

## Herpes and Shingles A Global Problem

In their lifetimes, most human beings will be exposed to a herpesvirus. This family of viruses (Herpesviridae) has been implicated in a wide range of diseases and conditions, including chickenpox, oral or facial herpes, genital herpes, mononucleosis, and corneal blindness. It is also likely that we haven't yet discovered all herpesviruses. One variety was discovered as recently as 1990, and researchers still aren't sure which diseases, if any, it causes in humans.

Herpesviruses are distinguished by their ability to lay dormant, or "hide" in the human body after primary infection. They then reappear during periods of reactivation. Researchers don't really understand the mechanism of reactivation. Although there is no effective cure for herpes, many studies have shown that herpes reactivation is more common among patients who have compromised immune systems, suggesting that a strong immune system is a good defense against herpes reactivation. To manage herpes, physicians try to reduce the number and severity of outbreaks.

Among the most well-known herpesviruses are:

- **Herpes simplex virus 1 (HSV1)**—HSV1 is extremely common, with the vast majority of adults showing evidence of exposure to the virus (eg, antibodies in their blood), even if they are not positive for HSV1 (Kasper DL et al 2004). This form of the virus is most often associated with oral or facial lesions that appear during childhood, although it can also cause genital infection.
- **Herpes simplex virus 2 (HSV2)**—Researchers estimate that about 20 percent of the US population has antibodies to HSV2 (Kasper DL et al 2004). This form of the virus is closely associated with genital herpes. Genital herpes caused by HSV2 is twice as likely to reactivate and recurs 8 to 10 times more frequently than genital infection with HSV1 (Kasper DL et al 2004).
- **Varicella-zoster virus**—This relatively common virus is responsible for chickenpox infections (varicella) and shingles (herpes zoster). The varicella-zoster virus is extremely common. Up to 90 percent of people are attacked by this virus, about half of them between the ages of 5 and 9 years. Almost all of the clinical cases of chickenpox are diagnosed in children and adolescents younger than 14 years. For more information on varicella-zoster virus, see the section in this chapter on Chickenpox and Shingles.

Although infection with herpes is primarily associated with oral, facial, or genital herpes, the herpesvirus can also cause infections in the following ways:

- **Herpetic whitlow**—Infection of the finger.
- **Herpes gladiatorum**—Also known as traumatic herpes. Infection anywhere on the chest, ears, face, and hands. This form of herpes is sometimes associated with wrestling because the rough contact between wrestlers helps spread the virus.
- **Herpes of the eye**—The most common cause of corneal blindness in the United States.
- **Infection of the central or peripheral nervous systems**—The herpesvirus accounts for up to 20 percent of the cases of sporadic viral encephalitis (swelling of the brain due to a virus) in the United States. Herpes can also cause herpetic meningitis.
- **Infection of the internal organs**—This includes herpes infection of the esophagus (HSV esophagitis), the lung (HSV pneumonitis), and the liver.
- **Neonatal herpes**—Neonates (infants younger than 6 weeks) can contract herpes during birth (if their mothers are infected with the virus) or if they are handled by someone who has oral or facial herpes. Neonates are the most likely to have herpes infections that affect the central nervous system or internal organs. Mortality among neonates with untreated herpes is 65 percent (Kasper DL et al 2004).

Genital herpes, which may be the most highly publicized form of the disease, is a widely misunderstood condition. Many people believe that genital herpes is only transmissible during active outbreaks of herpes (when herpes lesions are visible). They may also believe that herpes is relatively rare. In fact, herpes is much more common than many assume. Many people who have antibodies to herpes (they have been exposed to the virus) are not aware they have the disease; they suspect the condition only when they have seen pictures of herpetic lesions (Kasper DL et al 2004). Also contrary to popular belief, herpes is not transmitted only by direct contact with active lesions. It can be transmitted by people who do not have manifestations of the disease but who are shedding the virus or have subclinical symptoms or tiny lesions that are not visible to the naked eye. Studies have shown that HSV2 can be located on the genital tract regardless of the presence of symptoms (Kasper DL et al 2004). Condoms have been shown to reduce the transmission of herpes during periods of nonsymptomatic shedding.

Herpes symptoms depend on the form of the disease. Oral or facial herpes is often accompanied by inflammation of the gums and throat during the initial outbreak. Children who have this condition may have fever, malaise, inability to eat, irritability, and lesions in and around the mouth. Genital herpes is accompanied by similar symptoms, as well as lesions on the genitals. Among newly infected women, the cervix and urethra are usually involved. If the central or peripheral nervous systems are infected, a fever and neurological symptoms are often present during periods of virus activation.

Because herpes sometimes resembles other diseases (especially herpes that affects the skin, mouth, or central nervous system), it can be challenging to correctly diagnose. The most common method used to diagnose herpes is to isolate the virus in a tissue culture or to demonstrate HSV antibodies or DNA in scrapings from active lesions.

## ANTIVIRAL DRUGS

Conventional treatment of herpes relies on antiviral drugs that have been shown to reduce the severity of outbreaks and, in some cases, reduce the likelihood of transmission. These drugs include:

- **Acyclovir**—Acyclovir interferes with the virus' ability to replicate (Kasper DL et al 2004). Common side effects include nausea, vomiting, headache, diarrhea, dizziness, fatigue, anorexia, edema, and sore throat (Sra KK et al 2004).
- **Valacyclovir**—Valacyclovir is the salt version of acyclovir; it becomes acyclovir after being metabolized by the liver. Valacyclovir has a bioavailability three to five times greater than oral acyclovir. Common side effects, such as nausea, vomiting, headache, dizziness, and abdominal pain, are similar to those of acyclovir (Sra et al 2004).
- **Famciclovir**—Famciclovir is a precursor to the antiviral drug penciclovir. Penciclovir works in a similar manner to acyclovir. Side effects are the same as those for acyclovir and valacyclovir.

These antiviral drugs may be given intravenously or orally, depending on the severity of the outbreak and the location. They are effective in treating both herpes and shingles. In addition to these antiviral drugs, a number of topical medications are used in the treatment of herpes infections of the eye. These include trifluridine, vidarabine, idoxuridine, acyclovir, penciclovir, and interferon.

In recent years, clinicians have discovered strains of herpes that are resistant to acyclovir. Because the drugs are closely related, acyclovir-resistant strains of herpes are also cross-resistant to valacyclovir and famciclovir. These strains are most often detected in patients who have weakened immune systems, such as those with HIV or AIDS (Kasper DL et al 2004). In these cases, treatment with a very powerful antiviral called foscarnet, which must be administered with an intravenous (IV) pump, is sometimes effective. Foscarnet can cause severe adverse effects, including kidney disorders.

## *Herpes Vaccines on the Horizon*

Although it is possible to lower the risk of contracting herpes through the use of condoms and antiviral drugs, the ultimate prevention goal is a herpes vaccine that would inoculate the population against the virus.

While there is no herpes vaccine yet, researchers have made significant progress in developing one. Recently, an investigational vaccine has resulted in a significant reduction in genital herpes in women who had never been exposed to the virus (Tyler I 2005). For reasons that are not known, this particular vaccine did not protect men (Jones CA et al 2003).

While it appears that effective herpes vaccines are on the horizon, there are still significant research questions to answer, such as who should be vaccinated and when, and whether or not a vaccination that suppresses symptoms prevents transmission of the virus to other people (Stanberry LR 2004).

## CHICKENPOX AND SHINGLES

Chickenpox and shingles are both caused by the varicella-zoster virus, and infection is strongly reminiscent of infection with either HSV1 or HSV2. However, unlike HSV1 or HSV2, the virus is often transmitted through the respiratory tract.

Chickenpox is an extremely common and highly contagious childhood disease. It is usually benign, with an incubation period of up to 21 days after initial infection, and a disease course of 14 to 17 days. During the time the varicella-zoster virus is most active, the patient has characteristic skin lesions. The lesions cause intense itching, and there is a risk that the lesions will become infected due to scratching. The severity of the disease and the number of lesions varies from person to person. Adults with the disease who have weakened immune systems might run a fever. In fact, chickenpox in adults is considerably more dangerous than the benign childhood variety. Adults are more likely to have symptoms such as headache and pain as a result of chickenpox. A form of pneumonia (varicella pneumonia) is seen in about 20 percent of adults who contract chickenpox (Kasper DL et al 2004). The virus can also cause brain inflammation.

In the future, chickenpox will likely become less of a health issue. Since 1995, children in large numbers across the United States

have been vaccinated against the varicella-zoster virus. The results of this vaccination program have been dramatic: hospitalizations have declined by 88 percent and direct medical expenditures by 74 percent (Zhou F et al 2005). These benefits were seen across all age groups.

However, researchers still don't know the impact of the chickenpox vaccine on shingles. Shingles occurs when the varicella-zoster virus reactivates, usually in adulthood, and is characterized by a painful skin rash. Reactivation occurs in about 15 percent of people who have had chickenpox, and most often occurs in people aged 60 to 69, although it can occur in any age group.

Some researchers have hypothesized that vaccination in childhood would actually make an adult more susceptible to shingles later in life. However, this has yet to be proven in clinical studies (Jumaan AO et al 2005). In the meantime, vaccination against herpes zoster in adults has been shown to reduce the incidence of shingles (Oxman MN et al 2005).

Shingles is nine times more likely to develop in those infected with HIV. In the early stages of HIV infection, shingles symptoms are fairly typical (Wilkerson MG et al 1987). In more advanced infection, herpes zoster may take the form of repeated episodes of severe, prolonged, and sometimes atypical disease (such as varicella-zoster virus retinitis). Shingles is also more common in immunocompromised children and adults (including organ recipients and chemotherapy patients). It is important to treat these patients early and aggressively with antiviral drugs.

Like chickenpox, shingles is characterized by skin lesions. The lesions may be accompanied by severe, sometimes debilitating pain. An outbreak of shingles usually lasts between 7 and 10 days. It can take up to 2 weeks for the skin to appear and feel normal. Herpes zoster can also infect the nerves in the eye. This serious condition can result in blindness if not treated with antiviral therapy (Cunningham AL et al 2000; Liesegang TJ 1984; Liesegang TJ 2004; Ostler HB 1976; Schmader K 2001; Weinhoff ML 1976).

Pain associated with shingles that persists more than 3 months after other symptoms subside is known as postherpetic neuralgia. The characteristics of postherpetic neuralgia are spontaneous aching and burning, intermittent shooting pains, and extreme sensitivity (Johnson RW 2003). Postherpetic neuralgia is more common in older people. However, at least 50 percent of patients older than age 50 who had shingles report some degree of pain months after the resolution of the skin rashes (Kasper DL et al 2004). Several drug classes are used to treat postherpetic neuralgia, including tricyclic antidepressants (Baldessarini RJ 2001) and painkillers such as acetaminophen, glucocorticoids, and lidocaine.

### ***The Herpes Family of Viruses***

The herpes family also includes the following viruses:

- **Cytomegalovirus (CMV)**—Initial infection with CMV usually occurs during childhood and adolescence, but typically goes undetected. In healthy adults, the primary infection is usually mild and may present as fever, muscle pain, fatigue, and elevated liver enzymes. CMV may be dangerous in people who have weakened immune systems, such as organ transplant recipients and people with HIV/AIDS. The virus is spread from person to person through direct contact, sexual intercourse, or blood transfusions. CMV is excreted in saliva, urine, semen, cervical secretions, and feces (Crumpacker CS 2000).
- **Human herpesvirus 6 (HHV6)**—Human herpesvirus 6 is the primary cause of roseola infantum, a common childhood disease that is characterized by high fever and a red, raised rash on the neck and trunk (Straus SE 2000). Among older adults, it can also cause a mononucleosis-like syndrome. HHV6 can be found in secretions of healthy people (Straus SE 2000).
- **Human herpesvirus 7 (HHV7)**—HHV7 was discovered in 1990. Although no diseases have been conclusively linked to HHV7, it might be associated with pityriasis rosea, a benign skin condition characterized by scaly, pink, or dry raised capsules. Like HHV6, HHV7 can also be found in secretions of healthy individuals (Straus SE 2000a).
- **Human herpesvirus 8 (HHV8)**—HHV8 is associated with Kaposi's sarcoma (Schulz TF et al 1999; Straus SE 2000b). Latent HHV8 may target tumor suppressor pathways, leading to cell proliferation and tumor formation in people who have immune systems weakened by diseases such as HIV (Mesri EA et al 1996; Moore PS 2000; Sarid R et al 1999).
- **Epstein-Barr virus (EBV)**—EBV is the most common cause of infectious mononucleosis, which is characterized by fever, sore throat, and swollen lymph nodes. Complete recovery may take months (Niedobitek G et al 1997). Infection is common, with about 95 percent of the population having antibodies against the virus by age 30. Transmission of EBV is through exchange of saliva containing the virus.

## **HERPES AND THE IMMUNE SYSTEM**

It appears that herpes-specific T-cell immunity might be related to reactivation. Animal studies have shown that ultraviolet light, a weakened immune system, and trauma all contribute to reactivation of the virus (Kasper DL et al 2004). At this time, there are no drugs or agents that can cause a latent virus to stay hidden forever. The number and frequency of reactivation events depends on the site and on the nutrition and immune status of the host (Isada CM et al 2003; Murray PR et al 2002).

The Life Extension Foundation's approach to herpes management is based on the premise that a strong immune system can help reduce viral reactivation. People who have herpes can benefit from a nutritional regimen of supplements that studies suggest may fight the virus directly, as well as support a healthy immune system.

### ***What You Have Learned So Far...***

- The herpes family includes several related viruses, including HSV1, HSV2, and varicella-zoster virus. These viruses are extremely common, with the majority of the US population showing antibodies to viruses in the herpes family.
- The herpesviruses are distinguished by their ability to go into clinical dormancy, or a period in which they hide in the body before becoming reactivated. Herpes outbreaks are often characterized by skin lesions and fever, along with other symptoms.
- The varicella-zoster virus is responsible for chickenpox in children. After the initial outbreak, the virus can enter a long period of latency and reappear in the sixth decade of life as shingles.
- Both HSV1 and HSV2 can cause oral or facial lesions or genital disease. The herpesvirus can also infect the central nervous system, internal organs, and eyes. Neonatal herpes is usually passed from infected mothers to children during birth.
- Contrary to popular belief, genital herpes can be transmitted even when active lesions are not visible and symptoms are not present. People with the disease can shed the virus or may have lesions that are not readily visible.
- Conventional treatment for herpes relies on antiviral drugs that have powerful side effects. These drugs can help lessen the severity of outbreaks.
- Reactivation is associated with a weakened immune system, so patients with herpes might consider an immune-boosting nutritional program to strengthen their immune systems. Many supplements have been proven to fight herpes by boosting the immune system or by interfering with the virus's ability to penetrate cell walls.

## **ANTIOXIDANT DEFENSES**

Although there is no cure for herpesvirus infection, various supplements have shown the ability to reduce the severity and even the frequency of outbreaks. This might be due to their ability to support a healthy immune system (a weakened immune system has been associated with herpes reactivation).

Antioxidants are particularly important immune-boosting supplements. Multiple clinical studies support the theory that antioxidants are of benefit in the management of herpesviruses (Bhaskaram P 2001; Elmadfa I et al 1994; Grimble RF 1997; Sheridan J et al 1997).

### ***Vitamin A and beta-carotene***

Vitamin A plays a role in protecting the skin and mucous membranes from invasion of microorganisms. In 178 HIV-positive women with genital herpes, who were neither pregnant nor taking oral contraceptives, vitamin A levels were closely associated with cervical HSV shedding. Increased shedding was associated with decreased vitamin A (Mostad SB et al 2000).

Experimental studies have documented vitamin A's effectiveness against other herpesviruses. The strong antiproliferative activity exerted by retinoids (vitamin A derivatives) indicates these compounds may be useful tools in the management of EBV-related disorders in immunosuppressed patients (Pomponi F et al 1996).

Beta-carotene is the major precursor of vitamin A (Meisenberg G et al 1998). Studies show that long-term beta-carotene supplementation may be beneficial for immune, viral, and tumoral surveillance in aging individuals. In a controlled, double-blind study, the effects of 10 to 12 years of beta-carotene supplementation on natural killer (NK) cell activity were evaluated. Although no significant difference was seen in NK cell activity in the middle-aged groups, elderly men who took supplements of beta-carotene had significantly greater NK cell activity than the control group receiving placebo (Santos MS et al 1996).

## ***Vitamins C and E***

Vitamin C (ascorbic acid) is important in maintaining immune status. Vitamin C can strengthen white blood cell function and boost interferon levels. It is a free radical scavenger (Li W et al 2001) and protects tissues from oxidative stress and enhances the actions of vitamin E (De Souza MC et al 2000).

In one clinical trial, a water-soluble bioflavonoid/ascorbic acid complex (600 to 1000 milligrams [mg] of bioflavonoids and 600 to 1000 mg of ascorbic acid taken three to five times daily) was shown to be effective in the reduction of recurrent HSV1, reducing blisters and preventing disruption of vesicular membranes. Remission of symptoms was observed in 4 days (Terezhalmay GT et al 1978).

In another randomized, double-blind, placebo-controlled study on the topical treatment of recurrent mucocutaneous herpes, a pharmaceutical ascorbic acid formulation with antimicrobial properties (Ascoxal®) demonstrated the antiviral effects of vitamin C. A cotton pad soaked in the Ascoxal® solution was firmly pressed on the lesion for 2 minutes three times (with 30-minute intervals in between) for one day only. The treatment resulted in markedly reduced symptoms and fewer days of scab formation (Hovi T et al 1995).

High levels of vitamin C can protect levels of vitamin E in tissue and may contribute to the immune-enhancement of vitamin E (Chan AC 1993).

Vitamin E is a powerful antioxidant and free radical scavenger. A highly publicized study of vitamin E to boost immune function appeared in 1997 (Meydani M et al 1997). The double-blind, placebo-controlled study looked at healthy humans older than 65 years. Supplementation with vitamin E for 4 months improved clinically relevant indices of cell-mediated immunity.

## ***Zinc and selenium***

Zinc plays many roles in basic cellular function, including DNA replication, RNA transcription, cell division, and cell activation. Zinc is a specific activator of T-cells, T-cell division, and other immune cells. Zinc also functions as an antioxidant and stabilizes membranes against the oxidative effect of other minerals, such as iron and copper, by increasing the levels of catalase, superoxide dismutase, and glutathione-S-transferase. Zinc-deficient patients display reduced resistance to infection (Cuevas LE et al. 2005).

In a double-blind, placebo-controlled, randomized clinical trial that evaluated the effect of a zinc oxide/glycine cream on facial herpes in 46 patients, treatment reduced or shortened the duration of cold sore lesions (5 days) compared to placebo (6.5 days) when applied within 24 hours of onset of symptoms. The cream also reduced the severity of symptoms, particularly blistering, soreness, itching, and tingling (Godfrey HR et al 2001).

Selenium (an antioxidant with immune system–boosting properties) may help suppress the reactivation of herpesviruses by increasing immunity. A number of studies have shown that the combination of zinc and selenium enhances immunity in the elderly. A pioneering study published in *Lancet* (Chandra RK 1992) found that seniors taking modest doses of a multivitamin/multimineral supplement containing zinc and selenium showed a general reduction in infection and required antibiotics for significantly fewer days annually.

A more recent study brings the effect of zinc and selenium into sharper focus. This well-designed, randomized, placebo-controlled, double-blind study found that seniors taking these two minerals had significantly fewer infections over a 2-year period, but that vitamin supplementation alone did not have a major effect (Girodon F et al 1997). The zinc and selenium supplement cut the number of infections by nearly two-thirds, compared to placebo.

## ***Cimetidine: A Novel Approach***

Cimetidine (Tagamet®), an over-the-counter drug, helps reduce the severity of herpes outbreaks (especially in patients with shingles), as well as reduces the amount of time of active infection. It works by temporarily inhibiting T-suppressor cells. T-suppressor cells down-regulate the immune system after the pathogen has been destroyed. Because of the inhibitory effect on T-suppressor function, cimetidine therapy is contraindicated in patients who have had organ transplants or who have autoimmune disorders (Kumar A 1990).

The following studies appear to demonstrate the effectiveness of cimetidine against herpes:

- A combined *in vitro/in vivo* study evaluated the effect of cimetidine on herpes zoster. Treatment with cimetidine shortened the median time to initial pain reduction and to complete resolution of pain. It also promoted more rapid healing of skin lesions than did symptomatic treatment (Miller A et al 1989).
- In 221 patients with shingles who were given 200 mg of cimetidine three times during the day and 400 mg at night, disease

duration was reduced. It was suggested that use of cimetidine should begin even during the prodromal period, the time when the appearance of early symptoms may mark the onset of the condition (Kapinska-Mrowiecka M et al 1996).

- Patients with herpes labialis (oral lesions) and herpes keratitis (a herpes infection of the eye) showed a shortened duration and frequency of infection after treatment with cimetidine (van der Spuy S et al 1980).
- A case report in Canada appeared to show that cimetidine therapy reduced the expected length of the active phase of herpes zoster from 35 days to just 10 days (Hayne ST et al 1983).
- A paper presented at Michigan State University concluded that patients with herpes zoster who were given cimetidine exhibited enhanced immunity (Kumar A 1990).

Cimetidine is sold over the counter. Refer to the package insert for possible drug interactions.

### ***L-lysine: Active against Herpes***

L-lysine, an essential amino acid, has been studied for its ability to reduce the reactivation rate of herpes (Flodin NW 1997; Marcason W 2003). It works by inhibiting the action of L-arginine during viral replication. Proteins within herpes are rich in L-arginine. An altered ratio of L-lysine to L-arginine, in favor of L-lysine, has been studied for its ability to inhibit the virus. While the results of some studies have been mixed, the following studies have shown L-lysine's ability to inhibit herpes:

- In a double-blind, multi-centered, placebo-controlled study evaluating L-lysine for the prevention and treatment of recurrent herpes infection, one group received 1000 mg of L-lysine three times daily for 6 months. This group had significantly fewer outbreaks, less severe symptoms, and more rapid healing. The researchers said that L-lysine was an effective agent for reducing the occurrence, severity, and symptoms of herpes (Griffith RS et al 1987).
- In a second prospective, randomized, double-blind, placebo-controlled, cross-over study, oral intake of L-lysine (1248 mg daily) decreased the recurrence of herpes simplex in people with healthy immunity. A dose of 624 mg per day was not effective. L-lysine may also decrease the severity of symptoms associated with recurrences. Neither dosage shortened healing time (McCune MA et al 1984).
- In a double-blind clinical study examining the long-term prophylactic efficacy of L-lysine supplementation for herpes labialis, volunteers who had a history of frequent outbreaks were recruited. The treatment group received daily oral supplements of 1000 mg of L-lysine. The L-lysine treatment group had significantly fewer outbreaks than the control group. Volunteers who were taken off L-lysine generally showed a significant increase in the recurrence of lesions. Data revealed fewer lesions when a person's serum L-lysine concentration exceeded 165 nanomoles per milliliter (nmol/mL) and increased significantly as concentration levels fell below 165 nmol/mL. These results suggest that prophylactic L-lysine may be useful in managing selected cases of recurrent herpes labialis (Thein DJ et al 1984).

Foods rich in L-lysine include legumes, eggs, yogurt, fish, and chicken (Balch PA et al 2000; Jamison JR 2004). Taking L-lysine with vitamin C and bioflavonoids together has been shown to reduce the risk of herpetic outbreaks (Balch PA et al 2000).

### ***Propolis***

Propolis, a natural product from bees, is comprised of a complex of antiviral chemicals (especially flavonoids).

In one study, extract of propolis was tested against the herpesvirus both in vitro and in experimental animals. In the in vitro study, propolis caused a 50 percent reduction in herpes infection. Administration of propolis before or at the time of infection yielded the most significant results. However, even when the propolis was added 2 hours after infection, it still yielded 80 percent to 85 percent protection. In the animal portion of the study, a weak propolis solution prevented the appearance of herpes symptoms in rats and corneal herpes in rabbits (Huleihel M et al 2002).

In a multi-centered randomized study, 90 men and women with recurrent genital HSV2 were divided into two groups to compare the healing ability of propolis ointment with natural flavonoids versus acyclovir ointment and placebo. Ointments were applied four times a day for 10 days. At day 10, 80 percent of patients in the propolis group had healed. Forty-seven percent had healed in the acyclovir group, and 40 percent had healed in the placebo group. Investigators concluded that an ointment containing flavonoids was more effective in healing genital herpetic lesions and in reducing local symptoms than ointments containing either acyclovir or placebo (Vynograd N et al 2000).

### ***Thymus Extract***

Extracts of thymus have immune system-enhancing and restorative properties (Corey L 2000). In a randomized, placebo-controlled study, immunodeficient patients with recurrent HSV1 cold sores who were given bovine thymus extract (Thymostimulin) for 6 months had only 17 recurrences versus 62 in the control group. A significant increase in total white blood cells, lymphocyte count, and T-cell numbers was detected. Thymus extract may be useful in reducing the risk of viral reactivation in people who have weakened immune systems (Aiuti F et al 1984).

## **Lactoferrin**

Numerous studies have shown that lactoferrin, a whey protein found in human milk, and an antimicrobial, has powerful antiherpetic properties. Lactoferrin works by reducing the ability of HSV1 and HSV2 to penetrate cell walls (Andersen JH et al 2004). Studies have shown that:

- Lactoferrin reduced the appearance of skin lesions in mice infected with herpes (Wakabayashi H et al 2004).
- Lactoferrin works synergistically with acyclovir (Andersen JH et al 2003).
- Lactoferrin was able to lower the risk of infection in the eye among mice infected with herpes (Fujihara T et al 1995).

## **Dehydroepiandrosterone (DHEA)**

Reactivation of herpes and shingles has been associated with a weakened immune system. Among older people, who are more likely to get shingles, a reduced immune response might be caused by age-related changes in steroid hormones (Valenti G 2004a,b).

DHEA, a steroid hormone, is known to decline as people age. In a 1997 study (Khorram O et al 1997), scientists proposed that the oral administration of DHEA among elderly men would result in activation of their immune systems. Nine healthy men with an average age of 63 years were treated with a placebo for 2 weeks, followed by 20 weeks of DHEA (50 mg a day). After 2 weeks on oral DHEA, serum DHEA levels increased 3- to 4-fold. These levels were sustained throughout the study. Compared to placebo, DHEA administration resulted in:

- An increase of 20 percent in insulin-like growth factor (IGF)-I. IGF-I is thought to be responsible for some of the anti-aging, anabolic effects that DHEA has produced in previous human studies.
- An increase of 35 percent in the number of monocyte immune cells.
- An increase of 29 percent in the number of B-cells and a 62 percent increase in B-cell activity.
- A 40 percent increase in T-cell activity even though the total numbers of T-cells was not affected.
- An increase of 50 percent in interleukin-2 (IL-2).
- An increase of 22 percent to 37 percent in the number of NK cells and an increase of 45 percent in NK cell activity.
- No adverse effects were noted with DHEA administration (however, this was a short study with few subjects).

DHEA has been shown in numerous human and animal studies to boost immune function via several different mechanisms (Danenberg HD et al 1995; Loria RM et al 1996; Solerte SB et al 1999). A study in the Proceedings of the Society for Experimental Biology and Medicine demonstrated that, when older female mice were treated with DHEA, several markers of immune function improved (Inserra P et al 1998).

## **Garlic**

Garlic (*Allium sativum*) has substantial antiviral activity. Fresh garlic extract, in which thiosulfates are the active components, was virucidal against every virus tested, including HSV1 and HSV2. The predominant thiosulfate in fresh garlic extract is allicin (Weber ND et al 1992).

## **LIFE EXTENSION FOUNDATION RECOMMENDATIONS**

Once herpes is contracted (the primary infection), the infected person (host) will carry the virus for life. The goal of herpes management is to support a healthy immune system with nutrients that have been shown to reduce the severity and possibly even frequency of reactivation episodes. In addition, patients with herpes should avoid excessive consumption of foods that are rich in L-arginine, such as chocolate and nuts. This will enhance the effectiveness of L-lysine by altering the balance in favor of L-lysine.

The Life Extension Foundation offers specially compounded nutrient mixes, such as Life Extension Mix, which supply everything you need to support healthy immune function. Alternatively, you may choose to take individual supplements to help treat herpes and improve immune function. As always, it's best to launch a program of dietary supplementation under the supervision of a qualified physician. The Life Extension Foundation suggests:

- **Life Extension Mix**—Follow label directions.
- **Cimetidine** (Tagamet®)—200 mg three times daily and 400 mg at bedtime (800 mg at bedtime if you cannot take cimetidine throughout the day)
- **Vitamin A**—20,000 international units (IU) daily during outbreaks; 2500 to 5000 IU for maintenance
- **Beta-carotene**—25,000 IU daily for 7 to 10 days during outbreaks

- **Vitamin C** (ascorbic acid)—5 to 10 grams (g) of esterified or buffered vitamin C during outbreaks
- **Vitamin E**—400 IU of alpha-tocopherol or 359 mg of mixed tocopherols including gamma, delta, alpha, and beta tocopherols
- **Zinc**—30 mg daily
- **Lactoferrin**—300 to 900 mg daily during an outbreak; 300 mg daily for maintenance
- **Selenium**—200 micrograms (mcg) daily
- **L-lysine**—700 to 1400 mg daily to suppress outbreaks
- **Propolis**—500 to 2000 mg daily during outbreaks
- **Thymus extract**—2 capsules daily of Thymic Immune Factors
- **Garlic extract**—1200 mg of Kyolic garlic twice daily during outbreaks; 1000 mg for maintenance
- **DHEA**—100 to 200 mg daily if an outbreak appears imminent and during outbreaks until lesions disappear (blood testing is recommended after DHEA therapy to ensure adequate levels)

## HERPES AND SHINGLES SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

### Beta-Carotene

- Do not take beta-carotene if you smoke. Daily intake of 20 milligrams or more has been associated with a higher incidence of lung cancer in smokers.
- Taking 30 milligrams or more daily for prolonged periods can cause carotenoderma, a yellowish skin discoloration (carotenoderma can be distinguished from jaundice because the whites of the eyes are not discolored in carotenoderma).

### DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

### Garlic

- Garlic has blood-thinning, anticlotting properties.
- Discontinue using garlic before any surgical procedure.
- Garlic can cause headache, muscle pain, fatigue, vertigo, watery eyes, asthma, and gastrointestinal symptoms such as nausea and diarrhea.
- Ingesting large amounts of garlic can cause bad breath and body odor.

### L-Lysine

- Do not take L-lysine if you have hyperlysinuria or the rare genetic disorder hyperlysinemia.
- Consult your doctor before taking L-lysine if you have kidney failure or liver failure.

### Selenium

- High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
- High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
- Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

### Vitamin A

- Do not take vitamin A if you have hypervitaminosis A.
- Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, etretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
- Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial

hypertension), elevated serum liver enzymes, reversible noncirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

## Vitamin C

- Do not take vitamin C if you have a history of kidney stones or of kidney insufficiency (defined as having a serum creatine level greater than 2 milligrams per deciliter and/or a creatinine clearance less than 30 milliliters per minute).
- Consult your doctor before taking large amounts of vitamin C if you have hemochromatosis, thalassemia, sideroblastic anemia, sickle cell anemia, or erythrocyte glucose-6-phosphate dehydrogenase (G6PD) deficiency. You can experience iron overload if you have one of these conditions and use large amounts of vitamin C.

## Vitamin E

- Consult your doctor before taking vitamin E if you take warfarin (Coumadin).
- Consult your doctor before taking high doses of vitamin E if you have a vitamin K deficiency or a history of liver failure.
- Consult your doctor before taking vitamin E if you have a history of any bleeding disorder such as peptic ulcers, hemorrhagic stroke, or hemophilia.
- Discontinue using vitamin E 1 month before any surgical procedure.

## Zinc

- High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
- Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
- High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
- High doses of zinc may suppress the immune system.

For more information see the Safety Appendix

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