Questions & Answers about . . .

Behçet's Disease

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
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This booklet contains general information about Behçet's (BAY-sets) disease. It describes what Behçet's disease is and how it may develop. It also explains how Behçet's disease is diagnosed and treated. At the end is a list of key words to help you understand the terms used in this booklet. If you have further questions after reading this booklet, you may wish to discuss them with your doctor.

What Is Behçet's Disease?

The disease was first described in 1937 by Dr. Hulusi Behçet, a dermatologist in Turkey. Behçet's disease is now recognized as a chronic condition that causes canker sores or ulcers in the mouth and on the genitals, and inflammation in parts of the eye. In some people, the disease also results in arthritis (swollen, painful, stiff joints), skin problems, and inflammation of the digestive tract, brain, and spinal cord.

Who Gets Behçet's Disease?

Behçet's disease is common in the Middle East, Asia, and Japan; it is rare in the United States. In Middle Eastern and Asian countries, the disease affects more men than women. In the United States, the opposite is true. Behçet's disease tends to develop in people in their 20's or 30's, but people of all ages can develop this disease.

What Causes Behçet's Disease?

The exact cause of Behçet's disease is unknown. Most symptoms of the disease are caused by inflammation of the blood vessels. Inflammation is a characteristic reaction of the body to injury or disease and is marked by four signs: swelling, redness, heat, and pain. Doctors think that an autoimmune reaction may cause the blood vessels to become inflamed, but they do not know what triggers this reaction. Under normal conditions, the immune system protects the body from diseases and infections by killing harmful "foreign" substances, such as germs, that enter the body. In an autoimmune reaction, the immune system mistakenly attacks and harms the body's own tissues.

Behçet's disease is not contagious; it is not spread from one person to another. Researchers think that two factors are important for a person to get Behçet's disease. First, it is believed that abnormalities of the immune system make some people susceptible to the disease. Scientists think that this susceptibility may be inherited; that is, it may be due to one or more specific genes. Second, something in the environment, possibly a bacterium or virus, might trigger or activate the disease in susceptible people.

What Are the Symptoms of Behçet's Disease?

Behçet's disease affects each person differently. Some people have only mild symptoms, such as canker sores or ulcers in

the mouth or on the genitals. Others have more severe signs, such as meningitis, which is an inflammation of the membranes that cover the brain and spinal cord. Meningitis can cause fever, a stiff neck, and headaches. More severe symptoms usually appear months or years after a person notices the first signs of Behçet's disease. Symptoms can last for a long time or may come and go in a few weeks. Typically, symptoms appear, disappear, and then reappear. The times when a person is having symptoms are called flares. Different symptoms may occur with each flare; the problems of the disease often do not occur together. To help the doctor diagnose Behçet's disease and monitor its course, patients may want to keep a record of which symptoms occur and when. Because many conditions mimic Behçet's disease, physicians must observe the lesions (injuries) caused by the disorder in order to make an accurate diagnosis.

The five most common symptoms of Behçet's disease are mouth sores, genital sores, other skin lesions, inflammation of parts of the eye, and arthritis.

- **Mouth sores** (known as oral aphthosis [af-THO-sis] and aphthous stomatitis) affect almost all patients with Behçet's disease. Individual sores or ulcers are usually identical to canker sores, which are common in many people. They are often the first symptom that a person notices and may occur long before any other symptoms appear. The sores usually have a red

border and several may appear at the same time. They may be painful and can make eating difficult. Mouth sores go away in 10 to 14 days but often come back. Small sores usually heal without scarring, but larger sores may scar.

- **Genital sores** affect more than half of all people with Behçet's disease and most commonly appear on the scrotum in men and vulva in women. The sores look similar to the mouth sores and may be painful. After several outbreaks, they may cause scarring.

- **Skin problems** are a common symptom of Behçet's disease. Skin sores often look red or resemble pus-filled bumps or a bruise. The sores are red and raised, and typically appear on the legs and on the upper torso. In some people, sores or lesions may appear when the skin is scratched or pricked. When doctors suspect that a person has Behçet's disease, they may perform a pathergy test, in which they prick the skin with a small needle; 1 to 2 days after the test, people with Behçet's disease may develop a red bump where the doctor pricked the skin. However, only half of the Behçet's patients in Middle Eastern countries and Japan have this reaction. It is less commonly observed in patients from the United States, but if this reaction occurs, then Behçet's disease is likely.

- **Uveitis** (yoo-vee-EYE-tis) involves inflammation of the middle or back part of the eye (the uvea) including the iris, and occurs in more than half of all people with Behçet's disease. This symptom is more common among men than women and typically begins within 2 years of the first symptoms. Eye inflammation can cause blurred vision; rarely, it causes pain and redness. Because partial loss of vision or blindness can result if the eye frequently becomes inflamed, patients should report these symptoms to their doctor immediately.

- **Arthritis**, which is inflammation of the joints, occurs in more than half of all patients with Behçet's disease. Arthritis causes pain, swelling, and stiffness in the joints, especially in the knees, ankles, wrists, and elbows. Arthritis that results from Behçet's disease usually lasts a few weeks and does not cause permanent damage to the joints.

In addition to mouth and genital sores, other skin lesions, eye inflammation, and arthritis, Behçet's disease may also cause blood clots, and inflammation in the central nervous system and digestive organs.

Blood Clots

About 16 percent of patients with Behçet's disease have blood clots resulting from inflammation in the veins (thrombophlebitis), usually in the legs. Symptoms include

pain and tenderness in the affected area. The area may also be swollen and warm. Because thrombophlebitis can have severe complications, people should report symptoms to their doctor immediately. A few patients may experience artery problems such as aneurysms (balloon-like swelling of the artery wall).

Central Nervous System

Behçet's disease affects the central nervous system in about 23 percent of all patients with the disease in the United States. The central nervous system includes the brain and spinal cord. Its function is to process information and coordinate thinking, behavior, sensation, and movement. Behçet's disease can cause inflammation of the brain and the thin membrane that covers and protects the brain and spinal cord. This condition is called meningoencephalitis. People with meningoencephalitis may have fever, headache, stiff neck, and difficulty coordinating movement, and should report any of these symptoms to their doctor immediately. If this condition is left untreated, a stroke (blockage or rupture of blood vessels in the brain) can result.

Digestive Tract

Rarely, Behçet's disease causes inflammation and ulceration (sores) throughout the digestive tract that are identical to the aphthous lesions in the mouth and genital area.

This leads to abdominal pain, diarrhea, and/or bleeding. Because these symptoms are very similar to symptoms of other diseases of the digestive tract, such as ulcerative colitis and Crohn's disease, careful evaluation is essential to rule out these other diseases.

How Is Behçet's Disease Diagnosed?

Diagnosing Behçet's disease is very difficult because no specific test confirms it. Less than half of patients initially thought to have Behçet's disease actually have it. When a patient reports symptoms, the doctor must examine the patient and rule out other conditions with similar symptoms. Because it may take several months or even years for all the common symptoms to appear, the diagnosis may not be made for a long time. A patient may even visit several different kinds of doctors before the diagnosis is made.

These symptoms are key to a diagnosis of Behçet's disease:

- Mouth sores at least three times in 12 months
- Any two of the following symptoms: recurring genital sores, eye inflammation with loss of vision, characteristic skin lesions, or positive pathergy (skin prick test)

Besides finding these signs, the doctor must rule out other conditions with similar symptoms, such as Crohn's disease and reactive arthritis. The doctor also may recommend that

the patient see an eye specialist to identify possible complications related to eye inflammation. A dermatologist may perform a biopsy of mouth, genital, or skin lesions to help distinguish Behçet's from other disorders.

What Kind of Doctor Treats a Patient With Behçet's Disease?

Because the disease affects different parts of the body, a patient probably will see several different doctors. It may be helpful to both the doctors and the patient for one doctor to manage the complete treatment plan. This doctor can coordinate the treatments and monitor any side effects from the various medications that the patient takes.

A rheumatologist (a doctor specializing in arthritis and other inflammatory disorders) often manages a patient's treatment and treats joint disease. The following specialists also treat other symptoms that affect the different body systems:

- Gynecologist—treats genital sores in women
- Urologist—treats genital sores in men
- Dermatologist—treats genital sores in men and women, and skin and mucous membrane problems
- Ophthalmologist—treats eye inflammation

- Gastroenterologist—treats digestive tract symptoms
- Hematologist—treats disorders of the blood
- Neurologist—treats central nervous system symptoms

How Is Behçet's Disease Treated?

Although there is no cure for Behçet's disease, people usually can control symptoms with proper medication, rest, exercise, and a healthy lifestyle. The goal of treatment is to reduce discomfort and prevent serious complications such as disability from arthritis or blindness. The type of medicine and the length of treatment depend on the person's symptoms and their severity. It is likely that a combination of treatments will be needed to relieve specific symptoms. Patients should tell each of their doctors about all of the medicines they are taking so that the doctors can coordinate treatment.

Topical Medicine

Topical medicine is applied directly on the sores to relieve pain and discomfort. For example, doctors prescribe rinses, gels, or ointments. Creams are used to treat skin and genital sores. The medicine usually contains corticosteroids (which reduce inflammation), other anti-inflammatory drugs, or an anesthetic, which relieves pain.

Oral Medicine

Doctors also prescribe medicines taken by mouth to reduce inflammation throughout the body, suppress the overactive immune system, and relieve symptoms. Doctors may prescribe one or more of the medicines described below to treat the various symptoms of Behçet's disease.

- **Corticosteroids**—Prednisone is a corticosteroid prescribed to reduce pain and inflammation throughout the body for people with severe joint pain, skin sores, eye disease, or central nervous system symptoms. Patients must carefully follow the doctor's instructions about when to take prednisone and how much to take. It also is important not to stop taking the medicine suddenly, because the medicine alters the body's production of the natural corticosteroid hormones. Long-term use of prednisone can have side effects such as osteoporosis (a disease that leads to bone fragility), weight gain, delayed wound healing, persistent heartburn, and elevated blood pressure. However, these side effects are rare when prednisone is taken at low doses for a short time. It is important that patients see their doctor regularly to monitor possible side effects. Corticosteroids are useful in early stages of disease and for acute severe flares. They are of limited use for long-term management of central nervous system and serious eye complications.

- **Immunosuppressive drugs**—These medicines (in addition to corticosteriods) help control an overactive immune system, which occurs in Behçet's disease, and reduce inflammation throughout the body, and can lessen the number of disease flares. Doctors may use immunosuppressive drugs when a person has eye disease or central nervous system involvement. These medicines are very strong and can have serious side effects. Patients must see their doctor regularly for blood tests to detect and monitor side effects.

Doctors may use one or more of the following immunosuppressive drugs depending on the person's specific symptoms.

— **Azathioprine**—Most commonly prescribed for people with organ transplants because it suppresses the immune system, azathioprine is now used for people with Behçet's disease to treat uveitis and other uncontrolled disease manifestations. This medicine can upset the stomach and may reduce production of new blood cells by the bone marrow.

— **Chlorambucil or Cyclophosphamide**—Doctors may use these drugs to treat uveitis and meningoencephalitis. People taking either agent must see their doctor frequently because either can have serious side effects, such as permanent sterility and cancers of the blood. Patients have regular blood tests to monitor blood counts of white cells and platelets.

— **Cyclosporine**—Like azathioprine, doctors prescribe this medicine for people with organ transplants. When used by patients with Behçet's disease, cyclosporine reduces uveitis and uncontrolled disease in other organs. To reduce the risk of side effects, such as kidney and liver disease, the doctor can adjust the dose. Patients must tell their doctor if they take any other medicines, because some medicines affect the way the body uses cyclosporine.

— **Colchicine**—Commonly used to treat gout, which is a form of arthritis, colchicine reduces inflammation throughout the body. The medicine sometimes is used to treat arthritis, mucous membrane, and skin symptoms in patients with Behçet's disease. A research study in Turkey suggested that the medication works best for males with the disorder. Common side effects of colchicine include nausea, vomiting, and diarrhea. The doctor can decrease the dose to relieve these side effects.

— **Combination Treatment**—Cyclosporine is sometimes used with azathioprine when one alone fails. Prednisone along with an immunosuppressive drug is a common combination.

If these medicines do not reduce the symptoms, doctors may use other drugs such as methotrexate. Methotrexate

(Rheumatrex,* Trexall), which is also used to treat various kinds of cancer as well as rheumatoid arthritis, can relieve Behçet's symptoms because it suppresses the immune system and reduces inflammation throughout the body.

Rest and Exercise

Although rest is important during flares, doctors usually recommend moderate exercise, such as swimming or walking, when the symptoms have improved or disappeared. Exercise can help people with Behçet's disease keep their joints strong and flexible.

What Is the Prognosis for a Person With Behçet's Disease?

Most people with Behçet's disease can lead productive lives and control symptoms with proper medicine, rest, and exercise. Doctors can use many medicines to relieve pain, treat symptoms, and prevent complications. When treatment is effective, flares usually become less frequent. Many patients eventually enter a period of remission (a disappearance of symptoms). In some people, treatment does not relieve symptoms, and gradually more serious symptoms such as eye disease may occur. Serious symptoms may appear months or years after the first signs of Behçet's disease.

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What Are Researchers Trying to Learn About Behçet's Disease?

Researchers are exploring possible genetic, bacterial, and viral causes of Behçet's disease as well as improved drug treatment. For example, genetic studies show strong association of the gene HLA-B51 with the disease, but the exact role of this gene in the development of Behçet's is uncertain. Researchers hope to identify genes that increase a person's risk for developing Behçet's disease. Studies of these genes and how they work may provide new understanding of the disease and possibly new treatments.

Researchers are also investigating factors in the environment, such as bacteria or viruses, that may trigger Behçet's disease. They are particularly interested in whether *Streptococcus*, the bacterium that causes strep throat, is associated with Behçet's disease. Many people with Behçet's disease have had several strep infections. In addition, researchers suspect that herpesvirus type 1, a virus that causes cold sores, may be associated with Behçet's disease.

Finally, researchers are identifying other medicines to better treat Behçet's disease. TNF inhibitors are a class of drugs that reduce joint inflammation by blocking the action of a substance called tumor necrosis factor. Although serious side effects have been reported for TNF inhibitors, they have shown some promise in treating Behçet's disease. Examples of TNF inhibitors include etanercept and infliximab. Also, interferon alpha, a protein that helps fight infection, has

shown promise in treating Behçet's disease. Thalidomide, which is believed to be a TNF inhibitor, appears effective in treating severe mouth sores, but its use is experimental and side effects are a concern. Thalidomide is not used to treat women of childbearing age because it causes severe birth defects.

Where Can People Get More Information About Behçet's Disease?

- **National Institute of Arthritis and Musculoskeletal and Skin Diseases**
  NIAMS/National Institutes of Health
  1 AMS Circle
  Bethesda, MD 20892–3675
  301–495–4484 or
  877–22–NIAMS (226–4267) (free of charge)
  Fax: 301–718–6366
  TTY: 301–565–2966
  www.niams.nih.gov

- **National Institute of Dental and Craniofacial Research**
  National Institutes of Health
  Bethesda, MD 20892–2510
  301–496–4261
  www.nidcr.nih.gov

- **National Institute of Diabetes and Digestive and Kidney Diseases**
  National Institutes of Health
  Bethesda, MD 20892–2510
  301–654–3327 or
  800–860–8747 (free of charge)
  www.niddk.nih.gov

- **National Eye Institute**
  National Institutes of Health
  Bethesda, MD 20892–2510
  301–496–5248 and
  for professionals 800–869–2020 (free of charge)
  www.nei.nih.gov

- **National Institute of Neurological Disorders and Stroke**
  National Institutes of Health
  Bethesda, MD 20892
  301–496–5751 or
  800–352–9424 (free of charge)
  TTY: 301–468–5981
  www.ninds.nih.gov

- **American Academy of Dermatology**
  P.O. Box 4014
  Schaumberg, IL 60168–4014
  847–330–0230 or
  888–462–3376 (free of charge)
  www.aad.org

- **American College of Rheumatology**
  1800 Century Place, Suite 250
  Atlanta, GA 30345
  404–633–3777
  Fax: 404–633–1870
  www.rheumatology.org

- **Dermatology Foundation**
  1560 Sherman Avenue
  Evanston, IL 60201–4808
  (This organization is "research only." Contact should be made by U.S. mail or e-mail.)
  E-mail: dfgen@dermatologyfoundation.org
  www.dermfnd.org

- **American Behçet's Disease Association**
  P.O. Box 19952
  Amarillo, TX 79114
  800–7–BEHCET (234238) or
  800–723–4238 (free of charge)
  www.behcets.com

- **American Skin Association**
  150 East 58th Street, 33rd Floor
  New York, NY 10155–0002
  212–753–8260 or
  800–499–SKIN (7546) (free of charge)
  ww.skinassn.org

- **Arthritis Foundation**
  1330 West Peachtree Street
  Atlanta, GA 30309
  404–872–7100 or
  800–283–7800 (free of charge), or your local chapter (listed in the telephone directory)
  www.arthritis.org

- **Behcet's Organization Worldwide**
  1838 East 45th Street
  Wichita, KS 67216
  www.behcets.org

- **National Organization for Rare Disorders**
  P.O. Box 1968
  55 Kenosia Avenue
  Danbury, CT 06813–1968
  203–744–0100 or
  Voice Mail: 800–999–NORD (6673) (free of charge)
  www.rarediseases.org

Glossary

Anesthetic—Pain relief medicine that dulls feeling in the sore area. Doctors sometimes use an anesthetic to relieve pain caused by mouth and genital sores in people with Behçet's disease.

Aneurysm—Swelling of an artery due to a weakness in its wall.

Antibody—A special protein produced by the body's immune system that recognizes and helps fight infectious agents and other foreign substances that invade the body.

Aphthosis—Ulcers in the mouth or on the genitals. Oral or mouth aphthosis, also called aphthous stomatitis, is the most common symptom of Behçet's disease.

Arthritis—Literally means joint inflammation. It is a general term for more than 100 of the rheumatic diseases. Arthritis causes joint swelling, pain, and stiffness. Some people with Behçet's disease develop a form of arthritis that goes away after a few weeks or months and causes no long-term damage to the joints.

Autoimmune disease—A disease that results when the immune system mistakenly attacks the body's own tissues.

Blood vessels—Arteries, veins, and capillaries that carry blood through the body.

Central nervous system—This body system includes the brain and spinal cord. Its functions are to process information and coordinate thinking, behavior, sensation, and movement. In some people with Behçet's disease, blood vessels in the central nervous system become inflamed, causing headaches, stiff neck, and clumsiness.

Corticosteroids—Strong anti-inflammatory hormones that are made naturally in the body or synthetically (man-made) for use as medicine. They also are called glucocorticoids. The most commonly prescribed medicine of this type is prednisone.

Crohn's disease—Inflammation of the small intestine or colon that causes diarrhea, cramps, and weight loss.

Digestive tract—The body system that breaks down food. The digestive tract includes the stomach, intestines, pancreas, gallbladder, and liver.

Flare—A period of time when disease symptoms reappear or become worse.

Immune system—A complex network of specialized cells and organs that work together to defend the body against attacks by "foreign" invaders such as bacteria and viruses. In some rheumatic conditions, it appears that the immune system does not function properly and may even work against the body.

Immunosuppressive drugs—Medicines that reduce the immune response and therefore may relieve some symptoms of Behçet's disease.

Inflammation—A reaction of tissues to injury or disease, marked by four signs: swelling, redness, heat, and pain.

Meningitis—Inflammation of the membranes that cover the brain and spinal cord.

Meningoencephalitis—Inflammation of the membranes that cover and protect the brain and spinal cord. This condition sometimes occurs in patients with Behçet's disease.

Pathergy (a state of heightened reactivity)—A test that detects pathergic skin sensitivity is sometimes used to help diagnose Behçet's disease. The skin is pricked with a small needle and in some people, a bump appears after 1 or 2 days. This reaction is called positive pathergy.

Reactive arthritis—A form of arthritis that can develop after an intestinal or urinary tract infection. The disease causes pain and swelling around the joints and in the spine. People with the disease may also experience swelling of the eye and the reproductive and urinary tracts.

Streptococcus—A bacterium that causes infections such as strep throat. Doctors think that it also may trigger Behçet's disease in some people.

Thrombophlebitis—Inflammation of a vein and formation of a blood clot in the vein.

Topical treatment—Medicine, such as a cream or rinse, that is put directly on the affected body part.

Ulcerative colitis—Inflammation of the colon. Symptoms include stomach pain and diarrhea.

Uveitis—Inflammation of the inner eye that includes the iris, the tissue that holds the lens of the eye, and a network of blood vessels surrounding the eyeball called the choroid plexus.

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