Management of genital warts: a guide for GPs

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Genital warts are primarily a cosmetic problem; however, they can cause psychological distress and take some time to resolve. This article discusses the diagnosis of genital warts, the treatment options available and the GP’s role in management.

Genital warts are a sexually-transmitted infection (STI) caused by transmission of human papilloma virus (HPV). There are more than 100 genotypes of HPV, but most genital warts are caused by infection with types 6 and 11. Of patients infected with HPV types 6 and 11, more than 90% do not have visible genital lumps, and 95% of infections resolve spontaneously within two years with or without treatment.1

There are two other main types of HPV that cause genital infections – types 16 and 18. These do not cause warts and are instead deemed ‘high-risk’ infection and can lead to ano-genital carcinoma, such as cervical, vulval, penile and anal carcinoma. They are also a significant cause of oropharyngeal cancers.

The introduction of an HPV vaccination (see Box 1), which protects against types 6, 11, 16 and 18, has resulted in a significant decrease in the number of genital wart diagnoses in England, with a 3% decrease from 59,178 cases in 2017 to 57,318 cases in 2018. This decrease is largely due to the decline of HPV infection in younger women (the majority of whom would have received the HPV vaccine at age 12–13 years), with a 56% decrease in genital warts diagnoses among 15–17-year-old girls and a corresponding 46% decrease among 15–17-year-old boys between 2017 and 2018.2

Symptoms

Genital warts are fleshy lumps that appear on the external genitalia and perianal area in men and women. They can also be found inside the vagina, on the cervix and in the anus. They are not normally painful but can be itchy. Cervical, urethral and anal warts can also be associated with bleeding, and urethral warts can disrupt the urine stream.

Anal warts are found in 25% of infections, whether there has been anal sex or not. This is because HPV is spread by skin-to-skin contact, and during sex it is almost inevitable that there will be some contact between the anal skin and the infected region. However, intra-anal warts are normally only found when there has been penetrative anal sex.
Complications
Genital warts are primarily a cosmetic problem, but they can cause significant psychological distress, especially in cases that take many months to resolve. Recalcitrant warts may need surgery and this can result in scarring.

Diagnosis
Diagnosis of genital warts is made on the basis of a clinical examination in the first instance, although a biopsy to confirm the diagnosis needs to be considered if there is any associated depigmentation, pruritus, underlying immune deficiency or past history of intraepithelial neoplasia.

When assessing a patient with suspected genital warts, it is important to do a thorough examination of the genitalia and perianal skin. Where the lesions are very small, or not typical of warts, it may be necessary to examine them under magnification, such as with a colposcope. Women should have a speculum examination at their initial assessment to look for internal warts. If none are found at that point, then there is no need for a speculum examination at follow-up.

Where patients have perianal warts, routine proctoscopy is not required. However, proctoscopy is recommended if there are rectal symptoms such as bleeding, irritation or discharge, or if there are warts at the anal margin whose base cannot be visualised. If meatal warts are present, and the base of the wart cannot be visualised, then the patient should be referred for metatsonopy and/or urethroscopy.

Once the patient has been examined, it is very useful to record where any warts are on a genital map. This allows treatment progress to be evaluated, particularly if your clinical set-up means that the patient may see a different clinician at each review visit.

Differential diagnosis
A wide variety of skin conditions can present in a similar way to genital warts. It is therefore important that clinicians diagnosing warts have the necessary knowledge, skills and training to be able to distinguish between warts and incidental findings, such as pearly penile papules in men and the equivalent in women – vulvar vestibular papillomatosis. Warts can also be confused with molluscum contagiosum, skin tags, the nodules of chronic scabies infection, dermatofibromas and condylomata lata – the warty manifestation of secondary syphilis. Referral to specialist services for a second opinion should always be considered if there is no improvement with conventional treatments.

Treatment options
Recurrence rates are quite high after all forms of wart treatment, and there is also a relatively high failure rate for each treatment. This means that it is important to manage patient’s expectations, and ensure that they know that it may take some time to treat their warts. For the purposes of primary care, there are three possible treatments that can be used – podophyllotoxin cream, imiquimod cream or cryotherapy – with other treatments available in specialist centres. The guidelines on treatment of warts in patients with HIV are the same as for those without HIV.

Podophyllotoxin 0.15% cream is an antiviral therapy that is applied twice daily, morning and evening, for three consecutive days, following which treatment is withheld for the next four days. Residual warts can be treated with further three-day courses of twice daily application at weekly intervals, if necessary, for a total of four weeks of treatment. Direct medical supervision is recommended for areas of treatment greater than 4cm². Side-effects include redness, pain and ulceration.

There are currently three vaccines that have been licensed to protect against HPV – Cervarix (for types 16 and 18); Gardasil (for types 6, 11, 16 and 18,) and Gardasil 9 (for types 6, 11, 16, 18, 31, 33, 45, 52 and 58).

When the UK introduced the HPV vaccine into the national immunisation programme in 2008, the initial decision was to use Cervarix, and only give the vaccination to girls aged 12–13 years, in the hope that with 80% coverage, herd immunity would protect boys. In Australia, the national immunisation programme used Gardasil, starting from 2007. This led to a 93% reduction in genital wart diagnoses in women and an 82% decline in genital warts in heterosexual men by the fifth year of the programme. The programme was then extended to cover boys in 2013.

In the UK, Gardasil was introduced in 2012 and the STI data reported to Public Health England show a dramatic reduction in the incidence of genital warts in women aged 15–24 years in England in the following years (see Figure 1), and a corresponding decrease in men. From September 2019, the HPV programme in schools has been extended to include boys aged 12–13 years. Gardasil 9 is available from some private clinics but is not currently used in the national immunisation programme.

Box 1. HPV vaccination programme

Figure 1. Rate of new genital warts diagnoses in women attending sexual health services in England between 2009 and 2018. Source: Public Health England. Sexually transmitted infections and screening for chlamydia in England, 2018
Patients should stop using the cream if they have any pain or ulceration, and return to the clinic for review.

Imiquimod 5% cream is an immune response modifier that stimulates macrophages to release interferon alpha and other cytokines. The cream is applied three times a week (for example on Monday, Wednesday and Friday), before sleeping – and should be washed off six to ten hours after application. It can be used for four weeks before reviewing. Treatment should continue until clearance of visible warts, or for a maximum of 16 weeks. Patients should be told that there can be a delay before the warts start to respond. Imiquimod often causes local skin irritation and erythema. If, however, the patient experiences any bleeding, pain or ulceration then they should stop using the cream and return to clinic for review.

Cryotherapy involves the use of liquid nitrogen to effectively cause frostbite to the skin. Liquid nitrogen is applied directly to the lesion using a spray in the clinic, with a halo about 2mm thick around the lesion. For smaller warts, one single freeze for about 10–15 seconds is usually sufficient, and for larger warts up to three freeze-thaw cycles of 10–15 seconds may be required, ensuring that the wart thaws entirely between each cycle of freezing. Treatment should be repeated once a week for four weeks, at which point the patient should be reviewed to ascertain whether the treatment is working.

Freezing the skin results in heat transfer, cell injury and inflammation – the net result being cell death and necrosis, after which the wart falls off. This damage can of course occur to healthy skin cells as well as HPV-infected ones, so it is very important to apply the nitrogen spray only to the lesion itself. Always check that the patient is tolerating the procedure, and stop if they are in too much discomfort.

The main side-effect of cryotherapy treatment is a hypopigmented scar in the place where the wart was. This can take up to two years to resolve.

Dermatologists and GPs use cryotherapy for treating solar keratosis and seborrhoeic keratosis as well as warts and mol-
luscin contagiosum, but in a sexual health setting, cryotherapy is used only for the treatment of genital warts or molluscum contagiosum in the anogenital region.

**Specialist treatments**

There are some other options available for treating recalcitrant warts, such as the use of trichloroacetic acid or 5-flourouracil creams, electrocautery and surgical excision, but patients who require these treatments will normally need to be referred on to a specialist service.

**Pregnancy and breastfeeding**

None of the topical treatments for warts can be used in pregnancy. Cryotherapy can be used in pregnancy, by an experienced clinician, so this is an option for GP practices where cryotherapy is routinely available. If cryotherapy is not available, then pregnant women with warts should be referred to a sexual health clinic for diagnosis and treatment. Very rarely, warts can be passed on to the baby during delivery, and result in respiratory papillomatosis, but this is so rare that the presence of genital warts alone is not an indication for a Caesarean section. However, very large vulvovaginal warts can obstruct the birth canal, and this would necessitate a Caesarean delivery.

**Partner notification**

Partner notification is not recommended, but current sexual partners may benefit from a clinical examination in case they have undetected warts, and they should also ideally have an STI screen.

**The GP’s role in management**

With the right training, support and equipment, there is no reason why GPs cannot have a role in the diagnosis and management of genital warts, including the use of cryotherapy. The British Association of Sexual Health and HIV (BASHH) guidelines recommend that if GPs are treating warts that they should develop local treatment algorithms in conjunction with their local Level 3 genitourinary medicine service to ensure that patients have a robust referral pathway should they need specialist diagnosis and treatment.

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**Figure 3. Treatment algorithm for genital warts in men**

- **Urethral meatal warts**
  - Base of wart visible?
    - Cryotherapy once a week (if available) or refer to GUM
  - Base of wart not visible?
    - Refer to urology

- **Penile, scrotal or perianal warts**
  - Multiple warts
    - Podophyllotoxin twice daily for 3 consecutive days a week for up to 4 weeks
    - If not >50% better, switch to imiquimod 3 times a week for up to 16 weeks
    - Review after 4 weeks
  - One or few warts
    - Cryotherapy once a week (if available) or podophyllotoxin (see left)
    - If >50% better, continue with podophyllotoxin (NB. not licensed for >4 weeks’ use)
    - If not >50% better, switch to imiquimod (see left)
    - Review after 4 weeks
  - If no improvement, refer to GUM clinic for further treatment
The treatment algorithms for genital warts in women and men shown in Figures 2 and 3 are based on the one provided in the BASHH guidelines,4 with modifications to allow for a primary care setting. GPs and clinics will have different treatments available depending on their local policies, and practices should develop their own treatment algorithm in conjunction with their local genitourinary medicine service.

Conclusion
Although genital warts are a benign condition that can resolve with no treatment, they can cause significant emotional distress for some patients and need to be dealt with sensitively. Because the diagnosis is primarily made on clinical examination, it is important that clinicians who are diagnosing warts have the right training and experience to do so, and that there are clear referral pathways in place to enable patients to receive a second opinion should initial treatment options fail.

References

Declaration of interests
None to declare.

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