in an improved safety profile; but, only clinical outcomes are relevant to assess the risk, and large surveillance studies are warranted to confirm this hypothesis.

So far, the contraindications and warnings for use of current hormonal combinations also apply to the estradiol-based contraceptives.

## Recognition and Management of Atypical Forms of Diabetes

*Written by Rita Buckley*

### *Cystic Fibrosis-Related Diabetes*

Samuel J. Casella, MD, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire, USA, reported that cystic fibrosis-related diabetes (CFRD) has increased in concert with gains in long-term survival of cystic fibrosis (CF) patients, with rates as high as 40% to 50% in adult cohorts. CFRD has many features of type 1 diabetes mellitus (T1DM).

The multicenter Cystic Fibrosis-Related Diabetes Therapy Trial recently confirmed that insulin therapy is beneficial in CFRD patients, safely reversing chronic weight loss even before the development of fasting hyperglycemia [Moran A et al. *Diabetes Care* 2009].

In adult patients, a standard oral glucose tolerance test shows normal fasting glucose levels, but 2-hour glucose is ≥200 mg/dL. Unlike T1DM, macrovascular complications are rare in patients with CFRD, and microvascular complications are also less common. However, the diagnosis of CFRD has a major impact on the CF patient, because it is associated with decreased pulmonary function, poor nutritional status, and increased pulmonary exacerbations that lead to decreased long-term survival.

Though HbA1C values are lower in CF (likely due to decreased red cell survival), higher levels indicate poor control and are associated with decreased pulmonary function. Recent reports indicate that mortality rates can be improved with more effective treatment of the illness.

Recently, small pilot studies have suggested that low-dose insulin glargine may improve patient weight or pulmonary function in those with CF who have abnormal glucose tolerance without causing significant hypoglycemia [Mozzillo E et al. *Pediatr Diabetes* 2009; Bizarri C. *J Endocrinol Invest* 2006].

Despite the publication of a position statement on clinical care guidelines for CFRD that were published by the American Diabetes Association (ADA) and a clinical practice guideline of the Cystic Fibrosis Foundation [Moran A et al. *Diabetes Care* 2010], a query of the CF Registry showed significant variation in CFRD care among CF treatment centers. Screening rates remain low in many centers, and monitoring of patients with CFRD is suboptimal. The data also reveal significant variation in median HbA1C among the various CF treatment centers. Taken together, there appears to be ample opportunity for quality improvement in CFRD screening, monitoring, and outcomes.

### *Latent Autoimmune Diabetes in the Adult*

Stephen Clement, MD, Georgetown University Hospital, Washington, DC, USA, discussed the clinical characteristics, controversies, and therapies that are associated with latent autoimmune diabetes in adults (LADA). The nature and diagnosis of the disease remain controversial.

According to the ADA and the World Health Organization, LADA has no specific recognition or diagnostic criteria. However, the Immunology of Diabetes Society defines it as age of at least 30 years, a positive test for at least 1 of 4 antibodies that are found in T1DM (ICAs, GAD65, IA-2, or insulin), and no insulin treatment within the first 6 months of diagnosis [Naik RG et al. *J Clin Endocrinol Metab* 2009].

While there are still no universally accepted criteria for antibody testing in adult onset diabetes, many clinicians advocate the antibody assay only if there is a suspicion of LADA, based on a body mass index <25 kg/m$^2$ [Nambam B et al. *World J Diabetes* 2010]. However, a 5-point LADA clinical risk score had a sensitivity and specificity of 90% and 71%, respectively, in identifying LADA patients. The presence of only 1 feature/none had a negative predictive value of 99% [Kanungo A, Sanjeevi CB. *Ann NY Acad Sci* 2003].

Given the many studies that show a higher prevalence of glutamic acid decarboxylase antibodies (GADA) in LADA and the ease with which it can be assayed, measurement of GADA provides a screening procedure for detecting future β-cell dysfunction [Nambam B et al. *World J Diabetes* 2010]. A recent report demonstrated that 10% of patients who are diagnosed with type 2 diabetes have detectable serum levels of GADA. They usually progress to insulin dependency within a few years and are classified as having LADA [Akesson C. *Clin Exp Immunol* 2010].

Early instigation of insulin therapy is a must in LADA type 1 (high GADA levels) to delay the rapid islet cell failure. For those individuals with low GADA levels, classified as LADA type 2, the phenotype is very similar to type 2 diabetes, and the treatment strategy appears to be ambiguous [Nambam B et al. *World J Diabetes* 2010].