



Behçet's Syndrome Society

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Behçet's Syndrome

Behçet's Syndrome is named after a Turkish Professor of Dermatology who described the **main** features of the condition in 1937. It had previously been described as long ago as the 5th century BC by Hippocrates, by a Chinese physician in the 5th century AD and by a number of European physicians in the late 19th and early 20th century.

First, why is there a debate whether it should be called Behçet's Disease or Behçet's Syndrome? A syndrome is a collection of clinical features that may, or may not be one condition and may be the presentation of a number of similar conditions. As there are differences in the incidence of Behçet's Syndrome, and of its various manifestations, in different countries, and since we do not yet know the exact cause, some physicians prefer to keep an open mind and use the term Syndrome rather than suggest that we know that it is a single entity with a single cause in all cases by using the word Disease.

Secondly, there is a debate on how one should diagnose the condition. The diagnosis in the individual patient depends on the clinical acumen and experience of the physician. Various schemes of diagnosis have been suggested over the years, none of which are perfect. There is no diagnostic test for the condition. A test known as *the pathergy test* has been investigated over the years. It consists of pricking the skin of the forearm with a sterile needle and seeing if a red lump appears after 48 hours. This has been thought to be specific for the condition but is not considered as such now since it is not positive in all patients, the frequency of positive tests is falling over the years and some "normal" patients may have a positive test.

Diagnosis, therefore, depends on a high index of suspicion (see below) and, if necessary, referral of the patient to a physician who has considerable knowledge and experience of the condition. There are so-called "International classification criteria" but these are for research purposes to ensure that studies of (eg) pathogenesis or treatment include patients who are comparable in different centres. These criteria are **not** intended to be used for diagnosis in an individual patient.

The condition is most frequent in Turkey, North Africa and the Middle East and in South East Asia. In Western Europe it is rare but must not be overlooked. While there are differences in various studies it is generally found that women are more frequently affected in Europe, men in the Middle East and South East Asia and men have more severe manifestations.

The cause of the condition is not known. It has been demonstrated in laboratory tests that there is a major disturbance of the immune system but this is not thought to be the underlying cause. Some authorities have suggested an infective cause but this has never been convincingly confirmed. It is known that there is a strong genetic predisposition. Detection of some of the markers (like blood groups), or antigens, on the white cells in the blood, which are genetically transmitted, show a high incidence of one known as HLA-B51 compared to the general population. However this is not the

cause as most people with this marker do not have Behçet's Syndrome and conversely some patients with Behçet's Syndrome do not possess the HLA – B51 antigen. Nevertheless there is often a strong family history of the syndrome, or just a family history of mouth ulceration.

Studies of involved tissues in patients with Behçet's Syndrome shows white blood cells in and around blood vessels (i.e. inflammation) – and particularly around large and small veins. Large arteries may also be involved but this is relatively rare. While some authorities have labelled this as a *vasculitis*, which usually means injury or destruction of blood vessels, it is probably more accurate to call this a *vasculopathy* which means involvement of blood vessels of all sizes.

1) The more common features of the syndrome are:

i) Mucocutaneous:

Mouth Ulceration : this is recurrent, arbitrarily defined as occurring at least three times in any 12 month period and occurs in 98% of patients. Ulcers may be multiple or single, are usually painful and, depending on their severity, heal in 7 – 21 days. Although this is the most frequent manifestation it may not be the initial one, and other features may be present for a considerable time before the development of mouth ulcers.

Genital Ulceration: again this is recurrent and painful and occurs on the scrotum, less commonly on the penis, in the male and on the vulva and in the vagina in the female patient, in about 80% of patients.

Skin lesions: these include acne-like lesions, red tended swellings known as *erythema nodosum*, and occasional ulceration.

ii) **Eye involvement** occurs in up to 50% of patients: This depends on inflammation of the front of the eye around the iris, known as *uveitis*, and of the retina, known as *retinal vasculitis*. The former usually responds to simple treatment (such as eye-drops) but the latter is more serious and occasionally may lead to blindness. Eye involvement is most severe in young men with Behçet's Syndrome.

iii) **Arthritis or arthralgia** (joint pains): this may occur in about 50% of patients. Some patients may experience joint pains only without any outward evidence of joint inflammation. However when a true arthritis is present it is inflammatory as indicated by joint pain, stiffness, swelling, warmth and tenderness. The knees ** are most commonly affected followed by ankles, small joints of the hands and wrists and least commonly the shoulders and hips. The lining of the joints (*synovium*) has been shown to be inflamed (synovitis) but the appearance under the microscope is different from other inflammatory arthritides, eg rheumatoid arthritis. Permanent bone damage within the joint may occur both on x-rays and at surgery but rarely.

There has been considerable debate over the years whether the joints of the spine are involved in the inflammatory process (*spondylitis*) and although some cases have been described the consensus of opinion is now that spondylitis is not a part of the arthritis of Behçet's Syndrome.

2) Other features include:

i) **Thrombophlebitis:** inflammation of veins most frequently in the lower legs resembling a deep vein thrombosis.

ii) **Arteritis:** inflammation of arteries which may swell at points of weakness (*aneurysms*) or rupture causing bleeding into the tissues.

iii) **Pulmonary lesions:** arising from inflammation of the pulmonary arteries

iv) **Central Nervous System involvement:** due to inflammation around veins in the brain and thrombosis of large veins (known as dural sinuses) inside the skull.

v) **Gastrointestinal ulceration:** this is most frequent in the Far East and the ulceration usually involves the colon (the large intestine) which may bleed or perforate.

On this basis a high **index of suspicion** will be raised if the patient presents with two or three possible manifestations such as:

- i) Painful recurrent mouth ulcers and genital ulcers, OR
- ii) Painful recurrent mouth ulcers and an inflamed eye, OR
- iii) Painful recurrent mouth ulcers, genital ulcers and an inflamed eye, OR
- iv) Painful recurrent mouth ulcers, genital ulcers and inflamed joints, OR
- v) Painful recurrent mouth ulcers, genital ulcers and skin lesions, OR
- vi) Inflamed eye(s) and joints and skin manifestations, OR
- vii) Inflamed eye(s), thrombophlebitis and skin manifestations, OR
- viii) Painful recurrent mouth ulcers, an inflamed eye and a positive family history

These are not definite indications of the diagnosis and many other examples could be listed. They are situations in which the diagnosis is suspected and further advice may be sought.

Dr Colin Barnes, April 2008