CYTOMEGALOVIRUS

learn about the symptoms, diagnosing and treating this disease

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Cytomegalovirus (CMV) is a common virus. It can infect people of all ages, including unborn babies. Once a person gets CMV, it stays in his or her body for life. Medicines do not rid the body of CMV infection, but they are used to prevent and treat CMV disease. There are ways to prevent CMV disease. While the virus is nearly impossible to avoid in everyday life, there are ways to reduce your risk of CMV infection. This publication describes how CMV is spread, its symptoms, prevention and treatments.

CMV is a type of virus in the herpes family—the kind of viruses that also causes chicken pox, shingles and cold sores. CMV is also knows as human herpes virus type 5, or HHV5. Most people in the United States have the virus by the time they turn 40. Almost all gay and bisexual men are infected with CMV, and more than 3 out of 4 people living with HIV carry the virus. CMV is the most common virus passed onto a pregnant woman's unborn baby.

Most of the time, CMV does not cause disease. It may be a cause for mononucleosis, commonly called mono. Among people with damaged immune systems, including those living with HIV, being infected with CMV is a major risk of CMV disease, which might include the loss of sight and death. Unborn babies can also develop the disease.

How is CMV spread?

CMV is passed from person to person through close contact with body fluids, such as saliva, semen, vaginal fluids, blood, urine, tears and breast milk. You can get CMV when you touch these fluids with your hands and then touch your eyes, nose or mouth, which are mucous membranes. People can also get CMV through sex, breastfeeding, blood transfusions and organ transplants.

Contact with the saliva or urine of young children is a major cause of CMV infection among pregnant women, as well as among other children. For women who become infected with CMV for the first time during pregnancy, 1 out of 3 of them will pass the virus onto their unborn babies. This contrasts with women who already have CMV before their pregnancy, because less than 1% of them pass CMV onto their unborn babies. Therefore, if you're pregnant and do not have CMV at the start of your pregnancy, it's important to take measures to prevent CMV infection during your pregnancy. Developing babies who are infected with CMV during pregnancy have a high likelihood of hearing and/or vision impairment and mental retardation.

How do I prevent CMV infection?

CMV is easy to pass from one person to another. You may already have it, and your doctor can test for CMV infection. Uninfected people can take steps to lower their risk of infection.

If you are not already infected with CMV, washing your hands often and well and using condoms during sex may help prevent CMV infection. If you expect to get a blood transfusion or organ transplant, talk to your doctor about what can be done to lower your risk of infection. When possible, uninfected people should be given blood products and organs that are free of the virus.

CMV is common in young children so being careful around them will help prevent infection. Some suggestions include washing your hands after contact with children; after contact with their saliva, tears or urine; or after contact with objects that they've touched such as cups, pacifiers, utensils, toys and diapers. Refraining from touching your eyes, nose and mouth in these situations is important, as well as not sharing food or drinks with them. These activities may be nearly impossible to avoid while parenting, in households with children, day care centers and schools.

How can I tell if I have CMV infection?

When a person is first infected with CMV (called primary infection), it doesn't typically cause symptoms. If they are present, symptoms might include fatigue, swollen glands, fever and sore throat. Since these are also symptoms of other illnesses like the flu, most people don't know when they get CMV. This is why most primary infections are not diagnosed.

Several tests can be done to find CMV. These include blood or urine culture tests, blood tests to find either the virus or its antibodies, and body tissue samples. If the test comes back positive, it means you have CMV infection. However, it may not mean that CMV is causing any of the symptoms you may be feeling.

How do I prevent CMV disease?

There is a difference between CMV infection and CMV disease. While most people living with HIV also have CMV, not all will develop CMV disease. People with very low CD4+ cell counts are most at risk for CMV disease, but there are medicines that can help suppress CMV and prevent its disease.

The most effective way to prevent CMV disease is by getting the best care you can for your HIV—keeping your immune system intact, which in turn keeps CMV in check. Using effective anti-HIV therapy to maintain your immune health can help keep CD4+ cell counts above 200. A healthy immune system is your best defense against CMV becoming a problem. If your immune system shows signs of being damaged, taking CMV preventive therapy is an important decision to make.

While CMV can cause disease in many places in the body, one of the more common places it occurs in people with HIV is in the eye, as CMV retinitis. Seeing an HIV experienced eye doctor, called an ophthalmologist, is an important part of a comprehensive strategy to prevent CMV retinitis. He or she can recommend treatment before permanent damage occurs to your eyesight. For those at risk, regular visits usually occur every 3–6 months.

Finally, for those with very low CD4+ cell counts, taking preventive medicine for CMV might be part of a comprehensive strategy against CMV disease. The drug, ganciclovir (sold as Cytovene), is used to prevent CMV disease in people with CD4+ cell counts below 50 or with other signs of weakened immune systems. It can also be considered for children. Ganciclovir as preventive therapy may be not be desirable for everyone because of its side effects, lack of proven benefit, cost and risk for developing resistance to it. Talk with your doctor about the pros and cons of using ganciclovir to prevent CMV disease and decide if it's right for you.

Can I ever stop preventive therapy?

Yes, stopping preventive therapy seems to be safe if your CD4+ cell count goes above 100–150 and stays there for 6 months or longer. However, there are no guidelines for stopping preventive therapy in children. If the CD4+ cell count goes below 100–150 again, it is advised to restart CMV preventive therapy, especially if you've had CMV disease before. Consult your doctor and ophthalmologist when making these decisions.

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How can I tell if I have CMV disease?

CMV disease most often affects people with HIV when their CD4+ cell counts are below 50. You may also be at risk if you have a slightly higher count (50–100) and have had at least one other opportunistic infection, such as PCP, candidiasis or tuberculosis (TB). A test can measure the level of CMV in the blood. However, high levels of CMV do not always mean there's active disease somewhere in the body.

CMV can infect almost any part of the body, sometimes in more than one place at a time. In people with HIV, CMV seems prone to infect the eye. If you think you have symptoms that are detailed below, talk to your doctor as soon as possible.

DISEASE OF THE EYE:

The most common CMV disease in people with HIV is CMV retinitis, or damage to the back of the eye (retina). About 1 out of 4 people living with HIV will develop CMV retinitis, and it remains the leading cause of blindness among them. People with this retinitis sense blurred vision, blind spots or floating spots in the affected eye. Even if treatment is successful, damage to the eye can be permanent. Left untreated, CMV retinitis will lead to blindness.

DISEASE OF THE COLON:

CMV colitis is the second most common CMV disease in people with HIV. Symptoms include diarrhea, weight loss, loss of appetite, pain in the stomach or chest, blood in the stool, diarrhea and fever. These symptoms are common for many different conditions in HIV disease, which makes it difficult to tell whether they are due to CMV disease or from other diseases of the intestinal tract. It may take several weeks to show that CMV is the cause and not other infections such as fungi, bacteria, parasites or other viruses. CMV can also affect the upper gut including the stomach and small intestine, called CMV gastritis.

DISEASE OF THE BRAIN AND NERVES:

CMV can infect the brain in the form of CMV encephalitis. Symptoms include dizziness, headaches, seizures, personality changes and nervous system problems. Death can occur within weeks or months. When CMV infects the nervous system, it is called polyradiculopathy.

Symptoms include numbness, pain and tingling in the legs, feet, arms and hands, and the loss of muscle, urinary and bowel control. All of these symptoms look like those of other opportunistic infections, so CMV disease may be overlooked as the cause.

DISEASE OF THE THROAT:

CMV esophagitis affects the throat. It can lead to difficult and painful swallowing, chest pain, fever, mouth sores and hiccups.

DISEASE IN NEWBORNS:

Congenital CMV is the most common infection in newborns. About 1 in 10 babies born with congenital CMV have symptoms such as a rash, low birth weight, small head, jaundice, and large spleen and liver. Newborns at risk for congenital CMV should be tested for it within the first 3 weeks of birth. See the section "Concerns for children" for more information.

How do you treat CMV disease?

Most of the time, treating CMV disease happens in two stages: induction therapy and maintenance therapy. Induction therapy is used to treat the disease when it first appears and usually takes 2–3 weeks. Maintenance therapy is used to prevent the virus from causing disease again.

Treating CMV disease depends on the type of CMV disease (CMV retinitis, CMV colitis, or both, etc.) as well as how severe it is. People with CMV retinitis can take medicine by mouth, implants in the eye (ocular implants), injection or IV line. Because several of the drugs are given by IV, they may impose changes in a person's lifestyle. Below is a list of the six medicines now available for treating CMV disease.

These medicines can interact with many drugs, including some anti-HIV drugs and common over-the-counter drugs like NSAIDs. A good way to learn about possible drug interactions is by reading the full package insert of your prescription or talking to your doctor or pharmacist.

GANCICLOVIR (CYTOVENE):

Ganciclovir can be used to treat all forms of CMV disease. Ganciclovir is given through an IV line (intravenously in the vein) and as a pill. For induction therapy, it's given by IV (5mg per kg of body weight) twice a day for 2 to 3 weeks. For maintenance, it's given either by IV once a day for 5–7 days a week or by 1,000mg capsules 3 times a day. Possible side effects include low red blood cells (anemia), low white blood cells, low platelets, nausea, vomiting, diarrhea, constipation, stomach pain, loss of appetite, dry mouth, mouth sores, trouble sleeping, nervousness, depression, sweating and joint or muscle pain.

FOSCARNET (FOSCAVIR):

Foscarnet can be used to treat all forms of CMV disease. Foscarnet is given through an IV line. For induction therapy, it's given either 2 (90 mg per kg of body weight) or 3 times a day for 2 or 3 weeks. For maintenance, it's given once a day. Possible side effects include kidney damage, low red blood cells (anemia), nausea, diarrhea, vomiting, fever, stomach pain, loss of appetite, confusion, dizziness and headache. Foscarnet should be stored in a refrigerator and out of direct light.

Neither ganciclovir or foscarnet offers an advantage over the other in treating CMV disease. However, the drugs have different side effects, and people often choose one over the other based on which side effects are of more concern to them. The major side effect of ganciclovir is low neutrophil counts (neutropenia). These cells are important for fighting bacterial infections. The major side effect of foscarnet is kidney toxicity. In studies, 16% (ganciclovir) and 20% (foscarnet) of people stopped the drug due to these side effects. So they roughly occur at the same rate, but one or the other may be of a greater concern for a person based on their health status or risk of side effects from taking other therapies.

As with the trend in prescribing anti-HIV drugs, more often doctors are combining different ways to treat CMV disease. This includes using combinations of both IV ganciclovir and foscarnet and/or combining IV therapy with medicine that's taken orally or through ocular injection or implant.

VALGANCICLOVIR (VALCYTE):

Valganciclovir is the only approved oral treatment and is as effective as IV ganciclovir for treating CMV retinitis. For induction therapy, it's given as two 450mg tablets twice a day for 3 weeks. For maintenance, it's given as two 450mg tablets once a day. Possible side effects include low red blood cells

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(anemia), low white blood cells, low platelets, diarrhea, upset stomach, vomiting, stomach pain, loss of appetite, thirst, fever, constipation, headache, back pain, leg swelling and trouble walking or sleeping.

The benefit of using oral therapy for the first time in treating CMV is that it does not cause neutropenia. It avoids the possible complications, such as sepsis, that accompany giving medicines through an IV.

CIDOFOVIR (VISTIDE):
Cidofovir has been studied for CMV retinitis and may be effective for other forms of the disease. Cidofovir (5 mg per kg of body weight) is given through an IV line with probenecid (to help prevent kidney damage from the cidofovir). For induction therapy, it's given once a week for 2 weeks. For maintenance, it's given once every 2 weeks. Possible side effects include kidney damage, kidney failure and low white blood cells.

The benefit of cidofovir is that it only taken once a week, which greatly reduces the impact of twice a day IV therapy on daily life and routines. However, the increased risk of quite serious side effects, such as kidney damage, makes it less desirable to use. It is often used only when the other IV therapies no longer are suitable options due to resistance, failure or side effects.

GANCICLOVIR IMPLANT (VITRASERT):
This implant is only used for CMV retinitis and does not prevent CMV disease in other parts of the body, including the other eye. Ganciclovir implant is a pellet surgically implanted into the affected eye and changed every 6 months. For induction and maintenance therapy, it's given either 2 or 3 times a day for 2 or 3 weeks. Possible side effects include loss of white blood cells as well as discomfort from surgery and some loss of clear vision, both of which are usually temporary. The implant is often used together with oral valganciclovir or ganciclovir.

FORMIVIRSEN (VITRAVENE):
Formivirsen is used to treat CMV retinitis for patients who have failed the other therapies listed. Formivirsen is given as a shot into the affected eye. For induction therapy, it's given every other week for 2 doses. For maintenance, it's given once every 4 weeks. Possible side effects include minor pain, redness or swelling of the eye.

Ocular implants and injections do not prevent CMV disease throughout the body. However, when used together with IV or oral medication, they can be very effective at treating the localized disease in the eye and may save a person's eyesight.

Concerns for pregnant women

If you are pregnant or plan to become pregnant, a CMV test can help you know how careful you must be to prevent CMV infection. If the test is positive, it means you already have CMV and there's little chance that your unborn baby will be harmed by CMV—unless the infection occurred in the few months before your pregnancy. If the test is negative, the best way to protect unborn babies from CMV is by using good hygiene before and during pregnancy.

If your doctor determines that you had a new CMV infection during the pregnancy, this does not mean that your unborn baby is infected. In many cases, you can be infected with CMV without it spreading to the baby. The only way to know is by testing the newborn within the first 3 weeks after birth.

Scientists are looking at other ways to prevent congenital CMV. Currently, there are no treatments for pregnant women whose unborn babies may be infected with CMV. The current drugs used to treat CMV have serious side effects and are not approved for use in pregnant women.

Concerns for children

The main reason for trying to prevent congenital CMV is to prevent the type of disabilities that may occur after birth and during a child's lifetime. Although most babies born with congenital CMV grow up with normal health, others who have symptoms at birth are more likely to have permanent disabilities and symptoms that get worse.

Some symptoms may be present at birth while others appear months or years later. Some symptoms may go away while others may be permanent. These symptoms and disabilities can include hearing and vision loss, mental disability, and liver and spleen problems, among many others. If a newborn is found to have congenital CMV, it is advised to get his or her hearing and vision tested regularly.

A newborn has congenital CMV if the virus can be found in his or her urine, saliva, or blood within the first 3 weeks after birth. Congenital CMV cannot be diagnosed if the baby is tested more than 3 weeks after birth, since she or he could have been infected after birth. Babies infected after birth are not at risk for disabilities.

Your CD4 cell counts

When you get routine blood work done to keep track of your HIV disease, one common lab result includes CD4 cell counts. This count helps measure the health of your immune system.

CD4 cell counts are considered in the "normal" range when they're above 500. When they fall to 350 or below, people are encouraged to consider anti-HIV therapy to prevent further immune damage and to help prevent infections. When this count falls below 50, people living with HIV become more risk for CMV disease.

For more information on keeping track of your immune health, see Project Inform's publications, *Day One*, *Blood Work: Two Common Tests*, *Blood Work: A Useful Tool*, and *Strategies for Improving Your Immune System*.

How can I get the medicines to treat CMV?

The medicines used to treat CMV are available by prescription through a health care provider. Most states also cover these drugs through their ADAPs (AIDS Drug Assistance Programs). To check to see if you're eligible for your state's ADAP and to find out if these therapies are covered by it, contact your state department of public health, your state Office of AIDS, or your state ADAP. Information is also available through the AIDS Treatment Data Network at 1-800-734-7104, or visit *www.atdn.org* and click on "Access Project." People who lack insurance, Medicaid, ADAP coverage and can't otherwise afford the drugs can sometimes gain access to them through the manufacturers' Patient Assistance Programs.

- **Ganciclovir**: 1-800-772-5790, *www.rocheusa.com* (Hoffman LaRoche)
- **Ganciclovir insert**: 1-800-843-1137 (Chiron Vision)
- **Valganciclovir**: 1-800-443-6676, *www.rocheusa.com* (Hoffman LaRoche)
- **Cidofovir**: 1-800-226-2056 (Gilead Sciences)
- **Foscarnet, Foscavir**: 1-800-488-3247 (Astra Pharmaceutical)

What about resistance?

One of the concerns with some of the drugs used to prevent and treat CMV disease is the issue of resistance. CMV can become resistant to the drugs. It then becomes more difficult for the drugs to control CMV disease. As well, resistance to one drug may lead to developing resistance to others. Ganciclovir is one of the drugs that CMV can develop resistance to rather easily, as well as foscarnet and cidofovir.

What research is being done on CMV?

Currently, scientists are working to develop a vaccine and other methods that prevent CMV infection, especially for an unborn baby. There are several in Phase I and II studies, which is early research. The US Institute of Medicine has ranked the development of a CMV vaccine as a highest priority because of the lives it would save and the disabilities it would prevent. Scientists are also working to develop new medicines that may be more effective, cause fewer side effects, can be used in pregnant women, and are not as prone to resistance as the currently approved drugs.

the bottom line

- Most people in the US have CMV infection by the time they turn 40.
- Most of the time CMV infection does not cause disease. Disease usually happens in people with damaged immune systems with CD4+ cell counts below 50.
- Drugs do not clear CMV infection from the body, but they are used to control CMV disease.
- Preventing CMV infection can be difficult because of how common the virus is. The best way to help prevent infection is through changes in personal habits and interactions with others, especially around small children.
- Babies born to pregnant women who get CMV during the pregnancy can have disabilities later in life, especially if the baby has symptoms at birth. Changing your habits around how you interact with others, especially with small children, may help women not infected with CMV who are pregnant or planning to get pregnant to prevent getting the virus and passing it onto the unborn baby.
- There are several ways to prevent CMV disease. The best way is by getting the best care for your HIV and keeping your CD4+ cell count above 200. Regularly seeing a special eye doctor (ophthalmologist) will help catch damage that may occur from CMV disease in the eye.
- CMV retinitis (in the eye) is the most common CMV disease in people living with HIV. CMV disease can occur in different parts of the body at the same time. People who suspect they have symptoms of CMV disease should report them to their doctors as soon as possible.
- There are several drugs used to treat CMV disease. Most can have serious side effects and require short-term changes in lifestyle. Only one, ganciclovir, is used to prevent disease in HIV-positive people with low CD4+ cell counts, although its use may not be desired due to its side effects and possible drug resistance concerns.