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# Intrathoracic neural tumours

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**Davidson, K. G., Walbaum, P. R., and McCormack, R. J. M. (1978).** *Thorax*, **33**, 359–367.
**Intrathoracic neural tumours.** The experience of one regional thoracic surgical unit in managing intrathoracic neural tumours over a 25-year period is presented. Neural tumour was diagnosed in 55 patients, of whom 41 were asymptomatic. In 11 patients complete resection was not achieved—the reasons for this and its effect on the outcome of the patient are discussed. There were 52 posterior mediastinal and three lateral chest wall tumours. The pathological distribution was as follows—benign nerve sheath tumours (neurofibroma, neurilemoma) 39, ganglioneuroma 13, and neuroblastoma 3. One neurofibroma recurred as a neurosarcoma six years after its apparently complete resection and was removed by an extensive resection at reoperation. One neuroblastoma recurred within the spinal canal four years after incomplete excision at thoracotomy—this patient died subsequently of widespread metastatic neuroblastoma. No other tumour is known to have recurred.

Intrathoracic neural tumours are uncommon but account for about 75% of tumours of the posterior mediastinum (Curreri and Gale, 1949). The terminology of these tumours varies throughout the world, and the pathological classification into distinct types on the basis of the cell of origin can be difficult. In this paper the benign tumour arising from the Schwann cell is called neurilemoma and that arising from the nerve sheath is called neurofibroma. Occasionally features of neurilemoma and neurofibroma co-exist, and this mixed pattern is best accepted as a benign nerve sheath tumour without attempting further classification. The malignant form of these two tumours is neurosarcoma. Benign tumours of nerve cell origin, most of which arise from the autonomic nervous system, are called ganglioneuromas. There is, however, a complete spectrum of differentiation between the benign ganglioneuroma and the malignant neuroblastoma. Unfortunately, many of these tumours of nerve cell origin are large and, while in one area the appearances may be quite benign, it is common to find other areas where the cellular pattern is much less differentiated. This is further complicated by the fact that such tumours in young children may show areas of very poor differentiation and may yet behave as benign ganglioneuromas.

Tumours of the paraganglion cells—phaeochromocytoma and chemodectoma—have not been included in this series, although embryologically they may originate from neural crest tissue. The presentation and investigation of patients with intrathoracic neural tumours has been fully discussed elsewhere (Cruickshank, 1957; Morrison, 1958; Le Roux, 1960; Oosterwijk and Swierenga, 1968) —they are reviewed only briefly here. The pathological behaviour patterns are looked at in more detail with particular emphasis on those factors that determine outcome.

## Patients

Between 1949 and 1974, 55 patients with intrathoracic neural tumours were seen in this unit. The male to female ratio was 1 : 1·3, and the slight female preponderance is typical of that found in other series. The age range at presentation was 7 months to 63 years (average 33 years). The distribution of tumour type within the various age groups is shown in Fig. 1. As would be expected, most tumours of nerve cell origin, both benign and malignant, occurred in the younger age groups, and the average age of this subgroup was 18. The tumours affected left and right sides of the chest with equal frequency and were evenly distributed from apex of thorax to diaphragm (Fig. 2). There were 52 posterior mediastinal neural tumours and three neurofibromas arising from intercostal nerves of the lateral chest wall.

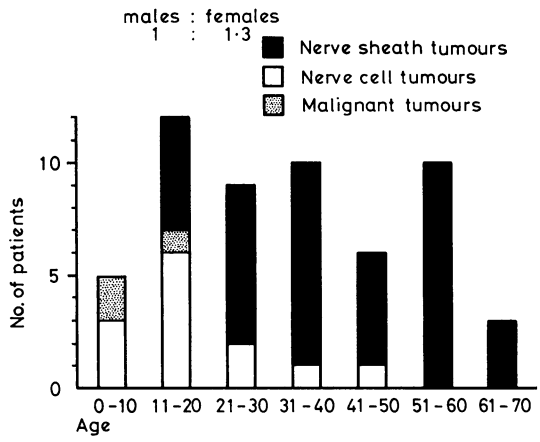



Fig. 1 *Relative incidence of different types of neural tumour in different age groups.*

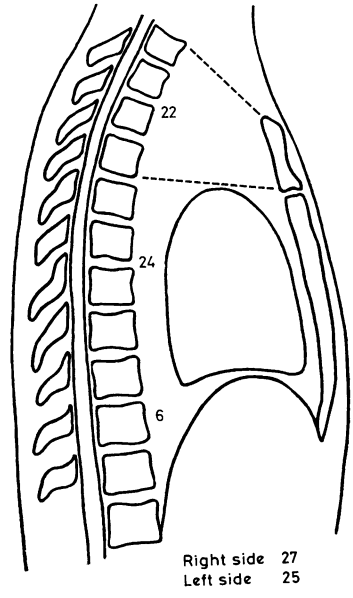



Fig. 2 *Anatomical distribution of neural tumours.*

## Presentation

In this series 75% of the patients were asymptomatic and their tumour was a chance finding on routine chest radiography (Table 1). Three patients had intrathoracic neurofibromas as manifestations of von Recklinghausen's disease. Neurological disturbances produced by these tumours were uncommon—only four patients complained of pain in the distribution of the nerves affected by their tumour. One baby with a large neuroblastoma in the right superior mediastinum presented with Horner's syndrome, as did one adult with a similarly situated benign tumour. One young man presented with symptoms and signs of spinal cord compression at midthoracic level, and was shown to have tumour both in his posterior mediastinum and in his vertebral canal. Respiratory symptoms were also uncommon, being associated mainly with the more bulky type of tumour. Two patients presented with cough and shortness of breath, the tumour in one of these being so large that it had to be cut into three pieces before it could be delivered from the chest. One patient presented with cough as his only symptom and one with breathlessness, but in neither case was the tumour remarkable as regards site or size, and the explanation of these complaints is not clear. Various other symptomatic presentations have been described—pneumonia, empyema, stridor, haemoptysis, hoarseness, and dysphagia, but none of these was seen in any of our patients.

Table 1 *Presentation of neural tumours*

| | | | |
|---|---|---|---|
| Chance radiographic finding | 41 | Neurological symptoms | |
| Von Recklinghausen's syndrome | 3 | Pain | 4 |
| Pulmonary symptoms | | Horner's syndrome | 2 |
| Dyspnoea | 3 | Spinal cord pressure | 1 |
| Cough | 3 | | |

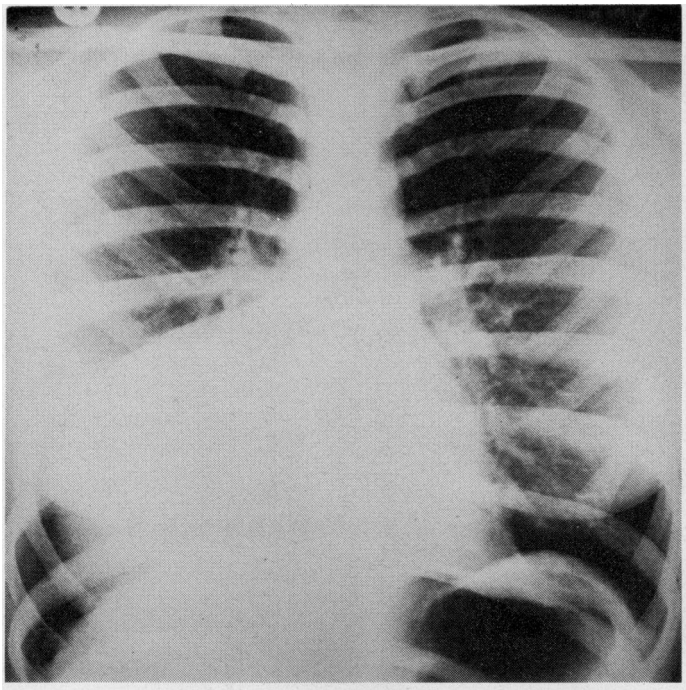
## Investigations

The classical radiographic features of mediastinal neural tumours (Parish, 1957—posterior situation, hair-line margin, uniform density, and D-shaped outline in the lateral projection—were present in most patients (Figs. 3a and b). Ten patients had associated rib deformities adjacent to the lesion, and all ten had benign tumours. Two of these ten patients were also recognised to have vertebral anomalies (Fig. 4).

Most patients underwent barium-swallow examination and, as would be expected, oesophageal displacement was occasionally seen in patients with large tumours. A minority in whom there was doubt about the diagnosis were subjected to bronchoscopy, but in no patient was there any bronchoscopic abnormality. In one patient who had an atypical radiographic appearance the diagnosis was made first at mediastinoscopy and confirmed subsequently at thoracotomy.

## Management

The policy of this unit has always been that all patients with suspected intrathoracic neural tumours should have thoracotomy and resection of



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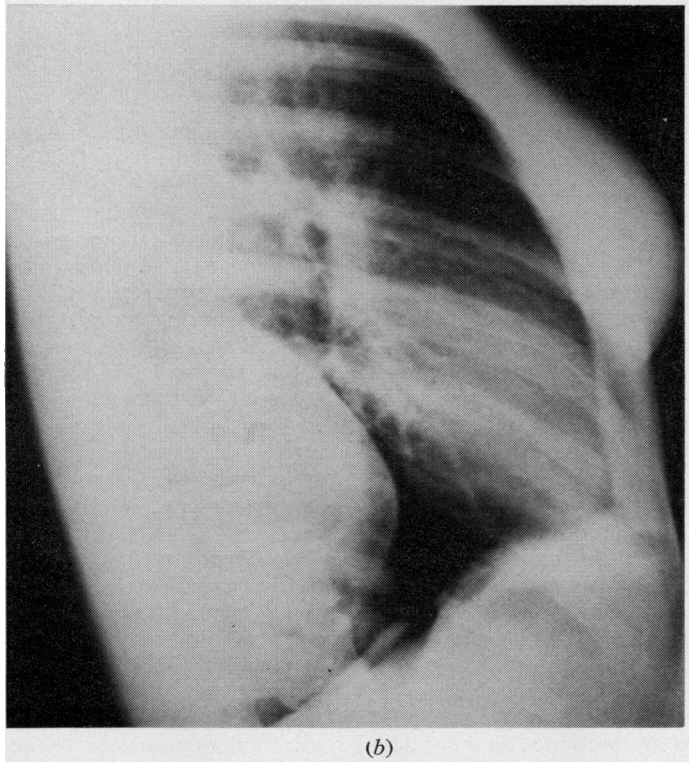

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Fig. 3(a) and (b) ***Chest radiographs showing typical posterior mediastinal neural tumour.***

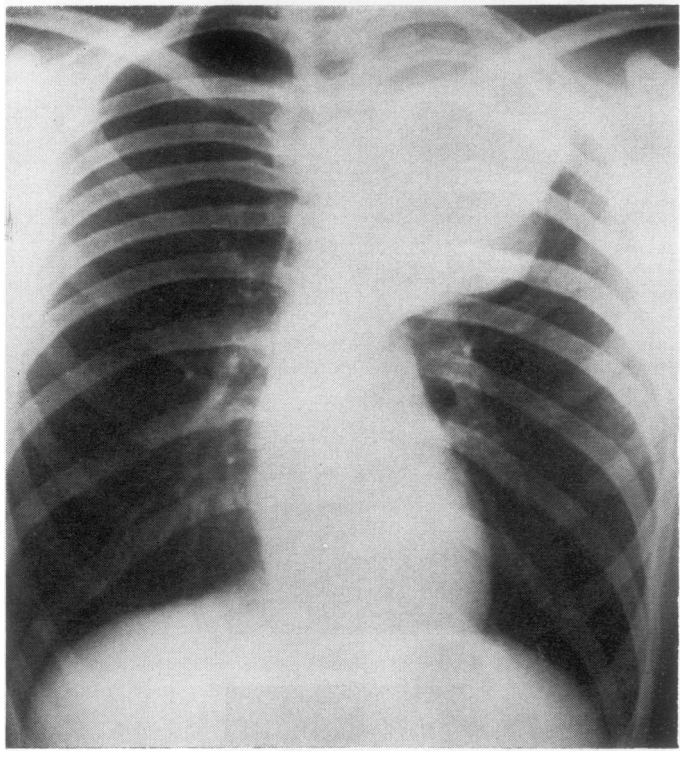


Fig. 4 *Chest radiograph showing large neural tumour with associated rib and vertebral abnormalities.*

their tumour because of doubt about the diagnosis and the possibility of malignancy. It is also clear that as a tumour enlarges it will produce pressure effects on surrounding structures, which may necessitate its excision. The surgical approach is lateral thoracotomy and the tumour mass, covered by pleura, is easily identified. The lung is not usually adherent to it, and the mass can be mobilised without difficulty. Division of the nerve or nerves of origin will have to be carried out, and division of intercostal arteries may also be required. In the benign tumour there is an easily developed plane between tumour and rib, the latter usually appearing bare of periosteum and often deformed by pressure of the tumour.

The objective of complete tumour removal was apparently attained in 80% of patients, and in no patient in this series was the resection accomplished without the division of one or more nerves. Up to four intercostal nerves have needed division, as have the sympathetic trunk and vagus from which tumours were originating. The reasons for failure to achieve complete resection and its effect on the patients are presented in more detail in Table 2.

There were found to be three situations in which neural tumours were deemed to have been incompletely resected:

DIRECT EXTENSION OF TUMOUR INTO INTERVERTEBRAL FORAMINA

Eight patients were found to have finger-like processes extending from the main tumour mass into one or more intervertebral foramina. In all of these patients there was residual tumour visible within the foramina after excision of all tumour accessible at thoracotomy. It is of interest that in all eight patients the tumours were of nerve cell origin, seven being ganglioneuromas and one a neuroblastoma. There were four male and five female patients in this group, and their average age was 15. Only one of the patients presented with symptoms that were clearly related to the intervertebral extension of his tumour. This was a young man with symptoms and signs of spinal cord compression at midthoracic level, confirmed by myelography and then laminectomy. Four patients in this group underwent myelography and three of these subsequently came to laminectomy. Intervertebral tumour was found in two of the three patients (cases 1 and 4). In these two cases the tumour was excised, but the outcome was very

Table 2 *Incomplete resection of neural tumours*

| | *Case* | *Age* | *Sex* | *Clinical features* | *Pathology* | *Outcome* | *Follow-up (years)* |
|---|---|---|---|---|---|---|---|
| Direct vertebral extension | 1 | 22 | M | Cord symptoms and signs | GN | Well | 10 |
| | 2 | 24 | F | None | GN | Well | 9 |
| | 3 | 7 | F | Dyspnoea | GN | Well | 11 |
| | 4 | 15 | F | None | NB | Recurred 4 years | |
| | | | | | | Died | 8 |
| | 5 | 4 | F | Cough and weight loss | GN | Well | 4 |
| | 6 | 15 | M | None | GN | Well | 5 |
| | 7 | 20 | M | Chest pain | GN | Well | 2 |
| | 8 | 14 | M | None | GN | Well | 8 |
| Cervical extension | 9 | 1 | F | Horner's syndrome | NB | Well | 10 |
| Multiple tumours | 10 | 19 | F | None | NF | Well | 8 |
| | 11 | 14 | F | None | NF | Well | 5 |

GN=ganglioneuroma; NB=neuroblastoma; NF=neurofibroma.

different. Patient no. 1 is alive and well and in full-time work ten years after surgery. Patient no. 4 remained well for four years after her original thoracotomy before symptoms of spinal cord compression developed. At laminectomy, dumb-bell-like tumour masses extended through the intervertebral foramina on both sides and although complete resection was attempted it was thought that it had probably not been achieved. The pathological appearances were regarded as those of neuroblastoma. Despite the attempted radical surgery, followed by radiotherapy, the tumour advanced, and the patient died of widespread metastases eight years after the original incomplete resection of her mediastinal tumour. The other seven patients in this group are alive and well at follow-up periods ranging from two to 11 years.

CERVICAL EXTENSION

Only one example of cervical extension was found (Table 2)— a young girl with a Horner's syndrome and a large mass in the posterior mediastinum on chest radiography. At operation, soft tumour filled the upper third of the right hemithorax, and there were long extensions into the neck and brachial plexus. At the posterior end of the first intercostal space was an enlarged soft lymph node that was excised along with all intrathoracic tumour, but the extensions into the neck and brachial plexus were not removed. The pathological appearances were those of neuroblastoma, which was also present in the excised lymph node. The neck and right upper thorax were irradiated subsequently but chemotherapy was not used. Ten years after resection she remains well, though the right upper thorax is shrunken and the overlying skin telangiectatic. There is no clinical or radiological evidence of tumour recurrence.

MULTIPLE TUMOURS

Of the two patients in this group (Table 2), one (case 10) was recognised to have had generalised neurofibromatosis in childhood and this had been confirmed by biopsy of a cutaneous lesion. Chest radiography, however, had shown the presence of a new mass in the posterior mediastinum and because of the possibility of malignancy it was thought that thoracotomy should be undertaken. Every visible nerve was studded with small tumours, and resection of only the main tumour mass was performed. Three months after thoracotomy she developed back pain and this was put down to a scoliosis, which had been present for several years. Myelography was carried out but did not show any evidence of intraspinal tumour, and it was thought that her symptoms were due to her scoliosis. A spinal fusion was carried out subsequently, and at this operation there was extensive paravertebral tumour, apparently separate from the mediastinal tumour. Eight years later she remains well, having no further treatment.

The other patient in this group (case 11) was not known to have generalised neurofibromatosis and was found to have a posterior mediastinal opacity. At thoracotomy, however, a tumour mass extended from the pleural dome to the azygos vein and nodules were present down the entire course of the vagus nerve to the diaphragm. The upper pole of the main tumour mass extended into the neck along the expected course of the vagus nerve. A low right cervical incision showed tumour along the vagus nerve to the level of the hyoid bone, above which the nerve appeared normal. The vagus was divided at this level and the main tumour removed. The mediastinal tissues were also apparently infiltrated by tiny nodules, and several of these were taken for biopsy. All specimens were neurofibromas, and there were multiple minute

neurofibromas throughout all the tissues. This case is unique in our experience in that other than the described tumour there was no evidence of generalised neurofibromatosis. She remains well five years after operation with no evidence of generalised neurofibromatosis or recurrent or residual tumour.

## Results and complications

In this series over 70% of tumours were benign nerve sheath tumours—neurofibromas (45%) neurilemomas (13%), and a mixed pattern with both neurofibroma and neurilemoma elements in them (13%). The remainder were all nerve cell tumours; benign ganglioneuromas (24%) and neuroblastomas (5%) (Table 3). The overall incidence of malignancy was only 6%—well within the reported range of 3% (Blades, 1946) to 19% (Morrison, 1958). The results and complications related to the excision of these tumours are presented in Table 4.

Table 3 *Relative frequency of neural tumours*

| | | | |
|---|---|---|---|
| Nerve sheath tumours | | Nerve cell tumours | |
| Neurofibroma | 25 | Ganglioneuroma | 13 |
| Neurilemoma | 7 | Neuroblastoma | 3 |
| Mixed pattern | 7 | Total | 55 |

Table 4 *Results and complications*

| | | | |
|---|---|---|---|
| Deaths | | Recurrence after complete resection | 1 |
| Related to neural tumour | 1 | Horner's syndrome | 5 |
| Unrelated | 1 | Sympathectomy of arm | 3 |
| Incomplete resection | | Brachial plexus signs | 2 |
| Vertebral extension | 8 | Left recurrent nerve paralysis | 1 |
| Cervical extension | 1 | | |
| Multiple tumours | 2 | | |

Of the 52 patients whose benign neural tumours were excised, none is known to have died as a consequence of tumour recurrence. One patient, however, had a benign neurilemoma excised from her right posterior mediastinum in 1957, and ten years later she presented with irresectable oat cell carcinoma of the bronchus. She died soon after presentation, and at necropsy there was no evidence of recurrence of her neural tumour. Eleven patients with mediastinal neural tumours, which it proved impossible to resect completely, have already been described. One of these, case 4, died as a consequence of recurrence of her neuroblastoma. The two patients with generalised neurofibromatosis are unchanged. None of the other eight patients is known to have tumour recurrence.

One of the three patients with lateral chest wall neurofibromas, an asymptomatic man of 28, whose tumour was apparently completely resected, developed multiple opacities in the same area six years after his original operation. Re-exploration showed two hard tumours adherent to the angles of the 4th and 5th ribs and a third lump adherent to or possibly even within the apical segment of the left lower lobe. All tumour tissue, along with 8-cm lengths of the 4th and 5th ribs, the intercostal muscles, and a portion of the apical segment of the left lower lobe, were resected. The pathologist reported that all three tumour masses were quite different from the original benign neurofibroma and now showed undoubted neurosarcoma. After operation the patient developed an empyema that needed further surgical treatment but he remains well at present with no evidence of tumour recurrence, though the follow-up period is only one year.

Two of the three patients with neuroblastomas have already been presented in the group of incomplete resections (cases 4 and 9). The third such tumour was in an 18-month-old boy who was found to have an abnormal chest radiograph during the investigation of diarrhoea, later shown to be due to salmonella infection. At thoracotomy, a tumour filled one third of the left hemithorax, and there was a posterior mediastinal pedicle extending from the 4th to the 9th intercostal bundles. Contributions to the pedicle came from four of these intercostal bundles, all of which required division, and resection appeared to be complete. The pathological features were those of neuroblastoma, in parts quite well differentiated. Four years later, without further treatment, he was well, with no clinical or radiological evidence of recurrence.

There were few complications of the surgical procedure itself, and these were mainly the predictable ones produced by division of the nerve or nerves from which the tumours originated. Thus, excision of five tumours from the superior mediastinum at the thoracic inlet (Fig. 5) produced Horner's syndrome. Three of these five were noted to have had a sympathectomy of the homolateral arm, and two of the same group also suffered damage to the anterior primary rami of the first and second thoracic nerves. One patient was found at operation to have a large left superior mediastinal tumour originating from the vagus nerve (Figs. 6a and b) and, inevitably, had a left recurrent nerve palsy after excision of the tumour. The lesion was reported to be a benign neurilemoma. No other major complications have been recorded in this series.

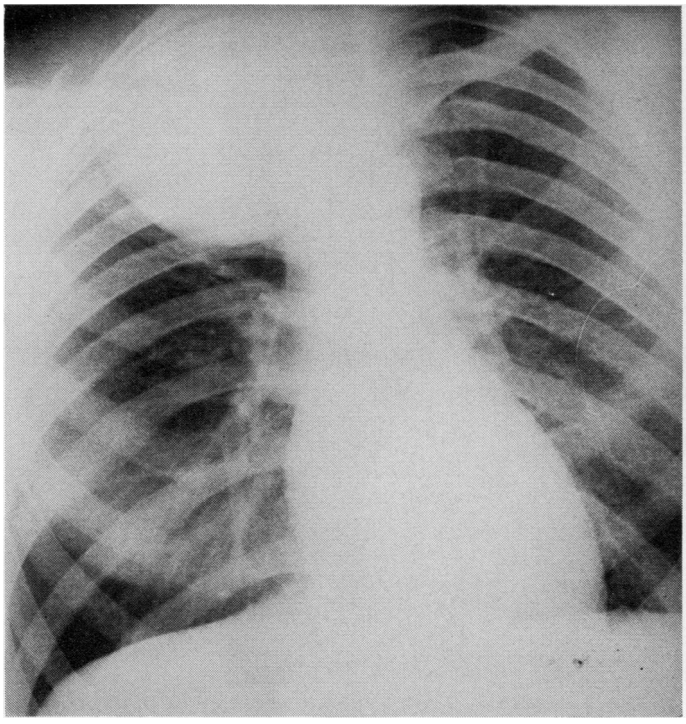


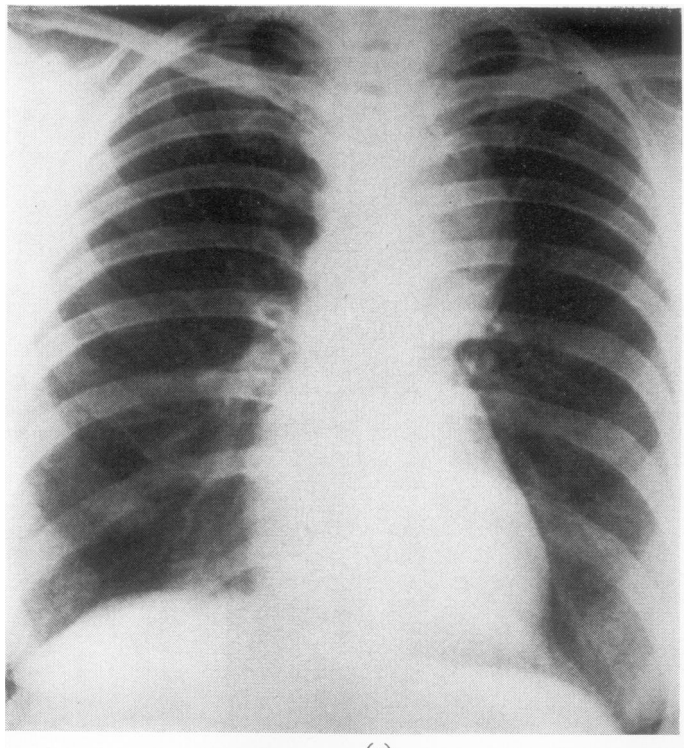
Fig. 5 *Chest radiograph showing large posterior neural tumour occupying much of right upper hemithorax.*

## Discussion

Analysis of this series of intrathoracic neural tumours illustrates some of the difficulties of pathological diagnosis and surgical management in this uncommon group of tumours. Because of doubt about the diagnosis, increasing size of tumour, and the possibility of malignancy, early surgical exploration and resection is a universally accepted policy. Most patients clearly present little problem if this objective is achieved—the asymptomatic patient, usually a young adult with a typical posterior mediastinal opacity, will have this tumour completely excised and its benign nature confirmed by the pathologist. This series suggests that in about 20% of patients complete resection at thoracotomy will not be possible. If there are dumb-bell-like extensions passing into intervertebral foramina, then the lesion is most likely to be a ganglioneuroma originating from the sympathetic trunk and the correct management is excision of all accessible intrathoracic tumour. This can be followed four to eight weeks later by myelography to assess the extent of the intervertebral tumour. Exploration for intraspinal tumour by laminectomy would then be undertaken only if the myelogram showed tumour at the relevant site.

If multiple tumours are present they are likely to be neurofibromas and may be manifestations of von Recklinghausen's disease. In this situation it is recommended that the main tumour mass should be excised, but clearly there is no point in attempting to excise multiple neurofibromas, which may well be minute and may affect virtually every nerve within the chest. There will always be a risk that this type of patient may eventually develop a neurosarcoma, but there is no known way of preventing this. In anteriorly situated neural tumours there is a higher incidence of malignancy (Efskind and Liavaag, 1950), but such tumours are very rare (Kent *et al.*, 1944).

The difficulties of the pathologist are perhaps greater than those of the surgeon, but the minutiae of pathological interpretation are beyond the scope of this paper and have been fully discussed elsewhere (Russell and Rubinstein, 1969). Nerve sheath tumours of mixed pattern are common, and the appearances may vary from section to section of the same tumour. To the surgeon, the distinction between neurofibroma and neurilemoma is of relatively little importance, although the latter is usually more encapsulated. Histologically, the appearance of the malignant neurosarcoma is usually quite distinctive and does not present a major diagnostic problem to the pathologist. The area of greatest concern in this field



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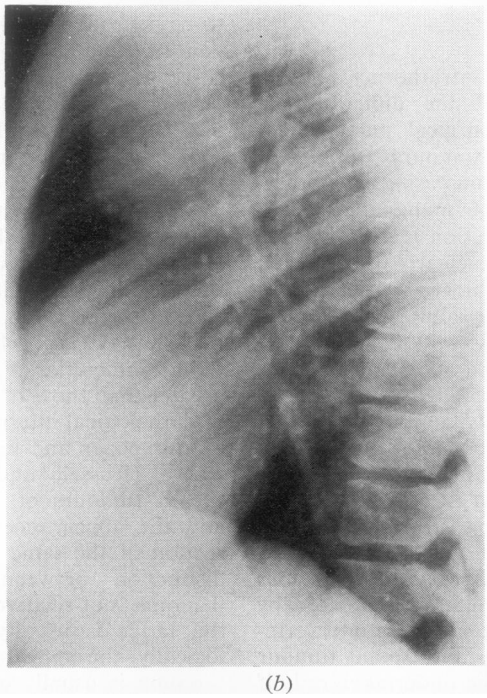

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Fig. 6(a) and (b) ***Chest radiographs showing ganglioneuroma originating from left vagus nerve.***

is in the interpretation of the nerve cell tumour, with benign ganglioneuroma at one end of the spectrum and undifferentiated neuroblastoma at the other. Between these two extremes, all varieties of differentiation are found, different degrees being seen in different parts of the same tumour. Prediction of tumour behaviour is particularly difficult in the young child where a certain lack of differentiation may be seen in a tumour that otherwise behaves in a wholly benign manner.

The policy of this unit has been that if a neural tumour appears to have been completely excised and is reported as a benign ganglioneuroma no further treatment is offered, and the patient is merely kept under observation for a prolonged period. If, however, a ganglioneuroma has been incompletely resected it is more difficult to be specific about the appropriate management—myelography should probably be carried out, but laminectomy only if intraspinal tumour is suspected radiologically. Nor is there universal agreement as to management when the excised tumour is reported as a neuroblastoma. When excision appears complete, it would seem reasonable to proceed with close observation, particularly if the patient is a young child, but also to consider either radiotherapy or chemotherapy at that stage. If resection were incomplete, or possibly incomplete, further treatment in the form of radiotherapy or chemotherapy or both is instituted. Following this policy, two of the three patients in this series who had neuroblastomas excised remain well four years and ten years after resection. Both of these were young children, and one was irradiated because of incomplete resection. The third patient with neuroblastoma died eight years after resection despite irradiation, with extensive recurrence of her tumour. The only other patient known to have recurrent tumour had a benign lateral chest wall neurofibroma excised, and this recurred six years later as a neurosarcoma—it was again resected and has not recurred to date.

Several authors have pointed out recently that in patients who present with typical posterior mediastinal neural tumours the likelihood of malignancy is low, and a reasonable course of action would be merely to continue with regular observation and perhaps avoid a thoracotomy. We have found, however, that it has not been possible to distinguish clinically or radiologically between benign and malignant tumours. With improvements in radiotherapy and chemotherapy, this distinction is becoming increasingly important. Doubt about the diagnosis and increase in size of the tumour mass remain indications for surgical excision. There has been no mortality from the surgical procedure itself, and the morbidity has been very small—almost entirely complications directly related to the excision of affected nerves. In addition, all three patients with neuroblastomas underwent radical surgery followed by radiotherapy, and in only one of these has the tumour recurred. Although primary intrathoracic neuroblastomas carry a less ominous prognosis than similar intra-abdominal tumours, it has been suggested (Koop *et al.*, 1955) that wide excision, even if incomplete, may lead to increased survival. For these reasons, we consider that the most appropriate management policy for patients with suspected intrathoracic neural tumours remains surgical excision.

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