Herpes Simplex.

Introduction

Genital Herpes is caused by a common virus known as Herpes Simplex. Because of certain differences in laboratory characteristics, scientists have designated herpes strains as either type 1 or type 2. Type 1 generally causes cold sores around the mouth, while type 2 generally causes sores on the genital area. In other words, most often, genital herpes is caused by herpes simplex virus type 2. However, the word "genital" actually refers only to the area of skin affected not to the virus type. In fact, a person may get genital herpes from the mouth of a sexual partner with an active herpes simplex virus type 1 infection (e.g., a cold sore) during oral sex. In this case, this person will get type 1 genital herpes. Genital herpes is a sexually transmitted disease (STD) and is usually passed on through genital skin contact with an area affected by an active herpes sore in the partner. After herpes is contracted, it usually causes a skin infection which clears by itself (or faster with treatment). After the illness is over, the virus in the skin has been removed from the area by the body's immune system. Between outbreaks, the virus hides in certain nerve cells (neurons) along the lower spinal cord in a place called the sacral ganglia. The virus will remain there in an inactive or latent phase, although it may reoccur from time to time and travel back down the nerve to the skin.

If you think you have genital herpes, go to a clinic or a Doctor to have it diagnosed. Diagnosis is made based on clinical symptoms and/or a viral culture. If you feel you are having your first or primary episode, this should be diagnosed through a blood test in combination with a viral culture. In some situations, genital herpes may be a simple diagnosis for the general practitioner. In others it may even elude the specialist. When symptoms and signs of herpes are "classical", that is, when a known exposure has taken place and sores have developed that are painful clustered vesicles (blisters) or ulcers on a red, inflamed base, the clinical diagnosis is clear-cut. Recurrences make herpes even more likely. Then, the virus itself is detected by a culture test from one of the sores, confirming the diagnosis. In order to make sure that no other diseases accompany the herpes, tests for syphilis, gonorrhea, Chlamydia, trichomonas and yeast are also performed.

Certain people with genital herpes can have mild intermittent symptoms. The only sore might be a pinpoint or single ulcer on the labia that lasts for a few days and reoccurs every six months. It may not hurt at all. The diagnosis may not even occur to the patient or the physician. A virus culture test to detect herpes in the sore should be performed during an active phase of infection. If the test is positive, herpes is likely to be the cause of the sore. A positive culture for herpes simplex virus from the skin means that you have herpes. The virus culture is so reliable, it is called the gold standard for this infection.

If the culture test is negative, however, herpes may or may not by the cause of the problem. The following issues need to be considered if a test comes back negative:

- was the test obtained during an active period? Even if it was, quite often herpes virus is not recoverable. **Correct timing of the virus culture is essential.**
- how was the test obtained?
- was the doctor's office far away from the laboratory? If so, the virus may not have survived the trip.
- how experienced is the laboratory? This varies.

If you suspect herpes and your doctor agrees, return again for virus culture at the first sign of a recurrence. The earlier the specimen is obtained, the better is the chance of an accurate test. In my experience, two visits will suffice, if the visits are early. If we suspect herpes very strongly, however, we will keep culturing until we find it. Rarely, four or five tests are necessary.

Blood Test

Blood tests have markedly improved the physicians' ability to properly counsel both patients and their partners. Herpes blood tests measure the body's immune response against the virus. Without infection there is no specific reaction to the virus. However, shortly after true viral infection the body responds to fight the infection. The herpes blood test measures the body's antibodies to herpes, the body's response to infection. A positive blood test indicates there are antibodies present, therefore viral infection has occurred; a negative test indicates antibodies are nonexistent. All herpes antibody tests do essentially the same thing. They do not directly measure virus but the body's reaction to the virus. To look directly for virus, one must test a sore containing virus and grow the virus in the laboratory. This has the advantage of determining the virus and its type.

Blood tests will not identify a sore or its position, but an accurate blood test could be used to help diagnose herpes in people who do not get sores and in people who get them only rarely. People who might want such a test would include:

- the partner who has no symptoms but who may have been the source of herpes
- the person with only one past episode whose culture was lost on the way to the lab
- the person who thinks he or she has been exposed to herpes but is not sure
- the couple who wants to give up safer sex precautions.

Unfortunately, the commercial tests available to your health care provider can be very confusing. Most herpes antibody (blood) tests are not truly type specific. Most antibody tests cannot accurately tell the difference between past infection with type 1 versus type 2. To further confuse things, even some widely used tests that are commonly called "type specific" are not accurately type-specific. Most commercial type specific tests are very poor at accurately differentiating antibody against herpes simplex virus type 1 from antibody

against herpes simplex type 2. Many of these inaccurate tests are commercially available and they may be easily accessible to your doctor.

Inaccurate type specific or non typespecific blood tests are still useful in some settings. For example, during a first episode, an antibody test may be used, in conjunction with viral culture and typing, to determine whether that culture proven episode is a true primary or a non primary. In this case, the blood test is not used to diagnose genital herpes but whether it's a true primary; the culture and typing of a lesion specimen was used to make the diagnosis of genital herpes.

Recently, true and accurate type specific antibody tests for herpes have been developed. These tests examine directly for the body's reaction (antibody production) against a type2specific glycoprotein, Gd (gG2). Very few laboratories test directly for this antibody, since commercial test kits are not routinely available for this purpose. Until new tests replace the old tests, you and your physician will have to interpret information obtained very carefully.

The Western Blot test is so specific that, as far as we can tell, there is virtually no chance for error of the type that shows a positive antibody to herpes simplex virus type 2 where none exists. On the other hand, there is always a small possibility that an antibodies to herpes simplex virus type 2 that is really present will go undetected by this method. This could happen in the case of a person who has not had time to make a good antibody response yet. In some cases, antibody may take as much as twelve or sixteen weeks to develop, especially if the primary infection was treated with an effective medication. In some rare cases, a person with culture proven, long-lasting, herpes type 2 of the recurrent variety will still have a negative Western blot after the sixteen weeks presumably because they just do not make enough of the necessary antibody for detection. This probably occurs less than 1 percent of the time.

The Western Blot is very, very sensitive probably 99 percent sensitive. It is also very accurate, with virtually no false positives (incorrect positive results). If a person is tested more than twelve or sixteen weeks after the possible exposure, and if the test is negative, and if the possible exposure was to type 2 herpes simplex virus, then it is very likely that bona fide infection did not take place. However, no test is absolutely without fault and this test, like all tests, should be interpreted by you and your physician, in the seeing of the clinical information, so that everyone understands all of the subtle details.

Other tests for gG2 (type2specific glycoprotein), called RIA, ELISA, or EIA (other names are also possible) may also be available. These tests can determine whether there has been infection we herpes simplex virus type 2, but they do not necessarily determine whether there has been infection with type 1. EIA tests are technically much easier to perform than the Western blot, with much of the assay actually done by machine. Unfortunately, commercial kit assays for antibody to gG2 are not yet available. This situation is very likely to change and soon. ELISA tests have been successfully used for this purpose, with one described from Atlanta, one from California, another from Sweden, and an adaptation from Australia.

Until then, if possible, be especially careful to check with your physician as to which test is being ordered and how the test will be interpreted before actually being tested. The test situation can be very confusing, because if your physician has ordered a so-called type specific EIA test that does not specifically check for antibody against gG2 or some other type 2 specific glycoprotein, then the test answer may be of no value and should not be interpreted. So called type specific tests that often give misleading test results are most often reported as "type 2:type 1 ratios." Always check this out with your physician.

When to do a Western blot

The following are some examples of real cases where we have found the Western blot test to be especially useful. Test results will be different for each person depending upon their own experience.

Example 1: A couple in a long-term relationship wish to be tested for herpes. One partner has genital herpes simplex virus type 2 proven by viral culture. The other partner is asymptomatic, although they have been together for several years. The partner wants to know if he or she is still at risk of getting genital herpes.

Serology Results: There is virtually never a need to perform a Western blot in a person with viral culture proven type 2 genital herpes simplex virus infection, since the viral culture (if it is positive) tells you the information you need. However, the partner should be tested. In this case, he or she is seropositive for HSV type 2.

Interpretation: This partner has genital herpes. He or she may have had genital herpes at the time the couple met, or asymptomatic transmission may have taken place at some point in their relationship. Either way, there is very little risk for the partner catching a second infection with type 2 herpes simplex virus. This couple can relax significantly their concerns about transmission of genital herpes since both already have proven infections. While there are cases of second viral strain transmission, the chance of that being a problem for this couple is very remote.

Example 2: A patient with a history of genital herpes is seen twelve months after recovering from genital sores diagnosed by only visual examination as probable primary genital herpes. A virus culture performed at the time was negative, but the patient's physician explained that the negative result does not rule out genital herpes. The patient was advised to return with an active episode for repeat culture, but none have been detected. The patient has had one monogamous relationship, which started just before the so-called primary infection, with a partner who has no history of genital symptoms. They commonly practice oral genital sex. Neither partner has cold sores.

Serology result: Both partners are positive for HSV type 1 and negative for HSV type 2.

Interpretation*:* Blood tests results must be interpreted in the clinical setting. It is very likely that the patient's partner does not have genital herpes. The patient's genital sores may have been a primary genital episode, but, if so, probably resulted from oral genital transmission of HSV type 1 from the partner. Regardless, the prognosis for a continuing low genital recurrence rate is excellent. Alternatively, these blood test results are consistent with both patient and partner having been exposed on the face to cold sores at some time in their lives, while neither has genital herpes at all. A third explanation would be that the partner transmitted herpes simplex virus type 1 to the patient by genital contact with asymptomatic genital herpes simplex virus type 1 sores. Alternative diagnoses to the patient's primary herpes diagnosis should be considered, especially if symptoms recur frequently. The serology test is only additional supportive evidence for the diagnosis. It does not determine where in the body exposure has taken place, and it must be interpreted cautiously and in connection with the clinical picture. This patient with genital sores should be quite certain that other causes of genital ulcer have been ruled out, since the precise is not yet know. In this case, the serology test has helped to rule out some things but has not specifically confirmed the clinical problem. It is very important that this patient be tested for syphilis to make sure that syphilis did not cause the ulcer, since syphilitic ulcers, left untreated, will improve and then remain dormant only to cause damage later on. The result above could be consistent with both patient and partner having immunity to herpes simplex virus type 1 from asymptomatic mouth cold sores and with one partner having transmitted syphilis to the other that has never been diagnosed or treated. Without a test, nobody will know.

Alternative Serology Result: Both partners are negative for both HSV type 1 and HSV type 2.

Interpretation: The initial diagnosis of genital herpes was probably incorrect. An alternative diagnosis should be considered, but if the infection remains inactive, the cause may never come to light. The syphilis test discussed above is crucial, although the result is likely to be negative. If sores are recurrent, one or more specialist physicians should be involved to try to sort out the proper diagnosis.

Summary

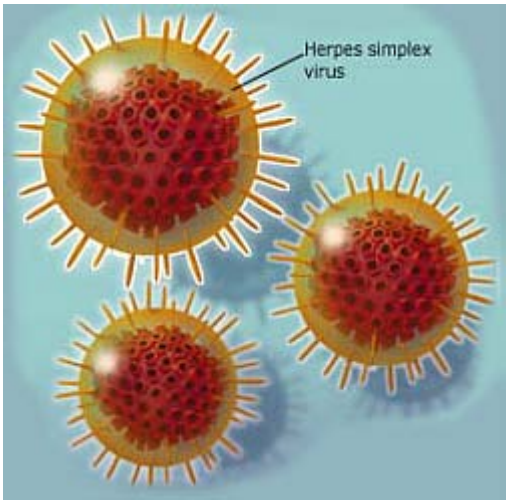
Type specific serology testing is especially useful in unusual presentations of herpes and in some asymptomatic cases. People with genital sores will still need to have a viral culture test from a sore for confirmation and typing. The culture test is more direct, less expensive and provides information about the specific sore and the symptoms. If you have a clear positive viral culture test that is typed (type 1 vs. type 2) there is almost never a reason to get a Western blot also.

A negative Western blot test performed correctly, means that genital herpes is very unlikely, although there is still a small chance of a false negative. A positive test for type 2 herpes strongly suggests the diagnosis of genital herpes, although the test does not determine the site of infection. Although most type 2 herpes is sexually transmitted and usually affects areas on or near the genitals of anus, there are type 2 facial herpes infections as well. Furthermore, since genital herpes can be caused by type 1 herpes simplex virus, a negative test for type 2 does not rule out genital herpes: it only makes type 2 genital herpes very unlikely, as long as the twelve to sixteen weeks' waiting period has passed. It may take up to twelve to sixteen weeks after infection for the serology test to show positive. Any test result should be interpreted with your physician.

Herpes Simplex Viruses

HSV-1 & HSV-2

Herpes Simplex Viruses belong to the family *Herpesviridae*. The HSV viruses are double-stranded DNA viruses and replicate in the nucleus of host cells. They have icosahedral capsids and are enveloped viruses. HSV also consists of eight different types of viruses. The most commonly known viruses associated with HSV are HSV-1 and HSV-2. HSV infections are very common and by adulthood, almost 80% of Americans have had an HSV-1 infection at some point. About 20% of all Americans have had HSV-2 infections. Most infections caused by HSV are asymptomatic. Once a person becomes infected with HSV, the virus becomes latent between infections and remains in the body for life. HSV viruses are usually spread through contact with lesions on the skin. HSV-1 and HSV-2 have no seasonal incidence and are found worldwide. Over 90% of children older than 2 years of age in undeveloped countries have the antibody to HSV-1.



Source : http://www.moondragon.org/images/herpessimplesvirus.jpg

This is an enveloped virion of HSV. The capsid is icosahedral and the envelope makes the virus more susceptible outside of the host cell.

Taxonomy: HSV-1 and HSV-2 viruses cause different types of infections in their hosts. HSV-1 causes gingivostomatitis, or oral herpes, which are cold sores along the oral mucosa and opening of the mouth. This type of infection occurs most often in children. About 80% of the American population has been infected by the time adulthood is reached. HSV-1 also causes keratitis which is an infection of the cornea, and can cause herpes encephalitis in older children and adults. HSV encephalitis is a rare disease and has a 70% mortailty rate. HSV is the primary cause of fatal sporadic encephalitis in the United States. HSV encephalitis is caused by HSV-2 in neonates and has a high association with immunocompromised patients. HSV-2 viruses can also cause genital herpes and neonatal herpes. About 85% of genital herpes infections are cause by HSV-2.

Pathogenesis: HSV viruses usually only infect humans although they can also be transmitted by dogs. Infections are spread through contact with secretions from lesions on the oral mucosa, genitalia, or areas where lesions have formed. Lesions develop on mucous membranes of the oral mucosa and genitalia after an incubation time period of 2 to 11 days. HSV is more readily transmitted when the virus is in its primary stage of development. The virus-infected cells are located at the base and along the edges of the lesions. The virus can still be transmitted from lesions that are old or scabbed. Also, asymptomatic patients can still transmit the virus without visible lesions present. Saliva and vaginal secretions contain the virus and the infection is spread through kissing, sharing drinking glasses, and through sexual contact. During latency of the virus, HSV-1 infects the trigeminal nerve root ganglion and autonomic ganglia of superior cervical and vagus nerves. HSV-2 remains in the sacral nerve root ganglion at the base of the spine. HSV infections can also be transmitted from mother to neonate and have a fairly high mortality rate of 60%, although infection obtained by this way is not as common.

Signs and Symptoms: Although many times HSV is asymptomatic, there are many signs to distiguish whether a person has an HSV-1 or HSV-2 infection. *Oral herpes,* is usually caused by an HSV-1 infection and has an incubation period of 2 to 14 days. In its primary stage, the virus is usually asymptomatic. When visible, the virus manifests into intraoral mucosa vesicles, which are inside the mouth and cannot be easily seen. The virus can also produce ulcerations which can be found on the buccal mucosa, posterior pharynx, gingival mucosa, and palatal mucosa. Since ulcerations may be found on the posterior pharynx, it may appear as pharyngitis. Recurrent infection usually causes lesions or infection of the lips and in the corners of the mouth where oral mucosa joins with skin. These lesions and ulcers create a burning sensasation which is typical of HSV infections.

source: http://www.moondragon.org/images/coldsore.jpg

Another sign of an HSV infection is the formation of *genital herpes* caused mostly by HSV-2. HSV-1 can also cause genital herpes and is the cause of infection about 33% of the time. In females, the infection appears as vesicles on the mucosa of the labia, vagina, or both. Infection can also occur in the urethra, on the cervix, or on the vuvla of the female body. In males, the infection affects the shaft, glans, and prepuce, and can also infect the urethra. These sypmtoms become less severe throughout recurrent infections.

HSV infection may also cause *ocular herpes*, or an infection of the eye. This will cause swelling of the eyelids and can also result in a corneal infection. HSV is the most common cause of corneal infections in the United States. Most infections only involve the epithelial layer of cells and with treatment, will heal completely.

Diagnosis and Laboratory Testing of HSV-1 & HSV-2

If an infection of HSV is suspected, laboratory testing is used to make a diagnosis. There are no non-laboratory tests to help confirm the disease in adults but if HSV is a supected congenital infection, a CT scan or MRI of the head should be done.

Common Laboratory Tests Performed To Detect HSV

Test	Expected Results for Healthy Subjects	Expected Results for Patients with HSV	Type of Test
ELVIS (Enzyme Linked Virus Inducible System)	Negative	Positive - Virus infected cells will result in fluorescence, which can be seen with the use of a light microscope. This test is serological and tests are	Screening - confirm with Western Blot

		performed on patient serum.	
DFA (Direct Fluorescent Anitbody)	Negative	Positive - Virus infected cells collected from a patient will fluoresce green under a microscope. This test is also serological and performed using patient serum.	Screening - confirm with Western Blot
NAATs (Nucleic Acid Amplification Tests)	Negative	Positive	Confirmatory
EIA (Serology)	Negative	Positive - Useful for primary infection only and detects IgM spike. Patient serum is tested for antibodies to HSV-1 and HSV-2.	Screening - confirm with Western Blot
POCkit	Negative	Positive - This test can be used in a doctors office and tests for the antibody to the virus. Enough antibody must be present for the test to positive. This test is specific for HSV-2.	Screening - confirm with Western Blot
PCR DNA	Negative	Positive - Indentification of Viral DNA is extracted. This test is extremely accurate.	Confirmatory
Western Blot	Negative	Positive - Identifies proteins from the virus	Confirmatory

Tests that are used to detect antibodies to HSV are positive only if there is enough antibody present to produce a positive result. Small amounts of antibody can produce a false negative and therefore a confirmatory test must be performed to ensure the result is correct. The Western Blot test is most often used since it is a very reliable way to detect HSV.

What are the long term effects of HSV?

After primary infection of HSV, the virus remains inside the host. Although the person may be asymptomatic, the virus is still in the body and becomes latent. As discussed before, HSV-1 stays in trigeminal nerve root ganglia and autonomic ganglia of superior cervical and vagus nerves. HSV-2 remains in sacral nerve root ganglia. Certain stimuli can reactivate the virus such as stress, caffeine, and sunlight. This would cause the virus to come out of latency and lesions will reappear. There is no cure for HSV, but treatments and testing are available. With treatment and while the virus is latent, a person may appear and feel completely normal. Although no symptoms are visible, reactivation of the virus is possible at a later time.

Who is at risk?

HSV does not have a higher incidence in patients with a medical or family history of HSV. This also does not help to diagnose the disease. However if a neonate contracts HSV, it is very likely it was transmitted congenitally during birth from the mother. HSV in neonates can cause HSV encephalitis. Mothers who are expecting should be tested if an HSV infection is suspected. HSV is a common infection throughout the world and traveling will not increase your risk of contracting HSV. People who are sexually active before age 17, have been sexually active for many years, and who have had many sexual partners are at a greater risk. Also, people infected with other STDs such as gonorrhea, syphilis, and HIV are more likely to be seropositive for HSV.

How can an HSV infection be prevented?

HSV can be prevented by limiting sexual partners and practicing safe sex. HSV-1 and HSV-2 can still be transmitted when no symptoms are present so be aware of who your sexual partners are. Also be aware of lesions on or around the mouth and genitalia. Avoid direct contact with lesions, saliva, mucosal secretions, and other secretions from an infected person. Health care workers should wear gloves to prevent herpatic whitlow, which is an HSV infection on the fingers. There is no vaccine available to prevent against HSV.

How is HSV treated?

HSV can be treated by the use of antiviral drugs such as Acyclovir and Vidarabine. Daily doses of these drugs interefere with the replication of the virus so the virus is unable to reproduce in the host. Therapy, with the use of antiviral drugs, can limit recurrences of the disease althought it cannot completely prevent further infection.

For more information on HSV visit Herpes.com

This website is part of a class assignment for Clinical Immunology and Virology at the University of Delaware. I am a Medical Technology student and my goal is to educate people on HSV and help them to know more about how to prevent contracting an infection due to HSV. My Home Page

Have any questions or comments?

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