
Genital Herpes and HPV

A Tale of Two Viruses

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HSV *Genital herpes*

Genital herpes is a sexually transmitted disease caused by herpes simplex virus-1 (HSV) or HSV-2. Since recurrences with HSV-1 tend to be less frequent, all patients should have virus typing done on one occasion.

The natural history of genital herpes consists of the first outbreak, followed by a variable period of latency and then reactivation resulting in another outbreak. Generally, the longer the patient has been infected, the less frequent and less severe the outbreaks.

Asymptomatic shedding is the presence of HSV on a mucosal or skin surface when the patient is unaware of symptoms or signs. This is when most HSV transmission occurs. The frequency of asymptomatic shedding is dependent on virus type and frequency of recurrences.

Predictors of asymptomatic shedding include time since disease acquisition and frequency of recurrences. Rates of asymptomatic shedding have been reported to be between 5% and 10% when tissue cultures are used; however, this figure increases significantly when more sensitive polymerase chain reaction technology is applied.

HSV *How is it diagnosed?*

Diagnosis relies on history, as well as on physical and lab exams. A history of recurrent episodes of genital lesions that

Mary's case

- Mary, 24, presents with a six-month history of recurrent episodes of genital irritation and pruritus.
- She has had three separate episodes just prior to menses.
- Over-the-counter antifungal creams have not been effective.
- Mary has been in a stable heterosexual relationship for one year and her partner is asymptomatic.
- There is no recent travel history.
- On exam, there is no regional adenopathy, but she has fissures and two very small ulcerative lesions involving the right labia majora.
- Vaginal/cervical exam is normal.



For more on Mary, go to page 74.

• Fact Box •

Did you know?

- While thousands of people become infected with genital herpes every year, only 20% are aware of their diagnosis.
- Although the true incidence of genital herpes is unknown, it is estimated one in five Canadians is infected.
- The incidence of neonatal herpes in the U.S. is about 1 in 7,500 births.
- Up to 70% of infants with HSV are born to asymptomatic mothers.

Table 1

Genital herpes treatment

First episode

Acyclovir	400 mg tid for 7-10 days
Famciclovir	250 mg tid for 7-10 days
Valacyclovir	500-1,000 mg bid for 7-10 days

Recurrence (patient-initiated)

Acyclovir	400 mg tid for 5 days
Famciclovir	125 mg bid for 5 days
Valacyclovir	500 mg bid for 3 days

Suppressive

Acyclovir	400 mg bid
Famciclovir	250 mg bid
Valacyclovir	500 mg qd/bid or 1,000 mg qd

tid: Three times daily
bid: Twice daily
qd: Daily

last two to seven days is useful in the diagnosis. It is also important to obtain a history of prodromal symptoms. If they are present, your choice of therapy may be affected. On exam, a cluster of vesicles on an erythematous base, painful ulcers or crusted lesions may be seen.

Clinical suspicion must be confirmed by viral identification. A swab of vesicular fluid or a swab from the base of the ulcer should be submitted for viral culture. As viral shedding is variable and may be as short as 48 to 72 hours, a negative culture does not necessarily rule out the diagnosis. Viral typing should be requested on one occasion only.

HSV How is it managed?

Management of genital herpes goes beyond drug therapy. Patients must be counselled to understand their infection, its recurrent nature and asymptomatic shedding. Available anti-viral medications include acyclovir, famciclovir and valacyclovir (Table 1). An advantage of the two new agents, famciclovir and valacyclovir, is a longer half-life, resulting in reduced dosing frequency.

Treatment of first episode disease will shorten the duration of illness and viral shedding, but will not prevent establishment of latency or the character or frequency of recurrences. Recurrent outbreaks can be controlled with either patient-initiated therapy or suppressive treatment.

For patient-initiated therapy, patients should be instructed to begin medications as early as possible, preferably during the prodromal stage. Valacyclovir has proved superior to the other agents in aborting lesions if it is initiated in the prodromal stage.

The most compelling reasons to recommend suppressive therapy are to control outbreaks and to reduce the risk of asymptomatic shedding. A recent transmission study demonstrated a 75% reduction in rates of disease transmission when patients were administered valacyclovir, 500 mg daily. Long-term suppressive therapy is not associated with any diminution of efficacy or emergence of viral resistance.

Patients should be encouraged to share their diagnosis with their sexual partner and be counselled in safer sex practices. Consistent use of condoms has been demonstrated to reduce the transmission of genital herpes.

In women who are pregnant, it is important to note that antepartum cultures do not predict the infant's risk of exposure to HSV at delivery; therefore, a careful assessment should be done at the time of delivery to determine the presence of prodromal symptoms or genital lesions. If either is present, a caesarean section should be undertaken.

Randomized, controlled trials have shown a significant decrease in recurrences, asymptomatic viral shedding and rates of caesarean delivery with the use of suppressive acyclovir. Acyclovir, 400 mg three times daily, should be considered from week 36 until delivery.

HPV HPV

Genital warts are caused by human papillomavirus (HPV). They are the most common viral sexually transmitted infection. The incubation period ranges from six weeks to 12 months, but may be longer. Most HPV infections are transient and clear within two years.

Over 70 genotypes of HPV have been identified. Genotypes are differentiated into low-risk and high-risk for the development of genital malignancies. Infection with one genotype is likely not protective against other types. Although treatment effectively removes the wart, it does not necessarily eliminate the virus, nor does it eliminate the possibility of recurrences; however, it may reduce the risk of transmission.

Table 2
Genital warts treatment

<i>Treatment</i>	<i>Clearance rate</i>	<i>Recurrence rate</i>	<i>Notes</i>
<i>Patient-applied:</i>			
Imiquimod cream	33-72%	9-19%	<ul style="list-style-type: none"> • For external lesions only • Cream applied sparingly 3 nights/week • Side-effects common, but limited to local skin reactions
Podophyllotoxin	37-91%	4-91%	
<i>Provider-administered:</i>			
Cryotherapy	27-88%	21%	<ul style="list-style-type: none"> • Used for extensive warts and cervical lesions • Treatment is repeated weekly until warts subside • Safe during pregnancy
Podophyllin	23-72%	23-65%	<ul style="list-style-type: none"> • Associated with local skin reactions • Potential for systemic toxicity
Electrocautery	61-94%	22%	<ul style="list-style-type: none"> • Painful • Requires specialized equipment
Laser	23-52%	60-77%	<ul style="list-style-type: none"> • Same as electrocautery
Surgical excision	35-72%	19-29%	
Trichloroacetic acid		63%	<ul style="list-style-type: none"> • Ideal for vaginal and cervical lesions • Safe during pregnancy

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A followup on Mary

What is her diagnosis?

- The clinical impression of genital herpes is confirmed by lab identification of herpes simplex virus, type 2.
- Syphilis serology is negative.
- Endocervical samples for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* and a vaginal swab for candida are also negative.

What should be done for Mary?

- Mary is counselled on the natural history of genital herpes, including:
 - the expected frequency of recurrences,
 - the likelihood that frequency will decrease with time,
 - the risk of asymptomatic viral shedding and
 - the importance of consistent safer sex.
- It is impossible to define how long infection has been present. Her partner may have genital symptoms he does not recognize to be genital herpes. He should be assessed and it may be appropriate to arrange for type-specific serology.
- Treatment options of episodic versus suppressive therapy are outlined for Mary (including the recent data on daily valacyclovir, 500 mg, significantly decreasing the risk of disease transmission when used with safer sex).
- Mary chooses suppressive therapy and arrangements are made to reassess her in one month.

HPV *How is it diagnosed?*

Genital warts are often asymptomatic. The classic appearance is one of warty growths on anogenital skin and/or mucous membranes. The warts are frequently multiple and polymorphic. They may be associated with pruritus, bleeding, pain or dyspareunia.


Diagnosis is generally made by visual exam of the genitalia and perianal region. A speculum exam should also be done to rule out the presence of vaginal or cervical involvement. Magnification by a hand lens or colposcopy is often useful. Anal warts should be examined by proctoscopy to assess the full extension of the lesions. Any atypical warts should be biopsied or the opinion of an expert sought before treatment is initiated. The most common way to detect cervical HPV is with a Pap smear.

HPV *How is it treated?*

Since no therapy has been shown to eradicate HPV, the goal of treatment is removal of exophytic warts and the amelioration of any symptoms and signs. As HPV is not eradicated with therapy, recurrence of warts may occur.

The choice of therapy is dependent on symptoms, site and extent of infection, the wishes of the patient and the availability of therapeutic modalities. Treatment of external genital warts may be self-applied or provider-applied (Table 2).

How can herpes and HPV be prevented?

All patients with either genital herpes or genital warts should be screened for other sexually transmitted infections and be counselled on consistent use of condoms, plus other forms of safer sex. Screening should include syphilis serology (rapid plasmin reagin [RPR], *Treponema pallidum* particle agglutination assay [TPPA]) and appropriate tests for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. 

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