The Arterial Supply to Experimental Metastatic VX2 and XY Tumors in Rabbit Lungs*

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SUMMARY

The developed blood supply to experimental metastatic lung tumors in rabbits has been investigated by a variety of injection technics. The purpose for carrying out these experiments was to determine whether there was a bronchial arterial supply to metastatic tumors in addition to the pulmonary artery supply which had previously been demonstrated.

Evidence for a bronchial arterial supply was obtained post mortem in many specimens in which the major bronchial arteries were clearly injected and in which this injection mass reached vessels in the tumors. Few or no ink particles were distributed throughout the normal-appearing portions of the lung. In all preparations tumors found near the hilus were injectable via the bronchial arteries. Tumors located at the periphery of the lungs, which were 3.0 mm. or larger, were injectable via both the bronchial and pulmonary arteries. However, tumors which were less than 3.0 mm. in diameter and which were located at the periphery of lungs gave evidence of a blood supply from the pulmonary artery alone. The circulation to tumors in the lungs of living rabbits was observed by quartz rod transillumination. During these in vivo injection studies it was noted that, when India ink was injected via the systemic circulation, it was conducted to the tumor.

The treatment of patients with pulmonary tumors includes radical surgery, radiation and/or drug therapy. In the last decade, regional chemotherapy by perfusion of the pulmonary vascular bed in the treatment of selected patients with pulmonary neoplasms has become a reality (6, 9, 10, 23, 25). Conceivably, this therapy could become even more effective if the blood supply to developing lung tumors were more thoroughly understood.

The human lung has two anatomically and physiologically different arterial supplies. However, controversy still exists as to the function of these two systems in providing a blood supply to metastatic tumors (11, 19, 24, 25, 30, 34). Although the bronchial circulation in humans may differ from that in rabbits, the results of these experiments in rabbits may contribute to a better understanding of the progressive modification of the blood supply to metastatic pulmonary tumors in humans.

The purpose of the following experiments was to define the arterial blood supply to metastatic pulmonary tumors in the rabbit. The questions which the present experiments have tried to answer are: “Do pulmonary arteries alone supply blood to pulmonary tumors? Do bronchial arteries proliferate to supply pulmonary tumors under any circumstances? If so, under what circumstances? Are there any circumstances in which a dual supply exists?”

MATERIALS AND METHODS

The VX2 rabbit tumor has been used extensively in research (5, 7, 8, 12, 14, 15, 20–22, 26, 27, 29, 31–33, 35) and is the tumor used in most of the experiments described below. A portion of the following investigations was carried out with the XY tumor found in this laboratory (12).

Cell suspensions of the tumor tissue used for initiating growth within the rabbits' lungs were prepared in the following manner. Whole tumors were removed from the thighs of host rabbits and were minced with scalpel blades. The minced tissues were then strained consecutively through sieves with graded openings of 1000, 575, 250, 74, and 37 μ. The tumor cells were washed with sterile saline, and, by the force of gravity, saline suspensions of clumps of cells which had passed through each sieve were made. One ml. of the cell suspensions was
were used—namely, those aggregations of cells having
and 36 the XY tumor. Three sizes of cell suspensions
the 74-n sieve and trapped on the 37-ti sieve, and those
ejonctions of methyl methacrylate (16) (six via the external
jugular vein and six retrograde via the abdominal aorta).

Part I.—Fifty-four rabbits were given injections of
tumor cells. Eighteen rabbits received the VX2 tumor
and 36 the XY tumor: Three sizes of cell suspensions
were sacrificed. Seventeen of the injected rabbits died
during this period when the tumors were growing.

Of the remaining 37 rabbits, twelve were given in-
jections of methyl methacrylate (16) (six via the external
jugular vein and six retrograde via the abdominal aorta). The rabbits were refrigerated for at least 24 hours, after
which interval the tissues were macerated in saturated
potassium hydroxide, leaving only the plastic casts and
remnants of bone.

Thirteen rabbits were injected via the external jugular
vein with either a 20 per cent solution of India ink in
saline or a 20 per cent solution of mercuric sulphide (ver-
milion red, Murray Williams Co.) in saline. The remain-
ing twelve rabbits were given injections via each XY tumor cell size suspension, and twelve rabbits were used for
each VX tumor cell size suspension. The tumors were
allowed to grow from 25 to 42 days, when the rabbits
were sacrificed. Seventeen of the injected rabbits died
after death. In Part II, observations were made on
vasculature of which had been injected with a medium
studied.

Part II.—Fifty-four rabbits were given injections of
the VX2 tumor cells, as in Part I, except that cell aggre-
gations which had been trapped on the 250-μ and 575-μ
sieves were also used. These tumors were allowed to
grow from 21 to 45 days. Twenty-four rabbits were of no
critical value to this study, because either they died be-
fore the experiment was completed, or they did not have
visible tumors in those parts of the lung which could be
surface-illuminated or transilluminated for in vivo study.

Although this series of experiments consisted of differ-
ent technical approaches to the “marking” of the circula-
through the tumors, preliminary procedures were
nearly identical. All rabbits were anesthetized with
pentobarbital sodium (26.4 mg/kg of body weight),
tracheotomies were performed, and ligatures were placed
loosely around both common carotid arteries. A midline
laparotomy was done, and a ligature was placed loosely
around the abdominal aorta just below the diaphragm.
A polyethylene tube (I.D., 0.062", O.D., 0.082")", fitted
with a valve connected to a syringe of heparinized saline,
was introduced into the caudal vena cava with the open
end of the polyethylene tube directed caudally. After
n cannulation of the vena cava, a mid-ternal incision was
made to expose the heart and great vessels. Care was
taken to leave both pleural cavities intact. The animal
was allowed to continue its own respiration, while a glass
cannula was inserted into the left ventricle. The cannula
was connected to a source of mammalian Ringer solution.
Following heparinization (4 mg/kg body weight) by
injection into the caval cannula, the animal was perfused
through the left ventricle with mammalian Ringer solution
at 37°C. The valve connected to the polyethylene tube
in the vena cava was then opened, and the perfusion was
continued until the solution draining from it was clear.
Immediately prior to the injection of any medium the
common carotid arteries and the abdominal aorta were
ligated in an attempt to direct the medium into the
bronchial arteries.

<table>
<thead>
<tr>
<th>Tumor cell and upper size limit of aggregations initially injected</th>
<th>Injection medium</th>
<th>No. rabbits dead before observation</th>
<th>Total no. rabbits in series</th>
</tr>
</thead>
<tbody>
<tr>
<td>VX2 tumor:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37 μ</td>
<td>India ink</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>74 μ</td>
<td>Mercuric sulphide</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>250 μ</td>
<td>Methyl methacrylate</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>(Total VX2 tumor)</td>
<td></td>
<td>(3)</td>
<td>(18)</td>
</tr>
<tr>
<td>XY tumor:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>37 μ</td>
<td>India ink</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>74 μ</td>
<td>Mercuric sulphide</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>250 μ</td>
<td>Methyl methacrylate</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>(Total XY tumor)</td>
<td></td>
<td>(6)</td>
<td>(36)</td>
</tr>
<tr>
<td>Total no. rabbits:</td>
<td></td>
<td>9</td>
<td>54</td>
</tr>
</tbody>
</table>
The different methods of injecting the marker were as follows:

1. In six rabbits a 20 per cent solution of India ink in saline was passed into the systemic arteries through the glass cannula in the left ventricle while the heart was still beating. As soon as the ink became visible within the wall of the left ventricle the pulmonary artery was tied off, and after 20–80 ml. of ink was injected, the great vessels were clamped with a small hemostat to prevent the injection medium from the lung vasculature.

2. In four rabbits the glass cannula used for perfusion was subsequently removed and replaced by a 13-gauge 1½-inch intravenous (Horsley) needle. This needle was inserted through the wall of the left ventricle into the base of the aorta and was secured with a ligature. The pulmonary artery was tied off to prevent any flow of the injection medium through it. The pulmonary veins were clamped near the left atrium. Fifty to 100 ml. of diluted India ink was injected into the aorta under pressures of 50–100 mm Hg. After the injection was completed the remaining great vessels leading to and from the heart were clamped.

3. In eight rabbits technic 2 was used, except that the pulmonary veins were left open during the injection to minimize any backflow of the injection medium as a result of pressure build-up.

4. In four rabbits 0.25-ml. streptokinase (10,000 units/ml) in 5 ml. normal saline was injected, following heparinization, into the caudal vena cava to initiate the dissolution of any blood clots which might have formed. The vascular system was flushed out with a 1.5 per cent hypertonic mammalian Ringer solution. Twenty per cent India ink, suspended in a 4 per cent gelatin in mammalian Ringer solution, was then introduced into the left ventricle via a Horsley needle. After the heart had stopped beating the needle was secured in the base of the aorta, and more India ink-gelatin solution, to a total of 100 ml., was injected. The pulmonary arteries and the abdominal aorta were then ligated, and a suspension of 35–60 ml. of mercuric sulfide in 10 per cent gelatin was injected. The remaining great vessels were then clamped.

5. In one rabbit, the vascular system was flushed out with a 1.5 per cent hypertonic mammalian Ringer solution, after which latex, rather than India ink, was injected into the systemic and pulmonary arteries. The pulmonary artery was cannulated through the right ventricle, and blue latex was injected under 40–50 mm Hg pressure. The aorta was then cannulated through the left ventricle, and red latex was injected under 80–90 mm Hg pressure. In this animal the pulmonary veins, as well as the right atrium, were cut just prior to the injection to lessen pressure build-up. Following the injection, the remaining great vessels were clamped.

6. In seven rabbits in which tumors had been growing for only 15–20 days the vascular system was not flushed, and the following procedure was carried out. The right or left common carotid artery was cannulated with a polyethylene tube which was passed retrograde until its tip was positioned at the base of the aorta or in the left ventricle (position confirmed at autopsy). The circulation to the pulmonary tumors was observed in vivo before, during, and following the injection of India ink into the cannulated carotid artery by a method described by Knisely et al. (17). In addition to direct observations, permanent records were made on 16-mm. Ektachrome film (Type ERB) with a Cinekodak camera.

The lungs of all rabbits were infused intratracheally by gravitational flow of 10 per cent neutral formalin. The formalin-expanded lungs were then suspended in a bath of the same fixative. After fixation, gross observations were made of the intact surface of the injected lungs and of the cut surfaces of thick sections of injected uncleared and cleared lungs. Measurements of tumor sizes were made by both gross and microscopic methods. Microscopic observations were also made of histological sections of these lungs stained with hematoxylin and eosin and with nuclear fast red (1).

The technics and materials used in Part II are summarized in Table 2, and the number of rabbits observed with each technic is summarized in Table 3.

RESULTS

A more peripheral distribution of tumors was noted in the lungs of rabbits which had been given injections initially of the tumor cells that had passed through the 37-μ sieve. With an increase in the size of injected tumor cell masses the resulting tumors were observed to be more centrally located.

When examined microscopically, the metastatic tumors, except those on the surface, were usually spheroid and were growing in all directions from a cluster of injected cells (Fig. 1). Tumors on the surface making contact with the visceral pleura appeared to be flattened (Figs. 4, 5). The tumors attained an average size of 2.0, 3.0, and 4.0 mm. at 15, 20, and 25 days, respectively, after injection.

The blood vessels within the tumors were tortuous in contrast to the normal pulmonary vessels which are straight (Figs. 2, 3). Tumors of approximately 2.0 mm. or less in diameter were composed of tightly packed cells, with blood vessels passing through them (Fig. 7). In tumors larger than 2.0 mm., a necrotic center existed which became more evident as the tumor increased in size. The necrotic center was composed of amorphous material in which no blood vessels were found (Fig. 5). In these larger tumors, the walls of the blood vessels adjacent to the necrotic center were extremely thin and were surrounded by viable-appearing tumor cells. These cells formed the growing front of the tumor and bordered normal-appearing lung parenchyma (Fig. 11). A few thin-walled blood vessels were also identified in this area.

An examination of cleared and uncleared specimens under low magnification, and the study of histological sections, revealed no differences in the vascular patterns of the XY and VX2 tumors of the same size. Therefore, in the remainder of this paper, the type of tumor will not be identified, since this information is not pertinent to this study.

Related to Part I.—In the lungs of twelve rabbits given injections of methyl methacrylate, craters representing the avascular necrotic portions of tumors were present on the surface. The rim of each crater was formed by the cast of injected vessels which supplied blood to the pro-
liferating portion of each tumor. These vessels emerged from the surrounding solidly injected lungs and were identifiable as pulmonary arteries and veins. The histological sections of the lungs of the thirteen rabbits given injections of India ink or of mercuric sulfide via the external jugular vein all showed similar patterns. In a majority of the lungs the injection medium was found in the pulmonary arteries and in the tumor vessels. In a few, the injection medium was found only in the pulmonary arteries.

In four of the twelve rabbits given injections via the abdominal aorta, no injection medium was found in the lungs. The lungs of the other eight rabbits injected via the abdominal aorta contained the injection medium distributed sparsely in both pulmonary and bronchial arteries; however, no injection medium was seen in the pulmonary tumors of these eight rabbits.

Related to Part II.—In all the rabbits given injections of India ink, the tracheal, bronchial, and tumor vessels were well injected, whereas only a few ink particles were found in the pulmonary arteries (Figs. 1—3). In many cases the pulmonary veins draining the tumor vessels were injected (Fig. 3).

All tumors found near the hilus were injected via the bronchial arteries (Fig. 9). Tumors located at the periphery of the lung and measuring 3.0—4.0 mm. in diameter were also injected via the bronchial arteries (Figs. 11, 12). Particles of ink were found in vessels along bronchioles leading toward the tumors (Figs. 6, 8). With the exception of those tumors adjacent to the largest bronchi, only a few tumors less than 3.0 mm. in diameter were found with a blood supply from the bronchial arteries (Fig. 10). The bronchial arterial supply to the tumor as related to

### Table 2
**Technics and Materials Used in in Vivo Observations**

<table>
<thead>
<tr>
<th>Technic</th>
<th>Vascular wash-out</th>
<th>Injection medium</th>
<th>Point of injection</th>
<th>Vascular barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Normal Ringer</td>
<td>India ink</td>
<td>Lt. ventricle</td>
<td>Delayed ligation of pulmonary artery</td>
</tr>
<tr>
<td>2.</td>
<td>Normal Ringer</td>
<td>India ink</td>
<td>Aorta</td>
<td>Pulmonary artery ligated before injection</td>
</tr>
<tr>
<td>3.</td>
<td>Normal Ringer</td>
<td>India ink</td>
<td>Aorta</td>
<td>Pulmonary artery ligated before injection</td>
</tr>
<tr>
<td>4.</td>
<td>Hypertonic Ringer</td>
<td>India ink + gel-</td>
<td>Lt. ventricle +</td>
<td>Pulmonary artery and abdominal artery ligated after ink-gelatin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>atin + mer-</td>
<td>aorta</td>
<td>injection and before mercuric</td>
</tr>
<tr>
<td></td>
<td></td>
<td>curic sulfide</td>
<td></td>
<td>sulfide injection</td>
</tr>
<tr>
<td>5.</td>
<td>Hypertonic Ringer</td>
<td>Latex (blue)</td>
<td>Pulmonary artery</td>
<td>Pulmonary veins cut before injection</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+ Latex (red)</td>
<td>+ aorta</td>
<td>Right atrium cut before injection</td>
</tr>
<tr>
<td>6.</td>
<td>None</td>
<td>India ink</td>
<td>Aorta or Lt. ven-</td>
<td>None</td>
</tr>
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<td></td>
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<td>tricle</td>
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</table>

### Table 3
**in Vivo Observations of Rabbits with Metastatic VX2 Lung Tumors**

<table>
<thead>
<tr>
<th>Upper Size Limit of VX2 Tumor Cell Aggregations Initially Injected ((a))</th>
<th>Technic and Injection medium</th>
<th>Total No. Rabbits Observed</th>
<th>No. Rabbits Dead or Discarded Before Observation</th>
<th>Total No. Rabbits in Series</th>
</tr>
</thead>
<tbody>
<tr>
<td>37</td>
<td>1. India ink 2. India ink 3.</td>
<td>20</td>
<td>19</td>
<td>39</td>
</tr>
<tr>
<td>74</td>
<td>India ink 4. India ink + gel-</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>250</td>
<td>atin + mer. sul. 5. Latex</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>575</td>
<td>6. India ink</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1000</td>
<td></td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Total No. Rabbits: 6</td>
<td></td>
<td>30</td>
<td>24</td>
<td>54</td>
</tr>
</tbody>
</table>
the size of tumor cell aggregations injected initially is presented in Table 4.

Four of the six rabbits given injections according to technic 1 demonstrated that the tumors were supplied by a bronchial artery. Two of the four rabbits given injections according to technic 2 showed evidence for such a bronchial arterial supply. Five of the eight rabbits given injections according to technic 3 also showed evidence for such a bronchial arterial supply. All four rabbits given injections by technic 4 showed evidence for a bronchial arterial supply to the tumors. As a result of this double-injection technic, the arteries and arterioles were filled with red material, whereas the capillaries and veins were filled with black material.

The results of the injection into one rabbit of latex (technic 5) were not satisfactory. The size of the latex particles and/or the early solidification of the medium prevented the filling of the small vessels.

In seven rabbits, in an attempt to observe the marking of tumor circulation in vivo (technic 6), the tumor vessels were observed prior to and as the India ink was injected. It was assumed that, if a tumor were supplied by a bronchial artery, ink particles would be seen within the tumor before particles appeared within the normal surrounding pulmonary arteries. India ink particles moving at a rapid rate, in a pulsatile fashion, appeared in tumors in three rabbits at least 10 seconds before ink particles were seen passing through any nearby pulmonary arteries. In seven rabbits, in an attempt to observe the marking of tumor circulation in vivo (technic 6), the tumor vessels were observed prior to and as the India ink was injected. It was assumed that, if a tumor were supplied by a bronchial artery, ink particles would be seen within the tumor before particles appeared within the normal surrounding pulmonary arteries. India ink particles moving at a rapid rate, in a pulsatile fashion, appeared in tumors in three rabbits at least 10 seconds before ink particles were seen passing through any nearby pulmonary arteries.

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The vascular pattern of the VX2 tumor in the rabbit lung described in the results of this investigation is similar to that of the rat adenocarcinoma described by Lewis (18) and to that of the VX2 squamous-cell carcinoma in the rabbit-ear chamber described by Wood (31).

The method of injection used in Part I of this experiment failed to give consistent evidence concerning the blood supply of pulmonary tumors. Dead rabbits with tumorous lungs were given injections of large quantities of a medium forced against stagnated blood. The medium was found in veins and in arteries within the lung tissue and in tumors of some rabbits. The injection medium did not fill vessels of the tumors or the pulmonary arteries consistently. In some instances the medium was found in the small capillaries of the lung but not in the pulmonary veins or arteries or in the vessels of a tumor. This method did not confine the distribution of the injection medium to the desired area of investigation and was therefore abandoned.

Because of the inconclusive results obtained from the post-mortem injections in Part I, in Part II the medium was injected slowly during life into rabbits with lung tumors. It was assumed that the medium would be more uniformly distributed throughout the lung by being in-
jected at normal intravascular pressures and that the results would show the characteristic vascularity of tumors located within various areas of the lung.

In technic 4, because the pulmonary artery was tied off prior to the injection of a portion of the India ink into the aorta and before the injection of the mercuric sulfide, the red medium should have been present only in the bronchial arteries. Boeles and De Ruyter (4), using a dye dilution method, could not present proof of any functional anastomosis between the bronchial and the pulmonary arteries of the rabbit. Their findings supported the report by Verloop (28) that anastomoses between the bronchial and pulmonary circulations in rabbits exist only at the capillary level.

By flushing the vascular system with hypertonic Ringer solution, it was thought that the interstitial spaces would be less distended with fluid. This would leave the capillaries open for better filling by the injection medium. However, there was no major improvement in the filling of the lung vessels when the hypertonic Ringer solution was used, compared with the use of normal Ringer solution. The careful guidance of the injection medium by tying off certain vessels and the distribution of this medium by the force of the animal's own heat beat were the major advantages of the technics of Part II over Part I.

The reason for using the various modifications of a basic technic in this investigation was to eliminate as many erroneous conclusions as possible which might have been made on the basis of one technic. Essentially the same results were obtained with all the modifications of the basic approach in Part II.

That a bronchial arterial supply to the lung exists in the rabbit has been reported by Asai (2), Verloop (28), and Blandin et al. (3). Using a radiographic technic, Asai (2) found that metastatic pulmonary tumors were supplied initially by pulmonary arteries and, as the tumors grew, that bronchial arteries joined as "secondary nutrient arteries" to supply tumors close to the hilus. Knisely and Mahaley (14, 15) observed the VX2 tumor in vivo in the lungs of rabbits and included comments about the blood supply to transplants and to metastases but did not define the source of the blood supply.

The results of this investigation support and add to Asai's findings. That tumors can be injected via bronchial arteries has been demonstrated. It is believed, from this study, that the location of a metastasis in the lung will determine what its initial blood supply will be. If the metastasis becomes lodged in a vessel near the hilus, a blood supply from the bronchial artery will quickly develop supplemental to a pulmonary arterial supply. On the other hand, if its growth is initiated some distance from the hilus, the pulmonary arteries may supply it for some time until a bronchial circulation develops to the tumor. The secondary invasion of additional arteries into tumors at the lung periphery depends on the growth of the tumor and its changing relationship to the normal lung tissue. The findings of this investigation suggest that, as the increasing mass of a tumor impinges upon pulmonary tissue, the probability of its encroaching on a bronchial arteriole is increased.

ACKNOWLEDGMENTS

The technical assistance of Miss Carolyn L. Hoffman and Mr. Burnett Robinson is gratefully acknowledged.

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FIG. 1.—Photograph of a freshly fixed expanded rabbit lung. The aorta has been injected with India ink particles. Superficial tumors(s) are visible immediately below the pleura. $d =$ deep tumor. × 2.

FIG. 2.—Photograph of the right middle lobe of the rabbit lung shown in Fig. 1. Specimen has been cleared in a mixture of benzyl benzoate and methyl salicylate. India ink particles are clearly visible in the bronchial vessels (bv), tumor vessels (tv), and pulmonary veins (pv). × 3.

FIG. 3.—Photograph of an injected tumor (location indicated by arrow in Fig. 1). This tumor on the diaphragmatic surface of the right lung measured 4 mm. in diameter. India ink particles are visible in tumor vessels (tv) and in the pulmonary veins (pv). × 6.
FIG. 4.—Photomicrograph of a histological section of a 3.0-mm. tumor located immediately below the pleura. The shape of the whole tumor is discoidal. Nuclear fast red stain, X 49.

FIG. 5.—Photomicrograph of a histological section through the middle of the tumor shown in Fig. 3. India ink particles (arrows) are visible in the tumor vessels and in the bronchial vessels. Nuclear fast red stain, X 23. b = bronchiole, pa = pulmonary artery.
Fig. 6.—Photomicrograph of a histological section of a 1.5-mm. surface tumor. Serial sections showed that the bronchiole (b) was associated with this tumor. Nuclear fast red stain, X 30.

Fig. 7.—Highest power photomicrograph of the tumor outlined in Fig. 6. Injected India ink particles are clearly visible in the tumor vessels. Nuclear fast red stain, X 100.

Fig. 8.—Higher power photomicrograph of the area outlined in Fig. 6. Injected India ink particles are visible in a pulmonary artery (pa), in bronchial vessels (b), and in a pulmonary vein (pv). b = bronchiole. Nuclear fast red stain, X 45.
FIG. 9.—Photomicrograph of a histological section of a 0.9-mm. tumor located near the hilus of the lung. Injected India ink particles (arrows) are visible in bronchial and in tumor vessels. B = primary bronchus. Nuclear fast red stain, X 50.

FIG. 10.—Photomicrograph of a histological section of a 2.0-mm. tumor located deep in the lung. India ink particles (arrows) are visible in bronchial vessels and in tumor vessels. Nuclear fast red stain, X 83.

FIG. 11.—Photomicrograph of a histological section of the 3.0-mm. surface tumor shown in Fig. 3, at a more superficial level than Fig. 5. India ink particles (arrows) are visible in bronchial vessels and in tumor vessels. b = bronchiole, pa = pulmonary artery. Nuclear fast red stain, X 94.

FIG. 12.—Photomicrograph of a histological section of a 3.0-mm. surface tumor (same tumor as shown in Fig. 11). India ink particles (arrows) are visible in bronchial vessels and in tumor vessels. b = bronchiole. Nuclear fast red stain, X 90.
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