Persistent hyperinsulinemic hypoglycemia in adults is usually caused by solitary benign insulinomas. Nesidioblastosis, a term that has been used to designate a functional disorder of the beta cells, is a rare cause of persistent hyperinsulinemic hypoglycemia in adults, but seems to have increased in frequency. The histopathologic criteria for adult nesidioblastosis are similar to those used for the diagnosis of the diffuse form of congenital hyperinsulinism in infants and include beta-cell hypertrophy, islet hyperplasia, and an increase in the beta-cell mass. However, the degree and extent of these features vary much more from patient to patient than in newborns. The cause of adult nesidioblastosis is not known, but the recently observed association with gastric bypass surgery in obese patients suggests that a reactive process possibly unmasks or induces a defect in the beta cell, resulting in its hyperfunction.