Visual acuity benefit often cannot be maintained in neovascular age-related macular degeneration if the frequency of ranibizumab injection is decreased from a monthly injection protocol. However, Protocol I demonstrated benefit with the use of anti-VEGF therapy for DME. Data showed that improved VA was maintained in these patients for more than 3 years of follow-up despite a decreasing number of intravitreal injections of ranibizumab: a median of 6 injections for the first 6 months, 3 injections in the second 6 months, 2 to 3 injections in the second year, and 1 to 2 injections in the third year [Diabetic Retinopathy Clinical Research Network *Ophthalmology* 2012; 2010].

Additional DRCR.net research in this field is underway. Protocol S and Protocol T are near completion. The noninferiority Protocol S study is comparing 2-year VA outcomes in patients with proliferative diabetic retinopathy treated with anti-VEGF therapy plus deferred panretinal photocoagulation (PRP) or standard, prompt PRP therapy. Protocol T is a comparative effectiveness study of three intravitreal anti-VEGF agents—aflibercept, bevacizumab, and ranibizumab—in patients with DME. The primary outcome is mean change in VA.

Treatment of Gestational Diabetes Improves Short-Term Outcomes in Offspring

Written by Nicola Parry

Matthew W. Gillman, MD, Harvard Medical School, Boston, Massachusetts, USA, discussed the relation between gestational diabetes mellitus (GDM) and macrosomia, neonatal morbidity, and childhood obesity. He shared data demonstrating that treatment of GDM improves short-term fetal and neonatal outcomes, but does not reduce obesity in offspring at the age of 4 to 5 years.

As the global pandemic of diabetes continues, increasing numbers of women of childbearing age are at risk for GDM and type 2 diabetes mellitus (T2DM). GDM may contribute to an intergenerational cycle of obesity and diabetes: A woman who enters pregnancy overweight or obese may gain excessive weight and retain more postpartum, leading to T2DM and cardiovascular disease (CVD) in the long term. Fetal growth and metabolism may also be altered, leading to child obesity.

Dr. Gillman discussed two trials that addressed the value of glucose control in GDM, both of which randomized ~1000 patients to therapy or observation. In the Australian Carbohydrate Intolerance Study in Pregnant Women [ACHOIS], the composite end point of serious perinatal outcomes included fetal death, bone fracture, shoulder dystocia, and nerve palsy [Crowther CA et al. *N Engl J Med* 2005]. In the study conducted within the Maternal–Fetal Medicine Units (MFMU) Network, the composite end point was stillbirth or perinatal death and neonatal complications, including hyperbilirubinemia, neonatal hypoglycemia, and hyperinsulinemia [Landon MB et al. *N Engl J Med* 2005].

In the ACHOIS study, there was a decrease in the main outcome measure of any serious perinatal complication with intervention (RR, 0.33; 95% CI, 0.14 to 0.75; $p = .01$). However, the MFMU study composite outcome was not significantly changed ($p = .14$). The incidence of large-for-gestational age (LGA) decreased significantly in both studies ($p < .001$), whereas shoulder dystocia was only significantly decreased in the MFMU study ($p = .02$). In both trials, maternal weight gain from diagnosis to term was significantly lower with intervention (mean 1.7 kg less in ACHOIS, $p = .01$; 2.2 kg less in the MFMU study, $p < .001$), yet birth injury and small-for-gestational age were not significantly changed.

The results of both trials indicated the benefits of treating mild to moderate GDM, in particular with respect to reduced incidences of macrosomia and LGA. Subsequent meta-analyses and reviews have also provided broad agreement on these benefits and risks, noted Dr. Gillman.

Since GDM has been hypothesized to cause obesity in offspring, a longer-term follow-up study of a subset of children from the ACHOIS trial compared the effect of treatment for mild GDM with routine care on the body mass index (BMI) of children aged 4 to 5 years. The main outcome was age- and sex-specific BMI. Although treatment of GDM substantially reduced macrosomia (5.3% vs 21.9%), there was no reduction in their mean BMI at age 4 to 5 years (0.49 in treatment vs 0.41 in routine care) [Gillman MW et al. *Diabetes Care* 2010].

Studies so far have therefore shown that GDM treatment reduces serious fetal and neonatal outcomes in the short term but do not show similar benefits in the longer term. However, the long-term findings are based on only 1 study. Additionally, GDM may affect weight in early infancy and again in later childhood, but not in early childhood; thus, even longer-term follow-up studies are required to address this question, Dr. Gillman concluded.