

Natural history of genital warts

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Genital warts were known to the ancients, and many Greek and Roman writers referred to them. The early history of the disease has recently been reviewed by Bäfverstedt (1967), who pointed out that some of the early synonyms for the lesions, particularly the words 'fig' and 'condyloma', have survived into modern times. In the Middle Ages, descriptions of diseases were less precise than in the ancient world, but some of the genital lesions described (Lanfranc, 1306) may have been warts.

The outbreak of syphilis in Europe at the end of the 15th century led to renewed interest in genital diseases, but at this time most genital lesions were attributed to the 'venereal poison', and no causal distinction was made between the diseases now known as gonorrhoea, syphilis, and genital warts. Even Hunter (1786), who gave a clear description of genital warts, regarded them as a manifestation of syphilis, and did not differentiate them from condylomata lata. The important recognition that genital warts comprised a disease entity unrelated to syphilis was first made by Bell (1793), and his work was later confirmed by Jourdan (1826) and Ricord (1838). But, as the belief that genital warts were due to syphilis was gradually abandoned, the erroneous view developed that they were connected with gonorrhoea (Pirrie, 1852); indeed, in the 19th century, they were sometimes referred to as 'gonorrhoeal warts'. But Aimé Martin (1872) pointed out that many patients with genital warts gave no history of gonorrhoea, and after the isolation of the gonococcus in 1879 it was realised that over half of the patients with genital warts showed no sign of it (Jadassohn, 1905).

Many 19th century writers thought that genital warts were caused by irritation of the epidermis by various agents such as dirt, decomposed smegma, and genital discharges (Astley Cooper, 1835; Bumstead, 1864). This 'non-specific irritant' theory was widely accepted for many years; Cronquist (1912) strongly supported it, and it was reaffirmed well into the 20th century (Kaplan, 1942).

The idea that genital warts might be related to skin warts was first postulated by Gémy (1893), who was struck by their histological similarity. Nevertheless, there are also histological differences between the various kinds of skin wart and genital warts (Allen, 1965). Moreover, some animals are known to develop two aetiologically distinct types of wart; for example, the rabbit is liable to warts on the skin and in the mouth, but these are causally unrelated (Allison, 1965). Thus, histological resemblances between some types of skin and genital warts may not prove aetiological identity. However, a close relationship between warts on the genitals and on the skin was suggested by two further pieces of evidence, one clinical and the other experimental. Clinically, it was observed that many patients with genital warts had warts on the skin as well (Rasch, 1895; Diday, 1900; Thibiérge, 1905; Frey, 1924). These observations were not controlled by recording the prevalence of skin warts in the population groups being studied, and are thus of limited value. In this connection, it should also be pointed out that in the group of people in whom skin warts occur most commonly, namely children, genital warts are exceedingly rare. Experimentally, the idea that genital warts were related to skin warts received some support from the inoculation of extracts of excised penile warts into the skin of other parts of the body which was followed, in some cases, by the development of plane or common warts at the inoculated sites. This technique had been successfully used by Ciuffo (1907), Serra (1908), and Wile and Kingery (1919) to establish the viral aetiology of skin warts. In the case of genital warts, the experiments were fewer and the results less convincing. To prove a common viral cause for skin and genital warts by this means, it would be necessary to inoculate successfully a cell-free filtrate of genital warts into the skin, and of skin warts into the genitals; the use of unfiltered extracts would not be acceptable, as living cells might be introduced and act as a tissue graft (Gross, 1961). Unfiltered penile wart extracts have raised skin warts on several occasions (Waelsch, 1918; Frey, 1924; Goldschmidt and Kligman, 1958), but filtered extracts only once (Serra, 1924). Vulval wart extracts have never been

used; and the crucial experiment of successfully inoculating an extract of skin warts into the genitals has never been carried out. For these reasons, the results of these experiments must be interpreted with caution.

Nevertheless, the evidence available convinced most observers that warts on the skin and genitals were caused by the same virus (Frey, 1924), and this 'unitary' theory has not been seriously questioned. But the emphasis on the present (or past) existence of warts on the skin in patients with genital warts led attention away from the important question of how often the disease is sexually transmitted. There has never been agreement about this. In the days when the 'non-specific irritant' theory was believed, most clinicians had seen cases in which both partners had genital warts, and to explain this it was suggested that among the irritants which could cause warts was one secreted by the warts themselves, and that this irritant could be sexually transmitted (Astley Cooper, 1835; Bumstead, 1864); others, however, denied that this could happen (Hill, 1868). The proponents of the 'unitary' theory thought that sexual transmissibility seemed likely on general grounds, but firm evidence was lacking, and this led Heller (1921) to observe that 'general considerations speak for it, but practical considerations are against it'. More recently, many observers have concluded that genital warts are sexually transmissible, although epidemiological evidence was not available (Jacobsen and Jones, 1938; Wilson, 1937; Goldman and Clarke, 1940; Harkness, 1950). A significant advance was made by Barrett, Silbar, and McGinley (1954), who were struck by the frequent appearance of penile warts in soldiers returning from the Far East who had had intercourse with native girls. They examined a group of women with vulval warts, all of them wives of soldiers who had recently returned from Korea and Japan, and found that all their husbands had recently had penile warts, the incubation period in the cases of the wives being 4 to 6 weeks. They did not record the incidence of skin warts in any of their patients, but they were impressed by the apparent sexual infectivity of the condition, and suggested that genital warts should be regarded as a venereal disease. Their work was severely criticised by Robinson (1954), Ronchese (1954), and others, who reaffirmed the 'unitary' theory, and stated that many skin diseases, such as scabies, might sometimes be sexually transmitted without this being the usual means of spread, and that this was true of warts as well.

Teokharov (1962, 1969) has recently reported studies of the epidemiology of genital warts. He found that warts on the skin were uncommon in

patients with genital warts, but that contact tracing showed a high sexual infectivity, two-thirds of those who had had intercourse with individuals with genital warts developing the disease subsequently, the average incubation period being 3.1 months. He concluded that genital warts comprised an independent viral venereal disease, different from non-genital warts.

There is, therefore, some uncertainty about the natural history of genital warts. On the one hand, it is suggested that the disease is merely part of the skin wart dermatosis. According to this theory, warts may appear anywhere on the body, and may spread from one part of the skin to another, from the genitals to the skin or from the skin to the genitals; the occasional sexual transmission of genital warts is regarded as of no more significance than that which may occur in other skin diseases with genital manifestations, such as scabies or fungal infections. On the other hand, it is believed that genital warts are an independent disease, sexual transmission being the usual, or perhaps only, means of spread, and any clinical connection with skin warts is denied. As regards the aetiology of genital warts, the first theory must mean causal identity of skin and genital warts; the second theory implies causal diversity, although this is not necessarily essential.

In the following study, the clinical characteristics and epidemiology of genital warts seen in a group of patients are described, in an attempt to clarify the natural history of the disease.

Clinical material and methods

332 patients with genital warts were seen by the author between October, 1967, and January, 1970; 191 were men and 141 women. Most of these patients came to the Department of Venereology, St. Thomas' Hospital; a few were seen at other hospitals.

At the first interview, the history was recorded as follows:

- (1) Age and race;
- (2) Duration of genital warts;
- (3) Presence of other genital symptoms;
- (4) Sexual activities during the 12 months before the warts appeared, with details of contacts;
- (5) History of warts of any kind in the past; whether any non-genital warts were present now.

The results of examination were recorded as follows:

- (1) In men, whether circumcised.
- (2) Size, number, appearance, and location of genital warts.

In men, the sites of wart formation were classified as fraenum, corona and coronal sulcus, glans, urinary meatus, inner surface of prepuce, outer

surface of prepuce, preputial opening, shaft of penis, scrotum, anus, and 'other'.

In women, the sites were classified as labia majora, labia minora, clitoris, urinary meatus, introitus (anterior, posterior, and lateral), vagina, cervix, perineum, anus, and 'other'.

- (3) Presence of other genital lesions or discharges.
- (4) Site and type of any warts found on the skin.

At the second interview, usually 1 week after the first, the diagnosis of any other genital infection was recorded when the results of the usual routine investigations became available.

Patients were encouraged to bring sexual contacts to the Department. In a few instances, contacts were found to be attending other venereal disease clinics, and the clinic records of the presence or absence of genital warts in these cases were noted. No uncorroborated statements by patients as to the presence or absence of warts in their contacts were accepted.

For purposes of comparison, a 'control group' was set up, consisting of 97 white men who had gonorrhoea but no genital warts. In each of these patients, a note was made of whether he was circumcised, and the skin was inspected for warts.

Results

RACIAL DISTRIBUTION

191 men were seen with genital warts, of whom twenty were Negroes, four Indians, one Chinese, and 166 (87 per cent.) white. During the year ended June 30, 1969, 67 per cent. of all men attending the Department for the first time were white.

141 women were seen with genital warts, of whom nine were Negroes, two Indians, two Chinese, and 128 (91 per cent.) white. During the year ended June 30, 1969, 69 per cent. of all women attending the Department for the first time were white.

In the present series, therefore, genital warts were relatively more common among white than coloured patients.

AGE INCIDENCE

Most of the genital warts were seen in young adults (Fig. 1). 67 per cent. of white men with the disease were between the ages of 16 and 25, the commonest age at onset being 22 years. The comparison in this respect with gonorrhoea, an exclusively sexually transmitted disease, is interesting. Fig. 2 shows the age incidence of genital warts in this study compared with that of gonorrhoea reported in a recent survey (Ödegaard, 1967). The curves show general similarity, and the commonest age at onset of gonorrhoea is also 22 years.

In women, the same general conclusions on age incidence can be drawn. Again, genital warts were

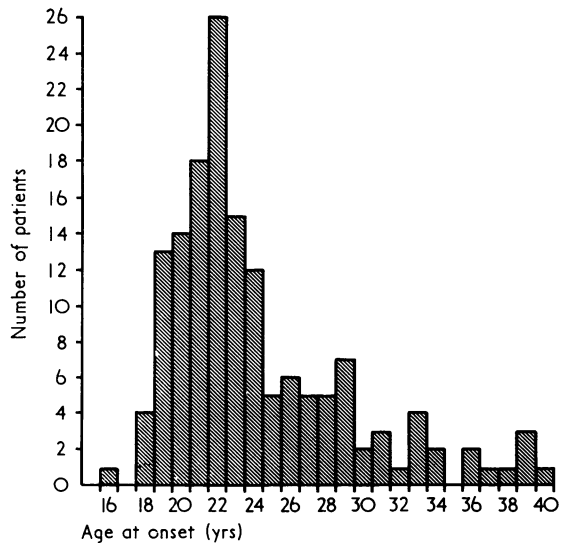


FIG. 1 Age at onset of genital warts (white men)

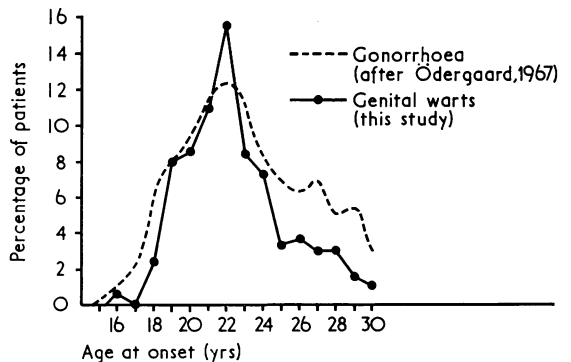


FIG. 2 Ages at onset of gonorrhoea and genital warts (men)

found mostly in young adults (Fig. 3); 82 per cent. of white women with the disease were between the ages of 16 and 25, the commonest age at onset being 19 years. Once more, the age at onset is comparable with that of gonorrhoea, likewise most common at the age of 19 years (Fig. 4).

MORPHOLOGY OF GENITAL WARTS

Genital warts show considerable morphological variation, but three clinical types can be distinguished, for which the terms *hyperplastic*, *sessile*, and *verruca vulgaris* are suggested. To some extent, the type of wart appearing depends on the site affected. Thus, in men, the fleshy *hyperplastic* wart was seen most often on the glans penis and on the inner lining

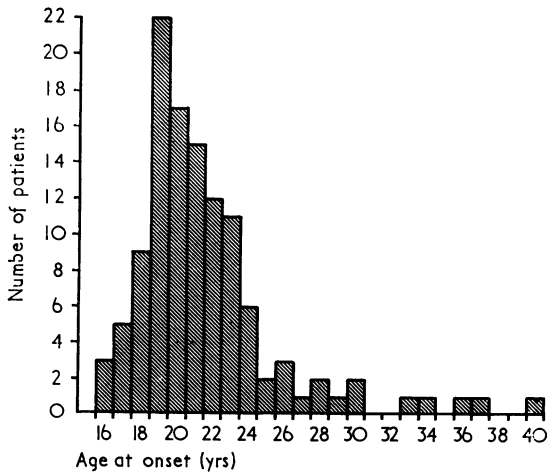


FIG. 3 *Age at onset of genital warts (white women)*

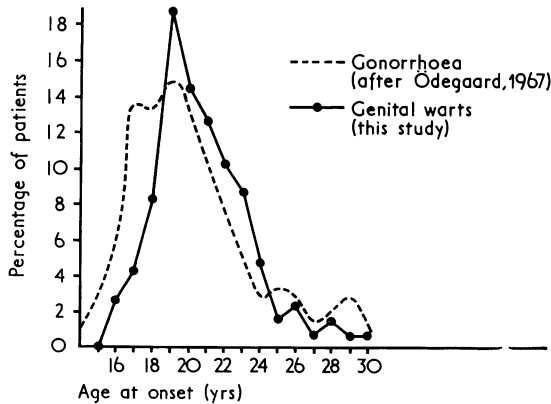


FIG. 4 *Ages at onset of gonorrhoea and genital warts (women)*

of the prepuce (Fig. 5); on these moist areas, the warts were sometimes quite large, but although moisture may affect their size, their morphology seems to depend rather on their location, as warts of the same type were seen in circumcised men (Fig. 6). Hyperplastic warts were also seen in the urinary meatus and in the terminal urethra (Fig. 7); their characteristically bright red colour here is probably due to the removal of surface debris by the passage of urine. Urethroscopy was carried out on patients with meatal warts if these were particularly large or recurred after treatment; extension of warts proximally into the spongy urethra was not seen in any patient, although it has been described (Morrow, McDonald, and Emmett, 1952).

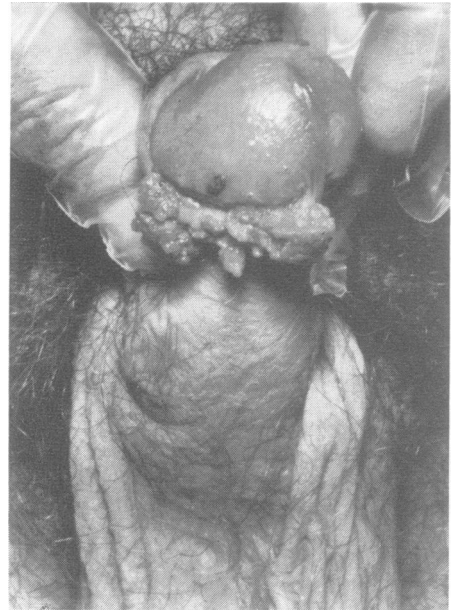


FIG. 5 *Hyperplastic fraenal and coronal warts, present for one month; the patient's sexual contact had vulval warts*

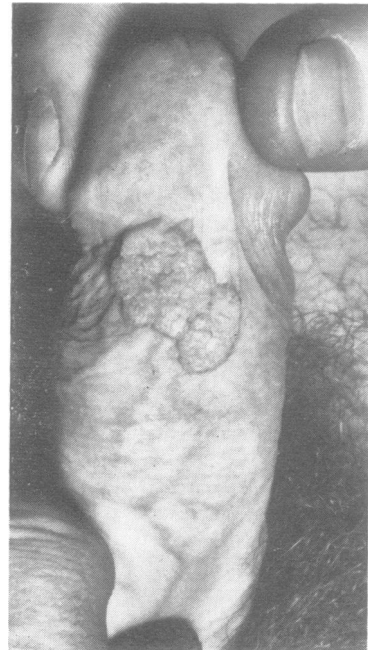


FIG. 6 *This wart formation had been present for 18 months. The patient's current contact had vulval warts of recent onset*

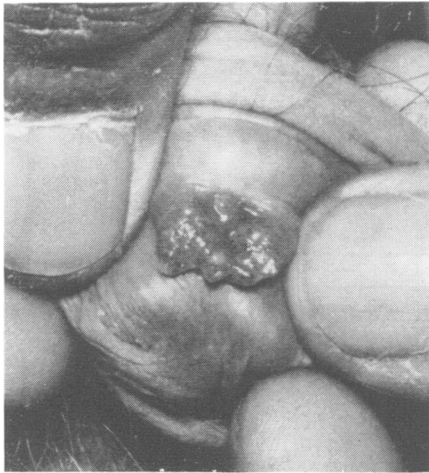


FIG. 7 Meatal warts. This patient had no other warts on the genitals

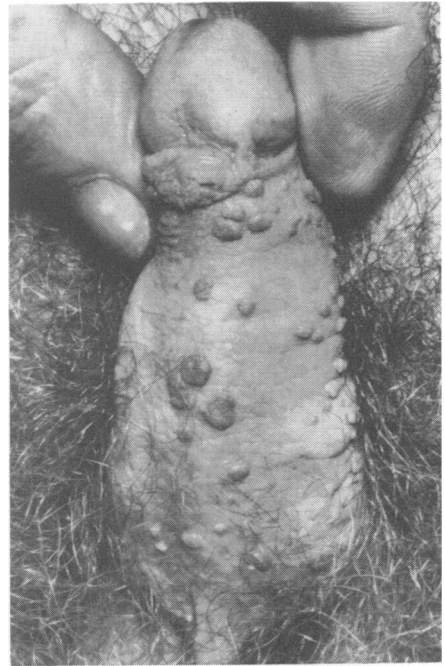


FIG. 9 Verruca vulgaris of penis. These warts had been present for over 3 years; the patient had had common warts on his hands for 10 years. His wife had no warts.



FIG. 8 Sessile warts on shaft of penis; duration 6 months

Smaller, discrete, *sessile* warts were observed on the shaft of the penis in some patients (Fig. 8); they were not seen on the glans, even in the circumcised. In some individuals, these were the only warts present, but in others they were associated with hyperplastic warts on the glans. Warts on the outer aspect of the prepuce were rare. Although sessile warts were usually multiple, coalescence of the lesions did not occur. They have some resemblance to plane warts on the non-genital skin, but are a little more conspicuous than these.

A third variety of wart was seen in only a few patients. These lesions were raised, multiple, and 2 to 3 mm. in diameter; morphologically and histologically they closely resembled common skin warts (Fig. 9). They were seen only on the shaft of the



FIG. 10 Typical early vulval warts of 2 weeks' duration. This patient's sexual contact had penile warts

penis, never on the glans, nor were they associated with warts of the other types. The possible significance of this *verruca vulgaris* type of wart will be discussed later.

In women, hyperplastic warts predominated (Fig. 10); these reached their largest size within the labia, where conditions are moist. It was not possible, as it had been in men, to differentiate hyperplastic and sessile warts. However, two patients were seen who had vulval warts of the *verruca vulgaris* type, resembling common skin warts (Fig. 11).

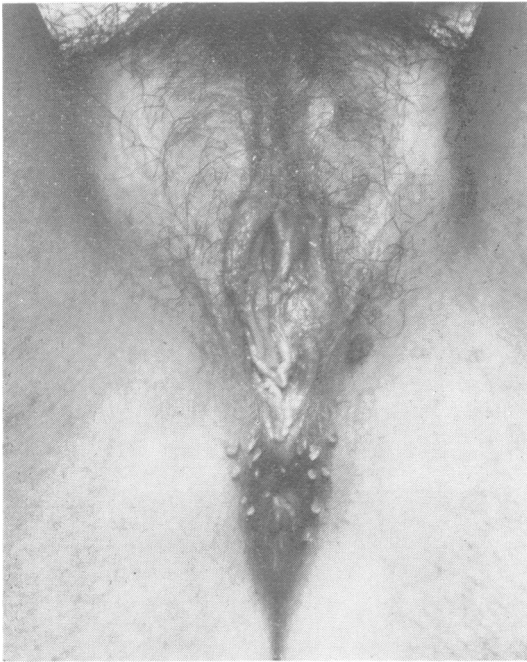


FIG. 11 *Vulval, perineal, and perianal warts of verruca vulgaris type. The patient also had common warts on the hands*

LOCATION OF GENITAL WARTS

Warts are not uniformly distributed over the genitals; some parts are more often affected than others. The distribution of warts on different parts of the genitals in men and women is shown in Tables I and II.

TABLE I *Distribution of genital warts in men*

Site	Percentage of patients affected
Fraenum, corona, and glans	52
Prepuce (all parts)	33
Urinary meatus	23
Shaft of penis	18
Scrotum	2
Anus	8

TABLE II *Distribution of genital warts in women*

Site	Percentage of patients affected
Posterior part of introitus	73
Labia minora and clitoris	32
Labia majora	31
Urethra	8
Vagina	15
Cervix	6
Perineum	23
Anus	18

The significance of the distribution of genital warts is seen more clearly in patients who have had the disease for only a short time, before there has been much secondary spread. The distribution of lesions in men who had had genital warts for a month or less is shown in Table III; the parts most often affected were the inner lining of the prepuce and the fraenum, followed by the corona and coronal sulcus, and then the urinary meatus. It is interesting that the classical studies of syphilis (Lambkin, 1908) showed that in this disease primary lesions occur most commonly in these same areas. The distribution of early lesions in women is shown in Table IV. Warts appeared first most often at or near the posterior part of the vaginal introitus and on the adjacent labia majora and minora.

TABLE III *Distribution of genital warts in uncircumcised men (duration 1 month or less)*

No. of patients	54
Site	
Prepuce (inner)	31
Fraenum	27
Corona and coronal sulcus	16
Meatus	10
Glans	3
Prepuce (outer)	0
Shaft	0

TABLE IV *Distribution of genital warts in women (duration 1 month or less)*

No. of patients	49
Site	
Introitus (posterior part)	40
Introitus (other parts)	3
Labia minora and clitoris	15
Labia majora	13
Vagina (lower half)	5
Vaginal vault	1
Cervix	2
Urinary meatus	2

An interesting feature of genital warts is their remarkably constant localization to site. In men, although large penile warts may involve the scrotum and anus secondarily and a few ill-developed warts may be seen in the pubic region, involvement of the abdomen or thighs seems to be very unusual. A similar situation exists in women with vulval warts,

and in both sexes a patient may have very large perianal warts but none on the buttocks. This confinement to one area seems to be a constant property of this type of wart.

FACTORS MODIFYING GENITAL WARTS

Circumcision

Genital warts are a little commoner in uncircumcised than in circumcised men. 79 per cent. of white men seen with warts were uncircumcised; in the control group of white men with gonorrhoea, 71 per cent. were uncircumcised. The type and distribution of warts were different in the circumcised; although warts at the urinary meatus were equally common in the two groups, warts on the shaft of the penis (mostly of sessile type) were much more often seen in circumcised men, in whom warts on the glans penis were rarer. Extensive wart formations were more common in the uncircumcised (Fig. 12).

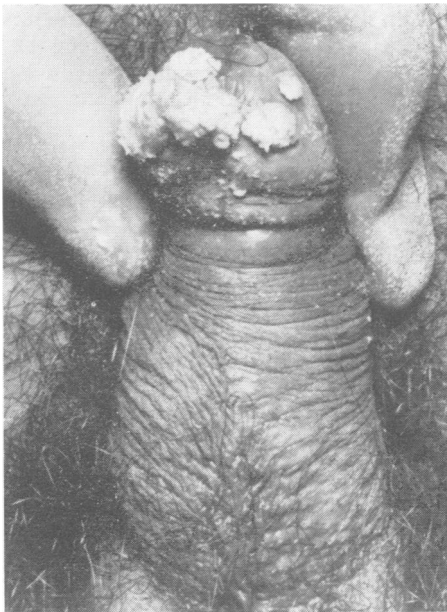


FIG. 12 Large hyperplastic penile warts. This patient had a phimosis and did not know that the warts were present

Other genital infections

Some patients with genital warts had other genital infections at the same time. In Table V, the incidence of these infections in white men with genital warts is compared with the incidence in 300 consecutive white patients without genital warts, who attended the Department from January 1, 1968, onwards.

TABLE V Comparison of incidence of genital infections in white men with and without genital warts

Disease	Incidence (per cent.)	
	With genital warts	Without genital warts
Syphilis (all forms)	1	1
Gonorrhoea	13	18
Non-gonococcal urethritis	21	37

A similar comparison in the case of women is made in Table VI. With the possible exception of candidiasis in women, other genital infections do not seem to be significantly commoner in those with genital warts than in those without them, and warts were no larger or more extensive in patients with

TABLE VI Comparison of incidence of genital infections in white women with and without genital warts

Disease	Incidence (per cent.)	
	With genital warts	Without genital warts
Syphilis (all forms)	1	1
Gonorrhoea	20	23
Trichomoniasis	16	14
Candidiasis	18	12

these infections. It is sometimes said that the extent of genital warts is affected by poor personal hygiene. This is difficult to assess; it may play a small part, but many large genital warts were seen in patients who were scrupulous in their personal cleanliness and in whom, indeed, the size of the warts caused much distress.

PREGNANCY

Genital warts in many women enlarge and extend considerably during pregnancy. Thirteen of the 141 women seen in this series were pregnant, and in ten of these pregnant women the warts were very extensive; in one patient they were so large that there was difficulty in delivery (Fig. 13, overleaf).

Spontaneous disappearance of these large warts in the puerperium has been described several times (Gorthey and Krembs, 1954; Hingorani and Kaur, 1961), and was observed in most patients here. It is not invariable, however. One woman was seen who had large vulval warts in two successive pregnancies; between the pregnancies, the warts regressed, but never disappeared completely.

INFECTIVITY OF GENITAL WARTS

This important question was studied by tracing and examining sexual contacts of patients with the disease. Since there was no information about how infectious genital warts were, or of their incubation period, the attempt was made to see contacts who had had intercourse with patients during the 9 months

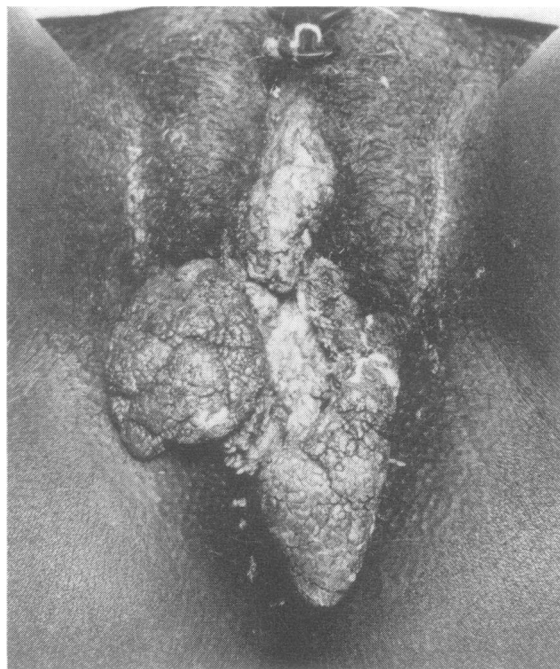


FIG. 13 *Massive vulval warts in a 17-year-old girl in the 36th week of pregnancy. Excision of the larger wart masses was necessary to facilitate delivery, but the remainder disappeared completely in the puerperium without further treatment*

before the warts appeared, and to follow up secondary contacts, who had had intercourse with them after the warts appeared, for the same length of time. As might be expected, this proved to be the most difficult part of this study.

In all, 97 people were seen who had had intercourse with individuals who were known to have had genital warts at the time, and 62 of these people were found to develop genital warts subsequently (Table VII). This gives an infectivity rate of 64 per cent.; the true figure could be higher than this, as it was not possible to follow up all secondary contacts for the full 9-month period. The incubation period showed a range of between 3 weeks and 8 months, the average being 2.8 months.

TABLE VII *Infectivity of genital warts*

Sex	No. of patients at risk	No. developing warts
Men	31	22
Women	57	31
Total	88	53

Note: In nine other cases, both partners had genital warts but it was doubtful who had developed them first.

There was other evidence of the sexual infectivity of the disease. Fifteen women were seen who had been virgins before they had had intercourse with men with penile warts; all developed vulval warts subsequently. Furthermore, several patients provided more than one positive secondary contact; for example, one patient produced three female contacts, all of whom developed vulval warts after having intercourse with him. Finally, three 'generations' of genital warts were observed on a few occasions, in which the disease appeared to have been transmitted from one patient to a second, and from the second to a third.

Not all those who had intercourse with individuals with genital warts developed the disease. The infectivity of the warts seemed to decrease with the length of the time they had been present; thus, the average duration of warts at the time of intercourse in the men whose contacts subsequently developed vulval warts was 3½ months, and in the men whose contacts did not develop warts it was 12 months. No doubt other factors affect the infectivity of these warts, or resistance to them, but these could not be assessed.

GENITAL WARTS AND SKIN WARTS

Is there any evidence that genital warts are causally related to warts on the skin? Skin warts are widespread, particularly in the younger people in whom, as has been seen, most genital warts occur, so the fact that a patient with genital warts has a skin wart may not be aetiologically significant; to establish an epidemiological connection between the two kinds of wart, it must be shown that skin warts are commoner in patients with genital warts than in a comparable population group without genital warts. Therefore, the incidence of skin warts in white men with genital warts was compared with that in a control group of white men who had gonorrhoea but no genital warts. The results are shown in Table VIII. It will be seen that there is no significant difference in this respect between the two groups.

TABLE VIII *Incidence of skin warts in men with and without genital warts*

Skin warts	166 white men with genital warts	93 white men with gonorrhoea
Common warts On hands	25	15
Elsewhere	2	1
Plantar warts	2	1
Total No.	29	17
Per cent.	17.5	18.2

It is also possible that the development of genital warts might be related to a sexual contact's skin warts; particularly if these warts were on the hands,

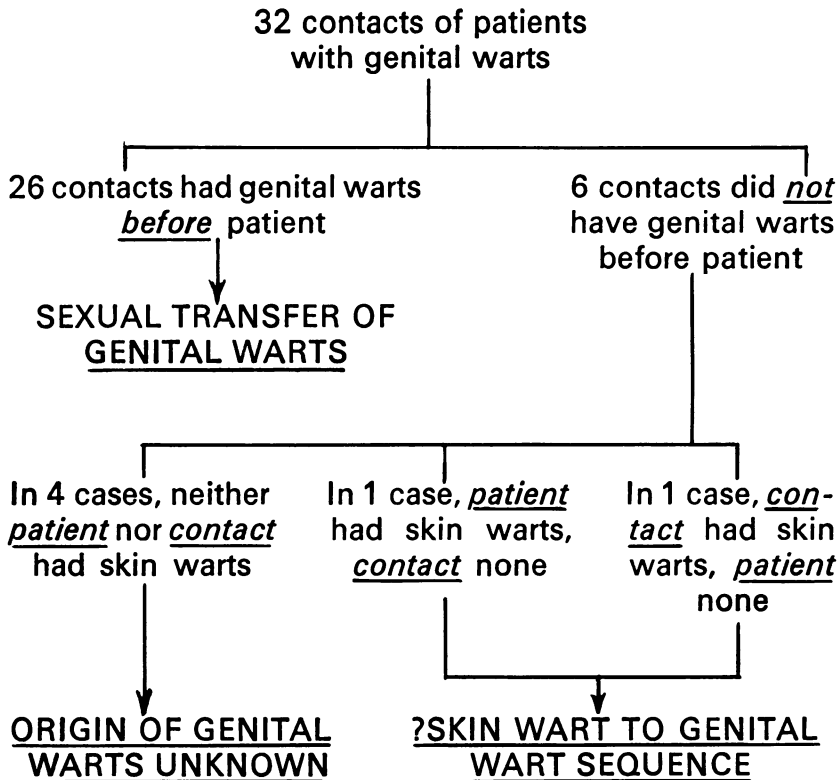


FIG. 14 Patients with genital warts and one primary contact

it is conceivable that any virus present might be transferred to the partner's genitals during love-play. To investigate this possibility in the simplest way, enquiry was restricted to patients with genital warts who had had sexual relations with only one person during the 9 months before the lesions appeared; it was also necessary that this primary contact should have been examined. 32 patients were found who satisfied these criteria; in them it was possible to see whether the contact had genital warts, and whether either had warts on the skin. The findings are shown in Fig. 14. The results do not suggest that a patient's genital warts often arise because a sexual contact has skin warts; in fact, they emphasize again the importance of sexual transmission in the aetiology of the disease.

In a smaller number of cases a close morphological and histological resemblance between the two types of wart was observed. As has been mentioned, a few patients have genital warts which look like common skin warts and resemble them histologically. Warts of this kind were seen on the shaft of the penis in four men. It is interesting that three of these men also had skin warts; two had common warts on

the hands, and one had them at the elbow—in this last case, the genital and skin warts resembled each other very closely (Fig. 15A, B, overleaf). In women this type of wart is more difficult to identify, owing to maceration of the lesions in the moist conditions on the genitals, but in one patient (Fig. 11), undoubted lesions of *verruca vulgaris* were seen on the vulva and perineum, and the diagnosis was confirmed histologically; she also had common warts on the hands.

Although rare, occurring in less than 1 per cent. of patients, these lesions do seem to form a distinct clinical sub-group. They are particularly persistent and difficult to treat; like common skin warts, they respond poorly to podophyllin.

Discussion

Genital warts are a disease of sexual maturity, and in age incidence the disease bears a close resemblance to gonorrhoea. It may be objected that this resemblance is due only to the fact that the group of patients with genital warts were seen in a department of venereology, and simply resemble the 'clinic population' in age. However, the infrequency of genital warts in dermatological, surgical, and gynae-

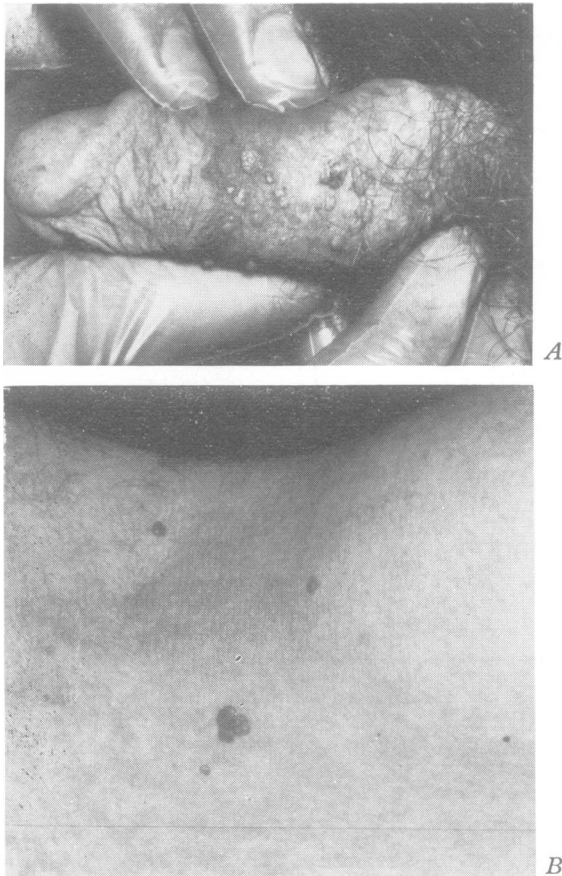


FIG. 15 *Verruca vulgaris* of the penis (A). Notice close morphological resemblance to common warts in cubital fossa of same patient (B)

ological practice has been noted several times (Ebergényi, 1939; Speiser, 1942); Rulison (1942) stated that the diagnosis of 'condyloma acuminatum' was made only 32 times in 250,000 patients who attended the New York Skin and Cancer Hospital between 1925 and 1934. On the other hand, genital warts are often seen in venereal disease clinics, so that the age of incidence recorded here is probably the true one, and the resemblance to gonorrhoea significant.

In men, it has been shown that genital warts most commonly appear first on the inner lining of the prepuce (if present) and the fraenum, followed by the corona and coronal sulcus, and then the urinary meatus, and the resemblance in this respect to the primary lesions of syphilis has been noted. It is likely that in both cases the location of lesions is related to trauma. Minor injuries to the penis during

coitus are not uncommon; abrasions may be seen on the inner lining of the prepuce and around the corona, and definite tears occur at the fraenum. The parts of the penis on which warts appear first seem to be those which are most often injured during intercourse; indeed, three patients were seen whose warts appeared first at the fraenum as the tears healed. In women, warts appear first most often at or near the posterior part of the introitus, a site at which minor abrasions and tears are often seen; again, there appears to be a relationship between genital trauma and the location of warts.

This association between genital warts and sexual activity does not, of course, prove that genital warts are a sexually transmitted disease; it has been postulated that sexual activity simply allows the entry of a causal agent already present on the genitals (Robinson, 1954). But it has been shown in this study that 64 per cent. of those who had intercourse with individuals known to have genital warts at the time subsequently developed the disease, and this high infectivity suggests that the passage of an infective agent by sexual intercourse from one person to another is the usual cause of development of the warts. The results obtained agree with those of Teokharov (1962), whose suggestion of an incubation period of 3.1 months is comparable to the period of 2.8 months found in the present study.

It is therefore suggested that in respect of age incidence, parts of the genitals affected in relation to trauma, and sexual infectivity, genital warts resemble diseases known to be sexually transmitted. The incidence of venereal diseases increases sharply in war time, and it is interesting that several workers have commented on the increased occurrence of genital warts during the second world war (Culp and Kaplan, 1944; Gersh, 1945), and during the Korean War (Barrett and others, 1954).

The relationship between warts on the genitals and warts on the skin will now be considered. The belief that they are aetiologically identical depends, in part, on the assertion that a large number of patients with genital warts have warts on the skin as well. This was not found during the present investigation. Although 17.5 per cent. of the white men seen with genital warts had warts on other parts of the body (mostly common warts on the hands), a similar proportion of the control group also had skin warts. There was, therefore, no epidemiological evidence that genital warts are often caused by the transfer of virus from skin warts to the genitals. In a small number of patients, however, the history given suggested that genital warts might have arisen in this way. For example, one woman with vulval warts said that she had only had intercourse with one

man, with whom she had been associating for a year. He was examined and was found to have three plantar warts but no genital warts. It is possible that his plantar warts were the source of her genital warts, although there are obvious difficulties in explaining how the transfer of the virus actually occurred. On the other hand, the man had had other contacts, and it is conceivable that he may have had genital warts which had spontaneously regressed, the presence of the plantar warts being only a coincidence. Alternatively, the woman herself may have had other contacts, although she denied it. It has been seen that, out of 32 patients admitting only one contact, in four cases the contact did not have genital warts, and neither patient nor contact had warts on the skin (Fig. 14). In these cases the origin of the genital warts is unknown. Bearing these circumstances in mind, it is concluded that epidemiologically a causal relationship between skin warts and genital warts is possible, but unproved. An analysis of a much larger number of patients and their contacts than has been attempted here would be needed to establish it.

In the small group of patients with lesions of *verruca vulgaris* of the genitals, there certainly does appear to be a morphological and histological resemblance between skin and genital warts, both of which are usually present in these patients. It is interesting that some early writers (Abraham and Davis, 1910) made a clinical distinction between warts on the genitals, which they thought were caused by the virus of skin warts, and *condylomata acuminata*, which they thought were due to irritation from genital discharges, but this distinction was abandoned when the idea that genital warts could be produced by chronic irritation was discarded. *Verruca vulgaris* of the genitals is certainly distinctive, and it is possible that the older clinicians were right in thinking that warts of this kind are caused by the action of the virus of skin warts on the genital epidermis. It must be stressed that this idea is virologically unproved; the laboratory techniques recently used in the study of genital warts (Almeida, Oriel, and Stannard, 1969) are not sensitive enough to characterize any virus present in such small lesions, and the question whether *verruca vulgaris* of the genitals is a virological as well as a clinical entity cannot be decided at present.

To summarize the question of aetiology, there seems little doubt that most patients develop genital warts because they have had sexual contact with an individual who also has them. No close clinical relationship with skin warts could be established, with the exception of *verruca vulgaris* of the genitals, occurring in a small minority of patients, which may be a special case. The nature of the infecting agent

in genital warts cannot be deduced from clinical studies; it can be identified only by virological investigation. Recent electron microscopic studies (Dunn and Ogilvie, 1968; Oriel and Almeida, 1970) have shown that a papillomavirus is present in low concentration in genital warts. However, further investigation (Almeida and others, 1969) has shown that this virus appears to be antigenically different from the virus present in common skin warts.

Once established on the genitals, the warts both enlarge and spread. The extent to which this happens does not seem to depend so much on the presence of other genital infections as on the presence of moisture; hence, the largest penile warts are seen under the prepuce, and the largest vulval warts within the labia. The role of the prepuce in genital wart development has been stressed by Gersh (1945). In women, pregnancy had a marked effect on the rate of growth of genital warts in many patients in this survey. Why this happens is unknown; Wilson (1937) suggested that the cause might be a raised local level of oestrogens; but other factors, such as increased vascularity or moisture of the parts during pregnancy, may be responsible. That this effect is reversible is shown by the regression of genital warts in the puerperium in most (but not all) cases.

The spread of warts from the genitals to the anus occurs in both sexes, but is more than twice as common in women; other genital infections, such as gonorrhoea and candidiasis also spread in this way, and in all these cases the backward flow of infected vaginal discharge is probably responsible. Warts which are *restricted* to the anus present special clinical and epidemiological problems, and will not be considered further here; a separate study of anal warts will appear in the near future.

Nine of the women seen with genital warts had warts on the cervix; in the cases of seven of these patients, there were warts on the vulva as well, but in two women (both with positive contacts), the warts were on the cervix only (Fig. 16, overleaf). Whether warts have any connection with other cervical diseases is not known and, indeed, cervical warts have been little studied. Raftery and Payne (1954) have reported two cases in which cervical biopsy revealed invasive squamous cell carcinoma associated with superficial cervical warts, and the possibility of malignant transformation of cervical warts appears to deserve further consideration.

What happens to untreated genital warts? Like warts on the skin, they may remain for a very long time; one man seen had had penile warts for more than 10 years. Conversely, genital warts, like skin warts, sometimes regress spontaneously, and this too was seen in a few patients. The reason for this

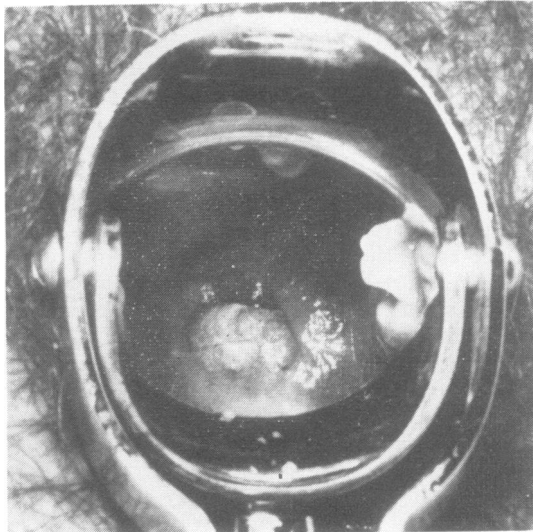


FIG. 16 *Warts on cervix uteri. This patient's sexual contact had penile warts. The first time she was seen, the cervix was normal, but one month later these warts had appeared. There were no warts on the vulva*

phenomenon is unknown, and is likely to remain so until the immunology of warts can be systematically studied. Malignant transformation of genital warts was not seen in any patients in this investigation. Nevertheless, it must be accepted as a rare complication, either as a locally invasive and destructive condition, the so-called 'giant condyloma' (Buschke and Loewenstein, 1932; Dawson, Duckworth, Bernhardt, and Young, 1965), or as a frankly malignant, metastasizing tumour (Sims and Garb, 1951; Davies, 1965). The occurrence of these rare but serious complications adds interest and perhaps importance to the study of this disease.

Summary

332 patients with genital warts (191 men and 141 women) have been studied at St. Thomas' Hospital, and the morphological varieties of these warts and the factors modifying their development have been described. It has been shown that the disease is one of sexual maturity, and that the age of onset closely parallels that of gonorrhoea. The sites at which genital warts first appear are those most often injured during coitus. Finally, there is evidence of a high incidence of genital warts in those who have had sexual relations with individuals suffering from the disease. It is concluded that in many ways genital warts behave like a sexually transmitted disease.

No epidemiological evidence was found of a

close relationship between genital warts and skin warts. Warts on the skin were no commoner in men with genital warts than in a control group, and previous suggestions that genital warts are often formed by the transfer of virus from skin warts to the genitals were not substantiated.

However, a very small number of patients with skin warts exhibited genital warts of distinctive appearance, resembling *verruca vulgaris*, and it is possible that genital warts of this type may be causally related to skin warts. With this exception, there was no clinical evidence of the nature of the infecting agent in genital warts, and its identification must depend on virological rather than clinical studies.

The distinctive appearance, rate of growth, and response to pregnancy of genital warts suggests that they may comprise a distinct disease entity, and the possible relationships between this and other genital diseases are briefly discussed.

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