Table 2. Screening Recommendations.

• Check complete lipid profile • If normal, reassess every 2 years (sooner if significant weight gain occurs)	LDL-C	<130 mg/dL (3.37 mmol/L) if no other risk factors
		<70-100 mg/dL (1.81-2.59 mmol/L) if metabolic syndrome
		<70 mg/dL (1.81 mmol/L) if T2DM, overt vascular, or renal disease
	Non-HDL-C	30 mg/dL (0.77 mmol/L) higher than LDL-C goal
	Triglycerides	<150 mg/dL

Besides modest increases in LDL-C, with a higher concentration of small, dense LDL-C, dyslipidemia in PCOS is also associated with a reduction in subclass HDL_2. This category contains more cholesterol molecules per unit of alipoprotein than HDL_3 and may put women with the syndrome at higher risk for coronary artery disease [Demacker PN et al. *Atherosclerosis* 1986]. Some studies also show decreases in apoA-1.

Lifestyle modification is first-line therapy, with low-fat diet and regular moderate-intensity exercise. Even without weight loss, moderate-intensity exercise (at least 30 minutes) a day can improve dyslipidemia in PCOS [Brown AJ et al. *Med Sci Sports Exerc* 2009].

Oral Contraceptives and CV Health

Written by Rita Buckley

Oral contraceptives (OCs) are the most commonly used form of birth control worldwide [Blackmore KM et al. *BMC Womens Health* 2011]. Estrogen and progestins have been used by millions of women as effective combined oral contraceptives (COCs). Their safety has been documented by years of follow-up, and serious adverse events that may be related to their use are rare in the young population that is exposed to these agents. Nonetheless, COCs are not risk-free. Regine Sitruk-Ware, MD, Center for Biomedical Research, Population Council, New York, New York, USA, discussed the risks, benefits, and strategic initiatives in the quest for safer and more effective OCs.

Although the balance between the benefits and liabilities of contraceptive steroids is generally positive, in particular when compared with the risks of pregnancy (especially in women with risk factors), cardiovascular (CV) and venous risks have been associated with surrogate markers, such as lipoprotein changes (eg, total cholesterol, total triglycerides, apolipoproteins, and very low low-density lipoprotein cholesterol) and coagulation factors (eg, factor VII, protein C, endogenous thrombin potential-based activated protein C resistance, and free protein S levels), that are induced by the synthetic steroids that are used in contraceptives. Thus, the dose of synthetic estrogen in ethinyl estradiol COC pills has been reduced to minimize the likelihood of ischemic stroke, myocardial infarction, and venous thromboembolism [Archer DF and Lasa IL. *J Womens Health* 2011].

Ethinyl estradiol (EE) exerts a stronger effect than natural estradiol (E2) on hepatic metabolism, including estrogen-dependent markers, such as liver proteins. EE's more powerful hepatic impact has been related to its 17α-ethinyl group, which prevents the inactivation of the molecule. Due to the strength of its activity, the administration of EE via a nonoral route does not prevent its impact on liver proteins [Sitruk-Ware R and Nath A. *Rev Endocr Metab Disord* 2011].

To circumvent the metabolic changes that are induced by EE, newer products that use more natural compounds, such as estradiol (E2) and estradiol valerate (E2V), have been introduced, as well as new formulations, including extended-cycle and continuous-use COC. They may offer improvements over their predecessors [Archer DF and Lasa IL. *J Womens Health* 2011].

Over the last 50 years, there has also been intense interest in the type of progestin that is used in COCs in an attempt to exploit novel properties and minimize adverse risks. The synthetic progestins that are used for contraception are structurally related either to testosterone (estranes and gonanes) or to progesterone (pregnanes and 19-norpregnanes).

Several new progestins that are closer to progesterone have been designed to bind more specifically to the progesterone receptor and to minimize side effects that are related to androgenic, estrogenic, or glucocorticoid receptor interactions. Dienogest, drospirenone, and the 19-norpregnanes (eg, Nestorone®, nomegestrol acetate, and trimegestone) have been combined with low-dose estrogen—EE, E2, or E2V. E2 and E2V induce fewer changes in coagulation markers than EE. However, the relevance to venous risk is not established. It is important, though, to note that the limited thrombotic risk that is observed with OC use is lower than risk during pregnancy

Risks and benefits of the newer progestins that are used in contraceptives depend upon molecular structure, the type and dose of estrogen that is used, and the route of administration. The lower impact of estradiol-based combinations on metabolic surrogate markers may result

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].