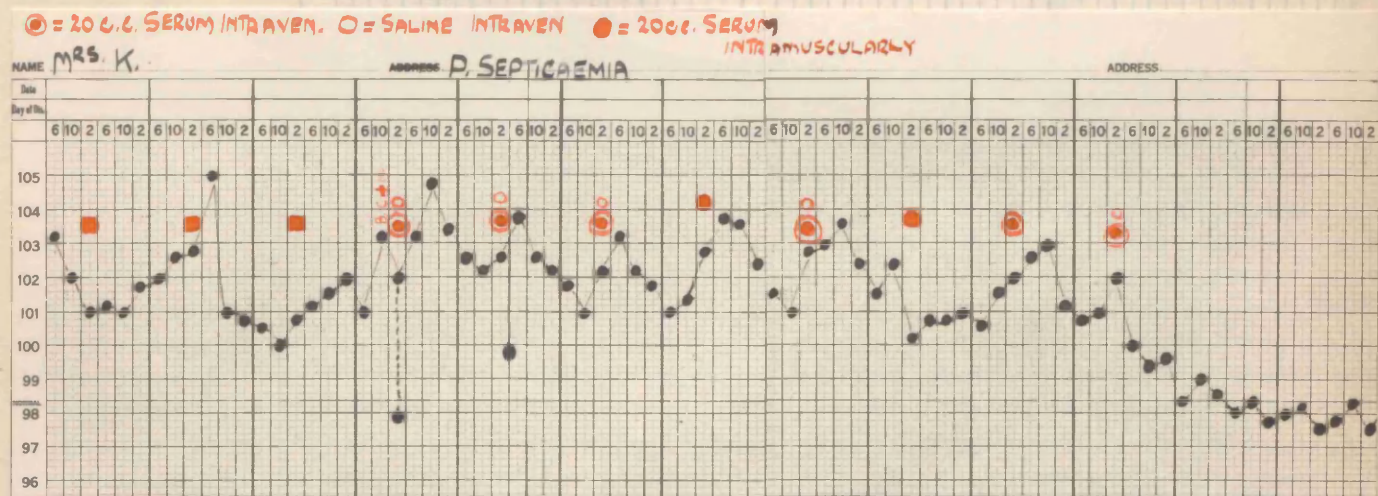
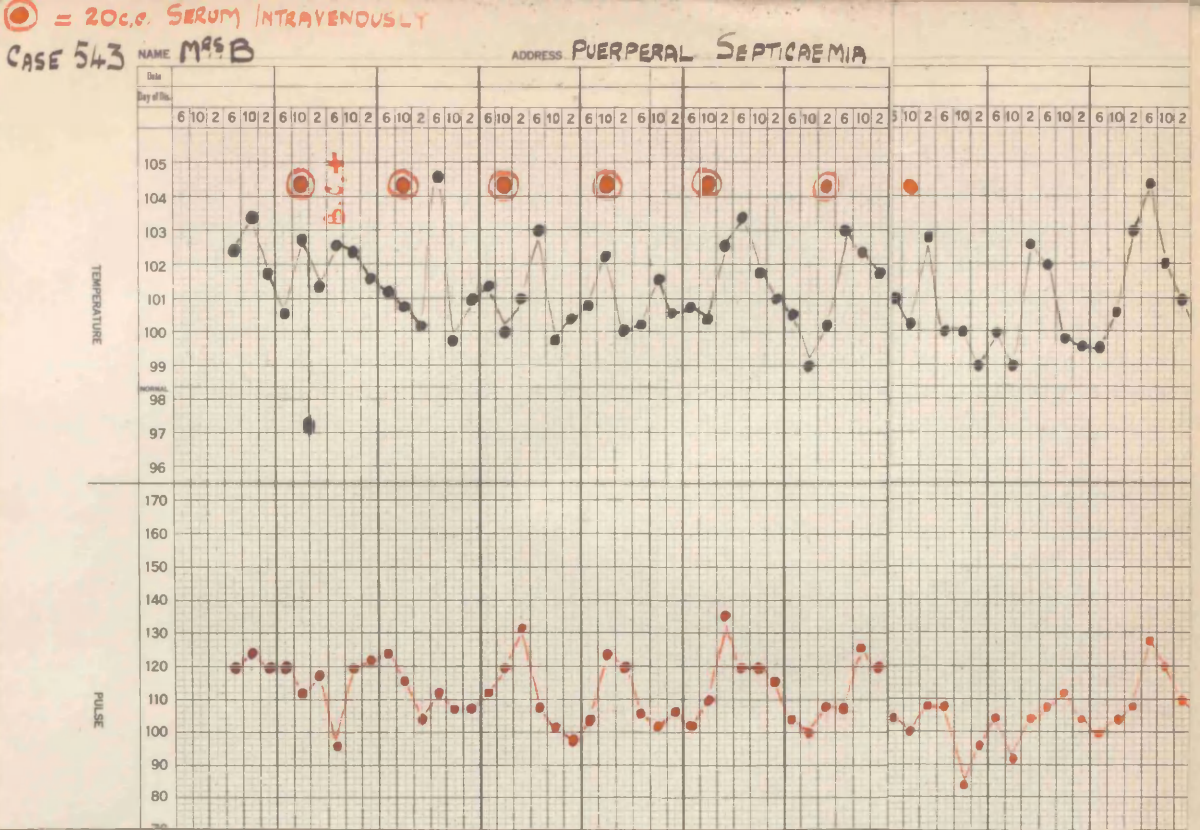
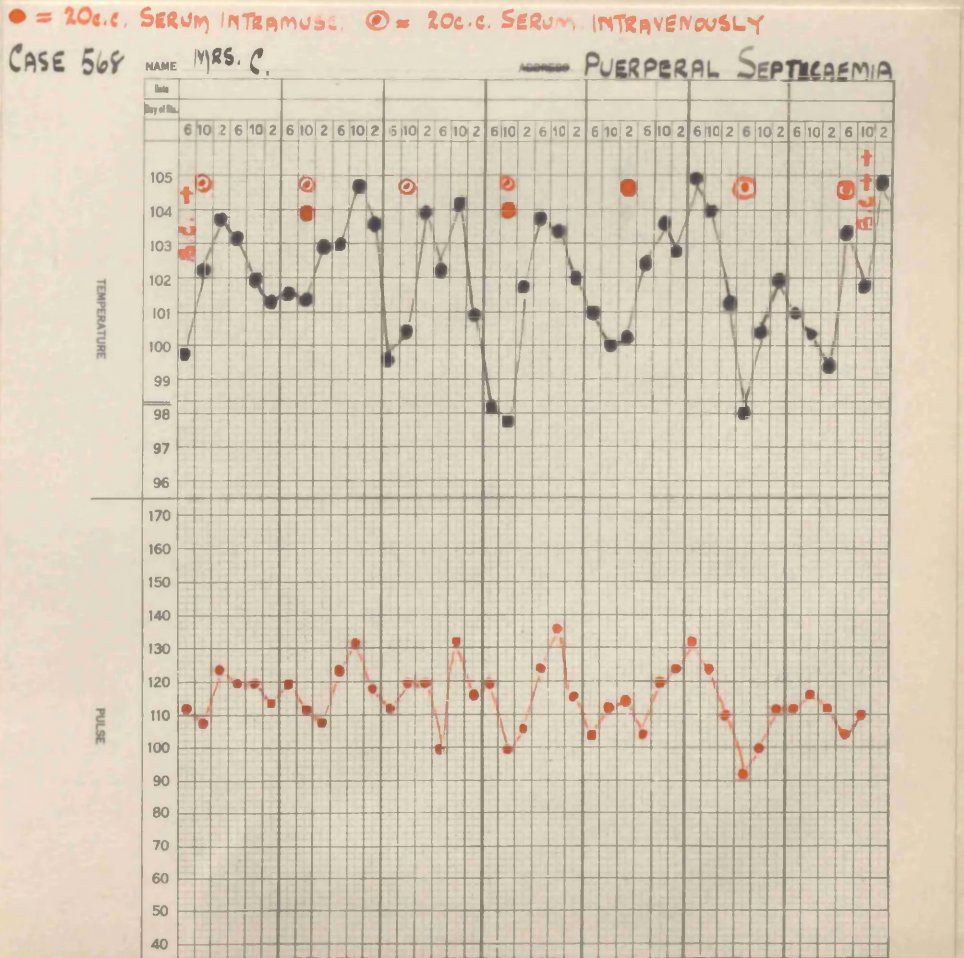


Figure 46.



few hours Case 568 was similar in many respects. This woman improved slightly after her first dose of serum, but neither temperature nor pulse took part in this effect. With repeated injections no general improvement was noted. The temperature became remittent, rigors were frequent, and blood culture became even more strongly positive than at the outset. As her chart shews, intramuscular injections were also given, so that the total dosage was almost 200 c.c.; yet she became gradually more and more septicaemic.

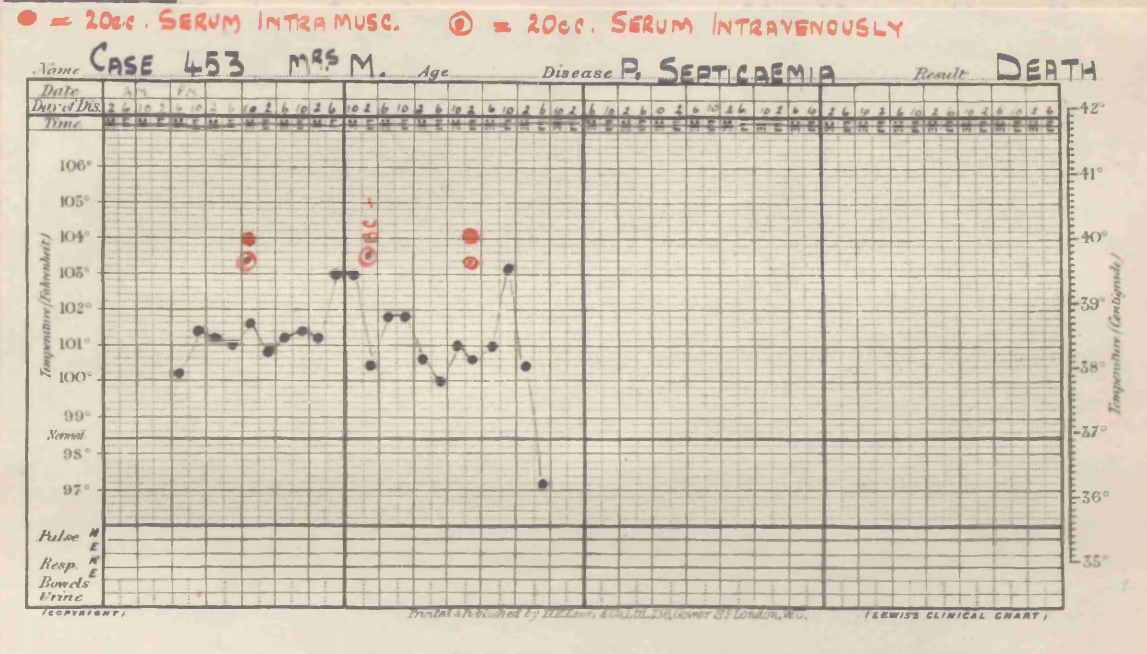
Figure 47.



CONCLUSIONS.

Case 453 illustrates the same lack of reaction, terminating in a fatal issue. There were no rigors in this case, no diminution of general symptoms, and absolutely no indication that any curative agent had entered the blood stream. Various writers lay stress on different aspects of the subject. Some claim that protein shock is responsible

Figure 49.



Many patients of this variety could be cited. These women were usually moribund when treatment was initiated and little effect was expected; but in a few a more hopeful outlook seemed justified, and the results were at the least disappointing.

Group IV patients treated by intravenous injections of serum may thus be classified into two main categories:-

I. A minority who benefited

- (1) (a) immediately and permanently.
- (b) immediately and partially, but gradually increased on repeated dosage.
- (2) (c) indefinitely; probably to a slight initial extent, but rapidly lost thereafter.

II. A majority who received no benefit.

CONCLUSIONS.

The interpretation of these results of serum administration in Puerperal Septicaemia is a matter of some difficulty. Various writers lay stress on different aspects of the subject. Some claim that protein shock is responsible for the effects of intravenous serum medication, rather than the neutralizing action of specific protective substances; and it is difficult to disprove such a theory, although the definite antitoxic effects obtained by intramuscular injection in less severe cases make the explanation an unlikely one. Bailey,⁽⁸¹⁾ in his analysis of 14 serum treated cases, states that parametritis developed and tended to localize the infection; but his charts do not adequately support his views, and Brodhead,⁽⁸²⁾ criticizing Bailey's results, sees no proof that the serum was of any value. The present investigation includes several women who did improve markedly, concurrently with the appearance of an extra uterine focus; but in no case was there any evidence that this localization resulted from serum administration. Finally, mention may be made of Burt White⁽⁸⁰⁾ who recently, after treating several cases - some with eminent success - comes to the conclusion that strong doubts must exist as to the specific action of serum on these patients.

The effects of serum in the cases under review appear to lead to the following conclusions:-

(1) Serum prepared against the Scarlet Fever type of streptococcus is not definitely bactericidal.

(2) This serum is antitoxic in a high degree to certain varieties of streptococcus. Its effect is entirely antitoxic, and the degree of this effect depends on whether the infection is by a scarlet fever type of organism or by one closely allied to it.

(3) In Septicaemia if the toxaemia is neutralized the patient becomes more able to deal with the bacterial part of her blood infection, and occasionally she is successful in this.

(4) The intravenous route, by flooding the whole system with antitoxin, gives a more rapid and fuller effect than the uncertain intramuscular method, where the serum is slowly absorbed and is rarely present in the blood in sufficient concentration to render the patient free of toxin. The sudden complete freedom from toxaemia produced by intravenous medication may allow the patient's own antibacterial reserves to come into action and inhibit, if not kill, the invaders.

(5) In many cases, however, although toxaemia is neutralized, bacteraemia persists and proves fatal.

(6) Probably in most instances the absence of effect is due to the fact that infection is not by a homologous organism, and the serum has therefore little or no antitoxic value for the patient who receives it.

Serum Anaphylaxis.

The cause of this phenomenon is still controversial. Anaphylaxis is, however, a factor of much importance in all types of serum treatment, and it is of special interest where the intravenous route is employed, or where repeated doses are given. This investigation, therefore, afforded excellent opportunities of studying its occurrence.

It is an established fact that the "incubation period" of anaphylaxis is roughly ten days, and that a serum injection may be repeated with complete safety, so long as a greater interval than this has not elapsed since the first dose was given. In a series of injections, therefore/

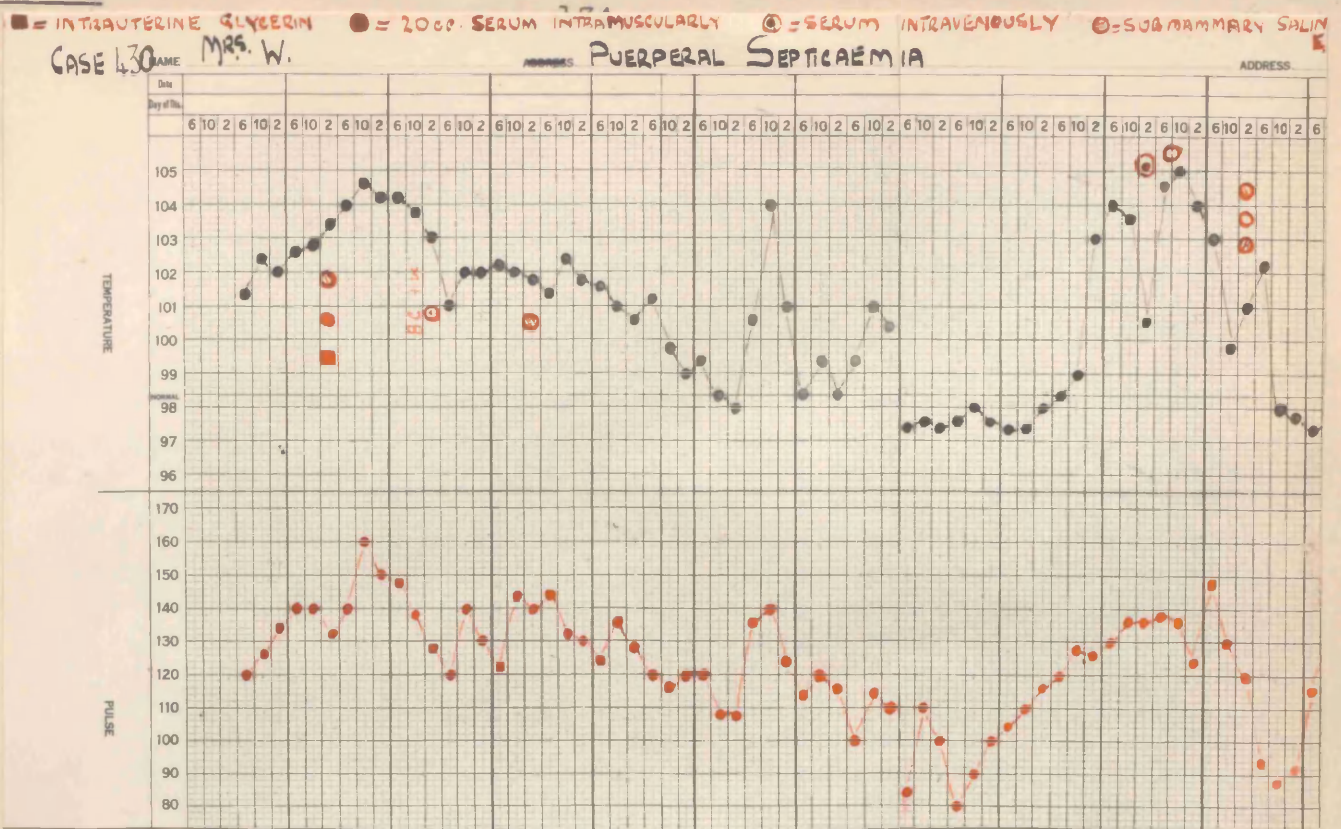
therefore, the date of the initial dose must be carefully kept in mind.

A few patients of the series developed serum sensitiveness. This became apparent on, or soon after, the tenth day; and was indicated by an urticarial rash, elevation of temperature and pulse, and such general symptoms as sickness, headache, and joint pains. Had an additional injection of serum been given at this stage, severe anaphylaxis would have resulted; and in a few instances such signs of sensitiveness did not develop until provoked by further dosage. Each injection was liable to produce its own sensitiveness, and there were a few patients who developed the above symptoms at regular intervals after each dose of their series. It has been claimed that the injection of a fair sized second dose of serum during the incubation period results in the production of a condition of anti-anaphylaxis, which again persists for an indefinite period; but such a statement has found no support in fact, in so far as the present investigation is concerned.

Martin,⁽⁸³⁾ among others, has suggested that grave anaphylaxis, comparable to that found in guinea pigs, never occurs in man. Definite and alarming symptoms occurred, however, in three cases, and in these followed administration by the intravenous route. Two of these had inadvertently received an additional dose of serum on the tenth day after their primary injection; but in the third case no previous serum had been given, and the patient appeared to have been naturally sensitive. In the second patient signs of anaphylaxis developed after only a few drops of serum had entered the circulation, but in the others the injection had been almost completed before symptoms occurred.

The first complaint was of dimness of vision and a "queer feeling," and this was rapidly followed by great dyspnoea/

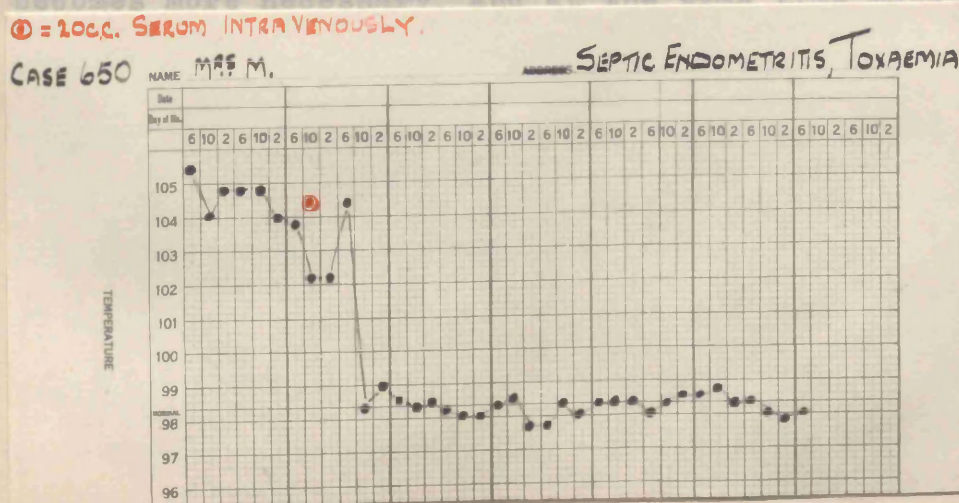
dyspnoea and cyanosis. At the same time the body became rigidly fixed by spasm, and teeth and hands clenched, the limbs extended, and the trunk arched. The pulse was at this stage imperceptible. This condition remained for about two or three minutes, and thereafter rapid recovery ensued. In all three cases, as the spasm relaxed, involuntary evacuation of bowel and bladder was noted, and violent retching with sickness supervened. Each appeared extremely collapsed and almost moribund for several hours, and in all severe repeated rigors occurred; but it is interesting to note that the ultimate recovery was excellent, and in the first patient it seemed extraordinary. This was Case 430. As her chart illustrates, this patient had proved Septicaemia on admission to hospital, but reacted indefinitely to several serum injections, one of which was intravenous. On the ninth day after admission, however, she again became very ill, and indeed was pronounced moribund. Pulse was poor and rapid, temperature high, and mild mania developed. The additional dose was then given, and before the needle had been withdrawn the violent reaction developed as above described. This injection was followed by great diminution of pulse rate and by complete disappearance of the general symptoms; and although the temperature again became elevated, there was no recurrence of the tremendous toxæmia present before the serum had been given. Her chart (Figure 50) does not adequately shew the great clinical improvement which resulted in this case.



The second patient (Case 405) also derived very definite general improvement, although temperature and pulse remained unsettled for some days thereafter.

The third patient, however, (Case 650) provided perhaps the most outstanding results. This woman when admitted appeared septicaemic, and on the following day blood culture was made and serum given. Anaphylaxis became apparent immediately afterwards; and within eight hours the temperature had fallen to normal levels, pulse rate was correspondingly diminished, and general symptoms rapidly vanished. Blood culture proved negative, and there was no subsequent relapse. This woman had no previous injection of serum, and there appeared no reason for the sensitiveness which she displayed.

Figure 51.



In view of these happenings, it seems definitely advisable that no additional serum be given after an interval of nine days from the primary injection, unless some means have been taken of determining whether serum sensitiveness has developed. The simplest method of doing so is by the injection of a small quantity of serum into the subcutaneous tissue of the forearm. About 1 c.c. is sufficient for this purpose, and sensitiveness will be shown by the appearance within an hour or two of an urticarial rash, either general or localized, round the area injected; and by the occurrence, to a greater or lesser degree, of the constitutional symptoms already recorded. In the absence of such effects, the full injection may be made with complete safety, four hours being usually allowed after the test dose, before this is done. Should signs of sensitiveness occur, however, steps must be taken to desensitize the patient; and this may prove a troublesome matter.

It must be realized that the small initial dose merely indicates whether or not sensitiveness is present, and does not by any means produce complete desensitization. The usual method of doing this is to give the dose in small amounts at half-hourly intervals beginning with a minute quantity such as .25 c.c. and gradually increasing with each injection. This applies to the intramuscular route. Where intravenous use is contemplated, desensitization becomes more necessary, and at the same time more difficult. Besredka⁽⁸⁴⁾ recommends the gradual introduction of large quantities of isotonic saline solution, the first 1 c.c. to contain 0.1 c.c. of serum, the next twice as much, and so on. Thus 50 c.c. of serum would require half a litre of saline and would entail one hour's work. Tuft⁽⁸⁵⁾ suggests that an intravenous desensitization or test should be employed with 10 c.c. of saline containing 0.1 c.c. of serum/

serum in all patients who are to receive intravenous treatment; but this proved unnecessary in the present investigation. There are other writers who advocate the giving of serum liberally without precautions, since anaphylaxis is rarely fatal, and is, in almost all cases, beneficial.

It is a wise precaution to have adrenalin solution at hand ready for injection should anaphylaxis occur, since .5 to 1 c.c. of a 1/1000 solution will abolish the symptoms almost instantly.

It is fortunate, however, that the question of desensitization does not often arise. If serum treatment is having any value, it will, in most cases, be effective before this ten-day limit; and it is usually only in cases of relapse that tests for sensitiveness must be made.

3. ARSENICAL PREPARATIONS.

The treatment of septic conditions by the intramuscular or intravenous injection of arsenical compounds is not entirely recent. When it was discovered that organic arsenic could sterilise the blood in Syphilis, many workers hoped that it might be of equal value in other septicaemic conditions, not only of protozoal, but also of pyogenic origin. The first demonstration of the conferring of bactericidal power on the blood serum by drug administration was made in 1912 by Sir Almroth Wright,⁽⁸⁶⁾ using quinine derivatives. He was concerned mainly with pneumococcal infections; but Douglas and Colebrook⁽⁸⁷⁾ in 1916 demonstrated that similar results followed the use of neosalvarsan in the case of staphylococci, and under the championship of Colebrook⁽⁸⁸⁾ and his co-workers arsenical preparations have recently/

recently come into much repute, especially in the treatment of streptococcal infections. It is claimed that in nearly all patients arsenic increases the power of the blood to kill these organisms, and that in every case the bacteriostatic power of the serum is very much enhanced. Kerr⁽²⁴⁾ and Morris⁽⁶⁵⁾ are among those who support these views, while Rivière,⁽⁸⁹⁾ Delmas,⁽⁹⁰⁾ and Pery⁽⁹¹⁾ also write enthusiastic reports of the curative and prophylactic value of this chemical.

The disadvantage of most arsenical compounds is that they are extremely irritant and are apt to cause severe local pain, or even abscess, if injected subcutaneously. Novarsenobillon (N.A.B.) is of this type. As a rule, however, if the preparation is painless, it is also useless as a bactericidal agent. The intravenous route has therefore been recommended by many workers, among whom Williams⁽⁹²⁾ may be mentioned. The preparations which are in most common use at the present time are, however, given by the intramuscular or subcutaneous route. Notable among these are Metarsenobillon, - advocated by Colebrook and his colleagues - and Sulpharsenol - praised chiefly by the French observers; and both of these drugs have been given an extended trial in the course of this investigation.

Metarsenobillon.

This substance is known more popularly under the name of M.A.B. Among the claims which are made for it are, firstly, that its injection is practically painless and rarely becomes the seat of abscess formation; that, secondly, it is well tolerated by all patients; and, finally, that if it is given in sufficient dosage it will cause marked increase in bactericidal power, and streptococci will be killed both in the blood and in the local lesion.

Of the total series, 89 patients received treatment by this means, and among this number 78 had, in addition, local glycerin injections.

Technique.

The routine used was that advocated by Colebrook, streptococcal infections as far as possible being chosen. In practice, since treatment must begin as early as possible, all seriously ill patients were regarded in this light until proved otherwise.

The drug is a fine yellow powder which dissolves readily in water, and is supplied in glass ampules each containing 0.3 gm. - the unit dose advocated in this disease. Immediately before the injection is made, 3 c.c. of distilled water are added to the powder. Solution quickly occurs, and the yellow liquid thus obtained is injected deeply into the muscles of the buttock or thigh. Colebrook insists that the needle should penetrate vertically to a depth of two inches, and he suggests that the area be firmly massaged thereafter to facilitate absorption and mitigate the local reaction. Four initial doses are given, and it is important that the following time intervals be allowed between these:-

1st - 2nd dose	---	6-8 hours.
2nd - 3rd dose	---	12-15 hours.
3rd - 4th dose	---	24 hours.

This sequence is so arranged that when the final injection has been given the arsenic will be in requisite concentration in the blood stream to give a bactericidal action, without toxic results to the body tissues and fluids. Any organisms previously present in the blood should have succumbed, therefore, and in the absence of septicaemia the serum should be fortified against further infection from the pelvic focus. The advocates of the treatment state, however, that additional doses/

doses of similar amount may be given, in order to maintain or increase this bactericidal action. The suggested intervals of such additional injections are:-

4th - 5th dose	---	48 hours.
5th - 6th dose	---	3 days.
6th - 7th dose	---	4 days.
7th - 8th dose	---	5 days.

These further amounts are in most cases rendered necessary by the development of signs that the blood stream has been again infected.

Concurrently with the above injections, it is advised that oral administration of Citric Acid solution be practised, in doses corresponding to two drachms daily of this drug. This procedure is said to make the blood less viscid, and to promote transudation of the arsenic-bearing lymph into the infected tissues. In the present investigation this precaution was duly taken, and every attempt made to obtain the excellent results reported by other workers.

Response to Treatment.

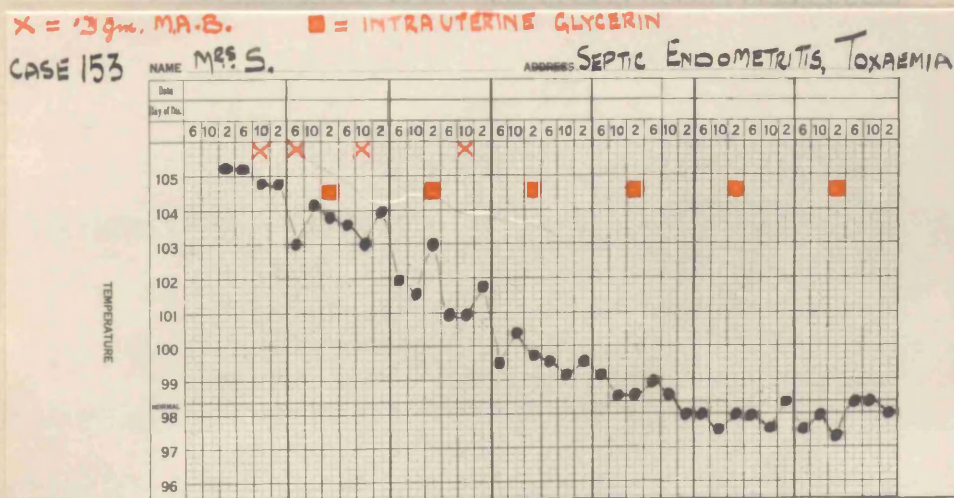
No patient gave evidence of definite toxic symptoms due to the drug, but although no abscesses formed at the site of injection the vast majority of patients complained of severe pain as a result of the treatment. This pain radiated down the thigh, persisted for several days after the injection, and was in a few cases the source of much annoyance for many weeks. The precaution of massaging the buttock for ten minutes after each injection was followed, but did not materially influence the incidence of the pain or its degree. In effect, the patients feared the injections, and the giving of a complete series was a triumph of persuasiveness on the part of the medical officer, and of long suffering/

suffering on the part of the recipient. In the case of very ill women, therefore, persistence of the treatment - in the absence of benefit - seemed scarcely justified.

Group II Cases.

A few of the milder degrees of infection appeared to shew some reaction, and in them the temperature and pulse gradually became normal during the four days occupied by the treatment. Case 153 was of this type. The local lesions consisted of septic endometritis with extensive lacerations of perineum, vagina, and cervix; and there was, in addition, marked general toxæmia. Arsenical treatment commenced on the evening of admission, and on the following day, glycerin injections were begun. During the first four days in hospital there was a gradual subsidence of temperature, and the pulse rate correspondingly diminished; while the general condition improved pari passu with these, and local sepsis rapidly cleared. Her temperature chart (Figure 52) illustrates this gradual improvement.

Figure 52.

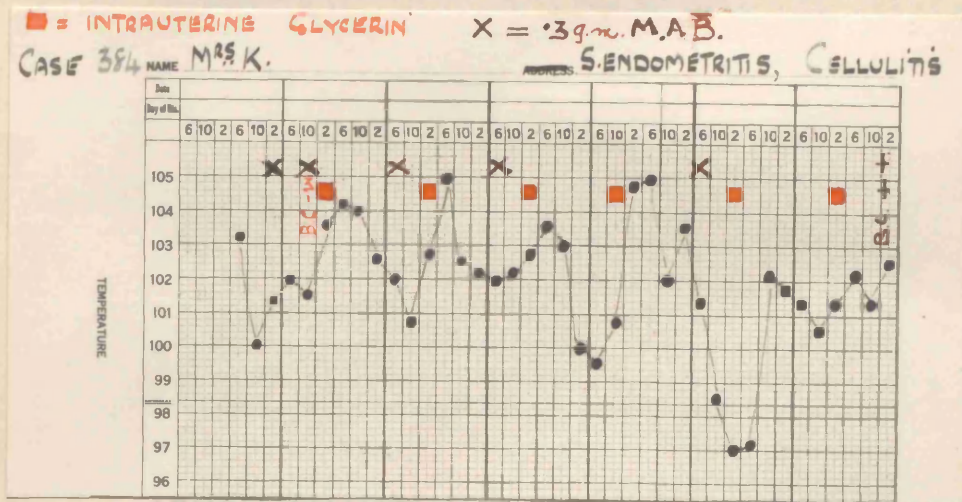


infection was completed. The arsenic may have been of some value in this case also. As the chart shows, however,

It is difficult, however, to assess how much of this effect was due to the arsenic, and how much resulted from the intensive local régime. This woman was eminently suited for glycerin treatment, and the gradual improvement is typical

strongly positive at the conclusion of the series. Repeated injections had absolutely no effect, and the patient gradually became moribund. Figure 56 shews this lack of reaction.

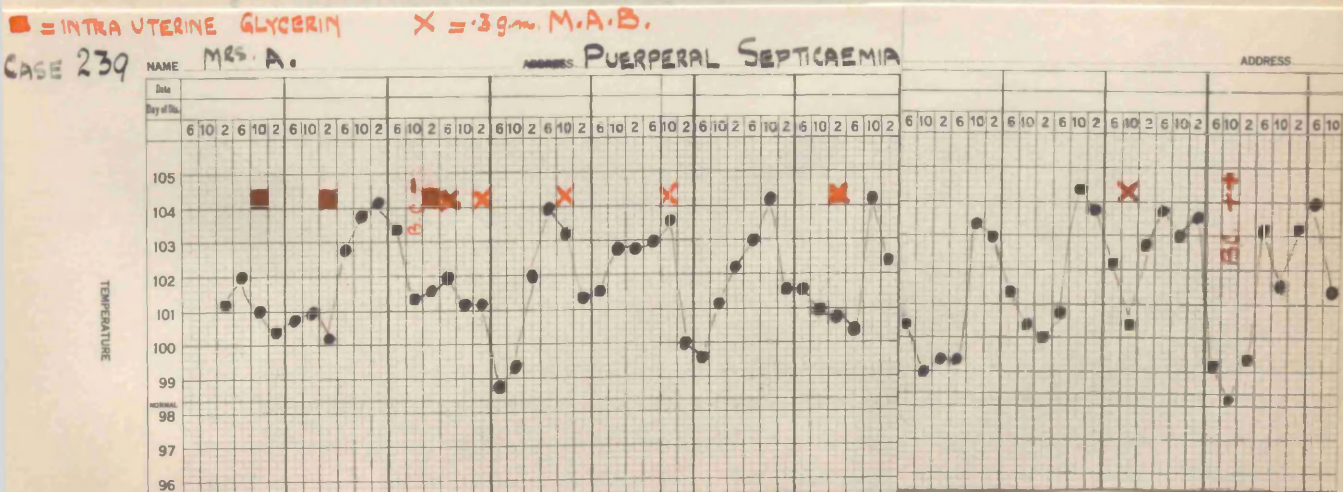
Figure 56.



Group IV Cases.

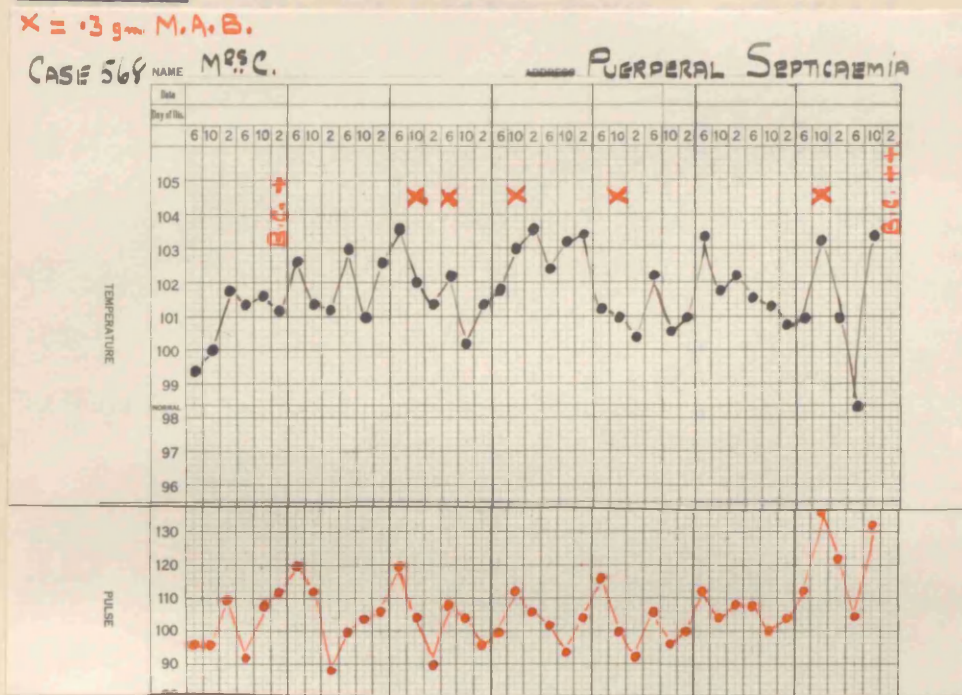
In these the results were consistently disappointing. Case 239 was of this group. This woman was septicaemic on admission, and foul retained products were removed from the uterine cavity - severe haemorrhage having rendered this interference necessary. Intra-uterine glycerin was given on this occasion, and on the following day a course of M.A.B. treatment was instituted. Blood culture proved negative at the outset, but was markedly positive after completion of the series and remained so in spite of additional dosage. The failure of the glycerin to prevent septicaemia must also be noted in this case.

Figure 57.



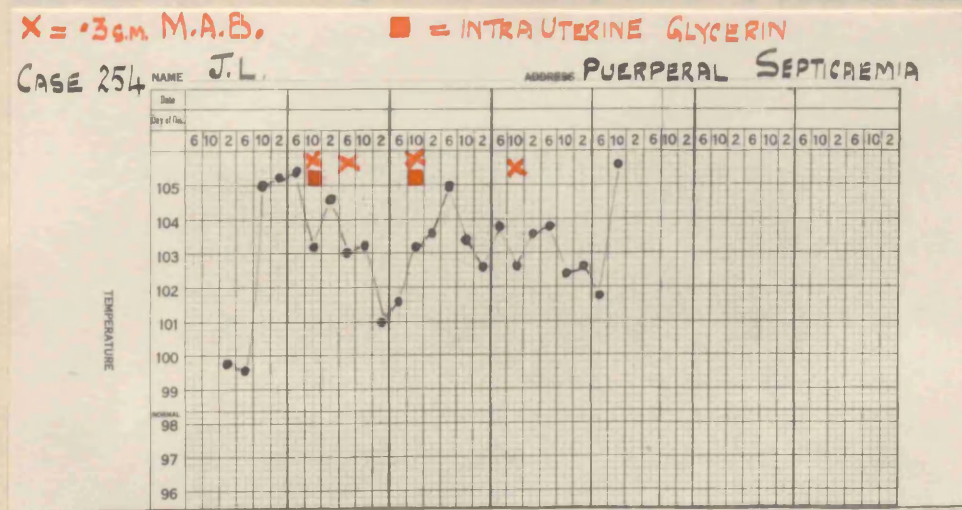
Case 568 was definitely septicaemic before adoption of arsenical treatment, and at its conclusion her blood gave an even more positive result. Her temperature and pulse, and above all the constitutional symptoms, were quite unaffected as a result of the drug.

Figure 58.



Case 254 illustrates again this lack of reaction. In spite of arsenic administration, this woman became progressively moribund, and died within five days of admission to hospital.

Figure 59.



There were many cases of this type.

Conclusions.

The results of treatment with this drug have been unsatisfactory from all points of view. Several of the less severe infections appeared to benefit; but all of these were receiving concomitant local treatment, and the real value of the arsenic was doubtful. In a few, however, the evidence points to the fact that some slight effect may have been due to the chemical injected.

Among the Group III patients treated by this means, many developed signs of Septicaemia and of spreading pelvic infection while the treatment was actually being pursued; and an analysis shews that blood examination became necessary to a much greater extent among these patients than among similar cases treated by other means.

In the Group IV series, arsenic proved entirely useless. No confirmed case of Septicaemia recovered as the result of this treatment; whereas in many, blood infection developed and increased, in spite of the injections.

Morris,⁽⁶⁵⁾ writing in 1929, reported excellent results from this line of treatment. Three cases of puerperal septicaemia recovered by this means, while a fourth shewed initial improvement, but died later. He states that in one case the blood, although previously yielding abundant growth of haemolytic streptococci, became sterile within five hours of her first injection; and he affirms that the arsenic was responsible for this immediate result. This patient was, however, obviously suffering from Pyaemia, and her course, which ended in cure, was very typical of this type of infection. A negative blood culture in such patients between, or even during, the rigors is by no means an uncommon occurrence. In other two of the cases cited by Morris, the improvement attributed to Metarsenobillon might reasonably have resulted from other factors. It is important to note, however/

however, that in all four cases the illness did not begin until two or even three weeks after the confinement. A late onset of this nature is usually followed by spontaneous, if protracted, recovery; and the problem of these patients is not to be compared with that of the acute primary or even secondary septicaemias which develop immediately after the confinement, or within a week of it. Amongst these, neither Morris nor Colebrook has so far adduced any examples of cure such as the serum treatment has occasionally provided, and certainly none of the present series shewed such a benefit.

Colebrook⁽⁶⁵⁾ asserts that Metarsenobillon can sterilize the blood, but like all other types of immunotherapy cannot penetrate to other organisms which are lodged in sheltered positions and out of reach of the bactericidal agents in the circulating fluids. The present experience is that with regard to both of these actions it is quite valueless. Of the women so treated, none affirmed that she was improved as a result of it - as was so often the case with serum treated patients; and there was in no case obvious indication of diminished toxæmia. In effect, none of the excellent results obtained by other workers were here observed; and the procedure was eventually abandoned as it did not justify the great pain and discomfort caused by it.

Sulpharsenol.

This is the organic preparation of arsenic favoured by French workers, both for its prophylactic and curative effect. Pery,⁽⁹¹⁾ found that, in Puerperal Fever, injections of Sulpharsenol, ranging from .05 to .24 c.g., were of great value when all other drugs failed; and Rivière,⁽⁸⁹⁾ encouraged by good results which he obtained when treating this disease, used it with excellent effect as a prophylactic measure in dosage/

dosage similar to that which Pery employed. Delmas, has also advocated the prophylactic use of Sulpharsenol, and suggests that it should be given as a routine measure after all accouchéments. His dosage is, however, one hundred times that of the above observers.

The value of Sulpharsenol is said to be in the elements of which it is composed. Its formula is interpreted as the acid salt of the acid sulphurous ether of methylolamino-arsenophenol; and it thus contains tetra-valent sulphur in addition to arsenic, both of which have a strong bactericidal and parasiticidal effect. As such, it is claimed to be infinitely superior to Novarsenobillon and Arsenobenzyl, and its activity has even been compared favourably with that of 606.

Sulpharsenol is a yellow powder which fumes slightly of sulphur and dissolves with some difficulty in sterile or distilled water. As available commercially, each dose is contained in a sealed sterile ampule, and this is dissolved in an appropriate quantity of sterile water - usually about 1 c.c. - immediately before use. The injection is made subcutaneously or intramuscularly, and has the advantage of being comparatively painless. Thus drug is also well tolerated, and rarely causes abscess formation.

Experience of this arsenical compound is confined to about twenty patients, and in none of these were any outstanding curative effects noted. Several patients received doses of 18 c.g. daily in the acute stages of their illness, without obvious diminution of toxæmia or temperature, and even in the milder types of infection the drug appeared valueless. As a vehicle for the administration of arsenic in the chronic phases it was, however, of some use. A few anaemic patients gave evidence of slight benefit after several injections of the above dose at intervals of three or/

or four days; but as these women were also receiving other tonic treatment, the part played by the arsenic is difficult to determine. In cases where there is a syphilitic basis there is likely to be a more definite result. On the whole, however, the drug appeared useless as a means of active treatment in this disease.

Conclusions.

The administration of organic arsenic has proved a disappointing line of treatment. Sterilization of the blood stream by means of metallic substances or other chemicals is a problem which has occupied the attention of many workers; and since Morgenroth and Levy⁽⁹³⁾ first shewed, in 1911, that mice infected with pneumococci could be saved by injections of "optochin," many other agents have joined the lists. On entering the blood stream, however, these appear to become fixed by the serum, proteins, the blood cells, or the tissues, and are thus rendered valueless. Moreover, Fleming's⁽⁹⁴⁾ work in 1924 made it clear that so much damage might be done to the normal protective elements in the blood - particularly to the leucocytes - that far more harm than good might result from such drugs in treatment. The border-line between the effective and the toxic dose must of necessity be very narrow; and although fifteen cubic centimetres of a solution may sterilize the blood, sixteen may produce disastrous and fatal effects on the vital tissues of the body.

Any antiseptic which is to be of value, therefore, must possess the double property of being toxic to the invading organisms and non-toxic to the blood and tissue cells - a power of discrimination which is almost human. When such a substance is discovered, the problem of Septicaemia will be on the road to solution; and in view of the excellent/

excellent results obtained along the same lines in the treatment of Spirochaetal conditions, there is still room for hope that Streptococcal infections may eventually prove vulnerable. The extreme delicacy of the spirochaete, and its comparative scarcity in the blood, must however be borne in mind. The streptococcus is a powerful organism which grows and remains alive readily in vitro, and in the blood of a septicaemic patient it is present in such numbers that any antiseptic which affects it must be both powerful and selective. For such a purpose organic arsenic, either as Metarsenobillon or Sulpharsenol, appears absolutely valueless.

4. MERCUROCHROME.

Mercurochrome is a phthalein derivative of mercury. This drug was first described by White, and was the outcome of research designed to find some organic preparation of mercury which would combine the strongly antiseptic properties of its inorganic salts while remaining free of their toxic effects. It is claimed that mercurochrome contains 26 per cent. of mercury, but that this is present in the non-ionised state and does not therefore exhibit normal coagulative powers. Thus the compound is able to exert fully its germicidal action in the presence of the albuminous body fluids and tissues in general; and it is recommended for this effect in such varied conditions as Gonorrhoea, Malaria, Leprosy, Scarlet Fever, Pneumonia, and several other diseases.

Many writers claim outstanding results from the administration of mercurochrome in various septic conditions; and as a bactericidal agent in Puerperal Septicaemia it finds many supporters. Among these are Young⁽⁹⁵⁾ and Mayes,⁽⁹⁶⁾ the latter maintaining that the incidence of puerperal sepsis may/

may be reduced by the routine adoption of 4 per cent. solutions of this drug in ordinary midwifery practice. Other observers deny the efficacy of mercurochrome, and recently Garrod⁽⁹⁷⁾ proved that it is a germicide incomparably weaker than is commonly supposed. It has been suggested also that the drug may even exert a harmful influence on the patient who receives it, and that degrees of mercurial poisoning may sometimes be produced. This toxicity is said to be the result of decomposition of the organic molecule, various intermediate products being formed. Reports of mercurochrome are on the whole good however.

In this investigation, experience of its action was limited to eight patients of Group IV, all examples of streptococcal septicaemia.

Technique.

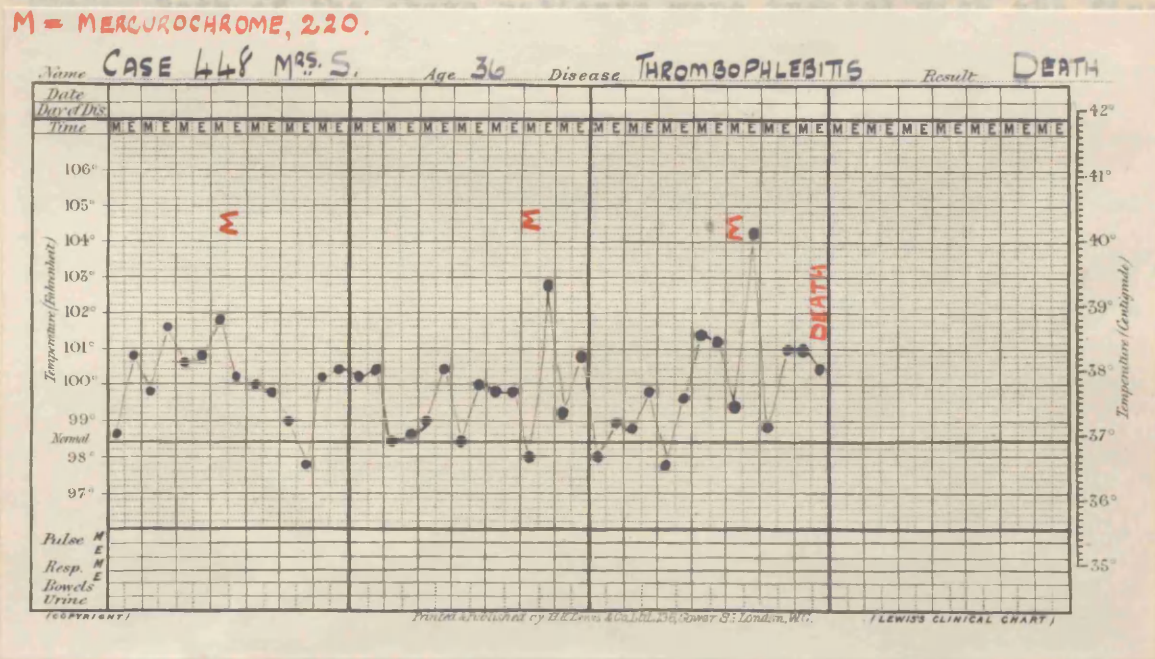
The drug is given intravenously. In the present series, two different preparations were employed. The first - Mercurochrome 220 - was a solution prepared for each patient in accordance with her body weight, 2-5 m.g. per Kilo being allowed, and the dose contained in 10 c.c. of normal saline solution. The second was a colossal brand prepared commercially. Recent clinical trials appear to shew that the therapeutic activity of mercurochrome is enhanced if the drug is dissolved in a sterile isotonic glucose solution; and in the colossal preparation above described, .1 mg. of the salt is added to 25 c.c. of this liquid immediately before use, from 10 to 25 c.c. of the resulting mixture being the requisite dose. Both preparations have a deep permanganate colour and are really dyes. Deterioration takes place rapidly on exposure to light, and great care must be taken in this respect, absolutely fresh solutions being employed on all occasions.

Case 543 — Streptococcal Septicaemia

Figure 62.

Several of the other patients may be cited, although here the results were entirely unsatisfactory. Figure 61 shows the temperature variations of a patient (Case 448) who died of thrombophlebitis and chronic pyaemia. Serum proved unavailing, and mercurochrome was tried, three injections being given. The first two produced no appreciable clinical effects, but after the third, signs of cardiac failure rapidly ensued; and although her condition had previously indicated a fatal termination, this occurred at an earlier date than had been anticipated.

Figure 61.

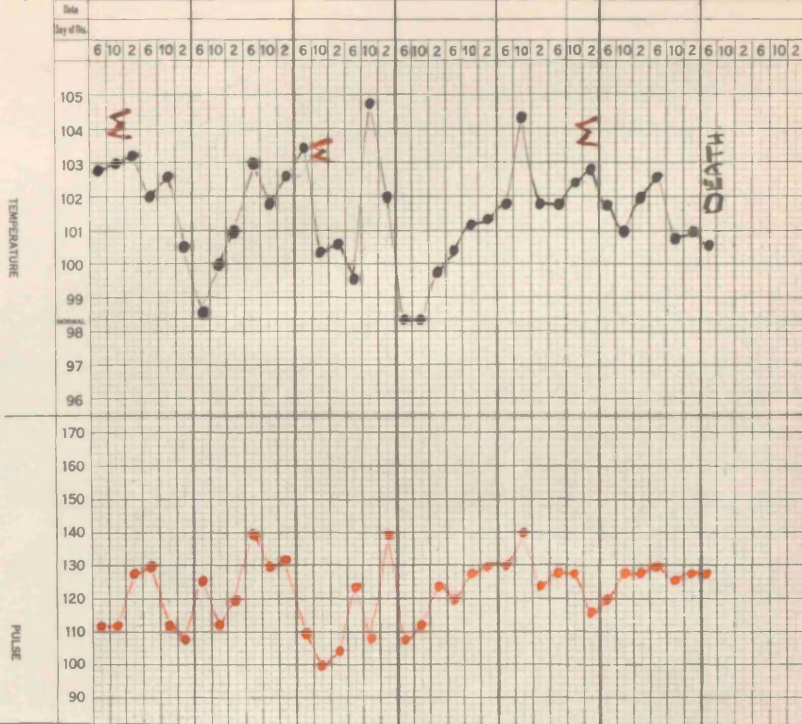


M = MERCUROCHROME, 220

CASE, 543 NAME MRS. B.

ADDRESS Puerperal SEPTICAEMIA

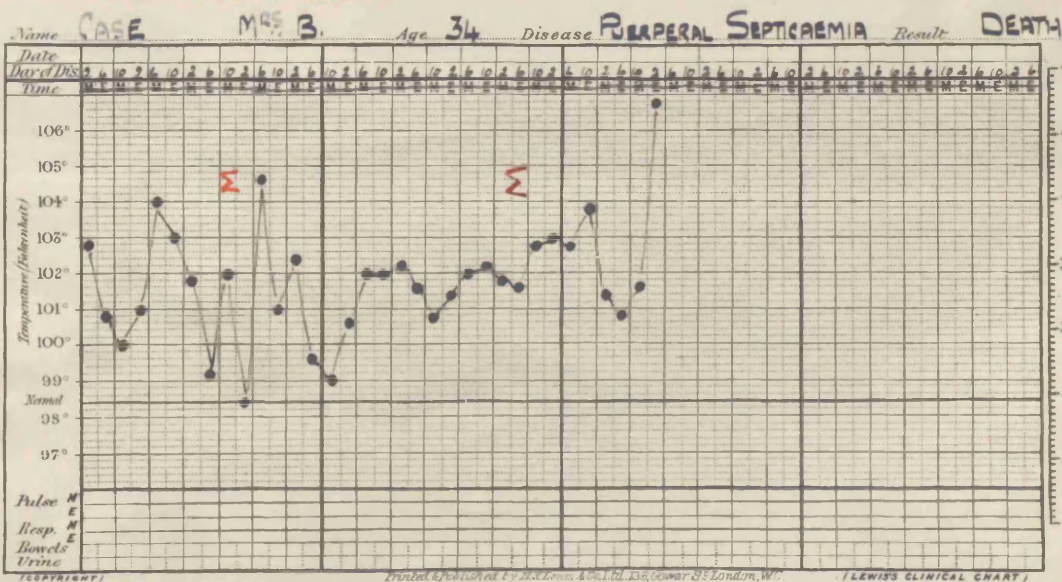
Figure 62.



Both of the above patients were treated with the first mercurochrome solution; and these rapid toxic symptoms seemed confined to this preparation. One case of primary septicaemia previously treated by other means received the mercurochrome glucose solution. Two injections of 20 c.c. were given without clinical response, and the case ended fatally.

Figure 63.

M = COLLOSAL MERCUROCHROME



effect in all toxic conditions. They may therefore be given as an adjuvant to other forms of general treatment, and are specially beneficial in Puerperal Septicaemia, since they not only make up the blood volume - frequently low on account of haemorrhages - but they also dilute the toxins in the circulating/

Conclusions.

It seems quite established that the administration of mercurochrome is not devoid of risk. Three of the patients so treated rapidly became worse and the fatal issue was precipitated. With regard to the patient who recovered so definitely, many other factors must be considered. The formation of localizing foci in arm and gland was almost certainly the real determinant, and how far this resulted from the mercurochrome injection must remain a debatable point, in view of the other methods of treatment previously pursued. It appeared, however, that the mercurochrome did turn the balance towards recovery. The mode of action of the drug is also doubtful. A few writers have affirmed that it has its basis in protein shock phenomena, but in this series there were no clinical evidences of such an action.

It is also obvious that mercurochrome has no miraculous properties in the treatment of streptococcal blood infections. In a disease so frequently fatal as Puerperal Septicaemia it may seem justifiable to take some risks in treatment, and it is expedient to explore all avenues of helpfulness; but the biochemistry of the blood is still obscure, and it does not appear advisable to tamper with it in such a haphazard manner as the use of mercurochrome and other antiseptic substances would imply.

5. SALINES.

Salines may be given rectally, subcutaneously, or intravenously, and are useful for their stimulant and diluting effect in all toxic conditions. They may therefore be given as an adjuvant to other forms of general treatment; and are specially beneficial in Puerperal Septicaemia, since they not only make up the blood volume - frequently low on account of haemorrhages - but they also dilute the toxins in the circulating/

circulating blood, and promote elimination by the kidneys and other excretory channels.

Throughout this investigation salines were therefore freely employed, and for this purpose the rectal route was most frequently chosen. Patients with severe pelvic infections, however, in many cases presented a marked degree of bowel irritation, and in these the subcutaneous route was used. This injection was given by gravity into the submammary regions, about one pint of isotonic saline being frequently absorbed without evidence of local discomfort, despite the fact that in most cases painful engorgement of the breasts had been present at the outset. The effect of such treatment was entirely adjuvant; and although many patients improved markedly concurrently with the daily administration of subcutaneous or rectal salines, other more specific methods were at the same time followed, and conclusions are not therefore permissible. It is to be noted that, even in septicaemic patients, abscess formation did not arise at the site of such injections.

For rapidity of action, however, the intravenous route appears most rational, and if the patient's veins were suitable, saline infusions were frequently given in this way. As before noted, practically all intravenous injections of serum were followed by from 100 to 150 c.c. of normal saline at blood heat, and in addition saline per se was frequently administered by this route in septicaemic, toxic, or collapsed patients. This injection was given slowly by means of a syringe in some cases, and by gravity through a funnel and tubing in a few others.

It is not to be expected that any specific effect should follow such a line of treatment, and no immediate results with regard to temperature, pulse rate, or toxæmia were observed in any of these cases. Some writers affirm that/

that if serum is diluted and followed by saline when given by the intravenous route severe rigors are inhibited; but there was no evidence of such an action, and rigors of equal severity appeared to follow both methods of injection.

French workers have recently shewn a tendency to pursue this line of treatment to the exclusion of all other methods, and for this purpose both isotonic and hypertonic solutions have been recommended by them. It is claimed that leucocytosis is stimulated by the higher concentration, and that septicaemia may be cured as a result of this; but although there is no doubt that saline injections are in all cases beneficial, they should be administered in addition to - rather than to the exclusion of - other more specialized forms of treatment.

6. VITAMINES.

The relationship between vitamins and disease has long been realized, and it is an established fact that definite deficiency conditions may arise from a dietetic lack of each of these accessory substances. It appears, however, that Vitamin A has an additional, less specialized, effect. The early researches of Mellanby and Green⁽⁹⁸⁾ led them to the conclusion that, apart from the promotion of healthy growth, the chief and most important function of this vitamin is to raise the resistance - either local or general, or both - to bacterial infection. Animals deprived only of Vitamin A died ultimately with multiple foci of infection, whereas control animals receiving Vitamin A remained in good health free from disease. In addition, animals which had developed infective lesions usually recovered completely if given in time abundant doses of this/

this vitamin. According to the same workers, the pregnant woman is in great danger of a deficiency of this nature. Not only her own body, but the rapidly growing organism within her, must receive adequate supplies, and if her daily intake is insufficient, any liver stores which she may have amassed are quickly depleted. It may be supposed, therefore, that the parturient woman usually enters her puerperium grossly depleted of Vitamin A, and is thus extremely liable to develop sepsis should suitable organisms be present.

Acting on this assumption, Mellanby and Green advocate the use of Vitamin A both as a prophylactic and as a cure for Puerperal Sepsis; and they adduce⁽⁹⁹⁾ impressive results from the pursuance of such a line of treatment. In a series of thirty cases cited by the above observers, dosage with this vitamin resulted in an immediate diminution of death rate from 100 per cent. to zero; and the patients so treated were with one exception completely recovered and dismissed from hospital within six weeks of its commencement. It would appear, however, that the effect of Vitamin A is to increase gradually the general resistance against the infective process, rather than to give the sudden reaction which is expected of a substance possessing specific bactericidal or antitoxic value.

Under the direction and advice of its originators, this method of treatment was followed in 86 patients of this series.

Technique.

The drugs used are of two kinds - preparation X and preparation Y. The former is the proprietary substance called Radiostoleum, while the latter is a special product made by Lever Brothers of Port Sunlight. Both are oily liquids which deteriorate on exposure to light, and must therefore be preserved carefully. If these preparations are/

are standardised by the colorimetric method of Carr and Price, (100) and the results compared with those of Cod Liver Oil, it is found that preparation X is on average ten times, and preparation Y one hundred and fifty times, as rich in Vitamin A as the above liquid.

The preparations are given by mouth, of X, two drachms twice daily (this being equivalent to about five ounces of cod liver oil), and of Y two minims hourly for twelve doses daily (this corresponding to about eight ounces of cod liver oil). Preparation Y is given only in cases of persistent sickness and when preparation X is not being well tolerated. The drugs have an oily taste, but if mixed with equal quantities of orange syrup, both become palatable, and little difficulty is experienced in this connection.

Response to Treatment.

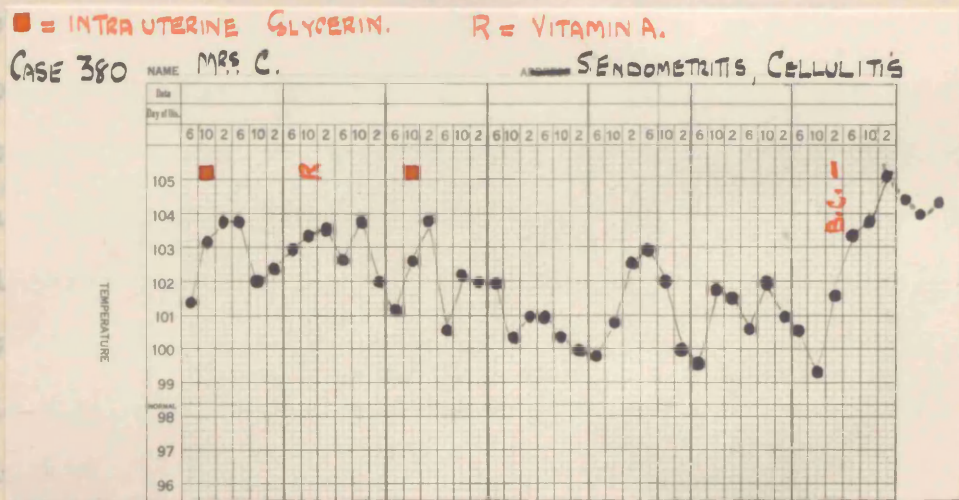
Preparation X was well tolerated, and the more concentrated drug was necessary in very few instances.

With regard to the patients of Group II and Group III, 68 of these received this form of treatment, either alone or in combination with local glycerin injections. In no case, however, could any definite benefit be traced to the administration of this drug. Temperature persisted, pelvic infections spread, and toxæmia was quite unaffected in spite of continued and adequate dosage. In one case bilateral phlegmasia alba dolens developed; in another fatal peritonitis supervened; and in five others septicaemic features became outstanding while the treatment was in progress.

Case 380 was of the latter series. This woman was on admission acutely ill, delirious, highly febrile, and in her fourth day of fever. Radiostoleum treatment commenced on the following day, and two glycerin injections were also given at the outset. In spite of this vitamin treatment, the temperature continued to swing in an irregular manner, toxæmia/

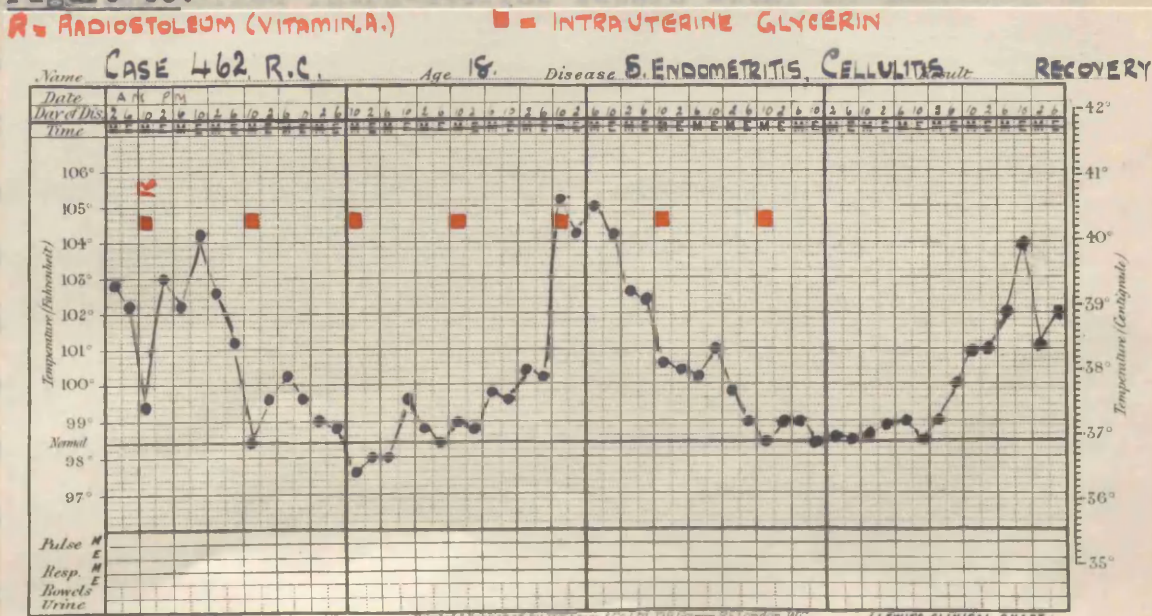
toxaemia increased, and at the end of a week clinical septicaemia was manifest. Several days later, blood culture revealed the presence of streptococci. Her chart (Figure 64) illustrates this complete lack of reaction.

Figure 64.



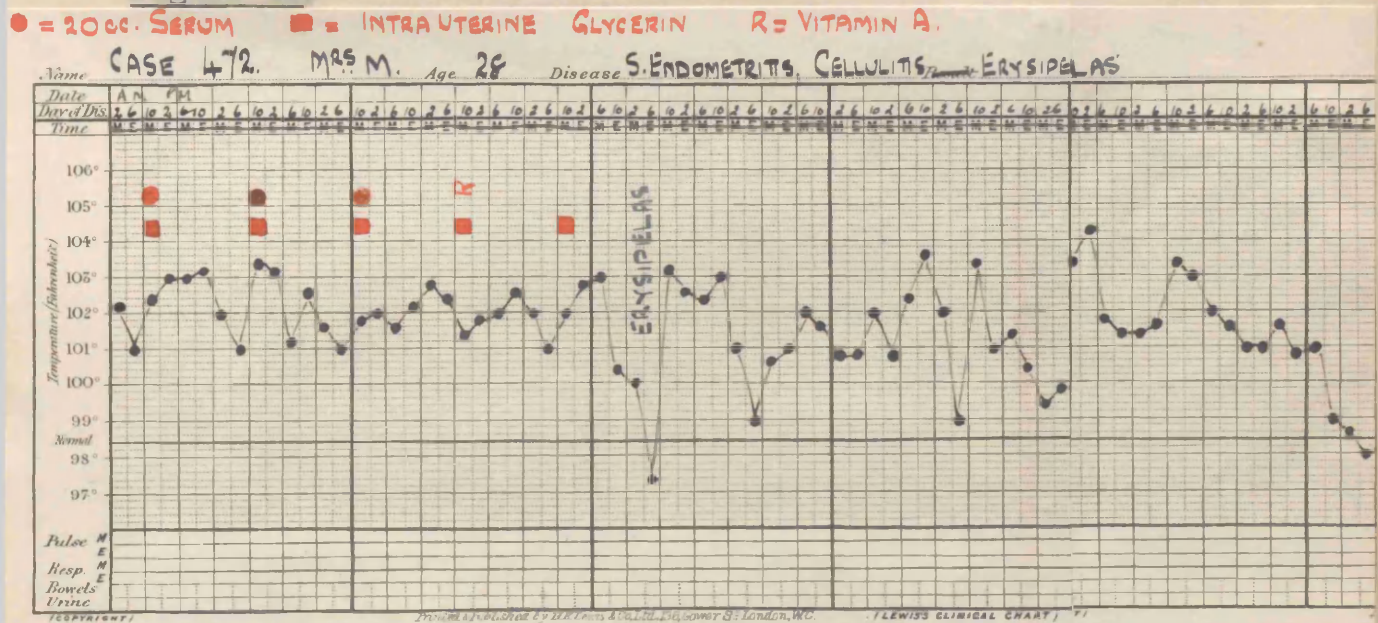
Case 462 was a typical Group III patient with marked intra-uterine sepsis and a moderate pelvic infection. Glycerin was given daily, and Radiostoleum was administered from the first day of admission. Although the intra-uterine condition cleared rapidly as a result of the local treatment, the extra-uterine sepsis progressed and remained active for several weeks. No obvious effect could be traced to the vitamin treatment, and the pelvic lesions merely followed their ordinary course.

Figure 65.



Case 472 gave rather misleading results. This woman also fell into the category of Group III, and in spite of the fact that streptococci were cultivated from the cervix and from the uterine pus, repeated doses of serum had no effect on the general symptoms. Radiostoleum treatment commenced on the fourth day, and soon thereafter the temperature became remittent - in marked contrast to the continuous pyrexia before noted. At the same time, however, a spread^{ing}, erysipelatous lesion of the perineum and buttocks developed; and as this focal lesion ran its course, the temperature and general disturbance gradually subsided. It is unlikely that the vitamin treatment had any real effect in determining this result.

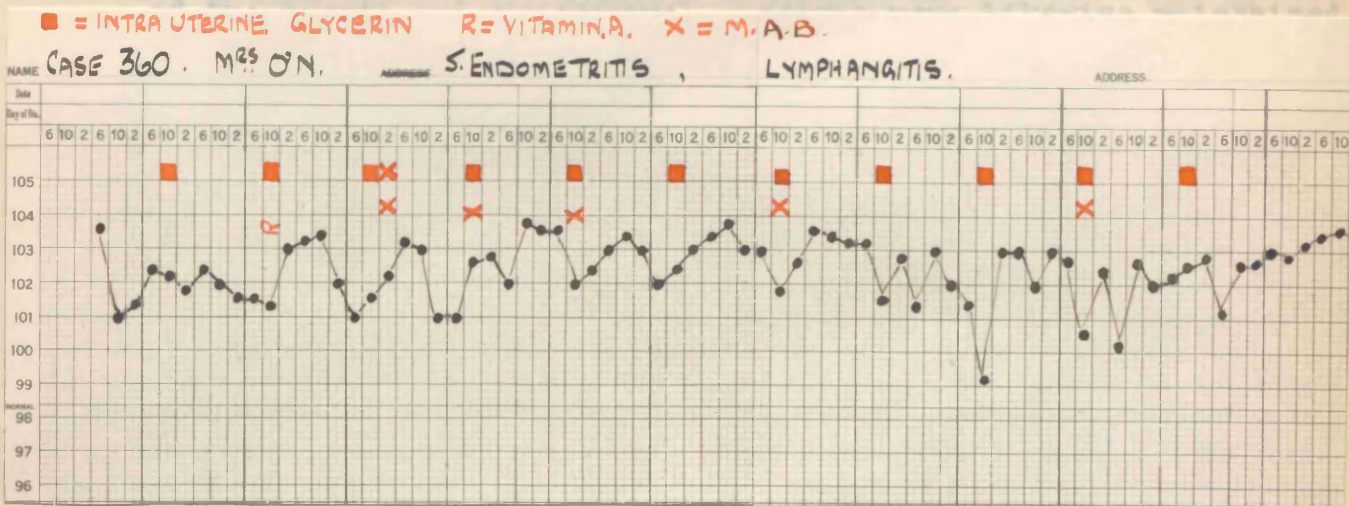
Figure 66.



Finally, case 360 may be mentioned. This woman presented marked intra-uterine sepsis with, in addition, a slight pelvic lymphangitis; and Radiostoleum was administered from the third day of admission. Toxaemia increased, however, so a course of M.A.B. treatment was initiated. At the conclusion of the series she was even more toxic than at the outset. By the end of the following week the temperature was consistently high, and clinically the patient was septicaemic, although blood examination proved negative. Glycerin treatment was pursued throughout, and its absence of/

of benefit, if not its positive harmful effects, are also noteworthy.

Figure 67.



It is in Group IV cases, however, that any conclusive signs of benefit should be apparent; and 18 women clinically and bacteriologically septicaemic received this form of general treatment. With two exceptions, all of these proved fatal; thus the death rate is 89 per cent. as opposed to the 0 per cent. adduced by Mellanby and his colleague. In the patients who died, there was no obvious effect from administration of either preparation, and the Septicaemia ran a short active course differing in no way from that observed with other forms of treatment. The two patients who survived are of some interest.

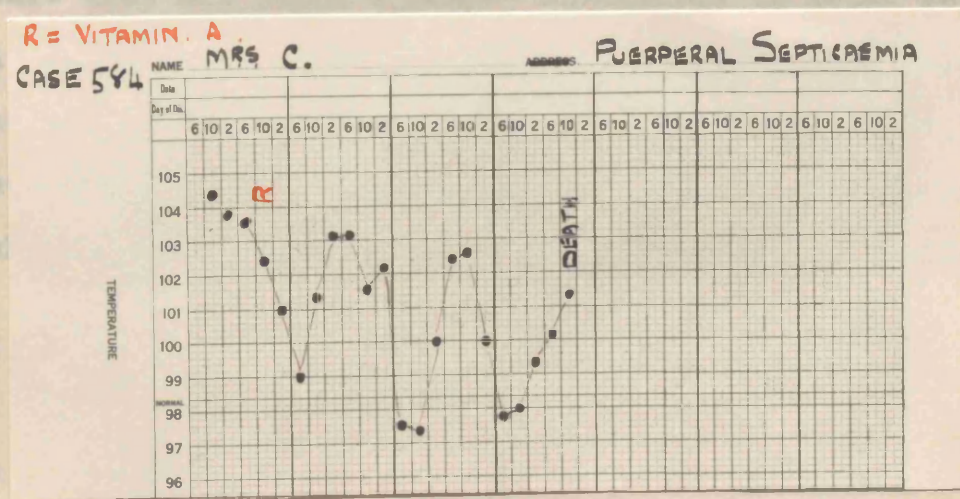
Case 239 had a well-established streptococcal septicaemia, which however presented pyaemic features and gave therefore, from the outset, a rather more hopeful prognosis. Vitamin A treatment was continued for six weeks, during which time $10\frac{1}{2}$ ounces of preparation X and one drachm of preparation Y were used; and at the conclusion of this period the patient was still highly febrile, emaciated, pale, sickly, and exhibiting frequent rigors. A further month elapsed before she was definitely afebrile, and/

Case 583 It has been suggested that signs of cardiac insufficiency occasionally develop after prolonged administration of this drug, but in neither of the two cases above cited were there any indications of such an action; and as has been noted in the latter case, there was already a predisposing cardiac lesion.

The exact value of the treatment in both of these patients is difficult of determination. The first would probably have recovered without Vitamin A, although the second may have benefited to some slight extent. It is to be remembered, however, that blood infection of the coliform type is not so consistently fatal as the streptococcal variety. Both cases certainly show that the effect of Vitamin A - if indeed it has any such - is one of extreme slowness. The advocates of the treatment admit that no immediate action must be expected, and the drug is therefore valueless in the acute virulent septicaemias. Examples of this type may be multiplied.

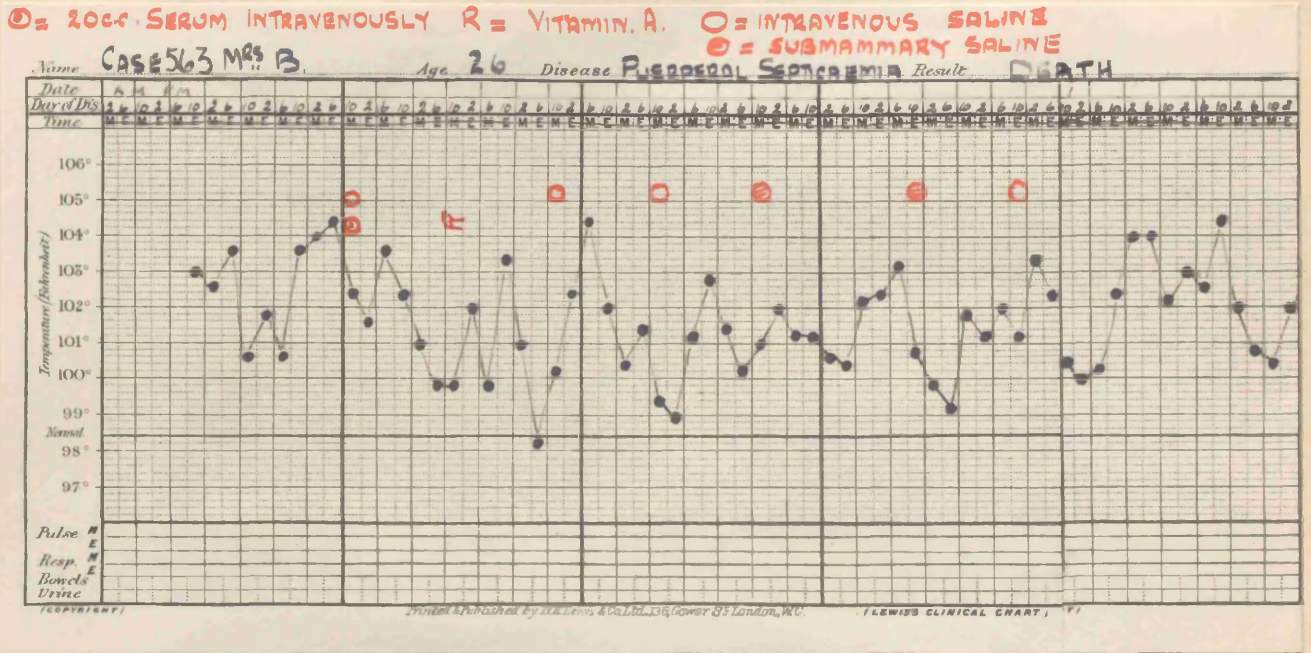
Case 584 illustrates this complete absence of effect in streptococcal septicaemia which proved fatal within four days of admission.

Figure 70.



Case 563 shows a more prolonged illness marked by frequent rigors and remittent temperature, terminating fatally 15 days after admission to hospital.

Figure 71.



STATISTICAL ANALYSIS OF TREATMENT.

The personal factor in determining the value of treatment is very potent; and while there can be no doubt that this estimate of a drug or method is in many cases the correct one, it is easy to become convinced of results which are not substantiated by facts. Standards which are impersonal, and therefore impartial, must, on this account, be employed, and criteria on which stress may be laid are:-

- (1) The average duration of primary pyrexia.
- (2) The average period of hospitalization.
- (3) The percentage number of patients developing complications.
- (4) The percentage mortality.

Considered in conjunction, these provide a fair standard on which comparisons may be based, although alone neither is infallible.

The importance of comparing patients whose infection is similar in severity and type has also been considered, and for this reason appropriate grouping has been practised; and since post abortum cases present problems of treatment slightly at variance with those of full time infections, these have been segregated throughout. Finally, it is to be noted that all patients within each group benefited from similar general hospital treatment.

Before this investigation was initiated, a conservative regime had been practised. Each patient received routine doses of liquid extract of ergot to the extent of half a drachm every four hours; and of quinine hydrochloride ten grains at similar intervals; both drugs being given orally. Women who appeared specially toxic received one injection (10-20 c.c.) of scarletinal antiserum, and in occasional cases of severe anaemia/

anaemia, Sulpharsenol was injected at later stages of the illness. Apart from an initial or later vaginal examination for the purposes of diagnosis, - or, in post abortum cases, for the removal of retained products, - no special method of local treatment was adopted, and no attempt was made to control the disease either locally or generally. Dependence was thus placed on gradual raising of the patient's resistance, by the usual methods of hospitalization, as the chief agent in controlling the infection. The series includes two hundred of such cases; and together with a few others similarly treated later, they form a number of controls, in the light of which the intensive methods may be judged and their true value assessed.

Many of the methods discussed in the preceding pages have been of an essentially adjuvant type, and were pursued in addition to the more specialized forms. These cannot therefore enter into a statistical analysis of this nature. Similarly, the small series of patients treated with mercurochrome had all received specific general remedies at an earlier date; and failure must therefore be attributed entirely to the earlier method. The statistical analysis is thus concerned with the following methods of treatment. Firstly, there is a strictly conservative routine - ergot and quinine alone being administered; and secondly a modified conservative regime - one dose of specific antiserum, in addition to the above drugs, being employed. In the third place, local treatment with glycerin is to be considered, and this may be pursued alone, or in combination with general remedies. Of these, specific serum must be analyzed, and its effects contrasted with those of arsenical preparations and of vitamins.

Group I Cases.

This group includes 112 patients, and of this number 76 were full time cases, the remaining 36 being post abortum infections. Within the group the following methods of treatment were adopted:-

- (1) Conservative - Ergot and Quinine.
- (2) Modified Conservative - (Ergot, Quinine,
(1 dose (10-20 c.c.) Scarletinal
(Antiserum.
- (3) Intra-uterine injections of Glycerin.
- (4) (Intra-uterine injections of Glycerin
(1 dose (10-20 c.c.) of Scarletinal Antitoxic Serum.
- (5) 1 dose (10-20 c.c.) of Scarletinal Antitoxic Serum
without local treatment.

The statistical results obtained by an analysis of these cases, are shown in the accompanying table.

TABLE 17.

Table shewing the relationship of type of treatment to average duration of primary pyrexia and hospitalization and to the complication rate in all cases of Group I.

FULL TIME CASES.

POST ABORTUM CASES.

Treat- ment.	No. of Cases	Primary Pyrexia (Days.)	Hospi- tal Treat- ment. (Days)	Compli- cation Rate. %	No. of Cases	Primary Pyrexia (Days.)	Hospital Treat- ment. (Days.)	Compli- cation Rate. %
E + Q	22	5.8	38.7	24.4	10	2.9	26.5	16.6
E+Q+S	23	3.9	33.3	13.2	8	2.1	23.5	-
G.	21	4.6	32.3	9.5	7	2.7	24.6	-
G+S.	6	4	28.3	-	5	2.6	24.8	-
S.	4	3.5	30.1	25	6	1.9	23.6	-

E = Ergot

Q = Quinine

G = Glycerin

S = Serum.

It appears therefore that with regard to Primary Pyrexia the conservative régime gives by far the largest figure, whereas modified conservative treatment or the use of serum alone is most effective. Glycerin alone is not so efficient as when in combination with serum. Similar results are met with in the abortion cases.

The period of Hospitalization is also at its highest when conservative methods are employed; but the lowest figure is obtained when intensive glycerin treatment is combined with the general antitoxic remedy provided by scarletinal antiserum. Serum treatment alone is, however, almost equally as effective as when intra-uterine medication is employed. The other methods give intermediate figures, glycerin given alone being slightly below the figure obtained by modified conservative routine.

The post abortum cases vary slightly from the above. In them serum given alone or combined with ergot and quinine appears to be most efficient. The glycerin groups are of slightly less value, while the strictly conservative routine is least effective.

The complication rate is found to be highest in the conservative group, and it is nil in the cases receiving glycerin and specific serum. The use of glycerin alone, or of serum alone, gives a higher rate; and the modified conservative routine provides a rate which is intermediate to both of these. Among the post abortum cases, only those treated on strictly conservative lines were followed by complications.

The mortality rate was nil in all types of treatment.

The following Conclusions may, therefore, be made:-

(1) In Group I cases, intensive local treatment with glycerin, if combined with a prophylactic or curative dose of serum, gives the best all-round results.

(2)/

(2) Serum, however, if given alone provides practically similar findings, the complication rate alone being higher; but it must be noted that the number of cases in both of these series is very small, and that no hard and fast conclusion can be drawn from statistics concerning either.

(3) Any method containing glycerin is followed by a low complication rate.

(4) Although Ergot and Quinine, if combined with Serum, give fairly good all round results, Ergot and Quinine, if given alone, form a combination in every way inferior.

In Post Abortum cases of this group, however,

(1) Any treatment which avoids local interference gives the best results with regard to primary pyrexia and hospitalization.

(2) If the strictly conservative routine is excepted, few complications are incurred by any form of treatment.

Group II Cases.

There were 348 patients in this group. Full time cases amounted to 249 of these, and post abortum sepsis accounted for the residual 99 patients. The methods of treatment employed were as follows:-

- (1) Conservative - Ergot + Quinine.
- (2) Modified Conservative (Ergot + Quinine.
(1 dose (20 c.c.) Scarletinal Anti-Serum.
- (3) Intra-uterine glycerin injections.
- (4) (Intra-uterine Glycerin injections.
(1 dose - 20 c.c.- Scarletinal Antitoxic Serum.
- (5) (Intra-uterine Glycerin injections.
(Metarsenobillon.
- (6) (Intra-uterine Glycerin injections.
(Vitamin A.

As in the foregoing group, the factors which require

to be taken into consideration are the duration of primary pyrexia and of hospitalization, and the complication rate; with, in addition, the mortality rate.

An analysis of the cases reveals the statistical results shewn in Table 18.

TABLE 18.

Table shewing the relationship of type of treatment to average duration of primary pyrexia and hospitalization, and to complication and mortality rates in all cases of Group II.

FULL TIME CASES.

Treatment.	No. of Cases	Primary Pyrexia (Days).	Hospital treatment. (Days.)	Complication Rate %	Mortality Rate. %
E + Q	16	6.6	39.3	35.3	6.3
E+Q+S	44	6.5	38.9	31.2	2.3
G	70	6.1	36.5	17.1	1.4
G + S	60	5.5	35.1	10.4	-
G + M.A.B.	35	7.8	37.1	28.6	2.1
G + V.A	24	6.2	37.6	25.0	8.3

POST ABORTUM CASES.

Treatment.	No. of Cases	Primary Pyrexia (Days).	Hospital treatment. (Days).	Complication Rate %	Mortality Rate %
E + Q	12	8.4	38.3	33.3	8.3
E+Q+S	32	7.5	34.7	28.6	-
G	14	6.5	30.3	21.4	7.7
G + S	26	5.9	30.0	17.4	-
G + M.A.B.	12	10	39.1	43	-
G + V.A	3	6.3	35.1	33.3	33.3

E = Ergot.

Q = Quinine.

G = Glycerin.

S = Serum.

M.A.B. = Metarsenobillon.

V.A = Vitamin A.

An analysis of this table shews that, with regard to the Primary Pyrexia there is but little variation in this under the various methods of treatment. These figures are at variance with the personal expectations, since theoretically Group II cases should shew very definite benefit as a result of intra-uterine medication, especially when the toxæmia is controlled by some form of general treatment. Glycerin in combination with serum gives the lowest average, however, although Glycerin with M.A.B. provides the highest figure; and similar results are noted in the post abortum cases. The high average of the M.A.B. group is disconcerting, but may be explained by the fact that in most of the women this form of treatment was followed by painful inflammation at the site of injection, and it was several days after the last dose before they were quite settled and afebrile.

With regard to the second factor - the duration of hospital treatment - a slight variation may be associated with the different methods which were followed. Glycerin and Serum form the most effective combination both in full time and post abortum cases, although in both, Glycerin medication without general treatment seems almost equally beneficial. This is to be expected, however, since drainage is the main necessity of this group. That much of the effect is due to the glycerin is proved by the fact that Serum, when combined with Ergot and Quinine, gives a much poorer figure. The combination of M.A.B. or Vitamin A with Glycerin does not appear to add in any way to its effectiveness.

The lowest complication rates in both full time and post abortum cases are obtained with intra-uterine glycerin treatment, and the result is slightly enhanced if a general remedy such as serum is concurrently given. Even when combined with M.A.B. or Vitamin A, glycerin medication is still followed by a lower complication rate than is obtained either with/

with the conservative or modified conservative régime. In the post abortum series there is an apparent deviation, since both M.A.B. and Vitamin A provide a very high rate. It is to be noted, however, that both of these comprised very few cases, and statistics concerning them are of necessity less satisfactory.

As the number of cases in this group is considerable, it is suggested that reliance may be placed on the low incidence of complications in the patients who received intra-uterine glycerin medication, either alone or in combination with general treatment by means of scarletinal antitoxic serum.

A consideration of the fatal cases reveals that in full time and post abortum series the combination of glycerin with serum gives a zero mortality, and that glycerin medication alone comes next in order of effectiveness. It is difficult to understand why patients treated with glycerin alone should provide a lower mortality rate than those who received an additional general remedy such as M.A.B. or Vitamin A - even if the action of these is regarded as nil. The figures which are available would almost indicate that the liability to fatal complications increased when arsenic or Vitamin A was administered. Whatever be the explanation, it seems apparent that, since almost all of the fatalities resulted from septicaemia, neither of the above remedies can prevent the development of this complication, however potent they may be in curing it once it has occurred. The only fatal cases in the post abortum series were patients treated only with Ergot and Quinine, that is, receiving no general treatment. The complication rate in the few cases treated with M.A.B. was, however, high, and if the arsenic prevented death, it certainly did not prevent spread of the disease.

It/

It is concluded therefore that in Group II cases -

- (1) Any treatment designed to promote drainage gives the best all round results.
- (2) A method which includes serum administration would appear to prevent the occurrence of septicaemia and of death; but unless glycerin is also given, there will be a high proportion of local complications due to pelvic spread from the intra-uterine focus.
- (3) Metarsenobillon and Vitamin A, even if given at the outset, do not prevent the development of septicaemia.
- (4) Post abortum cases, after evacuation of the uterus, have as a rule an uninterrupted recovery if simply protected by a moderate dose of scarletinal antiserum; the figures for complication rate and duration of hospital treatment being only slightly higher than those obtained when intensive local treatment is carried out.

Group III Cases.

Of the 228 cases in this group, full time births accounted for 187 infections, and the remaining 41 were of the post abortum type. The various methods of treatment which were employed were as shewn:-

- (1) Conservative - Ergot and Quinine.
- (2) Modified Conservative - (Ergot and Quinine
(1 dose (20 c.c.) scarletinal
(antiserum.
- (3) Intra-uterine glycerin injections.
- (4) (Intra-uterine glycerin injections.
(20 c.c. scarletinal antiserum.
- (5) (Intra-uterine glycerin injections.
(Metarsenobillon.
- (6) (Intra-uterine glycerin injections.
(Vitamin A.
- (7) /

treated by strictly conservative routine. Glycerin, if employed without general treatment, gives a period of pyrexia averaging almost a fortnight; but this is equalled when M.A.B. is also injected, and exceeded if vitamin A is used. Patients treated only by general methods provide a slightly higher figure. The modified conservative routine, however, compares favourably in this respect with the glycerin methods, apart from the combination of glycerin and serum above noted. As far as primary pyrexia goes, therefore, glycerin and serum method gives the best results; while the conservative routine without local or general treatment is least beneficial.

With regard to Hospitalization, it is found that the combination of glycerin with serum is again most useful, although the use of Serum alone and of glycerin alone are only slightly less effective. Vitamin A and M.A.B., either alone or when combined with glycerin, are much inferior, and in this category also are the conservative and modified conservative methods. It is to be remembered, however, that there were deaths in all series. Although several of the fatal cases had a long protracted illness before death, few survived beyond the average period for their series, and the duration of hospital treatment is thus comparatively low in those with the higher death rate.

Analysis of the various complication rates shews that the use of intensive serum produces outstanding results under this heading. If local treatment is given in addition, the complication rate rises. Indeed glycerin treatment alone, or when combined with general methods, provides a figure exceeding that obtained with the modified conservative routine. Vitamin A and M.A.B. are also both followed by a high rate.

The mortality rate is again lowest in the cases receiving general serum treatment without local interference, and/

and even the modified conservative routine gives a figure lower than all other methods. Glycerin alone, or in combination with M.A.B. or Vitamin A, yields a rate almost equal to that obtained even by the strictly conservative method; although when serum is given the figure is little above that for the modified conservative group.

The statistical analysis of the Post Abortum cases of this group is shewn in Table 20.

TABLE 20.

Table shewing the relationship of type of treatment to average period of primary pyrexia and of hospitalization and to complication and mortality rates of Post Abortum Cases of Group III.

Treatment.	No. of Cases.	Primary Pyrexia. (Days)	Hospital Treatment (Days)	Complication Rate %	Mortality Rate %
E + Q	3	14.3	45.7	33.3	33.3
E+Q+S	8	9.8	37.4	12.5	-
G.	3	11.6	38.8	33.3	-
G + S	8	9.5	37.3	25.0	12.5
G + M.A.B.	5	13.4	40.1	60.0	20.0
G + V.A	2	16.5	18.5	50.0	50.0
S.in.	3	20.0	41.1	66.6	-
M.A.B.	3	25.4	47.2	33.3	33.3
V.A	6	18.8	50.6	33.3	-

E = Ergot.

Q = Quinine.

G = Glycerin.

S = Serum.

M.A.B. = Metarsenobillon.

V.A = Vitamin A.

S.in = intensive serum.

It will be noticed that in all of the series the numbers concerned are very small. Statistics concerning them/

them should therefore be accepted with considerable mental reservation.

With regard to Primary Pyrexia, it is seen that the lowest figures are obtained in the cases treated with glycerin and serum, and in those dealt with on modified conservative lines. Disappointing results are obtained with repeated doses of serum and no local treatment. This is however explained by the fact that of the three cases in this series one developed secondary Septicaemia and the pyrexia was continuous from admission. In the M.A.B. group there was a similar case, and the average primary pyrexia thus reaches an abnormally high figure.

The figures for Hospitalization are an average for all cases, and are therefore materially affected by the fatalities in each series. Glycerin treatment alone, glycerin with serum, and modified conservative routine, give the lowest figures; but as the first of these series contained only three cases, only the two latter are comparable. Local treatment with glycerin when pursued in conjunction with general Vitamin A medication gives a low figure; but this is to be explained by the fact that the series contained only two cases and one of these proved fatal after a comparatively short illness. Apart from illustrating how misleading mere figures may sometimes be, there is really nothing to be learned from a survey of the figures in this column.

All types of treatment were followed by complications. Of the only comparable series - Glycerin with Serum, and the modified conservative method - the former had the higher rate; but it is unwise to draw any conclusions where so few cases are involved.

The complications occasionally appeared early in the illness, and in some of the other series might almost have been regarded as part of the original condition.

The/

The mortality rate was nil in the cases treated by repeated doses of serum, and in the modified conservative group. All the glycerin series contained fatal cases, although in the series treated with glycerin and serum only one death - from Peritonitis - occurred. The absence of fatality in the six cases of the Vitamin A group is interesting, but lends itself to interpretation and is therefore inconclusive.

It appears, therefore, that in Group III

(1) Although the use of intra-uterine glycerin injections - especially when in combination with general treatment by serum - may give a smaller period of initial pyrexia, this type of treatment is followed by more complications and by a greater death rate than are obtained by intensive serum administration without local interference.

(2) M.A.B. and Vitamin A, either alone or in conjunction with glycerin injections, give a higher complication rate and a greater mortality rate than any other method of treatment, with the exception of the strictly conservative routine.

(3) In Post Abortum Cases, - if the single fatality in the glycerin and serum group is taken into account - the best all round results are obtained by refraining from any local treatment. The advantages - if any - of repeated dosage of serum, instead of a small initial injection as in the modified conservative series, cannot be estimated with the figures available.

Group IV Cases.

This group consisted of 112 patients. Of this number 95 were full time and 17 post abortum infections. The methods of treatment which were employed were:-

- (1) Modified conservative treatment - (Ergot and Quinine
(1 dose (20 c.c.) Scar-
(letinal antiserum.
- (2) (Intra-uterine glycerin injections.
(M.A.B.
- (3) Vitamin A.
- (4) (Intra-uterine glycerin injections.
(Repeated intramuscular injections of serum.
- (5) Intravenous serum injections (Intensive Serum).

The results obtained in the Full Time Cases are shown in Table 21. On account of the high mortality rates it was not possible to determine complication rates for cases in this group, and this factor does not therefore enter into the statistical survey.

TABLE 21.

Table shewing the relationship of type of treatment to duration of primary pyrexia, duration of hospital treatment and mortality rate in Full Time Cases of Group IV.

Treatment.	No. of Cases	Primary Pyrexia (Days)	Hospital Treatment Days.			Mortality Rate %
			All Cases.	Fatal Cases.	Recovered Cases.	
E+Q+S	30	-	6.68	6.68	-	100
G + M.A.B.	8	-	6.3	6.3	-	100
V.A	15	30.7	^{20.5} 20.5	^{7.1} 7.1	57.5	⁸⁰ 80
G + S	10	22.6	^{24.3} 26.5	^{7.0} 5.75	48.9	⁵⁵ 60
S.in.	32	12.3	^{31.5} 23.6	^{17.1} 10.6	44.8	^{48.2} 68.8

E = Ergot.

Q = Quinine.

G = Glycerin.

S = Serum.

V.A = Vitamin A.

M.A.B. = Metarsenobillon.

S.in = Intensive serum (intravenous).

This is a group of cases which form the most searching test of any method of treatment, by reason of the fact that there is in them a more or less massive local infection associated/

associated with a grave constitutional disturbance. The results obtained, therefore, are materially worse than in the previous groups. A reference to the adjoining table shews that all patients treated by modified conservative routine, and those who received glycerin in conjunction with M.A.B., succumbed to their infection. These need not be further discussed. With regard to the remaining three series, it will be observed that the intensive serum treatment gives a materially lower average primary pyrexia than either of the other methods.

The question of Hospitalization is of interest from the point of view of the fatal as well as the recovered cases. In the former it may be regarded as a measure of the extent to which the treatment helped the patient to resist the disease if it did not save her life; and the method which prolongs life to the greatest extent is the direction in which most hope lies. When each series is subdivided in this way, therefore, Intensive Serum treatment is found to be of most value, while Vitamin A, Glycerin with M.A.B., modified conservative routine, and Glycerin with Serum come next and in the order given. There is, however, another important factor to be considered. Several of the series include patients who were admitted to hospital moribund and died within 48 hours. It is unlikely that in these patients, treatment, although given at the earliest possible moment, could have any real effect on the course of the disease. If they are withdrawn from their series, the revised order becomes Intensive Serum, Serum with local glycerin treatment, Vitamin A, modified conservative routine, and Glycerin with M.A.B. In Table 21 the small red figures indicate these corrected results. The great superiority of intensive Serum treatment thus becomes apparent. Patients receiving this survived twice as long as any other patients of the group, and those who recovered were fit for dismissal

four/

four days sooner than the glycerin series, and nearly fourteen days earlier than those who recovered as a result of Vitamin A treatment.

The question of complication rate is scarcely applicable in this group where so many cases proved fatal. Most patients shewed signs of spreading infections before death, and pyaemic foci frequently occurred.

With regard to mortality rate, it is to be noted that all patients treated on modified conservative lines, and all those treated with M.A.B., ended fatally. There were a few recoveries in the Vitamin A series, and in the intensive serum series a little more than half proved fatal. The lowest rate is, however, with the Glycerin and Serum patients; but a personal factor must here be presumed, since the cases chosen were probably of slightly less severity.

Analysis of the Post Abortum Cases reveals the figures found in Table 22.

TABLE 22.

Table shewing the relationship of type of treatment to average duration of primary pyrexia and hospital treatment, and to fatality rate in Post Abortum Cases of Group IV.

Treatment.	No. of Cases	Primary Pyrexia (Days)	Hospital Treatment Days.			Mortality Rate %
			All Cases.	Fatal Cases.	Recovered Cases.	
E+Q+S	4	-	6.0	6.0	-	100
G + M.A.B.	3	-	15.5	15.5	-	100
G + S	2	-	27.5	27.5	-	100
V.A	3	28	32.5	10.0	53	66.8
S.in.	5	9	9.8	2.5	42.9	8.0

E = Ergot.

Q = Quinine.

G = Glycerin.

S = Serum.

M.A.B. = Metarsenobillon.

V.A = Vitamin A.

S.in. - Intensive Serum.

These figures confirm those obtained in the preceding analysis of Full Time Cases. It is again to be noted that the number of cases is extremely small in each series, and that reliable statistical conclusions are not possible. There are certain points, however, to which attention might be drawn.

There were no recoveries as a result of either M.A.B. or modified conservative treatment; and while both of the cases who received local treatment with glycerin combined with general serum administration were also fatal, the resistance which they shewed was considerable. At first sight the recovery rate with the Vitamin A cases is disconcerting. It is to be remembered, however, that there were only three cases in this series, and although one recovered, the others rapidly proved fatal. The single patient who recovered was febrile for 28 days and subfebrile for an equal period, and was in hospital almost eight weeks before dismissal. An analysis of the patients in the series receiving intensive serum treatment reveals that two were moribund and died within 48 hours of admission to hospital, whereas the remaining two fatal cases reacted well to treatment for several weeks, but succumbed later to broncho-pneumonia.

The conclusions which may be made from this analysis are as follows:-

- (1) Puerperal Septicaemia, however treated, is a highly fatal disease.
- (2) Ordinary conservative methods are useless in treatment.
- (3) The combination of M.A.B. with glycerin treatment has no effect even on the mildest cases of either full time or post abortum groups.

(4) /

(4) Intra-uterine treatment with glycerin if pursued in addition to intensive serum treatment may be of value in the less severe infections where the patient can be moved without great detriment and the pelvic sepsis is mainly intra-uterine.

(5) Intravenous serum injections alone, or with the addition of saline infusions, give most hope of recovery in all cases. The period of life is increased in those who die, and the duration of hospital treatment is diminished in those who recover.

GENERAL CONCLUSIONS.

The foregoing analysis, it is suggested, proves conclusively that there can be no rule or system of treatment defined for this disease. Each patient must be considered individually and a method adopted which is suited to her particular needs. Some writers lay stress on the routine use of glycerin, while others claim that the combined action of lymph drainage and chemotherapy offer the greatest hope of recovery. Finally, there are those who maintain that the administration of Vitamin A is the only rational treatment for what they aver is essentially a deficiency disease. Such standardised methods of treatment can only pave the road to disaster.

The experience of Group I cases treated herein shews that these do not require any special intervention. A small dose of specific serum appears to prevent any tendency to generalized infection, and simple cleansing will supply any local attention which may be required. It is possible, however, that in the full time cases intra-uterine glycerin injections will/

will provide a better final result, that is, more complete involution; and as the statistics also shew, fewer complications will develop. Such a finding is not absolutely in accordance with the personal estimate, since it appeared that intra-uterine interference should be avoided in these mild cases. But although the immediate results of non-interference may be good, this assessment is prejudiced by the fact that such a method is followed by a higher complication rate. Intensive local treatment may thus eventually prove beneficial. Post abortum cases should, however, be left untreated locally, and in this respect the statistical analysis is in entire agreement with the personal findings.

The patients of Group II are those most suited for the glycerin regime. In these cases the chief aim of treatment is the establishment and maintenance of uterine drainage, and for such a purpose glycerin medication is both an effective and safe proceeding. The actual method of this action is still debatable, and it is probable that the glycerin is not alone of chief importance, but that the daily inspection and cleansing, and all the other elements of the régime are equally valuable. These women are, however, toxic to a greater or less extent, and some method of general treatment is therefore in addition necessary. For this purpose specific serum has proved most effective. Metarsenobillon - the *panacea* of so many observers - has been found valueless, and unjustifiable as a routine measure, and Vitamin A has been demonstrated to be equally disappointing. Conservative or modified conservative treatment is for patients in this group entirely unsatisfactory. These statistical results are on the whole in accordance with the personal estimate clinically obtained. There are, of course, variations of severity within the group, and some patients present such marked toxæmia at the outset that only after a few days can any local treatment/

treatment be with safety employed.

With regard to the post abortum series of Group II, the statistical and personal findings are however slightly at variance, since the former contra-indicates local treatment, whereas the latter justifies it. It has been shewn that if the retained products are very foul, a few daily glycerin injections appear to make digital curettage a less dangerous procedure. In many cases also there is a purulent blood stained lochia which persists for several days after the womb has been emptied; and although the glycerin is rarely retained in the small post abortum uterus, it acts very beneficially as a douche. A few women of this group however were found to have very septic retained products, and in these local interference had an adverse effect on the course of the disease. Thus they materially affected the average for the other cases. On the whole, intra-uterine treatment should therefore be employed, but with caution, in the post abortum cases just as in the full time infections of this group; and if prophylaxis is at the outset established, the risks of further spread are after all few.

In a consideration of the Group III cases, the main fact which emerges is the problem of determining the best mode of treatment. Patients presenting gross pelvic infection without much intra-uterine sepsis do not offer much difficulty, since the glycerin treatment is usually inapplicable. On the other hand, if there is marked intra-uterine sepsis, there is always a strong feeling that if intensive treatment were directed toward the basic septic endometritis, the remaining pelvic infection would automatically come under control. This theory is keenly supported by Hobbs, and he continues the glycerin injections even when the peritoneum has become acutely involved. Such teaching is not easy to justify in the light of clinical findings. The necessary manipulation, movement into theatre, raising of the/

the pelvic level, and alterations in position of the uterus all tend to spread the pelvic lesion; and no amount of glycerin medication will limit the spread of an infection from the pelvic peritoneum into the general abdominal cavity, or will cure the wider infection once it has developed. In a few such cases of spreading inflammation, intra-uterine treatment was pursued with disastrous effects, and instead of localization, further extension of the disease was merely produced. The chief difficulty lies in ascertaining that there is no pelvic effusion, or that the infection is not of the virulent type which requires only a little movement of the uterus to provoke its advancement to the peritoneal surface.

The conclusion arrived at, therefore, is that for the patients of Group III the general methods of treatment are in the main indicated. Intra-uterine injections of glycerin may be administered with safety in the mild infections, but in the more severe forms it should be discontinued, as local interference in all such cases should be minimal. The statistics shew that specific sera are a justifiable method of treatment, and that repeated doses should be administered in most instances. The patient should be placed in a suitable posture for uterine drainage, in the further hope that effusions will in this way be localized to the pelvic area. Should general peritonitis supervene, this strict régime should be adhered to without any further form of interference, laparotomy - even at the first sign of this complication - having proved of little value. This is the group in which any specific value possessed by Vitamin A will be apparent. Failing that, however, it may be relied upon to produce a general tonic effect which, by raising the general resistance, may result in a limitation of the local infection. Metarsenobillon with the uncertainty of its action and the discomfort following upon its injection has little to recommend it.

The post abortum cases of Group III present similar problems. Usually these infections are of a virulent spreading type, and once sepsis has progressed beyond the wall of the uterus it seems wise to refrain from pelvic interference as far as possible. Although intra-uterine treatment may be followed by temporary local benefit, signs of further involvement are sooner or later manifest. The statistics do not adequately represent this, but it is a fact which has always been impressive; and while there may be a few immediate recoveries after glycerin injections, it is on the whole advisable to restrict treatment to the intensive general remedies in these cases.

The statistical review of Group IV patients confirms generally the personal estimate obtained in practice. Many of the cases were moribund on admission, and although no avenue of attack was left unexplored, it was obvious from the outset that the various methods of treatment under review could not have even a transitory effect on the further course of the disease. There were a few, however, for whom judicious treatment probably turned the balance towards recovery.

The analysis shews that any conservative method is of no value at this stage of the disease - a finding which is in accordance with the clinical experience. It would appear that a more specific method of treatment is essential if blood infection is to be controlled; and that rapidity of action is of primary importance. The statistics shew that Metarsenobillon has neither of these attributes, and that in established Septicaemia this drug is valueless. It appears also that dosage with Vitamin A may benefit a few patients; but its action in this connection is so slow that any betterment might possibly be attributed to the bactericidal powers of the patient herself, or to the general effects of hospitalization. Those who recovered as a result of this mode of treatment were /

were febrile for many weeks and were in hospital for several months; whereas those who died gave little evidence of an enhanced resistance which could be traced to this source. It may be that in certain less virulent types of Septicaemia free administration of vitamins will result in a gradual increase of resistance towards the infection, until finally the invading organisms are overcome; but few cases of Puerperal Septicaemia are of this mild type, and when found they give much less cause for alarm than do the highly virulent infections which must be ruthlessly attacked before they have so affected the essential systems as to determine a fatal issue.

Specific serum of the scarletinal type has proved to be of some value in a minority of these cases, and here again the statistical findings are in correspondence with the clinical. Although a few patients react quickly to small doses of this serum - and in these the infection is presumably due to a homologous organism - there are others who appear to be more gradually affected and for them repeated dosage at daily intervals may prove beneficial. In a small number of the less virulent infections intra-uterine treatment may be pursued concurrently and with some advantage; but in the more serious forms local interference cannot be too strongly deprecated, and this is specially true of the post abortum type where the desire to explore the uterus is often very strong.

An analysis of the fatal cases in the whole series reveals the fact that in 69 per cent. of the total, death resulted from blood infection; and the vast majority of Group IV patients are therefore not materially affected by any of the methods here analysed. It is these cases which constitute the real problem of treatment in puerperal sepsis.

FINAL CONCLUSIONS.

An analysis of the lesions found in 800 cases of Puerperal Sepsis shews that they are capable of classification into four broad types of infection. In the first group the disease is limited to the lower parts of the genital tract, whereas in the second there is evidence of an intra-uterine infection. Spreading pelvic inflammation involving Fallopian tubes, cellular tissue, or peritoneum is found in the third group; while the fourth or final group includes all cases of blood infection without regard either to the virulence or extent of the local lesion. There are degrees of severity within each group; but on the whole the gravity of the infection increases, and prognosis becomes more uncertain in the sequence above given. A bacteriological examination also shews that the frequency of streptococcal infections increases in the same order; and that in the most serious type of the disease, this organism is present in the blood or uterus in 75 per cent. of cases, and is the determining factor in the ultimate issue.

A critical review of the results obtained in the treatment of the above cases shews that methods of local treatment are restricted to those included in Groups I and II. Of the various types of such treatment, intra-uterine glycerin injections gave the most satisfactory and reliable response; whereas the oral administration of Ergot and Quinine was not followed by the good results claimed by certain authors.

The patients of Group III and IV present special and individual problems. The majority of the fatal cases are in these series, and if the mortality from Puerperal Infection is to be controlled by treatment, it is essential that the measures directed against it should be along more specific lines. An analysis of these patients reveals the serious fact/

fact that in 70 per cent. of cases the streptococcus was the causal agent.

The problems of general treatment presented by these groups are essentially similar to those of the preceding groups, though of a more intense character. In all cases, irrespective of grouping, the use of a scarletinal anti-serum,-in default of a specific serum for the streptococcus of Puerperal Sepsis,-constitutes the only rational measure at present available. As applied to the less severe infections of the earlier groups, such a serum will have, in the main, a prophylactic value; but the more serious infections demand its administration intravenously at the outset, on repeated occasions, and in a dosage to be determined by the nature of the response obtained.

With regard to the other suggested methods of general treatment, - Metarsenobillon and Vitamin A - and taking the cases as a whole, this inquiry has demonstrated conclusively that they possess no remedial properties which justify their administration.

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