Hypomagnesæmia is a recognized complication of hyperparathyroidism (Hanna *et al.* 1961), due frequently to an increased urinary magnesium loss. This latter probably results from competition with calcium for tubular reabsorption. The low magnesium intake on account of anorexia and vomiting for some time pre-operatively, and the relative increase in bone avidity for calcium and magnesium post-operatively, are additional factors contributing to the critically low serum concentration encountered in this case.

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Riedel's Thyroiditis and Retroperitoneal Fibrosis

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Miss M W, aged 45

History: Presented November 1962, aged 42, with two months' rapidly progressive tender swelling of thyroid, giving rise to pressure in neck, breathlessness on exertion, tiredness and some weakness of voice.

Past history: No serious illnesses. Occasional pains in wrists but no history of arthritis. Unspecified anæmia in youth. No family history of thyroid disorders, no collagen diseases.

On examination: Clinically euthyroid. Very firm diffuse goitre, estimated weight 60–80 g, larger on the left, tender to palpation, no bruit. Trachea central, goitre poorly mobile on swallowing, no enlarged lymph nodes palpable in the neck.

Investigations: ^{131}I neck uptake: four hours 15%, twenty-four hours 26%, forty-eight-hour plasma activity 0·08%/l. Scintigram: symmetrical distribution of isotope but uptake confined to upper poles above the palpable swelling which was completely inactive. PBI 4·4 μg%, BMR −11%, serum cholesterol 190 mg/100 ml. Thyroid antibodies: immunofluorescence, CFT and hæmagglutination all negative. Anti-nuclear factors negative. Serum proteins 6·7 g/100 ml, electrophoretic strip normal. Hb 72%. WBC 4,800. ESR 77 mm in 1 hour (Westergren).

Operation: Thyroid needle biopsy (28.11.62) showed only cellular fibrous tissue but in view of the rapid growth of the goitre, as a malignant tumour could not be excluded, exploration of the neck was undertaken (7.12.62). It was found that the pretracheal muscles were welded to the thyroid mass. The pretracheal muscles had to be resected *en bloc* and peeled off the thyroid (Fig 1). The lower poles and isthmus of the thyroid were completely replaced with a hard white fibrous mass frozen to all surrounding structures and especially the main vessels, while the upper poles of the thyroid appeared normal. The isthmus was resected to free the trachea (Fig 2). The dense fibrosis of the lateral lobes could not be freed from vessels; they were reduced by shaving off consecutive slices and partially left *in situ*. The impression at the time was that of a perivascular disease.

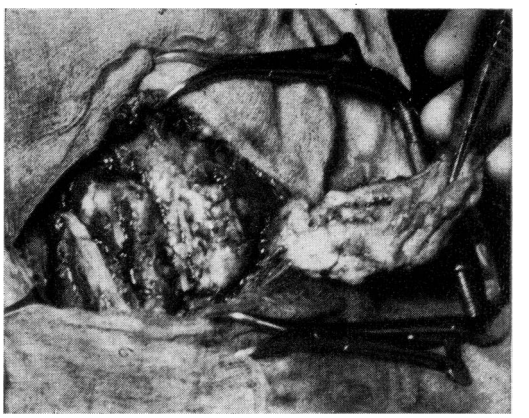

Fig 1 *Indurated thyroid exposed by block dissection of solid fibrous mass involving pretracheal muscles (held in forceps)*

Histology: Riedel's thyroiditis. Sections showed thyroid tissue infiltrated and almost replaced by cellular fibrous tissue. The fibrosis extended out

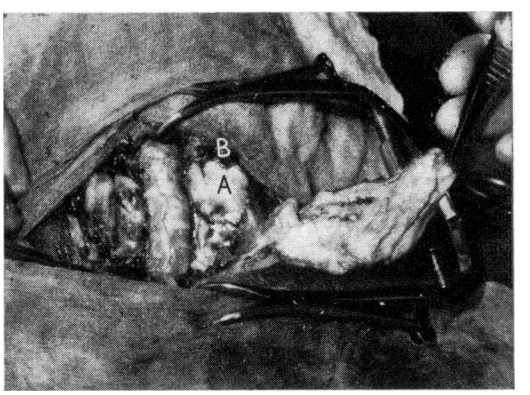

Fig 2 *The trachea was decompressed by shaving layers of solid fibrous tissue off the thyroid to leave fibrous remnant* (A) *– macroscopic normal upper thyroid pole* (B)

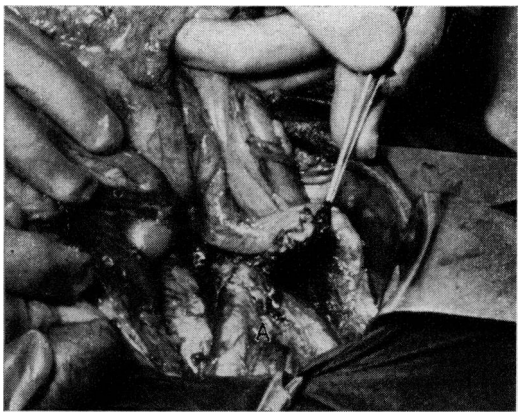

Fig 3 *Fibrous tissue plaque in front of aortic bifurcation (A) – a distal segment of the inferior mesenteric vessel was involved by a separate plaque*

through the capsule of the gland to involve adjacent muscle. There was a moderate inflammatory infiltrate consisting mainly of plasma cells and lymphocytes. Lymph nodes appeared normal. Biopsy of unaffected upper poles showed somewhat hyperplastic thyroid epithelium and a multifocal lymphocytic thyroiditis.

Progress: In January 1963 the patient developed intermittent claudication in the left calf and thigh. The pain came on after walking 50–100 yards and was relieved by rest; two weeks later (1.2.63) increasingly severe pain developed in the lumbar region, radiating to the umbilicus. At this time the posterior abdominal wall became tender on palpation in the centre of the abdomen. There were no urinary or gastrointestinal symptoms. The intravenous pyelogram showed normal upper urinary tracts. A provisional diagnosis of retroperitoneal fibrosis was made; this was confirmed at laparotomy but distribution of the lesion proved to be atypical. There was a mass of proliferating fibrosis anterior to the lower aorta, mainly involving branch vessels especially the inferior mesenteric artery; a distal segment of this artery was separately involved and obliterated. The lower aorta, the common and internal iliac arteries and the left iliac vein were carefully dissected, to free them from the dense fibrous tissue (Fig 3). The ureters were not involved. Histology again showed active fibroplasia surrounding the vessels containing nerves and ganglia, and a diffuse infiltration with lymphocytes and plasma cells.

Follow-up: Following operation the patient gradually improved. Abdominal pain disappeared within seven months and claudication gradually subsided within the next two years. Three years after onset of the disease, the thyroid remnants were impalpable and the patient remained euthyroid without substitution therapy. ^{131}I uptake: four hour 24%, twenty-four hours 48%, forty-eight-hour plasma activity 0·19%/l (small iodine pool). Scintigram still showed radioactivity confined to the upper poles of the thyroid. PBI 3·7 μg%. Thyroid antibody tests remained negative. There was no abdominal or lumbar pain. Aching in left thigh, knee and calf occurred only when hurrying. There was a firm thickening palpable on the posterior abdominal wall and an aortic bruit was audible. The femoral pulses were normal but there was a blowing bruit over both inguinal areas. The ESR remained raised to between 50–85 mm in 1 hour (Westergren) for one year; three years after onset it was 12 mm.

Comment

This case again raises the fundamental problem whether Riedel's thyroiditis originates within the gland and spreads out or whether it is part of a more generalized process and not primarily a thyroid disease. Occasional thyroid lesions lead to dense fibrous reaction but this does not usually spread deeply into the surrounding tissue; many of these lesions are fibrous variants of autoimmune thyroiditis and the majority of patients show a high titre of antibodies to thyroglobulin and microsomal fractions. It seems probable that the thyroid origin of the so-called 'Riedel's thyroiditis' has come to be accepted rather than proved.

The normality of the upper poles of the thyroid in this case was the finding which stimulated a critical examination of the distribution of the fibrous tissue. The extensive perivascular fibrosis with only partial and well-defined involvement of the gland suggested an extrathyroid origin. When abdominal symptoms subsequently developed, a diagnosis of retroperitoneal fibrosis seemed probable. The intra-abdominal fibrosis was unusual in that it involved branch vessels rather than the aorta or vena cava themselves.

The ætiology of Riedel's fibrosis remains obscure. No antibody reactions suggestive of an autoimmune process have been found in any of the 5 authentic cases of Riedel's thyroiditis studied in our laboratory since 1956. Two cases suggestive of a coexistence of Riedel's and Hashimoto's diseases are, however, recorded in the literature (Merrington 1948, Rose & Royster 1961) in which an invasive fibrosing process was present in one lobe and Hashimoto type thyroiditis in the other.

Tubbs (1946) reported a case of proliferating fibrosis in the retroperitoneum and in the mediastinum. Woolner *et al.* (1962) collected 20 cases of Riedel's disease and saw 2 patients with associated retroperitoneal fibrosis (Hache, Utz & Woolner 1962), one of whom also had involvement of the common bile duct. Riedel's disease

has also occurred in association with idiopathic mediastinal fibrosis (Hache, Woolner & Bernatz 1962). Milner & Mitchinson (1965) have found thyroid fibrosis at post-mortem in cases of retroperitoneal fibrosis. Mitchinson (1965) is of the opinion that retroperitoneal fibrosis is the end-result of an inflammation starting in adipose tissue, which would suggest a similarity with systemic Weber-Christian disease. Hardmeier & Hedinger (1964) consider the perivascular lesions in Riedel's thyroiditis to be related to Takayasu's arteritis and several authors now think that all these fibrosing disorders form an ætiologically related group (Tubbs 1946, Bartholomew *et al.* 1963, Woolner 1964, Hardmeier & Hedinger 1964). In a case described by Que & Mandema (1964) there was a history of Raynaud's phenomenon and interstitial pulmonary fibrosis with circulating antinuclear factors which suggested a relationship to the collagenoses.

On the present evidence it seems probable, therefore, that the Riedel process does not arise primarily in the thyroid, and furthermore there is as yet no direct evidence that it is an autoimmune disorder.

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Dr S Kumar (for Dr R Barton)

Meeting January 26 1966

Short Papers

Tissue-specific Anti-œstrogens

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The term anti-œstrogen has been in existence now for thirty years, but it has seldom been heard outside specialized laboratories until quite recently. Anti-œstrogens are now realized to be important in medicine. Unfortunately, many hundreds of compounds have been described as œstrogens, and the properties of some are certainly not common to others. Table 1 records some properties of the three main natural human œstrogens and the most widely used synthetic one; and clearly indicates that the œstrogenicity of a compound relative to another depends on the test chosen.

Consequently 'anti-œstrogen' can only have meaning in relation to a specific œstrogen under specified conditions. This is demonstrated in Table 2 where the anti-œstrone properties of various compounds are compared in the two classic œstrogen assays, Allen-Doisy and uterine weight test.

As in the case of the word œstrogen, the term anti-œstrogen has little meaning except in relation to a strictly specified situation. On the basis of its action in the Allen-Doisy test progesterone has been called the classic anti-œstrogen, yet the synthetic 19-nor steroids have progesterone-like actions in some tissues and œstradiol-like actions in others (Emmens *et al.* 1960). Norethisterone manages to combine progestational properties in the endometrium (Pincus 1956) with œstrogenic actions on the breast (Paulsen 1965) and anti-œstrogenic actions on the cervical mucus (Cohen 1965).

These observations are consistent with specific œstrogen receptors in the target organs. Noteboom & Gorski (1964) have shown quantitative competition between œstrogens for receptors at one site, and Jensen (1964) has shown similar quantitative competition between œstrogen and