

External Genital Warts: Report of the American Medical Association Consensus Conference

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A consensus process was undertaken to describe and evaluate current information and practice regarding the diagnosis, treatment, and evaluation of patients with external genital warts (EGWs) and their sex partners. This process developed a number of key statements that were based on strong evidence in the literature or reasonable suppositions and opinions of experts. Key statements included the following. In most cases, EGWs can be diagnosed clinically by visual inspection. No one treatment is ideal for all patients or all warts. Women with EGWs and female sex partners of men with EGWs are at increased risk for human papillomavirus-related cervical disease and, like all women, should be screened for cervical cancer. The diagnosis of EGWs in children requires a sexual abuse evaluation. Clinicians who treat EGWs have a responsibility to counsel patients and to provide information about the infectivity, diagnosis, treatment, and natural history of EGWs and general information about sexual health and other sexually transmitted diseases.

External genital warts (EGWs) are visible by gross clinical examination without instrumentation (e.g., colposcopy, anoscopy, and urethroscopy) and are one manifestation of human papillomavirus (HPV) infection. Internal genital warts and dysplasia, although important causes of disease and the subject of considerable attention in the medical literature, are not the focus of these consensus statements.

An estimated 24 million Americans are infected with HPV; between 500,000 and 1 million new cases of HPV-induced genital warts occur annually [1, 2]. In 1995, EGWs and internal genital warts accounted for >240,000 initial visits to private physicians' offices [2]. In the United States, 1% of sexually active men and women between the ages of 18 and 49 years are estimated to have EGWs [3]. The economic burden of HPV infection in the United States is substantial, estimated to exceed \$3.8 billion in total costs in 1997 (excluding the cost of HPV-related cervical cancer). This cost represents more than one-third of the approximately \$10 billion spent annually on common sexually transmitted diseases (STDs; excluding HIV infection) and related syndromes [2].

At least 70 HPV types are currently defined by their DNA genotype on the basis of the alignments of the nucleotide sequences of the open reading frames L1, E6, and E7 [4, 5]. HPV types that infect the genital area can be divided into low-

risk types (e.g., 6, 11, 42, 43, and 44) and high-risk types (e.g., 16, 18, 31, 33, 35, 39, 45, 52, 55, 56, and 58) on the basis of their association with anogenital cancers [6–15]. Most EGWs in immunocompetent patients are caused by HPV type 6 and sometimes HPV type 11 [7, 12]. HPV types that cause EGWs can also cause visible warts in the vagina, on the uterine cervix, and inside both the urethra and the anus [6, 10, 11, 16–19]. In addition to genital warts, these HPV types have been associated with conjunctival, nasal, oral, and laryngeal warts [20, 21]. Most infections with low- and high-risk types occur without evidence of EGWs, squamous intraepithelial lesions (SILs), or malignancy [22–25].

A variety of approaches to the diagnosis and treatment of patients with EGWs have been developed, often along the lines of individual medical specialties and subspecialties. In addition, our understanding of the pathogenesis, assessment, and treatment of EGWs has increased in recent years. The consensus statements in this article were developed to provide up-to-date information for practitioners with the ultimate goal of improving patient care.

Methods

Eleven questions were outlined initially by the three panel co-chairs (K. R. Beutner, G. A. Richwald, and M. V. Reitano) in collaboration with medical education staff of the American Medical Association. The first set of questions was circulated to all panel members, and a consensus on 11 key questions was achieved after three iterations of comment and revision. In addition, two key questions were expanded by the consensus panel co-chairs, and a total of 15 key questions provided a framework for the panel's deliberations and the selection of data sources (table 1).

EGWs are treated by clinicians from a variety of disciplines. Consequently, the panel of national leaders was multidisciplinary.

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nary, consisting of representatives from dermatology, family practice, gynecology/obstetrics, internal medicine, infectious disease, pathology, pediatrics, student health, urology, epidemiology, sociology, and health education.

The consensus statements were formulated following an extensive review of the literature. MEDLINE and other proprietary databases were used for extensive subject, key-word, and title-word searches for the preceding 11 years. Select MEDLINE searches were conducted for articles published before 1985. Data sources not found through database searches included abstract booklets, conference proceedings, and references identified from bibliographies of pertinent articles and books, companies, or manufacturers of therapeutic agents.

Preliminary position statements corresponding to the key questions were presented for detailed review and revision by the expert panel at a 3-day, closed meeting in January 1997. Small working groups and plenary session discussions were used to prepare written statements that were reviewed repeatedly by the entire expert panel. Two additional revisions of the statements were conducted by correspondence with the full expert panel. The final statement was approved by all panel members in May 1997.

Table 1. Key questions on EGWs of the American Medical Association Consensus Conference.

Evaluation and diagnosis
What is the basis for diagnosis of EGWs and perianal warts?
What are the indications for biopsy or other tests, such as detection of HPV DNA, to confirm the diagnosis of EGWs?
Therapy
What are the goals of therapy and acceptable therapeutic modalities for the treatment of EGWs?
What follow-up is recommended once EGWs are cleared?
Screening: women
Should women with EGWs undergo cervical cancer screening?
Should female sex partners of patients for whom EGWs or HPV-associated cervical disease are diagnosed be evaluated for EGWs?
Should female sex partners of male patients with EGWs undergo cervical cancer screening?
Screening: men
Should male sex partners of patients for whom EGWs or HPV-associated cervical disease are diagnosed be evaluated for EGWs?
When is anal cancer screening indicated?
Children and adolescents
How should children with lesions suspected of being EGWs be evaluated to confirm or rule out the diagnosis of EGWs?
How should children suspected of being sexually abused be evaluated for EGWs?
How should children with EGWs be evaluated for suspected child sexual abuse?
Patient counseling
How should patients be counseled about infectivity, transmission, risk reduction, and disclosure?
What gaps currently exist in patient education on EGWs and how should these gaps be addressed?
Health care provider education
What gaps currently exist in health care provider education of EGWs and how should these gaps be addressed?

NOTE. EGW = external genital wart; HPV = human papillomavirus.

Information supporting the panel's findings was rated using a two-tier, eight-category, quasi evidence-based method previously validated by the U.S. Preventive Services Task Force [26]. The strength and the quality of evidence supporting each recommendation were based on study design, efficacy, and clinical benefit. Whenever possible, the panel gave greater weight to study designs that were less subject to bias and inferential error. Where there was insufficient evidence, ratings were based on the clinical experience and judgment of the consensus panel.

Recommendations with strong evidence for substantial clinical benefit to support the proposition were rated as A; those with moderate or strong evidence that showed only limited clinical benefit were rated as B. When the evidence for efficacy was insufficient to support an affirmative or negative recommendation or evidence for efficacy did not outweigh the adverse consequences of use, the panel rated the proposition as C or optional. When evidence showed a moderate lack of efficacy or a moderate association with adverse outcomes, a recommendation was rated as D, generally not to be offered. When there was good evidence supporting poor efficacy or a strong association with adverse outcomes, the panel rated the recommendation as E. The quality of evidence was rated in three categories (I, II, and III). The categories were judged and ranked on the basis of evidence from one or more properly randomized, controlled clinical trials (I), one or more well-designed observational studies (i.e., nonrandomized clinical trial; cohort, case-control, or time series study; or noncontrolled experimental trials) (II), and opinions of respected authorities that were based on clinical experience, descriptive studies, and reports of expert committees (III) (table 2).

Consensus

Clinical Diagnosis

EGWs are visible warts that occur in the genital area, (e.g., penis, scrotum, perineum, vulva, perianal area, pubic area, upper thighs, and crural folds) [29, 59–62]. They appear as discrete lesions or may coalesce into confluent plaques [30, 36, 63]. The clinical diagnosis of EGWs in the immunocompetent patient by physical examination is reliable on the basis of a good correlation between physical findings and histological studies [31, 62, 64–67]. Clinical inspection, without the aid of instrumentation (i.e., colposcopy, anoscopy, and urethroscopy), is sufficient to diagnose most EGWs. EGWs are frequently multifocal, with one or more lesions on one anatomic site (e.g., vulva), or multicentric, with lesions on disparate anatomic sites (e.g., perineum and cervix) [30, 31, 35, 36, 61–70]. Thus, it is important to examine the entire lower genital tract for the presence of multicentric visible warts before treatment.

Bright light and magnification with a loop, hand lens, or colposcope may assist in diagnosis. Evaluation for visible intraanal warts by anoscopy is recommended for men and women with recurrent perianal warts and/or a history of receptive anal

Table 2. Key statements, strength of recommendations, quality of evidence, and supporting materials of the American Medical Association Consensus Conference.

Variable, recommendation	Strength of recommendation	Quality of evidence	[Reference(s)]
Diagnosis			
Clinical examination is sufficient to diagnose most EGWs.	A	III	
Mild acetic acid soaking should not be used routinely to screen patients for EGWs.	D	II	[27, 28]
Biopsy is seldom necessary to accurately diagnose EGWs.	D	III	
Detection and typing of HPV are not currently recommended for diagnosis or management of EGWs.	E	III	[29–33]
Treatment			
The goal of treatment for EGWs is the removal of symptomatic warts.	A	III	
Standard therapies for EGWs can eventually remove most warts, although no one treatment is ideal for all warts or all patients.	A	I and III	[34]
Clinicians should be knowledgeable about and have available to them at least one patient-applied treatment and one health care provider-administered therapy.	C	III	
Screening			
Sex partners of patients with EGWs should be evaluated for EGWs, screened for other STDs, and receive educational information.	B	III	[27, 35–41]
The value of referring sex partners of women with HPV-related cervical SILs for EGW screening is unknown.	C	III	[28, 39, 42, 43]
Women with EGWs should undergo cervical cytological screening.	A	II	[44–47]
Patients with external perianal warts or a history of receptive anal intercourse may be at increased risk for anal high-grade SILs, but routine screening is not currently recommended.	C	III	[48–55]
Children and adolescents			
The presence of EGWs in minors is rare and requires initiation of sexual abuse evaluation.	A	III	[32, 56–58]

NOTE. A = strong evidence for substantial clinical benefit to support the proposition; B = moderate or strong evidence that showed only limited clinical benefit; C = evidence for efficacy is insufficient to support an affirmative or negative recommendation or evidence for efficacy did not outweigh the adverse consequences of use (or optional); D = moderate lack of efficacy or a moderate association with adverse outcomes (generally not to be offered); E = good evidence supporting poor efficacy or a strong association with adverse outcomes; EGW = external genital wart; HPV = human papillomavirus; STD = sexually transmitted disease; SIL = squamous intraepithelial lesion; I = one or more properly randomized, controlled clinical trials; II = one or more well-designed observational studies; III = opinions of respected authorities that were based on clinical experience, descriptive studies, and reports of expert committees.

intercourse. If urinary symptoms of terminal hematuria or an abnormal urinary stream are present, the distal urethra and meatus should be visually examined, and a referral for urethroscopy should be considered.

There are four morphological types of EGWs: condylomata acuminata that are cauliflower-shaped [36, 71, 72]; papular warts that are dome-shaped (usually skin-colored) 1- to 4-mm

papules [71, 73, 74]; keratotic genital warts that have a thick, horny layer and may resemble a common wart or a seborrheic keratosis; and flat-topped papules that appear macular to slightly raised [71, 75, 76].

The morphological type is generally associated with one of the two major types of skin in the genital area: fully keratinized hair-bearing or non-hair-bearing skin and partially keratinized,

moist, and non-hair-bearing skin. Keratotic and smooth papular EGWs occur on fully keratinized skin, condylomata acuminata occur most commonly on moist surfaces, and flat-topped papular EGWs can occur on either surface.

Differential Diagnosis

The differential diagnosis of EGWs includes two types of morphological lesions: papules and flat erythematous lesions [77–82]. Genital papules include normal anatomic structures: pearly penile papules, vestibular papillae, and sebaceous glands or glands of Tyson. Acquired papules include the following: molluscum contagiosum, Crohn's disease, seborrheic keratosis, lichen planus, lichen nitidus, skin tags, melanocytic nevi, pseudoverrucous papules, and condylomata. Vulvar intraepithelial neoplasia, formerly called vulvar carcinoma in situ, is a papular pruritic lesion that may appear as a skin-colored, hypopigmented or hyperpigmented, warty lesion. Bowenoid papulosis is a condition marked by the presence of dome-shaped or flat-topped papules (usually 1–5 mm in diameter) that may have a hyperpigmented or bluish hue and may be clinically indistinguishable from the papular form of EGWs [83–86]. Histological examination of these papules shows high-grade intraepithelial neoplasia; bowenoid papulosis is usually associated with HPV type 16 infection [87, 88] but can also be associated with other high-risk types of HPV. A very rare manifestation of infection due to low-risk types of HPV is the Buschke-Löwenstein tumor, a form of verrucous squamous cell carcinoma [85, 89].

Flat erythematous lesions include psoriasis, seborrheic dermatitis, balanitis circinata associated with Reiter's syndrome, high-grade SILs, Bowen's disease, erythroplasia of Queyrat (Bowen's disease on the glans penis or basaloid [flat] carcinoma on the vulva), vulvar intraepithelial neoplasia, and squamous cell carcinoma [77, 80, 82, 85, 86].

Additional Diagnostic Approaches

Bright light and magnification may assist in the diagnosis of smaller EGWs. The value of using dilute (3%–5%) acetic acid solutions (i.e., "the acetowhite test") has not been established, and the positive predictive value of this test for EGWs is low [27, 28]. Some clinicians find that acetic acid soaking is a useful adjunct in diagnosing visible lesions suspected of being EGWs, particularly flat-topped papular warts [90]. However, acetic acid soaking is not recommended for screening individuals for EGWs, since acetowhite areas often are not EGWs [27, 28]. When the acetowhite test is used, care must be exercised to avoid overdiagnosis of EGWs, as acetowhite change occurs with many other conditions.

When the diagnosis is in doubt, referral to a practitioner experienced in the diagnosis of EGWs should be considered. Biopsy in cases of clinically diagnosed EGWs seldom is needed. However, biopsy should be performed when lesions are indurated, fixed to underlying structures, or ulcerated. In

addition, biopsy may be considered when individual warts are >1 cm, which raises the possibility of a Buschke-Löwenstein tumor; the diagnosis is in doubt; lesions do not respond to a standard course of therapy; lesions are pigmented, thus suggesting the possibility of bowenoid papulosis or high-grade SILs [85, 86]; and if disease worsens during therapy, which can occur when papulosquamous conditions such as lichen planus or psoriasis are treated with ablative therapeutic modalities. Biopsy may be indicated more often for immunosuppressed patients because high-grade SILs are more common in these patients than in immunocompetent patients and may be less often distinguishable clinically from EGWs.

Detection and typing of HPV have no proven benefit in the diagnosis or management of EGWs. Thus, routine detection and typing of HPV is not recommended currently for diagnosis or management of EGWs.

Cervical Cancer Screening

As with other sexually active women, all women with EGWs and those reporting contact with a sex partner with EGWs should have their history of recent cervical cancer screening documented [44]. Women with EGWs should undergo annual cervical cytological screening. After three negative annual screening tests, women may be screened at intervals recommended by reported guidelines that are supported by their health care provider [44].

Anal Screening

Patients with perianal warts (i.e., those visible on inspection without use of an anoscope), patients who are HIV-seropositive, and patients with a history of receptive anal intercourse may be at increased risk of anal high-grade SILs [44, 50]. There is no direct evidence that anal high-grade SILs progress to invasive anal cancer. By analogy with cervical cancer, it is possible that identification and treatment of anal high-grade SILs will reduce the incidence of anal cancer [49]. One recent study showed that anal cytology was useful in identifying patients with intraanal SILs [51]. However, more data are needed on the natural history of intraanal high-grade SILs, the performance of screening tests for intraanal high-grade SILs, and the efficacy of therapy for these lesions in preventing anal cancer before firm recommendations can be made on routine screening of the anal canal in patients with EGWs and/or a history of receptive anal intercourse.

Screening for Other STDs

Patients with EGWs should be evaluated for other STDs, many of which may be asymptomatic [1, 2]. This evaluation may include testing for chlamydial infection, gonorrhea, syphilis, vaginitis, hepatitis B, and HIV infection. The need to test for these STDs is greatest among sexually active patients under

the age of 25, a group accounting for two-thirds of all reported STDs in the United States [1, 2].

Treatment

The primary goal of treatment of EGWs is to eliminate warts that cause physical or psychological symptoms. Physically, EGWs often are asymptomatic but can be painful, friable, or pruritic. Emotionally, EGWs may be stigmatizing socially and a reminder of an STD. Treatment can induce wart-free periods, but the underlying viral infection may or may not persist. The elimination of warts may or may not decrease infectivity since EGWs may not represent the entire viral burden (e.g., internal sites and clinically normal skin may act as reservoirs for infection).

If left untreated, EGWs may resolve on their own, remain unchanged, or increase in size or number, and rarely, if ever, EGWs may progress to cancer [6–12, 16, 17, 91–94]. Treatment should be tailored to the patient's disease and needs as well as to available resources. At the present, no one treatment is ideal for all patients or all warts. Treatments can be classified as either patient-applied or health care provider-administered (table 3). Clinicians who treat patients with EGWs should be knowledgeable about and have available at least one patient-applied treatment and one health care provider-administered therapy.

Patient-applied treatments include podofilox solution and gel and imiquimod cream. Health care provider-administered treatments can be divided into topical therapy (e.g., cryotherapy, trichloroacetic acid [TCA], bichloroacetic acid [BCA], and podophyllin resin), simple office surgery (e.g., curettage, electrosurgery, scissor excision, and laser vaporization), and injectable therapy (e.g., IFN and 5-fluorouracil/epinephrine gel implant).

IFN, 5-fluorouracil/epinephrine gel implant, imiquimod, and podofilox have been systematically and prospectively evaluated in multicenter, placebo-controlled clinical trials. Other therapeutic modalities have been compared with alternative treatments or no treatment but have not been subjected to rigorous placebo-controlled study [34].

Podofilox solution or gel (0.5%) and imiquimod cream (5%) are patient-applied treatments. Podofilox is an antimetabolic agent, purified from podophyllum resin, that can destroy warts [97, 98]. Imiquimod is a topically active immune enhancer that stimulates production of IFN and other cytokines [99, 100]. Patients must be able to identify and reach the warts and to follow application instructions to successfully use these patient-applied therapies.

Cryotherapy destroys warts by cryocytolysis. Inadequate training in the use of cryotherapy frequently results in over- or under-treatment of warts, thus leading to poor efficacy and/or increased complications. Although the use of an injected local or topical anesthetic is not required, it can facilitate cryotherapy, particularly when a large number or a large area of warts is present. Podophyllum resin contains a number of antimetabolic compounds including podofilox (i.e., podophyllotoxin) and the two mutagens [101] quercetin and kaempferol. Podophyllin is usually compounded

as a 10%–25% suspension of resin in benzoin tincture [66, 70, 74, 102–105]. TCA and BCA are caustic agents that destroy warts by chemical coagulation of proteins.

Simple office surgery also can remove warts and often promptly provides a wart-free state. Once local anesthesia is achieved, EGWs can be physically removed and destroyed by curettage, electrosurgery, or tangential excision with a pair of fine scissors or a scalpel. These simple procedures are applicable to patients with limited, average, or extensive EGWs.

A therapeutic implant consisting of 5-fluorouracil, bovine collagen, and epinephrine injected beneath the wart has been shown to be effective [106, 107]. The mechanism of action of this implant is probably due to the antimetabolic effect of 5-fluorouracil. IFNs have antiviral, antitumor, and immune enhancing activity. Intralesional IFN has been shown to be effective; however, systemic administration has proved to be ineffective for EGWs [29, 30, 37, 38, 59, 68, 92, 102].

Concurrent use of multiple therapeutic modalities on a single wart is not recommended as routine treatment. Because of unproven efficacy, significant toxicity, and teratogenicity, patient-applied 5-fluorouracil cream is not recommended for routine treatment of EGWs.

Treatments for EGWs frequently disrupt skin integrity to varying degrees and for varying durations. Consequently, healing open sores (i.e., erosions and, rarely, ulcers) may increase a sexually active patient's risk of contracting or transmitting other STDs.

The average patient has a relatively small number of EGWs that can eventually be eliminated with most treatment modalities. Health care provider-administered topical treatments seldom work promptly in patients with large or extensive areas of EGWs. These patients should have surgical treatment or a patient-applied therapy to at least debulk their EGWs. Patients with limited disease (i.e., one to five warts) may benefit most from simple office surgery, cryotherapy, or other health care provider-administered treatments. Additional details on treatment are available in the Centers for Disease Control and Prevention's STD Treatment Guidelines [107a].

Many patients require a course of therapy rather than a single treatment. Studies have not systematically evaluated the patient-related and health care provider-related factors that influence the selection of therapy. Factors that may influence treatment selection include the following: size, morphology, and number of warts; anatomic site; patient's preference; patient's age and cognitive ability; and clinician's training and experience (table 4). The development of a comprehensive treatment algorithm for patients with EGWs would be desirable but is very difficult because of a number of reasons. Different specialties have effective but fundamentally different approaches to treatment. Many health care providers either do not have all therapeutic modalities available to them or are not trained in their use. Disease presentation and patient preferences vary widely.

For health care provider-administered topical therapies, experts recommend that if there has not been significant improve-

Table 3. Summary of patient-applied and health care provider–administered treatments for EGWs.

Therapy	Advantage(s) and disadvantage(s)	Contraindication(s) and pitfall(s)
Recommended treatment*		
Patient-applied		
Podofilox solution and gel	Patient applied, results are dependent on patient compliance	>10 cm ² of wart area; safety for use in pregnancy not known
Imiquimod cream	Patient-applied immune enhancer	Safety for use in pregnancy not known
Health care provider–administered		
Cryotherapy	Effective for moist and dry warts, pain (can be reduced by use of an anesthetic), safety and efficacy highly dependent on health care provider's skills and experience	Over- or underapplication
Podophyllin	Most effective on moist warts, relatively simple to use, unknown shelf-life, may contain mutagens, variable concentration of active components, limited value for dry warts	Pregnancy, large wart area, overapplication
TCA or BCA	Inexpensive, most effective for moist warts, relatively simple to use and safe during pregnancy, limited value for dry warts	Large area of friable warts, low viscosity results in spreading if overapplied
Office surgery		
Curettage, electrosurgery, and scissor excision	Prompt wart-free state, results depend on health care provider's skill and training, requires equipment, longer clinic visit, local anesthetic is mandatory	
Alternative treatment†		
Intralesional		
5-FU/epinephrine implant	Pain on injection, multiple visits	Pregnancy and breast-feeding
IFN	Immune enhancer, long time (weeks to months) to clearance, many (9–16) visits, systemic reactions, recommended dose limits treatment to patient with a small number of warts	Pregnancy, transplant patients, psychiatric disease
Surgery		
Laser	Prompt wart-free state, may require general anesthesia, results and safety dependent on health care provider's skill [95, 96]	Improper power settings damage normal tissues [95, 96]

NOTE. BCA = bichloroacetic acid; EGW = external genital wart; 5-FU = 5-fluorouracil; TCA = trichloroacetic acid.

* For routine or first-line treatments.

† Should be reserved for patients for whom other multiple recommended therapies failed or who are not appropriate candidates for other treatments.

ment after three treatment sessions or if complete clearance has not occurred after six treatment sessions, treatment should be changed or the patient should be referred. For patient-applied therapeutic modalities, treatment beyond the manufacturer's recommendations is not advisable. The risk-benefit ratio should be evaluated throughout the course of therapy to avoid overtreatment and a therapeutic course worse than the disease itself.

Persistent hypo- or hyperpigmentation is a common complication of ablative therapeutic modalities. Depressed or hypertrophic scars occur rarely [52, 108]. Ablative treatment can result in disabling chronic pain syndrome (e.g., vulvadynia) or hypesthesia at the treatment site [109]. Some experts report that patients with fair complexions seem to be the most susceptible to chronic pain syndromes following treatment of EGWs.

Pregnancy

Treatment during pregnancy requires some special considerations. EGWs should be treated during pregnancy, especially

since treatment will decrease the risk of obstetrical complications with delivery. Appropriate treatments for EGWs during pregnancy include TCA or BCA, cryotherapy, surgical removal, and laser ablation.

Posttreatment Follow-up

The benefit, frequency, interval, and type of follow-up care necessary after treatment of EGWs has not been studied. When appropriate, follow-up visits may be scheduled to document treatment outcomes (e.g., a wart-free state), manage complications of therapy, and evaluate for recurrence. A follow-up visit to document a wart-free state should be made available but is not necessary in all cases. Follow-up evaluation can also provide the opportunity for education and counseling of patients.

The need to monitor for complications of therapy will vary greatly on the basis of the patient's experience and cognitive ability, the number and location of warts, and the treatment modality used. Patients concerned about recurrence should be

Table 4. Some factors that influence the selection of treatment for EGWs.

Age	<p>Safety and efficacy of treatments for EGWs have not been studied in pediatric populations.</p> <p>When treating, attention should be paid to avoiding and controlling pain associated with treatment.</p> <p>Requiring a parent or guardian to apply a treatment that may be painful is questionable.</p> <p>Variations in the rate of psychosocial development in adolescence should be taken into account (i.e., cognitive ability to understand and carry out any treatment program, particularly patient-applied therapy).</p>
Pregnancy and lactation	<p>Safety of podofilox, imiquimod, and IFN in pregnancy is not known.</p> <p>5-Fluorouracil is a teratogen.</p>
Disease prevention: wart size, wart number, anatomic location, circumcision status (men), and epithelial presentation (fully keratinized vs. partially keratinized skin)	<p>Wart size and count: In general, health care provider-administered topical treatments are not ideal for large areas of warts, although they may have a debulking effect.</p> <p>Warts on moist (partially keratinized) surfaces and intertriginous areas appear to respond better to topical treatments than do warts on dry (fully keratinized) surfaces and open areas.</p> <p>Aggressive ablative or surgical therapy should be avoided over the clitoris, glans penis, urinary meatus, prepuce, and preputial cavity in uncircumcised men.</p>
Patient preferences and characteristics	<p>Tolerance of pain</p> <p>Preference for health care provider or patient application</p> <p>Duration of treatment and/or number of visits</p> <p>Cost of treatment</p> <p>Cognitive ability</p> <p>Ability to accurately identify and physically reach EGWs</p>
Health care provider preferences and characteristics	<p>Clinical training and experience</p> <p>Fiscal and physical resources</p> <p>Scheduling limitations</p>
Immunologic status	<p>Use of immunomodulators (i.e., imiquimod and IFN) should be avoided in allograft recipients, other immunosuppressed patients, and perhaps pregnant patients.</p> <p>Immunocompromised patients may have lower response and higher recurrence rates.</p>

NOTE. EGW = external genital wart.

offered an evaluation 3 months after successful treatment since most recurrences occur during this period. In immunosuppressed patients, recurrences of EGWs are much more common, and periodic follow-up evaluation for recurrence of EGWs may be necessary.

Sex Partner Evaluation

The benefit of evaluating sex partners of patients with EGWs has not been carefully studied. Evaluation does, however, provide an opportunity for education of sex partners about identification and prevention of EGWs, genital examination for EGWs, and, where appropriate, screening for other STDs.

The specific benefit of evaluating sex partners of women with HPV-related cervical SILs for EGWs is not known [110]. Although as many as one-half of male sex partners of women with cervical SILs may have evidence of genital HPV infection, relatively few have EGWs. It is unclear whether treatment of men with evidence of genital HPV infection influences the natural history of their female sex partner's cervical disease [27, 39, 42, 110]. There is little information available currently about the health effects of HPV-related cervical disease on female sex partners of women with HPV infection [43]. Just as in cervical cancer screening for women with EGWs, women who are sex partners of patients with EGWs should undergo cytological screening for cervical cancer at intervals recommended by reported guidelines [44]. The benefit of evaluating male sex partners of men with EGWs is not known, although an association between a history of self-reported receptive anal intercourse and perianal EGWs has been reported [108].

Infants, Children, and Adolescents

As in adults, diagnosis of EGWs in infants, children, and adolescents is based primarily on physical examination. The differential diagnosis and indications for biopsy, the acetowhite test, and detection and typing of HPV DNA are analogous to those for the adult population. Young children and adolescents may suffer emotional trauma when genital procedures are performed. Thus, examinations and treatments should be performed by knowledgeable practitioners after age-appropriate counseling and attention to pain relief.

EGWs are rare in the general pediatric population. Although some children appear to acquire EGWs in a nonabusive manner, the prevalence of confirmed sexual abuse is high among verbal children with EGWs [32, 53, 56]. The diagnosis of EGWs in a child requires that the clinician report suspected child abuse. The act of reporting does not imply that sexual abuse is confirmed but is a means to begin an evaluation process that may or may not confirm sexual abuse. State laws regarding the reporting of suspected child abuse or neglect should be observed. The clinician who fails to follow state law guidelines has the burden of ensuring the subsequent safety of the child. The American Academy of Pediatrics and the American Professional Society on the Abuse of Children have reported recommended standards for the evaluation of children for sexual abuse and STDs [56–58, 111].

Caring for adolescent patients is frequently complicated by a conflict between two ethical concerns: the adolescent's right to confidentiality and the need to investigate and protect the minor from potential abuse. Adolescents should be interviewed privately. Clinicians should explore whether forced sexual contact and physical contact have occurred and evaluate the safety of the home.

Patient Counseling

Health care providers have a responsibility to inform patients that EGWs are caused by infection with HPV, which is sexually

transmitted in most cases. Because HPV infection has neither a cure nor a well-defined natural history and is associated with the social stigma of an STD, addressing patient concerns about the potential chronic nature of the infection can be challenging and time-consuming. Accordingly, clinicians should use written educational materials or referrals to other sources of patient information. Ideally, patients should be counseled about three broad areas: the nature of EGWs, treatment protocols, and anticipatory guidance about the potential impact of EGWs on their lives.

Nature of EGWs

Given the gaps in scientific understanding of HPV, EGWs can be explained to patients in terms of “knowns” and “unknowns.” Knowns include the following: HPV infection is a viral infection that may or may not persist, HPV infection is most often sexually transmitted, and the HPV types likely to cause EGWs are not the same types associated with an increased risk of cervical cancer and generally do not cause infections that pose a serious long-term health risk. Women also can be assured that EGWs do not jeopardize their chances of giving birth to a healthy child.

Unknowns largely reflect uncertainty or controversy over the natural history of HPV infection. Although warts can be eliminated, underlying viral infection may or may not persist. The duration of infectivity after treatment of EGWs is uncertain. The high prevalence, long incubation period, and potential for asymptomatic transmission of HPV infection often preclude tracing an infection to a source sex partner. The source sex partner may or may not know that they have EGWs or HPV infection. Sexually active individuals with or without EGWs can be infected with and transmit low- and high-risk types of HPV.

Treatment Options

Although available treatments are often safe and effective, clinicians should explain, whenever possible, the rationale for treating vs. not treating EGWs and the rates of treatment failure and recurrence. Warts can recur after treatment. However, the recurrence rates after successful treatment with common therapeutic modalities have not been well characterized. Treatments can be characterized as removal of EGWs and possibly reduction of infectivity. Clinicians should explain the adverse effects of the available treatments, their costs, and the influence that special considerations (e.g., age and impaired immune function) might have on treatment and efficacy (table 3). Patients should be counseled about the time necessary to heal after treatment and the potential need for abstinence or use of barrier protection until the tissue is fully healed.

Anticipatory Guidance

A survey on genital HPV infection revealed that the major concerns of patients include determining the source of their

infection, understanding the risk of recurrence or reinfection, disclosing their infection to current and future sex partners, and protecting sex partners from infection [112]. It may be helpful to explain that a current or recent sex partner was not necessarily the source of infection nor do EGWs necessarily reflect infidelity in a monogamous relationship. Patients should be informed that following successful treatment, recurrences are common and may not represent reinfection.

Patient education should include that while treatment may reduce infectivity, HPV infection may persist after treatment and, therefore, future partners may be at risk. There is insufficient evidence to evaluate the effectiveness of condoms in preventing transmission of HPV infection. Nonetheless, patients should be counseled about the general guidelines for prevention of STDs, including the proven effectiveness of condoms in preventing many infections such as HIV infection and gonorrhea. There is no consensus at present on the necessity of fully disclosing one's HPV infection to sex partners. However, legal precedent from litigation on genital herpes may argue for disclosure, and some patients will benefit from guidance in this area. The need for regular Pap smears and screening for other STDs also should be discussed.

Conclusions

A diverse group of experts was able to reach a consensus on a number of key issues related to the diagnosis, treatment, management, and education of patients with EGWs and their sex partners. Some of these positions are supported by strong evidence in the literature, while others are reasonable suppositions based on the experience of experts in the field.

In the process of reaching a consensus, important areas for future research were identified, particularly the need to know when patients are infectious and the impact of treatment on infectivity. Comparative trials of available therapies are needed to firmly establish the relative efficacy and effectiveness, safety, and recurrence rates. It would be valuable to know the prevalence of other STDs in patients with EGWs and the impact of EGWs on the acquisition and transmission of other STDs. Patient self-diagnosis of EGWs is a comparatively basic fact for which the specificity and sensitivity need to be established. A better understanding of the route and frequency of nonsexual transmission of genital HPV infection in children, adolescents, and sexually active adults is needed.

Education about EGWs and other STDs needs to be expanded in medical school curricula and in the ongoing education of clinicians in training and practice (e.g., residencies, specialty organizations, and their accrediting bodies). Clinicians who care for patients with EGWs should counsel patients about all aspects of their diagnosis, including infectivity, transmission and recurrence of EGWs, and the relationship of HPV infection to cancers.

Patients with EGWs receive care from a wide range of clinical disciplines in a variety of clinical settings. It is hoped that development of these consensus statements will be the

beginning of a process that will increase clinicians' and patients' understanding of this STD. The strength of this article rests on a multidisciplinary consensus. Complementary educational materials for health care providers and patients need to be developed to elevate the quality of care and education provided to patients with EGWs and their sex partners.

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