Lesson of the Week

Prevalence of inappropriate drug treatment in patients with hyperthyroidism

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The treatment of choice for hyperthyroidism due to single or multiple functioning autonomous nodules with secondary suppression of extranodular tissue (Plummer's disease¹) is radioiodine as this results in a high cure rate with little inconvenience or morbidity and a low incidence of hypothyroidism.^{2,3} In contrast, the conventional treatment for toxic diffuse goitre (Graves' disease) is to give antithyroid drugs for six months to two years and if remission does not follow or early relapse occurs to give radioactive iodine or perform subtotal thyroidectomy.⁴

Autonomous toxic nodules and diffuse toxic goitre can usually be distinguished clearly by radionuclide thyroid scanning. Without an initial scan, however, prolonged and unsuccessful treatment of Plummer's disease with antithyroid drugs may be undertaken when the hyperthyroidism could have been treated earlier and more effectively by radioiodine or surgery.

The purpose of this study was to investigate the proportion of patients with undiagnosed Plummer's disease who had received long term treatment with antithyroid drugs.

Patients and methods

We reviewed 882 consecutive patients with hyperthyroidism who had attended the thyroid clinic at this hospital from 1975 to 1983. The patients had been referred either directly by their general practitioners or from other hospital clinics. Hyperthyroidism was confirmed biochemically by radioimmunoassay of serum triiodothyronine (normal range 1.2-3.0 nmol/l (0.78-1.95 ng/ml)) and serum thyroxine (normal range 70-150 nmol/l (5.4-11.6 µg/100 ml)), with a thyrotrophin releasing hormone test when indicated.⁵ Plummer's disease was diagnosed when (a) one or more areas of focally increased accumulation of tracer were found on the thyroid scan with suppression of the rest of the gland, (b) thyroid stimulating immunoglobulin was not detected in the serum, and (c) other systemic features of Graves' disease were absent (ophthalmopathy, pretibial myxoedema, and acropachy).

Radionuclide thyroid scanning was performed in all cases, usually at the first visit to the clinic. We injected 180 MBq (4.9 mCi) of ^{99m}Tc as sodium pertechnetate intravenously and performed imaging after 20 minutes with a gammacamera fitted with either a pinhole or a long nose parallel hole collimator. The uptake of radionuclide into the thyroid gland was calculated

A thyroid scan is essential in the investigation of patients with hyperthyroidism when other features of Graves' disease are absent and especially when thyroid nodules are present or a goitre is not palpable; without this Plummer's disease may be misdiagnosed

as the percentage of the injected dose trapped by the thyroid at 20 minutes, allowing for decay and correcting for background.

Results

One hundred and four of the 882 patients with hyperthyroidism had Plummer's disease with single or multiple nodules. Those with Plummer's disease due to a single nodule had a mean age of 58.6 years and those with several nodules a mean age of 60.8 years.

Single functioning autonomous nodules—Thirteen of the 63 patients with single functioning nodules had received at least one course of treatment with antithyroid drugs for six months or more before thyroid scanning was performed. The mean time between diagnosis of hyperthyroidism and scanning was five years, but in one case it was as long as 20 years. Many patients had received several courses with rapid relapse when drug treatment was stopped. Three of the 13 patients had not had a nodule palpated before scanning was performed. Eight of the 63 patients had no palpable nodule or goitre, and in 12 cases the nodule was palpated only after being located on the thyroid scan.

Multiple functioning autonomous nodules—Ten of the 41 patients with definite multiple functioning nodules had received at least one course of treatment with antithyroid drugs before the diagnosis was made on the radionuclide scan. The mean delay in diagnosis in this group was 4.9 years. Only one of these patients did not have a palpable goitre; all the others had easily palpable nodules.

Discussion

Twenty three patients—2.6% of all patients with hyperthyroidism and 22% of all patients with Plummer's disease who had been referred to the thyroid clinic—had received treatment with antithyroid drugs for long periods before single or multiple toxic nodules had been diagnosed. These patients had relapsed repeatedly after drugs were withdrawn before being referred for thyroid scanning. We assumed that a patient receiving antithyroid drugs for more than six months was being treated as having Graves' disease, with the intention of inducing or waiting for a remission. Less than six months of treatment may be used in preparation for treatment with radioiodine or surgery or to control complications such as atrial fibrillation. Toxic nodules do not normally remit naturally or in response to treatment with antithyroid drugs, and it can therefore be argued that patients receiving more than one course or long courses of antithyroid drugs have been treated inefficiently.

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Findings on palpation are not always a guide to the true functional findings and the cause of hyperthyroidism. Our results supported this, with only 40 out of 63 cases being correctly diagnosed before the thyroid scan was obtained.

Early diagnosis is particularly important in view of the excellent results achieved with radioiodine. Recent follow up studies (paper in preparation) of treatment of single hyperfunctioning nodules have shown that all patients could be rendered euthyroid, in most cases with only one dose of radioiodine, with no incidence of hypothyroidism in patients followed up for up to 10 years.³

We conclude that thyroid scanning is essential in the management of hyperthyroid patients who do not show the classical features of Graves' disease, especially when a nodule or a multinodular goitre is palpated and when no goitre is palpable. This would permit early and successful treatment of single and multiple hyperfunctioning nodules.

We thank Susan Finer and Susan Ellam for database assistance and advice and Toni Buckley for typing the manuscript.

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(Accepted 1 August 1985)

Occupationless Health

"He never got over losing his job": death on the dole

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In politics corpses matter: a few deaths may change policy in a way that an ocean of misery will not. Much energy has thus been devoted to arguing whether unemployment kills. From his aggregate studies (also known as time series analyses) Brenner has calculated that societies in which the number of unemployed increases by more than one million in five years will experience 50 000 more deaths from general illness and 167 000 more from cardiovascular causes,¹ but Gravelle has countered under the heading "Lies, damned lies, and time series results" by arguing that unemployment is "not important in explaining variations in general population mortality."² Scott-Samuel in his turn has attacked Gravelle for underplaying the results of an important study from the Office of Population Censuses and Surveys³ and offered his own calculation that male unemployment causes 3000 extra deaths a year in Britain.⁴

Aggregate studies before Brenner

Time series analyses relate measures of economic activity and stability with measures of health in different communities over varying periods of time. Brenner is the name most associated with these studies, but Fraser attempted comparisons between different countries more than 10 years ago,⁵ and Singer in the 1930s was using these techniques to try to find an association between unemployment and maternal and infant mortality and deaths from specific causes.⁶

He worked out differences in death rates from various causes for all the county boroughs in England and Wales from 1928-33 and tried to correlate these with changes in unemployment rate. After attempting to eliminate the effects of other variables he found statistically significant correlations between unemployment and maternal and infant mortality and deaths from diarrhoea and

enteritis, diphtheria, scarlet fever, and tuberculosis. Stern, however, has recently reworked these data and found that only the correlation with maternal mortality was significant.⁸

Morris and Titmuss tried to extend Singer's work in a paper published in 1940,⁹ and Farrow has recently summarised their work.¹⁰ They looked at deaths from rheumatic heart disease and unemployment rates in 83 county boroughs from 1927-38 and found correlations between unemployment, poverty, overcrowding, and mortality. The correlation between unemployment and mortality

Five years ago we were a happy, contented family. My husband had a good job. I was working at North Tees Hospital. We were able to buy a nice house, we had annual holidays. If we wished to buy anything we bought it. We had a little in the bank. Then my husband fell into ill health. He was made redundant, he was 54 then and because of his age was unable to find employment. I went on to full time working at the hospital. As the years have gone on—our savings went, no more holidays, no social life at all. We began to sell our possessions. The colour TV. Our lovely grandfather clock, our rings, watches, bits of silver and brass, our stereo—anything we could sell we sold to pay the ever rising cost of living, the bills which are more each time they arrive. My son is now 15 years old, he is a big boy with a big appetite. He seems to grow overnight. It is a nightmare trying to keep up with his clothes. He is in men's clothes now, which are very expensive. He's a good boy doing very well at school and we are determined that he goes on to higher education. I have been in ill health for two years, I'm sure it is all the worry and stress of trying to cope. Both my husband and I are ex-service. Is this what we fought for? Extract from a letter quoted in *Unemployment and the Family* by Jennie Popay.²⁷