Delfino A, Picciotto A: Kinetics of soluble tumour necrosis factor (TNF)-alpha receptors and cytokines in the early phase of treatment for chronic hepatitis C: comparison between interferon (IFN)-alpha alone, IFN-alpha plus amantadine or plus ribavirine. *Clin Exp Immunol* 136:507–512, 2004

- 7. Tsai SL, Liaw YF, Chen MH, Huang CY, Kuo GC: Detection of type 2-like T helper cells in hepatitis C virus infection: implications for hepatitis C virus chronicity. *Hepatology* 25:449–458, 1997
- 8. Eckels DD, Tabatabail N, Bian TH, Wang H, Muheisen SS, Rice CM, Yoshizawa K, Gill J: In vitro human Th-cell responses to a recombinant hepatitis C virus antigen: failure in IL-2 production despite proliferation. *Hum Immunol* 60:187–199, 1999
- Masaki N, Fukushima S, Hayashi S: Lower th1/th2 ratio before interferon therapy may favor long-term virological responses in patients with chronic hepatitis C. Dig Dis Sci 47:2163–2169, 2002
- Rosa D, Saletti G, De Gregorio E, Zorat F, Comar C, D'Oro U, Nuti S, Houghton M, Barnaba V, Pozzato G, Abrignani S: Activation of naïve Blymphocytes via CD81, a pathogenic mechanism for hepatitis C virus-associated B lymphocyte disorders. Proc Natl Acad Sci U S A 102:18544–18549, 2005
- 11. Sanyal AJ, Chand N, Comar K, Mirshahi F: Hyperinsulinemia blocks the inhibition of hepatitis C virus (HCV) replication by interferon: a potential mechanism for failure of interferon therapy in subjects with HCV and nonalcoholic fatty liver disease (Abstract). *Hepatology* 40 (Suppl. 1):179A, 2004

A Clinical Screening Tool Identifies Autoimmune Diabetes in Adults

Response to Fourlanos et al.

ourlanos et al. (1) report on a screening instrument designed to facilitate management of latent autoimmune diabetes of adults (LADA). They assert that in poorly controlled type 2 patients exhibiting two or more of five features (age <50 years, hyperglycemic symptoms, BMI <25.0 kg/m², and personal and family history of autoimmunity), the "logical" next step is confirmatory islet antibody testing (1).

Although the effect of routine use of the instrument on outcomes such as ${\rm HbA}_{\rm 1c}$ is unknown, the article raises important questions relating to the manage-

ment of clinically diagnosed type 2 diabetes. The authors state that LADA patients can require rapid escalation of oral therapy or early commencement of insulin (1). However, patients with severely deficient $\beta\text{-cell}$ function but insufficient LADA features still need insulin therapy. In addition, some LADA patients achieve reasonable initial glycemic control with oral agents (2), with insulin available should this strategy fail.

We have concerns that the LADA instrument fails to meet the necessary criteria for a valid screening tool (3). In their small study, Fourlanos et al. report a sensitivity of 90% and specificity of 71%. However, the positive predictive value is 21%, indicating that the probability of correctly diagnosing LADA is low. This, and the high false-positive rate (28%), suggest a limited ability to identify patients most in need of early insulin therapy.

The authors' apparent intention is to promote the instrument as part of usual care. Because of this, and since the American Diabetes Association does not recommend islet antibody testing in type 2 diabetes (4), why do the authors recommend serological confirmation (1)? Even in the case of children, in whom education, dietary counsel, and treatment differ markedly by diabetes type, autoantigens may be present in a substantial number with otherwise straightforward type 2 diabetes (4). One reason for antibody testing may be to characterize LADA patients fully for intervention studies (1), but this would only be appropriate in specialist centers.

We contend that the management of poorly controlled type 2 diabetes in adults should be based on detailed clinical assessment (including the LADA instrument components), review of glycemic control, implementation of strategies (including educator and dietitian input) that might improve adherence to self-management, a discussion of available therapies (including insulin), and adequate monitoring and support. The use of the LADA instrument and/or autoantibody testing appears redundant in this setting.

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References

- Fourlanos S, Perry C, Stein MS, Stankovich J, Harrison LC, Colman PG: A clinical screening tool identifies autoimmune diabetes in adults. *Diabetes Care* 29:970–975, 2006
- 2. Davis TM, Wright AD, Mehta ZM, Cull CA, Stratton IM, Bottazzo GF, Bosi E, Mackay IR, Holman RR: Islet autoantibodies in clinically diagnosed type 2 diabetes: prevalence and relationship with metabolic control (UKPDS 70). *Diabetologia* 48:695–702, 2005
- 3. Barratt A, Irwig L, Glasziou P, Cumming RG, Raffle A, Hicks N, Gray JAM, Guyatt GH: Users' guide to the medical literature. XVII. How to use guidelines and recommendations about screening. *JAMA* 281: 2029–2034, 1999
- 4. American Diabetes Association: Standards of medical care in diabetes (Position Statement). *Diabetes Care* 29 (Suppl. 1): S4–S42, 2006

A Clinical Screening Tool Identifies Autoimmune Diabetes in Adults

Response to Davis et al.

e thank Davis et al. (1) for their comments regarding the recent publication of a climinary ing tool for latent autoimmune diabetes in adults (LADA) (2). It is appreciated that the authors' routine management of "poorly controlled adult type 2 diabetes" incorporates the "LADA instrument components." However, our observations of the management of such patients by internists and diabetes nurse practitioners in the community are often contrary to the practice of the authors. Adults with suboptimal glycemic control due to declining β-cell function (often secondary to autoimmune disease) are underrecognized, leading to delays in commencing insulin therapy. The clinical screening tool was developed to aid primary care physicians and diabetes nurse practitioners to consider the pathophysiological process of autoimmune β-cell destruction. The authors cite that the positive predictive value of the clinical screening tool is low