

CARCINOMA OF THE LUNG *

AN ANALYSIS OF SEVENTY-FOUR AUTOPSIES

RIGNEY D'AUNOY, M.D., BJARNE PEARSON, M.D., AND BÉLA HALPERT, M.D.

(From the Departments of Pathology and Bacteriology, Charity Hospital and Louisiana State University School of Medicine, New Orleans, La.)

Two previous communications from this laboratory have dealt respectively with 40 cases of primary carcinoma of the biliary system¹ and 40 cases of primary carcinoma of the pancreas.² The present study deals with 74 cases of primary carcinoma of the lung. As in the previous communications, this report is principally concerned with the site and structure of the primary growth and with its spread locally and to distant parts. The clinical manifestations, their duration, and the immediate causes of death are also briefly considered.

Race, Sex and Age: The 74 cases of carcinoma of the lung were encountered in 6623 autopsies on individuals over 1 year of age performed between Jan. 1, 1931, and June 30, 1938 by the staff of the Department of Pathology of the Charity Hospital of Louisiana at New Orleans. Forty-seven patients were white (42 male, 5 female) and 27 negro (26 male and 1 female). The youngest patient was 21 and the oldest 75 years of age. One died in the 3rd, 4 in the 4th, 13 in the 5th, 33 in the 6th, 19 in the 7th, and 4 in the 8th decade of life (Tables I, II and III).

Site and Structure of Neoplasms: The main growth was located in the right lung in 38 cases and in the left lung in 33. In the 3 remaining cases the site could not be determined. In 35 cases the primary growth was located in one bronchus or the other, 6 in this group being located near or at the bifurcation of the trachea (Fig. 1). Twenty-eight growths were located in a branch of a bronchus (Fig. 2).

The diameter of the mass forming the primary growth varied from 2 to 15 cm. Ulceration of the bronchial mucosa was frequently observed, together with involvement of the bronchial wall and of the underlying pulmonic tissue. The affected bronchus was usually identified near the periphery of the growth and not

* Received for publication March 11, 1939.

TABLE I
Data on Patients with Squamous Cell Carcinoma

Number of case	Age yrs.	Sex and race	Site *		Spread		Clinical manifestations	Duration of illness mos.	Cause of death
			Right	Left	Regional	Distant			
S-1 33-1362	33	M W	B		Lymph nodes	Lymph nodes, pancreas	Pain, cough, dyspnea	3	Carcinoma
S-2 35-806	42	M W		B	Lymph nodes		Cough	6	Carcinoma
S-3 37-1021	42	M C		B U	Ribs		Pain, dyspnea, hemoptysis	9	Carcinoma
S-4 32-540	49	M C		B U	Lymph nodes	Lymph nodes	Cough, dysphagia	1	Carcinoma
S-5 32-277	50	M W			Lymph nodes	Lymph nodes	Pain, cough, loss of weight	5	Abscess of lung
S-6 32-1047	50	M C	Lung	Lung	Lymph nodes, pericardium	Liver, adrenals, skeleton	Pain, loss of weight	2	Carcinoma
S-7 38-233	50	M C		B	Lymph nodes		Hemoptysis	1	Carcinoma
S-8 31-371	51	M W		B U	Lymph nodes	Lymph nodes			Abscess of lung
S-9 34-309	51	M C	B		Lymph nodes	Liver, adrenals, pancreas	Pain, cough, dyspnea, hemoptysis	3	Carcinoma
S-10 36-1390	51	M W		Lung	Pleura		Pain	3	Carcinoma
S-11 33-448	53	M W		B U	Lymph nodes		Pain, dyspnea	2	Carcinoma
S-12 34-915	53	M C	B L		Lymph nodes		Pain	9	Abscess of lung
S-13 33-83	54	M W	B			Liver, pancreas	Cough, dyspnea, hemoptysis	6	Abscess of lung
S-14 33-275	54	M W	B L				Cough	5	Abscess of lung
S-15 37-526	54	M C	Lung		Pleura		Cough, loss of weight	5	Carcinoma
S-16 36-420	55	M W		B	Pleura	Kidney	Pain, cough, dyspnea	5	Carcinoma
S-17 38-176	55	M C	B L			Lymph nodes	Dyspnea, dysphagia	4	Carcinoma

* B = bronchus; U = upper; L = lower; M = middle.

S-18	37-1037	57	M W		B	Lymph nodes, pleura	Liver, skeleton, skin	Pain, cough, loss of weight	1	Carcinoma
S-19	33-563	58	M W	B	B	Lymph nodes		Cough	1	Carcinoma
S-20	37-885	58	M C	B L	B L	Lymph nodes		Dyspnea	1	Obstruction vena cava inferior
S-21	38-111	58	M C	B	B	Lymph nodes		Pain, cough, hemoptysis	1	Carcinoma
S-22	32-124	59	M W	B L	B L	Lymph nodes, pleura		Pain, cough, dyspnea	18	Abscess of lung
S-23	33-1277	59	M C	B U	B U	Lymph nodes, pericardium	Intestine	Cough, loss of weight, hemoptysis	12	Abscess of lung
S-24	38-114	59	M C	B	B	Lymph nodes, pericardium	Liver	Cough, loss of weight, hemoptysis	5	Carcinoma
S-25	36-1512	60	M W	B	B	Lymph nodes	Skeleton	Cough, loss of weight, hemoptysis	6	Carcinoma
S-26	32-967	61	M W	B L	B L	Lymph nodes, pericardium		Pain, dysphagia	5	Carcinoma
S-27	36-1083	61	M W	Lung	B	Lymph nodes		Pain	4	Carcinoma
S-28	37-333	62	M W	Lung	B	Lymph nodes, pleura, pericardium		Pain, cough, loss of weight, hemoptysis	12	Abscess of lung
S-29	38-55	63	M W	Lung	Lung	Lymph nodes, pericardium	Liver	Pain, dyspnea, loss of weight	7	Carcinoma
S-30	37-840	63	F W	B U	B U	Lymph nodes, pericardium	Kidneys	Pain	5	Carcinoma
S-31	35-1162	64	M W	B U	B U	Pleura		Pain, cough, loss of weight	4	Carcinoma
S-32	37-1237	64	M C	B	B	Lymph nodes	Lymph nodes	Pain, dyspnea	1	Carcinoma
S-33	38-376	64	M W	B	B	Lymph nodes	Liver, kidneys	Dyspnea, hemoptysis	7	Carcinoma
S-34	38-77	65	M W	B	B	Lymph nodes		Loss of weight	3	Carcinoma
S-35	36-342	68	M C	B	B	Lymph nodes		Dyspnea, loss of weight	6	Carcinoma
S-36	33-1082	73	M C	B	B	Lymph nodes		Cough		Abscess of lung
S-37	37-1031	74	F W	Lung	Lung	Lymph nodes				Thrombosis, coronary artery

TABLE II
Data on Patients with Reserve Cell Carcinoma

Number of case	Age yrs.	Sex and race	Site *		Spread		Clinical manifestations	Duration of illness mos.	Cause of death
			Right	Left	Regional	Distant			
R-1 33-59	21	M C		B U	Lymph nodes, pleura	Skeleton	Paralysis	1	Carcinoma, transverse myelitis
R-2 37-54	36	M W	Lung	B	Lymph nodes	Kidneys	Pain, dyspnea	4	Carcinoma
R-3 37-955	40	M C		B U	Lymph nodes		Pain, cough, loss of weight	1	Pneumonia, diffuse
R-4 32-354	46	M W		B U	Lymph nodes	Liver	Pain	4	Abscess of lung
R-5 36-304	47	M C	B	B	Lymph nodes	Kidneys, skeleton, meninges	Cough	4	Abscess of lung
R-6 32-112	48	M W		B	Lymph nodes	Liver	Dyspnea, loss of weight	3	Carcinoma
R-7 33-2	51	F C		Lung	Pleura	Liver	Pain, cough	1	Carcinoma
R-8 33-306	51	M C	Lung	Lung	Lymph nodes		Loss of weight, dysphagia	6	Carcinoma
R-9 37-1043	54	M W		B	Lymph nodes	Lymph nodes, liver, pancreas	Dyspnea	1	Lobectomy
R-10 35-180	56	M W	B L		Pleura		Pain	1	Carcinoma
R-11 31-99	57	M W	B U	B	Lymph nodes	Liver	Pain, cough	3	Carcinoma
R-12 36-212	57	M W		B	Lymph nodes		Cough, loss of weight, hemoptysis		Pneumonia, diffuse

* B = bronchus; U = upper; L = lower; M = middle.

R-13	58	M W	B		Lymph nodes				2	Abscess of lung
R-14	58	M W	B						6	Constriction vena cava superior
R-15	59	M W	B M		Lymph nodes				7	Carcinoma
R-16	60	M C	B		Lymph nodes, pleura		Liver, adrenals, pancreas			Carcinoma
R-17	61	M W		Lung	Lymph nodes		Liver, pancreas		1	Carcinoma
R-18	68	M C		B	Lymph nodes		Lymph nodes, liver		3	Carcinoma
R-19	68	M W	B L		Lymph nodes		Liver		6	Abscess of lung
R-20	72	M W	B L		Lymph nodes, pleura				6	Carcinoma
R-21	75	M W		B	Lymph nodes				24	Carcinoma

TABLE III
Data on Patients with Columnar Cell Carcinoma

Number of case	Age yrs.	Sex and race	Site *		Spread		Clinical manifestations	Duration of illness mos.	Cause of death
			Right	Left	Regional	Distant			
C-1 31-85	39	F W	B U		Lymph nodes	Lymph nodes	Pain	1	Constriction vena cava superior Carcinoma
C-2 34-163	48	M C		Lung	Lymph nodes, diaphragm	Lymph nodes, liver, pancreas	Pain, dyspnea	3	Carcinoma
C-3 34-747	48	M W	B		Lymph nodes	Lymph nodes	Pain, loss of weight, hemoptysis	3	Abscess of lung
C-4 36-346	49	M W	B		Lymph nodes		Cough, hemoptysis	7	Carcinoma
C-5 35-195	50	M W	B		Lymph nodes		Pain, cough	8	Abscess of lung
C-6 36-96	52	M W	B U		Lymph nodes		Pain, dyspnea	9	Carcinoma
C-7 37-439	52	M C	B		Lymph nodes, diaphragm		Pain, dyspnea	4	Lobectomy
C-8 38-434	52	M C	B L		Lymph nodes, pleura	Liver, adrenals, pancreas			Carcinoma
C-9 34-597	54	F W	B		Lymph nodes, pleura	Liver, adrenals, pancreas, spleen	Pain, dyspnea, hemoptysis	6	Carcinoma
C-10 35-1060	54	M W	B U		Lymph nodes			12	Carcinoma
C-11 36-160	61	M W		B U	Lymph nodes, ribs	Lymph nodes, adrenal	Cough, dysphagia	5	Carcinoma
C-12 38-222	62	M C	B		Lymph nodes	Adrenals, skeleton		1	Carcinoma
C-13 34-1295	64	M C	B		Diaphragm	Lymph nodes, skeleton	Cough	5	Carcinoma
C-14 35-442	65	M W		B L	Pleura, ribs	Adrenals, lymph nodes	Pain, cough, loss of weight	3	Carcinoma
C-15 34-952	67	F W	B L		Lymph nodes, pleura	Kidneys	Cough, dyspnea, loss of weight	5	Carcinoma
C-16 32-859	68	M W		B	Lymph nodes		Cough, hemoptysis	5	Carcinoma

* B = bronchus; U = upper; L = lower; M = middle.

in the center (Fig. 3). The primary growths and their metastatic foci varied in gross appearance, the variations seeming to depend principally on the rate of growth, the amount and character of the stroma, and such secondary changes as hemorrhage and necrosis, rather than upon the actual cellular structure of the tumor parenchyma. It was therefore impossible to set up definite criteria by which on gross examination the microscopic structure of the carcinoma could be predicted with any degree of certainty.

Following the histogenetic classification previously outlined by one of us (B. H.³), the neoplasms were divided into three groups on the basis of their microscopic structure — squamous cell, reserve cell and columnar cell carcinoma. Thirty-seven of the 74 neoplasms were squamous cell, 21 reserve cell and 16 columnar cell carcinoma.

The squamous cell carcinoma was usually composed of nests or sheets of tumor cells arranged more or less concentrically to form epithelial pearls (Fig. 4). In some growths the cells toward the center of the cell sheets disclosed varying degrees of keratinization (Fig. 5), or were transformed into scales or into cell débris (Fig. 6).

The reserve cell carcinoma was composed of sheets or solid masses of tumor cells, which formed no particular structure (Fig. 7). Usually the cytoplasm was scant and the cell borders hardly discernible. The nuclei of the cells were fairly uniform, ovate or elongated, and stained deeply. In some growths the cells seemed to be arranged in whorls (Fig. 8), in others there was a palisade arrangement of the peripheral cells (Fig. 9).

The columnar cell carcinoma was usually composed of columnar or cuboidal cells, and of solid masses of undifferentiated tumor cells. The columnar or cuboidal cells formed acinar or tubular structures which simulated in a haphazard way the normal epithelial structures of the air passages (Figs. 10 and 11). In some growths these cells were mounted on connective tissue stalks in a papillary arrangement (Fig. 12). Columnar cells forming acinar or tubular structures were occasionally observed in predominantly squamous cell growths.

In all three types of carcinoma of the lung there was a wide variation in the number of nuclei in mitosis. The amount and

density of the stroma, the degree of infiltration with lymphocytes and plasma cells, and the extent of areas of necrosis and hemorrhage also varied in the individual growths, as well as in different fields of the same growth.

Manner of Spread: Local extension with involvement of the regional lymph nodes occurred in 65 of the 74 cases (87.8 per cent), and extensive distant metastases in 41 (55.4 per cent). Metastatic foci were encountered in the liver 19 times, in the pancreas and suprarenal glands 8 times each, and in the kidneys and in the skeleton 7 times each.

Clinical Course: Thirty-seven of the 74 patients complained of pain in the chest, neck or epigastrium. Thirty-five complained of cough, with or without expectoration, 21 of dyspnea, 19 of loss of weight, 15 of hemoptysis, and 6 of dysphagia.

In the 65 cases in which information was available, the illness had lasted from 1 to 24 months, with an average duration of 5 months. The newgrowth was the principal lesion and the immediate or contributory cause of death in 71 patients.

COMMENT

The increasing importance of carcinoma of the lung as a clinical problem is made clear in such recent publications as those of Hruby and Sweany,⁴ Tuttle and Womack,⁵ Rabin and NeuhoF,⁶ Jackson and Konzelmann,⁷ Graham,⁸ Kennaway and Kennaway,⁹ Husted and Biilmann,¹⁰ Simons,¹¹ Mattick and Burke,¹² Edwards,¹³ Klotz,¹⁴ Matz,¹⁵ Howes and Schenck,¹⁶ Hochberg and Lederer,¹⁷ Tod,¹⁸ and Ochsner and DeBaKey.¹⁹ New opportunities for the analysis and clarification of some of its morphological problems are presented in the large series of cases studied at autopsy and reported in such recent communications as those of Geschickter and Denison,²⁰ Neely,²¹ Olson,²² Jaffé,²³ Lindberg,²⁴ Samson,²⁵ Rice,²⁶ Frissell and Knox,²⁷ Brines and Kenning,²⁸ Bauer,²⁹ and Koletsky.³⁰

There is an apparently wide variance in the conceptions of individual authors as to the histogenesis and structure of carcinoma of the lung. The available data have contributed materially to our knowledge, but no uniformity has as yet been attained in classifying these growths. The difficulty may be superficial, however, rather than essential. In our opinion a classification on a

histogenetic basis, combined with a nomenclature derived from the cell making up the growth, rather than from the structure which the cell forms, will go far toward simplification of the problem.

All carcinomas primary in the lung, it now seems clear, can be classified into one of three groups — squamous cell, reserve cell and columnar cell. The occasional overlapping of groups is not unexpected, since all carcinomas of the lung, we believe, are derived from a common ancestor cell, the reserve cell (Fried³¹).

SUMMARY

1. Seventy-four cases of primary carcinoma of the lung were encountered in 6623 autopsies on individuals over 1 year of age. Males and females were represented in the proportion 11:1. The age range was from 21 to 75 years. The average duration of illness was 5 months. Thirteen patients died in the 5th, 33 in the 6th, and 19 in the 7th decade of life.
2. In almost half of the cases the primary growth was located in one bronchus or the other.
3. Thirty-seven of the 74 cases were squamous cell, 21 were reserve cell, and 16 were columnar cell carcinoma.

REFERENCES

1. D'Aunoy, Rigney, Ogden, Michael Alexander, and Halpert, Béla. Primary carcinoma of the biliary system. A clinico-pathological analysis of 40 cases. *Surgery*, 1938, 3, 670-678.
2. D'Aunoy, Rigney, Ogden, Michael Alexander, and Halpert, Béla. Carcinoma of the pancreas. An analysis of forty autopsies. *Am. J. Path.*, 1939, 15, 217-224.
3. Halpert, Béla. Pathologic aspects of bronchiogenic carcinoma. *New Orleans M. & S. J.*, 1939, 91, 439-441.
4. Hruby, Allan J., and Sweany, Henry C. Primary carcinoma of the lung, with special reference to incidence, early diagnosis and treatment. *Arch. Int. Med.*, 1933, 52, 497-540.
5. Tuttle, William McC., and Womack, Nathan A. Bronchiogenic carcinoma: a classification in relation to treatment and prognosis. *J. Thoracic Surg.*, 1934, 4, 125-146.
6. Rabin, Coleman B., and Neuhof, Harold. A topographic classification of primary cancer of the lung; its application to the operative indication and treatment. *J. Thoracic Surg.*, 1934, 4, 147-164.
7. Jackson, Chevalier Lawrence, and Konzelmann, Frank W. Bronchial carcinoma — bronchoscopic biopsy in a series of 32 cases. *J. Thoracic Surg.*, 1934, 4, 165-187.

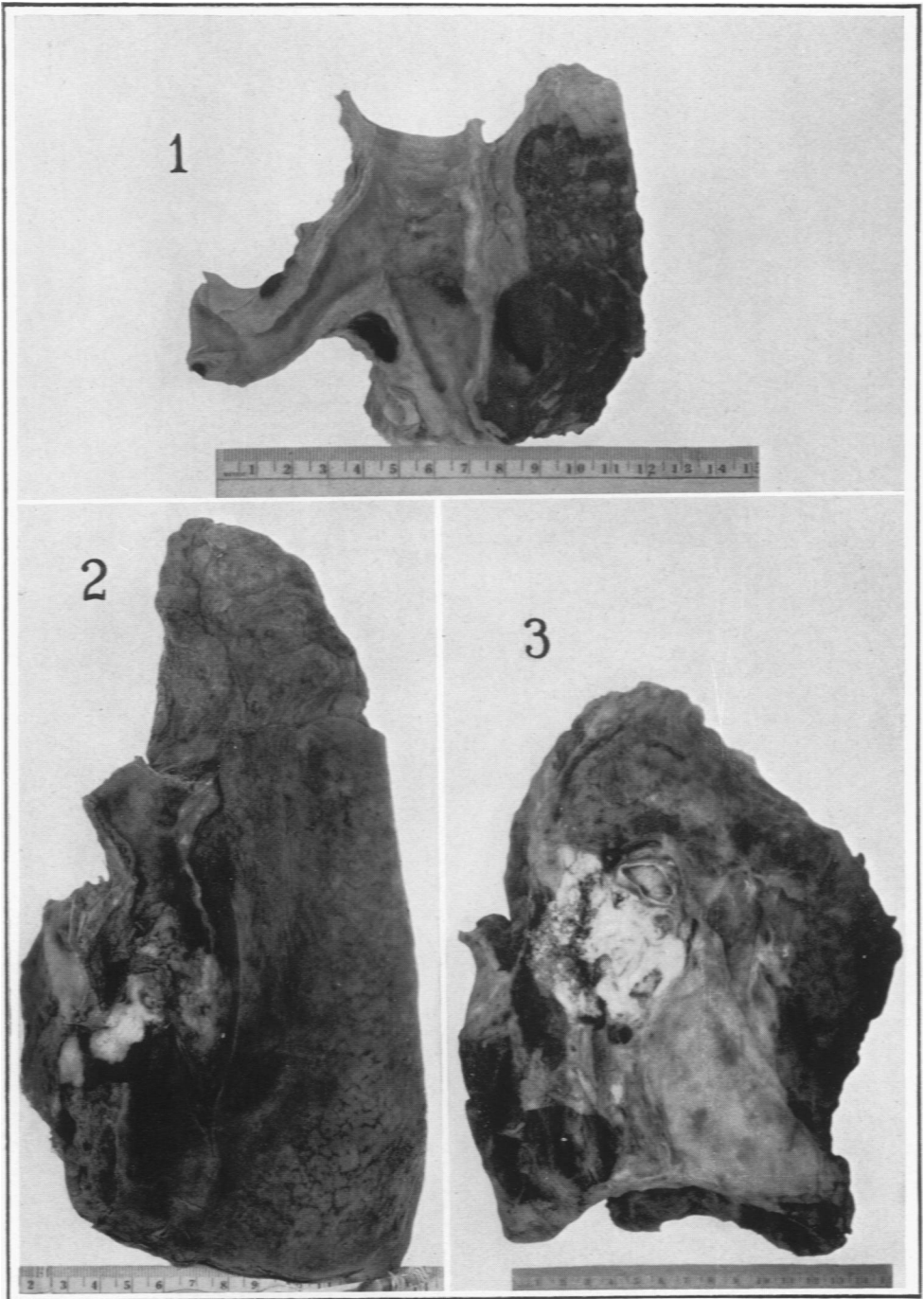
8. Graham, Evarts A. Primary carcinoma of the lung or bronchus. *Ann. Surg.*, 1936, 103, 1-12.
9. Kennaway, N. M., and Kennaway, E. L. A study of the incidence of cancer of the lung and larynx. *J. Hyg.*, 1936, 36, 236-267.
10. Husted, Erik, and Biilmann, Gerda. Primary cancer of the lung with reference to the frequency, etiology, pathological anatomy and histology of this lesion. *Acta path. et microbiol. Scandinav.*, 1937, 14, 141-196.
11. Simons, Edwin J. Primary Carcinoma of the Lung. The Year Book Publishers, Inc., Chicago, 1937.
12. Mattick, Walter L., and Burke, Eugene M. Primary bronchogenic carcinoma from the pathologic and radiologic points of view. *J.A.M.A.*, 1937, 109, 2121-2124.
13. Edwards, A. Tudor. Tumours of the lung. *Brit. J. Surg.*, 1938, 26, 166-192.
14. Klotz, Max O. Primary carcinoma of the lung. *Am. J. M. Sc.*, 1938, 196, 436-454.
15. Matz, Philip B. The incidence of primary bronchiogenic carcinoma. *J.A.M.A.*, 1938, 111, 2086-2092.
16. Howes, William E., and Schenck, Samuel George. Bronchogenic carcinoma. A study of eight autopsied cases. *Radiology*, 1939, 32, 8-18.
17. Hochberg, Lew A., and Lederer, Max. Early manifestations of primary carcinoma of the lung. *Arch. Int. Med.*, 1939, 63, 80-99.
18. Tod, M. C. Tumors of the lung, mediastinum, and pleura. *Edinburgh M. J.*, 1939, 46, 95-116.
19. Ochsner, Alton, and DeBakey, Michael. Primary pulmonary malignancy; treatment by total pneumonectomy; analysis of 79 collected cases and presentation of 7 personal cases. *Surg., Gynec., & Obst.*, 1939, 68, 435-451.
20. Geschickter, Charles F., and Denison, Robert. Primary carcinoma of the lung. *Am. J. Cancer*, 1934, 22, 854-877.
21. Neely, J. Marshall. Primary carcinoma of the lung; a pathological and clinical study based on eighty cases. *Nebraska M. J.*, 1935, 20, 247-252.
22. Olson, Kenneth B. Primary carcinoma of the lung. A pathological study. *Am. J. Path.*, 1935, 11, 449-468.
23. Jaffé, R. H. Primary carcinoma of the lung; review of 100 autopsies. *J. Lab. & Clin. Med.*, 1935, 20, 1227-1237.
24. Lindberg, K. Über die Histologie des primären Lungenkrebses. *Arb. a. d. path. Inst. d. Univ. Helsingfors*, 1935, 8, 225-473.
25. Samson, Paul C. Entdifferentiation in bronchogenic carcinoma. *Am. J. Cancer*, 1935, 23, 741-753.
26. Rice, Carol M. Primary carcinoma of the lung; a review of thirty cases. *J. Lab. & Clin. Med.*, 1936, 21, 906-909.

27. Frissell, Lewis Fox, and Knox, Leila Charlton. Primary carcinoma of the lung. *Am. J. Cancer*, 1937, 30, 219-288.
28. Brines, Osborne Allen, and Kenning, John Carl. Bronchiogenic carcinoma. *Am. J. Clin. Path.*, 1937, 7, 120-133.
29. Bauer, John T. A review of the primary carcinomas of the lungs and pleurae occurring in six thousand consecutive necropsies. *Bull. Ayer Clin. Lab., Pennsylvania Hosp.*, 1938, 3, 139-188.
30. Koletsky, Simon. Primary carcinoma of the lung; a clinical and pathologic study of one hundred cases. *Arch. Int. Med.*, 1938, 62, 636-651.
31. Fried, Boris Mark. Primary Carcinoma of Lung. Bronchiogenic Cancer. A Clinical and Pathological Study in Two Parts. Williams and Wilkins Co., Baltimore, 1932.

DESCRIPTION OF PLATES

PLATE 95

- FIG. 1.** Primary growth in the right bronchus at the bifurcation of the trachea. The neoplastic infiltration extends through the entire thickness of the wall (R 13).
- FIG. 2.** Primary growth in the hilus of the right lung in the wall of the bronchial branch to the lower lobe (R 20).
- FIG. 3.** Primary growth in the hilus of the left lung, arising from the bronchial wall. The bronchus lies along the anterior margin of the growth and not in the center (S 34).



D'Aunoy, Pearson and Halpert

Carcinoma of Lung

PLATE 96

- FIG. 4. Squamous cell carcinoma composed of nests or sheets of tumor cells arranged more or less concentrically to form epithelial pearls (S 14).
- FIG. 5. Squamous cell carcinoma. The cells toward the center of the cell sheets disclose varying degrees of keratinization (S 24).
- FIG. 6. Squamous cell carcinoma. The cells toward the center of the cell sheets disclose varying degrees of keratinization and a cell débris (S 13).

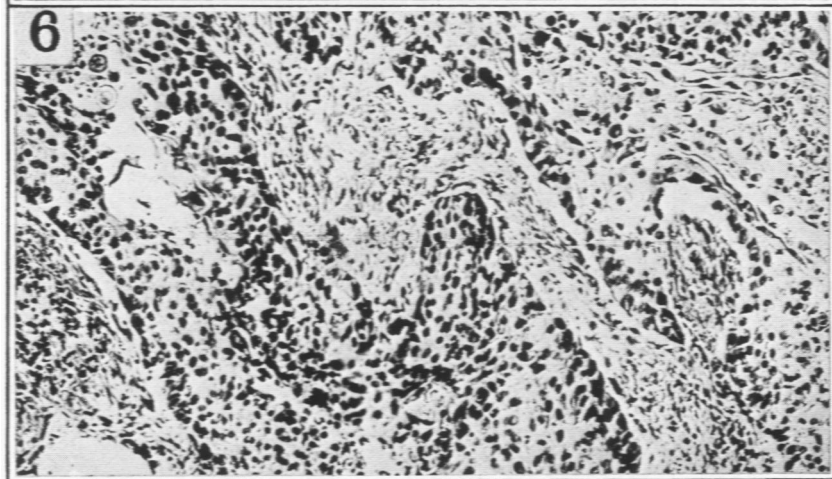
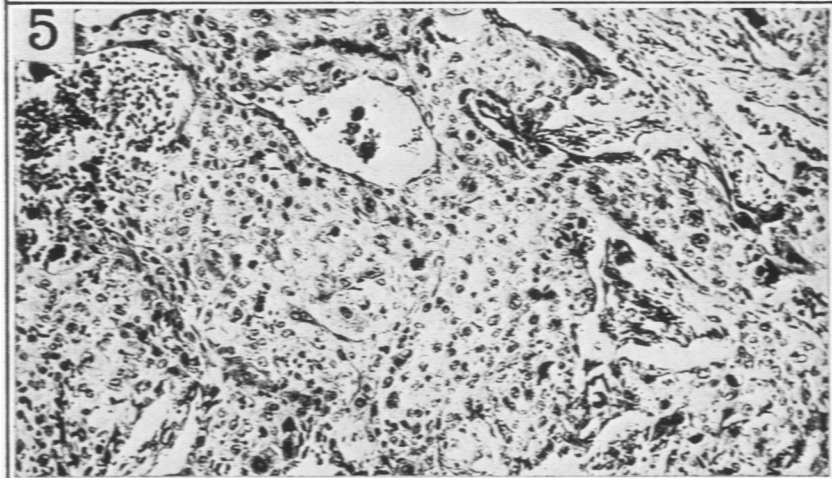
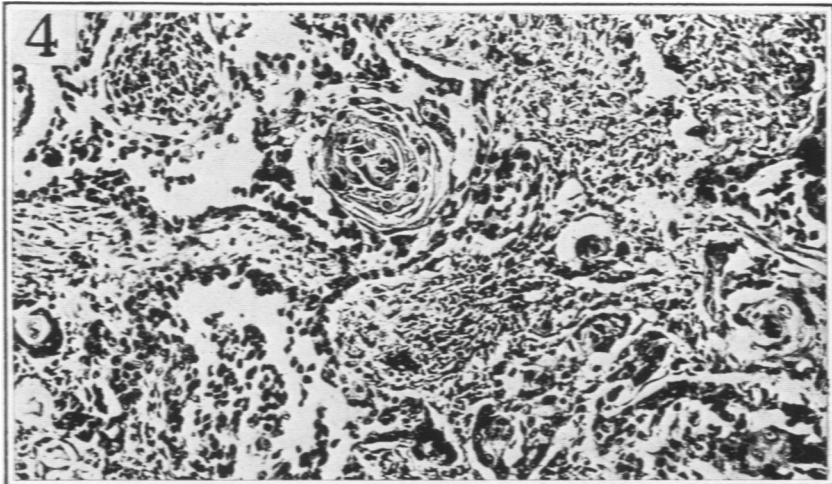


PLATE 97

- FIG. 7. Reserve cell carcinoma composed of sheets or solid masses of tumor cells forming no particular structure. The cytoplasm is scant and the cell borders hardly discernible. The cell nuclei are fairly uniform, ovate or elongated, and stain deeply (R 6).
- FIG. 8. Reserve cell carcinoma. The cells seem to have a whorl-like arrangement (R 19).
- FIG. 9. Reserve cell carcinoma. A palisade arrangement of the peripheral cells is seen (R 20).

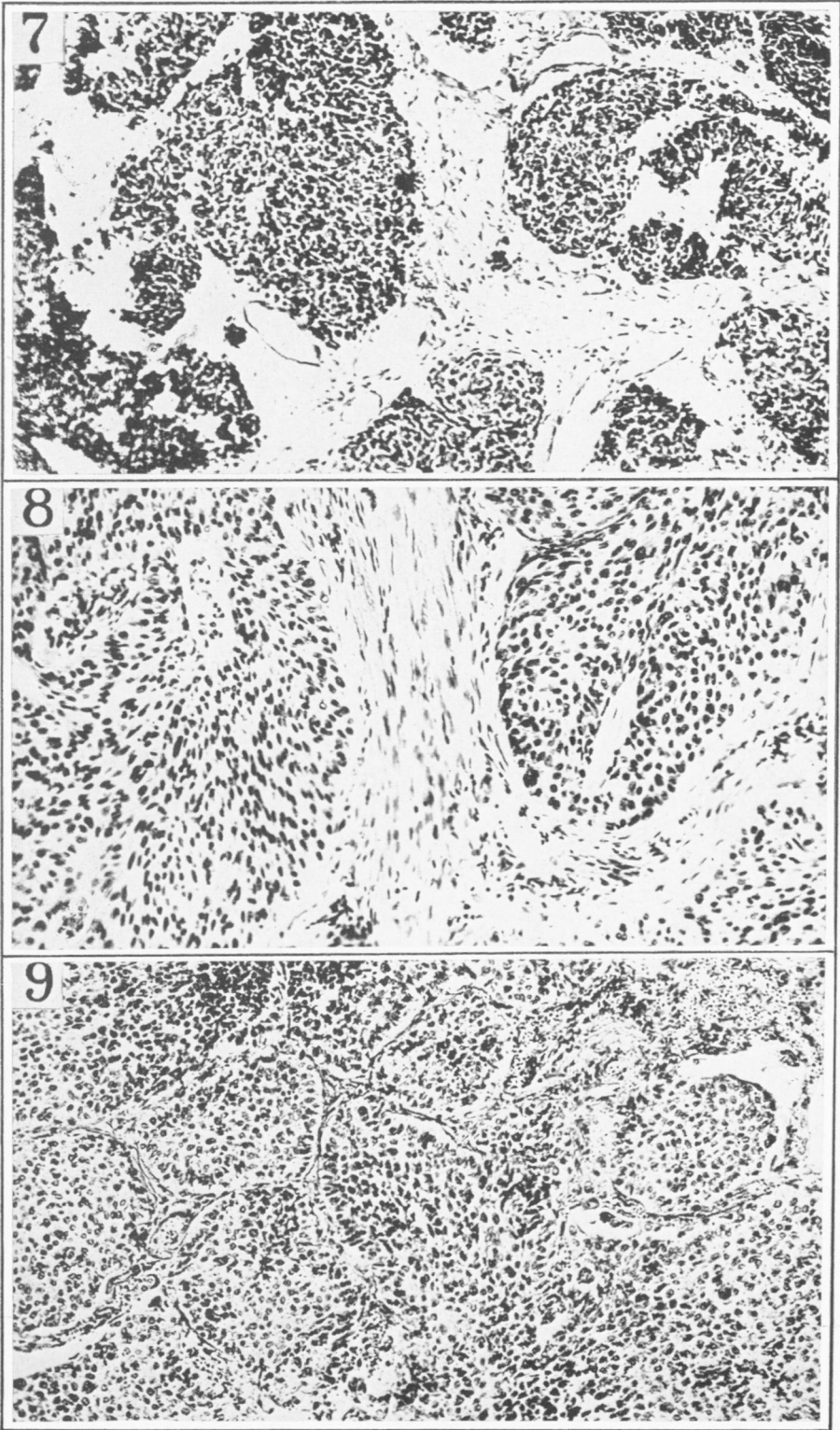


PLATE 98

FIGS. 10 and 11. Columnar cell carcinoma. The columnar or cuboidal cells, in acinar or tubular arrangement, simulate in a haphazard way normal epithelial structures of the air passages (C 12 and C 2).

FIG. 12. Columnar cell carcinoma. Tall columnar cells are mounted on connective tissue stalks in a papillary arrangement (C 11).

