arterial calcification, blood lipids and inflammatory markers, and changes in menopausal symptoms and sexual function. Seven hundred and twenty-eight women were enrolled in the trial, and 584 completed it.

In the oral formulation group (conjugated equine estrogen 0.45 mg/day), levels of HDL-C were increased, and LDL-C were decreased, compared with those in the transdermal formulation (50 µg/day 17β-estradiol) and placebo groups. However, there was no significant effect on CVD progression. This null effect on progression of carotid intimal medial thickening, however, at least indicates that CVD was not accelerated by hormonal treatment over 4 years. Additional treatment effects in women taking estrogen/progesterone included a reduction of menopausal symptoms (Figure 1) and prevention of bone loss (Figure 2) [Farr JN et al. *J Clin Endocrinol Metab* 2013].

Figure 1. Changes in Menopausal Symptoms Throughout the KEEPS Trial

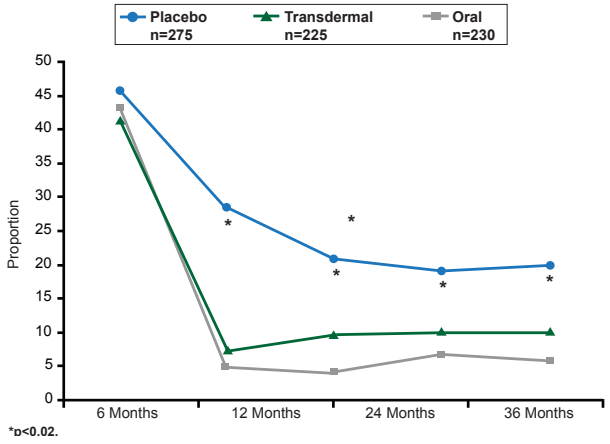

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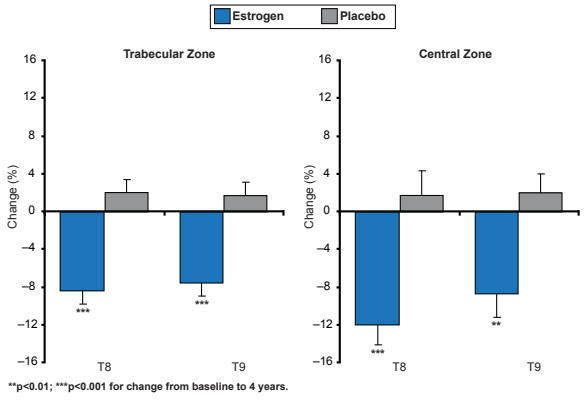
Figure 2. Changes in Bone Mineral Density Throughout the KEEPS Trial



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Dr. Miller concluded by emphasizing the need for further exploration of emerging data to determine whether hormonal treatment does have a preventive effect on CVD progression over a longer time period. She also stressed the importance of avoiding generalizations about the effects of hormone treatments in this era of personalized treatments. In particular, the different types, doses, and delivery modes of hormone treatments must be carefully considered in order to maximally impact the individual health of patients.

Individualized Diabetic Care Is Key for Athletic Success

Written by **Nicola Parry**

Anne Peters, MD, University of Southern California, Los Angeles, California, USA, discussed the challenge of caring for athletes with type 1 diabetes (T1D). Since athletic training and competition can markedly disturb blood glucose control, it can be difficult to manage diabetes in individuals who exercise excessively. Dr. Peters highlighted the importance of personalized care to optimize glycemic control for maximal health benefits and athletic success.

The Nutrition and Athletic Performance Joint Position Statement of the American College of Sports Medicine, American Dietetic Association, and Dietitians of Canada, most recently revised in 2009, suggests that athletes should eat 6 to 10 g/kg body weight of carbohydrates per day [*Med Sci Sports Exerc* 2009]. For many patients with T1D, this can represent a challenge in insulin dosing. Higher amounts of carbohydrates require larger doses of insulin but increased workouts may improve insulin sensitivity and lower insulin requirements. This balance between carbohydrate ingestion, exercise and insulin dosing can create a difficult balance for athletes to maintain.

Dr. Peters emphasized the need to understand the basics of exercise physiology. Muscles obtain glucose from their glycogen stores as a primary energy source, and once these sources are depleted, there is a balance between glucose production and uptake by exercising muscle. Immediately following exercise, in nondiabetic individuals, catecholamine levels rapidly decline and insulin increases, with restoration of muscle glycogen. Consequently, in individuals with T1D, glucose uptake may occur to such an extent that they become very sensitive to insulin and potentially hypoglycemic.

For individuals with T1D, the fear of hypoglycemia is the strongest barrier to regular physical activity, and is certainly a concept that athletes often struggle with [Brazeau AS et al. *Diabetes Care* 2008]. Although many athletes report reduced performance when their blood glucose levels are high, they conversely run into other problems if blood sugar

levels are low. Hypoglycemia can occur during exercise for various reasons, including:

- Insufficient carbohydrate intake
- More rapid insulin absorption
- Challenges in reducing basal insulin levels in individuals receiving injectable insulin
- Differences in insulin sensitivity before, during, and after exercise
- The potential for acute and delayed hypoglycemia

Studies have confirmed that decreasing the amount of insulin at the meal prior to exercise can lower the risk of hypoglycemia immediately after exercise [Rabasa-Lhoret R et al. *Diabetes Care* 2001]. Therefore, Dr. Peters recommends that athletes take half their usual insulin dose at the meal before exercise; then, if the blood glucose level is <150 mg/dL, a 15- to 30-g carbohydrate snack is advised. A carbohydrate intake of 15 to 30 g is subsequently recommended for every 30 minutes of exercise. After exercise, a 30- to 60-g carbohydrate snack should be given with half of the usual insulin dose, and it is important to work with the athlete to reduce the overnight basal insulin level to prevent development of delayed postexercise hypoglycemia.

Dr. Peters concluded that the key to diabetes management in athletes is personalized care to help tailor solutions for their individual needs. Since blood glucose response varies between individuals and also their sports, it is important to investigate each athlete's response to their different activities. In addition to working closely with a physician, athletes with T1D should work with a registered dietitian to optimize their nutritional requirements. She stressed that this approach, aided by technology such as continued glucose monitoring, enables optimal management of blood glucose levels during training and events, allowing the athlete with T1D to compete safely and effectively.

Endocrine Society Releases PCOS Guidelines

Written by **Emma Hitt, PhD**

The goal of The Endocrine Society's clinical practice guidelines for the diagnosis and treatment of polycystic ovary syndrome (PCOS) is to address the diagnosis and treatment of PCOS from adolescence to adulthood while avoiding overlap with any other Endocrine Society guidelines for disorders related to PCOS (eg, hirsutism). Richard S. Legro, MD, Penn State Hershey Obstetrics and Gynecology, Hershey, Pennsylvania, USA, discussed aspects of diagnosis of PCOS contained within the new guidelines.

There are currently 3 overlapping, yet unique, diagnostic criteria for PCOS: the National Institutes of Health (NIH) criteria, the "Rotterdam" criteria, and the Androgen Excess and Polycystic Ovary Syndrome Society (AES/PCOS) criteria. The Endocrine Society favors using the broader Rotterdam criteria, which encompasses the NIH and AES/PCOS criteria. However, phenotypic heterogeneity is present; for example, patients with hyperandrogenism typically experience more severe reproductive and metabolic symptoms than those without hyperandrogenism.

PCOS is associated with multiple morbidities, including infertility, obesity, cutaneous symptoms including acne and androgenic alopecia, mood disorders, sleep disorders, abnormal liver function, and a greater risk for cardiovascular disease.

Commonly employed treatments for PCOS include hormonal contraceptives, insulin sensitizers (eg, metformin), and antiandrogens. There are some controversies as to the safety and efficacy of these therapies. In a systemic review and meta-analysis of the adverse effects associated with PCOS treatment, common therapies for PCOS (above) were correlated with a low risk of severe adverse events [Domecq JP et al. *J Clin Endocrinol Metab* 2013]. A meta-analysis of lifestyle modifications in patients with PCOS demonstrated that lifestyle modifications reduce insulin resistance in overweight or obese patients [Prutsky G et al. *J Clin Endocrinol Metab* 2013]. In part based on this evidence, The Endocrine Society recommends (a) clomiphene citrate as the first-line therapy for infertility, (b) hormonal contraceptives as first-line for menstrual irregularities and hirsutism, and (c) lifestyle modifications (eg, exercise; calorie-restricted diet in the setting of overweight/obesity) as needed to improve cardiovascular disease risk factors. The Endocrine Society recommends that metformin be used as a second-line therapy in women with type 2 diabetes or impaired glucose tolerance who do not achieve adequate benefit with lifestyle modifications. In addition, PCOS patients with menstrual irregularities may be candidates for metformin therapy if they cannot take or do not tolerate hormonal contraceptives.

The treatment of PCOS in adolescence is less clear, as there are less data on which to base recommendations. In this population, the diagnostic focus should be on hyperandrogenism because oligo-ovulation and polycystic ovaries are often normal during reproductive development in adolescence. Suggested treatment approaches for well-established adolescent PCOS are similar to those for adults. When clinical and biochemical hyperandrogenism occurs in premenarcheal adolescents who are at least Tanner breast stage 4 (and other causes are excluded), treatment with hormonal contraceptives is suggested.