

HANDLING THE
HARD QUESTIONS:

*What Our Patients
Are Asking Us About*

BEHÇET'S DISEASE



The Purpose of This Document

Due in part to its uncommon nature, rheumatology nurses, nurse practitioners, and physician assistants are often challenged in answering questions from patients newly diagnosed with Behçet's disease. It is important to be able to properly and effectively communicate appropriate responses. This pocket guide includes a brief summary of evidence surrounding some of the most common—and challenging—questions that patients with Behçet's disease are asking their providers. We hope you find this guide useful for your professional development.



CONTENTS

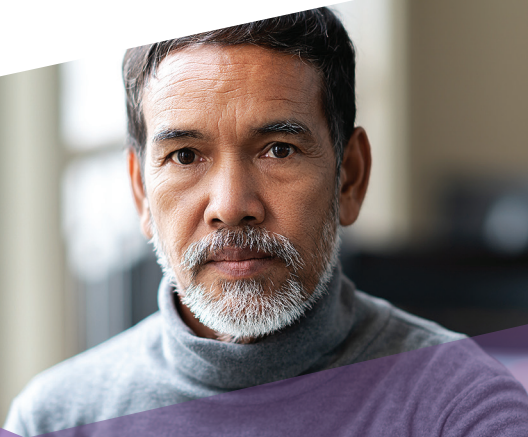
- 2** What is Behçet's disease?
- 5** How many people have Behçet's disease?
- 7** How do you know that I have Behçet's disease and not something else?
- 10** Can Behçet's disease be cured?
- 12** What are some of the other manifestations of Behçet's disease that I should be aware of?
- 14** Am I still going to be able to work/go to school?
- 16** Is my disease likely to get better or worse in the future?
- 18** What are my treatment options?
- 22** What can I do at home to help manage my disease?
- 24** Do I have to worry about my current or future children getting Behçet's disease? Will it impact my ability to get pregnant?

What is Behçet's disease?

Behçet's disease (or syndrome) is a rare inflammatory condition that affects the mucous membranes and skin. Patients with Behçet's disease may suffer from a combination of mouth ulcers, genital ulcers, skin lesions, and eye abnormalities that are caused by chronic inflammation. Due to its links to the autoimmune system, many patients with Behçet's disease are treated in rheumatology offices.

Behçet's disease is usually diagnosed in patients between 20-40 years of age, although it can initially present at any age. Several pediatric cases have been described, and these account for up to a quarter of all cases.¹⁻⁵

The condition is named for Hulusi Behçet, a Turkish dermatologist who first identified the combination of symptoms that are associated with Behçet's disease in 1937.⁶ For many years,



Behçet's disease was called "Silk Road Disease" because of its higher overall prevalence in the Far East and Mediterranean regions compared to the rest of the world.

Symptoms associated with Behçet's disease will often ebb and flow. The duration of acute attacks, which can last several days or weeks, depends on the location and severity of the symptoms. Attacks are followed by remission periods where symptoms subside, again, for varied lengths of time. The symptoms and severity of acute attacks will sometimes mirror each other, although at other times, they will differ. Again, why this happens is not entirely clear.

Studies have shown that Behçet's disease is a chronic inflammatory condition related to vasculitis that is occurring throughout the body.⁷ It is likely triggered by environmental factors in patients who have a genetic predisposition to the condition. One genetic factor that is linked to Behçet's disease is a gene called human leukocyte antigen (HLA) B*51. This gene is carried by most (but not all) patients with Behçet's disease.⁸ A genetic test is available to determine whether an individual carries the HLA-B*51 allele, and a positive test can confirm the diagnosis of Behçet's disease.

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How many people have Behçet's disease?

Behçet's disease is rare. In the United States, Behçet's disease is found in only 5.2 out of every 100,000 Americans.¹⁻³ This prevalence was determined as part of the 45-year Rochester Epidemiology Project conducted in Olmstead County, Minnesota. The project looked at whether there were any time trends in the incidence, prevalence, and clinical characteristics of Behçet's disease over a 45-year period. Results indicated that the incidence and prevalence of Behçet's disease in North America was comparable to other Western populations. The proportion of cases was found to be higher in women than other countries, and patients diagnosed with Behçet's disease had a higher than expected prevalence of ocular and central nervous system involvement.⁴



Geographically, Behçet's disease is most common in countries such as Turkey, Iran, Saudi Arabia, Iraq, Israel, and Japan.³ Some studies have shown a higher prevalence in women versus men, although there is no consistent pattern.

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How do you know that I have Behçet's disease and not something else?

The diagnosis of Behçet's disease is challenging. There is no specific test available to help diagnose the disease, and patients don't always present with a consistent pattern of symptoms. The complexity of Behçet's disease led one expert to term the condition, "A Great Imitator."¹ This is especially true when the symptoms commonly associated with Behçet's disease (mouth ulcers, genital ulcers, skin lesions, and eye abnormalities) don't appear all at once. Of course, these general symptoms are associated with many other conditions as well, adding to the challenge.

There is, however, some guidance available to help diagnose Behçet's disease. Perhaps the most



common clinical clue is mouth ulcers, which are present in 95% of patients at the time of diagnosis.²

To make the diagnosis of Behçet's disease, providers look for recurrent mouth sores (present at least three times in the last year) plus two of the following:

- Recurring genital sores
- Eye swelling or inflammation (possible vision loss)
- Skin sores
- A positive “pathergy” skin test — small red bumps from a needle prick

It can take months or years for all of the common symptoms of Behçet's disease to appear in a given patient, and some patients only develop some of these manifestations. Asking a patient to keep a diary of symptoms, including when they occur, can help build a clinical picture.

The best current criteria for diagnosing Behçet's disease is the International Criteria for Behçet's Disease (ICBD), last updated in 2014.³ The corresponding table outlines the ICBD scoring system, which is based on disease manifestations and a pathergy test.

ICBD Scoring System³

Symptom or Test	Point Value
Ocular lesions	2 points
Oral aphthosis	2 points
Genital aphthosis	2 points
Skin lesions	1 point
Central nervous system involvement	1 point
Vascular manifestations	1 point
Positive pathergy test	1 point

A patient scoring 4 or more points is classified as having Behçet's disease.

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Can Behçet's disease be cured?

As with many autoimmune diseases, there is currently no cure for Behçet's disease. It is a chronic, lifelong condition that must be carefully managed through a combination of proper medication, rest, exercise, and a healthy lifestyle. While many patients will see their symptoms subside for extended periods of time, there have been no reported permanent remissions.¹

As with other incurable conditions that cause chronic pain, Behçet's disease may have a deep psychosocial impact on patients who suffer from constant and repetitive attacks. The condition is associated with a greater risk for fatigue, depression, anxiety, and lower quality of life scores.^{2,3}



Symptoms that arise in patients with Behçet's disease are typically treated as they arise, with the goal to minimize the effects of each acute attack and reduce any long-term impact these attacks may cause if gone untreated.

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What are some of the other manifestations of Behçet's disease that I should be aware of?

Behçet's disease is a multi-system condition, meaning that it can affect a variety of body parts and organs. In the United States, the rate of occurrence for the most common symptoms is as follows:^{1,2}

- Recurring mouth sores (95%)
- Skin sores (up to 90%)
- Recurring genital sores (up to 80% or more)
- Eye swelling or inflammation (up to 75%)



Additional manifestations (and their occurrence rates) include the following:^{1,2}

- Joint problems/arthritis (50%)
- Neurological problems, such as meningitis, cranial nerve palsy, memory loss, impaired speech, balance, or movement (up to 30%)
- Stomach and intestinal problems (up to 25%)
- Vascular problems, such as blood clots or aneurysms (up to 18%)

The recurring manifestations of Behçet's disease usually heal without complications; however, some can cause serious morbidity, such as ophthalmological problems that lead to blindness if not aggressively treated. On the extreme end of the spectrum are vascular, neurological, cardiac, or pulmonary manifestations that have led to mortality in select patients with Behçet's disease.¹

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Am I still going to be able to work/go to school?

People with Behçet's disease typically lead productive lives. Symptoms can often be controlled by following a careful plan that includes medication, rest, and exercise. Adherence to a plan you develop and agree upon in consultation with your provider can help to relieve pain, treat symptoms that arise (especially during flares), and prevent significant complications. Studies have shown that effective treatment and a healthy lifestyle can lead to less frequent flares.¹

Because it can cause chronic pain, patients diagnosed with Behçet's disease may require a variety of methods to cope with the physical, psychological, and social aspects of living with the condition. Flares can negatively affect an individual's appearance, psychosocial status, personal relationships, daily activities, and general quality of life.²



A 2018 study used the Theory of Unpleasant Symptoms (TOUS) and Symptom Management Theory to understand symptoms of patients with Behçet's disease and coping methods commonly used. It made the following conclusions:²

- Behçet's symptoms affect the way that patients live
- Patients with Behçet's disease need symptom management. Those performing effective symptom management have fewer symptoms than those who do not.
- Healthcare providers should give patients detailed information about the symptoms of Behçet's disease and provide an effective symptom management strategy
- Healthcare providers should emphasize the importance of adhering to medical treatment, diet, and regular exercise and teach their patients how to cope with the disease

Patients with severe cases of Behçet's disease may become debilitated if their condition goes unchecked. Serious sequelae include blindness, meningitis, stroke, and aneurysms.

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Is my disease likely to get better or worse in the future?

The course of Behçet's disease is different for each patient. Some patients manage flares fairly easily while others have chronic symptoms that last for longer periods of time. Therefore, recommendations should be personalized to the individual and their circumstances (i.e., age, gender, stage of life, symptom severity, treatment regimen, and patient preferences).¹

Although disease manifestations may ameliorate over time in many patients, serious symptoms can also appear months or years after the first signs of Behçet's disease. Therefore, patients need to be aware that effective, consistent, and vigilant symptom management is optimal for managing



the disease. Those who accept the challenges of following treatment guidelines, adjusting to a lifestyle with continual medical monitoring, eating a healthy diet, and exercising regularly manage better than those who do not.² Patients must also learn to employ effective coping strategies to manage the social and psychological effects of living with chronic pain or disease.³

Flares associated with Behçet's disease may become more common, less common, or occur at the same frequency over the years. Progressive damage may occur, even in patients receiving treatment. A “light at the end of the tunnel” for patients with Behçet's disease—and all inflammatory conditions—may lie in ongoing clinical research.⁴

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What are my treatment options?

Treatments that are currently used to treat Behçet's disease are aimed at specific symptoms related to the condition, such as mouth ulcers or skin lesions. One option, apremilast, recently became the first and only approved treatment by the US Food and Drug Administration (FDA) for oral ulcers associated with Behçet's disease.

Many patients will receive a combination of therapies depending on their specific symptom profile. These may include corticosteroids and, especially in severe cases, chemotherapeutic agents, which are used to help prevent flares and minimize the effect of flares when they emerge. Your healthcare team will work with you to decide which options are best.



Some of the more common drugs used to treat Behçet's-related symptoms are included in the accompanying table.

In 2018, the European League Against Rheumatism (EULAR) published its guidelines for the treatment of Behçet's disease. Within these guidelines, there were five overarching principles:¹

- Behçet's disease is a condition that typically runs a relapsing and remitting course. The goal of treatment is to promptly suppress inflammatory exacerbations and recurrences to prevent irreversible organ damage.
- A multidisciplinary approach is necessary for optimal care
- Treatment should be individualized according to age, gender, type, and severity of organ involvement and patient preferences
- Ocular, vascular, neurological, and gastrointestinal involvement may be associated with a poor prognosis
- Disease manifestations may ameliorate over time in many patients

Patients with Behçet's disease usually need to see more than one clinician. A rheumatologist or advanced practice provider will often serve as the point person, managing a patient's pain and inflammatory disease, coordinating care with other professionals, and monitoring for any

side effects and improper drug combinations. Other specialties that may be involved include dermatology, gynecology, urology, ophthalmology, gastroenterology, hematology, and neurology. Other providers such as dentists, pain management specialists, and pulmonologists may also be needed in rare cases.

In patients with severe symptoms related to their disease, aggressive treatment with cytotoxic drugs and medium- to high-dose steroids are often necessary. Together with prednisolone, pulse cyclophosphamide, azathioprine, cyclosporine A, chlorambucil, and methotrexate can be considered

Behçet's Disease Medication Chart^{2,3}

Symptom(s)	Medicine	How it Works
Oral ulcers	Apremilast	Immune system anti-inflammatory
Skin ulcers General disease flare	Colchicine	Anti-inflammatory used to reduce swelling and pain
Genital ulcers General disease flare	Low-dose methotrexate with low-dose prednisolone	Immune system suppressor and steroidal anti-inflammatory
Chronic inflammation	Infliximab	Blocks the effects of tumor necrosis factor (TNF) alpha, a cellular substance that promotes inflammation
Genital ulcers	Pimecrolimus ointment	Immune system suppressor
Skin ulcers	Non-steroidal anti-inflammatory drugs (NSAIDs)	Reduces pain and swelling

depending on the severity of a patient's lesions. Patients who are resistant to the combination of cytotoxic drugs and prednisolone may be treated with a combination of cytotoxics alone.¹

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Significant Side Effects or Complications

Diarrhea, nausea, vomiting, depression, weight decrease

Interacts with other drugs, allergic reaction, nausea, vomiting, stomach pain, diarrhea

Infection, diarrhea, mouth sores, cough, shortness of breath, stomach pain, dark urine, numbness or tingling, muscle weakness, confusion, seizure, skin rash

Fever, sweats, chills, muscle aches, weight loss, cough, skin or sores on body, diarrhea, stomach pain, shortness of breath

Severe burning of treated skin, new symptoms of viral skin infection, worsened skin symptoms, swollen glands

Gas, bloating, heartburn, stomach pain, nausea, vomiting, diarrhea, and/or constipation

What can I do at home to help manage my disease?

During an Attack:

- Take medications as directed and on schedule
- See your team of healthcare providers as needed
- Eat nutritious and healthy meals
- Rest

During Remissions:

- Stay vigilant about monitoring symptoms and adhering to any ongoing preventative treatment



- Exercise. Many patients with Behçet's disease, especially younger patients, can continue to enjoy the same physical activities as they did prior to their diagnosis.
- Get enough sleep at night
- Eat nutritious and healthy meals

Researchers are studying the effects of different types of diet (e.g., vegetarian, Mediterranean, habitual) and exercise on patients with Behçet's disease.¹ Some people with the condition have suggested that a sensitivity to certain foods may trigger a flare. One study found that pineapple, nuts, lemons, and some cheeses made mouth ulcers worse in one-third of all patients who responded to a survey.^{2,3}

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Do I have to worry about my current or future children getting Behçet's disease? Will it impact my ability to get pregnant?

Women who are diagnosed during pregnancy or who are considering becoming pregnant have concerns about how pregnancy will affect their disease.

Behçet's disease does not appear to be linked to pregnancy complications, but some of the medications used to treat Behçet's can be harmful to an unborn baby. For this reason, it is best for any pregnancy to be planned and discussed first with your healthcare provider.¹



Little is known about how Behçet's disease affects the gestational period. A retrospective analysis from 1997 concluded that it did not represent a major risk during pregnancy, but a small number of serious vascular complications have been reported.²

Although very rare, cases of transient neonatal Behçet's disease have been reported in mothers who do and do not have the disease.²⁻⁴ The mode of transmission is unclear, but in most cases, the infant's symptoms were successfully treated without further complication.

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