LEUCORRHOEA IN PREGNANCY:

ADVANCES IN THE KNOWLEDGE OF ITS ETIOLOGY LEADING UP TO MORE RATIONAL TREATMENT, WITH A CLINICAL AND EXPERIMENTAL STUDY OF 408 CASES

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INTRODUCTION.

Many authorities say that leucorrhoea is the most frequent gynaecological complaint for which relief is sought and its importance depends on the inconvenience it causes the patient, the psychic factor involved, the accompanying irritation and the fact that it is frequently a guide to underlying disease.

There have been many definitions applied to leucorrhoea and the concepts in them have wide variation. For instance Munro Kerr[1] says that the term should include only those conditions in which there is merely an excessive amount of the normal whitish secretion referred to by the patient as "whites", and Davis[2] looks upon it as essentially a pathological state, calling it "the objective expression of a diseased condition", while Bland and Rakoff[3] aver that it is "an expression of some underlying disorder either functional or organic, having its origin in most instances in some lesion of the reproductive organs".

Although leucorrhoea may be classed as a minor ailment it is frequently a major annoyance to the patient, and although, in the majority of cases, it is of no danger to life and does not usually cause direct illness it is responsible for a large amount of distress, anxiety and local discomfort which, if long continued, can gradually wear down the health, both physical and mental, of the individual which in pregnancy is already under increased strain.

In recent years there has been much research on the nature and origin of the various types of discharge and fresh investigations have been made on the conditions which govern the normal vaginal secretions. The advances in the knowledge of its etiology and pathology, resulting in more rational treatment, have been of immense benefit to womankind.

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THE BACTERIAL FLORA OF THE VAGINA.

The early studies of the bacterial flora of the vagina were directed to the detection of pathogenic organisms whose presence in these situations might explain the occurrence of septic infections following childbirth. In 1887 Goenner[4] made a study of the vaginal secretion of pregnant women and stated that it did not contain the bacteria usually found in cases of puerperal infection, and that although organisms were present in abundance they did not grow on ordinary media. Later in 1892 Döderlein[5], when investigating the vaginal secretion of pregnant women, described the bacillus to which his name is attached and he demonstrated that the vaginal secretion of many pregnant women shows an extremely simple and almost homogeneous bacterial flora and his findings were corroborated by others, including Kronig[6] (1894). Because of the marked contrast between the simplicity of the bacterial flora of the vagina and the heterogeneous collection of organisms of the external genitals it was assumed that the vaginal secretions possessed bactericidal powers and this led Döderlein to study the cultural characters of the vaginal bacillus with a view to demonstrating this property. He found that considerable quantities of lactic acid

were formed by it and that in mixed cultures with staphylococci the latter were quickly killed by the resulting acid condition. As a result of his investigations he concluded that the bactericidal mechanism of the vaginal secretion in pregnancy was due to the acid produced in the secretion by the growth of the vaginal bacillus.

In 1899 Tissier[7] isolated from the stools of breast fed infants by anaerobic methods a gram positive, non-motile, non-sporing bacillus which produced acid but no clot in milk and which fermented certain of the carbohydrates without gas formation. In the following year Moro[8] reported the isolation from infants' faeces of a somewhat similar organism which was a facultative anaerobe and formed characteristic feathery colonies in deep beer-wort agar. From its supposed enrichment in acid medium Moro called the organism B Acidophilus. These acid resisting intestinal organisms have been included in the class of lacto-bacilli which have as their chief characteristic the formation of lactic acid. Orla-Jensen[9] (1919), however, separates the intestinal group from the true lactic acid bacilli because of the ability of the former group to reduce nitrates and show surface growth and a further distinction is their habitation to the intestinal canal. The aciduric group

of intestinal organisms is apparently saprophytic and is non-pathogenic to laboratory animals but a member of the group B Acidophilus odontolyticus has been regarded as the causal agent of dental caries. In this group of acid-resistant organisms must be included Döderlein's vaginal bacillus - the predominant organism in the healthy vagina after puberty and often present in practically pure culture during pregnancy. It has the morphological and cultural characteristics of the group and is possessed of the same acid resisting properties. These early discoveries of Döderlein and his contemporaries have stimulated other workers more recently to study the bacterial flora of the vagina in relation to leucorrhoea and although the general belief is still in accordance with Döderlein's view some doubt was cast on the protective ability of the acidophilus group of vaginal bacilli by Weinstein[10] in 1938 and again by Carter, Jones, Ross and Thomas[11] in 1940 who noted the occurrence of trichomonads in 9 patients whose smear showed only gram positive rods of Döderlein's type.

THE DEPOSITION OF GLYCOGEN IN THE VAGINAL EPITHELIUM AND ITS RELATIONSHIP TO OESTROGEN.

In 1920 Loeser[12] demonstrated the important rôle of Glycogen in the protective mechanism of the vagina. He showed that under constitutional conditions when the vitality was lowered the functioning power of the epithelium appeared to be lessened through loss of glycogen. In 1927 Lehmann[13] corroborated Loeser's view and stated that the exfoliation of superficial vaginal cells laden with glycogen was essentially defensive, while in the same year Dierks[14], from the examination of excised human vaginal mucosa, expressed the opinion that the vaginal mucosa had a strict dependence on the cyclic functional processes of the sexual apparatus.

Muira[15] showed in 1928 that man and monkey are the only animals in which glycogen has been demonstrated in the vaginal epithelium and those others examined were the cat, rat, dog, rabbit, guineapig (Muira[15]) and pig, lamb and squirrel (Bremicker[16]). He made observations on women following double ovariectomy which corroborated his experimental findings in monkeys in which after ovariectomy glycogen completely disappeared from the vagina.

In 1934 Cruikshank and Sharman[17] made a study of the vaginal epithelium from 63 patients of varying ages and found that a deep and well-formed vaginal epithelium containing abundant glycogen was found in the foetus and during the first few days of life, and that it changed gradually thereafter to a thin flat type devoid of glycogen. They found that this atrophic epithelium persisted until the onset of puberty when a marked change took place and the epithelium again became florid and was laden with glycogen. It persisted in this state until the menopause, when atrophy of the epithelium took place. There was thus shown to be a close association between the vaginal epithelium and ovulatory activity and Dierks[14] claimed to have produced an increase in the thickness of the vaginal mucosa in a young girl whose ovaries had been excised by the administration of ovarian-active substance. Cruikshank and Sharman[17] attempted to prove that not only is the deposition of glycogen in the vaginal epithelium dependent upon ovarian activity in a general sense but upon the presence of the female sex hormone oestrin in the circulation. They examined the urine of infants and showed that oestrin was present in excess in the urine of newly born children and that it rapidly disappeared during the succeeding days of life, while in no case was

anterior pituitary hormone demonstrable and they therefore concluded that this had passed via the placenta to the infant's circulation which they said explained the thickness of the vaginal epithelium in the infant.

THE HYDROGEN ION CONCENTRATION OF THE VAGINAL SECRETIONS.

It is generally accepted that the normal vaginal discharge of adult women is acid in reaction, but it is only within recent years that much attention has been given to its hydrogen ion concentration in association with the alterations which are developed in the individual by physiological changes and by disease.

Döderlein[5] himself, having postulated that the acidity was due to lactic acid formed by the vaginal bacillus, certainly noted that the acidity was reduced in certain pathological conditions involving infection, and later Menge[18] demonstrated that the acidity of the normal discharge is sufficient to kill streptococci in from 2½ to 70 hours, and therefore the conception developed that the acid reaction offers an element of protection.

Stroganoff[19] showed that the vagina contains bacteria throughout life and that the acidity varies with the flora, being higher during sexual maturity and especially during pregnancy when the vaginal bacilli are most numerous, and later Cruikshank and Baird[20] have also brought forward evidence to show that a high degree of acidity is normally maintained during pregnancy.

To keep up this acidity there must be a fermentable carbohydrate as a precursor and because of the presence of glycogen in the wall of the vagina it was considered by Kronig and Menge[21] that glycogen was possibly the substance concerned. However, Rother[22] and again Muira[15] showed by their experiments that serum and ascitic fluid enhanced the growth of Döderlein's bacillus only so far as these fluids contained glycogen but that glycogen is not fermented by cultures of the vaginal bacillus until it is converted to glucose by enzyme action. It has been suggested by Gragert[23] that the vaginal mucosa may contain a diastatic ferment which changes the glycogen to glucose.

Robert Cruikshank[24], in a paper on the conversion of the glycogen of the vagina into lactic acid, brought forward evidence to show that this is effected by Döderlein's vaginal bacillus, and more recently

Oberst and Plass[25] in 1936 studied the hydrogen-ion concentration of the human vagina, using a special capillary quinhydrone electrode, and found variations in the hydrogen-ion concentration at different stages in the menstrual cycle. They showed that immediately succeeding the onset of menstruation and after parturition there is a marked reduction in the acidity of the vaginal contents which may explain the relief of symptoms in cases of vaginal thrush and the increase in severity of symptoms in cases of trichomoniasis at these times. They also showed that the acidity varied with the character of the vaginal flora and was higher as the number of the vaginal bacilli of Döderlein increased, and they demonstrated that in general the pH was slightly higher in pregnant than in non-pregnant women and somewhat lower in the upper than in the lower vagina.

In 1940 Trussell and MacDougal[26] repeated the experiments of Oberst and Plass, using recently developed glass electrodes of a high degree of accuracy and permitting of rapid and accurate determinations in vivo, and they found that in late pregnancy the acidity is highest in the middle portion of the vagina with the region just inside the introitus being somewhat less acid and the cervix and upper vaginal fornices having an alkaline or only slightly

acid reaction. This last finding they considered due to the admixture of cervical mucus. Consistent with the observations by others that monilia are most frequently present in the more acid discharges while trichomonads are favoured by a less acid reaction, they found the monilia more easily cultivated from the middle vagina and the trichomonads from the upper portions near the cervix.

THE ASSOCIATION BETWEEN OESTROGENIC ACTIVITY, DEPOSITION OF GLYCOGEN, HYDROGEN-ION CONCENTRATION AND THE BACTERIAL FLORA OF THE VAGINA.

Cruikshank and Sharman[17] showed that when glycogen is present, as in the new-born infant and during the reproductive period, a homogeneous bacterial flora and highly acid secretion appear and that when glycogen is absent the secretion is scanty and alkaline and the bacterial flora usually varied. It seemed obvious to them that the glycogen was being utilised with the consequent production of acid which soon reached such a concentration that only acid-resistant bacteria such as Döderlein's bacillus could survive and multiply. They postulated that in this

way a defence mechanism is produced in the vaginal cavity capable of preventing the establishment there of foreign and possibly harmful bacteria.

It would appear, therefore, that there exists a direct association between the activity of the ovaries, the deposition of glycogen in the vaginal walls, the presence of the Döderlein bacillus and of lactic acid in the vaginal secretions and the experimental work has been corroborated by Muira[15] and Dierks[14] in their observations on the human subject following double ovariectomy. It is also highly probable that if there is a diastatic ferment present in the vaginal epithelium one function of oestrogenic activity may be to activate it and thus allow of the glycogen, whose deposition in the vaginal wall it aids, being converted into glucose, to be in turn split up by Döderlein's bacillus with the production of lactic acid.

In pregnancy it seems that the protective mechanism is developed to a high degree as pregnancy advances and the explanation of this phenomenon is probably associated with the over production of oestrin which occurs in pregnancy and which we believe is responsible for the deposition of glycogen in the vaginal epithelium. This increased deposition of glycogen may account for the excess of dis-

charge in some pregnant women which is proved to be non-pathogenic and which could not be explained away by increased varicosity or congestion of the parts.

We may conclude, therefore, that an obvious effort is being made to produce in the vagina, towards the end of pregnancy, a natural environment which is inimical to the entry of foreign pathogenic bacteria and one should bear this in mind before deciding to use antiseptics for disinfecting the vagina, and should find out first whether the natural mechanism of defence exists already as indicated by the hydrogen-ion concentration, the extent of deposition of glycogen and the bacterial flora present. In this connection Colebrook and Maxted[27] have shown that indiscriminate attempts to sterilize the vagina by mercurochrome, dettol, etc., or antepartum douches, have often resulted in the replacement of a non-pathogenic flora by other potentially pathogenic bacteria.

APPLICATION OF KNOWLEDGE TO CLINICAL WORK.

In the application to clinical work of the bacteriological findings in cases of pregnancy several workers have divided their cases into three main

groups corresponding to the 'grade of cleanliness', as it has been called (Schröder[28]). In the first group the vaginal secretion is described as being tough, milk white and highly acid, with a pH of 4.3 to 4.9. Numerous Döderlein bacilli are present and there are a few epithelial cells. In the second group the secretion is said to be thinner in consistency, the colour is yellowish, the pH is 4.6 to 5.0, some leucocytes are present and cocci are present in considerable numbers with a few Döderlein bacilli. In grade three the reaction is 5.2 to 6.8 and there are many pus cells. There are no Döderleins, but there are coliform organisms, staphylococci, diphtheroids, and sometimes yeasts and trichomonas vaginalis.

While it is true that there are definitely three distinct grades or types of bacteria into which cases may be divided, we do not always get the types of discharge and organisms in association as described above and it appears much more rational to divide cases into groups according to the causal agent concerned as there appears to be a definite relationship between the findings in the members of each group.

Liston and Cruikshank[29] in a series of 200 cases of leucorrhoea in pregnancy attempted to correlate the cause of leucorrhoea with the relative proportion

between epithelial cells and leucocytes, the character of the bacterial flora, the hydrogen-ion concentration of the vaginal contents and the state of the vaginal epithelium in respect of glycogen deposition. To assist them in their investigations Liston devised a vaginal sampling pipette which greatly facilitated their work. Having had experience in the use of this pipette, I am convinced that it is a piece of apparatus which in practice or at clinics would be a great boon, for it would enable the doctor to secure a good specimen in suitable medium from which much useful information could be obtained, and which could be examined at the convenience of the investigator.

Although they found no clear cut dividing line between the findings in the groups due to separate causal agents, yet the findings in each group were on the whole very consistent. Of 40 normal cases, epithelial cells were in excess of pus cells in all but 9 cases, the flora was Type I. in all except 1 case, the pH was between 4 and 5, approximating to 4 in all cases except 2 who had incontinence, and the glycogen content of the epithelium was abundant in all. Forty-nine cases of vaginal thrush were examined and in all of them, with only 2 exceptions, pus cells were more numerous than epithelial cells, the flora were somewhat varied, 13 being Type I., 19 Type II.

and 17 Type III., the pH was between 4 and 6 in those tested, and the glycogen was generally fairly abundant when examined.

Seventy five cases of trichomonas vaginalis were examined and in all of them pus cells were in excess of epithelial cells, 62 of the 75 shewed a Type III. flora and the pH readings shewed 23 between 5 and 6, 6 higher than 6 and 5 lower than 5 of the 34 tested, while glycogen was notably generally deficient.

Thirty one cervical cases were examined and in these pus cells were in excess of epithelial cells in all but 4 cases, 15 had Type I. flora, 9 Type II. and 7 Type III., the pH approximated to 5 and glycogen was generally deficient in the epithelial cells.

In the 4 gonococcal cases in the series pus cells were greater than epithelial cells in number and all of them had a Type III. flora. The other factors in this group were not estimated.

While in charge of the leucorrhoea clinic at the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, the author, working in association with Liston, continued investigations on the above lines and noted that although the history is often very suggestive of a particular infection and a typical case of each presents very definite clinical

characteristics upon which one can make a pretty accurate provisional diagnosis, yet the atypical case is frequently to the fore and we must rely upon the microscope for our diagnosis. We concluded from our observations that in the first instance a pretty clear distinction can be made between the normal and the abnormal on examining a fresh preparation made by mixing some of the discharge with normal saline on a slide, to which may be added a drop of 1% saffranin, and examining under the microscope either directly, while the patient is still on the table, when apparatus is available as was so at our clinic, or later from a specimen of discharge obtained by means of Liston's sampling pipette. In the normal case one finds:

(a) The number of epithelial cells is greater than the number of pus cells.

(b) Normal Döderlein flora are present which can be readily recognised by the experienced eye without staining.

(c) No parasites are seen.

(d) There is abundant deposition of glycogen in the epithelial cells as demonstrated by the golden brown staining of the epithelial cells when a drop of iodine is added.

(e) The pH is within normal limits, i.e. between 4 and 5, approximating to 4.

We found that any departure from these 5 findings generally meant that the case was abnormal and indicated the necessity for searching for a cause. We also concluded from our observations that the above factors in the vaginal discharge are not only helpful in coming to a diagnosis but are also an index of the degree and chronicity of infection and of the progress towards recovery when examined at intervals during the period of observation and treatment.

CLASSIFICATION OF LEUCORRHOEA.

Leucorrhoea may be divided into two broad groups - (a) physiological, and (b) pathological. In the physiological group of cases the vaginal mucosa becomes thicker with an accompanying hypersecretion during pregnancy due to increased production of oestrin, and also there is a further tendency to hypersecretion by reason of the increased varicosity at these times so that some excess of the normal secretions is to be expected and this in some cases may amount to an obvious discharge. The presence of this physiological discharge may give cause for great concern, especially to young introspective pregnant

women whose nervous system is temporarily less stable than normal, and care in explaining this mechanism will be fruitful in allaying nervous tension, with its possible sequelae, in such women. From the psychological aspect alone, therefore, leucorrhoea should never be looked upon lightly and we should take great pains not only to establish a correct diagnosis but also to gain the confidence of the patient and to explain to her in as far as is practicable the mechanism concerned.

Hudgins[30] subdivides the pathological group into (i) local infections and (ii) constitutional factors and I may record here his classification for, while parts of it are interdependent and overlap one another yet it embodies practically all the causes attributed to this condition, some of which, of course, are merely factors which play a part in the production of a soil suitable for the introduction and multiplication of pathogenic organisms.

A. Local Conditions:

1. Venereal
2. Pyogenic
3. Protozoal
4. Yeast-like fungi
5. Verminal
   - Oxyuris
   - Ascaris
6. Miscellaneous
   - e.g. Diphtheria
7. Chemical or irritant
   - e.g. over-douching or too strong solution.

8. Anatomical or Structural Abnormalities
   a. Uterine displacement
   b. Subinvolution
   c. New growths
   d. Foreign bodies
   e. Cervical ulceration
   f. Fistula

B. Constitutional Factors:

1. Anaemia
2. Endocrine disturbances
3. Debilitating diseases
4. Constipation
5. Circulatory or hepatic disease
6. Avitaminosis

THE MAIN CAUSAL AGENTS OF LEUCORRHOEA.

There are four main causal agents of leucorrhoea which account for the great majority of vaginal discharges and I propose now to deal with these in some detail in respect of the progress that has been made regarding them in recent years and of my own findings in a series of 408 consecutive cases examined at the leucorrhoea clinic of the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, of which I was in charge for a period of eighteen months.

These agents are Trichomonas Vaginalis Vaginitis, vaginal thrush, cervical conditions and gonorrhoea, this being the order of frequency of their occurrence in my series of cases. It is only within recent

years that particular attention has been paid to the importance of trichomonas vaginalis and the parasite of vaginal thrush (oidium albicans) as causal agents of leucorrhoea, and so far as gonorrhoea is concerned there has been such a striking reduction in its incidence that we have a relatively greater number of the less serious, though very distressing, cases presenting themselves at our leucorrhoea clinics. One must never, however, lose sight of the potential gravity of the case of gonorrhoea and although the reduction in its incidence since the introduction of the sulphonamide drugs has been very great there has been a relative increase in the last two years due to the present war conditions.

NORMAL CASES.

In my series of 408 consecutive cases there were 113 who had normal findings in respect of the relative number of epithelial cells, type of flora and glycogen deposition. A pH reading was taken of 24 of them and the average figure was 4.3, which is also a normal finding. The complaint in most cases was the noticeable presence of discharge which occasionally caused some local discomfort. On reassuring these patients after examination that no infection was present and after explaining to the more

intelligent of them the mechanism concerned, one was struck by the almost immediate relief from their exaggerated symptoms and in particular the relief afforded to their minds, for suggestion appears to play a big part in the mind of the pregnant woman.

GONORRHOEA.

Gonorrhoea is the most serious form of leucorrhoea both from the point of view of its pathogenicity and its sociological effects, but happily to relate its incidence has been greatly reduced by the recent introduction of the sulphonamide drugs, particularly sulphapyridine and sulphathiazole. Batchelor[31] states that the outstanding advantages of this new chemotherapy are many and far reaching, that it can be and is now being applied with success in all the manifestations of gonococcal infection and that acute gonococcal infections are subdued so quickly that complications seldom arise. Sommerville[32] (1941) in a series of 300 consecutive cases of gonorrhoea found complications in 5 (1.66%) but in 4 of them an exciting cause (alcohol) was demonstrable so that only in 1 case (0.33%) did the drug fail to prevent a complication. With regard to the untoward effects of this drug, rarely has there been a case in the literature of agranulocytosis or of haemolytic

anaemia, though occasionally the patients complain of headache, lassitude, nausea or vomiting, but seldom is it necessary to withhold the drug on account of intolerance. Sulphathiazole has proved to be less toxic with fewer side effects, but I have not used it in my cases in pregnancy in view of its reputed occasional damaging effect upon the kidney - a pyelonephritis with haematuria. Although as Mackenna[33] has explained it is unlikely that any permanent effects accrue from massive therapy, yet in pregnancy it is safer not to use sulphathiazole and to give a moderately intensive course of sulphapyridine in view of the strain which the kidney is already undergoing in the pregnant woman.

In my series of 408 consecutive cases I have had 19 cases of gonorrhoea = 4.7%. Of the 19 cases 7 were associated with a cervical erosion and 6 had also a trichomonad infection. The average pH was 5.67 of 7 tested, but this included 4 who also had trichomonads present. In all cases the flora was Type III. and pus cells were in excess of epithelial cells, and these reverted to Type I. and an excess of epithelial cells soon after the completion of the course of chemotherapy, except in three cases in whom there was an extensive cervical erosion which was still having treatment. Glycogen was found to be

generally deficient but this was most marked in the cases complicated by trichomonads and the amount of deposition steadily increased with improvement in the condition under treatment. All of them had been in the habit of taking liquid paraffin regularly as a laxative and only in two cases was there a complaint of nausea, but this did not prevent them persevering with the drug. The course adopted was to give one tablet four hourly and two at night for three days, followed by ½ tablet four hourly and one at night for four days, making a total of 30 tablets in one week. The patients took their tablets with a soda bicarbonate drink which prevented nausea in all but 2 cases and the gonococci were absent from their smears at their next attendance, in three days' time, with the exception of one case when it was discovered that she had not been taking the tablets as ordered. She was brought into hospital and soon both she and the condition were brought under control.

I am happy to be able to record that during eighteen months in the Simpson Maternity Pavilion, ending in April 1941, there was not one case of gonococcal ophthalmia neonatorum amongst the babies born in the hospital of mothers who had attended the Antenatal Clinic. One attributes this result chiefly to the fact that men, and women too, are presenting

themselves for treatment more readily, to the quick effect of the modern chemotherapy cutting short the opportunity for spread of infection and to the increasing number of women who are taking advantage of the antenatal clinics at which those complaining of discharge are referred for investigation to the leucorrhoea departments.

CERVICAL CONDITIONS.

Cervicitis and its attendant leucorrhoea are a real problem in pregnancy because of the greater discomfort and because of the traditional fear of premature labour if any therapeutic measure is used. The absence of evidence in the literature, however, suggests that the dangers of treating the gravid cervix are somewhat exaggerated. King[34] reports the use of the cautery in 48 women between the 20th and 30th weeks of pregnancy with good results. There was no premature induction of labour and comparison with 140 controls revealed no significant change in the length of labour, the incidence of operative delivery or the morbidity. He takes care to point out, however, that the cautery is not to be recommended routinely or to untrained individuals.

The etiology of cervical erosions still remains rather obscure. Many gynaecologists believe that

the most important causal factor is a chronic pyogenic infection resulting from a laceration of the cervix during labour. They say that after delivery the normal resistance to infection is reduced because the genital tract has been subjected to trauma and the normal acid reaction of the vagina has been rendered alkaline by the passage of lochia.

This may be the explanation in some cases but how are we going to account for the erosions found in primipara? 35% of my cases with cervical erosions were primipara. These cervical erosions possibly depend on the change in the pH of the environment. A woman with excessive cervical secretion will tend to show a change in the character of the epithelium about the os, becoming more like that of the cervical canal and thus appearing as a bright red erosion.

In my series of cases there were 142 = 34.8% with cervical conditions and of that number 45 were associated with a trichomonad infection, 20 with vaginal thrush and 7 with a gonococcal infection. The commonest abnormality among the patients of this group was a large cervical erosion and frequently in the parous women the cervix was noted to be lacerated and there was generally present a profuse muco-purulent discharge coming from it. Included in this

group were 6 cases of cervical polypus.

In all the cases of cervical erosion pus cells were more numerous than epithelial cells, and though the bacterial flora did not belong consistently to any one group, the larger erosions were generally associated with a Type III. flora.

The average pH readings of 18 of the uncomplicated cases tested was 5.2 and after treatment the average pH was 4.48, a reading approximating to normal. There was generally a deficiency in glycogen deposition, though this was not nearly so marked as in the trichomonad cases.

Treatment of cervical erosions in these pregnant women was confined to local applications of picric acid in glycerine followed on healing by painting with the more astringent iodine in alcohol solution except in the early months when the more effective method of cautery was employed.

More research upon the etiology, pathology and classification of this condition is required so that it may be possible to institute prophylactic measures.

TRICHOMONAS VAGINALIS VAGINITIS.

Although it is more than 100 years since the trichomonas was first described by Donné[35], yet it is only within recent years that much attention has

been paid to it as an important cause of leucorrhoea. There has been much controversy as to whether trichomonas vaginalis is a separate species or whether the organisms are interchangeable with those trichomonas found in the mouth and intestines. For instance Wenyon[36] and again Clifford Dobell[37] say that they resemble one another so closely that it is impossible to differentiate them, while Powell[38] in studying living and fixed stained specimens from cultures was convinced that each species retained its identity on culture. Brooke Bland and Rakoff[39] studied the subject in a series of 200 women and showed that women suffering from vaginal infection did not show an appreciably higher percentage of buccal and intestinal infection, and again Liston and Liston[40] in a series of 200 women attending a venereal diseases clinic on account of discharge found only 6 with a buccal infection, all of which showed the true characters of trichomonas in respect of their organelles and only 1 showed trichomonas from rectal cultures and it was typical of the species Pentatrichomonas ardindelteili. They expressed themselves as being convinced that trichomonas infections of the mouth and rectum have no connection with trichomonas infection of the vagina.

In recent years the increased interest in

trichomonas vaginalis and the improved methods for studying the organism have placed it as one of the chief offenders. Bland[41] reports the presence of the organism in 20% of all pregnant women examined and suggests that it may be harboured regularly with clinical manifestations only during pregnancy, and he also suggests that puerperal morbidity may result from this organism at times. In a recent paper on trichomonas vaginalis vaginitis in pregnancy Bland, Goldstein and Wenrich[42] expressed the opinion that under suitable conditions the organism may assume pathogenic proclivities similar to other organisms or in association with bacteria may give rise to serious local or ascending infection of the genito-urinary tract, particularly in the puerperium, while Schmid and Kamniker[43], Liss[44] and again Gragert[23] have investigated the effect of trichomonas vaginalis infection in pregnancy on the puerperal morbidity rate and they all agree that the presence of a vaginal infection with this organism in pregnancy greatly increases the danger of puerperal infection. The puerperal morbidity rate of patients manifesting a trichomonas vaginalis vaginitis antepartum was considerably greater than in those who did not exhibit this condition.

Liston and Cruikshank[29] wrote a very interesting

paper giving their findings in a series of 200 cases of leucorrhoea in pregnant women. They found 75 patients out of the 200 harboured trichomonads in their vaginae. In my own series of 408 cases, there were 148 with trichomonas present = 36.27%, and this agrees closely with the findings of Liston and Cruikshank referred to. The pH of 42 of these cases was estimated at their first attendance and the average figure was found to be 5.31. In 25 of these 42 the pH was repeated at intervals during the period of observation and treatment and there was an increase in the hydrogen ion concentration in 23 of the 25, the average figure for the last lot of readings being 4.56; which of course approximates to a more normal reading, showing that the pH can be taken as an index of the progress towards recovery. The two showing no increase in the hydrogen ion concentration were very resistant cases in whom the trichomonas were still present at the last reading of pH. In all the 148 cases with trichomonas pus cells were more numerous than epithelial cells at their first attendance and with clinical cure and disappearance of the parasites the relative proportion was gradually reversed again showing that this is a factor in the progress towards recovery. A finding which was most striking was that all of the cases showed a marked deficiency

in glycogen deposition, only differing slightly in degree, and that when the parasites disappeared after treatment the amount of glycogen deposition increased in all cases, although it did so more slowly in the more resistant cases.

In making a diagnosis of trichomonas vaginalis vaginitis it is necessary to pay particular attention to the actual demonstration of the organism. Although one can often make a pretty accurate guess at the cause, especially in acute cases, from the history, symptoms and appearance of the vagina and vulva, there is occasionally the atypical case and one has also to bear in mind the possibility of another co-existing infection masking the characteristic symptoms, and in particular one must bear in mind the potential gravity of the case of gonorrhoea together with the danger to the child in the development of a G.C. Ophthalmia Neonatorum with its drastic results in an untreated case. Nearly 50% of gonorrhoea cases suffer from trichomonas vaginalis infection also (Liston[45]).

The discharge was generally a copious greenish-yellow one and I have found it to be frothy in the great majority of cases. The insides of the thighs were reddened and frequently chafed, due to the constant irritation by the discharge, and although the

vulva was in most cases tender, only in 3 cases was there marked oedema of the labia minora. The vaginal mucosa presented a strawberry-like appearance, with raised haemorrhagic spots in the majority of cases, and the cervix frequently showed superficial bleeding points. In the subacute form there was less diffuse inflammation, the areas affected being patchy in their distribution, affecting particularly the urethra, the introitus and the vault of the vagina. There were some cases which because of their history I have labelled as chronic and in these there was very little abnormal to note on clinical examination beyond some patchy inflammation of the vault of the vagina.

It behoves us therefore in making a diagnosis to examine carefully the specimen of discharge for the presence of the parasite and this can generally be done while the patient is still on the table, thus allowing of treatment being started at once. I have found that placing a drop of the discharge in a little 1% saffranin in normal saline is less toxic towards the parasite than methylene blue so that it retains its characteristic active motility for a longer period and by this method a very good differentiation is made between the epithelial and pus cells which have taken up the stain on the one hand and the

parasite on the other. In most cases it is possible thus to make a diagnosis but nevertheless one always takes films to stain by a modified Leishmann method, as suggested by Liston, for confirmation when the pale blue staining of the organism and the organelles are readily recognised, and one also, in every case, takes smears from the urethra and cervix to stain by Gram's method in order to exclude the possibility of a gonococcal infection.

The treatments recommended for trichomonads are legion, ranging from vinegar douches to many varied suppository preparations. No one has been universally accepted but various writers have expressed their preference for some particular one.

The use of a douche may seriously remove the natural protective secretion of the vagina and in any case the concentration of the antiseptic is likely to be so slight as to render its action of no importance in the short time it may be present in the vagina, and for these reasons I am not in favour of its use.

I am of opinion that one should rather try to reestablish in the vagina the natural secretion in respect of its hydrogen ion concentration and bacterial flora, in addition to using local bactericidal agents. It is interesting to note in the Annual

Review of Biochemistry 1940[46] published by the Stanford University, California, that pyridoxin (Vit.B 6) has been shown to be essential for the growth of lactic acid bacteria, and again Stähler[47] in 1940 showed that in 10 cases of non-specific vaginal discharge, treatment by local application of 1 mgm. of riboflavin (Vit. B_2) daily in tablet form increased the acidity of the vaginal contents in 4 or 5 days and encouraged the growth of acid forming bacilli with reduction in the numbers of pathogenic organisms. In 10 other cases instillation of a solution of riboflavin was equally effective. It has of course been known for some time that in pregnancy there is a tendency towards deficiency of Vitamin B_1 as has been indicated by the Test for O.B.T. principle. Horwitz and Farley[48] found that 13 pregnant women from a total of 100 studied by a test in blood serum for the effect of Vitamin B_1 were found to be very low in titre and they concluded that there was frequently a deficiency in pregnancy. They also showed that the O.B.T. level can be raised by administration of yeast over a 4 day period and that deficiency of Vitamin B_1 in pregnancy has a definite effect upon the appetite - 7 of the 13 had hyperemesis and 6 had poor appetites. It has been the experience of the author that many of the pregnant women attending the

leucorrhoea clinic were in poor general condition and lacking in healthy appetite and 7 of those who were resistant to local treatment were given in addition Vitamin B orally in tablet form or as Bemax and in all of these there was a notable improvement in respect of their general condition, the hydrogen ion concentration and in the return of the normal Döderlein flora to their vaginal secretion. With regard to the local bactericidal agents, I have tried a number of the advertised remedies including storasol, devegan, carbarsone and picragol and have had good results from all of them although I developed a preference for carbarsone in view of its effectiveness, together with the fact that it is convenient for the patient and does not stain the clothing. I have found it important to continue the treatment for a period after apparent cure as there is no doubt that this condition has a tendency to relapse. Liston and Liston[40] are of the opinion that the explanation of repeated relapses may be that the trichomonas penetrate beneath the epithelium and are there protected against the effect of local drugs, appearing again when conditions are favourable for their propagation.

VAGINAL THRUSH.

Vaginal thrush is the form of leucorrhoea which gives rise to the most severe and annoying of symptoms. In many cases the irritation caused by the parasite is extreme and particularly so during the night so that there is loss of valuable sleep and the patient is often mentally disturbed to such an extent that her general health is affected and she is deprived of that calm serenity which is such an important state of mind during pregnancy.

In 1847 Robin[49] described and in 1853 named the parasite of thrush, Oidium Albicans, and in 1875 Haussmann[50] produced the disease in a healthy pregnant woman whose vagina was free from the parasite by inoculating her with material from an infected patient. Zopf[51] in 1890 was the first to place the organism in the genus monilia, calling it monilia albicans, and it is generally known by that name in America. We tend, however, in this country to prefer the long-established name Oidium Albicans for the commonest species of thrush-producing organism. Shelmire[52] (1925) points out that in order to recognise a thrush infection it is necessary to find septate pseudo-mycelial threads or hyphae as well as groups of spores (blastospores) in cluster-like arrangement in material from the lesions, and Liston

and Cruikshank[29] show how the mycelium and blastospores can be demonstrated either in wet films, made directly from the affected parts, or in dried films stained by Gram's method, and they point out that cultures are not necessary to make a diagnosis and may even cause erroneous diagnosis unless great care is taken to distinguish the thrush fungus from other yeast-like organisms which are widely distributed even in normal persons.

There is a definite relation between the virulence of the parasite, the susceptibility of the host and the persistence of infection. Bland, Rakoff and Pincus[53] in 1937 produced vaginal thrush in 29 women out of 50 subjected to inoculations with pure culture of strains of Oidium Albicans which had been isolated from cases of vaginal thrush of different degrees of severity and they found that whereas with organisms from severe cases they were successful in 5 out of 6 attempts they obtained only 4 successes out of 8 attempts using strains from symptomless cases. In a discussion which followed a paper by Carter, Jones, Ross and Thomas[11], Brooke Bland goes so far as to say that one should not make a diagnosis of vaginal mycosis on the basis of a positive culture alone, as many patients harbour a few of the organisms in the vaginal tract without exhibiting any symptoms or

signs of the disease even over long periods of observation. He is of opinion that when by some alteration in nature's method of fungistasis environmental conditions become favourable for the propagation of the parasites clinical phenomena supervene.

It has been noted by several observers that pregnant women are more susceptible to thrush infection than non-pregnant women. For instance Bland, Rakoff and Pincus[53], in the experiments referred to, collected the cases they inoculated into groups and compared 12 non-pregnant women with 12 pregnant women inoculated with the same strains. They found that only 4 non-pregnant women developed symptoms, while 10 out of 12 pregnant women contracted infection, and again Carter and Jones[54] in 1937 studied the vaginal flora of 114 apparently normal pregnant patients and of 100 apparently normal non-pregnant patients. Yeast-like fungi were isolated from 32% of the 114 pregnant patients and only from 14% of the 100 non-pregnant women, but none of them offered any explanation of this increased susceptibility during pregnancy. Brooke Bland and Rakoff[55] (1940) suggested that the explanation might be the increase in glycogen and vaginal acidity which they believe occurs during pregnancy, but actually the glycogen deposition, though good, is not greater than in normal

pregnant women. In 1940 Carter, Jones, Ross and Thomas[11] stated they had failed to find a factor which might explain the difference between the findings in pregnant and non-pregnant women and that they did glycogen stains on biopsy specimens of vaginal mucosa but could not satisfy themselves that this glycogen factor might explain the predominance of monilia infection in the vaginae of pregnant women.

In 1941 the author, in association with Liston (Liston and Chisholm[56]), investigated the relationship between glycosuria and vaginal thrush and we found that if appropriate arrangements are made for the collection of urine after a meal of patients suffering from vaginal thrush, one hundred per cent show the presence of glucose, and we therefore concluded that the thrush fungus shows a marked avidity for glucose when it establishes itself in human beings, provided that there is a suitable pH reaction of the moist surface upon which the thrush fungus is to develop, i.e. in the neighbourhood of 4.5, and this may explain the frequency with which diabetic patients suffer from vulval mycosis.

We noted the findings on routine examination of the urine of 308 patients who in one week attended the Antenatal Department of the Simpson Memorial Maternity Pavilion and of that number 98 had sugar

present when tested for by Fehling's solution, showing that on the normal diet of the average hospital class patient roughly 30 per cent of pregnant women pass glucose in their urine at some stage of their pregnancy, most frequently during the latter half of the period. We prepared blood sugar curves and examined the urine of 9 patients suffering from vaginal thrush while starving and again at intervals of half-an-hour after the ingestion of 50 grams of glucose. Three of the patients showed glucose in their urine even when fasting. After taking 50 grams of glucose all but one patient suffered from glycosuria and we proved that the sugar was glucose and not lactose by the formation of glucosazone crystals. The one exception had been put on a restricted carbohydrate diet for some time and previous to this sugar had been found in her urine. The blood sugar curve was within the limits of normality in all of the cases and they all exhibited a low renal threshold for glucose.

It appeared clear to us, therefore, that the trigor which lights up a thrush infection is glucose and this again must depend on some physiological upset associated with pregnancy which prevents the proper metabolism of carbohydrate and its deposition in the tissues as glycogen, there to be stored and ready

for use when required.

In my series of 408 cases of leucorrhoea in pregnancy there were 96 cases of vaginal thrush = 23.3%, and of that number 3 complained in the first trimester, 42 in the second and 51 in the third. I have found the history often very suggestive of this infection, the chief complaint being that of irritation, frequently so severe as to keep the patient from sleeping at night. The clinical appearance of a typical case of vaginal thrush is absolutely diagnostic - one hundred per cent of cases with this characteristic appearance have the parasite present. The vagina is coated with a thick bread-crumb like discharge in the form of plaques of a deep cream colour and there is evidence of external irritation around the region of the vulva. The diagnosis in this case can be made immediately by viewing under the microscope a fresh preparation made by mixing some of the discharge - an adherent plaque if possible - with a little normal saline or saffranin solution. The finding of the unstained refractile pseudo-mycelium of thrush together with the budding yeast-like bodies, properly called blastospores, makes the diagnosis. A smear may also be stained by Gram's method, when the parasite is seen to be gram positive.

The treatment of vaginal thrush has in the past been confined to the local application of a fungicide and the one most universally employed has been Gentian Violet. There is no doubt that Gentian Violet is an effective agent against the parasite of vaginal thrush and its use gives great relief to the patient, but we should if possible go further than the actual attack against the organism responsible. There should be four main objectives in treatment - (1) prompt relief of the pruritis: (2) destruction of the causative organism: (3) prevention of spread of infection to others: and (4) the establishing of conditions such that recurrence is unlikely to take place.

Gentian Violet in a 2% solution, when applied frequently to the vagina and vulva, after removing the adherent plaques with a solution of sodium bicarbonate and thereafter drying out, gives great relief to all patients and eventually gets rid of the parasite at least temporarily in many cases, but if steps are not taken to remove the factors which predispose to the infection, it is most probable that there will be a recurrence and this has been the disappointing result in many cases.

It was this experience by themselves and others, together with the fact that glycosuria in pregnancy

appeared to predispose to vaginal thrush, which prompted Liston and Chisholm[56] to make a study of glycosuria in pregnancy and its relationship to vaginal thrush infection. Having discovered that all the thrush cases at my clinic showed glucose in their urine when tested after the main meal of the day, and having proved by blood sugar estimations and the drawing up of blood sugar curves that this glycosuria of pregnancy is due to a low renal threshold associated with a lessened power to assimilate and store carbohydrate and is quite distinct from true diabetes, we proceeded to institute dietetic treatment in addition to the local applications by putting the patients on a restricted carbohydrate diet and the results in the previously resistant and recurring cases were remarkable.

The following is an example of one such case.

Mrs M., aet 28, para 0, 5 months pregnant, had slight discharge, but her chief complaint was that of irritation so severe as to keep her from sleeping at night. On examination on 20.12.40 there was evidence of external pruritis and the vagina was raw looking with some inspissated plaques of a yellow cheesy looking material which when examined microscopically contained the pseudo-mycelia and blastospores of vaginal thrush. The cervix was healthy and smears

taken from the urethra and cervix were G.C. negative. The flora was Type III. and pus cells were in excess of epithelial cells. Treatment with 2% Gentian Violet was commenced and reapplied twice weekly, and on account of her poor general condition and poor appetite she was instructed to take Bemax. By 24.1.41 she was very much improved, having no irritation and her smears were negative, with a return of the normal Döderlein flora. However, on 7.2.41 a few hyphae were again found and there was a slight return of the symptoms. It became evident that she had a tendency to relapse and that on stopping treatment the parasite would gain entrance and flourish again, with all its attendant effects. On 14.3.41 her urine was tested for sugar and only a trace was found, but she was asked to bring a specimen collected one hour after her dinner and this was found to contain a large amount of sugar, a golden yellow precipitate being obtained on the test with Fehling's solution and this was found to be glucose by the formation of glucosazine crystals. A blood sugar curve was done which proved to be quite normal, the readings being 92 mgm. % while fasting, and those at half hourly intervals after the ingestion of 50 grams of glucose being 127, 115, 111 and 88.

We then put her on a restricted carbohydrate

diet and on 4.4.41 the local appearances were normal, no parasites were present, the flora was Type I. and we discharged her on 18.4.41 looking very well and with no complaints.

On interrogation of the thrush patients I found that the diet of the great majority of them consisted largely of starchy foods such as potatoes, white bread and cereals, and these were taken at one main meal at mid-day. As Liston and I have shown that on the normal diet of the average hospital class patient, approximately 30% of pregnant women excrete an appreciable quantity of glucose in their urine, and that this glycosuria is temporary, intermittent and quite distinct from true diabetes, there being no hyperglycaemia, and also in view of the tendency towards deficiency of Vitamin B in pregnancy, which vitamin has been proved to be necessary for the growth of the lactic acid bacilli and which may be concerned with the proper assimilation of carbohydrate and its storage in the tissues as glycogen, we came to the conclusion, after the successful trial in clinical cases of vaginal thrush, that measures directed against the development of glycosuria of pregnancy will be a prophylactic against vaginal thrush infection. We therefore advocate a well balanced diet with adequate vitamin content, containing carbohydrates limited in

quantity or taken in less readily available form and evenly distributed during the day, and we consider it important that the urine of all pregnant women should be examined carefully for glucose, especially in the later stages, not only to detect diabetic cases, as is the usual reason for this practice in midwifery, but also that those with a predisposition to the development of vaginal thrush be discovered and the prophylactic measures described be instituted.

SUMMARY AND CONCLUSIONS.

1. Leucorrhoea is a frequent gynaecological complaint often causing distressing symptoms which may lead to impairment of general health and mental distress in introspective pregnant women.

2. The early studies of the bacterial flora of the vagina by Döderlein and his contemporaries have been a stimulus to much recent research into the conditions which govern the normal vaginal secretions.

3. A definite relationship has been shown to exist between the deposition of glycogen in the vaginal epithelium and the circulation in the blood of the female sex hormone oestrin.

4. A high degree of acidity is shown to be normally present in the healthy adult vagina and glycogen is presumed to be the fermentable carbohydrate responsible for its production. As glycogen is not fermented by cultures of the vaginal bacillus, it is suggested that the vaginal mucosa may contain a diastatic ferment which converts the glycogen to glucose, to be in turn split up by Döderlein's bacillus with the production of lactic acid.

5. On account of the high acidity which normally prevails during pregnancy, preventing all but highly acid-resistant bacteria such as Döderlein's bacillus to survive, it is considered that an effort is being made to produce a natural environment inimical to the entry and establishment of foreign pathogenic bacteria, and therefore the indiscriminate use of antiseptics and douches is to be deprecated.

6. A definite association has been proved to exist between ovarian activity, deposition of glycogen, the hydrogen ion concentration and the bacterial flora of the vagina, though the exact relationship has not yet been clearly established.

7. In clinical work a pretty clear distinction can be made while the patient is still on the examining table between the normal and the abnormal by microscopic examination of a fresh preparation of the discharge, and any departure from the normal findings in respect of relative number of epithelial cells, nature of flora, glycogen deposition and hydrogen ion concentration indicates the necessity of searching for a cause.

8. There are four main causal agents of leucorrhoea - Trichomonas vaginalis vaginitis, vaginal thrush, cervical conditions and gonorrhoea, in that order of frequency.

9. Gonorrhoea remains the most serious form of leucorrhoea but its incidence has been greatly reduced by the introduction of the recent chemotherapeutic agents. In

the author's series of 408 cases there were 19 cases of gonorrhoea.

10. The treatment of cervical conditions is quite effective, even in pregnancy, but more research upon the etiology and pathology of cervical erosions is indicated so that we can institute prophylactic measures. The author has found 34.8% of her cases to have cervical conditions.

11. In recent years the increased interest in trichomonas vaginalis and improved methods for studying the organism have placed it as one of the chief causal agents of leucorrhoea. Out of 408 consecutive cases studied by the author, 148 had trichomonads present = 36.27%. In this condition the optimum pH is between 5.3 and 5.7 and glycogen deposition is markedly reduced. An explanation is offered for the continued relapse in chronic cases.

Treatment should be directed to the reestablishing of normal conditions in the vagina in addition to the use of local antiseptics. Vitamin B is shown to be effective in improving the general condition of the patients and in encouraging the return

of the normal vaginal flora.

12. Vaginal thrush is the form of leucorrhoea producing the most distressing symptoms. In the author's series of cases 23% were found to suffer from vaginal thrush infection. Approximately 30% of pregnant women, on the normal diet of the average hospital class patient, show a glycosuria which is temporary and intermittent, and quite distinct from diabetes, there being no hyperglycaemia. Glycosuria is shown to be a predisposing cause of vaginal thrush, being present in all cases after the main meal of the day.

Treatment should be dietetic in addition to the local application of antiseptics. A well balanced diet is advocated with adequate vitamin content, particularly vitamin B, and limited carbohydrates evenly distributed throughout the day and given in less readily available form.

Careful and frequent examinations of the urine for sugar and correction of errors of diet thus revealed are prophylactic measures against vaginal thrush infection in pregnant women.

13. The treatment of leucorrhoea is no longer palliative but is rather therapy directed at specific disease entities - a change which is brought about by a better understanding of the various endocrine and constitutional factors which control the biological characteristics of the vagina, together with a better appreciation of the significance of various organisms which may be present in the lower genital tract, and, as our knowledge of the factors predisposing to the development of the causal agents of leucorrhoea expands, we are increasingly able to institute prophylactic measures against this distressing complaint.

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