

Repeated partial endoscopic resections as treatment for two patients with inoperable tracheal tumours

G. NAKRATZAS, J. P. M. WAGENAAR, M. REINTJES,
E. SCHEFFER, and J. SWIERENGA

*Department of Pulmonary Diseases, University Hospital, Leiden, and
Pathological Laboratory, University of Leiden, The Netherlands*

Nakratzas, G., Wagenaar, J. P. M., Reintjes, M., Scheffer, E., and Swierenga, J. (1974). *Thorax*, 29, 125–131. **Repeated partial endoscopic resections as treatment for two patients with inoperable tracheal tumours.** Two cases of tracheal tumour are described, one a carcinoid and the other an adenoid cystic carcinoma (cylindroma). Both patients were treated by repeated partial bronchoscopic resections. The patients are in good health nine and three years respectively after treatment.

We report two cases of tracheal tumour—a carcinoid, which is a rare occurrence in the trachea, and an adenoid cystic carcinoma, which is not an unusual type of tracheal tumour. These cases are of interest primarily because of the therapy applied. A complete resection was impossible owing to the size of the tumour. Irradiation did not seem favourable. Therefore, we chose repeated partial endoscopic resections.

CASE REPORTS

CASE 1 A 73-year-old man was sent to the Department of Thoracic Surgery of the University Hospital, Leiden for surgical treatment of a tumour of the trachea which had been diagnosed elsewhere in May 1964. He was complaining of intermittent haemoptysis, cough, stridulous respiration, and slowly increasing dyspnoea for two years. Physical examination at the time of his admission to hospital was negative except for inspiratory and expiratory stridor.

Radiographic investigation of the trachea (Fig. 1) revealed a polypoid tumour mass which was localized to the posterior wall and caused severe stenosis of the lumen of the trachea. Bronchoscopic examination (Fig. 2) confirmed this finding. The tumour mass was approximately 7 cm long and originated 2 cm below the vocal cords, from the pars membranacea. The surface was coarsely nodular and showed no ulceration. On expiration the lumen of the trachea was almost completely obstructed. Diagnostic biopsies were taken.

Pathological findings Microscopic examination of the tumour tissue revealed large areas of epithelial

cells, which were often polygonal, having a round or oval nucleus with a fine chromatin pattern and slightly eosinophilic cytoplasm. There was little nuclear pleomorphism and the tumour tissue as a whole had a uniform nuclear pattern. It contained numerous blood vessels lying in thin strands of connective tissue between groups of tumour cells. Only a few mitotic figures were seen. A narrow band of subepithelial connective tissue was free of tumour; the surface epithelium in most parts showed squamous metaplasia. This histological picture was entirely compatible with a carcinoid (Fig. 3); it remained the same throughout the years.

Enzyme activities were studied histochemically in this tumour tissue in 1965 and 1973 (Fig. 4). There was no change in the activities of the enzymes investigated. No activity of alkaline phosphatase was present in the tumour cells, but there were many capillaries with activity of alkaline phosphatase in the endothelial cells. The cells of this particular carcinoid tumour had an extremely high activity of adenosine-triphosphatase (ATPase). The activity of this enzyme is usually less in most carcinoid tumours but is never completely absent (Willighagen, van der Heul, and van Rijssel, 1963). The combination of the presence of many capillaries with activity of alkaline phosphatase in endothelial cells and activity of ATPase in the tumour cells is characteristic of carcinoid tumours: this combination is not seen in other tumours of the respiratory tract (Willighagen, 1973).

Therapy Complete resection of the tumour with reconstruction of the tracheal wall was impossible because of the size of the tumour and the patient's age. It was decided, therefore, to try to remove bronchoscopically as much tumour tissue as possible. For this purpose the patient was transferred to the

Requests for reprints: Dr. J. P. M. Wagenaar, Department of Pulmonary Diseases, Leiden University Medical Centre, Leiden, The Netherlands

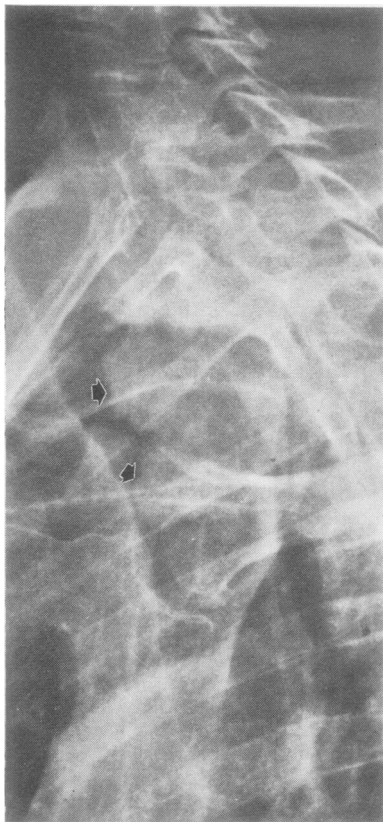


FIG. 1. *Case 1. Radiograph of the trachea, left anterior oblique position. The trachea is almost completely obstructed by a large tumour mass originating in the posterior wall.*

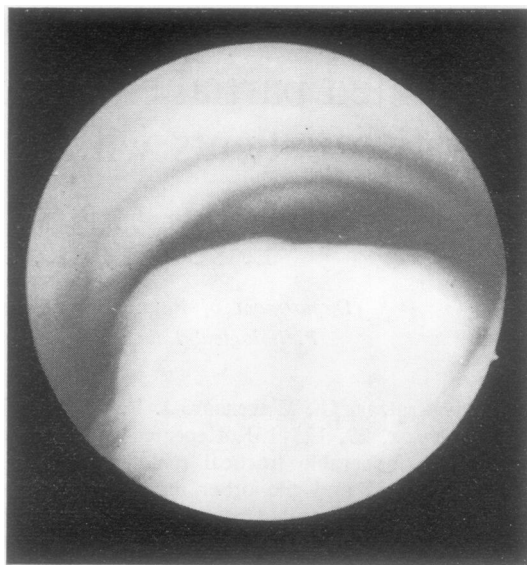


FIG. 2. *Case 1. The lumen of the trachea as seen at bronchoscopy is narrowed by a tumour mass originating in the pars membranacea.*

Department of Pulmonary Diseases. Bronchoscopy was performed under general anaesthesia. Bleeding from traumatized tumour tissue was easily controlled with electrocoagulation. Postbronchoscopic radiological examination of the trachea (Fig. 5) showed satisfactory restoration of the lumen. The radiological findings were confirmed bronchoscopically (Fig. 6). A few days later the patient was sent home in good condition; the stridulous respiration had disappeared completely. From 1964 to 1970 bronchoscopic treatment was repeated seven times with good results.

In January 1972 the patient was readmitted to hospital complaining of haemoptysis and dyspnoea; he had severe stridor. At bronchoscopy the tumour appeared to be of such a size that resection did not seem to be justified. In case of bleeding or oedema it might not have been possible to restore quickly the patient's ventilation. Therefore the procedure was

restricted to a minimal biopsy. Despite this a few hours later the patient suddenly developed severe respiratory insufficiency, presumably caused by bleeding or oedema at the site of the biopsy. Respiration was restored by immediate intubation. It was decided to perform a low tracheotomy to ensure adequate ventilation; the tumour was later removed in several bronchoscopic sessions. After two weeks the patient was discharged home in good condition without a tracheal cannula. The latest bronchoscopic examination in March 1973 revealed an adequate tracheal lumen.

CASE 2 A 64-year-old woman was admitted to our department in April 1970 because of haemoptysis and stridulous respiration. Physical examination did not reveal any signs except stridulous respiration. A tracheogram (Fig. 7) showed a clearly visible tumour localized to the posterior wall of the trachea. Bronchoscopic investigation confirmed this finding. An 8.5 cm long tumour mass was seen originating from the pars membranacea of the trachea. The tumour surface was coarsely nodular and without ulceration. The lumen of the trachea was severely stenosed.

Pathology The tumour tissue taken at biopsy from this patient originally showed the classic histological picture of an adenoid cystic carcinoma (Fig. 8). It consisted of sheets and cords of small cells with little cytoplasm and an oval basophilic nucleus; the cells were separated by stroma with fine collagenous

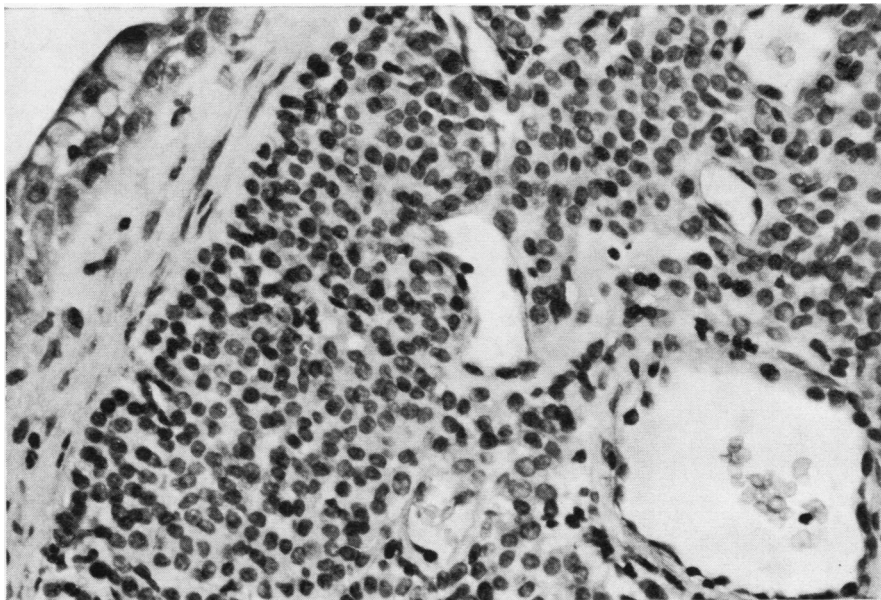


FIG. 3. Case 1. The histological picture is entirely compatible with carcinoid. Haematoxylin and eosin $\times 160$.

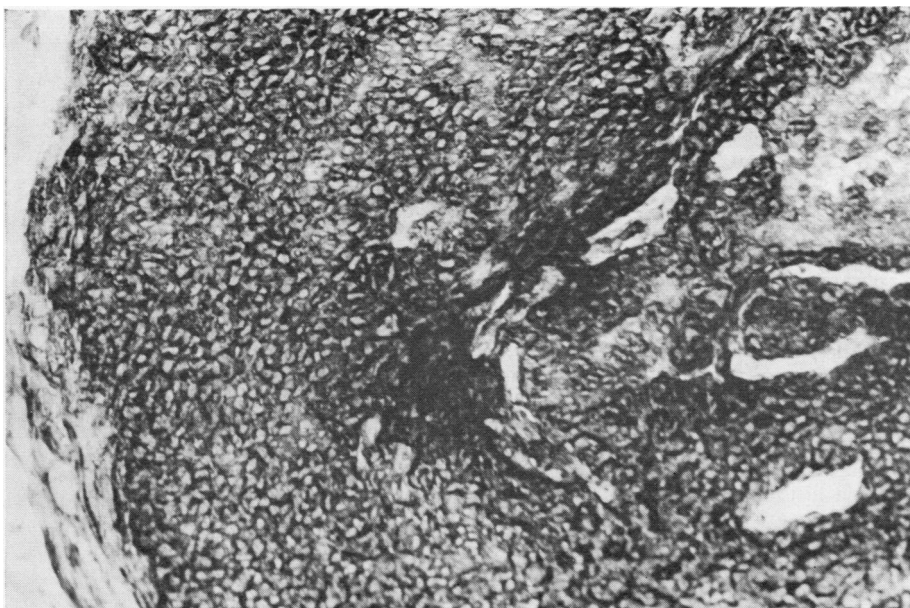


FIG. 4. Case 1. Intense activity of adenosinetriphosphatase (black precipitate of lead sulphide) in the cytoplasm of the tumour cells. The nuclei are negative $\times 200$.

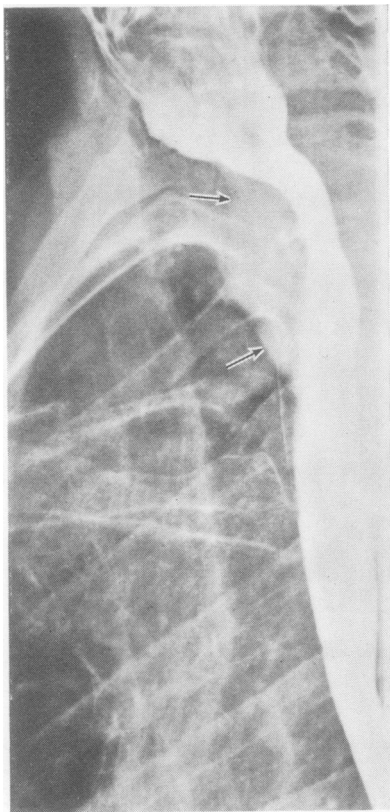


FIG. 5. Case 1. Radiograph of trachea and oesophagus after partial bronchoscopic resection of the tumour, left anterior oblique position.

fibres. The tumour cell sheets frequently contained one or more cyst-like spaces, sometimes with a cribriform appearance. The cyst-like spaces contained a slightly eosinophilic substance. Mitotic figures were not numerous. The tumour tissue extended to close beneath the surface epithelium of the tracheal mucosa; this epithelium in parts showed squamous metaplasia. Biopsies taken recently (January and March, 1973), however, showed tumour tissue consisting of rather large solid cells; mitotic figures were now quite numerous (Fig. 9). Progression to a less well-differentiated histological picture seemed to have taken place. In the part of the tumour investigated histochemically the activities of several hydrolytic enzymes were low. There was no activity of alkaline phosphatase in the tumour cells. The activity of this enzyme is characteristic of the well-differentiated parts of this type of tumour. In well-differentiated adenoid cystic carcinoma of the trachea the activity of alkaline phosphatase is seen in the cells of the



FIG. 6. Case 1. Bronchoscopic picture of the trachea after partial resection of the tumour.

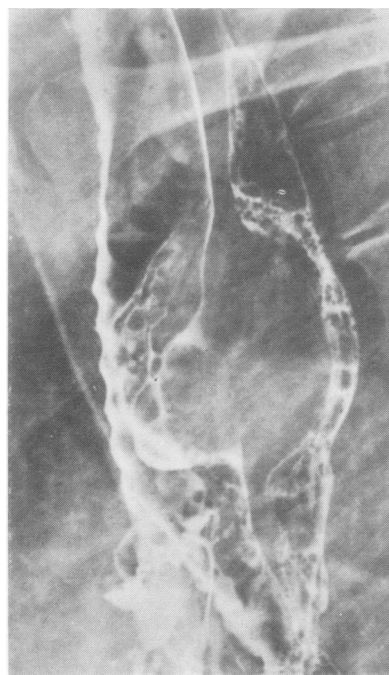


FIG. 7. Case 2. Tracheogram. A large tumour mass originating in the posterior wall of the trachea with indentation of the oesophagus.

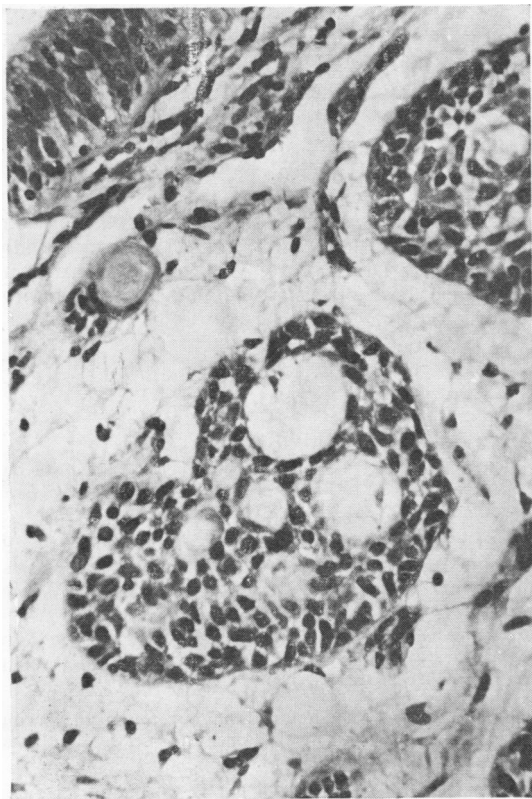


FIG. 8. Case 2. Original histological picture in 1970 shows a typical adenoid cystic carcinoma. Haematoxylin and eosin $\times 145$.

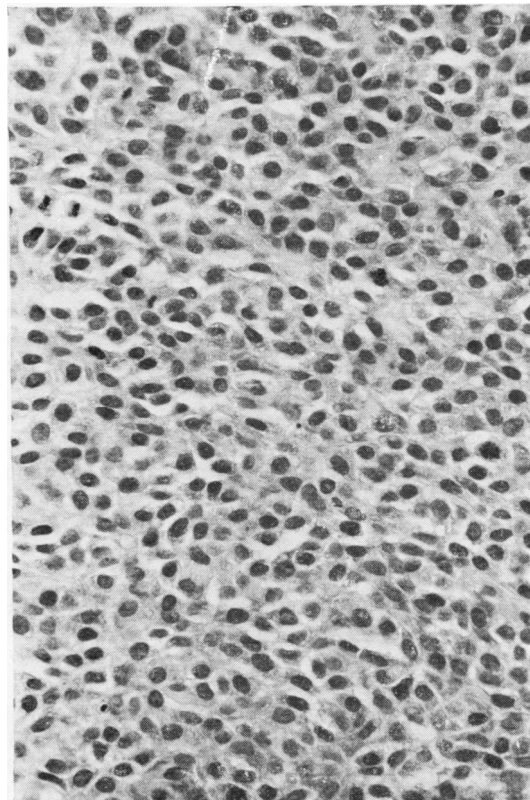


FIG. 9. Case 2. Histological picture in 1973 is much less typical of adenoid cystic carcinoma. Several mitotic figures are present. Haematoxylin and eosin $\times 145$.

narrow strands of tumour, and in the peripheral cells of the larger tumour cell fields (Willighagen *et al.*, 1963). The absence of activity of alkaline phosphatase could be explained by the progression shown by this tumour. (Unfortunately no tumour tissue was studied histochemically earlier.)

Therapy Because of the extent of the tumour mass a complete resection of the tumour and an end-to-end anastomosis of the trachea was not attempted. In view of this and of the good results of the treatment of the first patient it was decided to treat this patient by bronchoscopic resection of the tumour mass under general anaesthesia. After this treatment the stridor disappeared and the patient was discharged without complaints. Since 1970 the patient has had the same treatment six times without any complication. She remains well.

DISCUSSION

Primary tumours of the trachea are rare (Gilbert,

Mazzarella, and Feit, 1953; Salm, 1964; Ranke, Presley, and Holinger, 1962; Houston, Payne, Harrison, and Olson, 1969; Hajdu *et al.*, 1970). Among malignant primary tracheal tumours adenoid cystic carcinoma is relatively frequent. This is the second largest group in the series of Houston *et al.*, of Hadju *et al.*, and of Moersch, Clagett, and Ellis (1954), the most frequent type being squamous carcinoma. Adenoid cystic carcinoma is found most frequently in the oral cavity, the salivary glands, and the mucosa of the upper respiratory tract. It occurs also in the trachea and bronchi. It is believed to originate from the epithelium of the major and minor salivary glands and the mucous glands. In the trachea it is often situated on the posterior wall, where mucous glands are most abundant.

Adenoid cystic carcinoma shows strong infiltrative growth with fine strands of tumour cells

in the adjacent connective tissue. The tumour may grow considerably within the mucosa without visible alteration of the macroscopical features. The term adenoid cystic carcinoma has become generally accepted during the last 20 years (Reid, 1952; Moran, Becker, Brady, and Rambo, 1961). The term stresses the tumour's malignant nature and is preferred to the term cylindroma, which was introduced by Billroth in 1859. Despite its slow growth, distant metastases—though often late—are not infrequent.

Reid (1952), in a review of 45 cases collected from the literature and five personal cases, mentions distant metastases in 11 cases and metastases in regional lymph nodes in four cases. Moran *et al.* (1961) reported distant metastases in 15 of 36 cases. They mention a reported incidence of regional lymph node involvement ranging from 20 to 30%. The histological picture may progress to one showing much less differentiation (Reid, 1952; Zunker, Moore, Baker and Lattes, 1969).

Carcinoids of the trachea seem to be extremely rare. We found only nine cases mentioned in the literature (Weisel, Lepley, and Watson, 1961; Mathey *et al.*, 1961; Som, 1949; Suzuki *et al.*, 1964; Kononov, 1967; Habal and Murray, 1973). Carcinoids occur most frequently in the main bronchi. They are thought to originate from the argentaffin cells in the mucosal glands. Carcinoids are considered to be of low malignancy; according to Clagett, Allen, Payne, and Woolner (1964), metastases occur in 10% of cases, predominantly in regional lymph nodes. Spencer (1968) mentions 2 to 5% distant metastases.

Surgery is the treatment of choice for all tumours of the trachea. Several authors describe resection with end-to-end anastomosis as most favourable (Grillo, 1965; Mathey *et al.*, 1966). The size of the tumour may be a limiting factor. One should keep in mind the possibility of a greater extension of the tumour than may be diagnosed bronchoscopically or radiologically. This is an important reason for the occasionally discouraging results of resection. Results of irradiation treatment generally have not been very favourable in cases of adenoid cystic carcinoma (Zunker *et al.*, 1969). Surgical treatment was impossible in both our patients because of the size of the tumours. We elected endoscopic resection of as much tumour tissue as possible to restore the airway passage. Houston *et al.* (1969) described endoscopic resection as an important form of palliation for many patients with tracheal cancer. Our experience with the two patients presented here is in agreement with this statement. The procedure, however, is not without risks. The most

important of these are profuse bleeding from the tumour or an adjacent blood vessel and aspiration (Schaberg, 1959). Adequate electrocoagulation may prevent serious bleeding from tumour tissue. Endoscopic resection may be considered a useful alternative treatment for inoperable tumours of the trachea.

Histochemical investigations of tumour tissue from case 1 (1965 and 1973) and case 2 (1973) were kindly performed by Dr. R. G. J. Willighagen, Department of Applied Histochemistry, Pathological Laboratory, Leiden.

REFERENCES

- Billroth, T. (1859). Beobachtungen über Geschwülste der Speicheldrüsen. *Virchows Archiv für pathologische Anatomie*, **17**, 357. Quoted by Moran *et al.* (1961).
- Clagett, O. T., Allen, T. H., Payne, W. P., and Woolner, L. B. (1964). The surgical treatment of pulmonary neoplasms: 10-year experience. *Journal of Thoracic and Cardiovascular Surgery*, **48**, 391.
- Gilbert, J. G., Mazzarella, L. A., and Feit, L. J. (1953). Primary tracheal tumors in the infant and adult. *Archives of Otolaryngology (Chicago)*, **58**, 1.
- Grillo, H. C. (1965). Circumferential resection and reconstruction of the mediastinal and cervical trachea. *Annals of Surgery*, **162**, 374.
- Habal, M. B. and Murray, J. E. (1973). Argentaffin adenoma of the trachea. *The American Journal of Surgery*, **125**, 336.
- Hajdu, S. I., Huvos, A. G., Goodner, J. T., Foote, F. W., and Beattie, E. J. Jr. (1970). Carcinoma of the trachea. *Cancer (Philadelphia)*, **25**, 1448.
- Houston, H. E., Payne, W. S., Harrison, E. G., and Olson, A. M. (1969). Primary cancers of the trachea. *Archives of Surgery*, **99**, 132.
- Kononov, E. P. (1967). Carcinoid of the trachea. *Zhurnal Ushnykh, Nosovykh i Gorlovykh Bolezní*, **27**, 104. Quoted by Habal and Murray (1973).
- Mathey, J., Binet, J. P., Denis, B., Oustrières, G., and Fredet, J. (1961). Chirurgie des tumeurs primitives de la trachée. *Bronches*, **11**, 256.
- , —, Galey, J. J., Evrard, C., Lemoine, G. and Denis, B. (1966). Tracheal and tracheobronchial resections. *Journal of Thoracic and Cardiovascular Surgery*, **51**, 1.
- Moersch, H. J., Clagett, O. T., and Ellis, F. H. Jr. (1954). Tumors of the trachea. *Medical Clinics of North America*, **38**, 1091.
- Moran, J. J., Becker, S. M., Brady, L. W., and Rambo, V. B. (1961). Adenoid cystic carcinoma. A clinicopathological study. *Cancer (Philadelphia)*, **14**, 1235.
- Ranke, E. J., Presley, S. S., and Holinger, P. H. (1962). Tracheogenic carcinoma. *Journal of the American Medical Association*, **182**, 519.
- Reid, J. D. (1952). Adenoid cystic carcinoma (cylindroma) of the bronchial tree. *Cancer (Philadelphia)*, **5**, 685.

- Salm, R. (1964). Primary carcinoma of the trachea: a review. *British Journal of Diseases of the Chest*, **58**, 61.
- Schaberg, A. (1959). Bronchus-adenomen. *Nederlandsch Tijdschrift voor Geneeskunde*, **103**, 2296.
- Som, M. L. (1949). Adenoma of the bronchus; endoscopic treatment in selected cases. *Journal of Thoracic Surgery*, **18**, 462. Quoted by J. D. Reid (1952).
- Spencer, H. (1968). *Pathology of the Lung*, 2nd ed. Pergamon Press, London.
- Suzuki, C. *et al.* (1964). *Japanese Journal of Chest Diseases*, **23**, 505. Quoted by Huguenin-Dumittan *et al.* (1966).
- Weisel, W., Lepley, D. Jr., and Watson, R. C. (1961). Respiratory tract adenomas—a ten-year survey. *Annals of Surgery*, **154**, 898.
- Willighagen, R. G. J. (1973). Personal communication.
- , van der Heul, R. O., and van Rijssel, Th. G. (1963). Enzyme histochemistry of human lung tumours. *Journal of Pathology and Bacteriology*, **85**, 279.
- Zunker, H. O., Moore, R. L., Baker, D. C., and Lattes, R. (1969). Adenoid cystic carcinoma (cyclindroma) of the trachea. *Cancer (Philadelphia)*, **23**, 699.