BRONCHOGENIC CARCINOMA: THE DISTRIBUTION OF THE HISTOLOGICAL TYPES IN THE THREE RACIAL GROUPS OF CAPE TOWN

C. J. UYS and J. I. PEROLD, *Department of Pathology, Medical School, University of Cape Town, Observatory, Cape*

Within the last two decades a striking increase in the incidence of bronchial carcinoma in many countries has been reported. There have been isolated accounts of the situation in Southern Africa,[1-6] but on the whole the picture is incomplete, especially with regard to comparative studies between the various racial groups.

In Cape Town there are three racial groups, showing genetic as well as environmental differences, the latter being determined by a variety of factors, but notably by social status and racial customs. The geographic, genetic, dietary and cultural backgrounds of these groups have been fully reviewed by Brock.[7]

Firstly, there is a large White population of European origin whose mode of life does not differ significantly from that of people of privileged Western European descent living elsewhere. Next, the Cape Coloured people, who are of mixed European, Hottentot and Malay descent and genetically distinct from the Bantu, form a group of comparable size.[8] On the socio-economic scale the Coloured people occupy a position intermediate between the European and the Bantu, but their cultural pattern is more European than African.

Finally, the minority group in Cape Town, and the least privileged, are the Bantu. While many of them are permanently resident in Cape Town, a certain proportion migrate here temporarily from the Reserves in order to seek work, and return again after a period of 1 - 3 years. In the City this group is emerging from a tribal to a westernized mode of life.

In the evaluation of the incidence of lung cancer the more conventional assessment of mortality and morbidity rates cannot be applied to all groups. Mortality rates are available for Europeans in South Africa, but not for the other two racial groups. Thus, in studies which involve primitive communities, not only is there magnification of the difficulties encountered among similar projects in Western races, but also further snags may complicate the validity of such methods, and different approaches have to be adopted.[9]

Where there has been an increase in the incidence of bronchial carcinoma this has largely been due to an increase of squamous-celled and undifferentiated small-celled carcinomas and not of adenocarcinoma. On the basis of this, Kreyberg[10] has divided bronchial carcinoma into two broad histological groups: group I, which includes squamous-celled carcinoma and oat-celled carcinoma, and group II, which includes adenocarcinoma, bronchiolar-cell carcinoma, adenoma (benign and malignant) and salivary-gland tumours. He has demonstrated that the ratio of group I to group II tumours is an indication of the development of the new 'lung-cancer situation', and that this ratio could be used as a measure of the total incidence of lung cancer in areas where incomplete mortality and morbidity statistics are available. Other authors[11,12] have also stressed the value of this classification.

We have been conducting an investigation, the primary object of which is to determine the frequency and distribution of the various histological types of bronchial carcinoma in each of the racial groups, and possibly thus

provide an indication of the lung-cancer situation in Cape Town, especially since it is recognized that differences in the incidence of cancer in underdeveloped communities may reflect the influence of environment on carcinogenesis. Apart from the comparative aspects of the study under present conditions, it is of immediate importance to know to what extent the new lung-cancer situation has developed in the Europeans, who form a westernized community known to have a smoking rate among the highest in the world.[6]

METHOD OF INVESTIGATION

This survey includes all the cases of bronchogenic carcinoma diagnosed histologically in the Pathology Department of the University of Cape Town during the 11 years from 1950 to 1960 inclusive, from both postmortem and surgical material. Slides stained by haematoxylin and eosin were examined and evaluated by one of us without knowledge of the patient's age, sex and race. Where indicated, special stains, consisting of Southgate's mucicarmine for mucin, periodic-acid Schiff, Wilder's stain for reticulin, and van Gieson's stain, were used.

The material was classified into the following histological types: squamous-celled carcinoma, adenocarcinoma, small-celled carcinoma (oat-celled carcinoma), and large-celled anaplastic carcinoma. On morphological grounds we regard this as an acceptable classification, but by selecting it we have also attempted to conform, for comparative purposes, with surveys conducted by others.[12,14] A histogenetic difference between each entity is not necessarily implied.

If two types were observed in the same case, the neoplasm was classified according to the predominant pattern. For example, tumours were regarded as *squamous-celled* only if there was clear-cut evidence of either keratinization or of intercellular bridges. Even if some of these tumours showed minimal degrees of mucin secretion they were still designated as squamous-celled. A certain proportion of cases were less well-differentiated, and although suggestive of squamous-celled carcinoma, were placed among anaplastic large-celled carcinomata, if unequivocal prickles or keratin could not be demonstrated.

Adenocarcinoma included only those tumours composed of cylindrical columnar cells which formed clear-cut acini with or without mucin secretion. Where this pattern predominated, but anaplasia became evident in other sections, it was still regarded as an adenocarcinoma. On the other hand, where anaplasia predominated, although the indications only suggested that the origin lay in an adenocarcinoma, the neoplasm was classified as an anaplastic large-celled carcinoma.

Small-celled carcinoma formed a distinct group which showed the least variations morphologically.

The group *anaplastic large-celled carcinoma* showed the most marked morphological variations and histogenetically was the least distinct. From what has been said above it is clear that to a certain extent it forms a dumping ground for undifferentiated carcinomata that could not strictly be fitted into any of the above types. Others might well regard a certain number of examples of this group as adeno- or squamous-celled carcinoma. Mucin secretion was observed in a notable proportion of cases.

Alveolar-cell carcinoma and bronchial adenoma were classified as entities distinct from the above.

To assist in the classification of the tumour type in autopsy material, the secondary deposits at various sites were similarly classified, and their appearances were correlated with those of the primary tumours. There was complete agreement in the majority of cases, and observed differences were usually the result of dedifferentiation and did not indicate another histological type. Oat-celled carcinoma nearly always presented the same appearances in the secondaries, and in a few instances the accepted pattern was even better developed. A few primary squamous-celled tumours produced secondaries showing differentiation towards oat-celled carcinoma.

Biopsy specimens obtained by bronchoscope were used only if there was sufficient material to permit classification. Multiple specimens received from one patient over a period of time, including perhaps an ultimate autopsy specimen, were regarded as one case.

Owing to the selective influences that may apply, we feel that it is imperative in a study such as this to include both surgical and autopsy material. The importance of this has been stressed by other workers as well.[11,15,16]

RESULTS

This series consists of 274 cases of primary malignant disease of the lung, of which 126 were examined at autopsy, and 148 were based on surgical specimens suitable for histological classification. Only 27 cases were rejected from the material available as being unsuitable on the grounds that the specimens were too scanty. Six surgical specimens, although adequate from the point of view of histological classification, had incomplete data with regard to sex, age or race.

The number of cases of malignant disease of the lung among the three races is shown in Table I. From this it would appear that Europeans (168) far outnumber the Coloured (92), who in turn far exceed the Bantu (10).

TABLE I. MALIGNANT PULMONARY NEOPLASM—TOTAL NUMBER OF CASES WITHIN EACH RACIAL GROUP: 1950 - 1960

Race	*Postmortem material*	*Surgical specimens*	*Total*
European	77	91	168
Coloured	43	49	92
Bantu	6	4	10

However, these findings have more significance when viewed in the light of the total number of admissions to Groote Schuur Hospital during the period of the survey and of the age distribution of these patients. The admissions for Europeans (112,597) and Coloured (106,114) are very nearly the same, but those of the Bantu (23,353) constitute approximately a fifth of the individual totals of the other two racial groups.

Unfortunately, the distribution within the age groups of the total hospital admissions is not available to date, but an indication of this can be obtained from a similar analysis of the autopsy material within the same period (Table II) which shows that 55% of persons coming to autopsy over the age of 40 years are White, 35% Coloured and 10% Bantu.

TABLE II. AGE DISTRIBUTION OF POSTMORTEM EXAMINATIONS PERFORMED: 1950 - 1960

Age group (years)	*European*	*Coloured*	*Bantu*	*Total*
21 - 30	76	211	93	380
31 - 40	114	244	109	467
41 - 50	261	326	121	708
51 - 60	367	286	66	719
61 - 70	437	191	41	669
71 - 80	262	70	6	338
81+	85	28	3	116
Total	1,602	1,356	439	3,397
Over 40	1,412	901	237	2,550

The distribution of the histologically different tumour types within the total series is indicated in Table III. The occurrence of the different forms of bronchogenic carcinoma among the European and Coloured groups is illustrated in Fig. 1, while the 10 Bantu cases included 2 squamous-celled carcinomata, 1 adenocarcinoma, 5 oat-celled carcinomata and 2 large-celled carcinomata. These overall findings for all races indicate that squamous-celled carcinoma is the most frequent tumour type (39%), followed by oat-celled carcinoma (29%), with adenocarcinoma significantly the least frequent (8·5%).

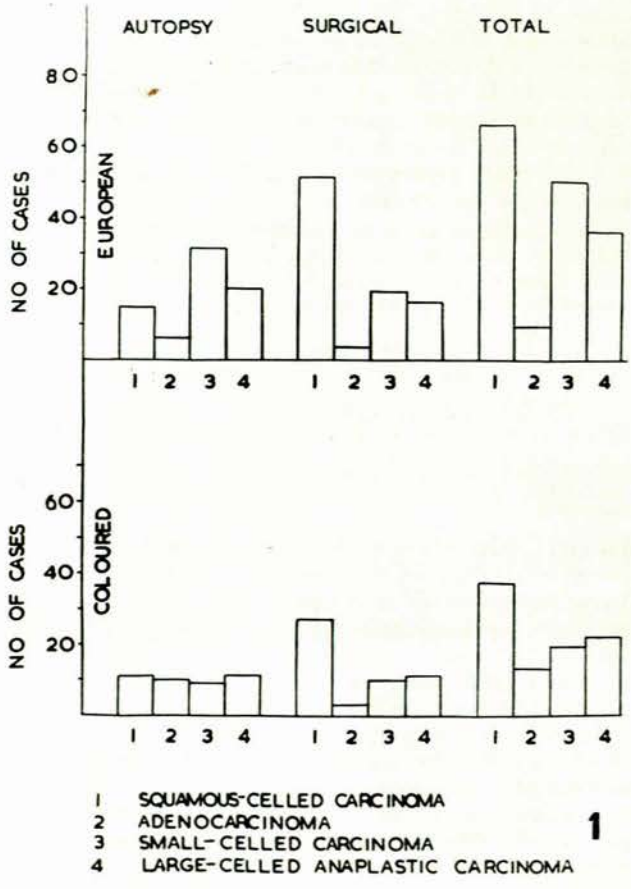

Fig. 1. Bronchogenic carcinoma: The frequency of tumour types in the European and Coloured groups.

TABLE III. PULMONARY NEOPLASM—DISTRIBUTION OF TUMOUR TYPES IN POSTMORTEM AND SURGICAL MATERIAL: 1950 - 1960

Histological type	*No.*
Squamous-celled carcinoma	107
Adenocarcinoma	23
Oat-celled carcinoma	77
Large-celled anaplastic carcinoma	61
Pleural mesothelioma	4
Alveolar-cell carcinoma	1
Metastasizing adenoma	1
Chondroma	3
Benign teratoma	1
Leiomyoma	1
Lipoma	1
Granular-cell myoblastoma	1
Bronchial adenoma	5

While this trend applies in the European and Coloured groups (Fig. 1) (there are not sufficient cases among the Bantu to be considered statistically), the difference between squamous-celled carcinoma and adenocarcinoma is not as marked in the Coloured subjects as in the European, and oat-celled carcinoma in the Coloured does not occupy so prominent a position. Fig. 1 also illustrates the necessity for including both surgical and autopsy material in a survey such as this, since each type is in itself subject to striking selective influences which are reflected in the distribution of tumour types.

The age distribution of the cases is shown in Table IV. It is apparent that the majority of cases for both European (86%) and Coloured (86%) fall between the ages of 41 and 70 years, with the Europeans showing a peak between 61 and 70 years and the Coloured showing a peak a decade earlier, between 51 and 60 years, corresponding to that of the total autopsy series for each of the races. It is thus quite likely that a similar trend in the clinical material may be the determining factor.

TABLE IV. AGE DISTRIBUTION OF BRONCHOGENIC CARCINOMA

Age group (years)	*European*	*Coloured*	*Bantu*	*Total*
21 - 30	1	4	—	5
31 - 40	6	6	4	16
41 - 50	22	22	1	45
51 - 60	54	34	—	88
61 - 70	66	24	3	93
71 - 80	16	2	2	20
81+	1	—	—	1

The age distribution of the tumour types in the European and Coloured groups is shown in Fig. 2, with no significant differences appearing to exist between tumour types in the two races.

The sex distribution of lung cancer is illustrated in Table V, and it is seen that, while a male preponderance is noted in all the races, it is most pronounced in the European and tails slightly off in the Coloured and the Bantu.

TABLE V. SEX DISTRIBUTION IN TOTAL AUTOPSY MATERIAL AND IN BRONCHOGENIC CARCINOMA: 1950 - 1960. MALE: FEMALE RATIO

Material	*European*	*Coloured*	*Bantu*
Total autopsies	1·5 : 1	1·2 : 1	2 : 1
Bronchogenic carcinoma	7·4 : 1	5·1 : 1	4 : 1

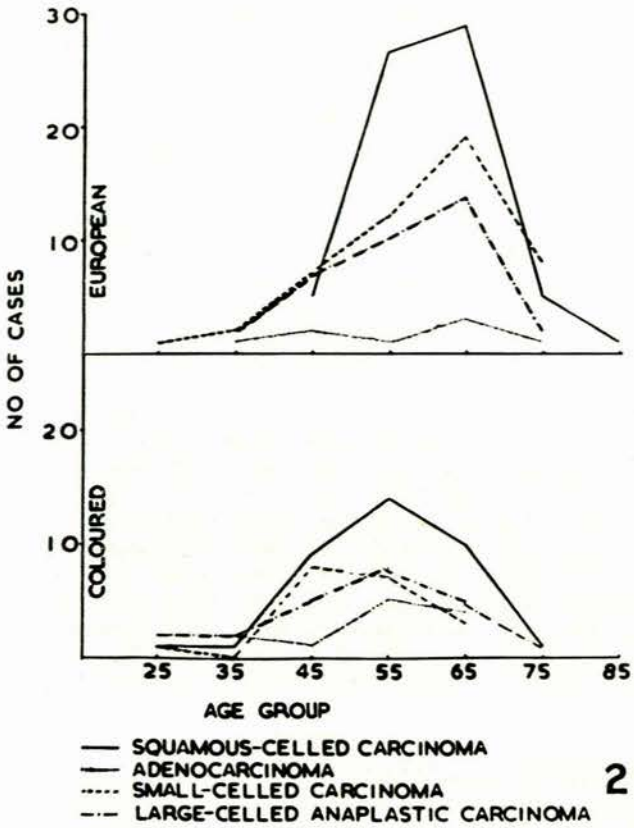

Fig. 2. Bronchogenic carcinoma: The age distribution of tumour types in the European and Coloured groups.

The sex distribution for each of the tumour types in the European and Coloured groups is shown in Table VI. It is seen that, while the male preponderance is most marked in squamous-celled carcinoma, it nearly approaches unity in adenocarcinoma, in both European and Coloured. The sex ratio of oat-celled carcinoma shows a similar trend in both races, but the male preponderance is not as striking as in squamous-celled carcinoma. This also applies to anaplastic large-celled carcinoma in Europeans, but not in the Coloured group where the sexes more nearly approximate one another. This latter discrepancy could possibly be due to the small number of cases in the Coloured group.

TABLE VI. SEX DISTRIBUTION WITHIN DIFFERENT HISTOLOGICAL TUMOUR TYPES

Tumour type	*Male*	*Female*	*Ratio*
European			
Squamous-celled carcinoma	63	3	21 : 1
Adenocarcinoma	6	3	2 : 1
Oat-celled carcinoma	44	6	7·3 : 1
Large-celled anaplastic carcinoma	33	4	8·2 : 1
Coloured			
Squamous-celled carcinoma	35	2	17·5 : 1
Adenocarcinoma	8	5	1·6 : 1
Oat-celled carcinoma	17	2	8·5 : 1
Large-celled anaplastic carcinoma	16	6	2·7 : 1

If these findings are considered in terms of Kreyberg's classification (Table VII), it is noted that in both the European and Coloured groups there is a marked preponderance of males with group-I tumours, whereas in both races the ratio of males to females approximates more closely for group-II tumours.

TABLE VII. SEX DISTRIBUTION ACCORDING TO KREYBERG'S CLASSIFICATION

Race	*Group*	*Male*	*Female*	*Ratio*
European	I	107	9	12 : 1
	II	8	5	1·6 : 1
Coloured	I	25	4	13 : 1
	II	9	7	1·3 : 1

If the ratio group I: group II tumours is considered in males only, the Europeans show a striking preponderance of group-I tumours, which is significantly greater than the group-I preponderance in the Coloured group (Table VIII).

TABLE VIII. RATIO OF KREYBERG GROUP I: GROUP II IN MALES

Race	*Group I*	*Group II*	*Ratio*
European	107	8	13·3 : 1
Coloured	52	9	5·8 : 1

COMMENT

The extent to which these findings can be compared with those of other workers in other countries is limited because of the varying nature of the material and the selective influences that apply. This objection may also apply to a comparison in the various race groups of the findings of our own material, although to a lesser degree. In this regard, however, it would be permissible to draw attention to similarities or differences in trends, rather than actual incidence, as stressed by Kreyberg's findings.[10]

In South Africa, Gordon[6] has drawn attention to the rising incidence of lung carcinoma among the Europeans, in whom the death rate has almost doubled over the decade 1950 - 1960, as in other high-incidence countries. Although there are several reports on lung cancer in the Bantu, no clear picture has emerged as yet, largely owing to the lack of reliable statistical data. Duchen,[3] on the Witwatersrand, demonstrated a significantly lower incidence in Bantu as compared with European males in an autopsy series, but also stressed that bronchial carcinoma could not be regarded as rare in the Bantu. Higginson and Oettlé,[4] from a study also conducted on the Witwatersrand, concluded that, while lung carcinoma was not rare in the Bantu of this area, the incidence was lower than that for both the Negroes and the Whites of the USA, but not significantly reduced in comparison with Denmark. At Kampala, Uganda, Davies[17] noted only 3 cases of lung cancer in a total of 286 male cancer patients. On the other hand Osburn[2] from Gwanda, Southern Rhodesia, felt that carcinoma of the lung in African males was almost as common in this district as among White males in the USA.

With regard to the Coloured population, the paucity

of data is even more pronounced. Higginson and Oettlé[4] stated that in the males of their series the incidence was significantly higher than that expected in the USA population.

The impression thus gained from the findings of these various workers is that the incidence of bronchial carcinoma is high among the Whites and possibly among the Coloured group as well, but that the Bantu in comparison show a lower incidence, although it is not a rare disease in them.

In our own material, the distribution of histological tumour types is similar in both the European and the Coloured groups. Squamous-celled carcinoma and oat-celled carcinoma are both far more frequent than adenocarcinoma, conforming to the tendency noted in other high-incidence countries.[10,14,18,19] Since the total number of admissions for European and Coloured patients in Groote Schuur Hospital are roughly equal, the fact of the large number of carcinomata in the European seems striking (Table I). However, attention has already been drawn to the fact that this might be a reflection of selective influences, such as the age distribution of the hospital admissions. Far more of the Coloured patients admitted fall within the earlier age groups, when carcinoma of the lung does not occur (Table IV). If the autopsy incidence only is considered in individuals over the age of 40 years (the age groups of all cases are available), it is noted that there is closer approximation of the incidence of bronchogenic carcinoma in the European and Coloured groups, this being 5·4% and 4·7% for the two races respectively. Using Kreyberg's[10] assessment of the extent to which the cancer situation has developed in a population group by comparing the ratio of group I: group II tumours in males (Table VIII), we find that both the European and Coloured show a pronounced preponderance of group-I cases, but this trend is significantly higher among Europeans. The values for both races are similar to those found in high-incidence areas.

The age distribution in the Europeans included in this survey also conforms with the accepted pattern. There is a pronounced increase from 40 years onwards, with the largest number of cases occurring between 50 and 70 years, and after 70 years there is a sharp fall-off. The same pattern is noted in the Coloured group, except that the peak seems to be a decade earlier.

The male: female ratio in both races shows a pronounced male preponderance for all tumour types except adenocarcinoma, in which the sex ratio is close to unity.

Unfortunately, not many conclusions can be reached with regard to the Bantu of this series. Firstly, it is obvious that all the common tumour types are represented in the 10 Bantu cases. This number is far lower than the totals of the European and Coloured groups, but if the total number of hospital admissions over the period under consideration, and the distribution within the age groups of all the autopsy material (which includes very few Bantu over the age of 40 years—Table II), are taken into consideration, then this figure becomes less significant. The autopsy incidence of bronchogenic carcinoma in cases over the age of 40 years is 1·7%, which is appreciably less than in the European and Coloured groups of this series. The total number of cases, however, is too small for analysis.

It would thus appear, from our findings, that while there is evidence that the new lung-cancer situation of Kreyberg[10] has developed in both the European and the Coloured racial groups of Cape Town, it is more pronounced in the European. The paucity of Bantu cases, possibly owing to selective factors, does not permit true evaluation of the situation in this group, but indications from this survey and from the literature are that the frequency would appear to be less than in either of the other groups.

If environment were the dominant factor responsible for lung cancer in these groups, one would expect the frequency among the three groups to be more closely approximated. All are exposed to atmospheric pollution; if anything the Coloured and Bantu more so. These findings possibly reflect more closely the use of tobacco by the three races. White South Africans are among the heaviest smokers in the world. There are fewer smokers among the non-Whites, and those who do smoke, especially among the Bantu, consume fewer cigarettes than the Whites.

SUMMARY

The distribution of histological tumour types of bronchogenic carcinoma in the European and the Coloured groups in Cape Town shows a significant preponderance of squamous-celled and oat-celled carcinoma over adenocarcinoma in both races. This trend conforms with that found in high-incidence countries, and on the basis of the Kreyberg classification may be taken as evidence that a high incidence of bronchogenic carcinoma exists in these two races also, more so in the European than the Coloured.

In comparison there are few cases of bronchogenic carcinoma among the Bantu in this series. While a lower incidence in this race may be partly responsible for this finding, it is also to a certain extent due to selective influences, principally the relatively early age of death among Bantu patients admitted to hospital.

We gratefully acknowledge the advice and criticism of Prof. J. G. Thomson, given during the preparation of this work. This investigation was supported by a grant from the Cancer Research Fund of the University of Cape Town.

REFERENCES

1. Duchen, L. W. (1954): S. Afr. J. Med. Sci., **19**, 65.
2. Osburn, H. S. (1957): Cent. Afr. J. Med., **3**, 215.
3. Dean, G. (1959): Brit. Med. J., **2**, 852.
4. Higginson, J. and Oettlé, G. (1960): J. Nat. Cancer Inst., **24**, 589.
5. Dean, G. (1961): Brit. Med. J., **2**, 1599.
6. Gordon, H. (1962): S. Afr. Med. J., **36**, 491.
7. Brock, J. F. (1961): Acta Un. int. Cancr.—monograph *Cirrhosis and Primary Cancer of the Liver in Trans-Sharan Africa*, p. 46.
8. *Idem* (1949): S. Afr. Med. J., **23**, 1000.
9. Higginson, J. (1953): *Ibid.*, **27**, 341.
10. Kreyberg, L. (1959): Acta Un. int. Cancr., **15**, 78.
11. Whitwell, F. (1961): Brit. J. Cancer, **15**, 440.
12. Herman, D. L. and Critenden, M. (1961): J. Nat. Cancer Inst., **27**, 1227.
13. Kreyberg, L. (1961): Brit. J. Cancer, **15**, 207.
14. Whitwell, F. (1961): *Ibid.*, **15**, 429.
15. Pederson, E. (1961): *Ibid.*, **15**, 712.
16. Kreyberg, L. (1954): *Ibid.*, **8**, 199.
17. Davies, J. N. P. (1957): Acta Un. int. Cancr., **13**, 891.
18. Spain, D. M. (1959): J. Nat. Cancer Inst., **23**, 427.
19. Kreyberg, L. and Saxén, E. (1961): Brit. J. Cancer, **15**, 211.