CORRESPONDENCE

Primary association of HLA-B51 with Behçet’s disease in Ireland

EDITOR,—I read with great interest the paper by Kilmarin et al. The incidence of 25% (six patients out of 24) of HLA-B51 among the 24 patients with Behçet’s disease is interpreted as showing a “primary association” between this HLA antigen and Behçet’s disease in Ireland.

In my opinion, the far reaching conclusions of these authors are questionable as the control group consisting of “96 healthy voluntary blood donors to the Blood Transfusion Service Board” may not be an adequate sample for comparison.

The HLA frequencies in the 24 patients with Behçet’s disease as outlined in Table 1 of their paper show that of the 52 HLA antigens tested, 21 antigens (40.3% frequency) were absent (0.00 frequency) in the group of Behçet’s patients and were present in the control group. Moreover, four other HLA antigens (of the 52 tested) were absent in the control group and detected only in the patient group. The absence of 46% of the tested HLA antigens in either group and their presence in the other group indicate unequivocally that the group of volunteers chosen as control for the frequency of the HLA-B51 is inadequate. This phenomenon exemplifies once again the need for proper controls in order to circumvent the unavoidable pitfalls of possible “clustering” of antigens among a small group of patients (or controls).

When dealing with small groups of patients, as in this study, the proper control group for comparison should be collected from a proportionate number of volunteers living in the same region or the same village as the patients. Preferably, patients attending the same ophthalmology clinic serving the area should serve as controls. For example, if two patients with Behçet’s disease were diagnosed and referred from clinic X, then eight non-Behçet’s patients (to form the same ratio for the total number of patients to controls—one to four—as performed in this study) from the same ophthalmic clinic should be included within the control group. This is especially important in countries where heterogeneous genetic haplotypes may be found in different regions.

It is undeniable that the most important findings of this study are the observations that all six Behçet’s patients with HLA-B51 were male and the fact that 18 other Behçet’s patients were negative for this antigen. Therefore, crucial data to be analysed would be comparison of the various HLA antigens among the HLA-B51 positive and HLA-B51 negative Behçet’s patients. Furthermore, the study of HLA haplotypes of the family members of these two groups (HLA-B51 positive and negative Behçet’s patients) may shed more light on whether HLA-B51 is truly associated with Behçet’s disease in Ireland or is only an incidental finding as a result of clustering of antigens in various regions in this country.

D. BENEZRA
Hadasah University Hospital, Jerusalem, Israel

Reply

EDITOR,—We would like to thank Professor BenEzra for the interest shown in our paper but wish to point out that the claim for a primary association between HLA-B51 and Behçet’s disease is strongly supported by the experimental data in our study. Although only 25% of our Behçet’s disease patients were B51 positive, when compared with the very low prevalence of HLA-B51 in the Irish population (2%, 372 of 16,682 healthy volunteer blood donors), and correspondingly in our control group (0%), a highly significant association is found suggesting a strong immunogenetic predisposition but also a multifactorial pathogenesis. BenEzra suggests that the absence of 42% (not 46% as quoted in his letter) of the tested HLA antigens in either the Behçet’s disease patient group or the control group, and their presence in the other group, “unequivocally” indicates that the group of volunteers chosen for the control group is inadequate. Clustering of HLA antigens may indeed occur in a small group of patients or controls, and as BenEzra admits, is an “avoidable pitfall associated with a small patient or control group. However, in our study this was due to the inevitably small Behçet’s disease patient group (and appropriate number of controls), owing to the low prevalence of Behçet’s disease in north western Europe, and not the inadequate nature of our control group. The outstanding Behçet’s disease association in our study was with HLA-B51, with a relative risk of 6.3 and corrected exact value of 0.002, comparable with previous reports from Japan and Turkey. Were clustering to have a significant effect, other spurious HLA haplotype associations would have been seen but were not, with none of the other HLA antigens showing a significantly increased frequency using the Bonferroni correction, even when an antigen was present in one group and absent in the other group.

We agree that in countries where heterogeneous genetic haplotypes are found in different regions, such as Israel, a proper control group should be from a proportionate number of volunteers living in the same region or village as the patients. In ethnic terms, however, the Republic of Ireland is a “village” and can be considered as one region with a high degree of ethnic homogeneity in this island population (periphery of north western Europe). As pointed out in our paper, there is only one blood donor service in the Republic of Ireland, operating nationally with one central tissue typing laboratory, allowing healthy voluntary blood donors to be used as representative of the general population, and thus an appropriate control group. Moreover, the geographic distribution of our Behçet’s disease patient group very closely matches the current Irish HLA genetic distribution from census data. We do not agree, however, that patients attending the same ophthalmic clinic serving the area should serve as controls, as despite this group has ophthalmic disease and the control group should be healthy, as in our control group.

Further data analysis is given in Table 1 showing that clustering of various antigens was not found in the HLA-B51 positive Behçet’s disease patients compared with the HLA-B51 negative Behçet’s disease group. This would make it extremely unlikely that the significant prevalence of HLA-B51 in Irish patients with Behçet’s disease was due to clustering of HLA antigens.

D. KILMARTIN
Department of Ophthalmology, University of Aberdeen Medical School, Aberdeen AB25 2ED

Table 1 HLA antigen frequencies in HLA-B51 positive and negative Irish Behçet’s disease patients

<table>
<thead>
<tr>
<th>Antigen frequency</th>
<th>HLA B51 positive (%)</th>
<th>HLA B51 negative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>3 (50.0)</td>
<td>9 (50.0)</td>
</tr>
<tr>
<td>A2</td>
<td>2 (33.3)</td>
<td>11 (61.1)</td>
</tr>
<tr>
<td>A3</td>
<td>1 (16.7)</td>
<td>3 (16.7)</td>
</tr>
<tr>
<td>A9</td>
<td>0 (0.0)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>A10</td>
<td>0 (0.0)</td>
<td>2 (11.1)</td>
</tr>
<tr>
<td>A11</td>
<td>2 (33.3)</td>
<td>3 (16.7)</td>
</tr>
<tr>
<td>A19</td>
<td>0 (0.0)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>A28</td>
<td>1 (16.7)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>A29</td>
<td>1 (16.7)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>A31</td>
<td>0 (0.0)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>A32</td>
<td>0 (0.0)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>A35</td>
<td>0 (0.0)</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>B7</td>
<td>1 (16.7)</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>B8</td>
<td>2 (33.3)</td>
<td>7 (38.9)</td>
</tr>
<tr>
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</tr>
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<td>2 (11.1)</td>
</tr>
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<td>1 (5.5)</td>
</tr>
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<td>1 (5.5)</td>
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<td>10 (55.5)</td>
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<tr>
<td>B57</td>
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<td>2 (11.1)</td>
</tr>
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<td>5 (33.3)</td>
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</tr>
<tr>
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<td>4 (22.2)</td>
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<td>2 (11.1)</td>
</tr>
<tr>
<td>DR14</td>
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<td>1 (5.5)</td>
</tr>
<tr>
<td>DR15</td>
<td>0 (0.0)</td>
<td>1 (6.7)</td>
</tr>
</tbody>
</table>

*Although not truly valid as n<10, percentages are given for comparison.

BOOK REVIEWS

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This is an ambitious book, written by 11 contributors from a variety of ophthalmic backgrounds compiled by Barbara Cassin with Dr Latif M Hamed as the medical content editor. Barbara Cassin was head of the orthoptic/
ophthalmic technology training programmes at the University of Florida for 18 years.

Starting with basic ophthalmic sciences, neuroanatomy, and optics the aim is to provide the technician and technologist a basic knowledge of, and sources of, information about ophthalmic technical skills. These include orthoptics, optometry, photography, perimetry, biometry, and a host of other assessment, recording, and measurement tools needed to provide vital information to the ophthalmologist. It concludes with a very useful section on abnormalities of the eye, eye disorders, and eye diseases and a comprehensive appendix. The beginning of each chapter states the learning objectives for that section and, at the end of the chapter, five multiple choice questions test for knowledge acquired.

The illustrations have been chosen for their clarity of information and come from a wide variety of credited sources, although they are somewhat cluttered on the pages among the two column text.

Since this is a reference book, it is somewhat disappointing that the only sequence of fluorescein angiography shown is a normal one, and all the frames of this are reproduced upside down!

This is an American book, and is aimed at, and succeeds in fulfilling its purpose to support, those working towards approved certification of the Joint Commission on Allied Health Personnel in Ophthalmology, such as COA (Certified Ophthalmic Assistant), COT (Certified Ophthalmic Technician), and COMT (Certified Ophthalmic Medical Technician). It is also background reading for the Ophthalmic Photographer's Society qualification or COPRA (Certified Ophthalmic Photographer and Retinal Angiographer). At present formal certification for some para-medical professionals is available within the UK—for example, optometrists and orthoptists, but not for others. This is probably due to some extent to the small numbers involved.

Eventually we may well change to follow the American model of multicertified individuals covered by most of the skills in this publication.

This book was published in 1995 and as such suffers already from becoming out of date. There are now many changes in our working practices, brought about by the advent of cheaper computerised digitised attachments to our existing equipment as well as totally new dedicated ones, such as scanning laser ophthalmoscopes, which it omits to mention the relevance of a chest x-ray. Because the listing of causes is alphabetical the reader may gain a false impression of commonality—for example, top of the list of causes of exophthalmos is listed “drug causes”. The most important clinical associations are highlighted here to indicate relative frequency. There are useful tables indicating association of diseases with age.

One main concern with such a text is the lack of references. Key references are given, but many of the associations listed may be questionable or possibly based on isolated case reports and the reader has no means of assessing this. For example, under causes of excess tears control of redness is probably listed (but oddly this condition is not listed as a cause of induced hypotropia). Under psychic causes of excess tears herpes simplex keratitis is listed!

In conclusion this book offers quick reference for those interested in rare associations. It is of no value to the postgraduate student studying for professional examinations and in many respects could be misleading, giving false impressions of the frequency of certain disease entities. It is of little value in looking up syndromes and may best find a place on the shelves of the ophthalmic equivalent of train spotters.

ALISON FARROW


It is testimony to this text’s popularity that this is its 6th edition and that it is written in six languages. Having read it for the first time I remain a little puzzled that it is indeed so popular. Having said this, it is not a book one reads as it is primarily a reference text offering over 700 pages of detailed diagnostic analysis of ophthalmic symptoms and signs (not diseases).

It is classified anatomically to a particular region of the eye (for example, orbit, extraocular muscles, cornea, conjunctiva, etc) and the reader then seeks a particular symptom or sign. The causes are then listed alphabetically thus offering fairly quick reference. The result is lengthy lists of associations and in this respect is useful in identifying rare associations and would be a useful addition to a departmental reference library. It is particularly exhaustive in relation to drug induced toxicity. It includes “diagnostic decision tables” at the end of some of the differential diagnosis lists. These list features of the history, physical signs, and laboratory tests that differentiate each of the more clinically relevant possible diagnoses and are quite helpful although of limited value in everyday practice.

Despite its exhaustive nature my fairly brief survey of this book in looking up a few examples identified a number of fairly obvious omissions or debatable inclusions. For example, in the differential diagnosis of lid tumours chalazion is not mentioned. In the investigation of orbital disease and cortical blindness no mention is made of magnetic resonance imaging as a useful investigation! In lacrimal disease it is recommended that the investigation of sarcoidosis includes a Kveim test but omits to mention the relevance of a chest x-ray.

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ST D ROXBURGH

CD-ROM REVIEW

Automated Perimetry; An Interactive Primer. By John Planagan, Graham Trope, Yvonne Buys. $120. Waterloo, Ontario, Canada: Lifelearn Eyecare, 1997.

The CD-ROM examines in detail over 20 cases using the Humphrey visual field analyser. The clinical range covered includes complicated and non-complicated cases of glaucoma at different stages of progression and, neurological cases including head trauma. These cases can be followed over a number of years with the help of over 300 sample fields, stereo photographs of the discs and computed tomograph scan images when appropriate.

The graphic presentations are clear with adequate explanations given in accompanying text. An interactive multiple choice facility allows individuals the opportunity to complete ongoing personal assessment of their knowledge.

The authors declare that they have attempted to create an easy to use case based interface to assist eyecare professionals in better understanding visual field interpretation. They must be congratulated for achieving what they set out to do. This publication will be welcomed by ophthalmic nurses, orthoptists, optometrists, and doctors starting their training in ophthalmology.

FERNANDO VALENZUELA

NOTICES

Glucoma Society (UK & Eire)

DAVID COLE TRAVEL FELLOWSHIP

The David Cole Travel Fellowship, instituted by Merck Sharp and Dohme in memory of Professor David Cole, will assist a visit to a hospital or research centre during the academic year starting 1 October 1998. The award will be equivalent to £2000. The purpose of the award is to enable the successful applicant to gain experience and knowledge in pursuit of a specific project related to glaucoma.

THE GLAUCOMA SOCIETY (UK & EIRE) RESEARCH GRANT

The Glaucoma Society (UK & Eire) research grant, sponsored by the International Glaucoma Association will be available for a research project clinically orientated to glaucoma for 1998. The award will be equivalent to £2500.

The grant may be used towards salary or project expenses or for buying equipment.

THE GLAUCOMA SOCIETY (UK & EIRE) RESEARCH AWARD

The Glaucoma Society (UK & Eire) research award, sponsored by Alcon Laboratories will be given in support of a research project related to glaucoma. The award will be equivalent to £2000.

These awards are available to both medical graduates and non-medical scientists resident in the United Kingdom or Ireland. They may be held concurrently with other awards.

For further details and application forms please contact: Dr S Nagasubramanian, Secretary, Glaucoma Society (UK & Eire), Glaucoma Unit, Moorfields Eye Hospital, City Road, London EC1V 2PD.

The closing date for applications is 10 June 1998.

Eye injuries worldwide

The latest issue of the Journal of Community Eye Health (no 24) concerns the magnitude of injuries worldwide. It covers the causes and prevention, health promotion and eye injuries, ocular injury pattern in Pakistan, primary care of eye injuries, and epidemiology in practice. For further information please contact Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V

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Residents' Foreign Exchange Programme
Any resident interested in spending a period of up to one month in departments of ophthalmology in the Netherlands, Finland, Ireland, Germany, Denmark, France, Austria, or Portugal should apply to: Mr Robert Acheson, Secretary of the Foreign Exchange Committee, European Board of Ophthalmology, Institute of Ophthalmology, University College Dublin, 60 Eccles Street, Dublin 7, Ireland.

9th British Association of Day Surgery Annual Scientific Meeting and Exhibition
The 9th British Association of Day Surgery Annual Scientific Meeting and Exhibition will take place at the Harrogate International Centre on 4–6 June 1998. Further details: Kite Communications, The Silk Mill House, 196 Huddersfield Road, Meltham, W Yorks HD7 3AP. (Tel: 01484 854575; fax: 01484 854576; email info@kitecomms.co.uk)

XVIIIth International Congress of Ophthalmology
The XXVIIIth International Congress of Ophthalmology will be held in Amsterdam on 21–26 June 1998. Further details: Eurocongress Conference Management, Jan van Goyenkade 11, 1075 HP Amsterdam, Netherlands. (Tel: +31-20-6793411; fax: +31-20-6737306; internet http://www.solution.nl/ico-98/)

First Combined International Symposium on Ocular Immunology and Inflammation
The First Combined International Symposium on Ocular Immunology and Inflammation will be held in Amsterdam on 27 June–1 July 1998. The meeting is sponsored by the International Ocular Immunology and Inflammation Society, the International Uveitis Study Group, and the Immunology and Immunopathology of the Eye Organisation. Further details: Professor Aize Kijlstra, The Netherlands Ophthalmic Research Institute, PO Box 12141, 1100 AC Amsterdam, Netherlands (email: a.kijlstra@amc.uva.nl)

2nd International Conference on Ocular Infections
The 2nd International Conference on Ocular Infections will be held on 22–26 August 1998 in Munich, Germany. Further details: Professor J Frucht-Pery, 2nd International Conference on Ocular Infections, PO Box 50006, Tel Aviv, 61500, Israel. (Tel: 972 3 5140000; fax: 972 3 5175674 or 5140077; email: ocular@kenes.com)

XVI Tuebingen Detachment Course
The XVI Tuebingen Detachment Course in retinal and vitreous surgery will be held 4–5 September 1998 in Odessa, Ukraine. Further details: Professor I M Logai, Director, The Filatov Institute, 49/51 Boulevard Francois, Odessa, 270061, Ukraine. (Tel:+38-0482-22 20 35; fax: +38-0482-68 48 51).

ICOP 98
The next International Conference in Ophthalmic Photography (ICOP) will be held on 19–21 September 1998 in Amsterdam. Further details: Mrs Gillian Bennerson, Senior Ophthalmic Photographer, Bristol Eye Hospital, Lower Maudlin Street, Bristol BS1 2LX. (Tel: 0117-928-4677).

IV meeting of the European Society for Out-Patient Eye Surgery (ESOPES)
The IV meeting of the European Society for Out-Patient Eye Surgery (ESOPES) will be held in Vittel, France on 9–11 October 1998. Further details: Mrs Nicole Charron, Director, Palais des Congrès, Av Bouloumie, BP 57, 8802 Vittel, France. (Tel: +33 329 08 18 30; fax: +33 329 08 6601.)

VIIth International Symposium on Graves' Ophthalmology
The VIIth International Symposium on Graves' Ophthalmology will be held on 27–28 November 1998 in Amsterdam. Further details: Amsterdam Thyroid Club, Department of Endocrinology, F5-171, Academisch Medisch Centrum, Meibergdreef 9, 1105 AZ Amsterdam, Netherlands.

Ophthalmic technologies
The 9th Ophthalmic Technology Conference will be held on 23–24 January 1999 during the International SPIE symposium on biomedical optics. Further information: The SPIE Organisation, PO Box, Bellingham, WA 98227-0010, USA. (Fax: (+1) 360-647-1445; email: www.spie.org/info/pw)

Laser eye injuries
A conference on the epidemiology, prevention, diagnosis, and therapy of laser eye injuries will be held in San Jose, California on 25–26 January 1999 during the International SPIE symposium on biomedical optics. Further information: The SPIE Organisation, PO Box, Bellingham, WA 98227-0010, USA. (Fax: (+1) 360-647-1445; email: www.spie.org/info/pw)

XII Congress European Society of Ophthalmology
The XII Congress European Society of Ophthalmology will be held in Stockholm, Sweden on 27 June–1 July 1999. Further details: Congress (Sweden) AB, PO Box 5819, S-114 86 Stockholm, Sweden. Tel: +46 8 459 66 00; fax: +46 8 661 91 25; email: soe@congrex.se; http://www.congrex.com/soe/
Primary association of HLA-B51 with Behçet's disease in Ireland

DAVID BEN EZRA

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