Latent autoimmune diabetes in the young

Editor – Latent autoimmune diabetes in the young (LADY) incorporates an increasing number of young patients with an initial insulin independent period. This is similar to latent autoimmune diabetes in adults (LADA), which masquerades as type 2 diabetes. The UK Prospective Diabetes Study estimated that 10–15% of patients with type 2 diabetes have latent autoimmune diabetes and that 58% of these patients require insulin within six years of diagnosis, irrespective of age.[1] The recent finding that early insulin therapy has favourable outcomes on β-cell function and glycaemic remission compared with oral hypoglycaemic agents in patients with newly diagnosed type 2 diabetes is an exciting prospect.[2]

With reference to the recent lesson of the month (*Clin Med* October 2008 pp 552–3), taking into consideration the asymptomatic 15-year-old girl's body mass index of 21.4 kg/m^2, consistent with ketonuria and raised blood glucose, favours the initiation of insulin treatment. It is of concern that the patient's β-cell function may have been left to deteriorate on sulphonylureas. In light of Weng *et al*'s finding a low-dose insulin regime may have been a better option to preserve β-cell function and prevent catastrophic outcomes such as diabetic ketoacidosis.[2]

It would be interesting to know the HbA_{1c} of the patient as Stene and colleagues demonstrated that normal but increasing HbA_{1c} may predict progression from islet immunity to overt type 1 diabetes, whereas random plasma glucose levels are less predictive.[3] Further, the human leukocyte antigen (HLA) status of the patient is not stated which could predict disease progression. The DAISY study implies that DR3/4 and the DQ8 genotype are predictive of disease progression. However 50% of genetic risk for type 1 diabetes is attributable to HLA region, including the insulin gene, CTLA-4, IL4/13 which all demonstrate a strong association.[4] Autoantibody testing is highly favourable in such patients as there is a strong association with progression to type 1 diabetes.[5] However, autoantibodies such as GAD65 must be repeated more than once to rule out false or transient positive results. In addition to existing markers of autoimmunity, data on a novel autoantibody ZnT8 suggest that this autoantibody may need to be tested to diagnose latent autoimmune diabetes.[6]

The possibility that LADY represents a growing proportion of cases seen in clinical practice, together with limited evidence to guide health professionals in treatment options, makes research into glycaemic control and preservation of β-cell function relevant in these patients. Screening and early detection of such patients may lead to a less severe onset and a milder clinical course following diagnosis.[7]

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In response

We thank Bering and Devendra for their comments. We agree that further research into preservation of β-cell function is highly relevant to patients with LADY though, of course, it is no more important than that in any other area of diabetes.

While we agree that early insulin therapy may preserve β-cell function, we would argue that progressive decline due to T-cell mediated destruction in type 1 diabetes is the norm. Extrapolation from the data of Weng *et al* based on type 2 diabetes and published only recently in 2008 does not allow the comment that the patient's β-cell function may have 'been left to deteriorate on sulfonylureas'.[1] Nor would we accept that automatic early treatment with insulin is more likely to 'prevent catastrophic outcomes such as diabetic ketoacidosis' than proper patient education and a supply of Ketostix®. Indeed, the psychosocial gains for a teenager (and other family members) treated with oral agents while maintaining excellent glycaemic control (as judged by the HbA_{1c} values stated) for four years should not be underestimated.[2]

It is clear that the patient's family history would have allowed her inclusion into research studies on the progression to type 1 diabetes and that, had she been so involved, she may well have been discovered earlier and, thus, have had a milder initial clinical course. We doubt, though, whether this justifies the cost of HLA typing outside of research studies especially when, as Bering and Devendra point out, the results are only as good as tossing a coin.[3] With regard to antibody testing we concur with the views expressed but feel that the role of ZnT8 only recently described needs to be explored in additional studies.[4]

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Clinical & Scientific letters

Letters not directly related to articles published in *Clinical Medicine* and presenting unpublished original data should be submitted for publication in this section. Clinical and scientific letters should not exceed 500 words and may include one table and up to five references.

A Royal College of Physicians lead on alcohol?

A distinguished colleague used to say that it took 100 years to achieve any worthwhile advance in public health. Disgusted by my failure to save the lives of most 50-year-olds with alcoholic cirrhosis, I decided 30 years ago that prevention was better than no cure and took up the cause of alcohol misuse. In the light of history, my impatience at the lack of progress may be misplaced, but it is still a long time since I wrote a paper in 1979 optimistically called 'Action on alcohol',[1] and another 10 years later on 'Action on alcohol at last'.[2] In the early 1980s I tried to promote alcohol misuse to the Royal College of Physicians (RCP) but was told by a senior Fellow that alcoholics (sic) were no part of a physician's business. The two RCP working parties that eventually followed have been half-hearted affairs – the first being confined to the physical damage (a relatively minor part of the problem) and the second implying that health professionals rather than doctors should take the blame, 'doctors…regarded alcoholics [that word again] as a bad bunch and don't want anything to do with them', said the secretary.

Now the RCP is supporting a European Forum, first mooted in 1993 and scuppered by Labour, which 'provides a valuable platform for open discussion on actions to reduce alcohol-related harm' and 'to review the evidence base'.[3] My heart sinks. The Cabinet Office spent six years reviewing evidence that could have been produced in a few hours by any expert in the field. We already have a pretty good idea what will and will not work in alleviating alcohol problems. Education and propaganda have repeatedly been shown to be ineffective and costly, yet the forum says 'it remains to be seen if action in the areas of education, information and commercial communication will reduce alcohol-related harm'.[3] Also I doubt if the current enthusiasm for targeting the young will help; after all, drinking alcohol, like smoking used to be, is a rite of passage. No wonder my welcome for the forum has been somewhat cool.[4]

Since 1960 the price of alcohol in Britain has halved relative to income, while average consumption has doubled; consumption closely mirrors cost and availability in both directions, and I hope epidemiologists are looking at the effects of the present financial meltdown on alcohol statistics. No less than three authoritative World Health Organization reports by international experts in the last 30 years have pointed out that increasing price and restricting outlets would have the greatest benefit, but this is anathema to public and governments.

What might the RCP do?

First, I believe the RCP could use its powerful advocacy with the medical profession and the public to *do* something rather than having endless discussions. Remember smoking? First, since most doctors know little about alcohol misuse, it should insist that all physicians are comprehensively taught the social and physical harms and at the least how to detect trouble and intervene early. Second, the RCP might consider adding addiction medicine to its list of specialties. This is a thriving specialty in the USA, and it is a disgrace that there is barely an academic unit in a British medical school devoted to alcohol and other addictions. Third, perhaps the RCP could provide support for a Richard Doll initiative in which doctors would be circulated about their drinking habits and incidence of alcohol disorders so as to highlight the profession's concern? Lastly, it must surely challenge the influence of a drinks industry that ignores or distorts the evidence or attempts to rubbish it,[5] claims that only a minority of drinkers, ie those who are dependent, are affected, ignores the voluntary code, brands its opponents covert prohibitionists, pleads job losses from increasing prices, an argument rejected by the RCP years ago,[6] and like big business worldwide has a malign influence on governments. Remember what happened to the tobacco companies when the medical profession's patience snapped? Surely we could try and emulate the success of that campaign – and drink to the achievement of this one?

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