THYROID DISORDERS IN THE NEWBORN

BY

IAN D. RILEY, M.D., M.R.C.P., D.C.H.
Paediatrician

AND

G. SCLARE, M.B., Ch.B.
Formerly Registrar in Pathology
Stobhill General Hospital, Glasgow

[WITH SPECIAL PLATE]

Disturbances of thyroid function in the newborn have been recorded at three periods in the history of thyroid disorder. The first cases were described before the discovery of the value of iodine prophylaxis in endemic areas, the second after its employment, and the third following the introduction of thiouracil. Three cases of this third type are described in the present paper.

Case 1

Male born normally at term on June 27, 1955. The mother, aged 28, was a primigravida and had had thyroidectomy for thyrotoxicosis in 1946. She was treated with 200 mg. of thiouracil daily for a recurrence in the same year. On January 5, 1955, she was not fully controlled on 100 mg. daily, and was admitted from March 31 to April 10 for stabilization. She was receiving 100 mg. daily at the time of her admission on June 9, and this was continued up to term.

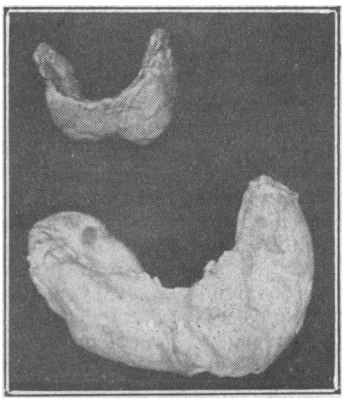
The infant weighed 5 lb. 1 oz. (2.296 kg.) at birth. Nothing abnormal was detected, there being no goitre. On the eighth day, when there was very slight thyroid enlargement, he was noticed to be sweating profusely and to have developed a sweat rash. He was irritable, his conjunctivae were suffused, and there was no increase in weight for the first 13 days. He was pale and his skin was hot to the touch, but his appetite was good. The irritability increased and the temperature showed an intermittent fluctuation between 97° and 100° F. (36.1° and 37.8° C.). Lugol's iodine, 5 minims (0.06 ml.) twice a day, was given with phenobarbitone, ¼ gr. (8 mg.) twice daily, and the weight then rose steadily. He was sent home on the twenty-sixth day weighing 6 lb. 3 oz. (2.807 kg.).

Case 2

Male born six weeks prematurely on December 16, 1954. The mother, aged 34, a primigravida, had been treated for thyrotoxicosis with methyl thiouracil, 100 mg. daily, and laevothyroxine, 0.1 mg. daily. Seven days before delivery, in spite of a tachycardia of 90 per minute, it was decided not to increase the thiouracil for fear of the effect on the foetus.

The infant weighed 4 lb. 4 oz. (1.927 kg.), and was cold and cyanosed with visible enlargement of the thyroid (Special Plate, Fig. 1). Next day the blood urea was 30 mg. and the blood cholesterol 104 mg. per 100 ml. By December 24 there was a tachycardia and the skin was moist and clammy. The baby was tremulous and hyperactive and had an irregular fever, mainly from 97° to 99° F. (36.1°–37.2° C.), but reaching 102° F. (38.9° C.) on one occasion. Cyanotic attacks developed with diminished air entry in the right lung, thought to be due to aspirated feeds. A week later, although no weight had been gained, he was no longer hyperactive and the thyroid was a little smaller, but he regained the hyperactivity and became very thin. The blood cholesterol on January 8, 1955, was 124 mg. per 100 ml. Lugol's iodine, 5 minims (0.3 ml.) three times a day, was started on January 21, but death occurred next day, when the infant's weight was 4 lb. 1½ oz. (1.856 kg.).

Necropsy showed the thyroid to be uniformly enlarged and to weigh 10 g. (see photograph). The gland was firm and its cut surface of fleshy appearance.



The uniformly enlarged thyroid found at necropsy in Case 2, compared with a normal gland.

Histology.—Although the interval between death and necropsy was 60 hours, autolytic changes were inconspicuous. The thyroid follicles varied little in appearance from one part of the gland to another. They were small, of irregular outline, and had a scanty colloid content which, in a very few instances, showed a solitary central vacuole. The lining cells were uniformly cuboidal, but there was marked variation in the size of their nuclei (Special Plate, Fig. 2). The stroma was unusually prominent (Special Plate, Fig. 3).

Case 3

Male born normally at term on June 26, 1944. The mother, aged 29, a primigravida, developed thyrotoxicosis during pregnancy and was treated with 200 mg. of thiouracil five times a day from April 27, 1944, reduced to three times daily on May 25 and to twice a day on May 30. For three weeks before delivery thiouracil was discontinued.

The infant weighed 6 lb. 1½ oz. (2.764 kg.) at birth. There was visible enlargement of the right lobe of the thyroid at this time, and it was remarked that the baby was "hypothyroid" in appearance. Tube feeding was employed, but frequent vomiting occurred, and on July 3 loose stools began to be passed. Death ensued on July 9.

Necropsy showed the body to be emaciated, with loss of nearly all subcutaneous and body fat. Histologically the thyroid was devoid of colloid, and the follicles were partially or totally occupied by desquamated epithelial cells. Nuclear variation of the type seen in Case 2 was not present.

Discussion

Endemic goitre in the newborn was first described by Fodere in 1796, and since that time many cases have been reported. In 1935 the condition was present in 50% of all newborn babies in Switzerland and accounted for 10% of the neonatal mortality in Freiburg im Breisgau (Aschoff, cited by Parmelee *et al.*, 1940). It is probable that both heredity and iodine deficiency are factors in the production of the condition, as it has become less common since prophylaxis with iodine came into use. Sporadic cases have also been reported with some frequency, and the clinical picture is similar. The mother usually, but not always, has a simple goitre, and the infant, as a rule, a nodular goitre. This may be so large as to cause death from respiratory obstruction (Peterson, 1911; Williamson, 1933; Mitchell and Struthers, 1933; Davies, 1943; Kunstadter, 1948; Seligman and Pescovitz, 1950; Schifrin and Hurwitt, 1951; Jones, 1951).

Thyrotoxicosis in the newborn was first described by White (1912); he had suspected the condition to be present before birth in the foetus of a thyrotoxic mother. Such cases are rare (Margetts, 1950). Goitre in the offspring of mothers who have received iodine either for goitre (Vérel, 1949; Skinner, 1924) or for some other condition (Parmelee *et al.*, 1940) has been reported. These goitres were transitory and diffuse rather than nodular.

Since the introduction of thiouracil it has been found that mothers treated with this drug may give birth to babies with goitres (Hubble, 1956). The babies may be otherwise normal or show signs of either myxoedema or hyperthyroidism. The condition usually subsides in a few weeks without treatment, but subsequent myxoedema has been reported (Elphinstone, 1953; Morris, 1953) and death has been known to ensue (Keynes, 1952). Such a goitre has been found in a six-months foetus at necropsy (Davis and Forbes, 1945), and it has also been seen in twins (Saye *et al.*, 1952). The goitre is usually diffuse, and on section hyperplasia with absence of colloid is seen. It is noteworthy that the histological appearances in our Case 2 are comparable in many ways with those seen in adult thyrotoxicosis, whereas many previous reports described hyperplasia of a type that commonly occurs in the normal newborn infant (Sclare, 1956). A raised level of protein-bound iodine was found by Bongiovanni *et al.* (1956). There does not appear to be any relation between the type of lesion in the mother and that in the child. Normal or goitrous mothers may give birth to normal or goitrous infants, and signs of toxicity may be present or absent in either (Eaton, 1945; Fischer, 1951; Salm, 1954; Koerner, 1954; Scarizza, 1954).

Investigations related to the problem include the discovery that the serum iodine level rises during pregnancy (Man *et al.*, 1951; Cooke and Man, 1956) and that the foetal thyroid has a greater affinity for iodine than that of the adult. It has also been shown that maternal thyrotropic hormone cannot pass the placenta (Nikitovitch and Knobil, 1955), but that thyroid hormone and thiouracil can do so (Freiesleben and Kjerulf-Jensen, 1947; Frisk and Josefsson, 1947). From these facts it would appear that thiouracil acts by depressing foetal thyroxine formation, thus inducing production of foetal thyrotropic hormone which in a few days leads to thyrotoxicosis. It is, however, probable that a hereditary factor also operates, and this might explain instances of identical disorders in mother and child.

The most important clinical question is to what extent the mother's thyrotoxicosis may be controlled without producing damage to the foetal thyroid. This is probably best answered by maintaining the protein-bound iodine above the normal level, and by substituting iodine for the thiouracil some weeks before delivery (Keynes, 1952); but the evidence for the value of this manœuvre is not conclusive, as the third case of the present series would suggest. Certainly if the condition of the mother demands thiouracil, the drug should not be discontinued.

Two of the three cases described here ended fatally, which suggests that the danger to the infant is substantial. Despite its failure in Case 2, iodine is probably the best drug to administer to the infant. Studies of the radioactive iodine uptake would help to elucidate the condition, but the danger at such an age renders the method inadvisable.

Summary

Three cases of goitre in the newborn are reported. In all three cases the mother had during pregnancy received treatment with thiouracil for thyrotoxicosis. Two of the infants died. The post-mortem appearances are described and illustrated.

The aetiology is discussed, and the question of treatment is reviewed in the light of cases described previously.

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ADDISON'S DISEASE IN A NINE-YEAR-OLD GIRL

BY

R. G. WELCH, M.D., M.R.C.P.

Senior Registrar to the Children's Department, St. Thomas's Hospital

[WITH SPECIAL PLATE]

The purpose of this paper is to record a further example of Addison's disease in a child—a very rare occurrence—and to draw attention yet again to the great change in the nature of the usual underlying pathological process that has taken place in the past ten years, coincident with, and probably resulting from, the high degree of control of tuberculosis now achieved.

Report of Case

The patient was a girl aged 9¾ years, the second of four children, the parents and the other children all being healthy. A few weeks after a mild attack of mumps she gradually became listless, felt weak, and lost her appetite. There were frontal headaches, especially on waking, and occasional epigastric pains. Giddiness on standing, stiffness and aching of the limbs, vomiting, and occasional double vision followed in a month or so with loss of weight. After four months, too weak even to get out of bed, she was admitted to hospital. She was ill, pale, and thin, but the only other findings were a slight evening pyrexia and a rapid sleeping pulse rate (about 110 per minute). B.P. 100/60 mm. Hg; E.S.R. 7 mm. in one hour; Hb 102%; W.B.C. 8,900 per c.mm. (lymphocytes 65%, monocytes 2.5%, neutrophil polymorphs 25%, and eosinophil polymorphs 6.5%). Mantoux 1:1,000 negative. Chest radiograph clear (a small heart shadow). Cerebrospinal fluid normal except for a chloride value of 670 mg. per 100 ml.

An intracranial tumour was considered and the patient was transferred to St. Thomas's Hospital. At this time a general increase in pigmentation was noticed, including a pigmented spot on the lip. She was very miserable, and lay curled up in her bed, moaning quietly. She drank fluids, but refused nearly all solids (in retrospect, the only foods she enjoyed throughout her illness were salty), and vomited daily. B.P. 105/80 mm. Hg. The electroencephalograph (E.E.G.) was abnormal; there were theta waves at 7 c.p.s. and fast activity at 20 c.p.s., seen in leads from all areas, but the record was dominated by asymmetrical irregular high-voltage (150–200 μV) slow waves at 2–3 c.p.s., of greatest amplitude in leads from the left cerebral hemisphere, and of lower frequency posteriorly. The E.S.R. was now 32 mm. in one hour.

The pigmentation increased rapidly over the next few days, and Addison's disease was considered. The day before

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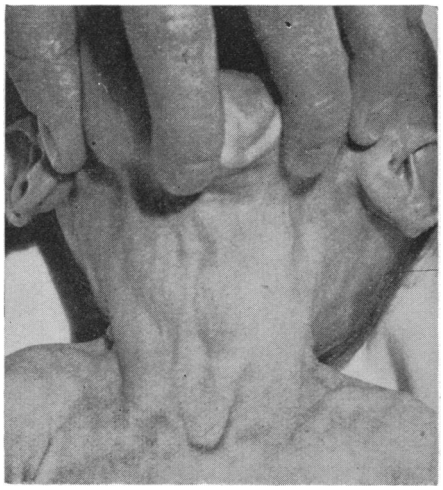

FIG. 1.—Case 2: Showing enlargement of thyroid.

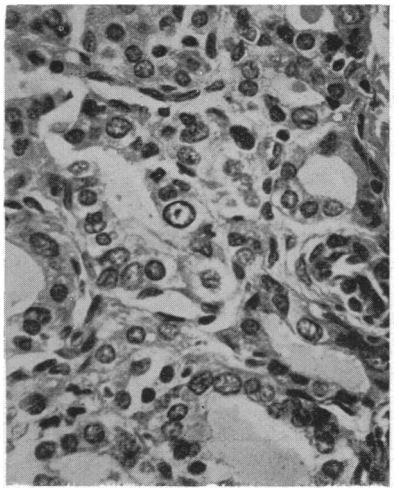

FIG. 2.—Case 2: Showing uniformly cuboidal lining cells with marked variation in size of their nuclei. (H. and E. ×400.)

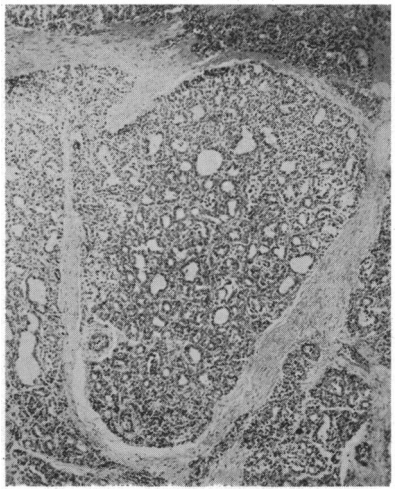

FIG. 3.—Case 2: Showing unusually prominent stroma. (Masson's trichrome. ×55.)

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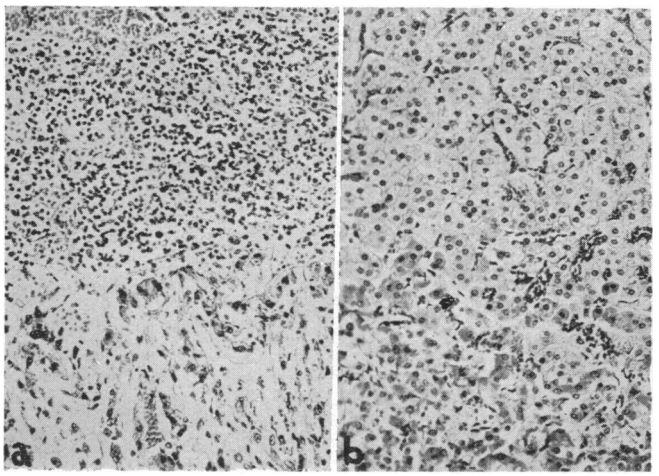

Sections of adrenal (*a*) from patient and (*b*) from healthy child of same age. (×120.)

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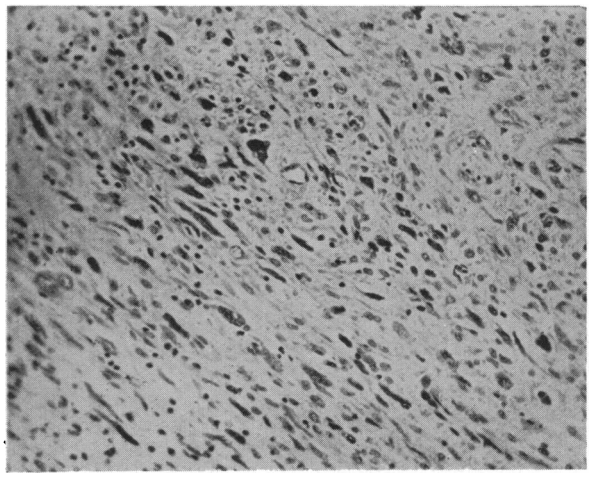

Photomicrograph of section of tumour. (×300.)

M. ELLIS AND P. WINSTON: CAROTID-BODY TUMOUR

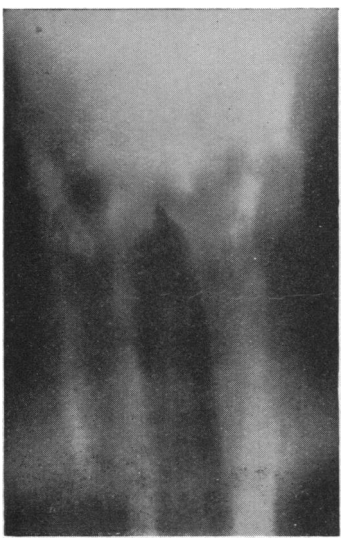

FIG. 1.—Tomograph of larynx, September 24, 1954. Left vocal cord relaxed.

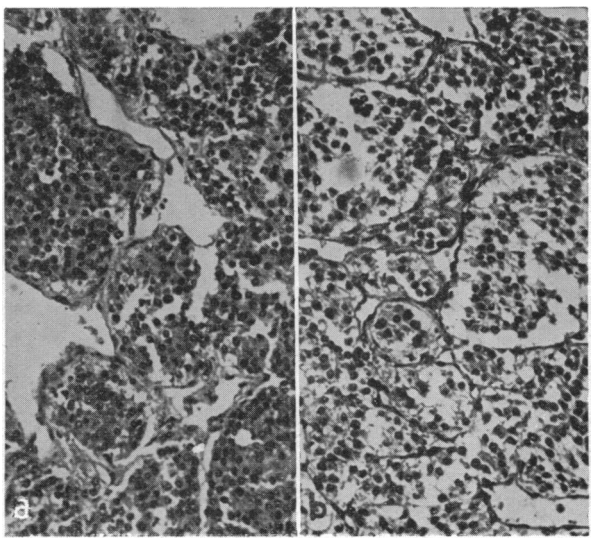

FIG. 2.—Photomicrographs of sections of tumour. (*a*, ×174; *b*, ×190.)

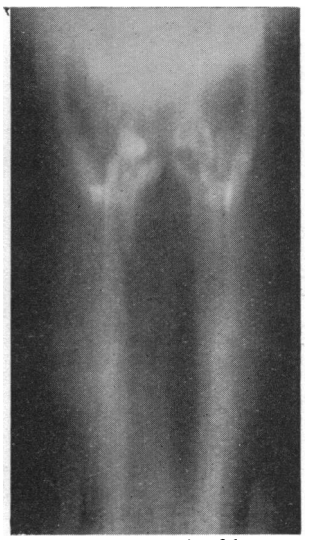

FIG. 3.—Tomograph of larynx, September 14, 1956. Left vocal cord unchanged.