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# PRIMARY CARCINOMA OF THE TRACHEA

BY

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[For Plates see pages 151-152]

Primary carcinoma of the trachea, in its rarity, contrasts with carcinoma of the bronchus, whose increasing frequency has been recognized during the last twenty-five years. Since von Bruns's publication of the statistics available up to 1898, the literature has been reviewed by Krieg (1908), Lombard and Baldenweck (1914), d'Aunoy and Zoeller (1931), and Culp (1938), the last of whom reviewed in detail all cases reported up to June, 1936. In this paper we describe a case of primary tracheal carcinoma closely resembling one of Culp's reported cases, and we review the literature, including new cases from the period June, 1936, to December, 1945.

#### HISTORY

In 1767 Lieutaud discovered a fibroma of the trachea at autopsy, making the first record of a growth in this situation. The first detailed study of a primary carcinoma of the trachea with a description of the histology was made by Langhans in 1871. In 1854 the laryngeal mirror came into use, and with this instrument Türck, in 1886, and Schrötter, in 1871, made the diagnosis of tracheal neoplasm in the living subject. To Killian, who in 1897 observed a tracheal tumour by endoscopy, Baratoux (1933) gives the credit for the first diagnosis of such a growth by this means.

### INCIDENCE

Autopsy statistics confirm the rarity of primary tracheal carcinoma. Culp's two cases were, respectively, the only ones in 9,000 autopsies at the Pathological Institute of McGill University and in 12,700 autopsies at the Montreal General Hospital. In 5,063 autopsies, however, Fraenkel (1921) found 7 cases, by far the highest incidence so far recorded, and, in contrast to this, Stenn (1935) noted that Wright, in 5,000 autopsies at Guy's Hospital, found none. Dorothy Russell, in a personal communication, informs us that 82 cases at the London Hospital in which the trachea was involved in carcinoma included not one of primary cancer. Negus, in a personal communication, states that he has seen, in all, five cases of primary carcinoma of the trachea, including Neilson's reported case (1930) and three cases as yet unpublished.

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The table gives the numbers of various types of primary tumour of the trachea published up to December, 1945, based on Culp's (1938) figures up to June, 1936, and a survey of the literature since that date.

TABLE
DETAILS OF PRIMARY TUMOURS OF THE TRACHEA RECORDED UP TO DECEMBER, 1945

Type of tumour						Cases recorded between 1898 and	Cases recorded up to December, 1945 (including Culp's series)	
						1936 (Culp, 1938)	Benign	Malignant
Papilloma				·.		63	67	
Adenoma	• •		• •			9	19	
Mixed (salivary)		• •	• •	• •		3	5	
Cylindroma	• •	• •	• •	• •		_1	1	
Intratracheal goi	tre	• •	• •	• •	1	28	31	
Carcinoma	• •	• •	• •	• •		147		187
	• •	• •	• •			. 5	5	1
	• •	• •	• •		1	36	36	
Chondroma	• •	• •		• •	וו			ł
Osteoma	• •		• •		· }	71	75	l
Tracheopathia o	steopla	astica	• •	• •	ال			1
	• •	• •				4	5	1
Rhabdomyoma		• •		• •			1	
Giant-celled turn	iour	• •	• •	• •			1	1
Sarcoma	• •	• •	• •	• •		31	Į.	34
Carcinosarcoma		• •	• •	• •		1	1	1
	٠:	• •	• •	• •	• • •	2	4	1
Haemangio-ende		ma	• •	• •	• • •		1	2
	• •	• •	• •	• •		<u> </u>	1	1
Amyloid tumour		: •	. • •		• • •	2	3	i
Histology undet	ermine	ed or o	doubti	ful		29		l

The division into malignant and non-malignant tumours in this table follows that of d'Aunoy and Zoeller (1931), who say of the mixed tumours of salivary type, "Although complex in character, no tumour of this type presents the stigmas necessary for classification as a malignant growth." We have, however, included two new cases reported by Cann (1938) as basal-cell carcinoma of mixed salivary type with the carcinomata, one tumour described by Palmer (1943) as an oncocytoma or mixed adenoma with the adenomata, and one case of mixed salivary type of tumour going on to myxosarcoma reported by Weinberg (1939) with the sarcomata. Segura (1913), whose case of cylindroma is included in Culp's survey, regarded this as a benign tumour developing near salivary glands; but further cases reported as cylindromata appear in each instance to be adenocarcinomata and have been tabulated with the carcinomata. D'Aunoy and Zoeller regarded the lymphoma as belonging to the class of so-called simple, local, or regional lymphomas or lymphadenomas in which infectious processes are suspected as aetiologically significant, and in this group we have included one benign growth described by Ellinger (1936) as a "lymphoplasmozytom." Cases of "tracheopathia osteoplastica"—a term used to describe the condition noted by Ewing (1940) as multiple exostoses of the trachea—have been included in this, as in past reviews, for the sake of completeness. A benign tumour showing marked degenerative changes, described by Bloch and Soulas (1937) as an amyloid tumour, has led to the addition of one new case in this group. The giant-celled tumour recorded by Cid and Bonilla (1941), and the rhabdomyoma by Andrén (1937), were regarded by these authors as benign neoplasms.

The tracheal tumours recorded up to December, 1945, can be summarized as follows:

Simple tumo		•••	•••	•••	253
Carcinomata					187
Other malign					38
Tumours of	doubt	ful hi	stology		29
Total			•••		507

Carcinomata form 37 per cent of all these tumours and 83 per cent of the malignant tumours. In Culp's review, out of 433 primary tumours, 147 (or 34 per cent) were carcinomata. Culp regarded 82 of the 147 as proven by histology; and Olsen (1939), adding 13 new cases, brought the total to 95; of these, 43 were adenocarcinomata, 42 squamous-cell, and 10 basal-cell carcinomata. The addition of 25 cases since then brings the total to 120 cases of established histology, with the following distribution of histological types:

Squamous-cell carcinoma	 50	(41%)
Adenocarcinoma	 56	(47%)
Basal-cell carcinoma	 14	(12%)

### CASE REPORT

A man aged 58 years was admitted with an irreducible umbilical hernia under the care of Mr. S. G. Clayton on Oct. 19, 1945. It was noted that he had been hoarse for one month, and this had been attributed to laryngitis, for he had had a husky voice with deafness and tickling in the throat on and off for two years. The hernia had been present for five years, increasing in size, but always reducible until the day of admission. On the following evening at 10 p.m. he complained of tenderness over the hernia, and passed one blood-stained loose stool; his temperature and pulse-rate, which previously had been normal, were raised to 99.5° F. and 100 per min. respectively. A diagnosis of strangulation was made, and operation was decided upon. He was given gas, oxygen, and ether anaesthesia, but in view of his "laryngitis" an endotracheal tube was not introduced. The sac was excised and seven feet of strangulated small intestine (gangrenous in two places) was resected, with end-to-end anastomosis.

On Oct. 22 he developed a cough with sputum, his temperature was 102° F., pulserate 120, and respiration-rate 24 per min., and a radiograph of his chest showed evidence of collapse of the left lower lobe. By Nov. 1 the lower lobe had re-expanded, and by Nov. 10 he was so well that he was considered fit for discharge, though his painless hoarseness persisted.

A month later he was seen at the surgical follow-up clinic. His general condition was good, but his voice was even more hoarse than before, and laryngoscopy then revealed a paralysis of the left vocal cord. There were no physical signs in his chest. A radiograph of the chest showed no abnormality, and the Wassermann reaction was negative.

On Dec. 21, some six weeks later, he was readmitted as an emergency case under the care of one of us (P. E.). He complained of progressive breathlessness during the preceding

ten days, and of three particularly bad paroxysms of urgent dyspnoea, each of which lasted over a minute. He again complained of hoarseness and weakness of the voice, and of cough of seven days' duration, with 6 to 8 oz. (180 to 240 ml.) of mucopurulent expectoration in the twenty-four hours. The sputum was not blood-stained, but he thought he had had a "nose bleed" fourteen days previously, during which he had coughed up a tablespoonful of pure blood.

On admission, the respiration was wheezing, laboured, and asthmatic in character, with stridor. There was no wasting, and no clubbing of the fingers. The chest was somewhat emphysematous, and the physical signs suggested collapse of the left lower lobe, with more widespread bronchopneumonia. His temperature ranged from 100° F. to 104° F., with a pulse-rate of 120 and a respiration-rate of 28 per min. Radiography showed collapse of the left lower lobe. Unfortunately the patient was far too ill for bronchoscopy, and died of asphyxia on Jan. 5, 1946, fourteen days after admission. Two days before his death he complained of dysphagia.

Autopsy.—This was done by one of us (H. W.). Arising on the posterior wall of the trachea in its lower third, at about the level of the subclavian arch, there was a tumour consisting of an intratracheal portion 19 mm. in diameter projecting about 6 mm. into the lumen of the trachea, and a larger extratracheal mass measuring 50 mm. × 30 mm. The dumb-bell appearance of the tumour is shown in Plate XIIIA and B. Macroscopically both portions of it appeared to arise from the wall of the trachea. There was no gross ulceration of the tracheal epithelium, the appearance in Plate XIIIB being an artefact due to removal of a portion of the growth for section. Over the posterior surface of the extratracheal part of the mass, the anterior wall of the oesophagus was acutely bent, but there was no ulceration of its epithelium.

There were metastases in the paratracheal glands at the level of the tumour, and in the glands of the tracheal bifurcation, but none in any viscus. Both lobes of the thyroid and its isthmus were well separated from the growth, and appeared normal. Careful examination excluded the possibility of an origin from the parathyroids, carotid body, or oesophagus; the macroscopic appearance suggested that the only possible origin was from the tracheal wall, as was confirmed by the histology.

Adhesions were present between the right diaphragm and the right lung base. The left lower lobe was consolidated, apparently as the result of long-standing segmental collapse. On the right side there was collapse of the lower lobe and extensive bronchopneumonia of the lower and middle lobes. In the abdomen, fine adhesions surmounted the region of the anastomosis which had followed resection of a large portion of the small bowel. The prostate showed slight benign hyperplasia of the middle lobe.

Histology.—Sections of the trachea (including tumour and normal mucosa), of the tumour near the oesophagus, and of lymphatic glands around the trachea and at the bifurcation of the bronchus, were fixed in formol saline and embedded in paraffin. Sections stained by haematoxylin and eosin were examined by Dr. J. N. Cumings, who reported as follows:

"The sections of the trachea show a large mass of tumour in the subepithelial region, with ulceration and loss of the surface epithelium. The tumour is composed of large masses of cells of a squamous character, with some fibrous tissue stroma between the sheets of cells (Plate XIVA). The cells show prickles in places, but there is no keratinization or cell nesting. The tumour cells approach the surface epithelium in a few places and mingle with the mucous glands in these regions (Plate XIVB). They appear to have arisen from the mucous glands, and to have undergone metaplasia into squamous cells. The surface epithelium does not appear abnormal in those areas in which it is present. Large areas of the tumour show a considerable degree of necrosis into pink granular material. The tracheal cartilages are surrounded by growth, and in a few places early invasion into

them has taken place. The growth appears moderately active, and a fair number of mitoses can be seen. All the glands sectioned show invasion by a squamous-celled carcinoma (Plate XIVC). The oesophagus is not invaded by growth. The tumour appears to be a tracheal carcinoma arising from mucous glands and showing extreme squamous metaplasia. All the neighbouring structures are normal, none of them showing any evidence of growth. Each of these other organs can be dissected out from the growth and trachea."

#### DISCUSSION

We have considered it convenient to discuss this subject from three aspects:
(a) diagnosis and clinical features; (b) histiogenesis and pathology; and (c) the relation of symptoms to lesions.

## Diagnosis and clinical features

In retrospect the significant features, when the patient first came under observation as an acute surgical emergency, were the progressive hoarseness and the transient collapse of the left lower lobe, thought to be a postoperative complication, but later seen to be due to the tracheal lesion and possibly aggravated by the anaesthetic.

The outstanding diagnostic features noted on his second admission were paralysis of the left vocal cord, revealed by laryngoscopy, and the wheezy respiration and progressive dyspnoea, with nocturnal paroxysms of an asthmatic nature.

In many cases of tracheal tumour, as in this one, the general clinical picture may suggest neoplasm, and the true site of the growth will be discovered by endoscopy. The orderly procedure outlined by Jackson (1938) in his discussion of benign tumours in the tracheobronchial tree forms the basis for the following discussion.

History.—Dryness and tickling of the throat with an irritating cough form the first complaint in many cases. Dyspnoea appears to be the most prominent symptom, and may be both inspiratory and expiratory in type, and influenced by posture. With neoplasms of the posterior wall, loss of weight may be an early symptom, and dysphagia, though prominent when the oesophagus is invaded, was a late development in our case despite considerable compression of this structure. Hoarseness and aphonia may appear at any stage of the disease. In almost every case symptoms are due to the primary growth and its extension rather than to distant metastases.

General medical examination.—Physical signs may be slight, and the patient may bear a deceptive appearance of good health. On the other hand, gross wasting and signs of serious disease may be obvious. Dyspnoea is the important symptom, and stridor the notable physical sign. Wheezing respiration—the asthmatoid wheeze described by Jackson (1938)—heard at the mouth and not at the chest wall, may be present. Both inspiration and expiration may cause stridor and, in some cases, slight pressure over the trachea may cause complete

respiratory obstruction. Foetor may be present. Malignancy may be suggested by metastases in the cervical nodes or the skin.

Finger clubbing, absent in our own case, does not appear to be a sign commonly associated with tracheal carcinoma. The chest may yield no physical signs, but, in the advanced case, pulmonary collapse or bronchopneumonia, as in the terminal stages of the case described, may appear. There may be signs of deposits in the mediastinal lymph nodes.

Laryngoscopy may be included in the general examination. Indeed, as in Türck's case (1866), the diagnosis may be attained by this means. Palsy of the left or of both vocal cords may be seen.

Blood examinations.—A positive Wassermann reaction may be misleading. The blood examination may show a secondary anaemia and a leucocytosis associated with a secondary infection.

Sputum examination.—While sputum examination for cancer cells is, in expert hands, of considerable value in the diagnosis of bronchogenic carcinoma, it does not appear to have aided diagnosis in the cases of tracheal carcinoma so far reviewed. With necrotic growths, however, malignant cells might well be demonstrated by this method.

Radiography.—In many cases radiography of the chest is negative. Indeed, a normal chest radiograph in cases of respiratory obstruction suggests a tracheal or mediastinal lesion. In the later stages, however, changes due to collapse, pneumonia, and metastases may, as in our case, make the diagnosis difficult. Vinson (1936), reviewing primary malignant disease of the tracheobronchial tree, found radiographic evidence in the lungs in 136 cases of bronchial tumours, while in one case in which the chest radiograph was considered negative a growth was present in the trachea.

Several tumours have, in fact, been demonstrated by radiography of the trachea itself. Andrén (1937), stressing the importance of the configuration of the posterior wall by a lateral view, quotes Maier's two cases (1927) and the one of Weiss and Biermann (1932), in which the diagnosis of primary tumour was made by radiography. Tinney, Moersch, and McDonald (1945) note the value of tomography and of radiographs taken after the instillation of iodized oil into the trachea. Andrén, moreover, believes that tumours giving rise to dyspnoea and wheezing respiration are large enough to enable a diagnosis to be made by radiography without the need of tracheography. Cann (1938) described the case of a woman aged 56 in whose radiograph, following the instillation of opaque oil, the intratracheal part of the tumour could be seen as a wavy outline due to the intermittent restriction on the tumour exerted by the tracheal rings—an observation which showed that intratracheal removal was impossible. opinion was that the value of the radiological information could not be overestimated since it also enabled high-voltage radiotherapy to be given with precision as to direction and level.

In our case the oesophageal deformity demonstrated at autopsy was so striking as to suggest that a barium swallow might have given valuable information.

Endoscopy and biopsy.—The diagnosis of tracheal tumour can be established in all cases by endoscopy, and confirmed histologically if biopsy is possible. As in Neilson's case (1930) of malignant stricture, however, even endoscopy may not demonstrate the carcinomatous nature of the lesion.

## Histiogenesis and pathology

We suggest the following classification:

- 1. Primary carcinoma arising from cells normally present in the trachea: (a) squamous-cell carcinoma, (b) adenocarcinoma, (c) basal-cell carcinoma.
- 2. Primary carcinoma arising from rests in the trachea of the epithelium of other structures, such as the oesophagus, thyroid, and remnants of primitive bronchial clefts.

While the relation of adenocarcinoma to the mucous cells of the trachea may be assumed, the occurrence of squamous-cell carcinoma in a structure normally devoid of this type of epithelium has caused much discussion. Culp cites Reichl (1893), Nager (1907), and others who were convinced that the tumours of their experience could best be explained on the basis of Cohnheim's theory of embryonal inclusions (1882). Robin and Mann (1937) point out that squamous epithelioma may originate in the thyroid, and quote Kauffmann's suggestion (1922) that it may be developed from primitive branchial cleft remains or from the thyroglossal duct.

Other workers think that metaplasia of the tracheal epithelium precedes squamous-cell neoplasm. Siegmund's observation (1922) of three squamous-celled carcinomata of the lung arising in bronchiectatic cavities is quoted by Culp in support of this theory, reinforced as it is by that metaplasia of columnar ciliated to transitional epithelium which has been observed in the air-passages of animals exposed to acute respiratory infections.

Olsen (1939), however, considers that "the original conception of Virchow concerning metaplasia of one cell into another is no longer tenable," and Cohnheim's hypothesis is considerably less valid. Regarding all neoplasms as originating in a universal basal-cell layer, he points out that, in the trachea, this layer gives rise to surface epithelial (ciliated columnar) cells, goblet cells, and the serous or mucous cells of the lamina propria. According to this theory, neoplasms do not arise by any change in these adult cells. The basal cells, however, by virtue of their embryonic nature, are capable of producing squamous cells which originate by protoplasia of embryonic cells and not by metaplasia of the adult cells which line the normal trachea.\*

<sup>\*</sup>Cann (1938) states: It is now widely accepted that carcinoma of the bronchi arise from the basal cell layer. Krompecher (1923), in a study of carcinoma arising in organs lined by columnar epithelium, decided that they all originate from proliferation of the basal cells.

Spread and metastases.—Direct invasion of the oesophagus is the most sinister mode of extension of the primary tracheal tumour. Figi (1930) states that metastasis as a rule develops late or not at all, but Culp found that in 91 instances where the presence or absence of metastases was recorded they were present in 62 and absent in only 29. Metastases appear to be more common with the squamous-cell growths. In contrast to the laryngeal carcinomata, as noted by d'Aunoy and Zoeller (1931), the tracheal growths may produce metastases in any part of the body; and Breslich (1930) stated the order of frequency of metastases as follows: peritracheal, cervical and tracheo-bronchial lymph nodes, lungs, liver, supra-clavicular and axillary lymph nodes, oesophagus, spleen, pancreas, kidneys, and skeletal structures.

Keeney (1937) notes the presence of metastases in the skin in a number of cases too small perhaps to warrant his suggestion that, if cutaneous metastases occur in a case of tracheobronchial obstruction, the primary growth is more likely to be located in the trachea than in the parenchyma of the lungs or in the bronchi.

Since the lymphatic vessels follow the course of the recurrent laryngeal nerve, this nerve on the left side is commonly involved when the growth is situated low in the trachea. With metastasis in the cervical nodes, both nerves may be affected with the production of bilateral paralysis of the vocal cords.

Site.—Culp's conclusion that the growth is most commonly situated on the posterior wall in the lower third is in agreement with the findings of other workers, and this was the site in our own case. In this region glandular epithelium predominates. The tumour is least often found in the upper third of the trachea. Annular growths appear to be very rare.

Age and sex.—Tracheal carcinoma appears to be more common in males. Between persons of 30 to 70 years of age, 90 per cent of cases analysed by Culp were distributed fairly equally, with but slightly increased frequency in the fifth and sixth decades.

### The relation of symptoms to lesions

Strauss (1922) states that the greatest channel of lymph absorption from the trachea is by way of the main trunks accompanying the recurrent laryngeal nerves. A left recurrent laryngeal palsy from compression of the nerve may, as Olsen points out and as occurred in our case, arise from lesions near the bifurcation, with involvement of the mediastinal nodes, while bilateral palsy of the cords may be produced by pressure on both nerves by cervical nodes infiltrated from a lesion higher in the trachea. The cause of other symptoms is apparent when the morbid anatomy is considered, but the complication of pulmonary atelectasis, present in our own and many recorded cases, is difficult to explain. Partial and intermittent obstruction of the airway may be the cause. In Plate IB the closer relation of the growth to the left than to the right bronchus is apparent,

and it was on the left side that collapse first occurred; yet this bronchus is unlikely to have been occluded by the growth, and the cause of the atelectasis may perhaps have been interference with ciliary action at the site of the growth.

### **TREATMENT**

From Olsen's (1939) study of cases at the Mayo Clinic it appears that squamous-cell tumours are less amenable to treatment than adenocarcinomata, and that Broder's index is useful in prognosis. His series includes, as did that of von Bruns (1898), a record of successful resection of the trachea. Olsen also gives an account of other methods, including surgical diathermy, the insertion of radon-seeds into the growth by endoscopic procedures, and x-ray therapy. Negus (1933) demonstrated the apparent cure of a man, aged 47, in whom the carcinoma was approached by splitting the thyroid and cricoid cartilages, radium needles, sewn into a rubber tube, being left in the trachea for six days. It is interesting to note that in two cases of primary carcinoma separately described by Figi (1930) and Leroux-Robert (1936), and in one case of laryngo-tracheal cancer reported by van den Wildenberg (1936), x-ray treatment for thyrotoxicosis had been applied some years before.

### SUMMARY

- 1. Recorded cases of tumours of the trachea are reviewed.
- 2. The clinical and pathological findings in a case of carcinoma of the trachea are described.
- 3. The diagnosis and clinical features, the pathology and histiogenesis, and the relation of symptoms to lesions in carcinoma of the trachea are discussed.

We are indebted to Prof. Dorothy Russell, Dr. J. N. Cumings, and Dr. D. N. Nabarro for help on the pathological side, and to Mr. V. E. Negus for a record of cases that have come under his care.

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