It is important to recognize this phenomenon to prevent an incorrect diagnosis of diabetes mellitus and inappropriate treatment with insulin.

REFERENCES

- Dubowski, K. M. (1962). An O-toluidine method for body-fluid glucose determination. *Clinical Chemistry*, 8, 215.
 Gour, K. N., and Bhargava, S. P. (1957). Biochemical studies in electric convulsive therapy. *Journal of Mental Science*, 103, 257.
 McIlwain, H., and Bachelard, H. S. (1971). *Biochemistry and the Central Nervous System*, 4th ed., p. 530. Churchill Livingstone, Edinburgh and London.
 Millichap, J. G. (1968). *Febrile Convulsions*, p. 58. McMillan, New York.
 Zellweger, H. (1948). Krampfe im Kindersalter. *Helvetica Paediatrica Acta*, 3, (Suppl. 5), 1.

Z. SPIRER,* J. WEISMAN, S. YURMAN, and N. BOGAIR
Department of Paediatrics 'A', Hadassah Hospital, and Tel-Aviv University Medical School, Tel-Aviv, Israel.

*Correspondence to Dr. Z. Spirer, P.O. Box 51, Tel-Aviv, Israel.

Neonatal thyrotoxicosis treated with propranolol

Neonatal thyrotoxicosis is a rare transient disorder related to the presence of long-acting thyroid stimulator (LATS) in the infant's blood. Treatment of the disorder has been based on iodides, sedatives, thiouracil drugs, and digoxin. As the condition is self-limiting and subsides spontaneously, control of symptoms through blockade of β -adrenergic receptors may be a more logical mode of therapy. Propranolol has been used in this way in the interval between the administration of radioactive iodine and its suppression of thyroid function (Hadden *et al.*, 1968; Shanks *et al.*, 1969). Recently a case of neonatal thyrotoxicosis has been described in which propranolol was used in conjunction with digoxin, phenobarbitone, propylthiouracil, and Lugol's iodine (Smith and Howard, 1973). This is the first reported case of neonatal thyrotoxicosis treated only with propranolol.

Case report

A male infant weighing 2720 g was delivered on 25 January 1972, by elective caesarean section at 38 weeks' gestation. The pregnancy had been complicated by moderate pre-eclampsia.

The mother, a 26-year-old primigravida, had had a

subtotal thyroidectomy in 1963 for thyrotoxicosis. Moderate exophthalmos, present before this operation, was still present. During the pregnancy the eye signs became more marked and the results of thyroid function tests were T_3 red cell uptake 8–10%, protein-bound iodine (PBI) 7.4–11.4 $\mu\text{g}/100$ ml. The fetus had persistent tachycardia with the heart rate greater than 180 beats/minute. The mother was treated during the last 10 days of pregnancy with carbimazole 20 mg 4 times daily, propranolol 40 mg 4 times daily, and diazepam. During this period the fetal heart rate was less than 150 beats/minute.

At birth the infant was noted to have a small goitre; there was no exophthalmos and he was not overactive. The heart rate was 130 beats/minute and there was no cardiac failure. Estimations of maturity confirmed that the infant was at 38 weeks. Thyroid function tests on the cord blood (Table) were in the thyrotoxic range (PBI

TABLE
Tests of thyroid function in infant

	T_3 red cell uptake (%)	PBI ($\mu\text{g}/100$ ml)
Birth	38.1	9.1
3 wk	38.1	16.0
7½ wk	15.5	6.2
(Normal)	(11.5–19.5)	

9.1 $\mu\text{g}/100$ ml, T_3 red cell uptake 38.1%). Further tests of thyroid function, T_4/T_3 ratio, and free thyroxine index were all in the thyrotoxic range.

The baby was kept under close observation. He remained well for the first 2 weeks, was not overactive, and slept for normal periods. His intake of milk (450 ml/day) was in keeping with his calculated requirements, though his weight remained static. However, by the end of the second week, signs suggestive of thyrotoxicosis were appearing and by 3 weeks the infant was obviously thyrotoxic (Fig.). He was hyperactive, irritable, and cried continuously. His appetite was voracious and he took 840 ml milk/day. His skin had become abnormally pink, hot, and velvety in texture. The eyes were more prominent and there was lid retraction. The heart rate was 180 beats/minute but there was no evidence of cardiac failure. EEG showed sinus tachycardia. There was a distinct tremor in all limbs. The results of thyroid function tests were PBI 16 $\mu\text{g}/100$ ml, T_3 red cell uptake 38.1%.

Treatment with propranolol (Inderal) was started with a dose of 0.5 mg 4 times daily, given as a solution added to his milk at the end of the third week. Daily increments in the dose were made over 4 days, until he was receiving 4 mg 4 times daily. On this treatment his behaviour assumed a more normal pattern and the heart rate slowed to 140–150 beats/minute. Improvement was most marked immediately after each increase in dose but with time this seemed to decline so that the dose had to be further increased over 2 weeks to 8 mg 4 times daily, which gave a plasma propranolol level (Shand, Nuckolls, and Oates, 1970) of 89 $\mu\text{g}/\text{l}$. 2 hours after a dose.

FIG.—Thyrotoxic appearance of mother and her 3-week-old infant.

At 6 weeks the tremor had disappeared and skin texture and colour were more normal. However, the infant still took large volumes of milk (1000 ml/day) and cried for long periods. Weight gain was marked and was approaching 500 g/week. Thyroid function tests performed at 7½ weeks were within the normal range, i.e. PBI 6.2 µg/100 ml, T₃ red cell uptake 15.5%. Treatment with propranolol was therefore stopped. At this time behaviour was normal except for an increased demand for food (784 ml/day); there was no tremor or irritability and skin colour and texture were normal. Neurological development was in keeping with his age. The heart rate was 130 beats/minute.

The baby was discharged home. His subsequent progress was uneventful and when seen at 6 months PBI was 6.4 µg/100 ml and T₃ red cell uptake 16.8%.

Discussion

Less than 50 cases of neonatal thyrotoxicosis have been reported since the first description by White in 1912. It is known that the clinical severity may vary from mild, requiring no treatment, to fulminant with rapid demise. Without treatment, or with iodides alone, mortality has been reported to be 12% (Samuel *et al.*, 1971). There is also a high fetal mortality. The standard treatment has been to give carbimazole or thiouracil, with or without thyroxine, to the mother and to treat the neonate with sedatives, iodides, carbimazole, or thiouracil combined with digoxin if required (Adams, Lord, and Stevely, 1964; Samuel *et al.*, 1971; Maisey and Stimmler, 1972). As propranolol will control the clinical and subjective evidence of adult thyrotoxicosis (Hadden *et al.*, 1968; Shanks *et al.*, 1969) while awaiting the

effect of radioactive iodine destruction of the thyroid, the transient nature of neonatal thyrotoxicosis suggests that this form of therapy would be useful. This has been confirmed in the present case. Since the effect of propranolol can only be assessed by clinical improvement, this baby was observed closely and given no sedatives. Propranolol reduced activity, heart rate, and skin blood flow. The effect of each increase in dose of propranolol was short lived, so that it had to be increased progressively to a maximum of 8 mg 4 times daily. The reason for this effect is unknown. The largest dose of propranolol, i.e. 8 mg, gave a plasma level 2 hours after administration of 89 µg/l. Though there is marked variation in the plasma levels of propranolol after oral administration in adult men (Shand *et al.*, 1970), it has been suggested on the basis of these observations that the oral dose of propranolol in a 4-month-old child would be 7 mg. Though the present infant was younger than this, a dose of 8 mg would not be unreasonable. As propranolol does not interfere with thyroid function (Hadden *et al.*, 1969), the PBI can be used as an index of thyroid activity. When the PBI had returned to normal in the present case, propranolol was discontinued with no return of symptoms.

Summary

Thyrotoxicosis developed 2 weeks after birth in an infant whose mother had thyrotoxicosis during the last few weeks of pregnancy. The infant was treated with propranolol until there was a spontaneous remission at 7½ weeks.

We thank Professor I. J. Carré for permission to publish this case; Dr. D. A. D. Montgomery for helpful advice, and Dr. J. G. Kelly for plasma propranolol estimations.

REFERENCES

- Adams, D. D., Lord, J. M., and Stevely, H. A. A. (1964). Congenital thyrotoxicosis. *Lancet*, **2**, 497.
- Hadden, D. R., Bell, T. K., McDevitt, D. G., Shanks, R. G., Montgomery, D. A. D., and Weaver, J. A. (1969). Propranolol and the utilization of radioiodine by the human thyroid gland. *Acta Endocrinologica*, **61**, 393.
- Hadden, D. R., Montgomery, D. A. D., Shanks, R. G., and Weaver, J. A. (1968). Propranolol and iodine-131 in the management of thyrotoxicosis. *Lancet*, **2**, 852.
- Maisey, M. N., and Stimmeler, L. (1972). The role of long acting thyroid stimulator in neonatal thyrotoxicosis. *Clinical Endocrinology*, **1**, 81.
- Samuel, S., Pildes, R. S., Lewison, M., and Rosenthal, I. M. (1971). Neonatal hyperthyroidism in an infant born of an euthyroid mother. *American Journal of Diseases of Children*, **121**, 440.
- Shand, D. G., Nuckolls, E. M., and Oates, J. A. (1970). Plasma propranolol levels in adults. *Clinical Pharmacology and Therapeutics*, **11**, 112.
- Shanks, R. G., Hadden, D. R., Lowe, D. C., McDevitt, D. G., and Montgomery, D. A. D. (1969). Controlled trial of propranolol in thyrotoxicosis. *Lancet*, **1**, 993.
- Smith, C. S., and Howard, N. J. (1973). Propranolol in the treatment of neonatal thyrotoxicosis. *Journal of Pediatrics*, **83**, 1046.
- White, C. (1912). A foetus with congenital hereditary Graves's disease. *Journal of Obstetrics and Gynaecology*, **21**, 231.
- P. J. PEMBERTON,* B. MCCONNELL, and R. G. SHANKS†
- The Neonatal Unit, Royal Maternity Hospital, Belfast, and the Departments of Child Health and Therapeutics and Pharmacology, The Queen's University of Belfast.*

*Present address: Princess Margaret Hospital for Children, Perth, Western Australia.

†Correspondence to Professor R. G. Shanks, Department of Therapeutics and Pharmacology, Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ.

The following articles will appear in future issues of this journal:

Annotation: Renin and hypertension in childhood. M. J. Dillon.

Use of a continuously recording intravascular oxygen electrode in the newborn. P. Goddard, I. Keith, H. Marcovitch, N. R. C. Robertson, P. Rolfe, and J. W. Scopes.

Fractional excretion of uric acid in infancy and childhood: index of tubular maturation. J. H. Passwell, M. Modan, M. Brish, S. Orda, and H. Boichis.

Persistent transitional circulation. R. Brown and D. Pickering.

Clinical evaluation of Sephadex gel filtration in estimation of bilirubin binding in serum in neonatal jaundice. J. Kapitulnik, T. Valaes, N. A. Kaufmann, and S. H. Blondheim.

The missing umbilical artery. I. Prospective study based on a maternity unit. E. M. Bryan and H. G. Kohler.

Teeth as indicators of exposure of children to lead. D. J. Stewart.

Plasma proteins in meconium from normal infants and from babies with cystic fibrosis. H. C. Ryley, L. Neale, T. D. Brogan, and P. T. Bray.

Incidence of growth hormone deficiency. J. M. Parkin.