

## The 10th International Conference on Behçet's Disease

*By Christos C. ZOUBOULIS (Germany)*



The 10th International Conference on Behçet's Disease is being held in Berlin on 27 -29 June 2002. It is the first such congress being under the auspices of the International Society for Behçet's Disease (ISBD). The Deutsches Register Morbus Adamantiades-Behçet e.V. and the Deutsche Forschungsgemeinschaft (DFG) are also supporting the conference.

A total of 199 scientific abstracts have been submitted from 24 different countries among which are Turkey (45), Germany (21), United Kingdom (20), Iran (18) and Japan (14) the number submitted from each country been shown in parenthesis. The abstracts were have been undergone peer review (H. Borgmann, G. Gross, W. Keitel, R. Keitzer, W. Kirch, I. Kötter, P.K. Kohl, L. Krause, F.R. Ochsendorf, H.-H. Peter, U. Pleyer, J. Reichrath, J. Sieper, R. Stadler, U.

## Behçet's Disease: The USA Scene



*By Kenneth T. CALAMIA (USA)*

Is the yellow brick road of the USA an extension of the Silk Road? What can we learn by examining Behçet's disease in an area where the prevalence is low? Does Behçet's disease even exist in the USA? I hope to examine these and other issues in this article.

I use the phrase "yellow brick road", from the famous American novel *The Wizard of Oz*, to mean travel and mobility in the USA. In the centuries when the silk road may have been responsible for the spread of the susceptibility genes or environmental agents responsible for the disease we now call Behçet's, travel was restricted, for a variety of reasons, along certain paths. These restrictions that tied people together no longer exist and, with modern travel, disease factors are no longer contained. Cultural and ethnic barriers are also becoming less restrictive as our globe shrinks. It is no longer tenable to think that a disease will remain localized to one region. Some may believe that the identification of Behçet's disease in the USA is as much of a fantasy as that found in Alice's travels, but I believe that our experience suggests that Behçet's disease is indeed alive and well in our country.

It may be that the study of Behçet's in an area of low prevalence, with a mixed gene pool from many countries, will serve to define the disease in a way that highlights critical essences and identify important variations. Like the variations in the clinical features, epidemiological characteristics, and genetics of the disease recognized in populations and ethnic groups near to the Silk Road, there seem to be differences in US patients, as there are in European patients, with this disorder. We see more females than males with the disease, less severe disease, generally, with less severe eye disease. Our patients are more likely to have central nervous system disease. Chronic pain and fibromyalgia, little studied as to the possible

Wollina, M. Zeitz, M. Zierhut). The results are under evaluation and the final program will be released shortly.

We now know the outcome of the young investigator awards. These are 500 US dollar travel grants given by the ISBD to those investigators aged 35 or less. After a stringent and blinded scientific peer review (H.Yazici, D. Haskard, S. Lightman and F. Kaneko) the following 8 investigators were awarded these bursaries out of a total of 31 applicants:

1. E. Chang (USA) for a survey of rheumatologists in the United States and Canada about the use of Pentoxifylline for mucocutaneous ulcerations in Behçet's patients.
2. J. Karasneh (UK) for whole genome screening of multicase families with Behçet's disease.
3. G. Kaymak (Turkey) for studying autonomic nervous system involvement in Behçet's disease.
4. N. Köktürk (Turkey) for studying CCR5 expression in Behçet's disease.
5. N. Molineri (France) for genetic studies indicating a Mendelian mode of transmission in the paediatric Behçet patients.
6. G. Lawton (UK) for work related to designing a disease activity index.
7. M. Treusch (Germany) for studying the influence of interferon-alpha on lymphocyte subpopulations.
8. V. Yilmaz (Turkey) for studying CXCR-2 polymorphisms in Behçet's disease.

The above will receive their bursaries at a special ceremony during the meeting.

The meeting opens on the afternoon of Wednesday 26th with business meetings. Starting the morning of the 27th and ending the late afternoon, of Saturday the 29th, there is a full scientific programme with such distinguished invited lectures as R. Winau (Germany), S. Beck (UK), P. Martus (Germany), R.J. Powell (UK), M. Bagglioni (Switzerland) and M. Bullinger (Germany). Other keynote lectures are also being planned based on the submitted abstracts.

The 2nd International Convention for Patients with Silk Route Disease (Behçet's Disease) will run parallel with the scientific meeting at the same venue. A formal joint session with the scientific meeting is scheduled for Friday, June 28, 2002.

The congress also has a full social program. A Get Together Party is being planned for the evening of Thursday, June 27, and a Cultural Event for the

cultural, psychological, and disease-related factors, appear to be a growing part of the disease in our country. One concern that we may not be dealing with the same Silk Road disease is the differences in the genes of our patients. O'Duffy has looked for HLA-B51 and for other Class I or Class II gene products in typical US Behçet patients and found no excess. More recently he has identified an association with HLA-DRB1\*04, present in 50% of 41 US patients of northern European extraction. Hopefully, as we learn all of the genetic influences to this disease, we may be able to recognize a common thread in Behçet patients worldwide, including US patients. Until that time, we hypothesize that disease associated gene is associated with different HLA genes among various ethnic groups, and that disease expression is dependent on this genetic substrate, similar to the effect of gender.

The prevalence of Behçet's disease in the US appears to be similar or even higher than that in some European countries. While few studies have been done, our estimate of the prevalence is 6.6 cases/100,000, from a population-based study of Rochester, Minnesota, settled largely by northern Europeans. What this means is that the disease is rare and, clearly, other disorders responsible for similar symptoms and findings must be excluded before a diagnosis is made. We have had little confidence in the sensitivity of the pathergy test we have underutilized it. However, we have found a positivity rate of 30% in US patients. Furthermore, the application of the "diagnostic criteria" for the diagnosis of the disease in individual cases will miss some patients. We found that our cases met the International Study Criteria in only 76% in a series of 164 US cases. The Classification Tree criteria were more sensitive, but likely would be less specific if used for diagnosis. The presence of skin lesions was an important finding in the diagnosis of US patients, supporting the suspicion that the disease is milder in our population. The presence of gastrointestinal disease, typical vascular lesions, central nervous system disease, and arthritis must be taken into consideration in the diagnosis. We do not hesitate to make a diagnosis of Behçet's disease when the disease is likely, in patients who lack genetic and ancestral ties to the Silk Road, when other disorders can be confidently excluded.

In one an early report from the United States in 1946, New York dermatologist Helen Ollendorff Curth, who had met the man, was one of the first to refer to this affliction as "Behçet's Syndrome". Numerous US cases and small series have appeared since that time. In the few larger series the threat of ocular disease, the typical findings in CNS disease, and treatment of these serious manifestations of Behçet's disease have been reported. We have favored the

evening of Friday, June 28. The Congress Dinner is scheduled for Saturday evening, June 29, 2002.

## **BD NEWS**

**EDITOR:** HASAN YAZICI, MD

**CO-EDITOR:** YALÇIN TÜZÜN, MD

**ASSOCIATE EDITORS:**  
SHIGEAKI OHNO, MD  
TOMOMI NISHIDA, MD, PhD

**ADDRESS:**

Department of Rheumatology,  
Cerrahpasa Medical Faculty,  
Istanbul University,  
Cerrahpasa, Istanbul, 34303, Turkey  
E-mail: hyazici@attglobal.net  
Fax & Tel: +90 212 588 48 83

use of chlorambucil for serious ocular and central nervous system disease, based on our uncontrolled experience and confidence in this agent. Our most recent experience with 164 patients with Behçet's disease, seen over 13 years was reported at the 9th International Congress in Seoul and published in the proceedings of that meeting. Underscoring the morbidity of the disease, 51% of the patients were affected with uveitis and retinal vasculitis was found in 20%. Large vessel disease was present in 23% of our cohort.

The American Behçet's Disease Association has been a valuable resource for US patients with the disease. Because of the rarity of Behçet's in our country, patients can find the names of interested and experienced physicians and a wealth of useful information. Bi-annual meetings are held for patients with experts in the field and adequate time to address individual concerns.

### **Selected References**

1. Moore SB, O'Duffy JD. Lack of association between Behçet's disease and major histocompatibility complex class II antigens in an ethnically diverse North American Caucasoïd patient group. *J Rheumatol* 1986; 13: 771-3.
2. Calamia KT, Davatchi F. Clinical characteristics of United States patients with Behçet's disease. In *Behçet's disease*. Edited by D Bang, E-S Lee and S Lee. Seoul, Design Mecca Publishing Co., 2000, pp 48-51.
3. Calamia KT, Davatchi F. Analysis of the sensitivity of diagnostic criteria in United States patients with Behçet's disease. In *Behçet's disease*. Edited by D Bang, E-S Lee and S Lee. Seoul, Design Mecca Publishing Co., 2000, pp 121-4.
4. Balabanova M, Calamia KT, Perniciaro C, O'Duffy JD. A study of the cutaneous manifestations of Behçet's disease in patients from the United States. *J Am Acad Dermatol* 1999; 41: 540-5.
5. O'Duffy JD, Robertson DM, Goldstein NP. Chlorambucil in the treatment of uveitis and meningoencephalitis of Behçet's disease. *Am J Med* 1984; 76: 75-84.
6. Zouboulis CC, Kietel W. The history of Adamantiades- Behçet's disease. Submitted 2002.



# Behçet's Disease Among Children

By Isabella KONÉ-PAUT (France)

---

From time to time Behçet's disease is observed among children. Cases occurring before 16 years of age have been mentioned for the last twenty years mainly as case reports. The first series of children with Behçet's disease emerged from the sixth international conference in Paris. In 1998 we have reported an international collaborative study of 86 cases. In recent years, the early manifestations of Behçet's disease have been increasingly studied however the delineation of these patients so called "paediatric" or "juvenile" still needs to be clarified.

## Epidemiology

Very little is known about the frequency of Behçet's disease among children. The frequency of patients with onset of symptoms before age of 16 varied from 3 to 24% in epidemiological studies coming from different parts of the world: for example, the German registry recorded 196 patients fulfilling the criteria of the BD classification tree in whom 13 only (6.9%) had "complete symptom complex" developing before or at 16 years of age. The Korean registry reviewed 1155 patients selected by the revised Shimizu classification: 30 among them completed their disease before 20 years (2.6%) and 8 before the age of 9 years (0.7). A French nation-wide survey in 1992 identified 17 children meeting the international criteria before 16 years estimating its prevalence at 1/600 000. We updated our survey during the year 2000 and identified 38 additional paediatric cases [total=55] reflecting increase physicians awareness of this disease.

## Clinical Features

The clinical features of definite BD in children resemble those seen in the adult however symptoms among children are frequently incomplete and not specific. The disease may start at any age including the first months of life and affects boys and girls equally. Recurrent oral ulceration is the leading symptom at onset. Other constitutional symptoms: bouts of fever, fatigue and abdominal pain may also be present but are usually underestimated. At this stage BD must be distinguished from other inflammatory periodic syndromes [FMF, Hyper IgD, Crohn's disease] and from congenital defects of mononuclear cells [cyclic neutropenia, chronic granulomatous disease]. Genital ulcers [30 to 90%] are less frequent than in adult and more likely observed after puberty. Erythema nodosum and acneiform lesions [45 to 90%] are predominant in Turks and Israeli patients. Skin hypersensitivity [15 to 60%] is uncommon in children from western countries. Neurological features: encephalomyelitis, aseptic meningitis and cerebral thrombosis may be the initial presentation of the disease. Their frequency varied from 15 to 40% and was higher and more severe in French and Saudi Arabian patients in our international study. Uveitis is less frequent than in adults [45% versus 60-80%] however its course is serious with 25% risk of blindness. Vascular complications are uncommon and thrombosis does not exceed 10% in any paediatric series. However multiple vein involvement and pulmonary aneurysm rupture are the leading causes of death in this age group in whom the mortality rate reaches 5%.

## Familial Aggregation

The familial occurrence of BD has been reported higher in patients from endemic areas such as Turkey, Korea and Tunisia. We have recently demonstrated that the recurrence-rate of BD was higher in parents and siblings of paediatric patients than in non-paediatric ones; in addition, the mean age of fulfilling the diagnostic criteria in familial cases was significantly lower than in sporadic

cases.

## Course and Prognosis

Both sex and ethnic origin influence the course of Behçet's disease in children. In most reports boys experienced a more severe course especially in terms of ocular and vascular complications. Patients from Eastern countries had predominant mucocutaneous features and pathergy phenomenon whereas Western patients had more digestive and neurological manifestations. Longitudinal studies are necessary to determine if the age of onset influences the overall prognosis of BD.

## Treatment

All treatments used for adult BD have been employed in paediatric patients following same schemes of prescription. However hard data about drug use in paediatric BD is very limited. Specific problems are assessment of disease severity and drug toxicity at this young age. Indeed such treatments interfere with growth rate and fertility. Guidelines for precise drug indications, doses and duration of treatment are needed for more effective and safer treatment of our paediatric patients with BD.

## Selected References

1. Koné-Paut I, Yurdakul S, Bahrabri S, et al. Clinical features of Behçet's disease in children: an international study of 86 cases. *J Pediatr* 1998; 132: 721-6.
2. Koné-Paut I, Geisler I, Wechsler B, et al. Characteristics of familial aggregation in Behçet's disease: High frequency of BD in siblings and parents of paediatric probands. *J Pediatr* 1999; 135: 89-93.
3. Zouboulis CC, Kötter I, Djawari D, et al. Epidemiological features of Adamantiades Behçet's disease in Germany and in Europe. *Yonsei Med J* 1997; 38: 411-22.
4. Gül A, Inanç M, Öcal L, Aral O, Koniçe M. Familial aggregation of Behçet's disease in Turkey. *Ann Rheum Dis* 2000; 59: 622-5.
5. Fresko I, Soy M, Hamuryudan V, et al. Genetic anticipation in Behçet's syndrome. *Ann Rheum Dis* 1998; 57: 45-8.
6. Bang D, Han Yoon K, Chung HG, et al. Epidemiological and clinical features of Behçet's disease in Korea. *Yonsei Med J* 1997; 38: 428-36.



## Behçet's Disease: Patient's Issues

*By Tomomi NISHIDA, MD, PhD (Japan)*

---

It's my great pleasure to describe the relationship between patients, physicians and other medical personnel centred on Behçet's disease. We had an opportunity to hold the first international convention for patients with Silk Road disease (Behçet's disease) at Hayama, Japan in 2000. Prof. Shigeaki Ohno of Hokkaido University, with whom I used to work at Yokohama City University, had been thinking how the patients with Behçet's disease would be able to get together, internationally. The 9th international Behçet's disease conference was held at Seoul, Korea and we tried to hold the first convention alongside the conference. I had assisted Prof. Ohno in all activities and I really think that it has been a great opportunity for me to learn many things.

Now, I would like to introduce myself. I am an ophthalmologist at Yokohama City University. My father is a patient with Behçet's disease and he lost his visual acuity when he was 30 years old, after 5 years of disease onset.

My situation is rather unique, because I am both a patient relative and a physician.

The estimated number of Japanese patients with Behçet's disease is about 16,000. There are two patient associations for Behçet's disease in Japan. One is in Hokkaido. The other association's main office is in Tokyo and its branches are located in many places in Japan except for Hokkaido, Shikoku and Kyushu districts. Membership to either organisation is totally voluntary.

For the 2000 patient convention we first started with an organising committee and prepared a preliminary programme. When we asked Prof. Ohno to become the head of this committee there was some discussion as to whether a patient or a physician should head such a committee. We finally decided that a physician should assume this position also taking into consideration such issues as being versed in English and the use of the Web. I personally think that appointment of Prof. Ohno, as the president of this committee has been helpful not only for the Japanese patients but also to patients at other parts of the world.

The organisation for the 2000 Patient Convention has thought me many things. In preparing for such a convention I would like to propose several points to keep up a good communication.

1. To be in constant communication with all parties involved;
2. To stay away from "strong" opinions.
3. To constantly keep a mind why I am work for patients; and finally
4. To refrain from considering a successful organisation and completion of a convention a personal feat.

To have regular international conventions is a great opportunity. I sincerely hope that the 2nd International Convention for Patients with Behçet's Disease being held alongside the 10th International Conference on Behçet's disease in Berlin will also be successful. After the first convention, we started a new non-profit organisation (NPO) with patients, medical personnel and volunteers. It is for patients, their families and friends with ocular inflammatory disease including Behçet's disease. A homepage is available its URL is: <http://www04.u-page.so-net.ne.jp/cd5/chatomo/npo/>

With this NPO we aim to address common problems together and help the patients in some

countries where there are severe economical problems. Next, we hope that general public will be more aware of Behçet's disease and the other diseases where aetiology is unknown. We especially aim to emphasise heredity and infection at this web site. More than half of the people that work in this NPO are volunteers that come from many professions. Myrah Kay is a professional singer and she helped in the first convention as a translator. She also put out a CD of her songs with the financial benefits directed to Behçet's disease. She is also tries to help our other activities as much as she can. She is an example and we need many more such examples from around the globe. Our patients would be happy to know that a lot of people are trying to be of help.

I, for one, will continue to help the patients as much as I can. My experience with my father will be, I think, be useful. Finally I introduce a letter to you all from my father, Minoru Nishida.

*Hello from Japan. I work as a president of NPO; ocular inflammation study group. It's a great organisation for me to tie up with a lot of people including patients, their families, doctors and volunteers. I am totally blind due to Behçet's disease, and I do not other patients lose their vision. I hear that the aetiology of Behçet's disease is still unknown, but a lot of research is under way.*

*To overcome Behçet's disease and help the patients in the world, I decided to establish the new NPO. It just started last October.*

*I am sincerely looking forward to get together again in Berlin in June.*

*Thank you very much. - Minoru Nishida, Japan.*



Dr. T. Nishida with father (Mr. Minoru Nishida)

With this issue BD News is starting a new column called "Patient's Letter". I hope many of our patients use this column to talk about their problems, hopes and expectations.

I sincerely hope the Berlin meeting will strengthen the care seeker and the care giver ties.

# A Touch of Confidence

By Jamal TAMIMI (Jordan's Friends of Behçet's Disease Patients Society, Amman- Jordan)

---

Several weeks ago a group of French tourists visited Petra (the ancient Nabatian Rose Rock City in the South of Jordan) as many other tourists do, but the uniqueness of this group was that they were blind. Those blind tourists were eager to touch the beauty of the rose rocks of Petra.

However the reason behind my interest in this group is that they symbolise how I think of Behçet's patients.

Doctors can influence the way that Behçet's patients think about their future, they can clarify the blurred thoughts of this disease, they can explore the possibilities of this disease, doctors can simply lay down the different roads one of which the patients can choose. But these separate roads can't be exclusively a doctor's responsibility. If doctors will only give recommendations for patients and ask them to think about their future, these advises might not be totally understood and the patient can still have indifferent attitudes toward his/her problem. So how could patients themselves play their vital role in drawing the blueprint of their lives? how could they do so during times when they are very much confused about their future.

We hope as Jordan's friends of Behçet's disease patients society to raise these questions during the 10th International Conference on Behçet's disease and hopefully to get some helpful answers.

I believe that increasing co-operation between doctors and patients, as this letter intends to do, and the participation of patients in the doctors conference, could lead to clarifying different aspects and mostly lifting the heavy psychological burden that Behçet's patients carry when looking at life.

We need from doctors to clarify more and more the idea of Behçet's disease, I certainly mean the simple idea of this immune disease and how can it affect our life. We need them to share with us their ideas about the disease course, how it comes and goes.

We need doctors to share with Behçet's disease societies ideas and ways to help their members think positively, hopefully and to grow confidence especially during the worst times.

We as patients do not want to touch the rock like those blind tourists did, but rather we need to grab an experienced hand to touch the rock of confidence.

## **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.