Letters to the Editor

HLA in relation to retinopathy, residual beta-cell function and age at onset in Type 1 (insulin-dependent) diabetic patients

Sir,

The possible rôle of genetic factors in the pathogenesis of microangiopathy was recently reviewed in *Diabetologia* by Barbosa and Saner [1] who have pointed out that most studies on Type 1 diabetic patients tend to show an increased frequency of HLA-B₁₅ or -DR₄ in association with severe or proliferative retinopathy. However, as discussed, by these authors [1] one Icelandic study [2] has suggested that HLA-B₁₅ positive patients might be less prone to develop retinopathy. This issue may be further elucidated by a recent report from Hoogwerf et al. [3] demonstrating a decline of C-peptide secretion in Type 1 diabetic patients with increased duration of the disease. In addition, the stimulated C-peptide response was found to be less marked in patients who were younger than 10 years old at the onset of diabetes. Furthermore, HLA-DR₄ positive subjects had higher mean C-peptide values than -DR₄ negative patients, irrespective of duration of the disease. The authors concluded that DR₄ positive patients might be blessed by a better preservation of beta-cell function and discussed that this might favour improved glycaemic control, and hence delay or postpone microvascular complications in the diabetic patient [4]. A previous study of the Icelandic Type 1 diabetic population [5] has demonstrated that a subgroup of patients without retinopathy after a diabetes duration of 20 years or more required significantly less insulin than those with retinopathy after a comparable duration of the disease. The mean ($\pm$ SD) age at diagnosis of diabetes in the retinopathy-free subjects was 30 ± 4 years and 70% were females. Late onset of diabetes and female preponderance are believed to characterize "autoimmune" diabetes [6]. In a study of Type 1 diabetic patients with thyroid disorders in Iceland [7] the age at the onset of diabetes was 38 ± 12 years and 80% were females. They tended to require less than average insulin doses, eye and kidney complications were relatively rare and a higher frequency was found for HLA-B₁₅ than -B₈ (relative risks 4.2 and 2.3 respectively).

Whether HLA-types are directly related to the age at onset of diabetes is presently controversial. HLA-DR₄ has been reported to be significantly increased in Type 1 diabetes with age of onset after 40 years [8]. Other authors were unable to find such an association in analysing different subgroups according to their age at onset up to the age at onset of 25 years [9]. Likewise, the frequency of HLA-B₁₅ is similar in patients diagnosed 0–19 years old compared to those with an age at onset of above 30 years in the Icelandic diabetic patients (unpublished).

In conclusion, HLA-DR₄ and probably HLA-B₁₅, because of the strong linkage disequilibrium between these two, appear to be related to better preservation of residual beta-cell function. This is demonstrated by a greater C-peptide response in HLA-DR₄ positive Type 1 diabetes patients. This may result in better glycaemic control in these patients and retard the development of long-term microvascular complications. These data may thus be compatible with the previous find-

ing of less retinopathy in HLA-B₁₅ positive Type 1 diabetic patients in Iceland.

Yours sincerely,
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Incidence of diabetes in Scottish children

Dear Sir,

The record lineage method used by Patterson et al. [1], and in their recent update [2], involves several assumptions, i.e. (1) that all new cases are admitted to hospital; (2) that recording of admissions is complete, and coding correct; (3) that all patients from outwith Scotland can be identified as such; (4) that all Scottish cases have onsets in Scotland (otherwise the first admission in Scotland will appear to be