because of pain and/or bleeding was considerably greater in Southampton than in Dublin. Interestingly, however, the incremental rate over consecutive three-month periods in each city was similar during the first year of use (Dublin 0·8%, 0·6%, 0·7%, and 0·9%, and Southampton 2·7%, 2·6%, 3·8%, and 3·0% respectively for each period). The rate of removal was not high during the first few months of use. The larger number of doctors in the Southampton clinic is bound to lead to a wider range of attitudes towards bleeding and pain, whereas the Dublin clinic arrangement leads to a more uniform approach.

There is another important difference between the two cities. Southampton has a liberal policy towards sterilization and termination of pregnancy for failed contraception which cannot be matched in Dublin. This gives an alternative outlet for the patient with I.U.D. complications, which tends to reduce motivation for a method such as the I.U.D. The lack of such alternatives in Dublin may force the I.U.D. user to tolerate discomfort at a level which would be unacceptable to the Southampton woman. The total family planning organization in terms of the range of alternatives in a given population must therefore be taken into consideration when examining any particular method of fertility regulation.

We acknowledge the help of the clinic staff in Southampton and Dublin and the data processing staff of the Family Planning Research Unit, University of Exeter, without whom this study would not have been possible.

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Hospital Topics

Screening for Hypothyroidism in Elderly Inpatients

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Summary

Routine biochemical screening for hypothyroidism in 2000 geriatric inpatients proved valuable and practicable and yielded 46 cases (2·3%). A non-specific clinical picture was particularly common, with less than a third of the cases showing "typical" signs and symptoms. Psychiatric manifestations, especially depression, were important and frequent and responded well to thyroxine. There was a preponderance of female cases of hypothyroidism and a strong association with other autoimmune diseases, notably pernicious anaemia and rheumatoid arthritis.

Introduction

Hypothyroidism is common in old age. We started routine screening tests for thyroid dysfunction in all patients admitted to the geriatric department of Northwick Park Hospital in 1970. The early experience, based on 300 patients, suggested that the incidence of both hypothyroidism and hyperthyroidism was higher than had been previously reported,[1] and we were thus encouraged to continue with screening.

When 2000 patients had been screened we re-examined our findings to see whether the earlier estimate of the incidence of hypothyroidism was reliable, but also to study the clinical picture of hypothyroidism in the elderly. We expected that this might be different from the textbook picture, which tends to be confirmed by series relying heavily on clinical diagnosis but might not be confirmed by the present series, in which identification was made on the basis of routine biochemical screening.

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Patients and Methods

Generally in the department[2] there is no waiting list, so that admissions include many cases of acute illness. Female admissions form 64% of the total, and the average age of the patients is 80 years, all being over 60. During the first 18 months the screening tests were the determination of protein-bound iodine (P.B.I.) by Auto Analyzer, and T-3-uptake by the Thyopac-3 test kit. Subsequently P.B.I. was replaced by T-4 estimation with the Thyopac-4 kit. In the interpretations we used a calculated free thyroxine index (F.T.I.), which is essential in view of the frequency of disturbance of thyroxine-binding proteins in these patients.[3] Two or more separate abnormally low F.T.I.s were minimum requirements in all but the most clinically obvious cases, in which a single low value was accepted. Determination of thyroid-stimulating hormone (TSH) by a double antibody radioimmunoassay technique[4] was used as a confirmatory test, while thyroid antibodies were sought in selected cases. Response to treatment also provided important confirmatory evidence.

The series represented about 95% of all patients admitted to the department, the remainder being largely accounted for by early deaths or patients who had been recently screened during a previous admission.

Results

Of the 2000 patients screened 46 (2·3%) were found to have undoubted hypothyroidism, this being a new diagnosis in 42 and representing relapse due to cessation or inadequacy of treatment in four. Where P.B.I. had been used the average F.T.I. was 1·85 compared with a normal range of 2·8-7·8,[3] and where T-4 had been used the average F.T.I. was 0·40 compared with a normal range of 0·55-1·60. None of the hypothyroid patients had had thyroid surgery or radioactive

iodine, lithium, or other antithyroid treatment and none had known pituitary disease.

Cases in which the diagnosis of hypothyroidism was uncertain and the investigation inadequate, usually because of early death or discharge, were excluded, as were several transient cases occurring after iodine medication, which were briefly reported on elsewhere.[5 6] The estimated 2·3% incidence of new cases of hypothyroidism is therefore conservative. Eleven patients had adequately treated hypothyroidism, giving a total incidence of 2·9%. As would be expected, the new cases contained a significant excess of women (85%, compared with 64% for all admissions to the department) but age was not significantly higher.

CLINICAL PRESENTATION

Classical Picture.—Only 13 of the 46 patients had classical signs and symptoms of myxoedema allowing them to be recognized as likely to be hypothyroid before the laboratory screening test results were available.

Non-specific Picture.—A non-specific picture was far more common. Such patients showed only a general deterioration of mobility and general health and sometimes apathy but had no classical signs or symptoms of hypothyroidism. Despite the vague nature of the symptoms, however, there was typically a clear response to thyroxine. A totally non-specific presentation occurred in 13 patients (28%), while 12 others (26%) had a similarly non-specific presentation but with some relevant associated disease or condition (rheumatoid arthritis in four, pernicious anaemia in four, and one instance each of Addison's disease, goitre, transient arthralgia, and deafness, which improved after thyroid treatment). A non-specific picture thus occurred in 54% of the series and accounted for 76% of the clinically unrecognized cases.

Psychiatric Presentations.—The remaining eight clinically unrecognized cases presented with psychiatric manifestations. Six patients presented with depression and two with paranoid symptoms. In addition, one case of classical myxoedema presented with acute delirium and one relapsed case with depression. Thus 10 patients (22%) had psychosis other than dementia. This was a significant excess when compared with a control group of 92 patients matched for age and sex, in which the incidence was only 6·5% (Fisher's exact test, $P = 0.011$). In contrast, there was no excess of dementia or of intellectual impairment as assessed by a simple orientation and memory test.[7] In no case did dementia improve with treatment of the hypothyroidism, whereas patients with the other psychoses recovered completely or improved greatly in each instance.

ASSOCIATED DISEASES AND FINDINGS

Among the 46 hypothyroid patients seven had pernicious anaemia, this being a new diagnosis in four. Six patients had rheumatoid arthritis, one Addison's disease of many years of duration, and one vitiligo. One patient presented with hypothermia, one with carpal tunnel syndrome, and another with a mild polyarthralgia, which disappeared rapidly when the hypothyroidism was treated. There was no excess of diabetes in the series.

Ischaemic Heart Disease.—Comparison with a control series showed no excess of ischaemic heart disease as judged by electrocardiography in the clinically unsuspected hypothyroid cases. The classical cases did show an excess, which failed to reach significance ($P < 0.1$). Four patients in this group had severe ischaemic changes on their admission electrocardiogram and two of these developed myocardial infarction after thyroid treatment was instituted despite cautious dosage. In one patient the infarct occurred three months after starting treatment and was followed by good recovery. The infarct in the other occurred six months after beginning treatment and proved fatal. In contrast, there were no infarcts in the clinically unsuspected group, though five had had severe ischaemia on admission.

Deafness.—Seven patients were deaf. In three, two of whom were clinically gross cases of myxoedema, there was complete recovery of hearing with adequate treatment of the hypothyroidism.

Macrocytosis.—A conspicuous feature of the series was that many patients, apart from those with pernicious anaemia, appeared to have a modest increase in mean corpuscular volume (M.C.V.), which tended to fall after thyroxine treatment. Out of 21 patients without pernicious anaemia who had duplicate determinations of M.C.V. before and after institution of thyroid treatment, 17 showed a fall in M.C.V., two no change, and only two an increase; the tendency to fall was highly significant (sign test, $P < 0.01$).

PATHOLOGY OF THYROID

The thyroid was examined post mortem in six cases. Four showed severe atrophy and two had multinodular goitre. One was a large goitre, which was one of only three recognized clinically in the series. The other was small, clinically inapparent goitre confined to the right lobe. It is noteworthy that some 26% of all patients from our department are found to have multinodular goitre at necropsy.[8]

Discussion

This series confirms the preliminary findings of a substantial increase in the number of diagnoses of hypothyroidism resulting from the routine biochemical screening of geriatric inpatients.[1] The incidence of 2·3% may be an underestimate but is far higher than earlier reports for hospital series,[9 10] which were not exclusively geriatric and not based on routine screening. It is more comparable with the incidence of clinical myxoedema (1·5%) found among geriatric patients by Lloyd and Goldberg,[11] but investigation of their cases was incomplete by today's standards, and our much lower incidence of clinically recognized disease (0·65%) suggests that their essentially clinical estimate may have been distorted both by the omission of atypical cases and by the inappropriate inclusion of old people whose physical appearance suggested myxoedema, a well recognized pitfall in old age.[12 13]

Biochemical screening for hypothyroidism has proved practicable in a busy geriatric department, and in our view the effort has been justified by the case yield (to which is to be added the not inconsiderable yield of thyrotoxicosis of approximately 1·1%). Many cases diagnosed had not reached a stage of clinically obvious myxoedema. This appears to be a positive advantage, for our experience confirms the view, quite widely held by geriatricians, that treatment of the gross case is hazardous despite cautious dosage regimens. Two of our patients with clinically recognizable disease had myocardial infarcts after treatment, one proving fatal. In contrast, treatment of the clinically unrecognized cases led to no such incidents.

While we regard routine screening of geriatric patients as the ideal, this may not always be possible. Selective screening may then be the necessary alternative, and our experience suggests that such selection should take account of the preponderance of women and the strong associations with other autoimmune disease, especially pernicious anaemia and rheumatoid arthritis, and should pay regard to depression, apathy, or a general "failure to thrive" as important indicators. We believe that the M.C.V. may also afford a useful pointer, indeed a far better one than cholesterol, which has so often been used in the past. Altogether 41% of our hypothyroid patients had a raised M.C.V. (92 fl or over) compared with 9% of an age-matched control group.

Measurements of TSH were not available for all patients in this series. Those that were available, however, indicated that the hypothyroidism was primary in all instances. TSH would be a useful addition to future screening studies, as a normal value effectively excludes primary hypothyroidism. This would be particularly helpful when the F.T.I. gives a borderline result.

One cannot automatically assume that screening of other groups of elderly inpatients—for example, those admitted to medical or surgical wards—would necessarily give similar yields of hypothyroidism. Nevertheless, this seems a sufficient probability to justify exploratory study. The potential value of screening apparently well old people at home is perhaps more uncertain. The findings of Taylor *et al.*[14] though somewhat equivocal, do suggest that a comparable yield might result. Here again further studies are needed.

Studies of this series of elderly hypothyroid patients diagnosed by routine screening have led us to modify our conception of the usual clinical picture. A non-specific presentation emerges as being particularly common, but depression is seen to be a striking and important feature. This is somewhat at variance with the classical descriptions of the mental changes in hypothy-

roidism. As Asher's graphic term "myxoedematous madness"[15] indicates, the earlier descriptions based on clinically obvious cases of myxoedema[16 17] stressed the occurrence of florid psychotic manifestations, depression being mentioned only parenthetically. In our relatively unselected cases depression totally overshadowed manifestations of this type.

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Requests for reprints should be sent to Dr. H. M. Hodkinson.

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Chlormethiazole in Treatment of Status Epilepticus

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Summary

Chlormethiazole (Heminevrin) was successful in controlling fits in seven out of nine episodes of intractable status epilepticus. It was administered as a constant intravenous injection at rates of up to 0·7g/h. No serious side effects were encountered, and the drug deserves wider recognition as a useful therapeutic agent in the management of status epilepticus.

Introduction

The management of status epilepticus has been transformed in recent years by the introduction of intravenous diazepam and thiopentone, which have largely replaced parenterally administered phenytoin, phenobarbitone, and paraldehyde. Nevertheless, some patients with status epilepticus fail to respond to these drugs. We have found chlormethiazole (Heminevrin) to be valuable in these cases. We report here its use in nine episodes of status epilepticus in eight patients seen over two years.

Chlormethiazole is a derivative of the thiazole nucleus of thiamine (vitamin B_1). It has anticonvulsant and sedative properties[1] and has been used in the management of acute alcohol withdrawal,[2] toxaemia of pregnancy,[3] and status epilepticus.[1] It may be given intravenously or orally, but because it has a half life of 46 minutes it should be given either by continuous intravenous infusion or at frequent intervals when prescribed orally. It is free from serious side effects and has little cardiorespiratory depressant action in therapeutic doses,[4] though apnoea has been reported in a child after an excessive dose.[1]

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Patients

The eight patients studied (three men and five women, aged from 19 to 67) were admitted to the Intensive Care Unit at the National Hospital, Queen Square, in "refractory" status epilepticus, one patient being admitted twice within six months. The clinical details of the patients are summarized in table I. Seven of them were in convulsive status epilepticus and one (case 6) was in focal motor status. Three had symptomatic epilepsy. One (case 1) had a progressive, diffuse encephalopathy of unknown aetiology which led ultimately to her death. Another (case 6) had an infantile hemiplegia. Case 7 was that of an alcoholic patient in whom status epilepticus was precipitated by a left hemisphere cerebrovascular accident. Contrast radiography showed no abnormality in the remaining five patients. Five out of the nine episodes of status were preceded by an alteration in the patient's antiepileptic drug therapy.

Initial Treatment

Before admission each patient had received diazepam (up to 20 mg intravenously as a bolus) and four had also been given intramuscular paraldehyde. Seizure activity during admission was assessed by clinical observation, E.E.G. sampling, and continuous respiratory monitoring. Previously administered anticonvulsant drugs were continued throughout the whole period of status epilepticus.

After admission the first drug given in all cases was diazepam at the rate of 8 mg/h in a continuous intravenous infusion (table II). In five cases the dose was increased to 15 mg/h. A higher dose caused respiratory depression without inhibiting seizures. In cases 2 and 3 doses up to 30 mg/h were tolerated but fits continued. Diazepam controlled status epilepticus in case 1 only by steadily increasing the dose to 60 mg/h over a period of seven weeks. Intravenous infusion of thiopentone at the rate of 125 mg/h was substituted for diazepam in cases 1 and 2. Both patients developed respiratory depression and needed assisted ventilation, one for four weeks and the other for nine days. Thiopentone controlled status in both cases but fits recurred if the dose was reduced.

Chlormethiazole Treatment

After diazepam or thiopentone had been stopped chlormethiazole in a solution of 0·8 g/100 ml was given by continuous