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.

REFERENCES

- Bongiovanni, A. M., Eberlein, W. R., Thomas, P. Z., and Anderson, W. B. (1956). *J. clin. Endocr.*, **16**, 146.
 Cooke, R. E., and Man, E. B. (1956). *Pediatrics*, **17**, 617.
 Davies, J. R. (1943). *J. Pediatr.*, **22**, 570.
 Davis, L. J., and Forbes, W. (1945). *Lancet*, **2**, 740.
 Eaton, J. C. (1945). *Ibid.*, **1**, 171.
 Elphinstone, N. (1953). *Ibid.*, **1**, 1281.
 Fischer, P. M. S. (1951). *S. Afr. med. J.*, **25**, 217.
 Fodere, F. E. (1796). *Ueber den Kropf und den Cretinismus*. C. F. Himburg, Berlin.
 Freiesleben, E., and Kjerulf-Jensen, K. (1947). *J. clin. Endocr.*, **7**, 47.
 Frisk, A. R., and Josefsson, E. (1947). *Acta med. scand., Suppl.* **196**, 85.
 Hubble, D. (1956). *British Medical Journal*, **1**, 875.
 Jones, D. B. (1951). *Amer. J. Path.*, **27**, 85.
 Keynes, G. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 173.
 Kunstadter, R. H. (1948). *J. Pediatr.*, **32**, 711.
 Koerner, K. A. (1954). *Ibid.*, **45**, 464.
 Man, E. B., Heinemann, M., Johnson, C. E., Leary, D. C., and Peters, J. P. (1951). *J. clin. Invest.*, **30**, 137.
 Margetts, B. M. (1950). *Proc. roy. Soc. Med.*, **43**, 615.
 Mitchell, D. S., and Struthers, R. R. (1933). *Canad. med. Ass. J.*, **28**, 27.
 Morris, D. (1953). *Lancet*, **1**, 1284.
 Nikitovitch, M., and Knobil, E. (1955). *J. clin. Endocr.*, **15**, 837 (abstract).
 Parmelee, A. H., Allen, E., Stein, I. F., and Buxbaum, H. (1940). *Amer. J. Obstet. Gynec.*, **40**, 145.
 Peterson, E. W. (1911). *Arch. Pediatr.*, **28**, 142.
 Salm, R. (1954). *J. Obstet. Gynaec. Brit. Emp.*, **61**, 831.
 Saye, E. B., Watt, C. H., Foushee, J. C., and Palmer, J. I. (1952). *J. Amer. med. Ass.*, **149**, 1399.
 Scarizza, P. M. (1954). *Minerva pediat. (Torino)*, **6**, 433.
 Schifrin, N., and Hurwitz, E. S. (1951). *J. Pediatr.*, **39**, 597.
 Sclare, G. (1956). *Scottish med. J.*, **1**, 251.
 Seligman, B., and Pescovitz, H. (1950). *N.Y. State J. Med.*, **50**, 1845.
 Skinner, H. H. (1924). *J. Amer. med. Ass.*, **82**, 1190.
 Vérel, D. (1949). *British Medical Journal*, **1**, 892.
 White, C. (1912). *J. Obstet. Gynaec. (Ludhiana)*, **21**, 231.
 Williamson, G. R. (1933). *J. Pediatr.*, **2**, 458.

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 9½ 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 μ V) 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

she died her blood pressure was 100/70 mm. Hg. Three hours after this was taken she collapsed and became pulseless. The plasma electrolyte values (in mEq per litre) were: sodium 119, potassium 5, chloride 94, and bicarbonate 24; blood sugar 80 mg. per 100 ml.; P.C.V. 44 c.cm. per 100 ml. She was given glucose saline containing hydrocortisone and noradrenaline intravenously and deoxycortone acetate (D.C.A.) and cortisone intramuscularly, but despite the administration of 120 mg. hydrocortisone, 100 mg. cortisone, 3 mg. D.C.A., and nearly 5 mg. noradrenaline in the next 23 hours the blood pressure never rose above 70/40 mm. Hg and she never became conscious. Three hours before death the plasma electrolyte values (in mEq per litre) were: sodium 124, potassium 5.2, chloride 100, bicarbonate 18; the P.C.V. was now 32 c.cm. per 100 ml. and the blood sugar 158 mg. per 100 ml.

Necropsy (Dr. H. Spencer) showed leaflike adrenals ($30 \times 10 \times 1$ mm.) each weighing about 0.75 g., which on cutting had no recognizable cortex. Histologically they showed adrenal atrophy (see Special Plate). No inclusion bodies could be seen. Apart from two small areas of perivascular lymphocytic cuffing on the outer part of the lentiform nucleus of the brain and chromatolytic changes in a few nerve cells of the pons and medulla, there were no other histological or anatomical changes of note.

Comment

This history of increasing weakness and loss of energy, of vomiting, loss of appetite, and wasting, and the development

of pigmentation, is characteristic of the condition which, untreated, progresses to a fatal crisis, precipitated perhaps by infection, trauma, surgery, or drugs such as morphine or the barbiturates, to which these patients are particularly sensitive. An increased liking for salt is often found—it occurred in 13 of the cases quoted in the accompanying table. The blood pressure may, as here, remain normal until the onset of the crisis. Lymphocytosis and eosinophilia, reflecting perhaps the low secretion of glucosteroids, are noted occasionally. The E.E.G. record showing diffuse high-voltage slow activity waves is typical.

Discussion

Jaudon (1946) found reports in the world literature of 62 proved cases of Addison's disease in children under 15 years, all but 13 of them being over 10 years. The underlying condition was tuberculosis in 53, atrophy in five, and "not demonstrated" in one, whilst in three the symptoms complicated hyperplasia of the androgen-secreting cells of the foetal cortex—mixed adrenal disease, a relatively more common condition best considered apart. Since then reports of a further 29 cases of uncomplicated Addison's disease have appeared, 22 in boys. The details are shown in the table.

Thus, including this present case, adrenal atrophy was the cause in 11 (55%) of the 20 proved cases, hypoplasia in four, and tuberculosis in only two (10%). In the 10 cases where the aetiology was less certain, only one had definite evidence of tuberculosis. Talbot *et al.* (1952) found tuber-

Summary of 29 Cases of Addison's Disease in Children Reported since 1946

	Sex	Age at Onset	Length of Illness	Pathology	Associated Conditions	Comments
Sikl (1948)	M	3 weeks	2 weeks	Hypoplasia (P.M.)		Treated from 7 months
Geppert, Spencer, and Richmond (1950)	M	Birth	20 months	" "		" "
Deamer and Silver (1950)	M	Few months	10 "	Probably hypoplasia		Survives. Treated from 18 months
Moore and Cermak (1950)	M	2 weeks	4 years +	Adrenal cysts (P.M.)		Treated with D.C.A.
Provenzano (1950)	M	Birth	7 months	Hypoplasia (P.M.)		Responded to A.C.T.H. at first
Garrahan, Sampayo, and Di Pietro (1952)	M	16 months	24 days	Atrophy (P.M.)		
O'Donnell (1950)	M	20 "	7 "	Fibrosis and calcification (P.M.)		Negro child. Septicaemia aged 1 month; normal then until crisis precipitated by otitis media
White and Sutton (1950)	F	2½ years	2 days	" "		Mentally and physically retarded. Sudden death in crisis precipitated by mild illness
Mautner (1954)	M	4½ "	12 hours	Calcification, cause not known (P.M.)	Internal hydrocephalus	Pigmented scar aged 4 months after vague febrile illness at 2 months. Retarded growth. Crisis at 9 years. Survives on treatment
Russell and Potter (1951)	M	9 "	" "	Unknown; no evidence tuberculosis		
Bickel and Stamm (1948)	F	7 "	7 months	Atrophy (P.M.)	Followed severe impetigo	
Bessman (1948)	M	5 "	3 "	" "		Presented as hypoglycaemia
Burdick, Warthen, Cassidy, and Welsh (1950)	M	5½ "	6 "	" "		Sister has thrush and Addison's disease
Craig, Schiff, and Boone (1955)	M	6½ "	3 "	" "	Moniliasis; ? hypoparathyroidism; pneumonia, empyema	Brother with moniliasis, coeliac disease, and hypoparathyroidism
	M	11½ "	3 "	" "	Moniliasis at 2½ years; ? coeliac disease at 4½ years; hypoparathyroidism at 6 years	
Leonard (1946)	F	10 "	2 years	" "	Moniliasis at 3½ years; ? hypoparathyroidism	No parathyroids found at necropsy
Broch (1946)	F	10½ "	18 months	" "	Hypoparathyroidism from 5½ years	
Laplane and Fritel (1948)	M	14 "	6 "	Tuberculosis (P.M.)		Pigmentation only for 18 months and then fatal crisis
Correa and Piera (1952)	F	12 "	18 "	" "		
Mouriquand, Dechavanne, and Laugel (1951)	M	11½ "	4 "	Unknown; probably non-tuberculous	Heart failure	After 4 months' treatment developed faintly positive Mantoux reaction, shortly before death. No other evidence of tuberculosis
Demirag (1947)	M	13 "	9 "	" "		
Mathesius (1947)	M	11 "	2 years +	Unknown; no evidence of tuberculous infection	Chronic malaria	Presented at age 10 with 3-year history of illness. Stunted growth
Briggs, Goodwin, and Wilson (1951)	M	8 "	3 "	" "		One year later 17-year-old brother died in 5 weeks of adrenal atrophy. Calcified abdominal glands
Patzerowa (1953)	M	12 "	2 years +	Unknown; no evidence of tuberculosis		
Papadatos and Klein (1954)	M	10 "	" "	Unknown; no evidence of tuberculous infection	Hypoparathyroidism at 5½ years	
Bernheim and François (1953)	F	12 "	3 "	Probably tuberculosis		Aetiology not considered at all by authors
Stanton, Jones, and Marble (1954)	M	10 "	2 years +	Unknown	Diabetes mellitus at 2½ years	

culosis to be a factor in only one of nine cases known to them. In so far, therefore, as can be judged from the evidence of published case reports, tuberculosis has now been displaced from its position as the commonest cause of Addison's disease in childhood, and atrophy must account for at least half the cases of this condition. A similar trend has been seen in adults in recent years. In adults atrophy is more common in the female, yet in these recently reported cases in children the reverse is true, a fact Jaudon (1946) also noted.

As to the cause of adrenal atrophy (adrenocortical contraction) nothing definite is known. The histological picture is clear-cut (Guttman, 1930): the parenchymal cells degenerate and disappear, shrinking away from the undamaged reticulum framework, which in time collapses, leaving no trace of the columnar zonal pattern. Both cortex and, to a lesser extent, medulla are infiltrated with lymphocytes, and there is usually no cicatricial or productive fibrosis. The condition has occurred in members of the same family—definitely in one case (Craig *et al.*, 1955), probably in two more (Briggs *et al.*, 1951; Smith and Higgins, 1952). It can be associated with disorder in other endocrine glands. Of these 11 proved examples of adrenal atrophy, clinical hypoparathyroidism was present in two and strongly suspected in two more. In two of the surviving cases where atrophy was suspected there is a further example with associated hypoparathyroidism and one with diabetes mellitus, the 47th example in the literature (Stanton *et al.*, 1954). In adults Addison's disease, particularly (but not always) when due to adrenal atrophy, has been found in association with both hypothyroidism and hyperthyroidism (Sorkin, 1949). Changes in the pituitary are found in Addison's disease from all causes, being secondary to the adrenal hypofunction. The adrenal changes in hypopituitarism are quite distinct from those of adrenocortical contraction (Crooke and Russell, 1935).

In the particular instance reported here the onset after mumps is of interest when one considers the effect of the mumps virus on testis, ovary, and pancreas. No inclusion bodies, however, can be seen on microscopy. The only other suggestions that this selective destruction of parenchyma cells might be viral in origin are from Weiner (1936), who found intranuclear inclusions in a case of atrophy in a middle-aged woman, and Friedman (1948) and others, who have noted a resemblance between the changes in this condition and those of certain liver diseases, particularly hepatitis—allowing for the different natures of the organ—and that there was some correlation in the rise in incidence of both conditions as seen at the United States Army Institute of Pathology. Yet, on the whole, it seems more likely that the relationship in time between the mumps and the onset of the child's final illness is only a coincidence.

Summary

A fatal case of Addison's disease due to atrophy of the adrenals in a girl of 9 years is reported. The picture of progressive weakness and listlessness, of vomiting and anorexia, and the development of pigmentation is typical of the condition. Until the onset of crisis her blood pressure was normal.

The recent literature on Addison's disease in children is reviewed. In the past ten years more than one-half of the cases reported with a known pathology have been due to atrophy of the adrenals (adrenocortical contraction) and only one-tenth to tuberculosis—a great change from the findings in a previous review of this subject. Over one-third of the cases showed evidence of a craving or increased liking for salt.

I wish to thank Dr. J. Forest Smith and Dr. John Anderson for permission to publish details of this case admitted under their care; Dr. H. Spencer and Dr. J. D. Pollitt for permission to quote from their reports; and my colleagues who gave their help and advice.

REFERENCES

- Bernheim, M., and François, R. (1953). *Pédiatrie*, **42**, 357.
 Bessman, S. P. (1948). *Clin. Proc. Child. Hosp. (Wash.)*, **5**, 173.
 Bickel, H., and Stamm, O. (1948). *Helv. paediat. Acta*, **3**, 53.
 Briggs, J. N., Goodwin, J. F., and Wilson, A. (1951). *British Medical Journal*, **1**, 115.
 Broch, O. J. (1946). *Acta med. scand.*, **125**, 371.
 Burdick, W. F., Warthen, R. O., Cassidy, J. E., and Welsh, W. W. (1950). *Amer. J. Dis. Child.*, **80**, 975.
 Correa, O., and Pica, A. (1952). *Rev. chil. Pediat.*, **23**, 110.
 Craig, J. M., Schiff, L. H., and Boone, J. E. (1955). *Amer. J. Dis. Child.*, **89**, 669.
 Crooke, A. C., and Russell, D. S. (1935). *J. Path. Bact.*, **40**, 255.
 Deamer, W. C., and Silver, H. K. (1950). *J. Pediat.*, **37**, 490.
 Demirag, B. (1947). *Ann. paediat. (Basel)*, **169**, 65.
 Friedman, N. B. (1948). *Endocrinology*, **42**, 181.
 Garrahan, J. P., Sampayo, R. R. L., and Di Pietro, A. (1952). *Arch. argent. Pediat.*, **37**, 220.
 Geppert, L. J., Spencer, W. A., and Richmond, A. M. (1950). *J. Pediat.*, **37**, 1.
 Guttman, P. H. (1930). *Arch. Path. (Chicago)*, **10**, 742, 895.
 Jaudon, J. C. (1946). *J. Pediat.*, **28**, 737.
 Laplane, R., and Fritel, D. (1948). *Arch. franc. Pédiat.*, **5**, 282.
 Leonard, M. F. (1946). *J. clin. Endocr.*, **6**, 493.
 Mathesius, V. J. (1947). *Pediat. Listy*, **2**, 160.
 Mautner, H. (1954). *Ann. paediat. (Basel)*, **58**, 354.
 Moore, F. P., and Cermak, E. G. (1950). *J. Pediat.*, **36**, 91.
 Mouriquand G., Dechavanne, D., and Laugel, J. (1951). *Pédiatrie*, **40**, 67.
 O'Donnell, W. M. (1950). *Arch. intern. Med.*, **86**, 266.
 Papadatos, C., and Klein, R. (1954). *J. clin. Endocr.*, **14**, 653.
 Patzerowa, T. (1953). *Pediat. pol.*, **28**, 416.
 Provenzano, R. W. (1950). *New Engl. J. Med.*, **242**, 87.
 Russell, A., and Potter, C. T. (1951). *Proc. roy. Soc. Med.*, **44**, 957.
 Siki, H. (1948). *J. Path. Bact.*, **60**, 323.
 Smith, T. W., and Higgins, A. R. (1952). *Milit. Surg.*, **110**, 180.
 Sorkin, S. Z. (1949). *Medicine*, **28**, 371.
 Stanton, E. R., Jones, H. W., and Marble, A. (1954). *Arch. intern. Med.*, **93**, 911.
 Talbot, N. B., Sobel, E. H., McArthur, J. W., and Crawford, J. D. (1952). *Functional Endocrinology from Birth through Adolescence*. p. 195. Harvard Univ. Press, Cambridge, Mass.
 Weiner, H. A. (1936). *Amer. J. Path.*, **12**, 411.
 White, F. P., and Sutton, L. E. (1950). *J. Pediat.*, **37**, 778.

AN UNUSUAL CASE OF CAROTID-BODY TUMOUR

BY

MAXWELL ELLIS, M.D., M.S., F.R.C.S.

Surgeon, Royal National Throat, Nose and Ear Hospital, London; Ear, Nose, and Throat Surgeon, Central Middlesex Hospital, London

AND

P. WINSTON, M.B., F.R.C.S., D.L.O.

First Assistant in the Professorial Unit, Institute of Laryngology and Otology, London

[WITH SPECIAL PLATE]

Aberrant parasympathetic nervous tissue often occurs near the great vessels of the neck. From this tissue a tumour called non-chromaffin paraganglioma may arise, sometimes near the bifurcation of the common carotid artery, where it is known as a carotid-body tumour, or occasionally near the exit from the skull of the internal jugular vein, where it is given the name of glomus jugulare tumour. These tumours are characteristically extremely vascular, and the carotid-body tumour is, in addition, closely attached to one or other of the carotid vessels by vascular connexions as well as adhesions, often simulating an aneurysmal dilatation. Excision of such a tumour may be impossible without also resecting a length of the adherent vessels.

As the tumour increases in size, pressure on neighbouring structures may occur, particularly the vagus and hypoglossal nerves and the sympathetic nerve trunk. The internal jugular vein is more often pushed aside than invaded. Harrington *et al.* (1941) state that 40–50% of carotid-body tumours become malignant, but Lahey and Warren (1947) consider this estimate is much too high. Metastases to cervical lymph nodes may occur, and very occasionally distant metastases.

I. D. RILEY AND G. SCLARE: THYROID DISORDERS IN NEWBORN

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. $\times 400$.) FIG. 3.—Case 2: Showing unusually prominent stroma. (Masson's trichrome. $\times 55$.)

R. G. WELCH: ADDISON'S DISEASE

Sections of adrenal (a) from patient and (b) from healthy child of same age. ($\times 120$.)

S. COPE: FIBROSARCOMA OF AURICLE

Photomicrograph of section of tumour. ($\times 300$.)

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, $\times 174$; b, $\times 190$.)

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