GONOCOCCAL VULVOVAGINITIS IN INFANTS AND CHILDREN: A STUDY OF 240 CASES

BY

CHUNILAL MUKHERJEE

From the Department of Obstetrics and Gynaecology, the Campbell Hospital Medical School, Calcutta

(RECEIVED FOR PUBLICATION AUGUST 25, 1949)

Gonorrhoea in women often produces minor symptoms. This explains the comparative infrequency of symptomatic gonorrhoea of the lower genital tract in out-patient clinics. Gonococcal infection of infants and children, on the other hand, at once attracts attention. Hence the reason why the incidence of vulvovaginitis infantum appears to be comparatively high. Nelson (1932) found the incidence of gonorrhoeal vulvovaginitis to be 11.8% and Mukherjee (1940) 11%. In a series of 2,464 cases in the female, diagnosed by bacteriological methods during 1933-46, we came across 240 cases of gonorrhoeal vulvovaginitis, a frequency of 9.7%.

Not all cases of vulvovaginitis are caused by gonorrhoea. Foreign bodies, non-specific infections caused by unhygienic conditions, threadworms, exanthematous fevers, monilia, and diphtheria account for a fair number. Fessler (1930) found gonorrhoea in two out of 25 cases, and Clauberg (1930) failed to cultivate the gonococcus from 70 children examined for the condition. Ruys (1935) found gonococci in 57 out of 292 children. During the period under review the total number of vulvovaginitis cases was 438, of which 240 (55%) were diagnosed as gonorrhoeal. This may appear to be high and is probably so, for most patients with simple catarrhal vaginitis do not report to hospitals for investigation and treatment. It may be of interest to compare the relative frequency of gonorrhoea with the other aetiological conditions causing vulvovaginitis in children (Table 1).

The incidence of gonococcal infection in any study of vulvovaginitis is dependent on the means employed for the detection of gonococci. The unreliability of smear examination alone has been shown by several observers (Clauberg, 1930; Ruys, 1935). This is because of the presence of Gram-negative cocci, which are often arranged in pairs, in the normal vagina. Greenhill (1945) suggested that to identify gonococci one must

TABLE 1
COMPARISON OF AETIOLOGICAL CONDITIONS CAUSING VULVOVAGINITIS

Nature of Infection	No. of Cases	Percentage
Foreign bodies	26	5.9
Non-specific infections ..	156	35.6
Diphtheria	2	0.5
Exanthemata	2	0.5
Mycotic	12	2.7
Gonococcal	240	54.9
Total	438	100.1

discover more than ten typical organisms intracellularly in the same slide, and two or more within the same cell. By a similar method it has been possible to eliminate no fewer than 31 cases in the present series. Subsequently culture and the progress of the patient demonstrated the usefulness of this simple suggestion. There is another difficulty in chronic or inadequately treated cases. In these the vaginal exudate is scanty, and leucocytes are fewer and more disintegrated. In these cases, even if Gram-negative diplococci are found in the smear they are frequently extracellular. A negative report in these cases does not completely rule out the possibility of a true gonococcal infection.

Cultural results are more reliable, provided the exudate is fresh and inoculated immediately. Clauberg (1930) was one of the earlier observers to emphasize the value of routine culture. Mascall (1933) also found a higher incidence of positive results on cultural examination. Cohn, Steer, and Adler (1941) showed from the results of 1,070 examinations that cultures were positive in 98.9% of cases, whereas positive results on smear examination alone obtained in 67.1%. These authors value cultural methods not only in diagnosis but also in follow-up treatment. In our series culture was not possible

in all cases, but the relative value of culture and smear examinations is tabled below (Table 2).

TABLE 2
COMPARISON OF CULTURE AND SMEAR EXAMINATIONS

Method of Examination	No. of Cases	Percentage
Culture + smear + ..	98	40.8
Culture + smear - ..	52	21.6
Culture - smear + ..	9	3.8
Smear (only) ..	81	33.8
Total	240	100

It would appear that culture was positive in 62.5% of all cases. Excluding the cases where cultural facilities were not available, positive culture was obtained in 94.3%, while smear examination was positive in only 61.0%. As a general rule more culture-positive cases are seen in chronic conditions. Incidentally, this increases the value of culture in assessing the criteria of 'cure.'

Mascall (1933) believed that the largest number of positive results could be obtained with the complement fixation reaction. His observation on cases at the London County Council clinic at Whitechapel showed 79.6% positive results with the complement fixation test, 66.8% positive results on culture, but only 45.4% by smear examination.

Age Incidence

The principal reason for the widespread infection of the vulva and vagina in the young is the absence of the normal protective acid vaginal secretion in these subjects. This also explains the rarity of gonococcal vulvovaginitis in very young infants. The youngest patient with gonorrhoeal infection of the vulva and vagina was reported by Wattie (quoted by Cruickshank and Sharman, 1934) in an infant of 5 months old. Wynkoop and Boggs (1926) in a study of 500 infants during the first two weeks after birth failed to detect a single case of vulvovaginitis of gonorrhoeal origin. In a similar study of 36 infants during the first 15 days after birth where the mothers had gonococcus in the lower genital tract before, and/or during labour, no case of gonococcal vulvovaginitis was detected. It is of interest to note, however, that 24 of them developed the infection between two and a half and 13 months after birth.

By far the largest number of cases are usually found in early childhood. Nelson (1932) found 44.9% of cases between 5 and 9 years of age. Mukherjee (1940) found the highest incidence in Bengal to be 45.6% in girls from 3 to 5 years of age.

The distribution of age of the cases in the present series was as follows (Table 3).

TABLE 3
AGE DISTRIBUTION OF PRESENT SERIES

Age	No. of Cases	Percentage
Under 6 months ..	4	1.6
6 months to 1 year ..	24	10.0
3 years to 5 years ..	114	47.5
5 years to 7 years ..	30	13.5
7 years to 9 years ..	19	7.9
Over 9 years ..	8	3.3

The youngest patient in this series was a girl of 2½ months and the oldest one was one of 11 years. The highest age incidence in this group was 3 to 5 years, as in a previous group which I reported in 1940.

Source of Infection

To trace the source of infection is difficult but important from the public health point of view. Boarding schools, dormitories, or infected bath tubs may account for an occasional case in India, or the sudden outbreak of an epidemic in an institution, but certainly in most cases these factors play a negligible role. Rape or superstitious beliefs account for a small number. In the majority, where the source can be traced, either a member of the family or a servant plays the rôle of carrier. In the present series the source of infection was apparently traceable in only 145 cases (60.4%) although 186 parents and immediate contacts were examined. Of these 81 (43.09%) harboured gonococci. In 86 cases the servant was examined and gonococci were discovered in 70. In 11 cases both the attendants and immediate family contacts harboured the infection. In five cases the infection was traceable to other children in the family, or to playmates.

Clinical Features

The incubation period could not be properly ascertained owing to difficulty in obtaining the history of the time of exposure. An attempt was, however, made to estimate it where the source of infection was detectable, but the result is not very satisfactory (Table 4).

The symptom which attracts attention is a discharge. This in the early stages is sero-purulent, but within 48 to 72 hours becomes frankly purulent. If cleanliness is not maintained the odour of decomposing pus is noticeable. The discharge is not as a rule sanguineous, but in three

TABLE 4
ANALYSIS OF INCUBATION TIMES

Incubation Period	No. of Cases	Percentage
Less than 24 hours	10	12.8
25-48 hours	22	28.2
49-72 hours	28	35.9
73-96 hours	18	23.1

hyperacute cases a sanguineous discharge was noticed. Incidentally it may be mentioned that a sero-sanguineous or sanguino-purulent vaginal discharge in infants has been found in all cases of foreign body vaginitis. The discharge of vulvovaginitis is of a remarkably irritating nature and in a few days (less than four days in 86% cases) signs of irritation of the vulva, groin, perineum, and peri-anal regions appear.

Dysuria was present in 194 cases (80.8%). Belladonna usually relieves this dysuria to a great extent. A considerable part of the complaint is probably due to urinary tract infection and spasm.

The first symptom observed in the patient was: (1) Discharge, 187 cases (77.9%); (2) vulval irritation, 47 cases (19.6%); (3) dysuria, 6 cases (2.5%).

Examination usually shows severe inflammation of the vulva. The labia are swollen, tender, and excoriated. The vestibule is bathed in pus, and is angry and congested. The urethral orifice is swollen and pouting, but infection of Skene's glands was never noticed, nor was Bartholin's gland affected. In one case the infection was so severe, and lack of cleanliness so pronounced, that noma of the vulva had developed before relief was sought. The extent of ulceration of the vulva is usually proportional to the infection. In such fulminating cases the nature of the basic infection is often missed, especially on culture, as secondary organisms grow exuberantly. This happened in no less than 23 (9.6%) of our cases. In such a predicament microscopical examination of a carefully prepared slide exposes the possibility of the nature of the underlying infection. It must be said, however, that as the secondary infection comes under control, culturing gonococcus from the vulvovaginal secretion becomes more easy.

Inspection of the vagina when the infection is acute is not only almost impossible but is also dangerous, for an acute flaring up of the infection is the usual consequence. Nevertheless, after washing the vulva under a gentle stream of normal saline, the degree of severity of the infection can be judged from the amount and nature of the vaginal discharge. Gentle milking of the vagina with the

little finger introduced into the rectum is all that is necessary. When the active infection is under control the state of the vaginal mucous membrane can be inspected with a Kelly speculum or an electric cystoscope. A small dose of luminal about one and a half hours before instrumentation helps to allay nervousness. The usual finding is a congested swollen mucous membrane bathed in a purulent exudate. In 79 cases (32.9%) superficial ulcerations were noticed. Evidence of infection is as a rule more marked in the lower half of the vagina than in the upper and on the posterior wall than on the anterior. The cervix often shares the vaginal infection (30%).

The spread of infection to the upper genital passages is rare, owing to the protective barrier of the cervix. Nevertheless exploration of the pelvis during rectal examination is sometimes rewarded. In our series only four children developed evidence of peritoneal involvement (1.68%). In a similar study by Schauflier (1940) of 266 infants and children with frank vaginal infections nine presented symptoms of pelvic involvement. Lees (1928) gives the frequency as no less than 5.5%.

In our series rectal symptoms were present in 14 cases or 5.8%. Rectal infection forms a hidden focus from which re-infection and relapse are frequent. Fraser (1925), Williams (1933), and Martin (1935) were some of the earlier observers to direct attention to this possibility. Fraser found rectal infection in 59 out of his 63 cases. Ruys (1935) observed it in all cases in his series. In an earlier report (1940) I found rectal infection in 82%. Material from the rectum was examined, by smear and culture, in 170 cases (70.8%) of this series. Culture was positive in 168 cases (98.8%); smear examination was positive in 124 cases (72.9%).

Collection of Material for Diagnosis

It is a mistake to collect the material from the vulva because extraneous organisms are so abundant in this region. The following method has been found useful.

Method. The vulva is washed under a gentle stream of sterile warm normal saline. A narrow, but strong glass pipette is then introduced into the vagina and a drop of exudate is collected from this region. Sometimes the pus is too thick for the calibre of the pipette. In these cases about $\frac{1}{2}$ to 1 ml. of sterile saline may be introduced before the material is collected. Inoculation in the culture medium on to hydrocele or ascitic fluid agar in petri plates is made immediately. After inoculation a smear preparation may be made with the remainder of the exudate and stained by Gram's method.

Examination of the rectal specimen formed a routine, except for the first 70 cases studied. The material was

collected with a strong wire loop from half an inch inside the anus after holding the child in an exaggerated lithotomy position and stretching the anal skin. Inoculation was done immediately. For a rectal smear the discharge collected on the loop may have to be mixed with a drop of sterile saline on a slide.

Complications

Complications are uncommon in gonococcal vulvovaginitis. Contrary to the usual expectation ophthalmia develops only rarely. I have found (1940) the incidence to vary from 1 to 5%. In the present series gonococcal ophthalmia developed in 18 cases (7.5%). It is, however, interesting to note that whereas in 14 cases the ocular infection followed the vulvovaginal lesion, in two the infection of the eye was primary. In the remaining two cases the parents declared the infection to be about synchronous. It is also interesting to note that in all these instances the mother was a carrier of infection.

Arthritis was also found to be uncommon. The joint most commonly affected was the knee. The onset is sudden and not infrequently it is confused with osteomyelitis of the lower end of the femur. The joint is swollen and a cutaneous flush may be present; pyrexia varies between 100.6 and 103° F. The tenderness is, however, limited to the joint, the bone ends being free. The lesion is of the mono-articular type. Williams (1926) considers this complication to be very frequent. In our series, however, it was encountered in only seven cases (2.9%). The knee was the seat of lesion in all, though in two instances the ankle was subsequently affected. Although the joint fluid was examined on nine occasions, gonococci were cultured only once. In no case did ankylosis or limitation of movement result.

King, Mascal, and Price (1936) drew attention to associated infection with trichomonas and stated that it interfered with the demonstration of gonococci. I can corroborate this statement. In the present series no less than 36 (15%) patients harboured trichomonas, besides eight, in which infection was suspected but could not be confirmed until about three weeks after the first observation, a total incidence of 17.5%. It has now been our practice to examine a hanging drop preparation of the vaginal discharge (diluted with saline) on three successive days before associated trichomonas infection is ruled out. In this connexion the case reported by Karnaky (1936) is interesting. Trichomonas infection makes gonococcal infection more resistant to treatment, besides causing the irritant vaginal discharge to persist even after the disappearance of gonococci. If the trichomonas infection is

missed initially it is usually detected later when leucorrhoea becomes persistent, but early detection shortens the course of treatment considerably. It has not been possible to detect the source of this obstinate secondary invader. The vaginal mucous membrane of infants is very susceptible to trichomonas infection. The mutation of *Trichomonas intestinalis* into *T. vaginalis in vivo* has been suspected but has not been actively proved. In 16 patients of the series intestinal trichomonas were detected in the faeces, but almost all these patients belonged to a class of society where personal hygiene was minimal. Of 86 'better class' patients only one showed this secondary infection.

Associated luetic infection cannot strictly be regarded as a complication, but it is important. Out of 198 cases in this series where a routine Wassermann test was done, 46 (23.2%) were positive. This cannot be accepted as it stands because of the possibility of inherited syphilis. If 37 cases, where the parents also had positive blood tests, are excluded, the incidence of associated syphilitic infection appears to be only 4.5% (nine cases). It may be pointed out that in eight out of these nine cases a history of rape was either present or suspected. It appears that the presence of an associated syphilitic infection, if inherited syphilis is excluded, indicates a criminal assault.

Treatment

For comparative study the results obtained in all cases are presented in relation to the form of treatment.

Orthodox Local Treatment. The total number of patients treated was 20. The treatment consisted of hip bath, vaginal irrigation, and instillation of silver nitrate or mercurochrome solutions.

Straightforward uneventful recovery was an exception; relapses were frequent, the course of therapy prolonged, and taxing to the patience of the parents and the medical attendant. The average duration of treatment was 12 weeks, while the minimum was 10 weeks and the maximum 26. If it is considered that all patients with relapse came back for treatment (an expectation which is extremely improbable) its incidence appears to be 20.0% (four cases). It was also noted that the relapses were more refractory to local treatment alone than the primary infection. The results of local therapy may, therefore, be considered unsatisfactory.

Sex Hormone Therapy. The total number of cases treated with sex hormones was 102. In 70 of these oestrogen therapy was combined with local antiseptic treatment. In the remaining 32 oestrogens

alone were employed locally. Lewis (1933) observed that female sex hormones in children produced proliferation of vaginal epithelium and the clearing up of the vaginal infection. But the effect of oestrogens is not confined to the vagina. Wither-spoon (1935) suggested that prolonged use of oestrogens might inhibit the pituitary and bring about secondary atrophic changes in the ovaries. It has, however, not been conclusively shown that such changes affect infants and children equally. Of the 102 patients of this series treated with oestrogens 31 have been followed up to the age of puberty and thereafter. The age of the menarche in this group may be tabulated here with advantage (Table 5).

TABLE 5
AGE OF MENARCHE OF CASES TREATED WITH OESTROGENS

Age of Menarche (years)	No. of Cases	Percentage	Normal Controls
11-12	8	25.9	38
12-13	12	38.4	29
13-14	8	25.9	21
14-15	3	9.7	9
15-16	—	—	3
Total	31	99.9	100

Table 5 shows that there is a tendency for a delayed menarche in the group of children treated with oestrogenic hormones in infancy, but it must be admitted that the number of cases is so small that the difference may be more apparent than real. In any case the advantages of oestrogen therapy in vulvovaginitis far outweigh the supposed fear of pituitary inhibition and ovarian atrophy. No difference in results has been observed between oral and parenteral treatments if the dosage has been adequate. Often both these means of administration have been combined.

NATURAL OESTROGENS. The preparations employed were 'progynon B oleosum,' 'ovocyclin P,' and 'menformon.' The number of cases so treated was 48 (64.4%, i.e. 20.0% of all cases). The dose employed was 1 mg. (10,000 I.U.). Except in the case of very small infants (up to 3 years) this was supplemented with a daily dose of 0.3 mg. (3,000 I.U.) of oestrogen dragees orally in divided doses. The course of treatment was checked by frequent vaginal smear and culture and estimation of the vaginal acidity. Improvement was invariably attended with a fall in the vaginal pH, often to the extent of 3.5 to 4. This substantiates the observation made by Karnaky (1936) who recorded recovery

in every case in a series of 140 when the pH was brought down to 3 to 3.5. He used dextrose-acid tablets which were inserted into the vagina. Oestrogens produce a similar effect in an indirect manner.

SYNTHETIC OESTROGENS. The preparation used was diethyl-stilboestrol. The number of cases treated in this group was 22 (35.6%, i.e. 9.1% of all cases). All patients had oral medication in doses of 1 mg. daily. Infants under 2 years of age were given 0.5 mg. It may be mentioned here that except in two cases no toxic symptoms were noted. These were manifested as vomiting and irritability which were relieved with small doses of calcium and sodium bicarbonate.

In both these groups the local treatment consisted of cleaning the vulva and vagina with 0.75% lactic acid and instillation of 2% mercurochrome in the vagina.

It was observed that with oestrogens (both synthetic and natural) considerable improvement occurred in about two and a half to three weeks, though for complete recovery the treatment had to be continued for five to six weeks, or longer. It must be mentioned, however, that examination for gonococci became negative on smear 10-14 days earlier than on culture. If reliance is placed on smear examination alone, the patient may still remain a carrier and as such, a source of danger.

Even after the vulva and vagina were free from infection rectal infection persisted, and acted as a focus of reinfection for the vagina, with subsequent relapse of the condition. In fact the incidence of relapses after oestrogen therapy was 15.7%. It was, therefore, considered necessary to institute treatment for the rectal condition while oestrogens were being administered for the vulvovaginal lesion, for in the absence of rectal infection relapse of vulvovaginitis never occurred after oestrogen treatment. The simplest remedy for the rectal infection was found to be 5% 'argyrol' suppositories. One of these is inserted into the rectum at bedtime and retained.

The change in vaginal acidity was noted as early as eight days after the beginning of treatment. Irrespective of what the initial pH value was (the highest recorded was 9.8), by this time a distinct though slight acid reaction was noted. A steady increase in acidity continued until about the end of the third week when a pH of 4.5 to 4.8 was the usual finding. By about the beginning of the fifth week the peak was reached and the level maintained for about a week after the treatment was over. The reaction returned near to neutrality by about the seventeenth day after the suspension of treatment. The highest acidity which was obtained in

the present series of cases was pH 3.2. In spite of full courses of oestrogens the pH did not fall below 5.3 in four cases. In these patients residual infection persisted in the vagina though the rectal infection was under control with 'argyrol' suppositories. Lactic acid jelly (1%) was instilled into the vagina three times a day and complete recovery followed.

Comparative refractoriness of the vaginal acidity was noted in 17 patients in none of whom did the pH fall below 6.4 after three weeks' treatment. Heavy infection with *Trichomonas vaginalis* was found in all of them. When this infection was controlled the normal curve of the vaginal acidity was regained.

The change in the vaginal smear was found to be more gradual than that of the reaction. Polymorphonuclear cells persisted until the disappearance of the infection, although partially keratinized epithelial cells appeared in the smear within two weeks of the beginning of treatment. A real 'oestrus smear' was not obtained till the vagina was free from infection.

The average duration of treatment in this series was 6.0 weeks (Table 6).

TABLE 6
AVERAGE DURATION OF TREATMENT

No. of Weeks	No. of Cases	Percentage
4	17	24.3
5	18	25.7
6	12	17.1
7	9	12.8
8	2	2.9
9	4	5.7
10	4	5.7
11-12	4	5.7

In eight (11.4%) cases of this series, although marked relief of symptoms was obtained, the vaginal secretion was not free from gonococci and the pH did not fall below 6.4. Cultures showed infection with staphylococci, which produce alkaline exudates.

These patients were subsequently treated with sulphonamides or/and penicillin and cured.

The criterion of cure was three consecutive negative reports on culture and smear examination, the last one after a provocative painting of the vagina with 1% silver nitrate solution. In 13 cases recurrence was noted within three to four weeks of recovery. The possibility of reinfection could be definitely eliminated in 11 patients. The incidence of relapse in this series may therefore be taken as 15.7% and the corrected recovery rate as 72.9%.

An inquiry was made into the difference in results obtained with natural and synthetic oestrogens (Table 7). It appeared that the synthetic product was slightly superior to oestradiol derivatives in its effects, besides being cheaper and more easily administered. Its toxic effects were not found to be marked in infants, and when present they were easily controlled.

Oestrogen Vaginal Suppositories. Thirty-two cases were treated with oestrogen vaginal suppositories. The preparations employed were 'kolpon' (organon) and stilboestrol jelly (10 mg. per g. tragacanth-glycerine jelly). Preliminary cleansing of the vulva and vagina with 0.75% lactic acid lotion was employed in all cases. No antiseptics were used, but the treatment of the rectal infection was not omitted. Results were found to compare favourably with oral and parenteral medication. The average course of treatment necessary was 5.0 weeks (Table 8). More than half the total number of cases needed only three to four weeks' treatment for complete recovery. By the tenth day considerable subjective improvement was often noted, while towards the beginning of the third week the vaginal discharge was scanty and seromucoid in nature in 29 cases (90.6%) of the series. A pH of 4.6 to 4.0 was usual about the middle of the third week. As with parenteral oestrogen therapy the initial change from alkaline to acid reaction took place in about eight to ten days, but once the acidity was established the fall in pH was

TABLE 7
COMPARISON OF RESULTS OBTAINED FOR NATURAL AND SYNTHETIC OESTROGENS

		No. of Cases	Course of Treatment			Cure	Relapse	Failure
			Maximum	Minimum	Average			
Natural oestrogens	..	48	12	5.5	6.6	38 (70.8%)	8 (16.6%)	6 (12.5%)
Synthetic oestrogens	..	22	10.5	4.0	4.7	17 (77.3%)	3 (13.6%)	2 (9.0%)

TABLE 8
DURATION OF TREATMENT WITH OESTROGEN VAGINAL SUPPOSITORIES

No. of Weeks	No. of Cases	Percentage
3	8	25.0
4	9	28.1
5	5	15.6
6	3	9.4
7	2	6.2
8	2	6.2
9	2	6.2
10	1	3.1

more or less steady and rapid. The rate of improvement was proportionate to the rate of attainment of this acid peak.

The treatment was without effect in three cases or 9.4%. The maximum vaginal acidity which was obtained in these cases was pH 5.2. Local treatment was continued for 12 weeks after which parenteral natural oestrogen therapy was employed for a further period of six weeks without any impression on the disease. Treatment with sulphonamides and penicillin subsequently cured these patients.

Permanent recovery was obtained in 26 cases or 81.1%. This is undoubtedly much less than the 98% cure reported by Te Linde (1938). Relapse occurred in three cases or 9.4%. The interval between apparent recovery and relapse was two to three weeks, which is shorter than after general oestrogen treatment. In these cases also the persistence of rectal infection appeared to be the cause of recurrence of symptoms.

UNTOWARD SYMPTOMS OF OESTROGEN THERAPY. Considering the dosage of oestrogens the incidence of untoward symptoms was negligible. They were not serious enough to call for withdrawal of the drug. In our series of 102 cases treated with oestrogens enlargement of the breasts was noted in 11 (10.8%). Of these, in eight cases the mammary changes were slight and just noticeable. In two cases where oestrogen injections were continued for over ten weeks the appearance of the mammary glands simulated that which is normally noticeable at or about puberty. In one case there was secretion, and pigmentary change was marked, though the hypertrophy was only moderate. Oestrogenic response of the breasts was more marked in the group treated with oral or parenteral oestrogens. Of the 72 cases subjected to general oestrogen therapy the breast changes were seen in nine or 12.5%, whereas these changes were noticeable in only two cases or 6.2% among the locally treated group. It was also observed that mammary

hyperplasia was more likely to develop in the higher age group children than in infants. Eight out of the 11 cases (72.8%) with noticeable changes in the breast were above the age of 8 years, and two were in the 6 to 7-years-old group. Only one case below the age of 3 years showed this change and it was only slight. The two cases where the change was marked were both over 9 years of age. In all cases, however, retrogressive changes set in within ten days of the cessation of the treatment except in the two cases where the hypertrophy was excessive, and persisted to some extent until puberty. Reversion to normal occurred in less than four weeks.

Vaginal bleeding is another untoward sequel. Though it is of no grave consequence it often causes anxiety. Schaufler (1947) noticed it in only two cases in his series. In our series of 102 cases vaginal bleeding occurred in only seven (6.9%). With the exception of one, where the bleeding appeared during the course of treatment, in all the haemorrhage was of the nature of oestrogen withdrawal bleeding and started six to eight days after the completion of treatment. In none was the haemorrhage excessive and it stopped spontaneously in four to seven days' time. In one case (aged 9 years 7 months) the bleeding was accompanied by cramp-like pain in the lower abdomen. All cases of vaginal bleeding belonged to the group of cases treated with parenteral and oral oestrogens. Here also, as in the preceding instance, susceptibility to vaginal bleeding appeared to increase with increase in age. Only one out of the seven cases was below the age of 7 years, four cases were over 9 years of age, and two between 8 and 9 years. There appeared to be some relation between vaginal bleeding and mammary congestion and hypertrophy, for all the seven cases in which vaginal bleeding occurred showed breast changes.

A sparse growth of fine pubic and axillary hair was noticed in four cases (3.9%), in all of which the treatment was continued for ten weeks or more. Two of these patients were over 9 years old, one just over 7, and another just under 5 years of age. In all cases spontaneous retrogression occurred in less than six weeks.

Sulphonamide Therapy

The advent of sulphonamides induced high hopes of success in the treatment of vulvovaginitis. This optimism has not been wholly rewarded. Hoffman, Schneider, Blatt, and Herrold (1938) reported cure in 75% of cases after one of two courses of sulphanilamide. Brown (1939) obtained a similar recovery rate, although she succeeded in curing 81.4% with a four-day course of sulphapyridine.

Lewis (1940) obtained a 90% recovery rate with this drug. Cohn, Steer, and Adler (1941) succeeded in obtaining negative cultures in all cases with sulphapyridine. Adair and Hac (1942) made a comparative study of the value of the different sulphonamide products and found that the rate of cure with sulphanilamide was 76%, with sulphapyridine 86%, with sulphathiazole 93%, and with sulphadiazine 96%.

In our series of 240 cases sulphonamides were administered to 83 patients. Sulphanilamide and sulphapyridine were used in only 10 and 13 cases respectively. Toxic symptoms appeared frequently when these drugs were used. These 23 cases have not been included in the series under review. Of the 83 patients considered here, 46 were treated with sulphathiazole and 37 with sulphadiazine. No special local treatment was given except cleansing and hip bath.

The dosage employed was 32 mg. per lb. body weight. With sulphadiazine in the case of feeble children a slightly smaller dose (24 mg. per lb. body weight) was employed. The initial dose was double the calculated dose. The maintenance dose was repeated every four hours. In the case of children weighing more than 15 to 16 lb. the dosage was so regulated that the total intake did not exceed 2 g. a day, and 16 g. during the whole course. This was found to be the maximum safe limit.

Within 48 hours of the administration of sulphathiazole or sulphadiazine subjective improvement was noted. The majority of cases showed a negative smear and culture in less than 96 hours, but it was found unwise to withhold the drug at the first negative reading, for in a number of such cases recurrence occurred. The minimum course of treatment compatible with recovery was found to be one of four days, and the maximum eight days, while the average duration of treatment was 5.9 days. The distribution was as follows:

4 days	..	11 cases (13.2%)
5 days	..	29 cases (34.9%)
6 days	..	32 cases (38%)
7 days	..	7 cases (8.4%)
8 days	..	4 cases (4.8%)

Lewis (1940) believed that if the patient did not improve after five days' treatment with sulphathiazole, sulphadiazine should be substituted after an interval of two to three weeks. In our experience, however, this observation was not substantiated, as the subsequent analysis of the results will show. Sulphathiazole-resistant cases also appeared to be resistant to sulphadiazine, but penicillin provided the remedy on these occasions. A change from sulphonamides even to oestrogens was found more

satisfactory than merely changing the type of sulphonamide.

Of the 83 cases presented in this series permanent recovery was obtained in 76 cases (91.5%). Progressive diminution of the coccal flora of the vagina and disappearance of the polymorphonuclear cells and macrophages were the characteristic features. Diphtheroids and certain strains of *E. coli*, however, persisted or appeared simultaneously with the disappearance of the pathogenic cocci. The change was observed on the second day in 69 out of 76 cases cured. In the remaining seven cases this change was noticeable between the third and fourth days. Once this change appeared the progress was steady and rapid. With complete recovery the vaginal secretion was found to consist of a few polymorphs and lymphocytes, immature vaginal epithelial cells, diphtheroids, *E. coli*, and occasionally enterococci and faecal streptococci.

The reaction of the vaginal secretion was also tested, but the only change which was noted was a diminution in the degree of alkalinity. The lowest pH recorded during sulphonamide treatment was 6.8. All the cured cases settled down to a pH of 7.2 to 7.5.

Failures were much less common than after oestrogen treatment, and the failure rate was 2.5%. In these two cases the symptoms were markedly ameliorated, and the vaginal discharge became scanty and white. Culture was positive in both. Obviously, an outcome like this is more dangerous than a frank failure, for the symptomatic relief may be mistaken for a cure while the child still remains a carrier and a source of potential danger.

In five cases (6%) the recovery was only apparent, for the condition relapsed. The interval between the apparent recovery and recurrence was eight days in one case, 12 to 13 days in three cases, and 17 days in the remaining one. In three out of these five cases the material collected from the rectum was negative for gonococcus on culture at the time of relapse.

All these seven cases where sulphonamides failed to establish a cure were put on a second course of the drug after an interval of three weeks (Table 9).

With a second course of treatment in the failure or relapse cases only one out of seven was cured. The other six were subsequently treated with oestrogens and penicillin with recovery in all cases.

Penicillin Therapy

Penicillin has been given ample trial in the treatment of gonorrhoea and found uniformly satisfactory. For this reason it was employed in the treatment of 35 cases of vulvovaginitis.

TABLE 9
ANALYSIS OF FAILED SULPHONAMIDE CASES

First Course of Sulphonamide	No. of Cases	Second Course of Sulphonamide	Result	
			Recovery	Failure
Sulphathiazole	2	Sulphadiazine	—	2
Sulphathiazole	2	Sulphapyridine	1	1
Sulphadiazine	1	Sulphathiazole	—	1
Sulphadiazine	2	Sulphapyridine	—	2

In the earlier part of the investigation the drug was given by three-hourly intramuscular injections but the treatment was found to be painful. In the last 20 cases penicillin was administered locally in the form of a jelly, the drug being introduced into the upper part of the vagina every three hours by means of an applicator of the type supplied with contraceptive jellies.

The dosage employed was the same for both intramuscular and local treatment, 10,000 Oxford units being given every three hours, one nocturnal dose being omitted. The vaginal jelly was made by adding mucilage of tragacanth and glycerine to concentrated penicillin solution in the proportion of 4:1 in order to make a concentration of 10,000 units per ml. The solution was loaded in a syringe and kept in a refrigerator. The applicator was sterilized each time after use and kept separately. With sensible and educated parents the instillation of this penicillin jelly into the vagina every three hours has never caused any difficulty.

In general, the results obtained were very gratifying. The course of treatment necessary was short, the average being 4.1 days. In two cases positive culture persisted in spite of eight days' continuous treatment and a total dosage of over 560,000 units. These have been regarded as failures.

The course taken by the disease treated with penicillin follows closely that under sulphonamide treatment. Enterococci and anaerobic streptococci persisted in all cases even after complete disappearance of gonococci. In all instances of recovery, the pH of the vagina settled down to 7.2 ± 0.2 . Rectal infection appeared to be slightly more persistent than that in the vagina, as in none of the cases studied did the rectum become negative on culture at the same time as the vaginal culture, and required 24 to 36 hours' further treatment. This applied equally to local and parenteral penicillin. In local penicillin therapy the rectum was also treated in the same manner as the vagina, i.e. by instillation of penicillin jelly with a separate applicator inside the rectum, about $\frac{3}{4}$ to 1 inch above the anal margin.

The immediate recovery rate was 94.3%, i.e. 33 out of 35 cases. This, however, did not represent the permanent recovery rate, for in two cases mild relapse was noticed. Reappearance of symptoms occurred in both cases within two weeks of the suspension of treatment. The clinical manifestations of relapse in both of them were of a mild nature. These patients were put on further courses of penicillin, but even with three full courses recovery did not occur. Each repeated course of penicillin brought about a temporary relief of symptoms, but neither smear nor culture was negative. These were probably examples of penicillin-resistant gonorrhoea. Taking into account these cases the corrected recovery rate was 88.6%.

Treatment of Relapse and Failure Cases

In our series of 240 cases, 42 (17.5%) fell into this unfortunate category. It will appear that the incidence of such cases was low in the penicillin and sulphonamide treated groups, whereas the orthodox and oestrogen treatment showed higher figures. It was found that repetition of the same line of treatment did not produce satisfactory results. The general principles which were followed are: (1) Oestrogen-resistant cases were put on a course of sulphonamides after a period of rest for two weeks, during which period nothing more than general cleansing was done. (2) Sulphonamide-resistant cases were put on penicillin and vice versa after a similar period of rest for two weeks. (3) As soon as the infection appeared to be coming under control in either group of cases, oestrogens were administered with a view to increasing the acidity and the local resistance of the vagina. This last measure was found to be immensely helpful as the results will show.

It will appear that by combined treatment in which oestrogens played a not negligible role, a total salvage of 41 out of 42 cases was obtained and a recovery rate of 98.6%. It will also appear that without combined oestrogen treatment there was generally a greater tendency to relapse.

TABLE 10
ANALYSIS OF DRUG RESISTANT CASES

Nature of Drug Resistance	No. of Cases*	Nature of Drug Employed	No. of Cases	Cure	Relapse	Failure
Oestrogen	31 (30.4%)	Sulphonamide	11	5	4	2
		Sulphonamide and oestrogen	20	19	-	1
Sulphonamide	14 (15.5%)	Penicillin and oestrogen	5	3	1	1
Penicillin	6 (14.6%)	Sulphonamide and oestrogen	6	5	1	-

* This number totals more than 42, as failures in one group are included in the next.

Subsequent Fate of Children with Vulvovaginitis

Oestrogens, penicillin, or sulphonamides frequently cure the vulvovaginal infection, but the question is: 'Will there be any relapse or recurrence after puberty, and will the disease in any way interfere with the future process of conception?'

This is an important sociological problem, so as many cases as possible were followed up through puberty and early married life.

It was found that 54 out of 78 traceable patients had attained puberty and menarche. Of these, 23 were married for a period of one to five years. Eighteen among the married group conceived within two to three years of marriage. Of the remaining five who did not conceive, four were married for less than two years and one was seeking treatment in a sterility clinic. It may be of interest to point out that one of those who conceived normally had developed signs of upper genital tract infection during the attack of vulvovaginitis. Though no positive conclusion can be arrived at, one may presume that the effects of vulvovaginitis on subsequent reproductive functions are not of considerable importance. Enquiry was made also about the menstrual history, but nothing outstanding was discovered, which could be due to the infection in childhood. Investigation, however, revealed that 71 among 78 cases traced showed considerable sex consciousness dating from soon after the disease. Records showed that 60 out of these 71 cases had

undergone energetic local treatment. This is a mild warning against the indiscriminate use of intensive local treatment in vulvovaginitis of young children.

Summary

Gonorrhoea accounts for probably not more than half the cases of vulvovaginitis in infants and children. Neither oestrogens nor penicillin nor sulphonamides offer an absolute therapeutic remedy. No matter what treatment is employed a certain number of cases appear to be resistant. With oestrogens a 72 to 75% cure is about the average which can be expected. With penicillin and sulphonamides a 90% recovery rate is a modest expectation. A comparative study of the results obtained with these three therapeutic measures is tabulated (Table 11).

The difference between results obtained with sulphonamides and penicillin is not striking. Sulphonamides, however, possess some toxicity and as such sulphonamide treated cases require to be watched carefully. The duration of treatment is about the same in both cases. Penicillin is at present expensive and the frequent medication necessarily is a drawback. The results of local penicillin treatment have been very encouraging and can be depended upon if the parents can cooperate.

Oestrogens also possess a distinct place in the treatment of vulvovaginitis. With the use of synthetic drugs expense is not a serious problem,

TABLE 11
COMPARATIVE STUDY OF RESULTS WITH OESTROGENS, SULPHONAMIDES, AND PENICILLIN

Nature of Therapy	Percentage of Cases*	Average Duration of Treatment	Cure (%)	Relapse (%)	Failure (%)
Oestrogens ..	42.5	5-6 weeks	75.5	13.7	10.8
Sulphonamides ..	34.6	5.9 days	91.5	6.0	2.5
Penicillin ..	14.6	4.1 days	88.3	5.7	5.7

* Twenty cases treated with local antiseptics only are not included.

but the course of treatment is prolonged and the recovery rate lower than with either sulphonamides or penicillin. The value of oestrogen therapy is, however, considerably increased in the treatment of relapsed or refractory cases. It is in these that the combination of oestrogens with either sulphonamide or penicillin is almost always rewarded with success.

REFERENCES

- Adair, F. L., and Hac, L. R. (1942). *New Eng. J. Med.*, **227**, 465.
- Brown, D. K. (1939). *Brit. med. J.*, **1**, 320.
- Clauberg, K. W. (1930). *Dtsch. med. Wschr.*, **56**, 524.
- Cohn, A., Steer, A., and Adler, E. L. (1941). *Amer. J. Syph.*, **25**, 329.
- Fessler, A. (1930). *Urol. cutan. Rev.*, **34**, 444.
- Fraser, A. R. (1925). *Med. J. S. Afr.*, **21**, 31; 73.
- Greenhill, J. P. (1945). 'Office Gynecology,' p. 66. Chicago.
- Hoffman, S. J., Schneider, M., Blatt, M. L., and Herrold, R. D. (1945). *J. Amer. med. Ass.*, **26**, 105.
- Karnaky, K. J. (1936). *Sth. med. J., Nashville*, **29**, 939.
- . Quoted by Greenhill, J. P. (1936). 'Year Book of Obstetrics and Gynaecology,' p. 438. Chicago.
- King, A. J., Mascal, W. N., and Price, I. N. O. (1936). *Lancet*, **2**, 18.
- Lees, D. (1928). *Edinb. med. J.*, **35**, *Trans. Obstet. Soc.*, 61.
- Lewis, R. M. (1933). *Amer. J. Obstet. Gynec.*, **26**, 593.
- (1940). *Trans. Amer. Neisserian med. Soc.*, (June 10-11). P. 34.
- Martin, C. L. (1935). *J. Amer. med. Ass.*, **104**, 192.
- Mascal, W. N. (1933). *Lancet*, **2**, 233.
- Mukherjee, C. L. (1940). *J. Obstet. Gynaec. Brit. Emp.*, **47**, 275.
- Nelson, N. A. (1932). *New Engl. J. Med.*, **207**, 135.
- Ruys, A. C. (1935). *J. Amer. med. Ass.*, **105**, 862.
- Sako, W., Tilbury, R., and Colley, J. (1945). *Ibid.*, **128**, 508.
- Schauffier, G. C. (1940). *Surg. Gynec. Obstet.*, **71**, 286.
- (1947). 'Pediatric Gynecology,' p. 148. Chicago.
- Te Linde, R. W. (1938). *J. Amer. med. Ass.*, **110**, 1633.
- Wattie, N. Quoted by Cruickshank, R., and Sharman, A. (1934). *J. Obstet. Gynaec. Brit. Emp.*, **41**, 217.
- Williams, P. F. (1926). *Amer. J. Obstet. Gynec.*, **11**, 487.
- (1933). In Curtis' 'Obstetrics and Gynecology,' Vol. II., p. 535. Philadelphia.
- Witherspoon, J. T. (1935). *Amer. J. Obstet. Gynec.*, **29**, 906.
- Wynkoop, E. J., and Boggs, E. O. (1926). *N. Y. St. J. Med.*, **26**, 894.