elsewhere. "Mixed" cultures are normally regarded as evidence of contamination. The bacteria isolated in these cultures could not have been skin contaminants, but were compatible with a genuine population of mouth and respiratory tract flora, particularly as the findings in both sets of cultures were consistent.

The discovery of denuding and ulceration of the respiratory tract epithelium at necropsy provides an obvious mode of entry, and since this is a well-established feature of influenzal infections it is perhaps surprising that multiple organisms do not gain access to the blood stream more often. The necropsy findings suggest that the damage in this case was probably unusually severe. Nevertheless, the phenomenon may not be so unusual, and would be detectable if blood cultures were obtained at an optimal stage in the course of such an illness before antibiotic treatment. There was no evidence of immune deficiency, as serum immunoglobulin concentrations were normal, and an adequate (fourfold) rise in viral agglutinin titres was shown. An initial lymphopenia is common in severe viral infections but could conceivably reduce the efficiency of an immune response to bacterial infection. An adequate polymorph response appears to have been developed, at least in terms of cell numbers, and there was no history of undue susceptibility to infection.

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Myasthenia gravis: acetylcholine-receptor antibody titres after thymectomy

Antibodies to the nicotinic acetylcholine receptor, recently shown in myasthenia gravis,[1 2] may be responsible for the characteristic neuromuscular block. Thymitis and thymomas are common in myasthenia, and thymectomy has long been known to alleviate the disease. It is not known how the thymus is implicated. If it were the source of the antibodies, as suggested by the presence of germinal centres containing B lymphocytes in the thymic medulla, there should be a rapid fall in titre after thymectomy. If, however, thymectomy merely removes the source of an antigen shared with striated muscle (nicotinic acetylcholine receptors are present in thymus tissue) any fall in antibody titre might be considerably delayed. This would also be the case if thymectomy acted via the removal of long-lived T lymphocytes. Furthermore, if the receptor antibody is responsible for the neuromuscular block there should be some correlation between the antibody titre and the clinical improvement after thymectomy. We have tested this hypothesis and report here our results.

Patients, methods, and results

We studied 21 patients with myasthenia gravis (see table)—14 with thymitis after thymectomy (group 1), three with thymomas after thymectomy (group 2), and four before thymectomy (group 3). Serum antibody titres were measured by competitive immunoprecipitation with human acetylcholine receptor labelled with ^{125}I α-bungarotoxin.[2] Titres exceeding $0{\cdot}619 \times 10^{-9}$ mol α-bungarotoxin precipitated/l are found only in patients with myasthenia gravis, the mean titre in myasthenia being $54{\cdot}3 \times 10^{-9}$ mol/l. The significance of the difference between two means for independent samples was determined by Student's t test.

There were no significant differences in mean antibody titres between group 1 when taken as a whole and groups 2 and 3 (table), possibly because of the small numbers of patients in groups 2 and 3. Patients in group 1 who had improved clinically after thymectomy—that is, with response A, B, or C[3]—however, had a significantly lower mean antibody titre than group 3, even when the patient with a thymoma (case 21) was excluded ($P<0{\cdot}01$).

In group 1 antibody titres fell with the increasing number of years since thymectomy ($0{\cdot}1>P>0{\cdot}05$). Of the patients in complete remission (response A), however, only one (case 11) had a titre within the normal range.

Clinical details and antibody titres in the 21 cases of myasthenia gravis

Case No	Sex	Years since thymectomy	Years from onset of myasthenia gravis to thymectomy	Initial grade of myasthenia	Response to thymectomy	Antibody titre $\times 10^{-9}$ mol/l
			Group 1			
1*	F	1	2	II	E	43·4
2	M	2	19	II	E	33·5
3	F	11	1	II	E	125·0
4	F	11	3/12	III	B	0·895
5	F	11	2½	III	B	0·349
6	M	16	3	II	B	12·8
7	F	20	7	II	A	11·4
8	F	21	1	II	A′	1·39
9	F	27	13	II	B	13·4
10	F	28	1	II	B	2·62
11	F	28	3/12	III	A	0·276
12	M	30	36	V	C	0·273
13	F	31	2	II	A	2·08
14	M	34	9/12	III	A	0·641
			Group 2			
15*	M	10	3	II	E	52·8
16*	F	2	2½	III	B	42·5
17*	M	1	1½	II	E	28·9
			Group 3			
18	F			II		2·08
19	F			I		68·6
20	F			III		21·6
21†	M			II		50·8

*Patients receiving steroids or steroids and immunosuppressant drugs at time of study.
†Thymoma found at subsequent operation.
Initial grade of myasthenia and response to treatment were assessed according to Osserman's[3] classification, as follows: A′, complete remission but subsequent exacerbation; A, complete remission; B, marked improvement with decreased anticholinesterase medication; C, marked improvement without decreased anticholinesterase medication; D, no improvement but decreased anticholinesterase medication; E, no change.

Two other patients with low titres (cases 5 and 12) were still taking small doses of pyridostigmine. Patients in group 1 who had had an abrupt, severe onset of generalised myasthenia (grade III[3]) all had normal or low titres. This was not explicable by earlier operation, as there was no correlation between time to operation and subsequent antibody titre.

Comment

These results suggest that clinical improvement is associated with a progressive decrease in anti-receptor antibody titre over several years. Hence a major source of antibody is probably not removed by thymectomy, as in that case the titre would fall more quickly. Thymectomy may remove an antigenic stimulus or cause a gradual decrease in T lymphocytes necessary for antibody formation by B lymphocytes. We have confirmed a reported fall[4] in the number of E-rosetting cells after thymectomy (unpublished observation). The association between clinical improvement and the fall in antibody titre after thymectomy is indirect evidence that anti-receptor antibodies have a pathogenic role in myasthenia gravis. A fall in antibody titre has also been reported after remissions induced by corticosteroids.[5] We are now performing long-term studies before and after thymectomy to further investigate this problem.

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