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50 Years Ago in *The Journal of Pediatrics*

Advances in Neonatal Thyrotoxicosis

Wilroy RS, Etteldorf JN. Familial hyperthyroidism including two siblings with neonatal Graves' disease. J Pediatr 1971;78:625-32.

Neonatal thyrotoxicosis is a rare, potentially life-threatening condition if not treated early. In 1971, Wilroy et al reported a multigenerational family with hyperthyroidism, including multiple infants born with thyrotoxicosis.

The past medical history included the maternal grandmother's death during removal of a toxic goiter; her daughter had also developed a goiter and exophthalmos as a teen requiring propylthiouracil, Lugol's solution, and subtotal thyroidectomy. Subsequently, she was euthyroid when she delivered a premature infant who died in the neonatal period and then a stillborn infant with a goiter with her second pregnancy.

Her next 2 pregnancies resulted in premature infants, both with microcephaly, a small anterior fontanelle, significant tachycardia, and advanced bone ages. One had exophthalmos and the other a significant goiter. Both children continued to have symptoms of hyperthyroidism, despite propylthiouracil treatment. Developmentally, 1 child was reported to have minimal intellectual disability, and the other had significant developmental delay as an adolescent. Long-acting thyroid stimulator assays were unavailable when they were neonates, but detectable at ages 8 and 9 years, respectively. At the time, it was hypothesized that maternal long-acting thyroid stimulator crossed the placenta and caused the hyperthyroidism. It was thought to be a brief condition that self-resolved and very little was known on the long-term effects of this condition.

Fifty years later, our understanding of the pathogenesis of neonatal thyrotoxicosis, its implications, prevention, and management has advanced significantly. Neonatal thyrotoxicosis continues to be rare and commonly caused by maternal Grave's disease. However, maternal Hashimoto thyroiditis, and nonautoimmune etiologies like genetic mutations that activate the thyroid stimulator hormone receptor and in the stimulatory G protein in McCune-Albright syndrome are described. Now, pregnant women with Grave's disease receive screening for thyroid receptor antibodies. If elevated, serial fetal ultrasound examination is performed to evaluate for fetal tachycardia, bone maturation, and the presence of a goiter.[1] Pregnant women are closely followed and receive therapy with antithyroid drugs to prevent fetal hyperthyroidism. Infants at risk are screened and monitored closely, and those born with thyrotoxicosis immediately start treatment with methimazole, instead of propylthiouracil given the risk of hepatic failure.[1]

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