Epidemiology of Adamantiades-Behçet's Disease

Christos C. Zouboulis, Priv.-Doz. Dr. med.

Department of Dermatology, University Medical Center Benjamin Franklin, The Free University of Berlin, Berlin, Germany

Correspondence and reprint requests to:

Christos C. Zouboulis, M.D.

Department of Dermatology

University Medical Center Benjamin Franklin

The Free University of Berlin

Hindenburgdamm 30

D-12200 Berlin

Germany

Tel.: 49-30-84452769 / Fax: 49-30-84454262

E-mail: zoubbere@zedat.fu-berlin.de

Running head: Epidemiology of Adamantiades-Behçet's Disease

Titre courant: L'epidémiologie de la maladie d'Adamantiades-Behçet

Abstract

Adamantiades-Behçet's disease is a universal disorder with varying prevalence, i.e. 80-370 patients per 100,000 inhabitants in Turkey, 2-30 patients per 100,000 inhabitants in Asia and 0.1-7.5 patients per 100,000 inhabitants in Europe and the U.S.A.. Certain ethnic groups are mainly affected, while the prevalence of the disease seems to be strongly dependent on the geographic area of their residence. These data indicate environmental triggering of a genetically determined disorder. The disease usually occurs around the third decade of life, however, early and late onsets (0-72 years) have been reported. Juvenile onset rates from 7 to 44% in different ethnic groups; juvenile disease is less frequent, i.e. 2-21%. Both genders are equally affected. Familial occurrence has been reported in 0-18% of the patients, mostly of Turkish, Israeli and Korean origin, and is increased in patients with juvenile disease. Oral aphthous ulcers represent the onset sign in the majority of patients worldwide (47-86%). Oral aphthous ulcers (92-100%), genital ulcerations (57-93%), skin lesions (38-99%), ocular lesions (29-100%) and arthropathy (16-84%) are the most frequent clinical features; sterile pustules (28-66%) and erythema nodosum (15-78%) are the most common encountered skin lesions. The positivity of pathergy test varies (6-71%) widely in different populations. HLA-B51 is associated with high relative risk for the disease in a small geographic area of the Mediterranean Sea countries and Southern Asia. Diagnosis can be established 2 to 15 years after the onset of the disease. Male gender, early development of the disease and HLA-B51 positivity are markers of severe prognosis (mortality rates of 0-6%).

Résumé

La maladie d' Adamantiades-Behçet est un desordre universel avec une prévalance variée rangeant de 80-370 malades par 100.000 d'habitants en Turquie, 2-30 malades par 100.000 d'habitants en Asie et 0.1-7.5 malades par 100.000 d'habitants en Europe et aux Etats Unis. Il y a des groupes ethniques qui sont affectés préférablement, mais il est évident que la prévalance de la maladie dépende de l'aréal géographique de la résidence. Ces dates indiquent que la maladie soit un desordre qui est déterminé par les gènes et qui est en plus provoqué par des facteurs d'environement. La maladie se manifeste normalement dans la troisième décade de la vie, mais il y a aussi des manifestations précoces et tardives (0-72 années). Le début de la maladie se présente en jeunesse dans 7-44% des cas et montre une dépendance des groupes ethniques. La maladie complète se montre rarement en jeunesse (2-21%). Les deux sexes sont également affectés. Dans 0-18% des cas on a observé une manifestation familiale, surtout chez les malades d'origine turque, israélienne et coréenne; et chez les malades qui montrent les premiers signes de la maladie en jeunesse. Les aphthes orales représentent le premier signe chez la majorité des malades dans le monde entier (47-86%). Des aphthes orales (92-100%), des ulcères genitaux (57-93%), des lésions dermatologiques (38-99%), des lésions oculaires (29-100%) et l'arthropathie (16-84%) sont les manifestations cliniques les plus fréquentes. Des pustules stériles (28-66%) et l'érythème nodeux (15-78%) sont les manifestation dermatologiques les plus fréquentes. La positivité du test de pathergie montre une grande variation (6-71%) en dépendance des différentes populations. L'antigène HLA-B51 est associé avec un risque augmenté pour le développement de la maladie dans un petit aréal géographique de la Méditerranée et de l'Asie du Sud. Le diagnostic de la maladie est èvoquée entre 1 et 15 années après sa début. Le sexe masculin, le début en jeunesse et la positivité de l'antigène HLA-B51 sont des marqueurs pour un pronostic sérieux (0-6% de mortalité).

Adamantiades-Behçet's disease is a rather rare disorder with wide distribution but varying prevalence around the world. It occurs endemically in the Eastern Mediterranean area and in Central and East Asian countries. The spread of these geographic areas along the old silk route and associated immunogenetic data support the hypothesis that the disease was carried over through the immigration of old nomadic tribes (1). Transfer of genetic material or of an exogenous agent may have been responsible for the expansion of the disease.

Prevalence

The highest prevalence of the disease has been reported in Turks living in Anatolia (Northeastern Turkey) with 370 patients per 100,000 inhabitants (2), while the overall prevalence in Asia is 20- to 30-fold lower and in Europe and the U.S.A. more than 150-fold lower (2-16) (Table 1). Single or a few cases have been reported in all continents.

Interestingly, in areas with many ethnic populations, certain ethnic groups were found mainly affected. In Taiwan, all 103 patients diagnosed between 1970 and 1988 were Chinese (17). In Iran, Turks presented a significantly higher prevalence than Caucasians and Semites, while no patient was found among Zoroastrians, who are isolated-living Caucasians (18). In Kuwait, Kuwaiti bedouins were not affected by the disease and there was only a prevalence of 1.58 per 100,000 Kuwaitis which was similar to the involvement of non-Arab populations (1.35 per 100,000 inhabitants), while 2.90 per 100,000 non-Kuwaiti Arabs were affected (12). In Berlin-West, Germany, the disease exhibited a prevalence of 20.75 per 100,000 inhabitants of Turkish origin compared to only 0.42 per 100,000 inhabitants of German origin in the year 1989 (5).

In populations with the same ethnic origin the prevalence of the disease seems to be strongly dependent on the longitude or the latitude of their residence. The prevalence in Turkish populations was calculated to decrease up to 18-fold by increasing distance from

Eastern Turkey towards a western direction (Table 1). On the other hand, the prevalence of the disease in Japan was assessed to decrease up to 30-fold by moving from northern to southern Japan and to be annihilated in Japanese living in Hawaii (10) and in the U.S.A. (11). A few patients of Japanese origin were found in Brazil (19). These data indicate (an) environmental factor(s) which possibly trigger(s) the onset or the development of the disease in genetically determined populations.

Studies comparing epidemiological features of the disease over time have found a throughout increasing prevalence, which may be due to the chronic character of the disease. In Japan, there were 6.3-8.5 patients per 100,000 inhabitants in the year 1972 (20), 8.3-10.0 patients per 100,000 inhabitants in the year 1984 (9) and 13.5 patients per 100,000 inhabitants in the year 1991 (9). In Berlin-West, Germany, 0.65 patients per 100,000 inhabitants were detected in the year 1984, 1.68 patients per 100,000 inhabitants in the year 1989 and 2.26 patients per 100,000 inhabitants in the year 1994 (5). In Rome, Italy, Adamantiades-Behçet's disease was found responsible for 3% of uveitis between 1968 and 1977, but for as much as 7.5% between 1978 and 1987 (21).

Incidence

Data on the incidence of the disease are rather sparing and ambiguous. In Japan, a country with well organized registration of patients with Adamantiades-Behçet's disease, 0.89 new cases per 100,000 inhabitants have been diagnosed in the year 1984 (9). In 1990, 0.75 new cases per 100,000 inhabitants have been registered indicating the reaching of a plateau after a rapid increase of incidence since 1972. In Taiwan, the yearly number of patients who first visited 6 major medical centers from 1979 to 1983 was about 5, while about 14 patients per year presented for the first time from 1984 to 1988 (17).

Age of Onset

The disease usually occurs around the third decade of life, an observation which is independent of the origin of the patients or their gender (5, 7, 9, 12, 13, 17, 19, 22-44) (Table 2). An average age of onset of 31.7 years was recorded in countries of East Asia, 26.5 years in Arab countries, 25.6 years in Turkey, 19.9 years in Israel, 25.9 years in Europe and 28.3 years in Americas. However, cases with early and late onset of the disease have also been reported and the age of onset ranges between the first months of life and 72 years.

The rate of patients with juvenile onset of the disease is varying among the several populations from 44.1% in Israel (32), 30.4% in the U.S.A. (38), 22.0% in Korea (22), 14.1% in Iran (45), 10.7% in patients of German origin (46), 7.6% in Italy (47) to 7.1% in Morocco (48). Juvenile disease is less frequent, its prevalence was estimated in France to be 0.17 patients per 100,000 inhabitants (49). Juvenile disease was reported in 20.8% of patients in Greece (50), 11.3% in Jordan (51), 8.6% in India (26), 6.1% in Turkey (52), 4.8 % of patients with German origin (46), 4.3% of patients in Iran (45), 4.3% in U.S. American patients (38), 3.5% in Morocco (48), 2.3% in Tunisia (53) and 1.5% of patients in Japan (20).

Sex Distribution

In contrast to old Japanese (54) and Turkish (55) reports of an androtropism, the male-to-female ratio drastically decreased in the last 20 years to currently reach an equal rate (9, 29, 56). Similar observations were made in Israel (32, 57) and Germany (5) (Fig. 1). Current epidemiological studies register an approximately equal male-to-female ratio in several populations (Table 2). An androtropism is still observed in Arab countries, while gynaecotropism is evident in some northern European countries and in the U.S.A.. Japanese studies has shown that there is a real increase in the numbers of female patients which is associated with a trend towards a milder manifestation of the disease (9).

Familial Occurrence

Familial occurrence is one of the major epidemiological features of Adamantiades-Behçet's disease. Interestingly, familial occurrence is more frequent in families with Korean (15.4%) than Japanese or Chinese (2.2-2.6%) origin ($p<0.001$, chi square test). Also patients with Arab, Israeli or Turkish origin presented higher frequencies of familial cases (2.0-18.2%) than European patients (0.0-4.5%; $p<0.001$, chi square test) (5, 13, 22, 26, 28, 30, 33, 34, 58-68) (Table 3).

In juvenile patients there is a higher frequency of familial occurrence than in adults, namely 16% vs. 2% in Morocco (69), 18% vs. 2% in France (49) and in Germany 25% vs. 8% (46). Recently, genetic anticipation in the form of earlier disease onset in the children compared with their parents has been identified corroborating the findings of higher frequency of familial cases in juveniles than in adults and the possibility of a genetic predisposition in Adamantiades-Behçet's disease (70).

Onset Manifestations

Oral aphthous ulcers represent the onset feature of the disease in the majority of the patients worldwide (47-86%) (5, 7, 13, 22, 27, 29, 32, 42, 44, 61, 71) (Table 4). Genital ulcerations (0-18%), skin lesions (0-27%) - especially erythema nodosum (0-19%) -, ocular lesions (0-35%), arthropathy (0-24%), neurological features (0-12%) and vascular involvement (0-3%) can also occur as onset lesions. The high frequencies of oral aphthous ulcers, genital ulcerations, skin and ocular lesions as onset lesions confirm the importance of these clinical features for diagnosis. Highly recurrent oral aphthosis, the most frequent onset symptom, is a warning signal for Adamantiades Behçet's disease. Fifty-two per cent of 67 prospectively evaluated patients with recurrent oral aphthosis (in average 10 recurrences per year) in Korea developed

Adamantiades Behçet's disease in 8 years after development of oral aphthous ulcers (72). Although it is also a frequent feature, arthropathy is unspecific and, therefore, does not support diagnosis if it occurs as onset symptom of the disease.

Clinical Findings

Oral aphthous ulcers (92-100%), genital ulcerations (57-93%), skin lesions (38-99%), ocular lesions (29-100%) and arthropathy (16-84%) are the most frequent features of the disease worldwide (5, 7, 9, 12, 13, 17, 19, 22, 23, 26-34, 38-42) (Table 5). Sterile pustules (28-66%) and erythema nodosum (15-78%) are the most frequent skin lesions. A positive pathergy test is reported in 6-71% of the different patients groups. A comparison of the frequencies of clinical features among patients of different ethnic origin revealed lower rates of positive pathergy test in patients in Europe, the U.S.A. and Brazil (32%) than in patients in the rest of the world (54%, $p<0.001$, chi square test) and higher rates of arthropathy in Europeans, U.S. Americans and Brazilian (62%) than in the latter group (41%; $p<0.001$, chi square test). Gastrointestinal features were assessed mor frequent in Japanese and Europeans (16%) than in Korean and Turkish patients (3%, $p<0.001$, chi square test). A comparison concerning the rates of ocular lesions in south-eastern European patients (Italian and Greek) and south-western as well as northern European patients has detected significantly higher rates in the former group (5).

Association of HLA-B51 with the Disease

HLA-B51 is significantly associated with Adamantiades-Behçet's disease (1). It is surprising, however, that none of the functional correlates of the disease appear to be restricted by HLA-B51. Current evidence is shifting towards the view that HLA-B51 is not involved directly in the etiology of the disease (74) but might be closely linked to disease-related gene(s) (75). On

the other hand, HLA-B51 was found to be a marker for unfavorable prognosis, especially an earlier development of the disease, ocular lesions and vessel involvement (5). HLA-B5-positive individuals of German origin as well as from other northern European countries were detected to present a lower relative risk to develop the disease compared to southern Europeans, especially patients from south-eastern European countries (5). It is interesting that the relative risk of HLA-B51 individuals to develop the disease does not follow the distribution of the HLA-B51 allele around the world (5, 14, 26-28, 31,32, 55, 59, 63, 64, 74, 76-99) (Table 6); it is increased in a small geographic area which well correlates with the major antic trade routes (100) (Fig. 2).

Course and Prognosis

Adamantiades-Behçet's disease is usually diagnosed with a delay of several years after the appearance of the onset sign, i.e. after 1 year in Israel (32), 2.1 years in Iraq (27), 3 in Germany (5), 4.7 in India (26), 5.1 in Spain (14), 6.1 in Turkey (29), 6.4 years in Saudi Arabia (28), 6.4 years in Korea (101), 7.8 years in Russia (102), 8 years in the U.S.A. (38, 103), 5-15 years in Japan (104). The disease exhibits a potentially severe course with mortality rates of 0 to 5.1%, mostly involving male patients (5, 9, 14, 26, 28, 66-68, 105-108) (Table 7). The real increase of female cases in Japan are associated with a decrease of the mortality rate, namely from 1% in 1972 to 0.4% in 1991 (9). Central nervous system, pulmonary as well as large vessel involvement and bowel perforation are the major life-threatening manifestations. On the other hand, blindness and the consequences of central nervous system involvement are the most disabling features. There is evidence that a lethal outcome is often due to delayed diagnosis and treatment. In addition to HLA-B51 positivity, male gender (5) and early development of systemic features (109) have been detected to be markers of severe prognosis, while juvenile onset does not predict unfavorable prognosis (32,

46, 110). Spontaneous remissions of certain or of all manifestations or have been observed in a part of the patients several years after the onset of the disease (23, 26, 61, 69, 104).

References

1. OHNO S, OHGUCHI M, HIROSE S, MATSUDA H, WAKISAKA A, AIZAWA M. Close association of HLA-Bw51 with Behçet's disease. *Arch Ophthalmol* 1982; *100:* 1455-8.
2. YURDAKUL S, GÜNAYDIN I, TÜZÜN Y ET AL. The prevalence of Behçet's syndrome in a rural area in northern Turkey. *J Rheumatol* 1988; *15:* 820-2.
3. IDIL A, GÜRLER A, BOYVAT A ET AL. Behçet's disease prevalence study over 10-year age in Park Health Care Center. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 99.
4. DEMIRHINDI O, YAZICI H, BINYILDIZ P. Silivri Fener köyü ve yöresinde Behçet hastaligi sikligi ve bu hastaligin toplum içinde taranmasinda kullanilabilecek bir yöntem. *Cerrahp Tip Fak Derg* 1981; *12:* 509-14.
5. ZOUBOULIS CHC, 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.
6. AL-DALAAN A, ALBALLAA S, ALSUKAIT M, MOUSA M, BAHABRI S, BIYARI T. The prevalence of Behçet's disease in Al Qassim region of Saudi Arabia. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 170-2.
7. SHAHRAM F, DAVATCHI F, AKBARIAN M, GHARIBDOOST F, NADJI A, JAMSHIDI AR. The 1996 survey of Behçet's disease in Iran, study of 3153 cases. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 165-9.
8. DAVATCHI F. Epidemiology of Behçet's disease in Middle East and Asia. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 42.
9. NAKAE K, MASAKI F, HASHIMOTO T, INABA G, MOCHIZUKI M, SAKANE T. Recent

epidemiological features of Behçet's disease in Japan. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 145-51.

10. HIROHATA T, KURATSUNE M, NOMURA A, JIMI S. Prevalence of Behçet's syndrome in Hawaii. With particular reference to the comparison of the Japanese in Hawaii and Japan. *Hawaii Med J* 1975; *34:* 244-6.
11. OHNO S, CHAR DH, KIMURA SJ, O'CONNOR GR. Clinical observations in Behçet's disease. *Jpn J Ophthalmol* 1979; *23:* 126-31.
12. MOUSA AR, MARAFIE AA, RIFAI KM, DAJANI AI, MUKHTER MM. Behçet's disease in Kuwait, Arabia. A report of 29 cases and a review. *Scand J Rheumatol* 1986; *15:* 310-32.
13. ASSAAD-KHALIL SH, KAMEL FA, ISMAIL EA. Starting a regional registry for patients with Behçet's disease in North West Nile Delta region in Egypt. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 173-6.
14. SANCHEZ BURSON J, GRANDAL Y, MENDOZA M, MONTERO R, REJÓN E, MARENCO JL. Clinical characteristics, HLA antigen and mortality in Behçet's syndrome in Spain. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 102.
15. CHAMBERLAIN MA. Epidemiological features of Behçet's syndrome. *In:* LEHNER F, BARNES CG, eds. Behçet's syndrome. Clinical and immunologic features. Proceedings of a conference sponsored by the Royal Society of Medicine. February 1979. London: Academic Press, 1979, 213-22.
16. O'DUFFY JD. Summary of an international symposium on Behçet's disease. *J Rheumatol* 1980; *5:* 229-33.
17. CHUNG YM, YEH TS, SHEU MM ET AL. Behçet's disease with ocular involvement in

Taiwan: a joint survey of six major ophthalmological departments. *J Formos Med Assoc* 1990; *89:* 413-7.

18. DAVATCHI F, SHAHRAM F, CHAMS C ET AL. Epidemiology of Behçet's disease in Iran. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 96-97.
19. BARRA C, BELFORT R JR, ABREU MT, KIM MK, MARTINS MC, PETRILLI AMN. Behçet's disease in Brazil – A review of 49 cases with emphasis on ophthalmic manifestations. *Jpn J Ophthalmol* 1991; *35:* 339-46.
20. MAEDA K, NAKAE K. Recent epidemiological review on Behçet's disease. *Asian Med J* 1977; *2:* 568-82.
21. PIVETTI-PEZZI P. Behçet's disease in 1988. *In:* FERRAZ DE OLIVEIRA LN, ed. Ophthalmology Today. New York: Elsevier, 1988: 81-93.
22. BANG D, YOON KH, CHUNG HG, CHOI EH, LEE E-S, LEE S. Epidemiological and clinical features of Behçet's disease in Korea. *Yonsei Med J* 1997; *38:* 428-36.
23. CHO MY, LEE SH, BANG D, LEE S. Epidemiological findings of Behçet's syndrome. *Korean J Dermatol* 1988; *26:* 320-9.
24. CHUN SI, SU WPD, LEE S. Histopathologic study of cutaneous lesions in Behçet's syndrome. *J Dermatol* 1990; *17*:333-41.
25. ARROYO CG, VOCTORIO NAVARRA ST, TORRALBA TP. Behçet's disease in a Filippino group of patients. *Philippine J Intern Med* 1993; *31:* 305-15.
26. PANDE I, UPPAL SS, KAILASH S, KUMAR A, MALAVIYA AN. Behcet's disease in India: A clinical, immunological, immunogenetic and outcome study. *Br J Rheumatol* 1995; *34:* 825-30.
27. AL-RAWI ZS, SHARQUIE KE, KHALIFA SJ, AL-HADITHI FM, MUNIR JJ. Behçet's disease in Iraqi patients. *Ann Rheum Dis* 1986; *45:* 987-90.

28. AL-DALAAN A, AL BALAA SR, EL RAMAHI K ET AL. Behçet's disease in Saudi Arabia. *J Rheumatol* 1994; *21:* 658-61.

29. GÜRLER A, BOYVAT A, TÜRSEN Ü. Clinical manifestations of Behçet's disease: An analysis of 2147 patients. *Yonsei Med J* 1997; *38:* 423-7.

30. BITAR E, GHAYAD E, GHOUSSOUB KH. La maladie de Behçet. A propos de 32 cas. *Rev Rhum* 1986; *53:* 621-4.

31. MADANAT W, FAYYAD F, ZUREIKAT H ET AL. Analysis of 150 cases of Behçet's disease Jordan. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 255.

32. KRAUSE I, UZIEL Y, GUEDJ D ET AL. Mode of presentation and multisystem involvement in Behçet's disease: The influence of sex and age of disease onset. *J Rheumatol* 1998; *25:* 1566-9.

33. HAMZA M, MEDDEB S. Behçet's disease in Tunisia. *Rev Rhum (Engl Ed)* 1996; *63:* 538.

34. BENAMOUR S, CHAOUI L, ZEROUAL B ET AL. Study of 673 cases of Behçet's disease. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 232.

35. JACYL WK. Behçet's disease in South African blacks: Report of five cases. *J Am Acad Dermatol* 1994; *30:* 869-73.

36. RIHOVÁ E, HAVLIKOVÁ M, MICHALOVÁ K, ROTHOVÁ Z, POCH T. Behcetova nemoc. *Cs Oftal* 1997; *5:* 298-304.

37. MITROVIC D, POPOVIC M, PAVLICA L ET AL. Ciklosporina A u lecenja Behçet-ove bolesti. *Vojnosanitetski Pregled* 1997; *54:* 321-5.

38. MANGELSDORF HC, WHITE WL, JORIZZO JL. Report of twenty-five patients from the United States with prominent mucocutaneous involvement. *J Am Acad Dermatol* 1996; *34:* 745-50.

39. BALABANOVA M, CALAMIA KT, O'DUFFY JD. A study of the cutaneous manifestations of Behçet's disease in patients from the United States. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 118.

40. ROCHA LACERDA R. Behçet's disease - clinical and immunologic study. Follow-up of 42 case studies over 10 years. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 185-8.

41. SCHERRER MA, VITRAL N, OREFICE F. Clinical study of Behçet's disease in Brasil. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 181-4.

42. MONTENEGRO V, DE ABREU AC, SCHAIMBERG C, GONÇALVES CR. Behçet's disease in 81 Brazilian patients. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 256.

43. ESGUEP AS, QUINTEROS IO. Behçet's syndrome: report of five cases. *J Oral Med* 1987; *42:* 25-29.

44. WAKEFIELD D, MCCLUSKEY P. Behçet's syndrome: ocular features in an Australian population. *Aust N Z J Ophthalmol* 1990; *18:* 129-35.

45. SHAHRAM F, SHAFAIE N, DAVATCHI F, NADJI A, AKBARIAN M, JAMSHIDI A. Juvenile Behçet's disease: Diagnosed before or after childhood? *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 180.

46. TREUDLER R, ORFANOS CE, ZOUBOULIS CHC. Twenty-eight cases of juvenile onset Adamantiades-Behçet's disease in Germany. *Dermatology*, in press.

47. PIVETTI PEZZI P, ACCORINTI M, ABDULAZIZ MA, LA CAVA M, TORELLA M, RISO D. Behçet's disease in children. *Jpn J Ophthalmol* 1995; *39:* 309-14.

48. BENAMOUR S, TAK-TAK T, MOUDATIR A ET AL. Juvenile Behçet's disease and juvenile onset Behçet's disease in Morocco. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 176.

49. KONÉ-PAUT I, BERNARD JL. La maladie de Behçet chez l'enfant en France. *Arch Fr Pediatr* 1993; *50:* 561-3.

50. KAKLAMANI VG, VAIOPOULOS G, MARKOMICHELAKIS N, PALIMERIS G, MARKAKI J, KAKLAMANIS PH. Correlation of the severity of Adamantiades- Behçet's disease with clinical and demographic parameters. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 238.

51. MADANAT W, FAYYAD F, ZUREIKAT H. Juvenile Behçet's disease in Jordan. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 178.

52. GÜRLER A, ERDI H, BOYVAT A. Clinical features of juvenile Behçet's disease. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 139-42.

53. HAMZA M. Juvenile Behçet's disease. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 377-80.

54. YAMAMOTO S, TOYOKAWA H, MATSUBARA J ET AL. A nation-wide survey of Behçet's disease in Japan. 1. Epidemiological survey. *Jpn J Ophthalmol* 1974; *18:* 282-90.

55. MÜFTÜOGLU AÜ, YAZICI H, YURDAKUL S ET AL. Behçet's disease: lack of correlation of clinical manifestations with HLA antigens. *Tissue Antigens* 1981; *17:* 226-30.

56. SAYLAN T, ÖZARMAGAN G, AZIZLERLI G, ÖVÜL C, ÖKE N. Morbus Behçet in der Türkei. *Zbl Hautkr* 1986; *61:* 1120-2.

57. CHAJEK T, FAINARU M. Behçet's disease. Report of 41 cases and a review of the literature. *Medicine (Baltimore)* 1975; *54:* 179-96.

58. GÜL A, INANÇ M, ÖCAL L, ARAL O, KONIÇE M. Sibling recurrence in Behçet's disease. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 98.

59. ARBER N, KLEIN T, MEINER Z, PRAS E, WEINBERGER A. Close association of HLA-B51 and B52 in Israeli patients with Behçet's syndrome. *Ann Rheum Dis* 1991; *50:* 351-3.

60. SHAHRAM F, CHAMS C, DAVATCHI F, NADJI A, AKBARIAN, JAMSHIDI A. Familial study in Behçet's disease, analysis of 1242 patients. *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 103.

61. HUI-LI S, ZHENG-JI H. Study on cutaneous lesions in Behçet's disease and meanings of relative laboratory parameters. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 325-30.

62. AOKI K, OHNO S, OHGUCHI M, SUGIURA S. Familial Behçet's disease. *Jpn J Clin Ophthalmol* 1978; *22:* 72-5.

63. MAKNI H, KOLSI R, KOLSI S ET AL. Clinical and immunological study of 26 cases of familial Behçet's disease. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 151-4.

64. FERNÁNDEZ MIRANDA C, PALACIO PÉREZ-MEDEL A, MARTÍNEZ-MARTÍN P, MONTALBÁN PALLARÉS MA, DOMÍNGUEZ ORTEGA L, RAMÍREZ DÍAZ-BERNANDO J. Enfermedad de Behçet. Presentación de 22 casos. *Rev Esp Reumatol* 1983; *10:* 37-43.

65. MASON RM, BARNES CG. Behçet's syndrome with arthritis. *Ann Rheum Dis* 1969; *28:* 95-103.

66. DE SOUZA-RAMALHO P, D'ALMEIDA MF, FREITAS JP, PINTO J. Behçet's disease in

Portugal. *Acta Medica Portug* 1991; *4:* 79-82.

67. KAKLAMANI V, VAIOPOULOS G, KAKLAMANIS PG. Behçet's diease. *Sem Arthritis Rheum* 1998; *27:* 197-217.

68. SENSI A, BARICORDI OR. Heritability of Behçet's disease. *Br J Dermatol* 1986; *114:* 748.

69. PIVETTI-PEZZI P. Behçet's disease in 1988. *In:* FERRAZ DE OLIVEIRA LN, ed. Ophthalmology Today. New York: Elsevier, 1988: 81-93.

70. BENAMOUR S, TAK-TAK MT, RAFIK M, ANRAOUI A. Juvenile Behçet's disease in Morocco. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 134-8

71. FRESKO I, SOY M, HAMURYUDAN V ET AL. Genetic anticipation in Behçet's disease. *Ann Rheum Dis* 1998; *57:* 45-8.

72. OSHIMA Y, SHIMIZU T, YOKOHARI R ET AL. Clinical studies on Behçet's syndrome. *Ann Rheum Dis* 1963; *22:* 36-45.

73. BANG D, HUR W, LEE E-S, LEE S. Prognosis and clinical relevance of recurrent oral ulceration in Behçet's disease. *J Dermatol* 1995; *22:* 926-9.

74. MIZUKI N, INOKO H, MIZUKI N ET AL. Human leukocyte antigen serologic and DNA typing of Behçet's disease and its primary association with B51. *Invest Ophthalmol Vis Sci* 1992; *33:* 3332-40.

75. GOTO K, MIZUKI N, OHNO S. Molecular genetic studies of Behçet's disease. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 102-105.

76. LEE S, KOH YJ, KIM DH ET AL. A study of HLA antigens in Behçet's syndrome. *Yonsei Med J* 1988; *29:* 259-62.

77. CHUNG Y-M, TSAI S-T, LIAO F, LIU J-H. A genetic study of Behçet's disease in Taiwan chinese. *Tissue Antigens* 1987; *30:* 68-72.

78. MINESHITA S, TIAN D, WANG L-M ET AL. Histocompatibility antigens associated with

Behçet's disease in northern Han Chinese. *Intern Med* 1992; *31:* 1073-5.

79. MEHRA NK, TANEJA V, KAILASH S, RAIZADA N, VAIDYA MC. Distribution of HLA antigens in a sample of North Indian Hindu population. *Tissue Antigens* 1986; *27:* 64-74.

80. GHARIBDOOST F, DAVATCHI F, SHAHRAM F ET AL. Clinical manifestations of Behçet's disease in Iran. Analysis of 2176 cases. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 153-8.

81. AZIZLERLI G, AKSUNGUR VL, SARICA R, AKYOL E, ÖVÜL C. The association of HLA-B5 antigen with specific manifestations of Behçet's disease. *Dermatology* 1994; *188:* 293-5.

82. ERSOY F, BERKEL AI, FIRAT T, KAZOKOGLU H. HLA antigens associated with Behçet's disease. *Arch Dermatol* 1977; *113:* 1720-1.

83. ALPSOY E, YILMAZ E, COSKUN M, SAVAS A, YEGIN O. HLA antigens and linkage disequilibrium patterns in Turkish Behçet's patients. *J Dermatol* 1998; *25:* 158-62.

84. BRAUTBAR C, CHAJEK T, BEN-TUNIA S, LAMM L, COHEN T. A genetic study of Behçet disease in Israel. *Tissue Antigens* 1978; *11:* 113-20.

85. HAIM S, GIDEONI O, BARZILAI A. The histocompatibility antigens in patients with Behçet's disease. *Acta Dermatol Venereol (Stockh)* 1977; *57:* 243-5.

86. ASSAAD-KHALIL SH. Clinical, genetic, immunological, and biochemical features of 180 Egyptian patients with Behçet disease. *In:* O'DUFFY JD, KOKMEN E, eds. Behçet's disease. Basic and clinical aspects. New York: Marcel Dekker, 1991: 269-77.

87. HAMZA M, BEN AYED HB, SOHIER R, BETUEL H. Frequence de l'antigene HLA-B5 au cours de la maladie de Behçet. *Nouv Presse Med* 1978; *7:* 3263.

88. CRESPO J. Incidence, clinical and genetic aspects of Behçet's disease in Portugal. *Rev*

Rhumatisme (engl ed) 1996; *63:* 538.

89. DE JESUS H, MARQUES A, ROSA M, DE COSTA T, QUEIROZ MV. Behçet's disease: Analysis of 43 cases. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 204-5.

90. VAZ PATTO J, FIGUEIRINHAS J, PARENTE M ET AL. HLA-B5 in Portuguese patients with Behçet's disease. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 109-10.

91. GONZÁLEZ-ESCRIBANO MF, RODRÍGUEZ MR, WALTER K, SANCHEZ-ROMAN J, GARCÍA-LOZANO JR, NÚÑEZ-ROLDÁN A. Association of HLA-B51 subtypes and Behçet's disease in Spain. *Tissue Antigens* 1998; *52:* 78-80.

92. PSILAS K, POLYMENIDIS Z, GEORGIADES G. Le HLA-B5 antigene dans la syndrome d'Adamantiades-Behçet. *J Fr Ophtalmol* 1979; *2:* 701-4.

93. PALIMERIS G, KOLIOPOULOS J, THEODOSSIADIS G, ROUSSOS J, TSIMBIDAS P. The Adamantiades-Behçet syndrome. Clinical and immunological observations. *Trans Ophthalmol Soc* UK !980; *100:* 527-30.

94. ZERVAS J, VAYOPOULOS G, SAKELLAROPOULOS N, KAKLAMANIS PH, FESSAS PH. HLA antigens and Adamantiades-Behçet's disease (A-BD) in Greeks. *Clin Exp Rheumatol* !988; *6:* 277-80.

95. MESSINI H, SPYROPOULOU M, PAPADEMITROPOULOS M ET AL. HLA-B5(51) genomic analysis in Greek patients with Adamantiades-Behçet's disease (A-BD): Correlation with certain disease characteristics. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 106-8.

96. KOUMANTAKI Y, STAVROPOULOS C, SPYROPOULOU M ET AL. HLA-B*5101 in Greek aptients with Behçet's disease. *Hum Immunol* 1998; *59:* 250-5.

97. O'DUFFY JD, TASWELL HF, ELVERBACK LR. HL-A antigens in Behçet's disease. *J*

Rheumatol 1978; *3:* 1-3.

98. OHNO S, CHAR DH, KIMURA SJ, O'CONNOR GR. Studies on HLA antigens in american patients with Behçet's disease. *Jpn J Ophthalmol* 1978; *22:* 58-61.

99. LAVALLE C, ALARCON-SEGOVIA D, DEL GUIDICE-KNIPPING JA, FRAGA A. Association of Behçet's syndrome with HLA-B5 in the mexican mestizo population. *J Rheumatol* 1981; *8:* 325-327.

100. CHAPOUTOT-REMADI M. Major trade routes and the "Silk Road". *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 22-29

101. KIM HJ, BANG D, LEE SH ET AL. Behçet's syndrome in Korea: A look at the clinical picture. *Yonsei Med J* 1988; *29:* 102-8.

102. ALEKBEROVA Z, MADANAT W, PROKAEVA T, YERMAKOVA N, POLJANSKAJA I. Clinical and genetic features of 35 patients with Behçet's disease from Commonwealth Independent States. *In:* WECHSLER B, GODEAU P, eds. Behçet's disease. International Congress Series 1037. Amsterdam: Excerpta Medica, 1993: 171-4.

103. O'DUFFY JD, CARNEY JA, DEODHAR S. Behçet's disease. Report of 10 cases, 3 with new manifestations. *Ann Intern Med* 1971; *75:* 561-70.

104. TANAKA C, HARAMOTO S, MATSUDA T ET AL. Studies on the clinical course of Behçet's disease. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 217-8.

105. CHAMBERLAIN MA. Behçet's syndrome in 32 patients in Yorkshire. *Ann Rheum Dis* 1977; *36:* 491-9.

106. YAZICI H, BASARAN G, HAMURYUDAN V ET AL. The ten-year mortality in Behçet's syndrome. *Br J Rheumatol* 1996; *35:* 139-41.

107. WECHSLER B, HUONG DU LT, MASSIN I ET AL. La maladie de Behçet en France. A propos de 60 sujets autochtones. *Ann Med Interne* 1988; *139:* 315-9.

108. PARK KD, BANG D, LEE ES, LEE SH, LEE S. Clinical study on death in Behcet's disease.

J Korean Med Sci 1993; *8:* 241-5.

109. SARYCA R, AZIZLERLI G, KÖSE A ET AL. The course of disease activity among 1127 Turkish adult Behçet's patients. *In:* HAMZA M, ed. Behçet's disease. Tunis: Pub Adhoua, 1997: 157-9.

110. SHAFAIE SF, DAVATCHI F, NADJI A, AKBARIAN M, JAMSHIDI A. Juvenile Behçet's disease: Diagnosed before or after childhood? *In:* OLIVIERI I, SALVARANI C, CANTINI F, eds. 8th International Congress on Behçet's Disease. Program and Abstracts. Milano: Prex, 1998: 180.

Table 1. World-wide distribution of Adamantiades-Behçet's disease

Population	Year	Prevalence per 100,000 inhabitants	
		Country	Region
ASIA			
Turkish			
Ordu region, Northeastern Anatolia (2)	1987		370
Ankara region (3)	1998		115
European part (4)	1981		80
Berlin-West, Germany (5)	1989		20.75
Saudi Arabian, Al Qassim region (6)	1997		20
Iranian (7)	1996	16.67	
Chinese (8)	1998	14.00	
Japanese (9)	1991	13.50	
Hokkaido region (9)	1991		30.50
Kyushu region (9)	1991		0.99
Hawaii (10)	1975		0.00
U.S.A. (11)	1979		0.00
Kuwait (12)	1986	2.10	
Kuwaitis (12)	1986		1.58
Non-Kuwaiti Arabs (12)	1986		2.90
Non-Arabs (12)	1986		1.35
AFRICA			
Egyptian, Alexandria region (13)	1997		7.60
EUROPE (5)			
Spaniard (14)	1998	7.50	
Italian	1988	2.50	
Germany, Berlin-West area	1994		2.26
German	1994		0.55
Portuguese	1993	1.53	
Swedish	1993	1.18	
British	1987	0.50	
Yorkshire region	1977		0.64
Scotland	1992		0.27
AMERICA			
U.S. American (15)	1979	0.12	
Olmsted County, MN (16)	1985	0.33	
Hawaii (10)	1975		0.00

Table 2. Demographic data on Adamantiades-Behçet's disease in a world-wide comparison

Country	Number of patients	Age of onset, y average	range (SD)	Male: Female
ASIA				
Japan (9)	1139	35.7		1.07 : 1
Korea (22)	1155	28.8	7 - 71	0.63 : 1
China (23)	328	27.9	4 - 58	0.69 : 1
Taiwan (17, 24)	156		10 - 50	2.47 : 1
Philippines (25)	9			2.00 : 1
India (26)	58	33.1	10 – 64	1.76 : 1
Iran (7)	3153	26.2	(± 9.7)	1.13 : 1
Iraq (27)	60	29.4		3.00 : 1
Saudi Arabia (28)	119	22.9	13 - 51	3.40 : 1
Kuwait (12)	29			3.10 : 1
Turkey (29)	2147	25.6		1.03 : 1
Lebanon (30)	32	22.0	3 - 45	1.50 : 1
Jordan (31)	150	25.2	(± 9.4)	3.40 : 1
Israel (32)	59	19.9	2 - 54	0.79 : 1
AFRICA				
Egypt (13)	274	26.2	(± 9.9)	5.37 : 1
Tunisia (33)	702	28.9	(± 9.9)	3.00 : 1
Morocco (34)	673	31.7	5 - 60	2.54 : 1
South Africa (35)	5			0.67 : 1
EUROPE (5)				
Russia	25	24.7	(±12.9)	0.56 : 1
Czech Republic (36)	9			2.00 : 1
Sweden	5	33.0	19 - 48	0.67 : 1
Scotland	15			0.36 : 1
England	53	24.7	10 - 61	0.96 : 1
Ireland	24	20.8	(± 7.5)	1.40 : 1
Germany*	96	24.5	0 - 72	1.00 : 1
Portugal	241	25.7	(±11.1)	1.01 : 1
Spain	31	26.0	15 - 48	1.38 : 1
France	126	28.5	2 - 64	1.57 : 1
Italy	155	25.0	5 - 53	2.44 : 1
Yugoslavia (37)	21			1.33 : 1
Greece	63	29.0	5 - 67	1.42 : 1
AMERICA				
U.S.A. (38, 39)	131	25.6	5 - 49	0.42 : 1
Brazil (19, 40-42)	197	30.2	9 - 61	0.91 : 1
Chile (43)	5			4.00 : 1
OCEANIA				
Australia (44)	12			2.00 : 1

* modified to include current data

Table 3. Familial occurrence of Adamantiades-Behçet's disease

Population	number of patients	rate (%)
ASIA		
Turkish		
Turkey (58)	170	18.2
Germany (5*)	101	15.5
Israeli (59)	38	13.2
Korean (22)	178	15.4
Indian (26)	58	13.8
Saudi-Arabs (28)	119	7.5
Lebanese (30)	32	6.3
Iranian (60)	1242	5.5
Chinese (61)		2.6
Japanese (62)	223	2.2
AFRICA		
Egyptian (13)	274	10.7
Moroccan (34)	673	5.6
Tunisian		
North Tunisia (33)	702	2.0
South Tunisia (63)	26	11.9
EUROPE		
Spaniard (64)	22	9.1
English (65)	33	3.6
German (5*)	96	3.2
Portuguese (66)	154	2.6
Greek (67)	64	1.3
Italian (68, 69)	177	1.3

* modified to include current data

Table 4. Onset manifestations of Adamantiades-Behçet's disease (%)

Nationality	Japan (72)	Korea (22)	China (61)	Iraq (27)	Iran (7)	Turkey (29)	Israel (32)	Egypt (13)	Europe (5)[a]	Brazil (42)	Australia (44)
Number of patients	85	1155	328[b]	60	3153	2147	59	274[c]	353	81	12
Oral aphthous ulcers	52	79	56	47	77	86	60	60	58-78	47	75
Genital ulcerations	4	7	10	10	10[d]	7	17	18	2- 7	-	8
Skin lesions	19	11	27	12		5	11	-	7-26	12	8
Folliculitis/sterile pustules			5			2	-		1		
Erythema nodosum			19			3	11		8-14		8
Superf. thrombophlebitis			-			1	-		1- 5		
Ocular lesions	21	3	4	13	12	1	-	23	1-18	35	25
Arthropathy	4	-	-	13	7	1	13	6	5-24	6	
Neurological features	-	-	-	2		-	-	3	0- 9	12	
Vascular involvement	-	-	-	2		-	2	3	-	-	
Other manifestations				2	9[e]						

Europe (5): England, n=39; France, n=133; Germany, n=96 (modified to include current data); Greece, n=63; Spain, n=22

[b] Multiple site onset lesions in 5%; [c] Multiple site onset lesions in 16%; [d] Mostly accompanied by oral aphthosis; [e] Mostly skin manifestations

Table 5. Clinical findings of Adamantiades-Behçet's disease (%)

ationality	Japan (9)	Korea (22)	Taiwan (17)	China (23)	India (26)	Iraq (27)	Iran (7)	Kuwait (12)	Saudi Arabia (28)	Turkey (29)	Lebanon (30)	Jordan (31)	Israel (32)	Egypt (13)	Tunisia (33)	Morocco (34)	Europe (5)[a]	U.S.A. (38, 39)	Brazil (19, 40-
umber of patients	3316	1155	103	328	58	60	3153	103	119	2147	32	150	59	274	702	601	714	131	197
ral aphthous ulcers	98	98	97	100	90	97	96	100	100	100	97	100	100	92	99	100	98-100	99	99
enital ulcerations	73	57	61	84	78	83	64	93	87	88	78	85	68	76	80	84	65-91	86	68
kin lesions	87	61	75	99	64	75	74	76	57	54	38	90	86	39			66-84	98	66
Folliculitis/sterile pustules		36		40		48	66		53	54	28				55	61	41-49	48	52
Erythema nodosum		55		64	47	55	23		47	47	19	41			20	15	25-78	37	36
Ulcerations		2		1							16					5	0-13	22	8
Superf. thrombophlebitis		3		4	24				13	11	6	7					4-29		
ositive pathergy test	44			66	9	71	61	34	18	57	71	55	46	70	50	68	12-52	33	6
cular lesions	69	29	100	40	43	48	59	69	56	29	59	46	49	76	50	67	35-69[d]	37	79
rthropathy	57	24	61	58	71	48	41	69	37	16	75	53	83	56	30	64	33-84	34	61
eurological features	11	6	3	2	4	2	4	14	44	2	19	28	15	26	17	14	11-48	18	8
ascular involvement	9		2	8	10	17	9	34	34	17	6	29	29	23[c]	17	21	10-37	14	17
astrointestinal features	16	4	15	9	5	10	9	21	4	3	13	19		10	1	13	5-60	-	6
ostatitis-Epididymitis[b]	6		6	6	-	22	11		4		3	28		16	4		2-44	-	17
hest disease			3	+	-		1	7	16	1	3	9		1	-	2	0-17	-	3
idney involvement			5	-	2		-	7	6	+		5			-	1	0-10	-	..-
ardiac disease			-	3	-		1	-	-	+		2			-	3	0- 7	-	4

Europe (5): Czech Republic, n=9 (36); England, n=46; France, n=133; Germany, n=96 (modified to include current data); Greece, n=63; Italy, n=141; Portugal, n=142; Russia, n=25; Spain, n=38; Yugoslavia, n=21 (37)

Male; [c] including cardiac disease; [d] Czech and Italian patients were excepted

Present lesions in less than 0.5% of patients

Table 6. Frequency of HLA-B51 antigen in patient groups and relative risk (RR) for Adamantiades-Behçet's disease

	Patients		Controls		
Country	n	HLA-B51+ in %	n	HLA-B51+ in %	RR
ASIA					
Japan (74)	91	57	140	14	7.9
Korea (75)	52	44	42	17	4.0
Taiwan (76)	51	51	128	11	8.5
China (77)	120	56	100	12	9.3
India (26, 78)	31	32	400		
Iraq (27)	52	62	175	29	3.9
Iran (79)		53		33	2.3
Turkey (5, 55, 80-82)	520	77	1106	26	9.2
Saudi Arabia (28)	85	72		26	9.0
Jordan (31)	68	74	43	23	9.2
Israel (32, 59, 83, 84)	126	75	790	21	11.5
AFRICA					
Egypt (85)	84	58	200	7	20.1
Tunisia (63, 86)	55	62	80	24	5.2
EUROPE (5)					
Russia	19	37	150	15	3.2
Great Britain	107	25	2032	9	3.3
Ireland	24	25	96	3	6.3
Germany*	70	37	1415	14	3.6
Switzerland	8	38		17	3.0
Portugal (87-89)	318	53	135	24	3.6
Spain (14, 64, 90)	100	42	452	21	2.7
France	105	51	591	13	6.7
Italy	57	75	304	22	10.9
Greece (91-95)	170	79	670	28	9.7
AMERICA					
U.S.A. (96, 97)	32	13	523	10	1.3
Mexico (98)	10	70	105	31	5.1

* modified to include current data

Table 7. Mortality in Adamantiades-Behçet's disease

Country	Number of patients	Lethal outcome n=	%	Male	Female	Duration of of follow-up (in years)
England (105)	32	2	6.25			
Turkey (106)	120	6	5.00	6	-	10
France (107)	60	3	5.00			3 (1-12)
Germany (5*)	96	4	4.17	2	2	1-20
Spain (14)	30	1	3.33			
Italy (69)	141	4	2.84	4	-	>10
Portugal (66)	156	4	2.56	3	1	>10 (up to 21)
Saudi Arabia (28)	119	3	2.52			
Japan (9)	3316		0.40			
Korea (108)	2200	7	0.32	6	1	6.5
Greece (67)	64	-	0.00			
India (26)	58	-	0.00			4

* modified to include current data

Legends to the figures

Fig. 1. Development of male-to-female ratio over time

Fig. 2. (a) Worldwide distribution of the HLA-B51 antigen in healthy populations and (b) relative risk for the development of the disease in several countries