CLINICAL GUIDELINE

External Anogenital Warts

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Lead Author:	Kay McAllister
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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

EXTERNAL ANOGENITAL WARTS

What's new

- Speculum examination is only required if internal warts are suspected (due to vulvovaginal symptoms or warts which may extend into introitus)
- Podophyllotoxin solution (0.5%) is preferred over cream (0.15%) formulation where it can be easily applied owing to slightly superior efficacy
- If inadequate response following 6 treatments of cryotherapy, for senior clinician review for consideration of alternative treatment
- Verrutop (nitrizinc complex) can be used in those who have exhausted all other treatment options, only those trained in application can administer this
- Reminder that Cryotherapy treatment SHOULD be recorded in NaSH Prescriptions.
- Refer to the service on NaSH as an internal referral, selecting 'Cryotherapy' as sub-category

Introduction

The UK National Guideline for the Management of Anogenital Warts (2024) can be found at www.bashh.org

Summary checklist for patients diagnosed with genital warts

Discussion points

- HPV infection; high population prevalence, variable incubation period and transmission issues
- Natural history of warts – 90% caused by HPV types 6 and 11
- Outcome of HPV infection – eradication unlikely
- Low risk for cervical cancer – different from "high risk" HPV types
- Several treatment attempts may be required before warts subside

Offer testing to identify concurrent STIs

Treatment options:

- Discuss objectives of treatment - removal of visible warts to achieve acceptable cosmetic outcome and limit unnecessary tissue damage
- Discuss methods of treatment – home therapies best unless contraindicated

Written information should be offered and documented.

If psychological distress is apparent, onward referral may be indicated.

Clinical Aspects

- Warts are diagnosed by visible inspection under good illumination.
- The differential diagnosis of warts includes physiological features, dermatoses and other infections such as molluscum contagiosum. If uncertain, get an opinion from a senior doctor at the time of presentation.

Proctoscopy is not routinely performed in patients with external genital warts at Sandyford, unless there are ano-rectal symptoms or the upper limit of wart area cannot be visualised at the anal margin. Intra-anal warts should only be treated if symptomatic. If uncertain, discuss with a senior doctor.

- Speculum examination is only required if internal warts are suspected (due to vulvovaginal symptoms or warts which may extend into introitus)
- Intrameatal warts that cannot be fully visualised should be referred to urology for urethroscopy.
- Most anogenital warts are benign and caused by HPV 6 and 11, which are of low oncogenicity. The presence of anogenital warts does not alter routine cervical screening intervals for those eligible.
- 10-20% of patients with warts at Sandyford will have other STIs. STI testing: HIV, syphilis and Chlamydia/gonococcal NAAT test is recommended when a patient presents with warts for the first time. Testing should be re-offered if there are new risks.
- Application of 5% Acetic Acid to reveal subclinical or latent infection is not recommended.
- Warts can appear or increase in size during pregnancy.

Wart Assessment at Sandyford

The following factors should be documented in the patient record.

1. Site(s) and distribution warts (vulva, urethral meatus, glans penis etc.).
2. Approximate number (single or multiple) and area of warts (more than $4cm^2$).
3. Morphology: keratinised or non-keratinised (those on moist, soft non-hair bearing tissue tend **not** to have a layer of keratin);
4. Any other notable features (e.g pigmentation).
5. Patient factors influencing therapy (e.g pregnancy, ability to re-attend).

Information giving

- Before information is given, an assessment must be made of the patient's existing preconceptions and concerns.
- Information should cover epidemiology, transmission, natural history, treatment, partner issues. The order and pace of information delivery may need to be varied to suit the needs of the patient.
- Written information should be offered and documented.

Epidemiology

- Visible warts represent only "the tip of the iceberg" (1-2%) of all individuals infected with HPV. Studies of HPV prevalence generally report much higher infection rates in young sexually active populations. PCR-based studies typically reporting prevalence values of 30-50%.
- HPV DNA is rarely detected in the genital tract of individuals who have never had sex. Risk of HPV acquisition rises with increasing numbers of sexual partners. However, prevalence in women with only one lifelong partner is as high as 20%.
- Prevalence of molecular evidence of HPV infection declines with increasing age.

- Smoking, hormonal factors (such as pregnancy) and immunosuppression are associated with an increased likelihood of HPV infection.
- Persistent infection (particularly with "high risk" types of HPV, such as HPV-16) is a key risk factor for HPV-related neoplasia.

Transmission

- Transmission of HPV occurs by direct skin-to-skin contact. Transmission studies in patients with visible genital warts have shown male to female transmission rates of 50% and female to male transmission rates of 70%.
- The high population prevalence of HPV infection and studies which show type-specific concordance between partners suggest high rates of sexual transmission, even when visible genital warts are absent.
- Consistent condom use has been shown to reduce the acquisition of HPV infection and genital warts (by 30 – 60%) and their use is advisable, particularly in a new relationship

Natural History

- The majority of individuals infected with HPV have no visible clinical abnormalities. However, warts may become clinically manifest at any time after infection, especially if there is immunosuppression (e.g. in pregnancy, with HIV co infection and in smokers).
- The location of visible lesions does not accurately reflect the original site of inoculation. (e.g. the presence of perianal warts does not imply anal intercourse has occurred)
- Treatment of sexual partners makes no significant impact on the natural history of genital warts.
- Smokers may respond less well to treatment than non-smokers.

Partner Notification

There is no reason to routinely see partners for visual inspection to exclude warts. Partners should attend if they have concerns about their sexual health or wish to have sexual health screening.

Management

See end of document for treatment algorithms

The objective of treatment is the removal of visible warts (to achieve an acceptable genital cosmetic appearance without causing unnecessary tissue damage). All treatments have significant failure and recurrence rates. Eradication of HPV is not an achievable goal with current therapies and treatment has no measurable effect on transmission rates between partners. Most patients seek treatment because of the psychological impact of visible wart lesions.

Treatment Notes

Topical treatment options:

Podophyllotoxin (Warticon/Condyline) is a purified extract of podophyllin. It is suitable for patients to self-administer and is available in both a 0.5% alcoholic solution (both brands and is more effective) and a 0.15% cream formulation (Warticon only in this form).

Podophyllotoxin solution (0.5%) is preferred over cream (0.15%) due to superior efficacy. Cream can be used if the area is difficult/impossible to visualise e.g. perianal warts as it is easier to apply. Treatment cycles consist of twice daily application for 3 days followed by 4 days rest for 4 cycles. Use for perianal lesions is "off licence" but RCT evidence suggests it is safe and effective at this site. Treatment should be discontinued if significant side effects develop (eg. soreness, ulceration). Sexual contact should be avoided soon after treatment because of possible irritant effect on the partner. Response rates at 4-6 weeks are generally in the region of 40-70%, but subsequent recurrence of lesions is common. Podophyllotoxin should never be used in pregnancy or on broken skin. Podophyllotoxin can be continued beyond its licensed duration where there is >50% wart clearance following 4 weeks of treatment.

Imiquimod (Aldara) is an immune response modifier. It is used for refractory warts which have failed to respond to other treatments, or warts which have been assessed by a senior doctor and are thought likely to be refractory to treatment (e.g. extensive carpet warts). Wart recurrence rates are lower with imiquimod, but it is currently reserved as a second line therapy (except for refractory warts) owing to its cost which is 2-3 times greater than podophyllotoxin. It should be applied 3 times per week (e.g. Monday, Wednesday, Friday) prior to normal sleeping hours and should remain on the skin for 6 – 10 hours. Use should continue until the clearance of visible genital or perianal warts or for a maximum of 16 weeks per episode of warts with 4 weekly review. Sexual contact should be avoided soon after treatment because of possible irritant effect on the partner. It should not be used in pregnancy or if having unprotected sex with a pregnant partner. Skin reactions are common, including erythema (61%), erosion (30%) and oedema (14%). Treatment should be discontinued if these are severe. Less severe reactions may subside with a treatment break. Rarely an intense local inflammatory reaction can occur after a few applications. Use with caution in solid organ transplant recipients and in individuals with autoimmune conditions.

If <50% reduction in wart volume after 8 weeks' of imiquimod, a switch to an alternative treatment should be considered. Advise the patient to contact the clinic if this is the case.

Cataphen *(Camellia sinensis*, folium (green tea leaf)) is an alternative second line treatment for warts unresponsive to podophyllotoxin. Mechanism of action is unknown. This should be applied three times per day to all external genital and perianal warts, for no longer than 16 weeks in total. Some irritation to treated areas can be expected. Application into the vagina, urethra or anus must be avoided. It is not necessary to wash off the ointment from the treated area prior to the next application. It should be washed off the treated area before sexual activity. It should not be used in pregnancy or breastfeeding. Effectiveness and recurrence rates appear to be similar to other topical treatments.

If there is <50% reduction in wart volume after 8 weeks', consider an alternative treatment.

Clinician-applied treatments:

Cryotherapy destroys warts by thermal induced cytolysis. It is the treatment of choice for intrameatal warts, and in pregnancy. It is labour intensive for the patient and service so should only be used when self-taken treatments are not possible. Treatment should be applied until a halo of freezing has been established a few millimetres around the treated lesion. A freeze, thaw, freeze technique should be used and the lesion held frozen for 10-20 seconds, depending on size. Response rates depend on size and chronicity of the lesions. This is not suitable for large warts and large clusters of warts unless other therapies are contra-indicated. See references relating to safety issues for use and storage of liquid gases. Product subject to risk assessment review. Cryotherapy treatment SHOULD be recorded in NaSH Prescriptions. It can be commenced by staff with relevant competency/experience in the Prescription section under 'Liquid Nitrogen (Application)'. Each prescription can have a maximum of 6 administrations, at which point a senior clinician should

review in regards to ongoing management. A new prescription should be written if it was initially prescribed more than 6 months ago.

Trichloro-acetic acid (TCA) treatment (to be administered by consultants only, if available). In 80-90% solution, this is directly corrosive to tissue. It should be used sparingly and is only to be initiated and applied by consultants. It is generally applied weekly and multiple treatment sessions are usually required to achieve clearance.

If <50% wart clearance achieved after 4 applications, switch to an alternative treatment should be considered.

Nitrizinc complex (Verrutop ®) is a clinician applied topical solution containing nitric acid, organic acids and zinc/copper salts which has a caustic action on warts and has shown similar efficacy to cryotherapy in one RCT among 120 individuals with previously untreated warts of <5mm diameter on the external genitals or perianal area. Several large case series also support its efficacy and tolerability. Drops of the solution are applied directly to warts via a capillary tube for up to four treatment sessions at fortnightly intervals. Irritation/pain can occur at time of application and after. This is only to be initiated in those who have exhausted all other treatment options, as guided by a consultant.

External surgical referral remains an option for large volume lesions and those unresponsive to medical therapies.

Dedicated warts service at Sandyford Central

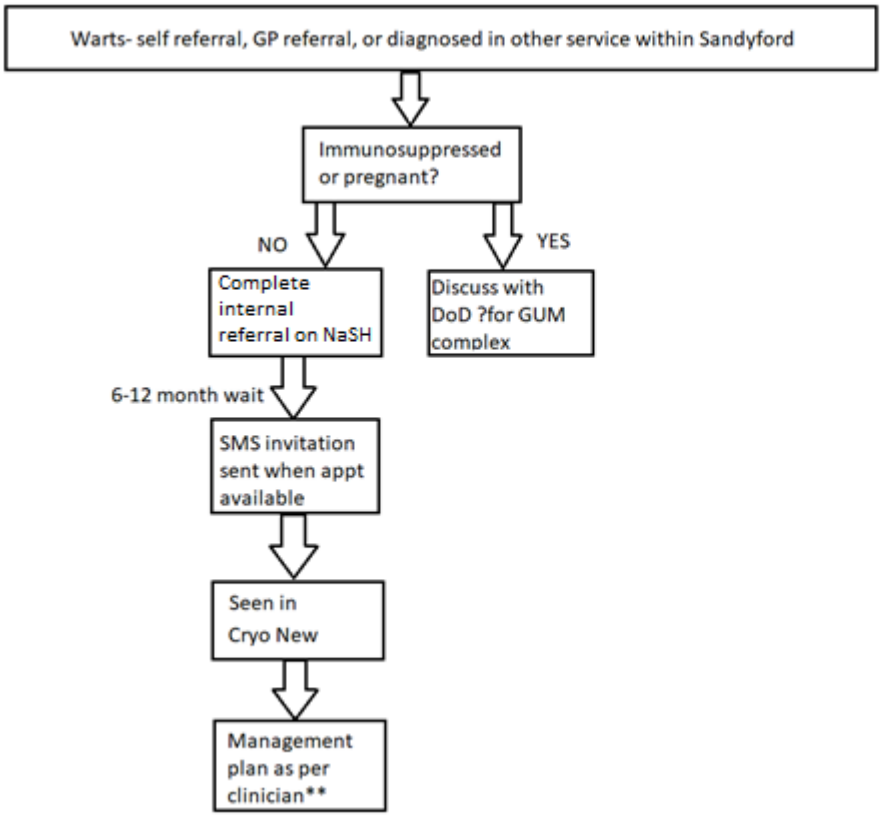
There is now a dedicated warts service at Sandyford. There is a waiting list to be seen. Clients are either referred by their GP or self-referred. Clients to be seen in this service should be referred via Internal Referral process, selecting 'Cryotherapy' as the sub-category. Please inform of the waiting time of 6-8 months. They will be sent an SMS with an invitation to book online once we can see them, please advise them of this and confirm their mobile number with them. Please initiate topical treatment if suitable in the meantime.

For any complex cases (background of immunosuppression, extensive warts in pregnancy) please discuss with the Doctor of the Day as these cases may be suitable for a GUM Complex appointment.

All clients are initially seen in a 'Cryo New' clinic for assessment, sexual health screening and management planning. They book this themselves online after receiving an SMS invitation, or by calling the secretary (whose number is included in the SMS).

Cryo Return lists are for those returning for cryotherapy treatments, after being seen in a Cryo New appointment. This is usually every 1-2 weeks, depending on appointment availability and client's preference. If a client has been seen in this service in the past 12 months, they can arrange further treatment through switchboard or the secretaries. If it has been longer than 12 months since they were last seen, they need to be added to the 'SC Warts Referrals' list and wait to be seen again for re-assessment in Cryo New.

Please see flowchart below:

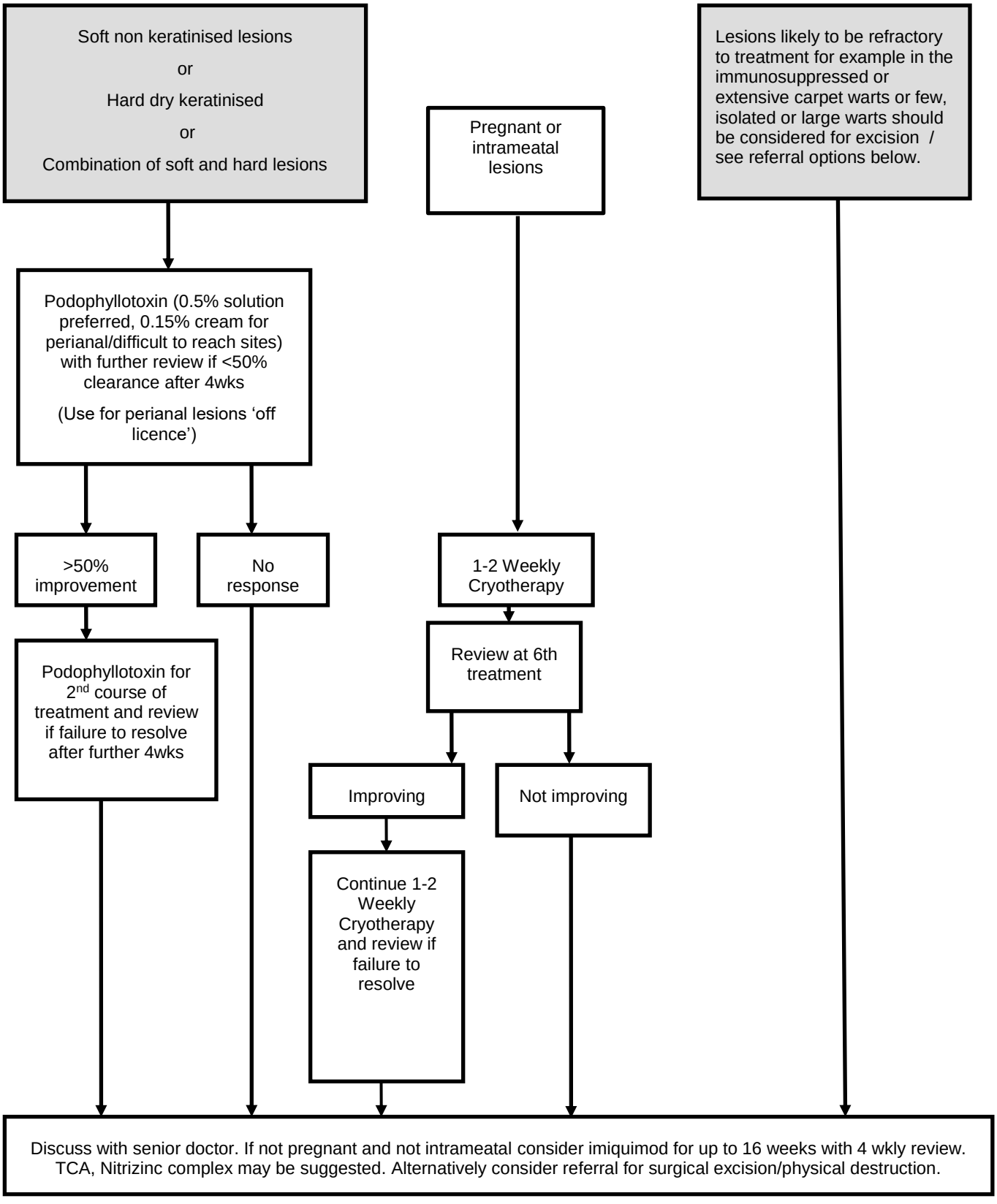


** Detailed in clinical notes- often either discharged with topical treatment, booked in to 'Cryo Return' for regular cryotherapy

References

British association for sexual health and HIV national guideline for the management of anogenital warts in adults (2024) https://www.bashh.org/_userfiles/pages/files/resources/agw_2024.pdf [accessed online June 2024]

2019 IUSTI-Europe guideline for the management of anogenital warts. [https://iusti.org/wp-content/uploads/2020/08/IUSTIHPVGuidelines2020.pdf] [accessed online June 2024]



If treatment algorithm isn't followed e.g. initiated on cryotherapy without trialling topical treatment first, please document reasons for doing so