Thyroid antibodies in patients before and during long term amiodarone treatment

	n	Positive thyroid antibodies*		No of days of treatment with amiodarone	
		Before amiodarone	During amiodarone	Mean (SD)	Range
Pisa and Cagliari:					
Short term (≤three months)	19	1	1	41 (26)	13-98
Long term (≥four months)	12	1	2†	284 (266)	119-1078
Worcester:					
Short term (≤three months)	1	0	0	90	
Long term (≥four months)	15	4	2	299 (91)	174-413

*Antibody titres greater than or equal to 1:100 were considered to be positive.
†One patient developed intermittently positive antimicrosomal antibodies.

Comment

Evidence of thyroid autoimmunity has often been noted in patients who develop hypothyroidism while receiving amiodarone.[2] Between 30% and 50% of patients who have hypothyroidism induced by amiodarone iodine have antithyroid antibodies.[1,2] Antithyroid antibodies are less common in patients who have hyperthyroidism induced by amiodarone iodine.[1,5] Monteiro *et al* reported the development of antimicrosomal antibodies in six of 13 patients treated with amiodarone for one month.[3] Two of these patients had slightly increased serum concentrations of thyroid stimulating hormone, and all were euthyroid with negative antibody titres six months after the amiodarone had been withdrawn. Rabinowe *et al* noted a high prevalence (60%) of antimicrosomal antibodies in 10 patients who received amiodarone, but no data are available for these patients before treatment.[4] One of their patients developed hyperthyroidism while receiving amiodarone and showed a considerable increase in immune region associated antigen positive T cells, often found in patients who have Graves' disease, which resolved within three weeks of withdrawing the amiodarone.

The results of our prospective study, however, which included patients treated with amiodarone for both short and long periods and from regions of differing ambient iodine intake show that amiodarone treatment does not seem to be associated with an increased incidence of antithyroid antibodies.

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Respiratory muscle weakness in Addison's disease

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Patients with Addison's disease may rarely present with wheezing due to asthma.[1] More commonly they have non-specific symptoms such as weakness, dizziness, and weight loss. We describe a patient who presented with dyspnoea on exertion that was related to severe respiratory muscle weakness.

Case report

A 63 year old retired caterer presented with a two month history of dry cough and wheezing. Her tolerance of exercise was 400 metres on the flat, she had no orthopnoea but became breathless on stairs. She smoked 20 cigarettes a day, had lost 6 kg over the past year, but denied any abdominal pain, anorexia, or blackouts. Her menstruation had been normal until the age of 50, and she had one son aged 36.

On examination she was deeply tanned with pigmented palmar creases and intraoral pigmentation. She had no axillary hair and scanty pubic hair. Her blood pressure was 95/70 mm Hg when supine and 85/75 mm Hg when standing. She had a widespread expiratory wheeze; peak flow was 150 l/min, forced expiratory volume in one second 1·3 l, and forced vital capacity 1·5 l. The plasma concentration of sodium was 129 mmol/l, potassium 4·5 mmol/l, and urea 8·6 mmol/l; haemoglobin was 136 g/l, white cell count $5·05 \times 10^{12}$/l (8% eosinophils), and erythrocyte sedimentation rate 9 mm in first hour. The results of tests of liver and thyroid function were normal. Plasma cortisol concentrations during three short tests with tetracosactrin were 120 nmol/l, 140 nmol/l, and 120 nmol/l, the lack of a cortisol response being confirmed by a long test with tetracosactrin. Luteinising and follicle stimulating hormone concentrations were both in the menopausal range (>50 U/l), and adrenocorticotrophic hormone was 266·7 pmol/l (normal 2·2-17·8 pmol/l). Respiratory muscle studies[2] showed low maximal static expiratory mouth pressure (34 cm H_2O; normal >32 cm H_2O), low maximal static inspiratory mouth pressure (14 cm H_2O; normal >24 cm H_2O), and reduced transdiaphragmatic pressure during maximal sniffs[3] (48 cm H_2O; normal >70 cm H_2O). Phrenic nerve conduction times were 9 ms (normal 5-9·5 ms). Maximal voluntary contraction of the quadriceps muscles was 9 kg (normal >29 kg).

Full replacement treatment with hydrocortisone acetate was started. Ten months later her breathlessness had improved such that she was able to climb two flights of stairs. Peak flow had increased to 315 l/min, forced expiratory volume in one second to 1·6 l, and forced vital capacity to 2·5 l. Maximal static expiratory mouth pressure had increased to 45 cm H_2O, maximal static inspiratory mouth pressure to 20 cm H_2O, and transdiaphragmatic pressure during maximal sniffs to 75 cm H_2O. Phrenic nerve conduction times were unchanged. Maximal voluntary contraction of the quadriceps muscles increased to 22 kg.

Comment

In Addison's disease generalised fatigue is common and is usually attributed to non-specific malaise rather than muscle weakness. Our patient, however, showed evidence of weakness in both respiratory and quadriceps muscles, suggesting that all skeletal muscles were affected. Phrenic neuropathy was excluded by the finding of normal conduction times in the phrenic nerve. Although electrolyte disturbances may have partially contributed, weakness in the respiratory muscles probably resulted mainly from myopathy. Thus just as steroid myopathy may be induced by Cushing's syndrome or by excessive corticosteroid administration, so a lack of corticosteroid also seems to result in muscle weakness and myopathy.

Our patient had airways obstruction that improved after treatment. She also had diaphragmatic weakness of moderate severity, which can produce dyspnoea on exertion[1]; this may improve as the diaphragmatic weakness resolves in cases in which a treatable cause for respiratory muscle dysfunction exists.[5] In our patient the strength of quadriceps muscle[5] and function of expiratory and diaphragmatic muscles returned to within the normal range after treatment; low values for maximal static inspiratory mouth pressures seemed to be due to poor technique, a not uncommon finding with this manoeuvre. We conclude that Addison's disease can cause myopathy which may affect the respiratory muscles.

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Carotenaemia in Alzheimer's disease

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Alzheimer's disease is the commonest type of dementia, during which patients may lose a considerable amount of weight.[1] Anorexia nervosa is a disease of the young in which there is also appreciable weight loss. Patients who have anorexia nervosa have hypercarotenaemia. There is no blood test for Alzheimer's disease. If plasma carotene concentrations were increased in this condition this would be of considerable interest.

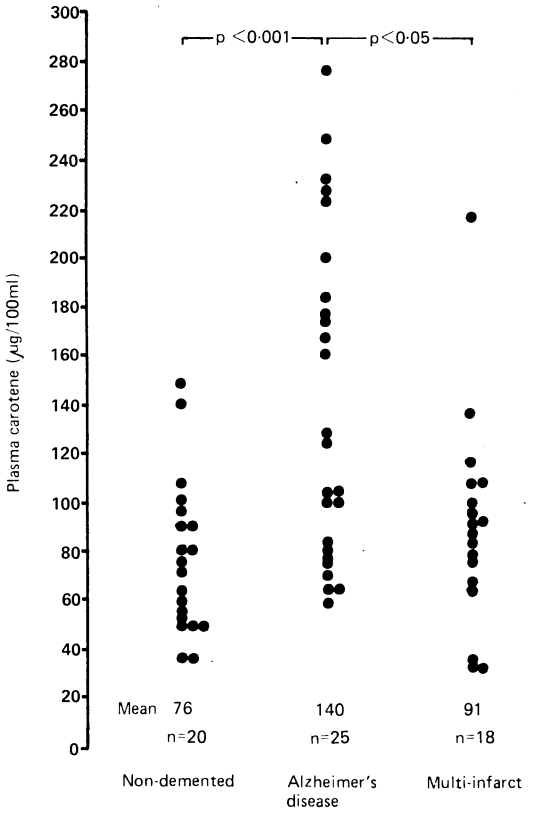
Patients, methods, and results

We studied plasma carotene concentrations in a group of elderly women who had Alzheimer's disease (mean age 86 (range 71-94)). Two control groups—namely, women who had multi-infarct dementia (mean age 83 (72-94)) and non-demented long stay elderly women (mean age 81 (70-89))—were also studied. Altogether there were 63 patients. Dementia was diagnosed from clinical criteria, and the Hachinski score[2] was used to differentiate patients who had multi-infarct dementia from those who had Alzheimer's disease. We measured plasma carotene concentrations spectrophotometrically and also studied the relation between plasma carotene and plasma vitamin A concentrations, as dietary carotene is a source of vitamin A. In addition, thyroid function and plasma lipid concentrations[3] were studied. Tests of thyroid function were performed on patients in all three groups, and lipid profiles were determined in the groups who had Alzheimer's disease and multi-infarct dementia.

A considerable difference in carotene concentrations was found among the Alzheimer group and the control groups (figure), but no significant differences in vitamin A concentrations were found. Lipid profiles were available for 12 patients in the Alzheimer group and 15 patients in the multi-infarct group. There was no significant difference between the mean values for the two groups. There were, however, significant differences ($p<0{\cdot}05$, Mann-Whitney U test) between the Alzheimer group and the non-demented group in total thyroxine concentrations (mean (SEM) 86·7 (3·4) nmol/l *v* 97·6 (4·9) nmol/l) and free thyroxine indices (168·2 (4·4) *v* 194·0 (10·3)).

Comment

Many patients who have Alzheimer's disease have increased plasma concentrations of carotene. Carotene is stored in adipose tissue, and it may be thought that weight loss itself leads to the carotenaemia. Patients who have other wasting illnesses, however—for example, disseminated malignancy—tend to have low plasma carotene concentrations.[4] Carotenaemia may arise as a consequence of increased carotene intake or be associated with diabetes mellitus, hypothyroidism, or hyperlipidaemia.[3]



Plasma carotene concentrations in patients who had Alzheimer's disease and two control groups

There is no reason to suspect an increased carotene intake in the patients with Alzheimer's disease; on observation their ward diet was no different from that of fellow patients. The difference in thyroid function was small and at most was likely to contribute only partly to the carotenaemia.

Dietary carotene is a precursor of vitamin A, the conversion occurring in the gut wall. Accordingly, a positive correlation between plasma carotene and plasma vitamin A concentrations would be expected. This was seen in the non-demented group (Spearman correlation coefficient 0·51; $p<0{\cdot}05$) but not in the Alzheimer group (Spearman coefficient 0·30), suggesting an abnormality in the conversion of carotene to vitamin A. The vitamin A concentration was not, however, lower than expected in the Alzheimer group, but the above hypothesis may still be