THE PROPORTION OF LUNG VESSELS BLOCKED BY ALBUMIN MICROSPHERES

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The number and diameter of vessels in the pulmonary circulation have been determined from a resin cast of a human lung. Assuming that microsphres (A) have a density of 1 gm/cc; (B) are perfectly spherical; (C) are of uniform diameter; and (D) will each block only one vessel—the percentage of pulmonary vessels blocked by 1 mg of albumin has been calculated. Spheres 60–90 μm in diameter block 0.31% of vessels, whereas smaller spheres 0.15 μm in diameter block 0.14%. Very large particles (525 μm) block only 0.12% of the pulmonary circulation, which suggests that they would not be more damaging than smaller spheres unless they produced another effect such as spasm in adjacent vessels. These results are in keeping with the clinical safety of lung scanning.

Weibel (*1*) estimated that there were 200–300 $\times$ 10^6 precapillaries in the human lung, and from this figure several authors (*2,3*) have calculated that albumin microspheres block less than 0.1% of pulmonary vessels in the normal subject. To obtain a more accurate estimate of the number of vessels blocked, we have measured a cast of the pulmonary vessels and calculated this number for different sizes of particles.

METHODS

The morphometric data. A resin cast was made of the pulmonary circulation of a 32-year-old woman who died from uremia (*4*). The number and diameter of all vessels from the pulmonary artery down to those of 800 μm diam (proximal zone) were measured with calipers. Three samples of branching structures with a main vessel just less than 800 μm diam (intermediate zone) were photographed through a dissecting microscope to include all branches greater than 100 μm (distal zone). Beyond 100 μm, the data of von Hayek (*5*) and Wagenwort, et al (*6*) for precapillaries were used.

The branching structure was described by the Strahler method (*7*) in which the most distal branches are defined as Order 1, and in the pulmonary system it would be the precapillaries. When two branches of Order 1 join, they form Order 2 branch; two Order 2 branches join to form a branch of Order 3. If branches of dissimilar order join, the resulting branch has the same order as that of the higher of the two daughter branches. An Order 3 branch may therefore supply two or more Order 2 branches (Fig. 1).

In the proximal and intermediate zones, the number of branches and their mean values of diameter follow geometric progressions with order. These have been interpolated with the known number and diameter of precapillary vessels to give an estimate of 17 orders in the complete system. The number of branches and their mean diameter in each order of the distal zone have been similarly estimated by interpolation. From the proximal and intermediate

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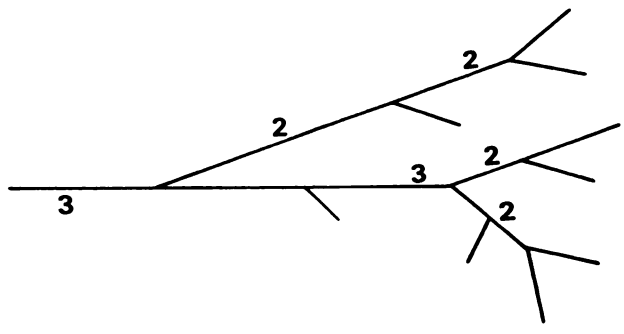

FIG. 1. Strahler ordering system.

TABLE 1. THE ORDER, DIAMETER, AND NUMBER OF VESSELS IN THE PULMONARY ARTERIAL CIRCULATION AND THE VOLUME AND NUMBER OF ALBUMIN SPHERES DERIVED FROM 1 MG OF THE PROTEIN

Pulmonary vessels			Albumin spheres		
Order	Number	Diam (μm)	Volume (cc)	No.	Percent of vessels blocked
10	1.09×10^{4}	525	7.576×10^{-5}	13.22	0.12
9	2.090×10^{4}	351	2.264×10^{-5}	44.17	0.21
8	7.152×10^{4}	224	5.885×10^{-6}	169.9	0.24
7	2.446×10^{5}	138	1.376×10^{-6}	726.7	0.30
6	8.373×10^{5}	90	3.817×10^{-7}	2,620	0.31
5	2.865×10^{6}	60	1.131×10^{-7}	8,842	0.31
4	9.802×10^{6}	40	3.351×10^{-8}	29,840	0.30
3	3.354×10^{7}	28	1.149×10^{-8}	87,030	0.26
2	1.148×10^{8}	20	4.189×10^{-9}	238,700	0.21
1	3.926×10^{8}	15	1.767×10^{-9}	565,900	0.14

zone data and the distal zone estimates, a statement of the complete arterial tree has been obtained as shown in Table 1.

Calculation of the proportion of vessels blocked. The percentage of vessels blocked by albumin microspheres has been calculated making the following assumptions:

1. One mg of albumin has been used.
2. No free albumin remains.
3. The particles are perfectly spherical and of uniform diameter.
4. Microspheres have a density of 1 gm/cc.
5. Only one particle blocks each vessel.

RESULTS

Table 1 shows the number and diameter of vessels of each order, and from these figures the number of spheres in each milligram of albumin and the corresponding percentage of vessels blocked have been calculated. Particles 60–90 μm in diam block a maximum of 0.31% of vessels, 15-μm particles 0.14%, and 525-μm particles 0.12%.

DISCUSSION

Measurement of the cast has yielded data down to vessels of 100 μm. Beyond this diameter the figures were obtained by interpolation with published data for precapillaries and provide the best current statement of the geometry of the pulmonary circulation. The assumptions made in calculating the proportion of vessels blocked tend to overestimate the result for the following reasons: the particles have a density greater than 1 because they settle out from saline solutions; and more than one particle may block each vessel. If the number of particles is small in proportion to the number of vessels blocked, the latter error is unlikely to be large.

The small number of vessels calculated to be blocked is in keeping with clinical experience of the safety of the technique. Many thousands of lung scans have been performed, and we are aware of only three fatalities (*8–10*). At autopsy in each of these patients, a further factor was operative: Dworkin and his colleagues (*8*) cited a case of carcinomatous emboli, and Vincent, et al (*9*) and Keeling (*10*) cited cases of severe pulmonary hypertension.

Experimental work on high dose has been confined to animals. Taplin (*11*) showed that the LD_{50} for dogs was approximately 40 mg/kg, and Mishkin (*12*) found that 7.15 mg/kg was required to raise their pulmonary artery pressure. Because there is no detailed information on the branching system in the dog lung, projection of these dose figures to man is difficult, so that assessment of a safe dose based on body weight is probably unjustifiable.

Vincent, et al (*9*) have proposed that large particles (300 μm diam) may be more toxic than those of 10 μm, but our results suggest that this is unlikely to be due to an increase in the proportion of vessels blocked. Other damaging effects might occur due to vessel spasm in the lung or large particles lodging in the cerebral circulation in patients with right-to-left shunts. A final technical point is that very large particles impair picture quality.

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