

# Surgical treatment for myasthenia gravis

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**ABSTRACT** A new surgical technique for thymectomy is presented. Three hundred and seventeen patients with myasthenia gravis and 20 with thymomas who had myasthenic symptoms were operated on. The new surgical approach—a small transverse sternotomy—was used in 257 cases (in 240 patients with myasthenia gravis and 17 with thymomas) and conventional median sternotomy in 80. In myasthenic patients small transverse sternotomy enabled radical thymectomy to be performed with an uneventful postoperative course and very good cosmetic results. There were no hospital deaths among patients with myasthenia gravis after thymectomy. The long term results, assessed after 18–24 months, were good: the total remission rate was 39.5%, and there was a great improvement in 48.5% and an improvement in 9%. After thymectomy about 30% of patients received supplementary treatment with prednisone. A correlation between the duration of symptoms and the result of thymectomy was established: the shorter the duration of myasthenia gravis the better the results. In the small group of 20 patients with thymomas two died in hospital. In 12 patients with encapsulated thymic tumours the long term results were similar to those in patients with myasthenia gravis, whereas in patients with infiltrating thymic tumours the results were unsatisfactory.

## Introduction

Thymectomy for myasthenia gravis, first used by Sauerbruch in 1912,<sup>1</sup> was introduced again by Blalock in 1939<sup>2</sup> and became a widely used procedure in the last two decades, when large series of cases proved this treatment to be beneficial to patients with myasthenia.<sup>3–10</sup>

The conventional surgical approach to the thymus is through a median sternotomy.<sup>11–14</sup> This incision, however, is rather large in relation to the size of the thymus to be removed, and thus is not acceptable to some patients, particularly young women, for cosmetic reasons. On the other hand, the transcervical approach,<sup>9, 15–17</sup> which is cosmetically superior, has given rise to much controversy about whether it permits radical thymectomy to be achieved or whether some residual thymic tissue may be left unnoticed in the mediastinum.<sup>18–20</sup>

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## Patients and methods

Since 1972 317 patients with myasthenia gravis and 20 with thymomas who had myasthenic symptoms have been operated on in the department of surgery of the Institute of Tuberculosis and Chest Diseases in Warsaw. Most of our patients were diagnosed in the department of neurology of Warsaw Medical Academy, but some had been referred from other neurological centres in Poland. All patients were followed up personally.

As indications for surgery we accepted proved or suspected thymomas, a rapid increase of myasthenic symptoms, a lack of response to cholinergic drugs, and advanced myasthenia with bulbar and respiratory symptoms. In all cases the clinical diagnosis was supported by a positive response to cholinergic drugs, including the tensilon test, and by electromyography: if the classical repetitive stimulation test was not conclusive, then positive single fibre electromyography was used. Pneumomediastinography and, in the last 48 cases, computed tomography also confirmed the diagnosis.

Of the 317 patients, 252 were women, the female to male ratio being 3.9:1. Young people predominated (fig 1). Forty one per cent of patients were aged 20–30

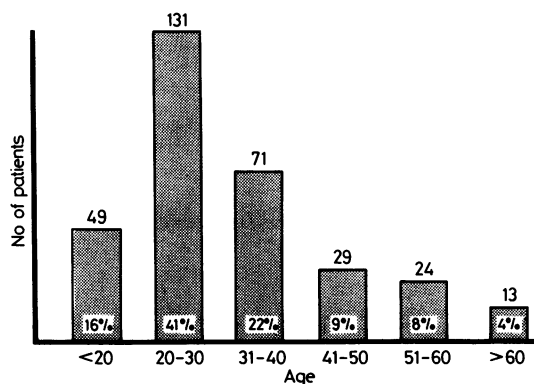


Fig 1 Age at operation in 317 patients undergoing thymectomy. There were 252 females and 65 males (female:male ratio 3.9:1).

years and 16% were below 20; we also, however, operated on 13 patients (4%) aged over 60.

Only eight patients (2.5%) were operated on who were in group 1 by the Osserman classification.<sup>21</sup> Four among these were suspected of having a thymoma that had not been found, and four others had double vision to such a degree that it made normal life very uncomfortable; they did not respond well to cholinergic drugs. Fifty nine patients (19%) were in group 2A and suffered mild generalised myasthenia gravis with ocular symptoms. Two hundred and fifty patients (78.5%) in groups 2B and 3 had surgery because of advanced symptoms. About 20% of patients suffered respiratory disturbances, and 11 of these were on ventilators at the time of surgery. Twenty nine patients received steroids before surgery with no improvement.

### Surgical technique

The first 80 patients were treated by conventional thymectomy through a median sternotomy. In 1978<sup>22</sup> we started to operate by a "small transverse sternotomy", and now this approach is used for all patients except those suspected of having an infiltrating thymoma.

A semicircular skin incision about 6 cm long is made just below the sternal angle, and subsequently the sternum is divided with a Gigli saw in the 2nd intercostal space (fig 2). With proper retraction of the divided sternum, good inspection of the anterior mediastinum and radical thymectomy are both possible. The internal thoracic arteries are very rarely ligated, and only if damaged accidentally. The thymus is retracted downwards and dissected (blunt dissection is usually preferred). Care is taken to dissect free the innominate vein and ligate the thymic veins. After re-

moval of the specimen one Redon suction tube is left in the mediastinum for 24 hours. If the pleural cavity is opened, it is drained by another Redon tube. The sternum is sutured with two wire stitches.

### Results

There were no hospital deaths among patients with myasthenia gravis, whereas two patients with infiltrating thymic tumours died in the postoperative period.

The postoperative course in most patients was uneventful. Two cases of wound suppuration and one pneumothorax requiring the insertion of an additional suction tube were observed. In one case it was necessary to resuture the sternum. In another case there was some bleeding from the innominate vein requiring extension of the incision and placing of stitches on this vessel.

In the first 24 hours after the operation no cholinergic drugs were administered. Usually they are started on the second postoperative day, at one third to one half of the preoperative dose. Minimal or no analgesic drugs are needed.

After operation 45 patients (14%) needed artificial

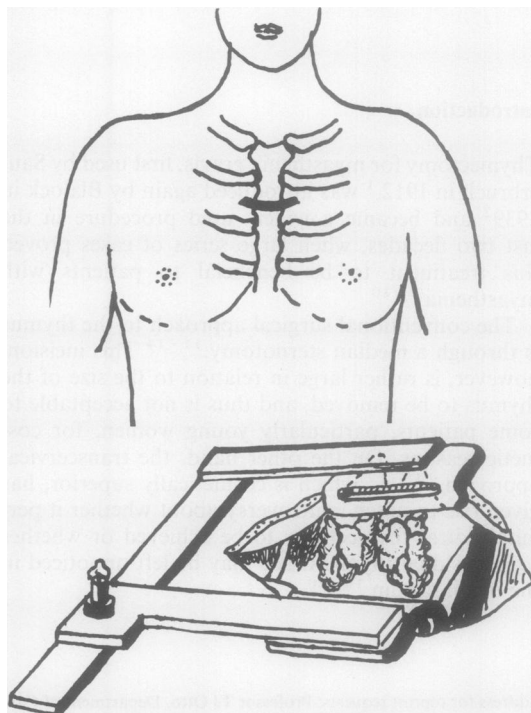


Fig 2 Small transverse sternotomy showing division of sternum at the level of the 2nd intercostal space.

ventilation, usually for three to five days. All of the patients who had been on the respirator before the operation were in this group. The longest time on a respirator was 14 days, in one case with a good outcome.

Two groups of patients were compared: 80 operated by median sternotomy and 257 operated by small transverse sternotomy. Indications for surgery and clinical classification were identical in the two groups. Statistically there was no significant difference between these two groups of patients, either in the early or the late results; but the postoperative course and cosmetic results were better in the latter group. As there were no statistical differences both groups are presented together.

#### MYASTHENIA GRAVIS EARLY RESULTS

The early results of thymectomy for myasthenia gravis in 317 patients were estimated about two weeks after the operation when the patients were being discharged (fig 3). At this stage the results were as follows: total remission (A) 8.5%, marked improvement (B) 42.5%, slight improvement (C) 40.5%. Eight and a half per cent of patients did not show improvement. The results improved, however, with the passage of time. All patients were followed up.

#### Results up to two years

Two hundred and fifty seven patients were reviewed from one and half to two years after the operation, by which time the full effect of thymectomy could have been expected; the results were satisfactory (fig 3). Total remission (A) occurred in 102 (39.5%), and considerable improvement (B) in 125 (48.5%). Only five patients did not show any improvement (D). Two patients (<1%) died during this period of observation; one death was not connected with myasthenia gravis, while the other was due to pulmonary complications.

Ninety eight patients (31%) received supplementary treatment with prednisone. In this group were all patients who had received it before the operation, as well as those patients who did not show improvement within three weeks of thymectomy, and who had presented with advanced bulbar or respiratory symptoms. Some patients who improved after thymectomy but had a relapse after a few months also received prednisone. The usual dose of prednisone was 80 mg on alternate days and this was maintained until improvement appeared (average four weeks), after which the dose was gradually decreased; but prednisone was given for up to six months or more. Ten patients have been receiving prednisone 20 mg a day for over five years; six of these have not been responding to cholinergic drugs. All these patients are symptom free and live and work normally, but when

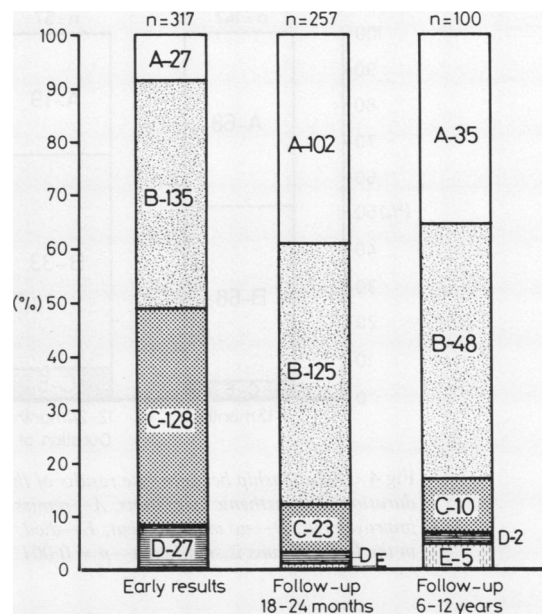


Fig 3 Results of thymectomy for myasthenia gravis as estimated two weeks after the operation and 18-24 months and six to 12 years later. All patients were followed up; the difference in numbers is due to length of observation. A—remission; B—great improvement; C—slight improvement; D—no improvement; E—died.

prednisone is stopped ocular and bulbar symptoms reappear.

The side effects of prednisone treatment occurred mainly in women: 40% had menstrual disturbances, weight increased in 30% of patients, and there was one case of osteoporosis of the thoracic vertebra. We did not observe cataract or diabetes among our patients taking prednisone. Thirty patients who did not improve with prednisone were subsequently treated with azathioprine or cyclophosphamide with satisfactory results.

#### Late results

Analysis of the long term results for all the operated patients showed a correlation between the duration of symptoms before the operation and the percentage of poor results (fig 4). Thus the shorter the duration of myasthenia gravis the better the results. This correlation was statistically significant ( $\chi^2 = 57.47$ ;  $p = 0.001$ ).

Every thymus that was removed was examined histologically; follicular hyperplasia of the thymus was diagnosed in about 70%; in the rest rudimentary thymus comprising adipose tissue and thymic foci or thymic cysts was found.



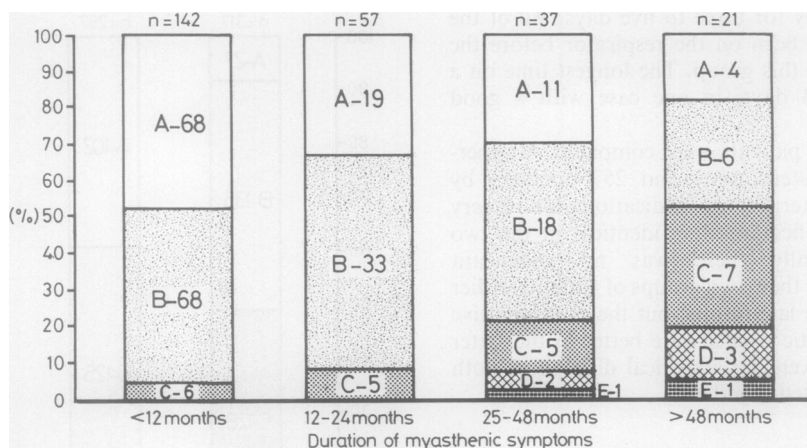


Fig 4 Relationship between late results of thymectomy for myasthenia gravis and the duration of myasthenic symptoms. A—remission; B—great improvement; C—slight improvement; D—no improvement; E—died. The observed difference in distribution of results in the four columns is significant— $p = 0.001$  ( $\chi^2 = 57.47$ ).

Electron microscopy was not relevant. No correlation between the number of germinal centres and the outcome of treatment was proved.

In one hundred patients the follow up interval after operation was six to 12 years. This was a most interesting group to investigate. It was found that in about 12% of patients with full remission and in about 20% of those with great improvement 18–24 months after thymectomy late relapse occurred three to five years later. All of these were examined by computed tomography. Reappearance of thymic tissue was not observed in any of these patients, there was no indication for surgical treatment, and no second operation was performed. Most of these 33 patients improved with steroid treatment; five improved after radiotherapy to the mediastinum.

The final results of treatment of these 100 patients may be considered satisfactory (fig 3). Total remission (A) amounted to 35% (23% after thymectomy alone, 12% after thymectomy and immunosuppression). Great improvement (B) was seen in 48% and some improvement (C) in 10%. Five of the 100 patients died during this long follow up. The causes of death were: pneumonia (two cases), cancer of the stomach (1), suicide (1), sclerosis lateralis amyotrophica (1).

Twenty women, including eight treated with steroids, after thymectomy gave birth to healthy children.

As in the group of patients examined 18–24 months after thymectomy, no significant correlation was found between the final results of treatment and the age and sex of patients or the severity of symptoms before the operation. The correlation between the du-

ration of symptoms before the operation and the final results of treatment was confirmed.

#### THYMOMA

The number of patients operated on because of thymoma with myasthenic symptoms is in our experience rather small. There were 12 patients with encapsulated thymic tumours (stage I<sup>23-26</sup>), which were resected radically. All patients after operation were submitted to x ray treatment. In six of the 12 it was also necessary to start and continue steroid immunosuppressive treatment. There was no evidence of recurrence or metastases of thymoma in any of these patients. The final results of treatment of this group of patients were: remission in five patients (two having continuous steroids treatment); great improvement in six patients (three having steroids); some improvement in one patient (having steroids). The observation time was from one to nine years (mean five years).

There were eight patients with infiltrating thymic tumours. Six (Stage II) were submitted to total excision, and two (Stage III) to palliative operation. From the former group two patients died, two and four years respectively after the operation, due to metastases, and four are alive for two to six years, mean four years. All of them were submitted to cobalt-therapy and chemotherapy. In two total remission (A) was achieved, in one marked improvement (B), and in one slight improvement (C). Both patients who had palliative operations died in hospital a few weeks later due to pulmonary complications.

## Discussion

The results of surgical treatment of myasthenia gravis are now very good. There are virtually no deaths in hospital. Improved postoperative management makes myasthenic and cholinergic crises uncommon and only a few operated patients require controlled respiration.

The advantages of thymectomy in the treatment of myasthenia gravis have been well demonstrated.<sup>5 7 8 23 24</sup> There is still some controversy regarding the surgical approach to the thymus.<sup>23</sup> In our opinion both the median sternotomy and the transcervical approach have some disadvantages: median sternotomy is cosmetically not acceptable and in itself is quite a big procedure; whereas the transcervical approach may not permit radical excision.

We propose the use of the small transverse sternotomy, which gives good exposure of the thymus, an uneventful postoperative course, and good cosmetic results. Long term results after thymectomy for myasthenia gravis through this approach are similar to the results achieved with median sternotomy in our own patients and to the results reported by others.<sup>23</sup> We must emphasise, however, that small transverse sternotomy provides limited exposure of the mediastinum and for that reason is not suitable for excision of large infiltrating thymomas.

Analysis of the results for the group of 100 patients with the longest follow up showed that recurrence of myasthenia gravis did occur, although it was relatively rare (12–20%). Patients with recurrence of symptoms reacted well to steroids, and with such treatment returned to the clinical state previously observed.

There is no doubt that steroid treatment considerably influenced our long term results. Once the beneficial effect of prednisone on myasthenia gravis was proved<sup>25 26</sup> we began to use it when the early result of thymectomy was not entirely satisfactory (group C and D), and when relapse occurred. This obscures the effect of thymectomy on myasthenia gravis in about one third of our patients; it is possible but unproved, that some of the patients who shortly after thymectomy were treated with prednisone would have improved without it with the passage of time. In general, prednisone was beneficial to the patients, particularly to those with recurrence of symptoms. We are therefore in favour of this supplementary treatment after thymectomy for myasthenia gravis.

The conclusions from our limited experience with thymomas are similar with those of others.<sup>23 27–29</sup> The prognosis of patients with a thymoma depends on its invasiveness. In patients with encapsulated thymic tumours undergoing radical excision results simi-

lar to those with myasthenia gravis may be expected.

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## References

- Schumacher CH, Roth P. Thymektomie bei einem Fall von Morbus Basedowi mit Myasthenie. *Mitt Grenzgeb Med Chir* 1912;**25**:746–65.
- Blalock A. Thymectomy in the treatment of myasthenia gravis. *J Thorac Surg* 1944;**13**:316–39.
- Keyness GL. The results of thymectomy in myasthenia gravis. *Br Med J* 1949;ii:611–6.
- Keyness GL. Surgery of the thymus gland. *Lancet* 1954;ii:1197–208.
- Eaton LM, Clargett OT. Present status of thymectomy in the treatment of Myasthenia Gravis. *Am J Med* 1955;**19**:703–15.
- Simpson JA. Evaluation of thymectomy in myasthenia gravis. *Brain* 1958;**81**:112–45.
- Perlo VP, Arnason B, Poskanzer D, et al. The role of thymectomy in the treatment of myasthenia gravis. *Ann NY Acad Sci* 1971;**183**:308–15.
- Perlo VP, Poskanzer DC, Schwab RS, et al. Myasthenia gravis; evolution of treatment in 1355 patients. *Neurology* 1966;**16**:413–39.
- Papatestas AE, Genkins G, Kornfeld P, Horowitz S, Kark AE. Transcervical thymectomy in myasthenia gravis. *Surgery* 1975;**140**:535–40.
- Papatestas AE, Alpert L, Osserman RS, Kark AE. Studies in myasthenia gravis: effect of thymectomy. *Am J Med* 1971;**50**:465–74.
- Cohn HE, Solit RW, Schatz NJ, Schlesinger N. Surgical treatment in myasthenia gravis. *J Thorac Cardiovasc Surg* 1977;**68**:876–84.
- Faulkner SL, Ehyai A, Fisher R, Fenichel G, Bendner H. Contemporary management of myasthenia gravis. The clinical role of thymectomy. *Ann Thorac Surg* 1977;**23**:348–52.
- Wolfe W. Surgical management of myasthenia gravis. *Ann Thorac Surg* 1972;**14**:645–9.
- Rzepecki W, Lukasiewicz M, Emeryk B. Ocena wartości leczenia miastonii wycięciem grasicy. *Pol Przegl Chir* 1979;**51**:1155–64.
- Grille G. Thymectomy through the neck. *Surgery* 1966;**59**:213–5.
- Klingen G, Johansson L, Westerholm GJ, Sundström C. The transcervical thymectomy with the aid of mediastinoscopy for myasthenia gravis: eight years experience. *Ann Thorac Surg* 1977;**23**:342–7.
- Kirschner PA, Osserman KE, Kark AE. Studies in myasthenia gravis. *JAMA* 1969;**209**:906–10.
- Jaretzki A, Bethes M, Wolff M, et al. A rational approach to total thymectomy in the treatment of

- myasthenia gravis. *Ann Thorac Surg* 1977;**24**:120-7.
- 19 Kuzin M, Szkrob O, Sołybkow W, Ippolitow J. Chirurgicznoje leczenie generalizowanoj miastenii. *Chirurgia* 1981;**2**:72-81.
  - 20 Masaoka A, Monden Y. Comparison of the results of transsternal simple, transcervical simple and extended thymectomy. *Ann NY Acad Sci* 1981;**377**:755-64.
  - 21 Osserman KE, Genkins G. Studies in myasthenia gravis: review of a twenty year experience in over 1200 patients. *Mt Sinai J Med* 1971;**38**:497-537.
  - 22 Otto T, Strugalska H, Kudelski Z. Postępy w chirurgicznym leczeniu miastenii. *Pol Przegl Chir* 1981;**53**:1:23-34.
  - 23 Oesterhius HJGH. Myasthenia gravis. Edinburgh: Churchill Livingstone, 1984:62-3, 68-72.
  - 24 Viets HR, Schwab RS. Thymectomy for myasthenia gravis. Springfield, Illinois: Charles C Thomas, 1960:117-30.
  - 25 Warmolts JR, Engel WK. Benefit from alternate-day prednisone in myasthenia gravis. *Neurology* 1971;**21**:412-7.
  - 26 Warmolts JR, Engel WK. Benefit from alternate-day prednisone in myasthenia gravis. *JAMA* 1972;**286**:17-20.
  - 27 Bergh NP, Gatzinski P, Larsson S, Lundin P, Ridell B. Tumors of the thymus and thymic region; clinico-pathological studies on thymomas. *Ann Thorac Surg* 1978;**25**:91-8.
  - 28 Masaoka A, Monden Y, Nakahara K, Tamioka T. Follow up study of thymomas with special reference to their clinical stages. *Cancer* 1981;**48**:2485-92.
  - 29 Wilkins WE, Castleman B. Thymoma; a continuing survey at the Massachusetts general hospital. *Ann Thorac Surg* 1979;**28**:252-6.