CONGENITAL GOITRE

A REVIEW WITH A REPORT ON THREE CASES OF SUFFOCATIVE GOITRE IN THE NEWBORN

J. H. LOUW, CH.M., F.R.C.S., *Professor of Surgery, University of Cape Town and Head of the Department of Surgery, Red Cross War Memorial Children's Hospital, Cape Town*

The term 'congenital goitre' is applied not only to thyroid enlargements which are present at birth, but also to those which begin to develop during the first few weeks of life. In either case the most important aspect of the condition is its tendency to cause serious respiratory obstruction—the so-called suffocative or obstructing goitre in the newborn.[9,20] The seriousness of the respiratory obstruction caused by goitres of even moderate size in newborn babies has been recognized for more than a century, and as recently as in 1936 Aschoff[2] reported that goitres accounted for 10% of the neonatal mortality in Freiburg, Germany. Relief of the suffocation by operation is often necessary and may prove life-saving.

It is the purpose of this paper to report 3 cases of congenital goitre with suffocation and to discuss the pathogenesis, clinical presentation and management of goitres in the newborn.

CASE REPORTS

Case 1

A.D., a White female infant aged 1 month, was admitted to the Red Cross War Memorial Children's Hospital on 10 September 1960 suffering from severe respiratory distress and a large swelling in the neck which had been present since birth. The mother's pregnancy and confinement had been normal. She had at no time suffered from any physical disorder, but had taken a mixture containing iodides during the pregnancy for 'asthma'.

The infant was suffering from obvious respiratory obstruction with dyspnoea, cyanosis and severe inspiratory stridor. There was a soft symmetrical swelling in the region of the thyroid which was, at first, thought to be a lymphangioma. The swelling was the obvious cause of the respiratory obstruction, which was partially relieved by hyperextension of the neck. X-ray of the neck showed the presence of a soft-tissue swelling with considerable forward displacement and kinking of the trachea (Fig. 1). There were no signs of hypo- or hyperthyroidism.

Conservative management by hyperextension of the neck failed to relieve the obstruction, and the child suffered from frequent cyanotic attacks with intense stridor especially during feeding. After 2 days, on 12 September 1960, the neck was explored. The swelling was found to be due to a diffuse, symmetrical enlargement of the thyroid gland, and a tracheostomy was performed.

The tracheostomy did not provide the desired relief and the infant was treated with thyroxin, 0·05 mg. daily, to promote shrinkage of the gland, and by continued hyperextension of the neck. However, after 3 weeks there was still no real improvement and the child developed frequent attacks of severe respiratory obstruction. A subtotal thyroidectomy was, therefore, performed on 3 October 1960. At the operation it was noted that the lateral lobes of the gland extended posteriorly between trachea and oesophagus, producing acute forward kinking of the trachea. The tracheostomy tube was left *in situ*.

After the second operation there was complete relief of the respiratory obstruction. Progress was retarded by wound sepsis and difficulty in weaning her of the tracheostomy, which was removed 2 weeks postoperatively. For a while she had some difficulty in swallowing, but this gradually subsided and she was discharged from hospital on 25 December 1960 on a maintenance dose of 0·025 mg. of thyroxin daily.

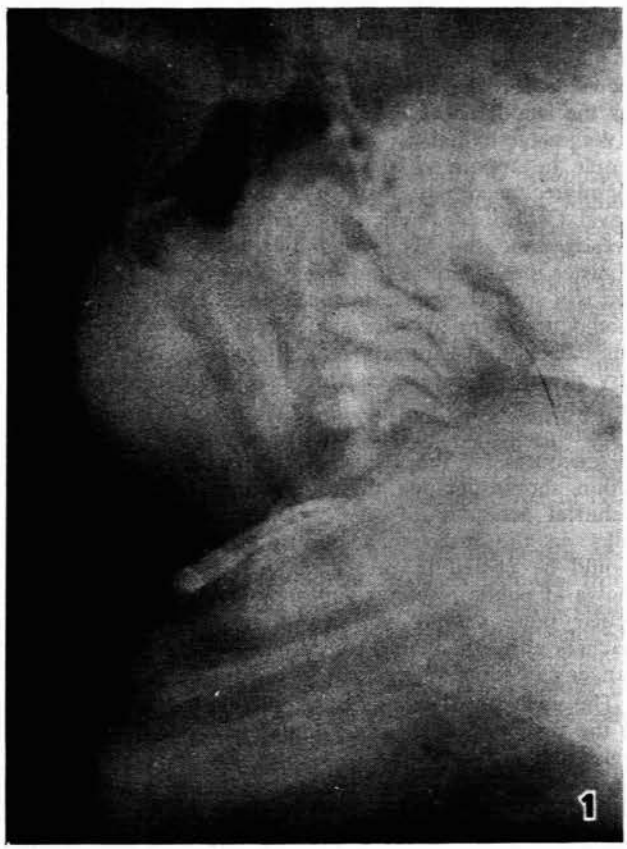

Fig. 1. Case 1. Lateral X-ray of neck. Note the soft-tissue shadow of the goitre and the forward angulation of the trachea so characteristic of these cases.

During the following 3 months she returned to hospital on a number of occasions because of stitch abscesses in the neck and pneumonia. After that she recovered completely and has thrived ever since. On 22 August 1962 the disfiguring scar in her neck was excised, and in March 1963, at the age of two and a half years, she was perfectly well and normal in every respect. She is still being maintained on thyroxin, 0·025 mg. daily.

The thyroid tissue which had been removed weighed 40 G., and histological examination revealed a simple colloid goitre with considerable, although not uniform, distension of the acini by well-stained colloid and flattening of the lining epithelium.

Case 2

E.P., a White male infant aged 1 day, was admitted to the Red Cross War Memorial Children's Hospital on 4 January 1962 suffering from respiratory obstruction, stridor and a large swelling in the neck. The mother's pregnancy and confinement had been uncomplicated, and at no time had she suffered from a thyroid disorder. However, she was an asthmatic who had taken iodized expectorants for years, including the period of her pregnancy.

The neck swelling had the typical trilobed appearance of a congenital goitre (Fig. 2) and was soft, smooth and sym-

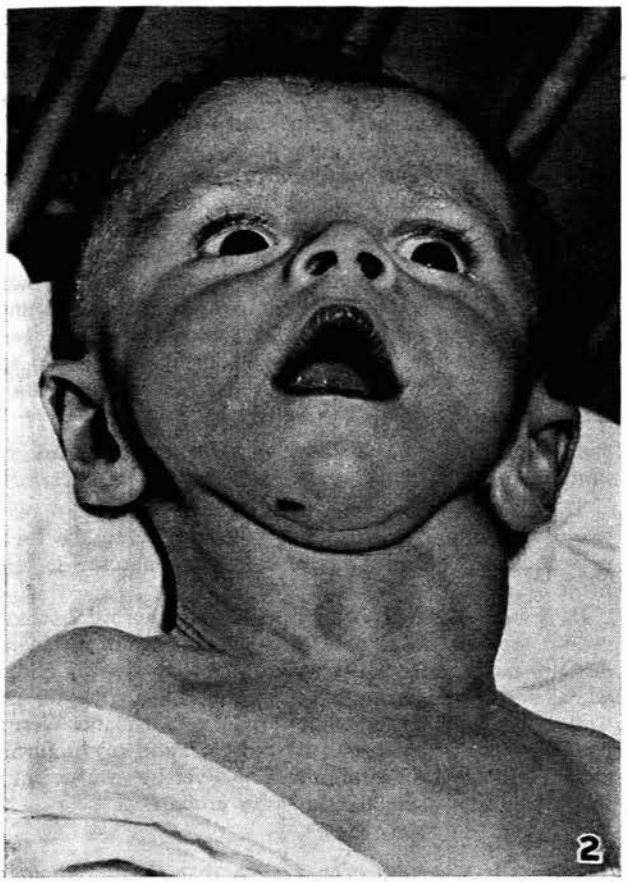

Fig. 2. Case 2. Note the trilobed appearance of the goitre and hyperextension of the neck.

metrical. The child held his head in the hyperextended position, and any flexion of the neck immediately produced severe stridor with serious respiratory obstruction. X-ray examination revealed considerable forward angulation of the trachea. There were no signs of hyper- or hypothyroidism, but the heart was considerably enlarged.

Because of the extreme angulation of the trachea the anaesthetist anticipated great difficulties with intubation, and it was therefore decided to treat the child conservatively by hyperextension of the neck and thyroid hormones. In the first instance triiodothyronine, 25 mg., was given to obtain a rapid initial effect in addition to thyroxin, 0·1 mg. daily. The child soon developed signs of hyperthyroidism and on the fifth day the medication was reduced to 0·05 mg. of thyroxin daily. There was some initial regression of the thyroid swelling and the neck measurement reduced by about ¾ inch during the first 3 weeks. Thereafter the swelling remained static and, although there was no obvious respiratory obstruction while the neck was well extended, the slightest flexion precipitated stridor and cyanosis, while sternal recession and tachypnoea persisted even with the neck fully extended. At this stage it was observed that the child was mentally abnormal and blind.

Four weeks after admission, during which time the course of the illness had been complicated by the development of pneumonia, diarrhoea and thrush, the child showed signs of hyperthyroidism — hyperactive, hyperirritable and hyperkinetic, with persistent tachycardia and tachypnoea and radioactive ^{131}I uptake of 42%. Thyroxin was, therefore, discontinued.

In view of the child's poor general condition, his mental state and the blindness, surgery was deemed inadvisable. He continued to deteriorate, developed staphylococcal and monilia infections and eventually died on 3 May 1962 at the age of 4 months.

Postmortem examination revealed a marasmic child with a large goitre, obstructive emphysema of the lungs, a large hypertrophied heart with fibroelastosis of the right ventricle, oesophagitis and gastritis. The lateral lobes of the goitre measured 4·6 × 4·6 × 2·5 cm. and they practically surrounded the trachea and oesophagus, almost meeting behind the oesophagus, but the tracheal lumen was circular and not occluded. The gland weighed 50 G. and had a uniformly yellow, 'glassy' appearance with occasional fibrous trabeculae

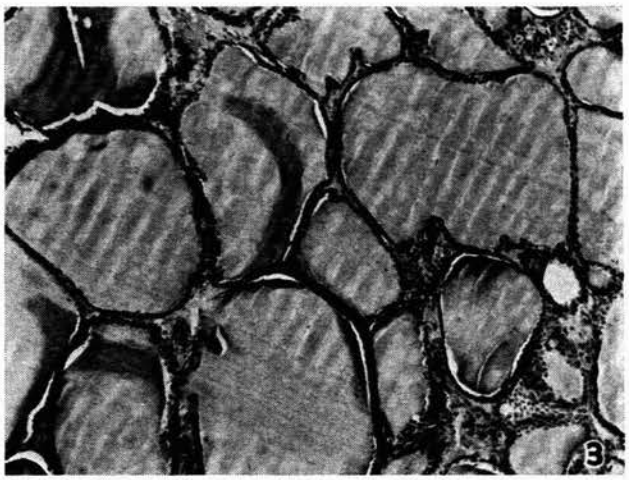

Fig. 3. Case 2. Histology of goitre (X 100). Note the enormous follicles distended by colloid and lined by low cuboidal epithelium.

traversing the gland. Histological investigation revealed a typical colloid goitre (Fig. 3).

Case 3

F.H., a Coloured female infant aged 1 day, was admitted to the Red Cross War Memorial Children's Hospital on 8 March 1963 with respiratory obstruction and a swelling in the neck. The mother's pregnancy and confinement had been normal, and at no time had she suffered from a thyroid disorder. However, she was a tuberculotic who had been treated with para-aminosalicylic acid before and during the pregnancy.

The swelling in the neck was a typical soft, trilobed con-

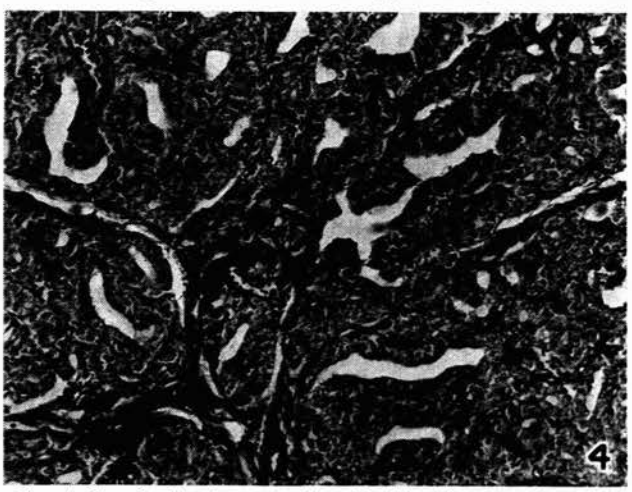

Fig. 4. Case 3. Histology of goitre (X 100). The photomicrograph shows tremendous follicular hyperplasia, but the follicles are indistinct and distorted, the large epithelial cells frequently being aligned in cords or tubules rather than in regular round or oval follicles. These features are compatible either with congenital goitrous cretinism, which is often produced by administration of antithyroid drugs, or with so-called familial goitrous cretinism.

genital goitre. The child kept the neck hyperextended and there was slight respiratory obstruction with stridor on crying and on flexing the neck. X-ray examination revealed well-marked forward angulation of the trachea. There were no signs of hypo- or hyperthyroidism.

On 11 March 1963 a subtotal thyroidectomy was performed. The gland was diffusely enlarged with the lateral lobes curling around the trachea and oesophagus, displacing the former forward. A tracheostomy was at first omitted, but was done later because of postoperative haematoma. Substitution therapy with thyroxin, 0·1 mg. daily, was commenced immediately after the operation.

The postoperative course was satisfactory, but difficulty was experienced in weaning the infant of the tracheostomy tube. Three weeks postoperatively it was noticed that the infant was developing xanthelasma of the scalp and the serum cholesterol was 288 mg. per 100 ml. The thyroxin dosage was, therefore, increased to 0·15 mg. daily.

The thyroid gland was uniformly enlarged, the right lobe measuring 3·8 × 2·5 × 2 cm. and the left lobe 2·8 × 2·8 × 2 cm. The gland was firm in consistency and the cut surfaces of both lobes had a fleshy appearance. Histological investigation revealed hyperplasia of the follicles, which were small, devoid of colloid and lined by relatively tall cuboidal epithelium (Fig. 4). The nuclei were round or oval with a reticular chromatin pattern, centrally situated in the cells. A well-defined lobular pattern was present.

DISCUSSION

Congenital goitre is said to be very rare today, and most current textbooks on paediatric surgery devote hardly any space to the subject. However, the condition used to be very common in endemic regions of Europe at the turn of the century, and as recently as 1936 Aschoff[2] reported that the thyroid was larger than normal in two-thirds of infants that came to autopsy in Berne, Switzerland. In recent years there have been an increasing number of reports of congenital goitres in infants whose mothers have received thiourea compounds or iodine during pregnancy, and it is possible that the incidence of thyroid enlargement in the newborn is appreciably greater than is generally suspected because slight or even moderate enlargements may be missed owing to the difficulty of examining the neck of a small baby. The condition, therefore, cannot be dismissed as a clinical curiosity, particularly in view of the grave risk of suffocation.

In considering the development of congenital goitres, the activity of the thyroid gland during foetal and neonatal life must be examined with some regard to the passage of TSH and thyroid hormones across the placenta in either direction. Consideration must also be given to the maternal environment, the use of drugs and genetic factors which might influence the development of the foetal thyroid.

Activity of the Thyroid in Foetal and Neonatal Life[24]

The secretory cells of the foetal thyroid become regularly arranged only 3 - 4 months after conception; at 6 months some storage of glandular secretion or colloid can be seen in occasional vesicles and by the eighth or ninth month most of them are filled. Biologic activity of the thyroid cells appears early and perhaps before they assume their vesicular arrangement in the gland. It has been shown that radioactive iodine is collected by the human foetal thyroid by the 12th week after conception, and thyroxin has been demonstrated in the human embryo at the third month. The gland has clearly demonstrable biologic function by the middle of gestation, and the human foetus seems to be able to provide its own thyroid hormone independent of the maternal supply for some time before birth. Nevertheless, measurements of hormone iodine suggest some sort of equalization with maternal factors across the placenta. During the 3 - 7 days immediately following birth, the infant's hormone-iodine rises by some 25 - 50% above that in cord plasma, and radioactive iodine uptake studies suggest that this is due to transitory physiological hyperthyroidism.

Pituitary activity, including secretion of TSH, probably starts early in foetal life. From observations in animal experiments and in anencephalic human foetuses it seems clear that the pituitary is active during foetal life and responsible for the normal development of its various target organs.

Passage of TSH and Thyroid Hormones across the Placenta

There is some evidence that maternal TSH can reach the foetus, but it is clear that it cannot reach the foetus in sufficient concentrations to supply the natural development of the target organs.[9,18,24]

It is believed that enough maternal thyroid hormone crosses the placenta to assist the development of the foetus, because most congenitally athyroid infants appear normal when born. In human experiments, using thyroxin and triiodothyronine tagged with ^{131}I, Grumbach and Werner[8] have shown that maternal thyroid secretion might furnish some of the foetal requirements and yet be insufficient to allow complete skeletal and brain growth.

Maternal Environment

Iodine. It has long been known that the development, size and function of the foetal thyroid may be altered by an *inadequacy of iodine* in the maternal diet.[24] Pregnancy itself increases the activity of the maternal thyroid with elevation of the protein-bound iodine in the blood and therefore the daily iodine requirements of the pregnant mother are increased. If her iodine intake is low, it may not be sufficient to meet the needs of both mother and child, and this may affect the foetal thyroid in two ways:

1. If both the maternal and foetal serum-iodide concentration (which are usually equal) remain subnormal, both maternal and foetal thyroids will accumulate iodine to form thyroid hormone and consequently enlarge owing to the presence of excessive colloid.

2. If the mother has a subnormal amount of circulating thyroid hormone, the foetus may not receive sufficient maternal thyroxin to supplement its own for its needs. This will stimulate an increased output of TSH by the foetal pituitary with consequent hyperplasia of the thyroid.

Whatever the mechanism may be, it is well known that infants born in endemic goitrous regions, where dietary consumption of iodine is low, show a definite tendency to thyroid enlargement although the mother need not have obvious thyroid disturbance. Similar changes have been accurately reproduced by Marine[15] in experiments with the offspring of partially thyroidectomized dogs. Successive litters of puppies could be made either normal or goitrous by administration of small amounts of iodine in the maternal diet.

On the other hand, it has also been established that an *unusually large intake of iodine* by the mother may in-

duce enlargement of the foetal thyroid.[9,15] Iodides cross the placenta freely, and it has been shown that if the serum level remains elevated for long periods, release of thyroid hormone from the gland may be almost completely inhibited. This results in stimulation of the foetal pituitary with consequent thyroid hyperplasia.[15]

TSH. Grave's disease in the mother is occasionally associated with the development of goitre in the newborn infant.[7,24] Although this is usually due to the therapy rather than the maternal disease *per se* (see below), excessive amounts of maternal TSH, which may persist after surgical or other treatment, may be responsible for hyperplasia of the foetal gland.

Drugs. There are now many reports of the development of goitres in the infants of mothers who had been treated for hyperthyroidism during pregnancy by thiouracil and other antithyroid drugs.[1,5,9,12,16,15,19] Thiouracil interferes with the synthesis of thyroid hormone and thus causes hyperplasia of the thyroid either directly or by promoting an increased secretion of pituitary TSH. Animal experiments have shown that the drug crosses the placenta and it is also excreted in breast milk. The effect on the human foetus is believed to be by transplacental passage of the drug itself with subsequent stimulation of foetal TSH production and resultant thyroid hyperplasia.

Genetic factors. At least 5 inborn errors of thyroid metabolism have been identified to date and there are probably many others which may be responsible for the development of goitres.[3] Usually the maternal thyroxin is sufficient to maintain the foetus, who is born apparently normal but develops goitre later. Sometimes, however, congenital goitre may be present.

Arising from the above the following types of congenital goitre are recognized.

1. Deficiency in Maternal Iodine Intake

Congenital goitres in endemic areas are almost invariably due to gross deficiency in maternal iodine intake. It was, therefore, rife in endemic areas of the European Continent before prophylactic iodine therapy was introduced, and Aschoff[2] in 1936 reported that goitre was present in 50% of all newborn infants in parts of Switzerland. In 1924 Skinner[22] reported 12 cases of congenital goitre collected from the endemic goitre belt of the North-West, USA. In 1928 he discussed a group of 900 women who received prophylactic iodine therapy during pregnancy and no case of congenital goitre occurred in their infants.[23] The same has happened in Europe since the introduction of prophylactic iodized salt.

The gland in these cases is uniformly and often considerably enlarged producing the typical trilobed mass situated high in the neck of the infant. In the young infant no secondary adenomatous changes are found.[25] The frequency and degree of associated hypothyroidism varies in the different geographic regions of endemic goitre, e.g. the incidence of cretinism is much higher in the Alps, Carpathians and Himalayas than in goitrous districts of the USA.[2,29] It would appear that if enough iodine is available to permit the compensatorily enlarged gland to produce an adequate amount of hormone, the patients remain euthyroid; if not, some degree of hypothyroidism develops.[29] On the other hand, other factors in addition to iodine deficiency may play a role because about half of 'endemic cretins' have no goitres.[2]

The histological pattern varies. In infants who are not hypothyroid the gland is uniformly hyperplastic with small follicles containing a moderate amount of colloid —the so-called microfollicular goitre.[25] In those with cretinism the goitre consists of very large follicles lined by flattened epithelium and distended by masses of colloid giving the cut surface a glassy, translucent appearance.[25]

It is agreed that these goitres are due to insufficient quantities of ingested iodine. If the deficiency is corrected postnatally, the goitre usually disappears, but if it persists, the gland may reach an enormous size although it usually remains a *diffuse* colloid goitre throughout childhood.

2. Ingestion of Large Amounts of Iodides by the Mother

It has been well established that congenital goitres may occur in infants born of mothers who have received large amounts of iodide medication.[29] Of 32 cases of suffocative goitre reported in the American literature, 9 of the mothers had been on heavy iodide therapy throughout pregnancy and 3 on a combination of iodides and thiouracil.[15] In 2 of the cases here reported the mother had received iodides for asthma. In most of the reported cases the mother has been euthyroid and the iodide therapy has been for asthma, but congenital goitres have also followed the use of iodides for maternal hyperthyroidism.[4] On the other hand, Wilkins[29] reports a case of a child who developed a goitre while receiving a mixture of sodium arsenite and potassium iodide for asthma and in whom the goitre disappeared after the arsenic was stopped although the iodide was continued; this suggests that other factors may be implicated.

The glands of infants born of mothers who have received iodides are uniformly enlarged and firm. In none of the infants has there been evidence of hyper- or hypothyroidism. Histologically the glands have shown a varied picture with evidence of hyperplasia and/or colloid storage.[25]

3. Exophthalmic Goitre

In 1912, under the heading of 'A Foetus with Congenital Hereditary Graves' Disease', White[28] described a case of a premature baby born with signs of hyperthyroidism. The mother had had Graves' disease, which could only be poorly controlled, for the last 4 months of pregnancy. In 1951 Fischer[7] reported a similar case in South Africa. The mother had been inadequately treated on propylthiouracil and Lugol's iodine. The infant developed symptoms of thyrotoxicosis on the 3rd day, but thyroid enlargement was not noticed until the 6th day. Koerner[14] has also reported a congenital goitre with exophthalmos and hyperthyroidism, while Skelton and Gans[21] reported congenital thyrotoxicosis, hepatosplenomegaly and jaundice in 2 infants born of exophthalmic mothers. In all reported cases the thyroid has been diffusely, uniformly, and only moderately enlarged,[25] and in no case has the gland been responsible for suffocation. The gland is firmer and more solid than usual, and because of its great vascularity, darker in colour.[25] Histologically there is well-marked hyperplasia, and the cells are tall and apparently increased in number.[25] It is rare for adenomatous goitres to cause symptoms of hyperthyroidism before the age of 20 years

and no case under 15 years of age was encountered in a large series collected at the Mayo Clinic over a period of 35 years.[10,11]

Talbot[27] states that neonatal hyperthyroidism tends to occur if thyroid is administered during pregnancy, and that if the infants weather the first 3 weeks of life, they are usually normal thereafter. That the thyroid hormone, derived from the hyperactive maternal thyroid, could *per se* affect the baby, seems highly improbable, however. Firstly, in at least 2 of the reported cases there was a time lag between birth and the full development of signs; secondly, it has been shown that thyroid hormone crosses the placenta with difficulty and thirdly, it is known that an excess of thyroid hormone depresses TSH, and consequently enlargement of the thyroid in the baby would *not* be expected.

Wilkins[29] mentions that infants born with congenital goitres owing to ingestion of goitrogens or iodine by the mother may develop thyrotoxic symptoms or even thyroid crises when the infantile thyroid is released from the blocking effect of the drugs owing to continued hypersecretion of TSH by the infantile pituitary. A similar mechanism may be responsible for some cases of congenital exophthalmic goitre; on the other hand, this condition might be due to the effect of maternal TSH which may remain excessive in hyperthyroid women who have been surgically or otherwise rendered euthyroid. However, it is not known for how long this hormone could continue to exert its effect post partum, nor does this explanation account for the lag period before the development of the full-blown picture in the infants.

Neonatal hyperthyroidism must be distinguished from hyperthyroidism developing in older infants and children. In the latter group there is no history of maternal thyrotoxicosis, the babies are normal at birth, signs of thyrotoxicosis appear after the age of 6 months, and the condition is progressive until arrested by treatment.[7]

4. Ingestion of Goitrogens by the Mother

Various goitrogenic drugs have been shown to cross the placenta.[29] In contrast, thyroxin and triiodothyronine do not cross the placenta freely in sufficient quantities to fulfil the needs of the infant completely.[29] It is therefore not surprising that there are a considerable number of reports of congenital goitres occurring in infants born of mothers who received antithyroid drugs during pregnancy. Most of the reports have concerned infants whose mothers had been treated during pregnancy for thyrotoxicosis with thiourea derivatives. Reports of congenital goitre following maternal therapy by thiocyanates, PAS, sodium arsenite and cobalt compounds are also on record.[9,18,25,29] There have been a few reports of death of the foetus with signs of severe intra-uterine hypothyroidism from excessive doses of antithyroid compounds.[29] The mother of our third patient received PAS throughout pregnancy.

The gland is uniformly, symmetrically and usually moderately enlarged, although it may reach a tremendous size.[25] It is usually deep red-brown in colour and of a meaty consistency. In most cases the infants are euthyroid, but some infants have shown mild signs of hypothyroidism manifested by sluggishness, poor peripheral circulation and an osseous development less than that of the normal newborn.[29]

A few cases have been reported with more classical signs of cretinism with epiphyseal dysgenesis, and in them the mothers had received very large doses of propylthiouracil during pregnancy.[29]

Histologically there are diffuse changes in the gland. The follicles are indistinct and irregular in shape with the cells arranged in cords or tubes rather than around oval follicles.[29] The glands are obviously hyperplastic with tall, closely packed cells having no clear basement membrane. There is very little fibrous stroma and colloid is never present.[25] In some cases the appearances have been so bizarre as to suggest carcinoma.[25]

The goitres develop from the effect of the antithyroid drugs on the foetal thyroid, which is prevented from synthesizing its hormones. After birth the infant is released from the blocking effects of the drug (provided he is not breast fed, because the thiouracil compounds are also excreted in milk), so that the thyroid promptly recovers its normal function and the goitre disappears in a few weeks (and so do the signs of hypothyroidism if they have been present). Occasionally during this period thyrotoxic symptoms or even a thyroid crisis may develop owing to excessive secretion of thyroxin by the hyperplastic gland when released from the thyroid-blocking effect of the drug.[29]

5. Defect in Thyroxin Metabolism

In a small group of *goitrous cretins* the infants have the ability to take up iodine but cannot convert it into thyroxin because of a congenital enzymatic deficiency.[25] In contrast to the 'athyrotic' type of cretinism, the goitrous form shows a high familial incidence with multiple siblings affected.[29]

Although both goitre and hypothyroidism may be present at birth, more frequently the patient is hypothyroid at birth and has a gland of normal size which later enlarges if the hypothyroidism is not corrected. The glands are at first diffusely and symmetrically enlarged and composed of hyperplastic follicles with little or no colloid. Later (at 6 - 8 years) they tend to become nodular with numerous encapsulated nodules of pleomorphic structure resembling adenomas or carcinomas.[25,29] The thyroid enlargement is due to the fact that with inadequately treated hypothyroidism there is a compensatory increase in TSH which leads to hyperplasia of the gland. Although the nodules resemble carcinoma microscopically, no cases with malignant extension or metastases have been reported.[29]

Possibly related to familial goitrous cretinism are the congenital goitres occurring in infants whose mothers give no history of iodine deficiency nor of the ingestion of goitrogens or iodide. The goitres tend to be soft and diffuse and sometimes disappear, but they may persist and be accompanied by mild signs of hypothyroidism. This condition is also apt to be familial and may be due to an inborn defect in the ability of the child's thyroid to synthesize thyroid hormones,[29] and if the error is severe, the foetus may develop a goitre so large as to cause dystocia at delivery.[3]

6. Nodular Goitres

Nodular goitres are very rare in childhood, but when they do occur the nodules are true neoplasms.[25] The

adenomas may be single or multiple and of any variety—macro- or microfollicular, foetal, embryonal or Hürthle-cell. All have a complete capsule, a different appearance to the surrounding thyroid, uniformity of cellular characters and evidence of growth. Such goitres are extremely uncommon in the neonatal period, but at least 2 cases of Hürthle-cell tumour with suffocation have been reported in the newborn.[17,26]

The main significance of nodular thyroids in children arises out of the fact that statistics show that 27% of thyroid nodules in children are carcinomatous.[21] The great majority of these are papillary in type. More cases occur in non-goitrous than in goitrous regions, and there is a history of irradiation to the thyroid in 20% of cases. Carcinoma of the thyroid is more common after 5 years but may occur at any age. Harples *et al.*,[12] in reporting 59 cases of thyroid cancer in childhood, cite a case of a child born with a large solitary mass in the thyroid which, on removal at the age of 6 months, proved to be a thyroid carcinoma; there was no history of the mother having been irradiated.

From the practical point of view it should be kept in mind that a nodular thyroid may be mistaken for the typical trilobed swelling usually encountered in diffuse enlargement and the lobulated mass of Hashimoto's disease.

7. Unusual Causes of Thyroid Enlargement

Acute bacterial infection of the thyroid may occur during the neonatal period as part of a generalized septicaemia. We have encountered one such case caused by *E. coli* septicaemia. Subacute thyroiditis (de Quervain) is extremely rare in childhood, and we have not found a report of a case in a neonate. Hashimoto's disease is said to be the most common form of 'thyroiditis' in childhood,[3] but has not yet been reported in the newborn.

Haemangioma, lymphangioma and teratoma are not uncommon in the neck. Not only should these lesions be differentiated from goitres but occasionally they arise in the thyroid gland itself.[29]

MANAGEMENT

The treatment of congenital goitres depends upon the severity of respiratory obstruction and the cause of the goitre. In most instances the goitre is not sufficiently large or wedged to cause pressure symptoms and therefore urgent surgical therapy is not necessary. Furthermore, in the majority the goitre is due to the use of iodine or antithyroid drugs during pregnancy, and therefore retrogresses spontaneously within a few weeks.

Obstructive Goitres

When the goitre is large enough to cause respiratory obstruction, surgical relief of the obstruction is often necessary. In the first place the infant's neck should be kept in the hyperextended position, which will provide some relief. If the respiratory distress is not completely relieved by positioning, and especially if it worsens, urgent surgical intervention is called for. The effects of increasing hypoxia may be insidious and unrecognized until the time remaining for surgical relief is seriously diminished. Even with slight and/or intermittent obstruction there may be progressive cardiopulmonary effects with the development of irreversible changes.[9,15] This was probably a contributory factor to the death of our second patient, who was treated conservatively. We are convinced that the effects of hypoxia should be anticipated and prevented by timely surgical intervention. Of the 32 cases of suffocative goitre reported in the literature, 18 were treated expectantly with 10 deaths.[18]

The type of surgical treatment is important. Tracheostomy alone is likely to fail because the obstruction may be too low down and especially because of the forward angulation of the trachea.[9,15] Packard *et al.*[18] collected from the American literature 13 cases of obstructive goitre treated by operation; 3 of these had emergency tracheostomy without thyroid resection and all of them died. In our first patient the initial tracheostomy failed to control the respiratory obstruction and would no doubt have terminated in a fatality had the thyroid not been removed subsequently.

Thyroid resection is the treatment of choice. Among the 13 cases collected by Packard *et al.*[18] 10 were treated by resection of varying amounts of thyroid and all recovered. To this they add a case of their own, and the success in our 2 patients treated by thyroidectomy provides further evidence of the value of the procedure. The extent of thyroid resection is important. It is reported that Malgaigne in 1851 was the first to treat a congenital goitre by section of the isthmus,[6] and as recently as 1957 Wilkins[29] recommended 'splitting or resecting the isthmus of the thyroid'. It must be pointed out, however, that this simple procedure is likely to prove as ineffectual as tracheostomy, for the following reasons: Firstly, the lateral lobes tend to obstruct the trachea low down in the neck and even in the upper mediastinum. Secondly, the goitre nearly always encircles the trachea almost completely with the lateral lobes extending well behind the trachea and displacing it anteriorly with acute forward angulation (Fig. 1) which is, in fact, the principal mechanism of obstruction. This was well illustrated by our second case, who came to autopsy where it was found that there was no encroachment on the lumen of the trachea despite the significant functional obstruction that had existed before death. The point is also illustrated by the remarkable relief of obstruction obtained by hyperextension of the neck and failure of tracheostomy to provide a clear airway. In both the babies operated upon by us it was noted that the tracheal kink could not be corrected until the lateral lobes had been well mobilized, extracted from behind the trachea, and resected. In the case reported by Packard *et al.*[18] removal of the left lobe, the isthmus and an anterior slice of the right lobe failed to provide the desired relief. This necessitated a second operation 2 days later when it was found that the right lobe, which extended far posteriorly, was responsible for continued forward angulation of the hypopharynx.

In view of the above, it is strongly recommended that the whole thyroid gland should be well mobilized and extracted from behind the trachea by division of the tethering bloodvessels, followed by resection of the isthmus and partial resection of the lateral lobes to allow the trachea to regain its natural situation. In the 2 infants treated by us the remnants measured approximately 1·5×1×1 cm. (This is the approximate size of a normal neonatal thyroid which weighs 2 - 5 G.). In successful resections reported

in the literature the amounts of thyroid removed ranged from 6 to 65 G.[18] Postoperative thyroid replacement therapy is necessary to prevent the development of hypothyroidism.

The need for concomitant tracheostomy with its attendant difficulties in management is debatable. In most of the cases reported in the literature it was not necessary. However, there are a number of factors which might render it essential. These include laryngeal oedema, collapse of the softened trachea or its compression by blood clot, and failure to correct the angulation completely owing to *elongation* of the trachea. In our first patient tracheostomy, which had anteceded thyroidectomy, was maintained because the infant had already become accustomed to it. In the second patient compression by haematoma and persistent angulation of the elongated trachea necessitated tracheostomy. While we appreciate the risks of tracheostomy in small infants, including the difficulties in weaning the infants of the tubes and in providing continuous close and expert postoperative care, we do not hesitate to carry out the procedure after operations on the neck because of its great value in maintaining a clear airway and allowing easy clearance of the lungs. (Our success in managing these cases has been largely due to the assistance of Dr. P. M. Smythe of the medical department who has had extensive experience with tracheostomies in neonatal tetanus.)

Non-obstructive Goitres

In patients without respiratory obstruction the treatment depends upon the cause of the goitre.

Iodine deficiency. Although endemic goitres without hypothyroidism sometimes respond to iodine therapy, there is usually no decrease in size of the gland, particularly if it is very large.[29] Furthermore, in neonates it may be impossible to distinguish these goitres from those arising from enzymatic defects or the use of antithyroid drugs for which iodine may be dangerous (*vide infra*). These goitres are, therefore, best treated by thyroxin, which puts the gland to rest so that much less colloid is formed and the goitre gradually diminishes in size and may disappear.

Ingestion of iodides or goitrogens. In these patients iodine should not be given because the gland may become larger and firmer owing to deposition of colloid and lead to respiratory obstruction. This was well illustrated by a case reported by Williamson.[20] The child was born with a typical congenital goitre which was treated expectantly. At the age of 13 months syrup of iodine was prescribed because the goitre had not yet disappeared. The goitre suddenly enlarged and caused respiratory embarrassment which demanded immediate partial thyroidectomy. On the other hand, thyroid hormone in full substitution doses leads to rapid decrease in the size of the gland and eventual disappearance of the goitre.[29] The recommended dose is ¼ - 1 gr. (45 - 60 mg.) of desiccated thyroid or 0·075 - 0·1 mg. of thyroxin daily. If results are not obtained the daily dose should be increased by 1 gr. of thyroid extract (0·1 mg. thyroxin) at weekly intervals until the goitre reduces in size or signs of toxicity develop. After the goitre has disappeared the dose of thyroid should be gradually reduced over a period of a few weeks and then discontinued to allow the infant's gland to resume normal function.

A mother who is receiving an antithyroid drug should not be allowed to breast-feed her infant since these compounds are secreted in the milk.

Enzymatic defect. In the rare cases of non-endemic goitrous cretinism in which the goitre is present at birth, the thyroid enlargement may disappear under thyroid therapy and reappear when it is discontinued. In neglected cases that develop adenomatous changes at a later age (6 - 12 years) the nodules are unlikely to disappear on thyroid treatment and thyroidectomy is indicated.[3,29] As in all nodular goitres in children, the possibility of malignancy must be seriously considered and therefore surgery becomes a matter of urgency (*vide infra*).

In the somewhat related cases of congenital goitre of unknown origin the goitre may disappear spontaneously, but usually thyroid therapy is required.

Nodular goitres. Surgical treatment is always necessary because almost one-third of thyroid nodules in childhood are carcinomatous.[21] Surgery is the only effective means of curing thyroid cancer in children because most of the carcinomas are of the papillary type which do not take up radioactive iodine. Moreover, irradiation in any form should be avoided in small infants.

Exophthalmic goitre. Neonatal hyperthyroidism tends to be self-limiting, and in mild cases the infant may be tided over the illness simply by rest, rehydration, and a high-calorie, high-vitamin diet.[7] The addition of 2 minims of Lugol's solution to the formula twice a day may be beneficial.[7] In the rare, severe cases it may be necessary to give small doses of propylthiouracil for a short period. Although thyroidectomy still has a limited place in the treatment of thyrotoxicosis in older children,[29] surgery is not indicated in the neonate.

SUMMARY

Three cases of suffocative goitre in the newborn are reported. In two of these the mother had taken iodized expectorant mixtures during pregnancy and in the third the mother had been treated with para-aminosalicylic acid. In the first patient tracheostomy failed to relieve the obstruction and subsequent thyroidectomy had to be performed. The second patient was treated conservatively, but died at the age of 4 months owing partly to the effects of chronic hypoxia. The third infant was successfully treated by immediate thyroidectomy. All the infants received thyroxin therapy.

The causes of congenital goitre are discussed, including iodine deficiency, excessive iodine intake especially in the form of iodized expectorants, the use of antithyroid drugs, maternal thyrotoxicosis, enzymatic defects in thyroxin metabolism, and neoplasms.

The management depends on the severity of respiratory obstruction and the cause of the goitre. Respiratory obstruction is best treated by thyroid resection because of the elongation and acute forward angulation of the trachea; tracheostomy is valueless and so is simple division of the thyroid isthmus. In most cases concomitant thyroxin therapy is necessary.

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