method, at the highest range of Po_2 can be accounted for by differences in the blood-gas factors of the two electrodes. Johnstone (1966) found similar results when he tested the microelectrode system up to a Po_2 of 200 mm. Hg.

In this study the Po_2 of blood specimens stored at 37° C. for three hours fell at the rate of 2.3 mm. Hg/min. when the mean initial Po_2 was 680 mm. Hg. This agrees with the figures of Asmussen and Neilsen (1961), Rhodes and Moser (1966), Laver and Seifen (1965), and Greenbaum, Nunn, Prys-Roberts, and Kelman (1967). It was also found that the Po_2 fell at the rate of 3.0 mm. Hg/min. during the first hour, 2.5 mm. Hg/min. during the second hour, and 2.3 mm. Hg/min. during the third hour. The decreasing rate of decline in Po_2 with time is explained by the consideration that at constant oxygen consumption by blood cells there will be a greater fall in Po_2 when the initial Po_2 is high compared with that found when the initial Po_2 is low. This is due to the shape of the oxygen dissociation curve. Thus the error in Po_2 caused by storing blood for a given time will be greater at high initial Po_2 values than at low values. Though it has been shown that the rate of decline in Po_2 of blood stored at room temperature is much less than that found when it is stored at 37° C., considerable errors will still be caused if there is much delay in measurement. Since storage of blood samples at 4° C. virtually abolishes oxygen consumption, there is an obvious need to store blood samples in ice if measurement has to be delayed. Since metabolism will proceed until the blood temperature reaches 4° C., capillary tubes are more efficient for storage of samples than glass syringes, which have a longer and variable lag cooling time (Kelman and Nunn, 1966). The total unsuitability of plastic syringes as storage vessels for blood samples in which Po_2 measurements are to be made is also shown in this study, contrary to the finding of Laver and Seifen (1965).

Since it has been shown that the microelectrode is capable of as accurate measurement as the macroelectrode and that a glass capillary tube is as efficient a storage vessel as a glass syringe, discrepancies between arterial and capillary Po_2 measurements can arise only from errors in sampling technique. The capillary bed of the thumb pulp is not a suitable site for obtaining arterialized capillary blood for this purpose even if the skin temperature is raised to 37° C. by heat or the skin is massaged with thurfyl nicotinate. In the normally perfused subject the capillary bed of the ear lobe will, however, provide a sample which gives the same Po_2 value as a simultaneously drawn arterial sample, after the ear lobe has been massaged with thurfyl nicotinate for three minutes, or even after massage alone for the same time. Since Po_2 measurements are most commonly required in either anoxic or hyperoxic patients it is of significance that the ear lobe massaged with thurfyl nicotinate for three minutes will give Po_2 values—in these two categories—which are in close statistical agreement with arterial oxygen tension.

It can be said, in conclusion, that the use of the oxygen microelectrode system with capillary blood specimens obtained from the ear lobe after massage with thurfyl nicotinate for three minutes affords a method of obtaining Po_2 measurements on capillary blood which are in close agreement with arterial Po_2 in normal, hyperoxic, and hypoxic subjects.

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Long-term Follow-up of Surgically Treated Thyrotoxic Patients

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Brit. med. J., 1968, 3, 643-646

Summary: Review of 123 patients whose thyroidectomy for thyrotoxicosis had been performed more than five years previously showed that there were no deaths attributable to surgery, while one hundred patients (81.3%) had been rendered euthyroid. Varying degrees of hyperthyroidism had occurred in 15 (12.2%), and six of these were first diagnosed at follow-up. Hypothyroidism was present in eight (6.5%). Long-term complications of operation were found in 20 patients—subjective voice disturbance in 13, unsightly scars in 4, and hypoparathyroidism in 3.

Introduction

The treatment of thyrotoxicosis is far from ideal. All current methods have their own advocates, but all have a significant incidence of complications. Radioiodine (^{131}I), which in the 1950s seemed to be gaining pride of place in the management of thyrotoxicosis, certainly in the over-40 age group, has come under serious criticism, mainly because of the high incidence of subsequent myxoedema. As a result surgery has again been advocated as the treatment of choice in the majority of cases. However, there is a lack of data on the long-term effects of thyroid surgery for thyrotoxicosis comparable to that available for ^{131}I therapy.

In view of this it seemed worth while to report on the outcome of thyroid surgery in a group of thyrotoxic patients, all of whom were treated in one surgical unit and all of whom had been followed up for at least five years after thyroidectomy.

Material

In the Southern General Hospital, Glasgow, records showed that 185 patients had been treated for thyrotoxicosis by partial thyroidectomy during the years 1953 to 1960. On perusal of

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individual case records 13 cases were rejected on the basis of insufficient evidence to sustain a preoperative diagnosis of thyrotoxicosis. Of the remaining 172 patients 41 could not be traced and eight had emigrated. Follow-up revealed five deaths in the series, yielded acceptable up-to-date clinical information on three cases without personal review, and procured personal examination of 115 patients—a total follow-up of 123, or 71%. Of these 123 patients 114 were female and nine were male.

Their average age at operation was 36 years, the average length of preoperation history two years, and the average stay in hospital after operation day 8 days. The average length of follow-up was nine years and the minimal follow-up interval five years 4 months. At operation the youngest patient was aged 14 years, and the oldest 72.

In 71 cases (57.7%) operation was considered the treatment of choice and medical treatment was restricted to preparation for surgery. In 52 cases (42.3%) surgery was undertaken after "failed" medical treatment. This failure took the form of unsatisfactory control or recurrence in 32 cases, increasing size of gland while under treatment in 7 cases, developing pressure symptoms in 2 cases, and drug toxicity in 11 cases.

The drugs used in the medical treatment of the "failed" 52 cases were methylthiouracil in 29, carbimazole in 22, and potassium perchlorate in 12.

The surgery was unequally divided among four surgeons, though the vast majority of operations (95) were performed by one of them. However, in all cases the essential techniques were similar. The strap muscles were not divided. The superior vascular pedicle was divided between ligatures and the inferior thyroid artery was tied in continuity. The recurrent laryngeal nerve was not deliberately exposed.

Methods of Assessment

Thyroid Status.—A clinical assessment of the patient's thyroid status was recorded. Fifteen presented at review with the diagnosis of postoperative myxoedema or recurrence already made and supported by laboratory findings. In all other cases arrangements were made for a laboratory assessment. This consisted of protein-bound ^{127}I in every case, radioiodine studies (24-hour gland uptake of ^{131}I and 48-hour protein-bound ^{131}I) in 73 subjects who lived near enough to Glasgow to make this feasible, and T_3 resin sponge test where indicated. Two patients failed to attend for laboratory tests. These were clinically euthyroid. One clinically thyrotoxic patient attended but refused to submit to any tests. These three patients have been allocated to the appropriate groups on the basis of this clinical assessment. Nine patients were considered to have equivocal laboratory findings. Repeat tests allowed them to be allotted to euthyroid or appropriate abnormal category.

Immediate Postoperative Complications.—Retrospective information from the case sheet and the patient with a view to assessing the immediate operative morbidity was collated under the headings of wound infection, tetany, psychological upset, and thyroid crisis.

Long-term Postoperative Complications.—The patient's views on persistent voice change and the disadvantages of this, if any, were recorded. Where these views or the interviewer's impression suggested any possibility of cord damage indirect laryngoscopy by a specialist was obtained; 36 cases were so examined. The patient's attitude to the scar was noted and an objective aesthetic assessment made by one of us (A.D.M.). The patient was directly questioned for a history of cramps or paraesthesia in the face or extremities. Chvostek's test was performed. Blood was obtained by venepuncture with minimum compression, and serum calcium and plasma proteins were estimated. Calcium was estimated by edetic acid titration in alkaline medium, murexide being used as an indicator (Wilkinson, 1957), and proteins were calculated by the Technicon Automated method. Correction of the serum calcium for protein variation was done by using the nomogram of McLean and Hastings (1935).

Results

There were no operative deaths. During the period of follow-up five deaths occurred, none of which could be related to thyrotoxicosis or complications of its management. The causes of deaths in the five patients are given in Table I.

TABLE I.—*Deaths During Follow-up of Patients Having Partial Thyroidectomy for Thyrotoxicosis*

Age at Death	Sex	Interval (in Years) Since Operation	Cause of Death	Thyroid Status at Death
62	F	3	Cerebral haemorrhage	Euthyroid
72	F	3	Coronary thrombosis	Euthyroid
47	F	5	Carcinoma of breast	Euthyroid
63	F	10	Carcinoma of ovary	Euthyroid
65	F	11	Bronchopneumonia	Euthyroid

Thyroid Status

The results of surgery are shown in Table II. One hundred (81.3%) were euthyroid. We have listed one patient separately as a failure of operative treatment, since the thyrotoxic state was never satisfactorily controlled by an inadequate thyroidectomy. At operation haemorrhage during mobilization of the second lobe prevented adequate resection. The gland was of the toxic diffuse type and preparation had been with thiouracil and iodine.

TABLE II.—*Results of Surgery on Thyroid Function*

Group	Total No.
Euthyroid at death or follow-up	100 (81·3%)
Recurrence after surgery	14 (11·4%)
Hypothyroid after surgery	8 (6·5%)
Surgical failure	1 (0·8%)

Of the 14 cases of recurrence after surgery eight were diagnosed before follow-up and six at follow-up (see Fig. 1). Among the six recurrences diagnosed at follow-up five were of a mild nature in symptom-free patients. No patient required a second operation. Six of those with previously diagnosed recurrences had been treated with ^{131}I.

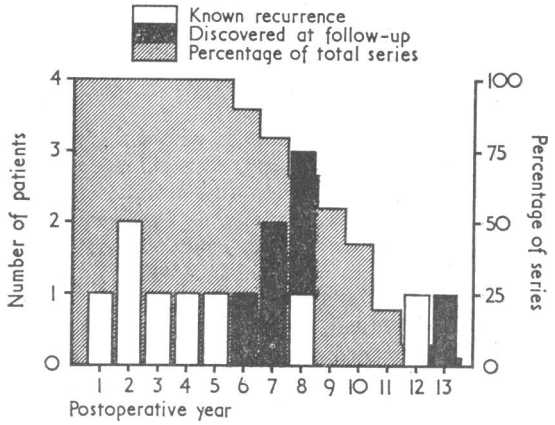

FIG. 1.—Recurrent thyrotoxicosis after surgery.

Of the eight hypothyroid patients seven were diagnosed before follow-up and one was discovered at review (see Fig. 2). The thyroid histology had been reported by the pathologist as being "typical of Hashimoto's thyroiditis" in one frankly thyrotoxic case; another had serological evidence of thyroid antibodies as shown by a positive antithyroglobulin precipitin test.

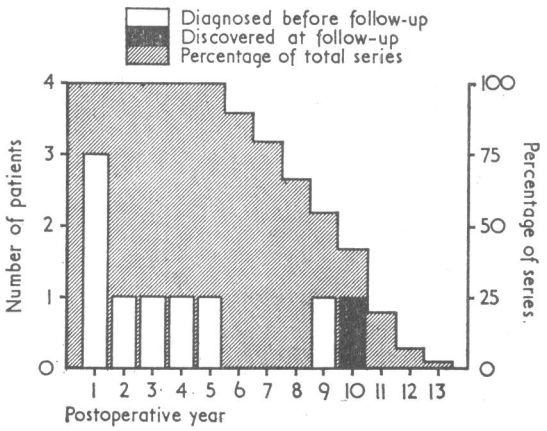

FIG. 2.—Hypothyroidism after partial thyroidectomy.

Immediate Postoperative Complications

No serious postoperative complication occurred (see Table III). Only one patient was taken back to the theatre, and that was eight hours after thyroidectomy for evacuation of a haematoma. The four cases of tetany responded promptly to oral and intravenous calcium. Some degree of immediate postoperative voice impairment was common, but we found it impossible to make an accurate retrospective assessment of this from case records or the patient's recollection.

TABLE III.—*Immediate Complications After Thyroidectomy*

Wound infection sufficient to delay discharge from hospital	2
Wound haematoma sufficient to delay discharge from hospital	4
Requiring tracheostomy	Nil
Chest infection sufficient to delay discharge from hospital	1
Tetany	4
Psychological upset (required admission to general ward for three weeks postoperatively)	1
Thyroid crisis	Nil

Long-term Complications

Voice Disturbance.—Of the 36 patients examined by laryngoscopy seven showed evidence of cord damage—that is, 5.6% of the total series: two had a completely immobile cord, and the other five had some degree of abductor palsy. None of these was bilateral and none required any form of remedial surgery. Thirteen patients, including five of the seven mentioned above, considered the change in their speaking voice a disability, though in none of these 13 could there be said to be any marked voice distortion in normal conversation. All patients were asked about change in their singing voice as distinct from their speaking voice. The vast majority claimed that there had been some permanent impairment of vocal range or control. This was of course a subjective comment, though two enthusiastic amateur choristers had to give up this activity.

Scar.—Six scars were considered unsightly at follow-up. Two were keloids, for which various forms of treatment had been given with limited success, and four were puckered scars which had resulted from persistent wound sinuses after operation. Each patient was asked if his or her scar had proved a social embarrassment, and, while many confessed that it had been so initially, every one at the stage of follow-up accepted his or her scar with equanimity.

Hypoparathyroidism.—Table IV shows the range of serum calcium values at review. One patient who developed tetany on the first postoperative day has since been on calcium and calciferol intermittently. On review, though on calcium and calciferol at the time, her serum calcium was only 7.1 mg./100 ml. Only one of the other three patients who had postoperative tetany showed a low calcium on review. The other two patients, from personal history and perusal of case records, had symptoms of hypocalcaemia associated with a low serum calcium for periods of one and two years respectively after operation but were asymptomatic and normocalcaemic on review. One patient without history of postoperative tetany or symptoms referable to hypocalcaemia was found to have a serum calcium of 9.2 mg./100 ml., which when corrected for plasma protein was just below the normal range. If this patient is included then a total of 3 (2.4%) showed objective evidence of hypoparathyroidism at review.

TABLE IV.—*Hypoparathyroidism After Partial Thyroidectomy*

Serum Calcium (Mg./100 ml.)	No. of Patients	In Hypoparathyroid Range when Corrected for Protein	No. Symptomatic
7·0–7·5	1	1	1
7·6–8·0	—	—	—
8·1–8·5	—	—	—
8·6–9·0	7	1	—
9·1–9·5	23	1	—
9·6–10·0	51	—	—
10·1–10·5	27	—	—
10·6–11·0	4	—	—

Discussion

Assessment of the thyroid function at postoperative follow-up of the patients in this series shows very satisfactory results comparable to those from similar series of surgically treated patients (Green and Wilson, 1964 ; Roy *et al.*, 1967). They are better in this respect than the results of ^{131}I treatment in a series of 908 thyrotoxic patients previously reported from the Royal Infirmary, Glasgow (McGirr *et al.*, 1964). Wilson (1967) reported a much higher incidence of postoperative hypothyroidism.

It is interesting that in the present series of surgically treated patients, in contrast to most ^{131}I treated series, only one subject was found to be hypothyroid on follow-up in whom the diagnosis had not already been established. On the other hand, almost half (six out of 14) of the cases of relapse of thyrotoxicosis were not diagnosed before our review ; a fact largely explained by the mild nature of the recurrence in these patients. Our experience differs from that of Roy *et al.* (1967), who found that almost half the thyrotoxic and hypothyroid cases had not been diagnosed before follow-up. However, the duration of follow-up in their series is shorter than in the present one. The incidence of relapse of thyrotoxicosis and that of hypothyroidism probably bear an inverse relation to each other, depending on how radical the thyroidectomy had been. Thus the type of abnormal thyroid state to be found on follow-up will vary from series to series. This is in contrast with ^{131}I therapy, where there is an almost negligible relapse of thyrotoxicosis but an incidence of hypothyroidism which tends to increase with the length of follow-up.

The complications directly attributable to surgical trauma were considered under the headings of "immediate" and "late." Twelve patients (9.0%) were judged to have immediate, though not serious, complications of surgery. On review some long-term morbidity from surgery was found in 20 patients (16.3%): 13 had subjective voice disturbance, four had unsightly scars, and three had hypoparathyroidism. This incidence of local complications of surgery is higher than in the series of Roy *et al.* (1967) but is comparable to that of Wade (1960–1), Asper (1960), and Green and Wilson (1964).

It might be argued that our search for recurrent laryngeal nerve damage and minor degrees of hypoparathyroidism was less than perfect. While admitting this, our criteria for diagnosing such defects seemed to us to represent clinically significant disability rather than minor degrees of dysfunction, such as diminished parathyroid reserve on edetic acid infusion, the clinical significance of which is not clear (*Lancet*, 1966). Though in the present series voice change did not constitute a major disability to any single patient, it is our impression that the risk to the singing voice, with or without apparent recurrent laryngeal nerve damage, constitutes a relative contraindication to offering thyroidectomy to, for example, a professional singer. The recurrent toxic group were free of other postoperative complications, but the smaller group of eventual

hypothyroid patients included two with cord damage and one with an unacceptable scar. It is of interest that in the group of four patients with postoperative tetany two showed objective evidence of cord damage. This association of hypoparathyroidism and recurrent laryngeal nerve damage has been pointed out by Shearman *et al.* (1965) and is clearly related to the extent of gland mobilization at operation.

The present findings add to the information on the long-term results of subtotal thyroidectomy for thyrotoxicosis. Thyroidectomy is an effective treatment for this serious disease. It shares this role with ^{131}I therapy. Comparisons of these two forms of treatment are inevitable and necessary. On the basis of such comparisons Green and Wilson (1964) and Byrd *et al.* (1960) have favoured surgery, while Bowers (1965) was less certain. Block (1967), in a recent review, indicates the need for offering therapy on an individual basis and against the background of services available—for example, a skilled thyroidectomist and local laboratory facilities. In either case long-term surveillance is necessary. As regards ^{131}I therapy this surveillance may be more simple in that there appears to be only the one but not unlikely complication—namely, hypothyroidism. Surgery offers a greater chance of establishing a permanent euthyroid state, though the range of possible long-term complications is wider and less predictable.

We wish to thank Mr. R. B. Wright, senior surgeon, Southern General Hospital, Glasgow, who initiated this review and provided helpful criticism. We are indebted to Professor E. M. McGirr, University Department of Medicine, Glasgow Royal Infirmary, and Dr. W. S. T. Thomson, biochemist, Southern General Hospital, for providing laboratory facilities to Drs. R. Miller and I. J. Kerr, of the ear, nose, and throat department, Victoria Infirmary, Glasgow, who carried out the laryngoscopies.

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Role of Mites in Allergy to House Dust

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Brit. med. J., 1968, 3, 646–647

Summary: One hundred and thirty-two patients known or suspected of allergy to house dust were skin-tested with pure extracts of four varieties of dust mites. The results show that both Dermatophagoides culinae and D. pteronyssinus probably played important parts in sensitizing susceptible people, as did Glycyphagus destructor and G. domesticus in some cases. In some patients these results enabled successful desensitization against the dust to be carried out, and for corticosteroid therapy to be stopped. Hence the use of mite extracts is considered to be an important advance in the diagnosis of allergy to house dust.

Introduction

The researches of Voorhorst *et al.* (1967) in Holland directed attention to mites as the prime factor in house-dust allergy, and particularly to one species, *Dermatophagoides pteronyssinus*, as the source of the antigen. This work stimulated an interest in other mites inhabiting house dust, such as *Glycyphagus destructor* and *Acarus siro*, particularly by Pepys *et al.* (1968) and Feinberg and Hill (1968). Both have concentrated their attention on the closely related *D. culinae*, which is much easier to breed in the laboratory; and the latter also investigated *G. destructor* and *G. domesticus*, which have been found in abundance in some houses of asthmatic patients in the Trent River Valley where the terrain is low-lying and flat with a network of canals, giving conditions not dissimilar to those in the Netherlands.

Materials and Methods

Since October 1967, when pure mite extracts first became available for experimental purposes, patients known or suspected to be sensitive to house dust were skin-tested with the available extracts. Dome Laboratories house-dust extract for prick testing was used for comparison and for nasal provocation testing. All extracts were coded to avoid observer bias, and many different batches were tested for potency, some standardized in protein nitrogen units (P.N.U.), and others on a weight/volume basis. Made up in 50% glycerol saline the material has remained stable at room temperature for over six months.

The mites were grown on dog-meal with added yeast, and the extracts were essentially free from antigens derived from the culture medium. Control tests with extracts of culture medium were invariably negative (Feinberg and Hill, 1968).

Results

The results of skin-testing with four varieties of mite extract are given in Table I. Four cases were positive for *D. culinae* but negative for *D. pteronyssinus*, the reactions to the latter being generally less intense. *D. pteronyssinus* was never positive when *D. culinae* was negative, but three cases gave a good positive for crude dust extract when all the mite extracts were negative, suggesting sensitivity to other allergens in the dust. Reactions to *G. destructor* were sometimes intense, while those to *G. domesticus* were seldom markedly positive.

In many cases skin reactions resembled those to grass pollen in intensity, particularly to *D. culinae*, the weal diameter often being 5 to 8 mm., and the flare 25 to 35 mm. Clear-cut specificity of skin-test response was frequently seen to different species of mites.

TABLE I.—*Prick-test Results From Different Mite Extracts*

Prick Test	House Dust	*D. culinae*	*D. pteronyssinus*	*G. destructor*	*G. domesticus*
Positive	97	127	76	47	27
Negative ..	35	5	13	85	20
No. of patients..	132	132	89	132	47

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