

## Meningitis

Meningitis is inflammation of the tissue covering the brain and spinal cord (the meninges). Reports of the illness date to the 16th century, and the disease was first accurately described in 1805 (Rosenstein NE et al 2001). Meningitis is characterized by swelling of the meninges; increased pressure inside the skull blocks the flow of blood to the brain, starving the brain of nutrients and oxygen. Encephalitis, which is actual inflammation of the brain, can occur along with meningitis.

People with meningitis usually have fever, severe headache, and stiff neck and neck pain. Almost any type of movement can cause the neck pain, and it may even be impossible to lower the chin to the chest. Seizures are associated with the acute forms of the disease. In severe cases, meningitis can be fatal.

Other symptoms include nausea and vomiting, dizziness, sensitivity to light, rashes, and weakness. Babies and older adults may not experience stiff neck. However, babies may lose their appetite, have a shrill cry, and be difficult to soothe, or conversely they may be extremely sleepy or lethargic.

Symptoms such as tiredness and lightheadedness can last for several months after recovery from the acute form of the disease. Resulting problems range from headaches, nausea, loss of balance, and stiff neck to brain damage and hearing loss. Long-term complications include brain damage, hearing loss, vision problems, and persistent seizures.

### **Warning!**

If meningitis is even remotely suspected, seek immediate medical assistance.

Bacterial meningitis is not a disease to be taken lightly. It is a degenerative, rapidly progressing disease that can result in death or permanent disability. If bacterial meningitis is suspected, patients are urged to go to a doctor (go to a hospital emergency department if necessary) for appropriate testing and prompt intravenous antibiotic treatment. Patients with suspected meningitis should get medical care as quickly as possible.

### **Diagnosing Meningitis: The Spinal Tap**

If a patient has symptoms of meningitis, his or her physician may order a lumbar puncture, commonly called a spinal tap.

During a spinal tap, a needle is placed in the lumbar (lower) portion of the spinal canal and a small sample of cerebrospinal fluid (CSF) is removed. After the CSF is removed, it is cultured (the sample of CSF is incubated for a few days under conditions that promote the growth of microorganisms). If bacteria grow in the fluid, the type of bacteria causing the meningitis can be determined, and the most effective antibiotic can be prescribed.

Because viral meningitis is caused by a virus and not a bacterium, there will be no growth in the culture medium. This is why viral meningitis is also sometimes called aseptic meningitis.

Other tests (other than a culture of the CSF) can give results in minutes to hours.

## CAUSES

Meningitis is usually caused by infection from a bacterium or virus that has penetrated the nervous system. Most cases of meningitis are caused by bacterial or viral infection, although meningitis can also be caused by other conditions, such as allergic reactions to drugs, fungi, or parasites.

Viral meningitis is responsible for most cases of meningitis and is also usually (although not always) less severe than bacterial meningitis.

Bacterial meningitis is a serious disease that can cause death or permanent brain damage if not treated by a physician immediately. Acute bacterial meningitis is most common in children aged 1 month to 2 years. However, localized outbreaks can occur in self-contained groups living in close quarters, such as college students living in dorms or people living in military barracks. Elderly people and those who have compromised immune systems (such as patients with HIV/AIDS) are also at risk.

Although the mortality from bacterial meningitis has dropped in recent years, the Centers for Disease Control and Prevention (CDC) reports that 10 percent to 14 percent of people who have bacterial meningitis die, and 11 percent to 15 percent of people who recover are disabled (CDC 2005 [meningococcal disease]).

## TREATMENT AND PREVENTION

If bacteria are the cause, the meningitis will be treated with intravenous antibiotics. If the patient is very sick and bacterial meningitis is suspected (but not yet proven with a culture), antibiotics are generally started before the specific bacteria are identified. In most cases, two or more antibiotics will be prescribed to kill the bacteria. Treatment may also include analgesics to relieve fever and pain, corticosteroids to decrease inflammation, and fluids to maintain electrolytes and prevent dehydration.

In recent years, anti-inflammatories for the treatment of bacterial meningitis have attracted significant research attention. Although this form of the disease is caused by bacteria, the majority of the damage resulting from meningitis is associated with an inflammation cascade that is touched off by an immune system response.

Antibiotics are used to treat only bacterial infections, therefore they are ineffective in treating viral meningitis (also, overuse of antibiotics leads to drug resistance). People usually recover from viral meningitis in a couple of weeks. Treatment includes analgesics for the pain and fever, rest, and fluids to prevent dehydration. There are 25,000 to 50,000 hospitalizations in the United States from viral meningitis each year (CDC 2005 [viral meningitis]).

In recent years, researchers have made a number of advances against meningitis, ranging from the introduction of vaccines that target the pathogens that cause meningitis to a deeper understanding of how inflammation is crucial to the disease course. During meningitis, the immune system is activated to produce a host of pro-inflammatory chemicals, including tumor necrosis factor-alpha (TNF-alpha) and various interleukins (Pathan N et al 2003). This immune-modulated inflammation causes much of the damage associated with meningitis. In the future, anti-inflammatories are expected to play a major role in conventional meningitis therapy (Pathan N et al 2003).

Because meningitis is contagious, people should practice good hygiene (wash hands frequently and thoroughly). The organisms are spread by breathing them in; they are rarely contracted by touching contaminated surfaces.

See a doctor if you have been exposed to someone with meningitis. Close contact with a person who has bacterial meningitis is enough to warrant prophylactic (preventive) antibiotic therapy.

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

- Meningitis is an inflammation of the tissue lining of the brain and spinal cord, and is usually caused by bacteria or viruses. Viral meningitis is more common, and generally less severe, than bacterial meningitis.
- The major symptoms of meningitis are severe headache, neck pain, and fever.
- Bacterial meningitis is a severe problem that requires immediate medical assistance and intravenous antibiotic treatment. If untreated or not treated promptly, bacterial meningitis can lead to death or brain damage.
- Viral meningitis has no specific treatment, but people usually recover at home with analgesics, rest, and fluids.
- Anyone who suspects that they or someone they know (especially a child) has meningitis should see a doctor or go to an emergency department immediately.
- The inflammation associated with meningitis is caused by a widespread immune response to the invading bacteria or virus. Thus, it is likely that anti-inflammatory strategies may play a significant role in future therapy.

## BACTERIAL MENINGITIS

Many people who carry bacteria associated with meningitis will never develop the disease. In some people, however, for reasons that are not fully understood, the bacteria will migrate through the body's outer immune defenses (for example, through nasal passages) and into the bloodstream (Pathan N et al 2003).

Acute bacterial meningitis is dangerous and needs to be diagnosed and treated with antibiotics as quickly as possible. In the past, it was fatal in more than 50 percent of the cases. However, with better and earlier treatment, fatality has dropped to 10 percent to 14 percent. Nevertheless, about 15 percent of survivors have long-term disabilities, including hearing loss and brain damage (CDC 2005 [meningococcal disease]). If acute bacterial meningitis is suspected, the person should see a physician and receive treatment immediately.

The most common strains of bacteria that cause meningitis are *Streptococcus pneumoniae* (in about 50 percent of bacterial cases),

*Neisseria meningitidis* (in about 25 percent of bacterial cases—and in up to 60 percent in cases that involve children), and *Listeria monocytogenes* (in about 10 percent of bacterial cases—almost exclusively in newborns and the elderly) (Kasper DL et al 2004).

In recent years, the causes of bacterial meningitis have changed because of vaccines that targeted *Haemophilus influenzae* and, to a lesser extent, a newer *N. meningitidis* vaccine that was approved in January 2005 (Bilukha OO et al 2005). Previously, these two bacteria were responsible for most bacterial meningitis infections. *H. influenzae* type b used to be the most common cause of meningitis in infants, but since the *Haemophilus influenzae* Serotype b (Hib) vaccine was introduced in 1985 the number of children in the United States who get meningitis from this organism has decreased by 95 percent (Beers MH et al 2005; CDC 2005 [Hib]). Today, *S. pneumoniae* accounts for about half of all bacterial cases.

Symptoms classically associated with bacterial meningitis include fever, headache, and stiff neck. In more than 75 percent of cases, changes in mental status occur, ranging from lethargy to coma, although some patients may become agitated and even combative. Nausea, vomiting, and sensitivity to light are also common symptoms. Seizures occur in up to 40 percent of patients.

There are several classes of drugs used to treat bacterial meningitis, including antibiotics, inflammation suppressors, and pain relievers. Antibiotics are used to kill the organism causing the infection. The other treatments are used to manage symptoms associated with the disease. If seizures occur, antiseizure drugs (such as phenobarbital and phenytoin) may be administered. When patients have trouble breathing, they may be administered oxygen, or they may require assisted ventilation.

In the future, anti-inflammatory medications are expected to play a larger role in meningitis therapy (Pathan N et al 2002). The inflammatory reaction associated with meningitis is at least partly modulated by proteins in the brain called tyrosine kinases (Angstwurm K et al 2004; Sokolova O et al 2004). They are involved in the inflammatory reactions in the brain and in the movement of bacteria across the blood-brain barrier. Inhibitors of tyrosine kinases, including supplements such as genistein, may decrease the severity of inflammation and the ability of bacteria to cross the blood-brain barrier, which could possibly prevent infection and limit damage (Sokolova O et al 2004).

## **VIRAL MENINGITIS**

Viral meningitis is the most common form of the disease (Romero JR et al 2003). About 90 percent of cases (in which the virus has been identified) are caused by enteroviruses, mostly coxsackieviruses and echoviruses (CDC 2005 [viral meningitis]).

Until recently it was difficult to identify which virus was causing viral meningitis, and, once bacteria were ruled out, further tests were not commonly done. However, because of the concern in recent years about West Nile Virus (which can also cause meningitis); more tests using the polymerase chain reaction technique have been performed to identify the viruses. The Epstein-Barr virus has also been found in the CSF of patients with meningitis (Volpi A 2004). The viruses that cause measles, mumps, and chickenpox can also cause meningitis. Vaccines against these diseases may be partly responsible for the decrease in viral meningitis in children (Beghi E et al 1984).

Mollaret's meningitis is a rare, recurrent viral meningitis that is painful but not generally life-threatening. The herpes simplex viruses, HSV1 and HSV2, have been associated with Mollaret's meningitis (Schmutzhard E 2001).

Viral meningitis is generally treated with analgesics, bed rest, and fluids. Acyclovir or valacyclovir, drugs used to treat herpes, may be useful for treating patients with Mollaret's meningitis (Schmutzhard E 2001).

As with bacterial meningitis, the inflammatory cascade is an important contributor to the damage caused by viral meningitis, and anti-inflammatory therapy will probably develop into an important part of therapy in the near future (Pathan N et al 2003).

## **OTHER TYPES OF MENINGITIS**

Meningitis can also occur after certain medical procedures, such as catheter-based intervention for cerebral aneurysm (Meyers PM et al 2004). Chemical meningitis can occur as a result of drug use. In these nonbacterial or viral conditions, the disease is characterized chiefly by inflammation, making anti-inflammatory therapy potentially more important.

Chronic meningitis can occur after infections with tuberculosis, Lyme disease, AIDS, or syphilis, as well as in noninfectious disorders such as some cancers of the brain or blood (for example, leukemias and lymphomas) (Beers MH et al 2005).

Fungal infections are usually only a problem in people who have weakened immune systems, such as people with AIDS or in people who have had their spleens removed. Usually the fungus responsible is a species of *Cryptococcus*, an encapsulated yeast (Beers MH et al 2005). These infections start when a person breathes in fungal spores from contaminated soil; the infection in the lungs is usually cleared by the immune system. Only when the immune system is weak do these infections progress to meningitis.

For more information on strengthening the immune system or on HIV/AIDS, please see the following chapters:

- Strengthening the Immune System
- HIV/AIDS

### NUTRITION'S ROLE IN MENINGITIS

Although much of the research is still preliminary, exciting discoveries are being made on the role of nutrients in meningitis, especially anti-inflammatories and antioxidants. Evidence suggests that much of the damage caused by bacterial meningitis is due to overactivation of the immune system (Pathan N et al 2003). This immune response is thought to be caused primarily by bacterial endotoxin, a poison (present in the bacteria) released when the bacterial cell disintegrates. Studies have clearly shown that the degree of severity of bacterial meningitis is linked to the level of endotoxin (Brandtzaeg P et al 1989).

Once in the bloodstream, endotoxin binds to a protein, appropriately called endotoxin-binding protein. This alters the endotoxin, enabling it to activate macrophages and other inflammatory cells. Once activated, these cells secrete pro-inflammatory chemicals including TNF-alpha, interleukin 1(b), and interferon. At the same time, immune system cells called neutrophils are activated, releasing yet more inflammatory chemicals and enzymes, which damage blood vessels and the inner lining of body cavities (Klein NJ et al 1996). The result is widespread inflammation and damage.

By looking at the disease as an inappropriate immune response that touches off an inflammatory cascade, researchers are studying exciting new therapies to reduce the damaging consequences of meningitis. While these studies are ongoing, the Life Extension Foundation believes that nutrients that fight inflammation can safely be considered in helping reduce the inflammation associated with meningitis. Some of these nutrients include:

- **Genistein** — Genistein is an isoflavone and phytoestrogen. It inhibits the activity of tyrosine kinases, which are directly involved in both the inflammation associated with meningitis and the ability of bacteria to cross the blood-brain barrier. This suggests that genistein may help reduce the severity of the disease and have a preventative effect (Sokolova O et al 2004).
- **Essential fatty acids** — Essential fatty acids, including the omega-3 and omega-6 fatty acids, have powerful anti-inflammatory effects. A proper ratio of omega-3 fatty acids, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), to omega-6 fatty acids (linoleic acid) is vital to good health. The omega-3 fatty acids have been shown in hundreds of published studies to reduce inflammation through the reduction of prostaglandin E 2, a hormone-like chemical that promotes inflammation. Although there have been no studies that examined the use of essential fatty acids in meningitis, if the recent research implicating widespread inflammatory damage in meningitis withstands scientific scrutiny, supplementing with EPA and DHA may have some benefit.
- **Perilla leaf extract** — Perilla leaf extract contains luteolin and rosmarinic acid, which have both shown anti-inflammatory effects in animal studies (Ueda H et al 2002). Again, although no studies have been performed testing Perilla leaf extract's effect on meningitis, the extract's anti-inflammatory effects may have some benefit.
- **Rosmarinic acid** — Rosmarinic acid is contained in large amounts in extract of Perilla leaf. Studies have shown it to have anti-inflammatory action through the inhibition of cytokines and other inflammatory mediators in human asthma subjects (Sanbongi C et al 2004).

Antioxidants have also attracted attention among meningitis researchers. Studies have found that patients with meningitis have oxidative stress caused by reactive nitrogen species in bacterial meningitis (Kastenbauer S et al 2002). In a mouse model of bacterial meningitis, the internal antioxidant superoxide dismutase (SOD) was studied for its ability to limit oxidative stress that caused damage to the ears. SOD, given by injection, was found to significantly reduce damage to the cochlea (Ge NN et al 2004).

Two studies have explored the relationship between the antioxidant vitamin C and bacterial meningitis. In some cases, the CSF of children with meningitis showed elevated levels of vitamin C, while other studies showed a marked deficiency in vitamin C, suggesting that vitamin C is involved with the body's defense against free-radical associated damage (Caksen H et al 2004; Heinz-Erian P et al 1985). Vitamin C's decrease in the CSF of patients with bacterial meningitis seems to be correlated with the increase in reactive molecules in the brain (Kastenbauer S et al 2002; Koedel U et al 1999). Together, these results suggest that vitamin C supplementation may be helpful in treating patients with bacterial meningitis.

Melatonin is another nutrient studied in association with meningitis. The CSF of patients with viral meningitis tends to have higher concentrations of melatonin. This suggests that melatonin may play an immunomodulatory role in viral meningitis (de Oliveira Silva S et al 2005). In an exciting new animal study, rabbits received melatonin at 20 milligrams per kilogram (mg/kg) of body weight. Researchers found that the rabbits, given the melatonin simultaneously with infection, had higher levels of SOD and lower levels of dangerous reactive nitrogen species. This suggests that melatonin had protective effects against infection (Gerber J et al 2005).

## ***A Word From Life Extension Foundation***

The Life Extension Foundation and its founders have devoted themselves to pushing the knowledge of health beyond rigid, conventional boundaries. Although individual components of the information given here have been published in studies, there have been no clinical trials to support these recommendations in their entirety. In some cases, we are basing our recommendations on observations gleaned from decades of experience.

However, these supplements may help ward off an infection in the first place, which would naturally reduce the chances of developing meningitis.

The following supplements have been used at the first sign of a viral or bacterial infection.

- **Cimetidine (Tagamet)** —An over-the-counter heartburn drug that also boosts immune function by reducing T-suppressor cells (Mitsuishi T et al 2003); 800 milligrams (mg) each day is the recommended dose.
- **Pure Gar garlic** — This garlic has proven antiviral properties (Josling P 2001). Don't eat immediately after ingesting the garlic. Expect a strong sulfurous odor. A 1600 mg daily dose is suggested.
- **Kyolic aged garlic extract** —This type of garlic, at a dose of 3600 mg per day, has unique immune-boosting properties independent of Pure Gar garlic (Kyo E et al 2001).
- **Dehydroepiandrosterone (DHEA)** —A dose of 200 to 400 mg early in the day may boost the immune system. DHEA has shown powerful immune-enhancing and antiviral properties (Danenberg HD et al 1995; Padgett DA et al 2000).
- **Lactoferrin** —A dose of 1200 mg a day may boost natural killer cell activity and can kill certain viruses (Swart PJ et al 1998; Waarts BL et al 2005).
- **Zinc** —A number of studies have shown that, if zinc lozenges are taken within 24 hours of the onset of cold symptoms, the severity and duration of the cold are reduced (Hulisz D 2004). Take two lozenges (24 mg each) every 2 hours when awake. This is a very high dose of zinc and should be continued for only a few days to avoid toxic side effects.
- **Melatonin** —At a high dose, 10 to 50 mg at bedtime, melatonin may help boost the immune system (Maestroni GJ 1999) and facilitate deep, restorative sleep, which is needed to ward off infection.

## **LIFE EXTENSION FOUNDATION RECOMMENDATIONS**

There are a number of supplements that have been shown to reduce inflammation and, while the research is still preliminary, it is reasonable when dealing with a serious condition such as meningitis to take every possible precaution. Nutritional therapy has identified many substances that can reduce inflammation and may help reduce inflammatory damage associated with meningitis.

The Life Extension Foundation's approach to meningitis is based on new research that probes the link among inflammation, oxidative stress, and meningitis. Viral meningitis often resolves on its own, but we favor an aggressive approach to limit any damage from the disease. In addition to aggressive medical therapy such as intravenous antibiotics, the Life Extension Foundation suggests:

- **Life Extension Mix**—Follow label directions.
- **Vitamin C**—2.5 to 6.0 grams (g) daily
- **SODzyme**—2000 milligrams (mg) daily
- **Genistein**—135 mg soybean powder extract, standardized to supply 55.5 mg of isoflavones
- **EPA and DHA**—700 to 1400 mg of EPA; 500 to 1000 mg of DHA
- **Rosmarinic acid**—100 to 200 mg daily (contains 50 mg of Perilla leaf extract)
- **Melatonin**—1 to 3 mg at night

## **MENINGITIS 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:

### **EPA/DHA**

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

## Melatonin

### Do not take melatonin if you are depressed.

- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea.

## 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.

For more information see the Safety Appendix

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