Mice share with men the peculiarity of having tumors of the lung among the most common neoplasms. However, the lung tumors of mice are very different from the common cancer of the lung in man. The latter arises in the bronchi, leads to occlusion of the bronchi with its sequelae of atelectasis, abscess formation, unresolved pneumonia, fibrosis, and empyema, and is almost unexcelled in the extent of its widespread metastasis. The tumors of the lung of mice arise in the subpleural regions from the alveolar epithelium, and invading the bronchi in the form of papillary ingrowths do not often lead to the widespread necrosis and suppuration common to human lung cancer.

Of particular importance is the absence of metastasis. In the recent series of papers on the production of experimental lung tumors no mention whatever can be found of the occurrence of metastases, with the exception of papers by Campbell and by Magnus. Campbell (2) produced lung tumors by dusting mice with road dust, and of 26 cases thus produced there were metastases in three— one in the heart and two in the kidney. He comments on the fact that these were the first metastases to be observed in England, and also that this was the first case of metastasis to the heart. In a later paper (3) he reports that in 10 mice with tumors of the lung induced by extract of cardboard, one tumor gave rise to metastases in the mediastinal nodes and pleura. Magnus (5) produced tumors of the lung by giving 1,2,5,6-dibenzanthracene by stomach tube to mice, and observed one metastasis to the liver and one to the suprarenal. These are all the cases of induced lung tumors with metastases that we can find.

Of metastases in spontaneous tumors, the record seems equally blank, for no metastases are recorded in the great number of spontaneous tumors observed, except in a paper published from this laboratory in 1914 (6). Here were reported the spontaneous occurrence of 160 lung tumors observed in 6,000 mice, of which 4 showed metastasis outside the lung. This was the first, and until recently the only, example of metastases of lung tumors, and served to establish them as true neoplasms. Since that time we have observed many more instances of lung tumors, both with and without metastases.

Of 147,132 mice coming to autopsy in the Slye laboratory, where every mouse is allowed to live out its span of life, 2,865 mice had lung tumors, or about 2 per cent. Since a considerable proportion of the mice do not live to tumor age, the figure of mice of tumor age would be raised to about 3 per cent. Of these lung tumors, 104 showed metastases outside the lungs, or 3.6 per cent. All these showed metastases in the mediastinal lymph nodes, many of them also showed growths along the chest wall and on the diaphragm. Only 10 showed metastases to other locations; namely, 5 in the kidney, 3 in the heart (Fig. 1), 1 in the seminal vesicle, and 1 in the skull. There were also 284 tumors that were unquestionably malignant, as shown by metastases throughout the lung, making a total of 388 malignant growths, or 13.6 per cent of the lung tumors. Of the rest, a considerable number were probably malignant, as shown by invasion of the bronchi, and it was difficult to decide whether some were multicentric or metastatic and so were included as multicentric benign growths. The experimental study of lung cancer has shown that the growth begins in the alveolar walls, frequently extends into the bronchi, and presents no sharp distinction between malignancy and benignancy. There is equal difficulty in distinguishing between benign and malignant spontaneous tumors. Sometimes tumors that would be considered benign on the basis of structure and lack of invasive character are found to give rise to metastasis, while other tumors of wild growth fail to produce metastatic growth. All observers comment on the infrequency of mitotic figures, and the lack of this sort of evidence of malignancy.
The Occurrence and Pathology of Spontaneous Carcinoma of the Lung in Mice

H. Gideon Wells, M.D., Maud Slye, Sc.D., and Harriet F. Holmes
From the Otho S. A. Sprague Memorial Institute and the Department of Pathology, University of Chicago, Chicago, Illinois

(Received for publication March 10, 1941)

Mice share with men the peculiarity of having tumors of the lung among the most common neoplasms. However, the lung tumors of mice are very different from the common cancer of the lung in man. The latter arises in the bronchi, leads to occlusion of the bronchi with its sequelae of atelectasis, abscess formation, unresolved pneumonia, fibrosis, and empyema, and is almost unexcelled in the extent of its widespread metastasis. The tumors of the lung of mice arise in the subpleural regions from the alveolar epithelium, and invading the bronchi in the form of papillary ingrowths do not often lead to the widespread necrosis and suppuration common to human lung cancer.

Of particular importance is the absence of metastasis. In the recent series of papers on the production of experimental lung tumors no mention whatever can be found of the occurrence of metastases, with the exception of papers by Campbell and by Magnus. Campbell (2) produced lung tumors by dusting mice with road dust, and of 26 cases thus produced there were metastases in three—one in the heart and two in the kidney. He comments on the fact that these were the first metastases to be observed in England, and also that this was the first case of metastasis to the heart. In a later paper (3) he reports that in 10 mice with tumors of the lung induced by extract of cardboard, one tumor gave rise to metastases in the mediastinal nodes and pleura. Magnus (5) produced tumors of the lung by giving 1,2,5,6-dibenzanthracene by stomach tube to mice, and observed one metastasis to the liver and one to the suprarenal. These are all the cases of induced lung tumors with metastases that we can find.

Of metastases in spontaneous tumors, the record seems equally blank, for no metastases are recorded in the great number of spontaneous tumors observed, except in a paper published from this laboratory in 1914 (6). Here were reported the spontaneous occurrence of 160 lung tumors observed in 6,000 mice, of which 4 showed metastasis outside the lung. This was the first, and until recently the only, example of metastases of lung tumors, and served to establish them as true neoplasms. Since that time we have observed many more instances of lung tumors, both with and without metastases.

Of 147,132 mice coming to autopsy in the Slye laboratory, where every mouse is allowed to live out its span of life, 2,865 mice had lung tumors, or about 2 per cent. Since a considerable proportion of the mice do not live to tumor age, the figure of mice of tumor age would be raised to about 3 per cent. Of these lung tumors, 104 showed metastases outside the lungs, or 3.6 per cent. All these showed metastases in the mediastinal lymph nodes, many of them also showed growths along the chest wall and on the diaphragm. Only 10 showed metastases to other locations; namely, 5 in the kidney, 3 in the heart (Fig. 1), 1 in the seminal vesicle, and 1 in the skull. There were also 284 tumors that were unquestionably malignant, as shown by metastases throughout the lung, making a total of 388 malignant growths, or 13.6 per cent of the lung tumors. Of the rest, a considerable number were probably malignant, as shown by invasion of the bronchi, and it was difficult to decide whether some were multicentric or metastatic and so were included as multicentric benign growths. The experimental study of lung cancer has shown that the growth begins in the alveolar walls, frequently extends into the bronchi, and presents no sharp distinction between malignancy and benignancy. There is equal difficulty in distinguishing between benign and malignant spontaneous tumors. Sometimes tumors that would be considered benign on the basis of structure and lack of invasive character are found to give rise to metastasis, while other tumors of wild growth fail to produce metastatic growth. All observers comment on the infrequency of mitotic figures, and the lack of this sort of evidence of malignancy.