Myasthenia Gravis and Elderly People

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Summary
Myasthenia gravis is probably commoner than previously suspected, the annual incidence being nearer 9—10/ million than earlier figures of 2—4/million. The current study found an annual incidence in Croydon of 9.1 per million (95% confidence limits 5.7—13.8 per million). Of the 22 patients (59%) seen in Croydon with newly diagnosed myasthenia gravis during the past 7 years, 13 were aged over 60. In a separate study of the age distribution of positive acetylcholine receptor antibody assays, 51% were 60 years or above in 1991, and 64% in 1994. The peak age in both sexes was 70—80, and numbers were greatest in men aged 60—80.

Introduction
The usually cited pattern of myasthenia gravis (MG) is that the incidence is 2—4/million [1—4] with a peak age of onset in women in the twenties and a less clear but later onset in men [5, 6]. Most series have found that only 6%—20% of cases start after the age of 60 [5—7]. Presumably because of this view, little has been written about MG in elderly people, and the standard geriatric textbooks reflect this. Only Herishanu et al. [8] have specifically reported on a group of elderly myasthenic patients from Jerusalem where 15 out of 33 patients (45%) were 60 or over.

In this study, two separate approaches have been used to look at the possible incidence of MG in the elderly population. Firstly, the experience of the single-handed Consultant Neurologist in Croydon is reported because 59% of the patients were 60 or over.

In the second approach, the age distribution of positive acetylcholine receptor antibody (AchRab) assays was studied by the supraregional immunology laboratory at Birmingham Heartlands Hospital during two study periods in 1991 and 1994 to determine the percentage of patients aged 60 and above.

Results
Clinical study: Croydon has a population of 330 000. Between 1987 and 1994 (the study period was 7 years and 4 months), 22 Croydon residents were seen and newly diagnosed with MG by the sole Consultant Neurologist in Croydon. This gives an annual incidence figure of 9.1 (95% confidence interval 5.7 to 13.8) per million. The possibility that other patients could have been referred to Centres outside Croydon cannot be excluded. Thirteen of these 22 patients (59%) were aged 60 and over. The age range was 60—84 years. Men predominated in the elderly group, with nine men and four women, 11 of the 13 were AchRab positive. Nine presented with generalized disease and four with only ocular disease. The only patient amongst these 22 who had a thymoma detected was aged 74.

The bulk of the deaths and complications occurred in the elderly group. Three patients died. An 82-year-old woman died of severe gastrointestinal haemorrhage after failing to respond to steroids, azathioprine and plasma exchange. A 74-year-old man died after removal of his thymoma, from severe generalized disease complicated by Pseudomonas septicaemia. A 68-year-old woman died at home with fairly well controlled disease. It is not definitely known whether her myasthenia contributed to her death. She also had chronic obstructive airways disease and Parkinson’s disease.

Two serious complications were encountered: a 64-year-old man required hospital admission for a major steroid psychosis, and a 71-year-old woman developed gross lymphopenia on azathioprine. The nine patients under 60 ranged in age from 17 to 59 years. Women predominated, with seven women and only two men. Six of the nine presented with ocular disease. Five were AchRab positive. Although three had thymectomies, there were no major complications in these patients, but the 59-year-old man died from small-cell lung cancer 1 year after diagnosis. The delay between the development of symptoms and establishing the diagnosis was less in the younger patients by an average of 2 months. (The average delay to diagnosis was $\frac{1}{2}$ months in the under-60 group, and $\frac{3}{2}$ months in the 60-and-over group.) These differences are summarized in the Table.

Acetylcholine receptor antibody study: The age distribution of the positive AchRab samples received at the supraregional immunology laboratory at Heartlands Hospital, Birmingham, was studied over two separate periods during this 7-year study, first in 1991 and then in 1994. In the pilot study from 1 January to...
In the second study period, all the positive assays in the whole of 1994 were reviewed. There were 294 positive assays; patients' ages were known in 264 cases of which 170 (64%) were aged 60 and above.

These samples contained no repeat assays. In the samples, there was, as before, a rising incidence of positive assays in men with a peak between 70 and 79 years. In women, there was again a bimodal distribution with a smaller peak in the 40–49-year-old group, and the largest peak at 70–79. The overall ratio of male : female samples was 1 : 1. In men, 75% of samples were from the over-60 group, and in women, 54%. Forty samples came from patients aged 80–89.

**Discussion**

Although this is a small study, the incidence figure for Croydon of 9/million is relatively high. This is, however, in close agreement with two other recent studies. Sorensen and Holm [9] found an incidence of 10.4/million in Viborg County, Denmark, and Phillips et al. reported the incidence in Central and Western Virginia to be 9.1/million. In Viborg County, 36% of the patients were 60 or over, and in Virginia, 44%. Both figures are less than the 59% found in Croydon. The main conclusion of all the recent studies is that MG is not as rare in the elderly population as previously reported. It is likely that these higher incidence figures represent better case ascertainment, particularly in elderly people.

It is possible that the age distribution of MG may show racial differences. Chiu et al. [11] compared a series of Taiwanese Chinese with a similar number of Caucasians and found there were far fewer older Chinese patients than Caucasians. It is also, of course, possible that, as in earlier European studies, older patients are not being diagnosed.

The particularly striking peak age in men over 70 has now been reported in at least four recent epidemiological studies [9, 10, 14, 15]. The excess mortality and morbidity in older patients which was found in our series has also been previously reported [8]. Donaldson et al. [12], however, found no excess mortality in patients over 50, but did find an excess of steroid-related complications.

Compston et al. [13] divided their 68 patients into three subgroups. Those under 40 with a predominance of women, those over 40 with a male predominance, and those with thymomas who had no clear age distribution. In the under-40 group there was an association of MG with HLA-DRw3 and in the older group with DRw2.

The use of the AchRab as an epidemiological aid seems suitable in MG for three reasons. Firstly, it seems likely that all suspected cases will have the antibody requested; secondly, the assay is only carried out in a small number of centres, and thirdly, there is no significant false-positive rate. The current study looked at all the positive assays in two study periods in 1991 and 1994. In both series, there was a clear excess of
positive assays from patients over 60. It is not yet clear from the epidemiological literature whether older patients may be more likely than younger ones to be antibody positive. The clear-cut bimodal age distribution in women, with a smallish peak in younger women and a larger one in older women, is in agreement with the findings of Somnier et al. in Denmark [14].

The suggestion of an apparent change in the incidence pattern of MG towards a predominance in the elderly population will need to be addressed further in larger studies, as this could have major implications for the way the disease is managed in the future.

References

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