Histology of bronchial carcinoma in relation to prognosis¹

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The treatment of bronchial carcinoma by resection, when it is possible, has become the method of choice. A success rate of about 30%, as five-year survival, is generally agreed, and the Birmingham figures were recently reported by one of us (Taylor, 1960), giving 28·9% alive at five years and 21·4% alive at 10 years. These figures were from all types of bronchial carcinoma. It has been suggested that the histological character of the growth may considerably affect the results of treatment, even making an operation not worth while for some types.

To investigate this point we have analysed the 2,847 cases diagnosed at the United Birmingham Hospitals from 1948 to 1956 inclusive. In 973 cases histological identification of the type of growth was obtained by bronchoscopy, operation, or necropsy.

Of these, 40 were placed in a category classified as 'mixed', adenocystic carcinoma (cylindroma) or carcinoid (malignant adenoma) and therefore excluded, leaving a total of 933. The primary source of these histological specimens is shown in Table I.

TABLE I
PRIMARY SOURCE OF HISTOLOGICAL SPECIMENS

Source	No. of Patients
Bronchoscopy	341 (37%)
Resection	364 (39%)
Necropsy	228 (24%)
Total	933 (100%)

Of the 341 found by bronchoscopy, 101 were resected and seven came to necropsy. In all, 465 were resected. (Actually in the total 2,847 cases there were 586 resections as some operations were done in hospitals of the Region. The overall resection rate is therefore 21%.) It has been possible to compare the histology found in 108 cases by bronchoscopy with that subsequently found in 101 of them by resection and in 7 of them at necropsy to assess the reliability of bronchoscopic diagnosis.

HISTOLOGY

The histological identification of bronchial carcinoma is open not only to differences of personal interpretation but also to differences of classification. All our cases have therefore been personally reviewed by one of us (N. K. S.) and we have adopted the classification described in detail by Shinton (1961). Briefly, this divides bronchogenic carcinoma into four main types: adenocarcinoma, squamous carcinoma, oat-cell carcinoma, and undifferentiated (anaplastic) carcinoma.

ADENOCARCINOMA This has cubical or columnar cells arranged as acini and showing mucin secretion.

The group includes 'acinar and trabecular polyhedral cell', 'solid alveolar', 'mucoid', and 'mucus' carcinomas.

¹ Based on a paper given to The Thoracic Society in Paris in July 1962

SQUAMOUS-CELL (EPIDERMOID) CARCINOMA This has stratified squamous cells usually with keratinization but sometimes cell-nest formation ('pearls').

The group includes 'transitional cell' and 'round cell and squamous' carcinomas.

OAT (OR SMALL)-CELL CARCINOMA This has small round, oval or spindle-shaped cells with hyperchromatic nuclei and scanty ill-defined cytoplasm arranged in masses, anastomosing ribbons or rosettes.

UNDIFFERENTIATED (ANAPLASTIC) CARCINOMA This has no specific structural or cellular characteristics.

The group includes 'medullary', 'large', 'pleomorphic', 'polygonal', 'polyhedral', 'spheroidal', and 'clear' cell carcinomas.

It was our policy to classify these tumours according to the most differentiated tissue seen. Where more than one type of differentiation was present they were placed into a 'mixed' category. Forty tumours were classified as 'mixed', adenocystic carcinoma (cylindroma) or carcinoid (malignant adenoma), and excluded from the present series. The distribution of histological types in the total number studied and in those found at bronchoscopy is shown in Table II and conforms to most published series except that the number of adenocarcinomas is smaller.

TABLE II

COMPARISON OF HISTOLOGICAL TYPES

Histology	All Patients		Bronchoscopy Patients	
	%	No.	%	No.
Adenocarcinoma	5.0	47	1.5	5
Squamous carcinoma	56.9	531	62.5	213
Oat-cell carcinoma	31.2	291	34.3	117
Undifferentiated (anaplastic) carcinoma	6.9	64	1.7	6
Total	100	933	100	341

RELIABILITY OF BRONCHOSCOPIC DIAGNOSIS

In assessing the different treatments in relation to the histology of the growth a pre-treatment diagnosis must be available and accurate. Of the 341 cases in this series diagnosed histologically from bronchoscopy, 101 came to resection and seven others came to necropsy. In each case a comparison of the histology was made.

The sections were examined 'blind' without knowledge of their relationship. There was agreement between the histological reports of the bronchoscopic biopsies and the operation or necropsy specimens in 98 of the 108 cases. All the differences

were from specimens obtained by biopsy showing squamous cell carcinoma and subsequently from operation or necropsy showing anaplastic carcinoma. The latter were then up-graded into the higher differentiated, *i.e.*, squamous cell, group for further analysis, according to the policy already stated.

Bronchoscopy therefore in this series is reliable in 90% of cases and the tissue most accessible to biopsy seems to be the most differentiated part of the tumour. Whitwell (1961), analysing 344 cases, found no disagreement in those with adenocarcinoma, 1.7% difference with squamous carcinoma, 1.5% difference with oat-cell carcinoma, and 31% difference with 'carcinoma simplex'. He found higher differentiation in the operation specimen than in the bronchoscopic biopsy specimen and assumed that the main specimen will give the more correct report because so much more tissue is examined histologically. While this may be a reasonable assumption, it seems to us from our results that the bronchial part of the growth may well be more morphologically typical and active than deeper parts in the lung where infection and necrosis have their effect.

Differences in reporting may occur in two ways, either by different histologists recognizing different appearances or by their using different terminologies. In this series these factors had accounted for a difference in 17% of the original reports before the sections were all rescrutinized by one of us.

RESECTION

During the years 1948 to 1956 inclusive 586 patients were resected (465 at the United Birmingham Hospitals) out of the total of 2,847, giving an average rate of 20.6%. The rate varied during the period between 16.8% and 25.9%. A bronchoscopic histological diagnosis was made in 341 patients and of these 101 (30%) were resected, the details being shown in Table III. It should be noted that most were squamous or oat-cell growths, the numbers of other types being very small.

Survival after resection can reasonably be assessed at five years. It was shown in our earlier paper (Taylor, 1960) that most deaths after resection

TABLE III

RESECTION RATE OF 341 PATIENTS WITH BRONCHOSCOPIC DIAGNOSIS

Histology	Total	Resection Rate	
		No.	%
Adenocarcinoma	5	1	20.0
Squamous carcinoma	213	77	36.2
Oat-cell carcinoma	117	23	19.7
Undifferentiated (anaplastic) carcinoma	6	0	0
Total	341	101	30

TABLE IV

FIVE-YEAR SURVIVAL AFTER RESECTION FOR BRONCHIAL CARCINOMA

Histology	All Resections			Bronchoscopically Diagnosed		
	Total	Survivors	%	Total	Survivors	%
Adenocarcinoma	23	3	13.0	1	0	0
Squamous carcinoma	328	81	24.7	77	20	26.0
Oat-cell carcinoma	85	11	12.9	23	4	17.4
Undifferentiated (anaplastic) carcinoma	29	2	6.9	No cases		
Total	465	97	20.9	101	24	23.8

occurred in the first three years and only a few of the five-year survivors failed to survive 10 years. All the patients have been followed up for five years or to their previous death. The comparison of histology with prognosis is shown in Table IV. Of the total of 465 resections the five-year survival is 21%, and those diagnosed by bronchoscopy before resection follow the rates for the whole group quite closely. It should be noted that the actual numbers of adenocarcinomas and undifferentiated (anaplastic) carcinomas are too small for significant consideration.

DISCUSSION

The relation of histology to prognosis is not easy to assess accurately. After starting with a large number of patients, by the time one has reached the final analysis of five-year survival for effective resection of a particular histological type they have diminished very greatly, and for those with a pre-operative histological diagnosis the final numbers are indeed small. In this series, however, squamous carcinoma of the bronchus was found twice as often as oat-cell carcinoma, could be resected nearly twice as often as oat-cell carcinoma, and after resection the patient had nearly twice the chance of surviving five years. The numbers for the other types of carcinoma were all so small at each analysis as to be insufficient for reasonable assessment.

Comparison with other reported series of five-year survivals after resection shows considerable variation and a number of these are summarized in Table V. The most striking differences are in the figures for adenocarcinoma which vary from 0 to 54%. The squamous carcinomas are much more uniform.

We have considered the possibilities of geographic distribution of variation of histological incidence and identification, as emphasized by Siddons (1962) in his own series of resections, and also a difference of case selection and resection rate. There is a very considerable variation of incidence of adenocarcinoma reported in different series (Shinton, 1961)

TABLE V

REPORTED FIVE-YEAR SURVIVALS AFTER RESECTION FOR BRONCHIAL CARCINOMA

Author	Adeno- carcinoma (%)	Squamous Car- cinoma (%)	Oat- cell Car- cinoma (%)	Undifferen- tiated (Anaplas- tic) Carcinoma (%)	Total Resec- tions
Bignall and Moon, 1955	41	36	—	26	453
Kirklin <i>et al.</i> , 1955	54	20	9	25	844
Gibbon <i>et al.</i> , 1957	1	24	—	13	145
Gifford and Waddington, 1957	0	38	0	19	464
Paulson, 1957	22	17	0	0	444
Collins, 1958	9	21	0	4	333
Clagett, 1960	28	33	15	27	584
Spjut <i>et al.</i> , 1961	18	24	12		225
Christiansen and Smith, 1962	1	13	—	2	
Siddons, 1962	41	36	—	31	250
Present series	13	25	13	7	465

whereas squamous carcinomas are much more uniform. We have dealt in detail with the difficulties of histological classification. The selection of cases and the resection rates are very similar in all series and do not seem to have any bearing on individual prognosis of the histological type.

What conclusions may therefore be drawn? From our figures squamous carcinoma is diagnosed in life most often and is most amenable to resection and the patient has a better chance of survival than those with other types of bronchial carcinoma. Oat-cell carcinoma is more malignant and the results of resection are not so good. It is possible, therefore, that other forms of treatment, and in particular radiotherapy, may prove to be more effective for oat-cell carcinoma and they demand critical trial. The position for adenocarcinoma remains most confused.

Pre-treatment identification of the cell type seems essential and bronchoscopy is the best way of providing this in most patients. Examination of the sputum, pleural fluid or pleural biopsy may show the histology but generally a direct view of the growth provides the most likely source of reliable histological material as well as assessing the situation macroscopically. We have shown that when a biopsy is obtained it does give a reliable indication of the type of growth present as long as there is agreement among pathologists about classification.

SUMMARY

From 1948 to 1956 there were 2,847 patients with bronchial carcinoma in the United Birmingham Hospitals, of whom 99 (3.5%) survived five years; all but two had had a resection.

The classification of histology was based on four main groups: adenocarcinoma, squamous cell

carcinoma, oat-cell carcinoma, and undifferentiated (anaplastic) carcinoma. There were 933 patients in these groups, of whom 465 had a resection and 97 (21%) survived five years.

The five-year survival after resection of adenocarcinoma was 13%, of squamous carcinoma 25%, of oat-cell carcinoma 13%, and of undifferentiated carcinoma 7%.

Bronchoscopic histology is reliable. The biopsy and subsequent operation or necropsy specimen agreed in 90% of 108 cases.

Bronchoscopic histology was obtained in 341 patients. Of these, five had adenocarcinoma (1.5%) and one was resected but did not survive; 213 had squamous carcinoma (62%) and 77 were resected, of whom 20 (26%) survived five years; 117 had oat-

cell carcinoma (20%) and 23 were resected, of whom four (17%) survived five years. Six patients had undifferentiated carcinoma (1.8%) and none was resected.

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