Genetic thrombophilia was no more prevalent than in the general population.

Finally, we confirm that LAC and aCL >30 GPL units are the main thrombophilic factors associated with thrombosis in SLE. The role of free protein S and homocysteinaemia remains unclear. Prospective studies, with serial sampling, are needed to elucidate which others factors may play a part.

Authors' affiliations

D Barcat, J Constans, C Conri, Médecine Interne et Pathologie Vasculaire, Hôpital Saint-André, 1, rue Jean Burguet, 33075 Bordeaux, France
V Guérin, A Ryman, Hématologie, Hôpital Pellegrin, 3, place Amélie Raba-Léon, 33076 Bordeaux, France
J P Vernhes, Rhumatologie, Hôpital Robert Boulin, 33500 Libourne, France
C Vergnes, Hématologie, Hôpital du Haut Lévêque, 33600 Pessac, France
F Bonnet, X Delbrel, P Morlat, M Longy-Boursier, Médecine Interne et Pathologie Infectieuse, Hôpital Saint-André, 1, rue Jean Burguet, 33075 Bordeaux, France

Correspondence to: Dr D Barcat; damien.barcat@chu-bordeaux.fr

Accepted 20 January 2003

REFERENCES

1 **Love PE**, Santoro SA. Antiphospholipid antibodies: anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and non-SLE disorders. Ann Intern Med 1990;112:682–98.
2 **Horbach DA**, van Oort E, Donders RC, Derksen RH, de Groot PG. Lupus anticoagulant is the strongest risk factor for both venous and arterial thrombosis in patients with systemic lupus erythematosus. Thromb Haemost 1996;76:916–24.
3 **Wahl DG**, Guillemin F, de Maistre E, Perret C, Lecompte T, Thibaut G. Risk of venous thrombosis related to antiphospholipid antibodies in systemic lupus erythematosus. Lupus 1997;6:467–73.
4 **Tomas JF**, Alberca I, Tabernero MD, Cordero M, Del Pino-Montes J, Vicente V. Natural anticoagulant proteins and antiphospholipid antibodies in systemic lupus erythematosus. J Rheumatol 1998;25:57–62.
5 **Sorice M**, Griggi T, Circella, Lenti L, Arcieri P, Domenico di Nucci G, *et al*. Protein S antibodies in acquired protein S deficiencies. Blood 1994;83:2383–4.
6 **Kiraz S**, Ertenli I, Benekli M, Haznedaroglu IC, Calguneri M, Celik I, *et al*. Clinical significance of hemostatic markers and thrombomodulin in systemic lupus erythematosus: evidence for a prothrombotic state. Lupus 1999;8:737–41.
7 **Ferro D**, Quintarelli C, Valesini G, Violi F. Lupus anticoagulant and increased thrombin generation in patients with systemic lupus erythematosus. Blood 1994;83:304–5.
8 **Petri M**, Roubenoff R, Dallal GE, Nadeau MR, Selhub J, Rosenberg IH. Plasma homocysteine as a risk factor for atherothrombotic events in lupus erythematosus. Lancet 1996;348:1120–4.
9 **Fijnheer R**, Roest M, Haas FJ, De Groot PG, Derksen RH. Homocysteine, methylenetetrahydrofolate reductase polymorphism, antiphospholipid antibodies, and thromboembolic events in systemic lupus erythematosus: a retrospective cohort study. J Rheumatol 1998;25:1737–42.

HLA class II allele polymorphism in Hungarian patients with systemic lupus erythematosus

E Endreffy, A Kovács, L Kovács, G Pokorny

Ann Rheum Dis 2003;**62**:1017–1018

Recently, a comprehensive study was published on HLA class II DNA typing in a large cohort of European patients with SLE.[1] Independently of this collaborative study, we have examined similar DRB1, DQA1, and DQB1 allele polymorphisms and clinical features in Hungarian patients with SLE.

Fifty patients with SLE (48 female; mean age at the time of the examinations 41 years (range 21–76)) and 50 healthy blood donors matched for age and sex with the controls were examined. Genotyping of HLA-DRB1 alleles was carried out with the Dynal RELI SSO HLA-DRB kit, and the DRB1*15/16 subtyping by the method of Ota *et al*.[2] DQA1 determination was performed by the method of Ota *et al*.[3] The DQB1 typing was carried out with the INNO-LiPA DQB kit. A χ^2 test with Yates's correction was used for statistical analysis. The significance levels ($p<0.05$) were adjusted by using Bonferroni's correction to eliminate chance associations (pc value). Odds ratio (OR) values were also calculated.

The main clinical manifestations were articular involvement (92%), anaemia (72%), leucopenia (54%), pericarditis and/or pleuritis (54%), and nephritis (32%).

The DRB1*1501, DRB1*03, and DRB1*07 alleles occurred more frequently in the patients with SLE than in the controls (12/50 (24%) *v* 3/50 (6%); 20/50 (40%) *v* 10/50 (20%) and 17/50 (34%) *v* 6/50 (2%), respectively; ORs 4.4, 2.25, and 3.2, respectively). The DQA1*0102 and *05011 alleles were also more common in the SLE group than in the controls (25/50 (50%) *v* 13/50 (26%), and 20/50 (40%) *v* 9/50 (18%), respectively; ORs 2.23 and 2.3, respectively). Of the DQB1 alleles, *0201 and *0602 were detected more frequently in the patients with SLE than in the controls (20/50 (40%) *v* 8/50 (16%), and 11/50 (22%) *v* 2/50 (4%), respectively; ORs 2.87 and 6.05, respectively). After the Bonferroni's correction the above mentioned differences did not reach significance.

In contrast, the DRB1*04 and DRB1*11/12 alleles were less common in the patients with SLE than in the controls (3/50 (6%) *v* 16/50 (32%) and 15/50 (30%) *v* 25/50 (50%)). The *04 allele was linked with resistance to leucopenia (pc=0.01), the *11/12 alleles with resistance to discoid skin lupus (pc=0.001). The 1106 subtype of the DRB1*11 alleles occurred only in the patients with SLE (4/16 (25%) *v* 0/25 (0%)).

Connections between the genetic and clinical characteristics were as follows: the DRB1*1501 positivity was less frequent in the patients with than in those without lupus nephritis (LN) (3/16 (19%) *v* 15/34 (44%)). In contrast, the DRB1*03 and DRB1*07 alleles were more frequent in the patients with than in those without LN (8/16 (50%) *v* 11/34 (32%) and 7/16 (44%) *v* 8/34 (24%)). In the patients with pleuritis and/or pericarditis, only the DRB1*07 positivity was more frequent than in the patients without serositis (12/27 (44%) *v* 3/23 (13%)). The *07 allele was detected more frequently in the patients with one or more severe renal, cardiorespiratory manifestations than in the patients without these potentially fatal features of the disease (16/36 (44%) *v* 0/14 (0%)). In the patients with anti-SSA and anti-SSB positivity the renal and cerebral involvement was more common, but the differences were not significant (4/8 (50%) *v* 9/33 (27%) and 2/8 (25%) *v* 3/33 (9%)).

A comparison with the results of the comprehensive European study showed that agreement was complete for the increased prevalence of the DRB1*1501, DRB1*03, DQA1*0102, DQB1*0201, and DQB1*0602 alleles in the

patients with SLE. We could not detect increased frequencies of the DQB1*0303 and DQB1*0502 alleles in our patients with SLE, and our patients with DRB1*1501 positivity exhibited a milder clinical course and a negative correlation with LN.

Authors' affiliations
E Endreffy, Department of Paediatrics, Albert Szent-Györgyi Medical and Pharmaceutical Centre, Korány fasor 14–15, Szeged, Hungary
A Kovács, L Kovács, G Pokorny, Department of Rheumatology, Albert Szent-Györgyi Medical and Pharmaceutical Centre, Korány fasor 14–15, Szeged, Hungary

Correspondence to: Dr E Endreffy; endreffy@pedia.szote.u-szeged.hu
Accepted 29 March 2003

REFERENCES

1 **Galeazzi M**, Sebastiani GD, Morozzi G, Carcassi C, Ferrare GB, Scorza R, *et al*. HLA class II DNA typing in a large series of European patients with systemic lupus erythematosus. Medicine (Baltimore) 2002;81:169–78.
2 **Ota M**, Seki T, Fukushima H, Tsuji K, Inoko H. HLA-DRB1 genotyping by modified PCR-RFLP method combined with group-specific primers. Tissue Antigens 1992;39:187–202.
3 **Ota M**, Seki T, Namura N, Sugimura K, Mizuki N, Fukushima H, *et al*. Modified PCR-RFLP method for HLA-DPB1 and DQA1 genotyping. Tissue Antigens 1991;38:60–71.

HLA-B27 in patients with a permanent pacemaker

J Bruges-Armas, C Lima, D Simas Lopes, V Schneider, J P Paisana Lopes, A Ferreira Gomes, J G Coelho Gil, M J Barreiros, M J Peixoto, F Garrett, F Laranjeira, A R Couto, T W O'Neill, G Herrero-Beaumont

Ann Rheum Dis 2003;**62**:1018

Conduction disturbances are a well recognised extra-articular manifestation of ankylosing spondylitis and other spondyloarthropathies (SpA),[1 2] disorders which are strongly associated with the HLA-B27 gene. Some, though not all studies, suggest an association between the presence of SpA and/or HLA-B27 and the occurrence of cardiac conduction disorders.[3–7] This study aimed at determining the prevalence of SpA in a group of patients with a permanent pacemaker, and discovering whether these patients were more likely to be HLA-B27 positive than a group of controls.

Seventy six men and 51 women (mean age 73 years) with a permanent pacemaker who attended the cardiology department at the Hospital of Angra do Heroísmo (Terceira island, Azores) were assessed clinically for the presence of spondyloarthritis. All had pelvic radiographs performed and blood taken for HLA-B27 typing (polymerase chain reaction with sequence-specific primers).[8] Pelvic radiographs were assessed by two qualified observers (JBA and CL) and, if sacroiliitis was suspected a computed tomographic scan of the sacroiliac joint was performed. SpA was diagnosed according to the European Spondylarthropathy Study Group (ESSG) criteria.[9] Fifty men and 80 women (mean age 53 years) recruited from a population based register for participation in a screening survey of vertebral osteoporosis acted as a control group. These subjects had blood taken for HLA-B27.

Eighty one of the patients had evidence of atrioventricular conduction disturbances and the remaining patients had a pacemaker implanted for other reasons (auricular fibrillation/flutter, sick sinus disease, congenital diseases). Two patients with pacemaker had bilateral sacroiliitis; one a 56 year old man had had surgery for aortic insufficiency four years previously and had complete atrioventricular block. He was HLA-B7 positive, but had no history of inflammatory back pain or spondylitis on *x* ray examination. The other, a 72 year old man was HLA-B27 positive, though did have inflammatory back pain and severe spondylitis. The underlying cardiac abnormality was mobitz type 2 atrioventricular block. Based on the ESSG criteria the prevalence of SpA was 0.8%. HLA-B27 was present in six (5%) patients with a permanent pacemaker and nine (7%) of the control group (χ^2=0.24; p=0.63).

In summary, in this observational study patients with a permanent pacemaker were no more likely to be HLA-B27 positive than a group of population controls.

Authors' affiliations
J Bruges-Armas, C Lima, D Simas Lopes, V Schneider, J P Paisana Lopes, A Ferreira Gomes, J G Coelho Gil, M J Barreiros, M J Peixoto, F Garrett, F Laranjeira, A R Couto, Departments of Immunogenetics, Cardiology and Radiology, Hospital de Santo Espirito de Angra do Heroísmo, Azores, Portugal
T W O'Neill, ARC Epidemiology Research Unit, Manchester, UK
G Herrero-Beaumont, Department of Rheumatology, Institute Jimenez Dias, Madrid, Spain

Correspondence to: Dr J Bruges-Armas, Department of Immunogenetics, Hospital de Santo Espirito de Angra do Heroísmo, 9700 Angra do Heroísmo, Azores, Portugal; jacome.armas@netc.pt

Accepted 24 February 2003

REFERENCES

1 **Bottiger LE**, Edhag O. Heart block in ankylosing spondylitis and uropolyarthritis. Br Heart J 1972;34:487–92.
2 **O'Neill TW**. The heart in ankylosing spondylitis. Ann Rheum Dis 1992;51:705–6.
3 **Bergfeldt L**, Edhag O, Vedin L, Vallin H. Ankylosing spondylitis - an important cause of severe disturbances of the cardiac conduction system. Prevalence among 223 pacemaker treated men. Am J Med 1982;73:187–91.
4 **Bergfeldt J**, Moller E. Pacemaker treated women with heart block have no increase in the frequency of HLA-B27 and associated rheumatic disorders in contrast to men - a sex linked difference in disease susceptibility. J Rheumatol 1986;13:941–3.
5 **Bergfeldt L**. HLA B27-associated rheumatic diseases with severe cardiac bradyarrhythmias. Clinical features and prevalence in 223 men with permanent pacemakers. Am J Med 1983;75:210–15.
6 **Bergfeldt L**, Möller E. Complete heart block - another HLA B27 associated disease manifestation. Tissue Antigens 1983;21:385–90.
7 **Peeters AJ**, ten Wolde S, Sedney MI, de Vries RRP, Dijkmans BAC. Heart conduction disturbance: an HLA-B27 associated disease. Ann Rheum Dis 1991;50:348–50.
8 **Bunce M**, O'Neill CM, Barnardo MCNM, Browning MJ, Morris PJ, Welsh KI. Phototyping: comprehensive DNA typing for HLA-A, B, C, DRB1, DRB3, DRB4, DRB5 & DQB1 with 144 mixes utilizing sequence-specific primers (PCR-SSP). Tissue Antigens 1995;46:35.
9 **Dougados M**, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A, *et al*. The European Spondylarthropathy Study Group Preliminary Criteria For The Classification Of Spondylarthropathy. Arthritis Rheum 1991;34:1218–27.