



# BD NEWS

NEWSLETTER FOR BEHÇET'S DISEASE

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## New Dates for Antalya 2004

With the Berlin conference now history, we are looking forward to the new international conferences: 2004 in Antalya, Turkey and 2006, in Lisbon, Portugal.

PLEASE NOTE THAT THE DATES FOR THE ANTALYA CONFERENCE HAVE CHANGED FROM 24-27 OCTOBER 2004 TO 27-31 OCTOBER 2004.

This was due to the recent change in the dates of the American College of Rheumatology Meeting from 7-12 October 2004 to 16-21 October 2004. As organizers we felt that these new dates would give too little "to be back home time" to our colleagues planning to attend both meetings.

Scientific highlights of the Berlin

meeting presented by H. Yazici can be found on Rheuma21 ([www.rheuma21st.com](http://www.rheuma21st.com)) and by I. Fresko in Clin Exp Rheumatol 2002;20 (Suppl26) S.59-64), in the second special and peer-reviewed supplement of Clinical and Experimental Rheumatology devoted to Behçet's disease and familial Mediterranean fever. A brief summary of the patient meeting in Berlin by B. Seaman can be found in this issue. We also understand the proceedings for Berlin, to be published by Kluwer are being prepared.

Editors



J. Crespo

## Epidemiology of Behçet's Syndrome in Portugal

By Jorge CRESPO\*, José VAZ PATTO\*\*, Rui PROENÇA\*\*\*, Portuguese Study Group for Behçet's Disease (Portugal)



J. Vaz Patto

Since January 1993, the National Study Group from Portugal brings together physicians from different specialties, which share a common interest in this clinical syndrome. As a result, it was possible to obtain a population of 241 patients from whole the country (121 males/120 females, average age = 38,6 ± 11,8 years), with diagnostic criteria defined by the ISGBD. With a population of almost 10 million people, this stands for a prevalence of 2,5 / 100.000.

The following can be said about BS in Portugal: BS is a condition of early onset, usually between 2nd and 4th decades (average age of onset from first symptom = 25,8 ± 11,1 years). Recurrent oral ulceration, present in all our patients, is the first manifestation of disease in 78% of cases. Ocular involvement is the most disabling, being observed in 74 % of cases. From these, 80 % presented bilateral involvement, with any kind of permanent visual impairment in 52 %. Anterior uveitis was found in 61% of cases, posterior uveitis in 40%, panuveitis in 36% and retinal vasculites in 31%. Cutaneous findings were observed in 82 %, with pseudofolliculitis found in 62 % of the total and erythema nodosum in 46%. Genital ulcers were observed in 80 % of cases. A positive pathergy test was seen in 40 %. Joint manifestations, not a diagnostic criterion, were the first clinical finding in 7 % of cases. As a whole, 85 %

of patients showed some joint involvement. Articular pain was mechanical in 46%, inflammatory in 42% and mixt in 12%. It was peripheral in 83% and axial in 12%; polyarticular in 97% and monoarticular in only 2% of cases. Other manifestations such as vascular problems were present in 26% of cases (superficial thrombophlebitis in 18%, deep venous thrombosis in 7% and arterial aneurysms in only 1% of patients). Central nervous system was diseased in 22%, with headache as the principal complaint in 12%. Gastrointestinal complaints were found in only 3%. The clinical diagnosis of BD usually takes a long time (7,0 ± 7,5 years)

from the time onset of first symptom. Initially there is an inevitable delay in diagnosis of 4,0 ± 4,7 years (range: 0-21), the time period during which the patient develops the necessary clinical manifestations to make up the diagnostic criteria. This could be observed among 95 of our patients among whom it was possible to ascertain the age of onset for each symptom (Fig. 1).

Recurrent oral ulceration is a frequent finding in the family members of BD patients, being observed in 42 % of first and second-degree relatives. HLA B51 is found positive in 60 % of cases, defining a relative risk of 8,5 for our country.

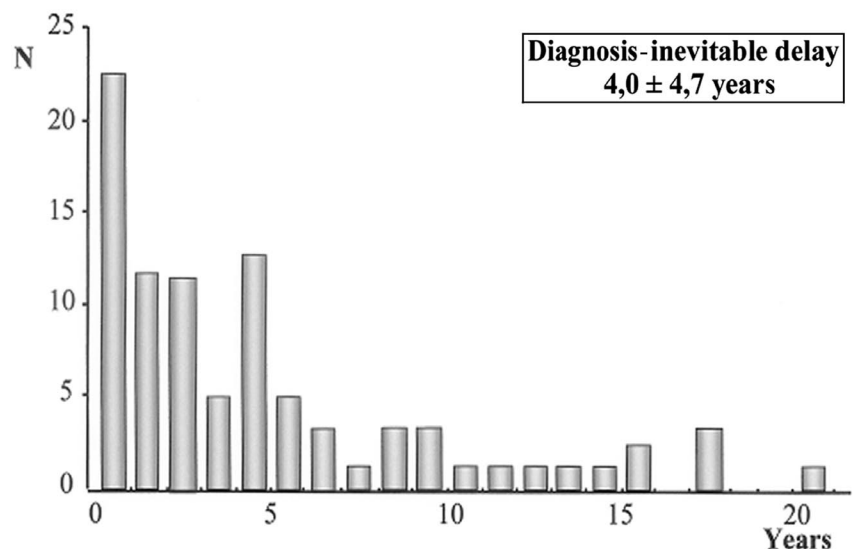


Figure 1. The time elapsed between the time of onset of the first symptom to the time fulfilling the diagnostic criteria among 95 Portuguese patients with Behçet's syndrome

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I. Krause

# Behçet's Disease in Israel

By Ilan KRAUSE & Abraham WEINBERGER (Israel)



A. Weinberger

Ethnic origin is one of the factors that may modulate the prevalence and expression of BD. It was previously reported that BD has diverse clinical expression in various geographical areas, e.g. the pathergy reaction is considered highly sensitive and specific for BD in patients from Turkey and Japan yet is frequently negative in patients from Western countries, or gastrointestinal involvement, which occurs in about one-third of patients from Japan, but rarely in Mediterranean countries. The expression of BD in Israel is largely influenced by the heterogeneous ethnic distribution of the population.

## Genetics

The prevalence of HLA-B5 among Israeli patients with BD ranges from 53%-84% according to various series. Among the HLA-B51-positive patients, B\*5101 was found to be the predominant allele, identified in 62% of all BD patients and 78% of Jewish BD patients. HLA-B\*5108 and B\*5104 alleles were identified in 23% and 15% of B51-positive BD patients, respectively. The HLA-B\*5201 allele was identified in all HLA-B52-positive patients and controls. The MIC-A A6 allele was found to be significantly more frequent in Arabic but not in Sephardi Jewish patients. In stratification analysis of the Arab subgroup on the confounding effect of MIC-A A6 on HLA-B51 association and vice versa, BD was distinctly associated only with HLA-B51. A possible association between BD and FMF in Israeli patients was recently studied. The prevalence of BD was reported to be higher in FMF than in worldwide populations with a predominance of BD. FMF-BD cases and FMF or BD controls were comparable in most demographic, clinical, and laboratory aspects studied. The severity of FMF was of intermediate grade and the extensiveness of BD was limited. It was suggested that BD should be included among the vasculitides complicating FMF. In a recent study, however, BD and FMF were found as two separate entities that have only a mild trend toward a higher-than-expected association. Nonetheless, there was no mutual effect of FMF on BD or vice versa.

## Epidemiology and Demographic Aspects

Studies on the prevalence of BD among various Israeli populations are still

lacking. In a recent study performed in an Israeli Arab town, a prevalence of 12/10,000 was found, that concurs with findings in other Mediterranean and Asian countries. BD was observed to occur earlier in males than in females. The first manifestation of BD in children was almost exclusively in the form of oral ulcers, while older patients had a large proportion of non-oral aphthosis as their first disease manifestation. Interestingly, disease onset at an older age was positively correlated with increased disease spectrum. Juvenile BD in Israel is probably common, and is frequently associated with HLA B5 positivity. The disease seems to run a less severe course in children than in adults. In a study comprising 100 Israeli BD patients, disease expression was compared between Jewish and Arab patients, and among Jewish ethnic groups. There were no statistically significant differences between Jewish and Arab patients with respect to male:female ratio, prevalence of HLA-B5, age at disease onset, or disease duration. Disease expression and severity score were also similar in the two groups, but the Arab patients had a higher rate of posterior uveitis. Among the three largest Jewish ethnic groups, patients of North African origin had a significantly higher rate of ocular disease, mainly in the form of anterior uveitis. These patients also had higher rates of arthritis, overall vascular disease, deep vein thrombosis, and neuro-Behçet, without reaching statistical significance. The disease severity score in this group was significantly higher compared to the other Jewish ethnic groups, implying that the disease in Israeli Jewish patients is most severe in those originating from North African countries.

## Clinical Manifestations and Associations

We have studied the expression of recurrent aphthous stomatitis (RAS) in Israeli BD patients, and the correlation between major or minor RAS and systemic expression and severity of the disease. The frequency of major RAS was significantly higher compared with a control group of patients with idiopathic RAS. The BD patients with major RAS had significantly more relapses of oral ulceration in a year, higher numbers of oral ulcers per relapse, and longer duration of aphthous episodes, compared with patients with minor RAS. Oral ulcers also appeared at a significantly younger age in patients with major than with minor RAS. However, the systemic expression of the

disease, as well as the disease severity score, were similar in patients with major and minor RAS. The results of this study indicate that major RAS is common in Israeli patients with BD, and is associated with a more severe, repeated and prolonged oral disease. Nevertheless, the presence of major RAS in BD does not predict a more severe systemic illness. A positive pathergy reaction was documented in high rates among Israeli BD patients, yet was not associated with an increased risk for specific mucocutaneous or systemic manifestations of the disease, and probably does not predict a more severe disease course. The main patterns of BD expression in Israeli patients were evaluated applying factor analysis. Five factors were derived, which accounted for 69% of the variance of the matrix. Factor 1 represented the association between folliculitis and genital ulceration; Factor 2 represented the association between papulo-pustular rash and gastrointestinal symptoms; Factor 3 represented the inverse association between superficial vein thrombosis and erythema nodosum; Factor 4 represented the correlation between deep vein thrombosis and neuro-Behçet and Factor 5 represented joint disease. No difference was found between males and females in relation to factors 1, 2 or 5, but males had higher scores in factors 3 and 4. Factor 3 was significantly higher in patients with HLA-B5 compared to HLA-B5-negative BD patients. Factors 1 and 3 were higher in patients with adult onset of the disease while factor 2 was higher in patients with childhood-onset BD.

The prevalence of thrombophilic factors known to induce intravascular clotting and their relationship with thromboembolic complications was assessed by several groups. A significant number of patients had elevated levels of anti-cardiolipin Abs but they were not associated with venous or arterial thrombosis. Similarly, no correlation was found between any thrombogenic factor and other clinical manifestations of the disease.

## Autoantibodies and Animal Models

We recently reported the presence of  $\alpha$ -tropomyosin antibodies in several patients with BD. Our studies in rats showed that immunization with  $\alpha$ -tropomyosin may induce a disease resembling Behçet, namely arthritis, uveitis and

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# The 2<sup>nd</sup> International Convention for Patients with Behçet's Disease

By Barrie SEAMAN (UK Behçet's Syndrome Society)

The 2<sup>nd</sup> International Convention for Patients with Behçet's Disease was held in Berlin, 27-29 June 2002. Thanks to the kind co-operation of Prof Zouboulis and the ISBD, the Convention was able to share facilities and some joint events with the 10<sup>th</sup> International Conference held at the same venue on the same dates.

The meeting was attended by 35 delegates from six countries; Denmark, Germany, Japan, Jordan, Portugal and UK, who enjoyed a varied programme of presentations and lectures, together with excellent social events. Delegates attended at their own expense though some received assistance from their own country's support group. The opening day included patient contributions on their varying experiences of health care and treatment around the world and, in the afternoon, presentations on the work of support groups. A business meeting of support group representatives was held later and a committee elected to progress work towards a larger and better attended convention in Turkey in Oct 2004.

The second morning was organised by the German Support Group and described many features of their health system and the way in which it affected Behçet's patients. It included an address by Dr Klaus Fritz, dermatologist, and Adeltraud Müller, leader of the recently formed Selbsthilfegruppe "Leben mit Behçet". Later, after lunch, the Convention President, Prof Shigeaki Ohno gave a lecture on 'The role of genetics in Behçet's Disease and immunological features'. Then, for the first time at a patients convention, a 'question and an-

swer' session was held with a Medical Panel composed of Prof Susan Lightman (Chair), Dr Richard Powell and Dr Fritz. Day 2 was concluded with a joint session with the Medical Conference called 'Patients inform the ISBD'. There were four patient presentations to the doctors and researchers with introduction and summing up by the ISBD President, Prof Colin Barnes. The evening entertainment on the second day was a memorable visit to the Komische Oper, Berlin for a performance of Verdi's *Traviata*.

On the final day delegates received a moving lecture from Dr Wafa Madanat about the situation for patients in Jordan and the work and aims of their support group. Following group photos the Convention was formally closed with the wish that we meet again in 2004 in Turkey. A very enjoyable congress was completed in the afternoon with a sightseeing coach tour of Berlin.

## IMPORTANT ANNOUNCEMENT

You can now visit The International Society for Behçet's Disease Website at:

<http://www.behcet.ws>

Please contact Prof. Yalçın Tüzün (the Webmaster) at:

[yalcintuzun@superonline.com](mailto:yalcintuzun@superonline.com)

for any business and inquiries related to the website.

## Patient's Letter

Mr. Refaat EL-AGROUDY (Egypt)

I would like to introduce myself as an old Egyptian patient 60 years old, who suffered from Behçet's disease. I am a chemist, and married since 30 years. I have 3 childrens, Khalid, a 29 years old engineer, Haytham, a 28 years old army officer (MARTYR), Reem who is 26 years old and she is married. My small family is all in good health, with no history of my disease.

**Past History of My Illness:** In 1975, I had my first attack with redness in the left eye, which got inflamed and swollen. The diagnosis of Behçet was determined during that period. I remember that during that period in the 70s, there were about 25 patients diagnosed with this disease in Cairo. The right eye developed a very sever attack in 1980, from which it did not recover. The right eye developed a high intraocular pressure, and within few months, this eye had become totally blind. The left eye started to develop a slight cataract, which led me in 1986 to undergo an operation.

**Report:** During the attacks of Behçet's disease, I received treatment for 10 years from 1075 to 1985 as follows:

-In Egypt and in the UK, I was treated with corticosteroids as tablets and eye drops and with Atropine eye drops. Each attack was treated at least for 2 weeks.

-In France, the treatment was more effective with corticosteroids injections in the conjunctiva with Cenaktin injection (for activation of cortisone secretion

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## Behçet's Disease in Israel

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dermatitis. This experimental model may help in understanding the pathogenesis of BD, and serve as an animal model for new treatment modalities. We also reported recently, for the first time, on a strong association between anti-*saccharomyces cerevisiae* Abs (ASCA) and BD. ASCA were not linked to a specific clinical manifestation of BD nor with a more severe disease course.

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C. Vasconcelos

# Patient Association for BD Patients in Portugal

By Cláudia VASCONCELOS & Lucinda CALEIRA (Portugal)

As a patient organisation in Portugal our approach to Behçet's disease has considerably changed since the Berlin conference. The conference was a privileged opportunity to achieve several goals aimed for a long time, because the ideal conditions for communicating were met. The meeting with patients from different countries such as England, Germany, Japan, Denmark, other acquaintance with other organizations and associations of patients from those and other countries made us aware of our need and showed us it was the right moment to the create a Portuguese Support Group for people with Behçet disease.

Therefore, with the helpful and generous cooperation of some Portuguese doctors, Jorge Crespo and José Vaz Pato, indispensable for our association, and thanks to the international cooperation, mostly from the English Patient Association, the roots of the Portuguese Association for Patients with BD were established.

At this very moment, different ways to establish contact with the patients are

already available:

- ☐ A phone support line  
00 351 936022796
- ☐ An internet site at  
<http://behcetportugal.com.sapo.pt>,
- ☐ An e-mail address at  
[behcets@netcabo.pt](mailto:behcets@netcabo.pt).
- ☐ Leaflets with general information about the Behçet Disease, are about to be distributed in order to reach people with non internet connection.

We are also preparing new leaflets with more specific questions like the effect of Behçet Disease in the Eyes, Behçet Disease and the Nervous System and others.

The goals of the association are being developed and we are open to different invitations and requests to talk with people interested in Behçet Disease.

Among our activities we were invited to the International Days of the Portuguese Institute of Rheumatology, held in December 2002 in Lisbon. We felt honoured since the journeys had contributions of well-known, prestigious, national and international personalities, connected to the Behçet Disease research.

The next international conferences for Behçet's Disease are already confirmed. They will be held in 2004 Antalya, where we hope to be represented, and in Portugal in 2006 where our association will play a very active role.

We are looking forward to the conference in our country because we expect to have a large number of Behçet patients and theirs relatives to attend so that they can understand how a rare disease like Behçet develops and be a everyday problem for some of us.

Finally we are very thankful to the International Behçet Society for its decision to have the 2006 conference in our country.

## Patient's Letter (Continued)

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from the superarenal glands). Also atropine eye drops were applied.

-In Russia, I received treatment similar to that in Egypt and in the U.K. in addition to eye drops formed of diluted solution of honey.

-In 1980, I had glaucoma in the right eye which ended in blindness after 5 months. I think that there was a relation between the past treatment with corticosteroids and contamination, which happened after the operation, and led to the other 3 operations which followed it.

Since then, there is no Behçet's attacks in the eye but sometimes, an oral ulcer might develop. 3 things helped me to survive with all these disease problems;

\* First, I deeply believe in God and I am sure God is giving me strength and help.

\* Second, my personal will and internal power helped to face such experience.

\* Third, I followed the instructions of my doctors to the letter.

### Present status of my illness:

1. Now, I am suffering only from ocular troubles; complete blindness of the right eye and diminishing vision in the left eye (6/12 with glasses).

2. My daily program is very important to keep myself always in a good shape, so, I have daily small frequent meals full of fresh vegetables, fruits (to have vitamins and minerals in natural form), red meat (of young age animals) fresh fish, small amounts of food that contain fats, carbohydrates and have daily big amount of water and fresh juice and keep away from candy and spicy foods. This my dietary habits which is running side by side with my daily 1 hour of walking, keeping away from smoking and air pollution as much as possible by enjoying weekends regularly and having 1 month summer vacation by sea side where fresh air and good climate are available.

At the present time, I have treatment just for arteriosclerosis and hypertension. Drawing your kind attention that I am still working as a chemist beside being the head of a political socialist party.

Finally my recommendation for doctors is to go on constant researching to

find earlier and better methods for diagnosis and wording on trials to have effective treatment, and for patients, they have to believe in God and to be sure that strong will must lead to success and also I advise them to keep following investigations and follow doctors' advices. I stress on the help provided by families to patients that give hope and relief to them.

I hope that doctors will develop more effective treatment for this disease and I hope the best recovery for all Behçet's disease patients.

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