TABLE IV—Acute hepatitis B among health service staff* (England only)

Staff category	1975-9			1980-4		
	Mid-period number	No of reported cases of acute hepatitis B	Average annual rate per 100 000	Mid-period number	No of reported cases of acute hepatitis B	Average annual rate per 100 000
Surgeons	10 372	6	12	11 282	14	25
Physicians	43 828	27	12	47 900	26	11
Laboratory staff:						
Medical	2 232	3	27	2 490	2	16
Scientific	14 291	13	18	15 339	28	37
Nursing staff	391 953	131	7	423 841	95	4
Dentists	14 354	12	17	15 337	13	17
Staff in institutions for mentally handicapped	28 000	43	31	39 163†	52	27

*Staff who acquired the infection while working abroad were excluded from both five year periods.

†Figures supplied by the Department of Health and Social Security. The 1980-4 mid-period number includes staff in small community units, who are not included in 1975-9.

a patient who had undergone a transplant operation who was a known highly infective carrier, but she could not recall any accidental inoculation or contamination. The other worked in a unit in which there were no carrier patients; the time of the onset suggested that the infection had been acquired before beginning work in the unit. None of the infections in health service staff were fatal.

Table IV shows the average annual incidence of hepatitis B estimated for the various staff groups. The denominators are derived from *Health and Personal Social Services Statistics for England 1982*.⁴ Actual numbers of staff were used when available; otherwise whole time equivalents were used. Since data for Wales and Ireland are presented differently, rates were estimated for England only.

The rates for staff of institutions for the mentally handicapped during the two periods are not comparable as the number of staff in 1980-4 was considerably increased by staff in small community units, who were not included in the figures for 1975-9. The rate for nurses decreased from 7 per 100 000 in 1975-9 to 4 per 100 000 in

1980-4. There was little or no difference between the rates for physicians and dentists. The rates for surgeons and laboratory scientific staff were twice as high as those found in 1975-9.

Although the increased incidence during 1980-4 in two groups is a cause for concern, the annual average numbers of infections, on which these rates were based, were small—for example, three surgeons, six laboratory staff. Nevertheless, these infections should be prevented by active immunisation of staff at high risk.

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Lesson of the Week

Resolution of dyskinesia and the "on-off" phenomenon in thyrotoxic patients with Parkinson's disease after antithyroid treatment

T H CARADOC-DAVIES

Many patients with Parkinson's disease develop complications of long term treatment with compounds containing levodopa. These complications include the "on-off" phenomenon and dyskinesia and develop after two or three years of treatment in some 15-40% of patients.¹ Thyrotoxicosis has been reported in association with Parkinson's disease in patients with severe tremor, and in three cases the tremor subsided with treatment of the endocrine disorder.² I report two patients who developed late side effects of treatment of Parkinson's disease which were reversed by correcting co-existing thyrotoxicosis and examine the postulated mechanism.

Symptoms and signs of thyrotoxicosis may easily be dismissed as late complications of levodopa in patients receiving this drug for Parkinson's disease; only a high index of suspicion and a therapeutic trial of antithyroid medication will yield the correct diagnosis

Case 1

A 66 year old woman with a seven year history of Parkinson's disease well controlled for four years with levodopa-carbidopa (Sinemet) presented with a four month history of night terrors, depression, dyskinetic movements, and episodes of freezing typical of the "on-off" phenomenon. She admitted

Department of Medicine, University of Otago, Dunedin, New Zealand
T H CARADOC-DAVIES, FRACP, senior lecturer

to weight loss, palpitations, and heat intolerance and to symptoms of depression with loss of appetite, early morning waking, and depressed affect.

Examination showed her to be anxious and sweaty with pronounced choreiform movements of the head and trunk. The thyroid was smoothly enlarged on the right and her pulse was 110/min at rest. There was moderate rigidity of cogwheel type with bradykinesia and an intermittent pill rolling tremor. She scored 8/10 on a simple mental state questionnaire.³ Modification of the levodopa regimen (smaller, frequent doses) achieved no improvement. Thyroid function studies showed hyperthyroidism with serum total thyroxine concentration 155 nmol/l (normal 68-141), serum triiodothyronine resin uptake 1.00 (normal 0.68-1.04), serum adjusted thyroxine concentration 155 nmol/l (normal 57-124), and serum triiodothyronine value 2.7 nmol/l (normal 1.2-3.2). A 400 µg thyrotrophin releasing hormone stimulation test produced an impaired response, with a thyroid stimulating hormone concentration of 1.3 mIU/l at zero time and 4.7 mIU/l at 20 minutes (difference 3.4; normal change >5.0). Carbimazole 10 mg three times a day was introduced and increased to 15 mg thrice daily. After two weeks the choreiform movements had improved, and when reviewed after four weeks her freezing episodes had stopped. She received a course of radioactive iodine and remained well for two years taking Sinemet, with no recurrence of the on-off phenomenon or dyskinesia.

Case 2

A 77 year old woman with a 15 year history of Parkinson's disease treated with amantadine and Sinemet was referred for assessment of dystonic head movements. She admitted to weight loss and intolerance of heat. Examination showed a thin, anxious woman with a small nodule in the right side of the thyroid, tachycardia of 130 beats/min, and constant bobbing of the head and neck to the left. She had minimal rigidity and scored 10/10 on the simple mental state questionnaire. Thyroid function studies showed hyperthyroidism, with serum total thyroxine concentration 147 nmol/l, serum triiodothyronine resin uptake 0.93, serum adjusted thyroxine concentration 137 nmol/l, and serum triiodothyronine value 3.0 nmol/l. A 200 µg thyrotrophin releasing hormone stimulation test showed an absent response (thyroid stimulating hormone concentration 1.4 mIU/l at zero time, 1.3 mIU/l at 20 minutes). Carbimazole 10 mg thrice daily was begun and within four weeks her tachycardia had settled to below 100 beats/min. By review at eight weeks her head movements had disappeared, she had gained weight, and she was less anxious. Carbimazole was reduced to 5 mg three times a day and she remained clinically euthyroid. After three months a repeat thyrotrophin releasing hormone stimulation test showed an improved but still impaired response (thyroid stimulating hormone 3.6 mIU/l at zero time, 5.3 mIU/l at 20 minutes, difference 1.7).

Discussion

Thyrotoxicosis may be difficult to diagnose in patients with Parkinson's disease because symptoms of sweating, weight loss, and irritability may be attributed to their extrapyramidal disease or drugs⁴ or to depression, which occurs in 40% of these patients at some time in their disease.⁵ It has been reported that weight loss is the only common symptom in elderly patients with thyrotoxicosis and occurs in three quarters or more, while the classical signs of thyrotoxicosis (weight loss, agitation, exophthalmos, tremor, and tachycardia) may be absent in the elderly.⁶ The withdrawn appearance of a patient with "apathetic thyrotoxicosis" may be similar to that of a patient with Parkinson's disease, especially in the elderly, who tend to have more akinesia and rigidity than tremor.

Our first patient complained of symptoms typical of patients who have been taking levodopa for several years, with choreiform movements and on-off phenomenon, both of which suggest late complications of treatment. The psychiatric disturbance led to her being admitted initially to the psychogeriatric service, with later transfer to the geriatric assessment unit, where the correct diagnosis was made. In both cases the impaired response to the thyrotrophin releasing hormone stimulation test might have been discounted because of levodopa treatment, and a therapeutic trial of carbimazole was the only way to resolve the diagnostic dilemma.

Response to the thyrotrophin releasing hormone stimulation test is impaired in patients with Parkinson's disease taking levodopa but not in those not taking the drug⁷; this may, however, be an artefact, patients with more severe disease needing levodopa and having a poor response owing to their disease rather than the drug. Levodopa

suppresses release of prolactin from isolated pituitary cells stimulated by thyrotrophin releasing hormone⁸ and it is assumed that this effect holds for the release of thyroid stimulating hormone. This makes the thyrotrophin releasing hormone test less discriminatory in patients taking levodopa. As an additional problem, the response to the thyrotrophin releasing hormone stimulation test may be impaired in up to a quarter of healthy elderly people over 80 not taking any drugs (unpublished observation). Hence a high index of suspicion on clinical grounds, a therapeutic trial of antithyroid medication, and monitoring of the clinical response is the only way of deciding whether the diagnosis is correct.⁹

The on-off phenomenon and dyskinesia may be induced by overdosage with levodopa,¹⁰ and chorea has been reported as a manifestation of hyperthyroidism.¹¹ It is tempting to suggest that the excess thyroxine sensitised the postsynaptic receptors to dopamine and induced the abnormal movements which were abolished by correct treatment.

In conclusion, these two cases show the difficulties in diagnosing thyrotoxicosis in patients receiving levodopa for Parkinson's disease and that restoring a euthyroid state may ameliorate some of the late complications of levodopa which may develop when these conditions coexist.

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Is there any reason to suppose that occasional local use of an oestrogen cream (Premarin vaginal cream) for postmenopausal atrophic vaginitis carries any increased risk of thromboembolism?

One gram of Premarin vaginal cream contains 0.625 mg of conjugated oestrogens, and a standard daily dose can increase plasma oestradiol to follicular phase levels, even though systemic absorption may be less with vaginal than with oral preparations.¹ Conjugated oestrogen treatment after the menopause has a variety of biochemical effects that could theoretically be either adverse or beneficial. For example, the effects on plasma lipids include an increase in high density lipoprotein cholesterol² (which might protect against cardiovascular disease), and the effects on the clotting mechanism include a reduction in the main coagulation inhibitor antithrombin III (which could predispose to thromboembolism).³ Nevertheless, epidemiological studies have shown no convincing link between postmenopausal oestrogen use and cardiovascular disease or thromboembolism.⁴—JAMES OWEN DRIFE, senior lecturer in obstetrics and gynaecology, Leicester.

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