Alterations in Regional Pulmonary Blood Flow in Patients with Congenital Heart Disease Studied by Radioisotope Scanning

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SUMMARY
External scintillation scanning of intravenously administered ¹³¹I-labeled macroaggregates of human serum albumin (¹³¹I-MAA) was employed to evaluate the distribution of pulmonary arterial blood flow in 61 normal subjects and in 100 patients with various congenital cardiovascular malformations. Intra-aortic administration of ¹³¹I-MAA demonstrated that blood flow through subclavian-pulmonary artery anastomoses is directed principally to the lung on the side of the anastomosis; the relative concentration of ¹³¹I-MAA in each lung after intravenous injection provided an index of the patency of the anastomosis or of the development of pulmonary atresia or pulmonary hypertension. In contrast to the findings in patients with a patent subclavian-pulmonary shunt, scans obtained from patients with a patent ductus arteriosus did not reveal a separation of the systemic arterial and systemic venous inflows to the lungs. The patency of superior vena caval-right pulmonary arterial anastomosis could be assessed after injection of ¹³¹I-MAA into an upper-extremity vein.

Anomalies characterized by increased pulmonary blood flow or elevated pulmonary arterial pressures, or both, increased the ratio of pulmonary blood flow in the lung apices relative to that in the dependent lung zones. Anomalies characterized by elevated pulmonary venous pressure, such as cor triatriatum and mitral regurgitation, were readily detected by demonstrating both a decrease in blood flow to the lung bases as well as an increase to the apices. Thus, in patients with known pulmonary arterial hypertension (mean pressure, > 30 mm Hg) the ratio of upper to lower zone blood flow was always significantly higher if the arterial hypertension was accompanied by venous hypertension. For this reason, lung scans facilitated the screening of patients with pulmonary arterial hypertension for surgically correctable lesions such as cor triatriatum and mitral stenosis.

The method described is technically simple, without risk, easily applicable to large numbers of patients, and provides clinically important information concerning many forms of congenital heart disease.

Additional Indexing Words:
¹³¹I-albumin macroaggregates Superior vena cava-pulmonary arterial anastomosis
Bronchial circulation Subclavian-pulmonary arterial anastomosis Gravity
Pulmonary arterial hypertension Pulmonary venous hypertension

It has recently become possible to determine the distribution of pulmonary blood flow in an accurate and reproducible manner by scintillation scanning of the lungs after the infusion of ¹³¹I-labeled macroaggregates of human albumin (¹³¹I-MAA).¹-⁴ In the present study lung scans were employed to investigate the patterns of regional pulmonary blood flow (PBF) associated with a variety of congenital cardiac malformations, to evaluate features of the bronchial circulation in selected patients with cyanotic heart disease, and to define the

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alterations in the patterns of pulmonary perfusion which follow operations such as superior vena cava-pulmonary arterial anastomosis and subclavian-pulmonary arterial anastomosis.

It is recognized that, because of the influence of gravity on the low pressure pulmonary vascular bed, normal erect subjects have greater blood flow to the lung bases than to the apices. In patients with pulmonary venous hypertension, there is a relative increase in blood flow to the apices and a decrease in perfusion to the lung bases, and it has been shown that a linear relationship exists between the magnitude of the shift of blood flow toward the apices and the level of mean left atrial pressure. Investigations utilizing inhaled or injected radioactive gases have demonstrated that left-to-right circulatory shunts also increase blood flow to the apices and reduce the normal differences in perfusion between lung apex and base. Thus, the present investigation was also designed to study the distribution of PBF in patients with congenital heart disease in an effort to distinguish those with pulmonary arterial and venous hypertension from those with pulmonary arterial hypertension alone.

Methods

Scintillation scanning after administration of $^{131}$I-MAA to patients in the supine position was employed to obtain data concerning the relative PBFs to the right and left lungs. Except when specified, $^{131}$I-MAA was administered by the intravenous route to all of the patients studied. The relative perfusion between lung apex and base was determined after intravenous administration of MAA to patients who were in the erect posture. Thyroid uptake of $^{131}$I was blocked with Lugol’s solution which was administered for 10 days starting the evening prior to the injection of $^{131}$I-MAA. High specific activity (up to 3 mc/mg) radioalbumin aggregates (10-90 $\mu$) were used, providing count rates in excess of 5,000 cpm above background. A dose of 10 to 300 $\mu$c was administered during a 5-minute period of quiet breathing. Less than 50 $\mu$c and 0.10 mg of protein was injected intravenously into every patient in whom a right-to-left shunt was present or suspected, and in all instances of left heart or aortic root injection.

The particle distribution of $^{131}$I-MAA provides a precise delineation of pulmonary arterial blood flow because the concentration of radioactivity that accumulates in the lungs is directly proportional to the blood flow. The particles of albumin are too large to pass through the pulmonary capillary bed and are therefore trapped at the capillary and precapillary levels. The pulmonary extraction efficiency exceeds 80%, and an appreciable error is not introduced by recirculation because the particles not trapped by the lungs are extracted from the blood in the systemic capillary bed. With intra-aortic injection, the $^{131}$I-MAA reaches the lungs by way of the bronchial circulation unless a direct systemic-pulmonary arterial shunt is present. Significant metabolic breakdown of the $^{131}$I-MAA does not occur during the period of scanning. Considerable data concerning the hemodynamic, immunological, and radiation safety of the dose and preparation have been collected.

Details concerning the method of displaying, recording, and quantifying the output of the scintillation detector have been described elsewhere. The scanning was performed within 1 hour of $^{131}$I-MAA injection with the patients in the prone position and the detector mounted above them. Although the patients lay prone throughout scanning, the distribution of observed radioactivity in the lungs was that which was present at the time of injection. A conventional radioisotope scanner and a focussed collimator were employed. Horizontal rectilinear scanning was performed at a constant speed while the face of the detector was kept equidistant from the skin surface throughout the procedure. The level of radioactivity recorded in any region of the scan image of the lung is proportional to the blood flow to that area. Therefore, the distribution of blood flow to the lungs can be expressed as a percentage of the total activity of one or both lungs.

To compare the blood flows between the apex and base, the right lung was divided into three equal longitudinal segments from the apex to the top of the diaphragmatic leaf. The ratio of concentration of radioactivity between the upper and lower thirds, designated "U/La," was calculated and taken to represent the ratio of blood flow per unit of lung tissue in these two regions. Observations made for the vertical distribution of blood flow in the left lung were not analyzed in detail since the data from the patients with congenital heart disease were compared with those obtained from patients with mitral valve disease in whom a greatly enlarged heart often obscured the counting field in the left lung.

The specific diagnosis was confirmed at cardiac catheterization for each patient. Anglo-
cardiography and cardiac operation provided additional confirmation in many of the patients reported. The magnitude of intracardiac shunting was determined at cardiac catheterization by either the $^{85}$Krypton inhalation test or by oximetry. The ratio between the pulmonary and systemic vascular resistances was calculated from the formula:

$$\text{PVR/SVR} = \frac{1}{\text{QP/QS}} \times \frac{\text{PA}_m - \text{LA}_m}{\text{SA}_m - \text{RA}_m} \times 100,$$

where PVR = pulmonary vascular resistance; SVR = systemic vascular resistance; QP = pulmonary blood flow in L/min; QS = systemic blood flow in L/min; PA$_m$, LA$_m$, SA$_m$, and RA$_m$ = the mean pressures in the pulmonary artery, left atrium, systemic artery, and right atrium in mm Hg, respectively.

**Results**

**Distribution of Pulmonary Blood Flow to Both Lungs**

In 48 normal subjects in whom $^{131}$I-MAA was infused in the supine position, the average distribution to the right lung was $53 \pm 2.3\%$ (sd) of the total concentration of radioactivity. This partition of the PBF agrees closely with data obtained from bronchopulmonary flow.

**Peripheral Pulmonary Stenosis or Atresia of One Pulmonary Artery**

In five patients with unilateral stenosis of the right main pulmonary artery (mean pressure gradient in excess of 4 mm Hg), the fraction of the total PBF to the right lung averaged $47.1 \pm 2.5\%$, a value significantly less than normal ($P<0.02$). In one patient with a 5 mm Hg pressure gradient between the pulmonary trunk and the left main pulmonary artery, the left lung received 41.2% of the total PBF (normal = $47 \pm 2.4\%$). In four patients in whom multiple bilateral sites of pulmonary arterial narrowing were detected angiographically, blood flow to the right lung averaged $51.1 \pm 1.5\%$, a value not significantly different from normal. Of interest was the observation that in none of these four patients did the scans show ischemic areas similar to those observed after pulmonary embolism, suggesting that either pulmonary arterial collateral vessels provided adequate perfusion to the lung parenchyma distal to the sites of stenosis or the ischemic areas were too small to be detected by scanning (that is, <2 cm$^2$).

In two patients with pulmonary hypertension and atresia of the left main pulmonary artery, sequential intravenous and intra-aortic injections of $^{131}$I-MAA clearly distinguished pulmonary arterial from bronchial collateral flow (fig. 1). The scans following aortic injection showed considerable radioactivity in the left lung, reflecting the large flow to that side through bronchial arteries. Although the entire right ventricular output entered the right pulmonary artery in these patients, a

![Figure 1](http://circ.ahajournals.org/)

*Chest roentgenogram and lung scans after intravenous (left) and aortic root (right) administration of $^{131}$I-MAA into a patient with atresia of the left main pulmonary artery and a ventricular septal defect. The right lung receives all of the pulmonary arterial blood flow (left) while the left lung is supplied exclusively by the bronchial arterial collateral circulation.*
The distribution of pulmonary blood flow after intravenous $^{131}$I-MAA in patients with tetralogy of Fallot before and after subclavian-pulmonary arterial anastomosis. The patient whose right lung received 95% of the isotope had a patent aortic-right pulmonary arterial anastomosis and thrombosis of the left main pulmonary artery.

A small amount of radioactivity was also detected in the right lung after injections into the aortic root; this indicated some perfusion of this lung through bronchial collaterals, presumably due to obstructive changes in the pulmonary vascular bed.

**Subclavian-Pulmonary Anastomosis**

The relative distribution of PBF after intravenous injection of $^{131}$I-MAA was normal in 16 patients with tetralogy of Fallot studied preoperatively (average PBF to right lung = 52.7 ± 2%; fig. 2). Similarly, scans following intravenous injection into three patients with pulmonary atresia and ventricular septal defect who had undergone successful subclavian-pulmonary anastomosis from 3 weeks to 11 months earlier revealed normal distribution of perfusate (average = 52.5% to the right lung; fig. 2). Also, in four patients with tetralogy of Fallot and absence of, or markedly reduced, flow through a subclavian-pulmonary anastomosis, there were no differences in the distribution of intravenously administered $^{131}$I-MAA between the preoperative and postoperative lung scans.

In contrast to the patients with pulmonary atresia or nonfunctioning anastomoses, an average of only 36.3% of the total PBF was detected in lung on the same side as the anastomosis (fig. 2) after intravenous administration of $^{131}$I-MAA to 13 patients with a patent subclavian-pulmonary shunt. Of particular interest were the findings in two of these patients in the early postoperative period, one with a barely audible continuous murmur and the other with no murmur, who did not show an initial change from the perfusion pattern observed preoperatively. At follow-up study several months after operation, both children had become acyanotic, had loud continuous murmurs, and reexamination at this time revealed a marked relative reduction in radioactivity in the lung on the side of the anastomosis. In an additional patient with a patent aortic-right pulmonary artery shunt and thrombosis of a left subclavian-pulmonary anastomosis and main left pulmonary artery, essentially no perfusion of the left lung was observed after both intravenous and aortic root administration of $^{131}$I-MAA.

To delineate the cause of the asymmetry in perfusion in the patients with patent subclavian-pulmonary shunts, lung scans were performed after aortic root injection of $^{131}$I-MAA into five such patients (fig. 3), and into a sixth patient in whom the anastomosis was known to be occluded. In the patients with a patent anastomosis, an average of 65.1% of the isotope injected into the systemic circulation was detected in the lung on the same side as the shunt, whereas the patient with a nonfunctioning shunt showed essentially equal quantities of bronchial blood flow to both lungs.
Superior Vena Cava-Pulmonary Anastomosis

In a child with tetralogy of Fallot and a patent superior vena cava-right pulmonary anastomosis, the infusion of $^{131}$I-MAA, into an upper extremity vein resulted in distribution of radioactive particles to the lung on the same side as the anastomosis; particles were distributed almost entirely to the opposite lung after injection of the isotope into a lower extremity vein (fig. 4).

Patent Ductus Arteriosus

In nine patients with patent ductus arteriosus the right lung received $52.4 \pm 2.5\%$ of the $^{131}$I-MAA after intravenous injection. In five of these patients, when $^{131}$I-MAA was injected into the left ventricle or aortic root at the time of cardiac catheterization, $54.9 \pm 2\%$ of the radioactivity was detected in the right lung. Thus, the distribution of $^{131}$I-MAA administered either intravenously or directly into the systemic circulation was not significantly different from the distribution of intravenously administered $^{131}$I-MAA in normal subjects. After intravenous administration of $^{131}$I-MAA to a tenth patient with a patent ductus, $65\%$ of the total radioactivity was detected in the right lung; a similar distribution was observed 6 months and again 1 year after successful closure of the ductus. In this patient stenosis of the left pulmonary artery had been excluded at cardiac catheterization. Thus, although markedly asymmetric flow to the lung existed, unlike the patients with a patent subclavian-pulmonary anastomosis, it was not due to a separation of the systemic arterial from the systemic venous inflows to the lungs.

After scanning the lungs of an eleventh patient with a right-to-left shunt through a ductus, we were prompted to examine the systemic distribution of the $^{131}$I-MAA. In such patients desaturated pulmonary arterial blood is shunted into the descending aorta, so that it would be anticipated that radioalbumin aggregates would be trapped selectively in the systemic capillary bed of the lower, as opposed to the upper, extremities after intravenous injection of $^{131}$I-MAA. In the aforementioned patient with a right-to-left shunt through a ductus, radioactivity emitted from the ventral metatarsal surface and the mid-palm of the hand was counted for 5 minutes with a scintillation detector used routinely for thyroid counting, equipped with a 2-by-2 inch NaI crystal (TI) and flat field collimator. The accumulated radioactivity in the lower extremities was found to exceed that recorded from the upper extremities by an average of

Figure 3

Chest roentgenogram and lung scans after aortic root (left) and intravenous (right) administration of $^{131}$I-MAA; patient had tetralogy of Fallot and a patent right subclavian-pulmonary arterial anastomosis. Shunted blood was distributed predominantly to the right lung (left), while systemic venous blood was diverted to the left lung (right).
30 ± 6%. In contrast, when the same technique was employed in 11 patients with right-to-left intracardiac shunts and four patients with patent ductus and left-to-right shunts, the uptake of radioactivity over the upper extremities was 24 ± 7% higher than that over the lower extremities. Thus, it would appear that shunt reversal through a ductus may be detected by simple counting of the radioactivity that accumulates in the extremities.

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Table 1

<table>
<thead>
<tr>
<th>Subject</th>
<th>Diagnosis</th>
<th>U/L</th>
<th>PAm (mm Hg)</th>
<th>LAm (mm Hg)</th>
<th>SAm (mm Hg)</th>
<th>Qp/Qs (L/min)</th>
<th>PVR/SVR (%)</th>
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<td>88</td>
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<td>86</td>
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<td>19</td>
<td>8</td>
<td>114</td>
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<td>16</td>
<td>4</td>
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<td>2.2/1</td>
<td>6</td>
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<tr>
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<td>16</td>
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<td>1.5/1</td>
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<td>1.1/1</td>
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<td>44</td>
<td>2</td>
<td>79</td>
<td>0.85/1</td>
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Abbreviations: U/L = upper/lower ratio; ASD = atrial septal defect; VSD = ventricular septal defect; PPH = primary pulmonary hypertension; PAm, LAm, and SAm = pulmonary-arterial, left atrial, and systemic arterial mean pressure, respectively; RAm = right atrial mean pressure; Qp/Qs = pulmonary/systemic flow ratio; PVR/SVR = pulmonary/systemic vascular resistance \( \left( \frac{1}{Qp/Qs} \times \frac{PAm - LAm}{SAm - RAm} \times 100 \right) \).

Distribution of Pulmonary Blood Flow Within One Lung

In 13 normal subjects in whom \(^{131}\text{I}-\text{MAA}\) was infused during quiet respiration while they were erect, the ratio of isotope distribution per unit of lung volume in the upper third of the right lung to that in the lower third (U/L) was 0.43 ± 0.08 (fig. 5). U/L averaged 0.55 ± 0.09 in 10 patients with intracardiac left-to-right shunts and normal pulmonary arterial pressure, a value significantly higher than normal (\(P < 0.02\); fig. 5, table 1). In ten patients with intracardiac shunts accompanied by elevated pulmonary arterial mean pressures (in excess of 30 mm Hg) and pulmonary vascular resistances, U/L averaged 0.68 ± 0.10 (fig. 5, table 1), a value significantly higher than that obtained from the normal subjects (\(P < 0.005\)) and from the patients with left-to-right shunts and normal pulmonary arterial pressures (\(P < 0.01\)). In five patients with idiopathic pulmonary hypertension, U/L averaged 0.66 ± 0.07 (fig. 5, table 1). U/L was significantly lower in all of the patients with pulmonary arterial hypertension and normal levels of pulmonary venous pressure than in 25 patients reported on previously\(^2\) with both pulmonary arterial and pulmonary venous hypertension (U/L = 1.09 ± 0.28) (\(P < 0.001\); figs. 5 and 6). Moreover, U/L never exceeded 1.00 in the absence of pulmonary venous hypertension, regardless of the
pulmonary arterial pressure. Thus, at any level of mean pulmonary arterial pressure above 30 mm Hg, U/L was significantly higher in the patients with pulmonary venous hypertension than in those with pulmonary arterial hypertension alone (fig. 6).

Discussion

Until recently, the accurate topographical analysis of pulmonary perfusion necessitated techniques, such as pulmonary arteriography, bronchospirometry, and the injection or inhalation of radioactive gases. Inherent limitations in each of these methods prevented their widespread application to clinical problems. Because of its safety and technical simplicity, scintillation scanning of the lungs has made it possible to derive information concerning the regional partition of pulmonary blood flow in patients with a wide variety of cardiopulmonary disorders. In the present investigation, lung scanning provided particularly useful information concerning the fate of patent systemic arterial or systemic venous-pulmonary arterial anastomoses in patients with cyanotic heart disease and has allowed the distinction of patients with pulmonary arterial hypertension from those with both pulmonary arterial and venous hypertension.

In 1962, Fragoyannis and Kardalinas\(^4\) compared the histological appearance of the small pulmonary arteries in each lung after systemic-pulmonary arterial anastomosis. They observed differences in the caliber and muscular content of the medial layer of these vessels which suggested that the lung on the side of the anastomosis received the major portion of blood flowing through the artificially created shunt. Subsequently, Fort and associates\(^5\) demonstrated in animals with subclavian-pulmonary arterial anastomoses that the major proportion of the blood shunted from the subclavian artery passed to the lung on the side of the anastomosis, and that the shunt flow diverted a major part of the right ventricular output to the lung on the side oppo-
Subclavian-Pulmonary Artery Anastomosis

1. PATENT ANASTOMOSIS
2. NON-FUNCTION OF ANASTOMOSIS
3. PULMONARY ATRESIA
4. PULMONARY HYPERTENSION

Diagrammatic representation of the postoperative relation between systemic arterial and venous blood supply to the lungs in patients with tetralogy of Fallot. (1) When a subclavian-pulmonary anastomosis is patent, the lung on the same side as the anastomosis receives most of the oxygenated, shunted blood (solid black) while unsaturated, systemic venous blood (stippled gray) is diverted to the opposite lung. The development of a more symmetric distribution of either venous or shunted blood suggests that the anastomosis is (2) thrombosed, (3) patent in the presence of pulmonary atresia, or (4) patent in the presence of pulmonary hypertension. SVC = superior vena cava; IVC = inferior vena cava; RA = right atrium; RV = right ventricle; PA = pulmonary artery; LA = left atrium; LV = left ventricle; Ao = aorta.

Site the anastomosis. This finding is consistent with those reported in patients in an earlier communication from this laboratory, as well as by Tauxe and associates and Massumi and co-workers. The present study indicates that, together with routine clinical assessment of the patient, intravenous lung scans obtained serially following systemic-pulmonary anastomosis may provide information concerning the patency of the shunt, the severity of right ventricular outflow obstruction, and the development of pulmonary hypertension (fig. 7). It would appear that, although total pulmonary blood flow is increased after subclavian-pulmonary anastomosis, the augmented flow to the lung on the side of the anastomosis is largely composed of oxygenated shunted blood, while the flow...
to the opposite lung is largely unsaturated systemic venous blood (fig. 7). In addition, a patent shunt changes the distribution of blood entering the main pulmonary artery from the right ventricle, diverting most of the systemic venous return to the lung on the side opposite the anastomosis. The distribution of shunted blood becomes more symmetrical postoperatively if the severity of right ventricular obstruction increases, or the shunt through the subclavian-pulmonary artery anastomosis diminishes markedly or ceases (fig. 7). The latter may occur if thrombosis develops at the anastomosis or if pulmonary arteriolar vascular obstruction develops. These two possibilities may be differentiated with relative ease by determining the size of the pulmonary arteries on a plain chest roentgenogram. On the other hand, if symmetrical distribution of intravenously injected particles occurs in patients who have maintained clinical improvement postoperatively, then it may be assumed that an increase in the degree of pulmonary stenosis has occurred.

It may be anticipated, therefore, that in any individual patient, serial lung scans will afford a simple means for following the patient's condition postoperatively. It may also be anticipated that serial lung scans will permit an estimate of the patency of superior vena cava-pulmonary arterial anastomoses. If the anastomosis is patent, infusion of \(^{131}\text{I}-\text{MAA}\) will produce a scintiscan of the right lung only; on the other hand, the left lung will be visualized after an injection into a vein in the lower extremity (fig. 4). Obstruction at the site of the anastomosis leads to the retrograde flow of superior caval blood to the inferior vena cava via the hemiazygous venous pathway. Thus, postoperatively, relative increases in the radioactivity detected in the left lung after injection of \(^{131}\text{I}-\text{MAA}\) into an upper extremity vein suggest that malfunction and perhaps imminent thrombosis of the anastomosis exist.

Garfunkel and Kirkpatrick, and Whitley and associates have observed patients with patent ductus in whom decreased vascularity of the left lung was a prominent roentgenographic feature and both a primary decrease in perfusion, and unilateral overaeration have been postulated as being responsible for the asymmetric appearance of the lung fields. That the former may sometimes be the case is suggested by our patient, mentioned earlier, in whom asymmetric pulmonary arterial blood flow persisted after closure of a ductus. However, it is also clear that in an occasional patient the ductus may insert at a more peripheral site into the left pulmonary artery, and Ankeney and Tauxe and associates have each reported one such case in which the flow through the ductus entered the left lung exclusively, with the blood ejected from the right ventricle being diverted into the right pulmonary artery.

The clinical value of lung scanning in patients with pulmonary hypertension is based on the well-known fact that the normal pulmonary circulation has a low perfusion pressure and the distribution of blood entering the lungs is considerably influenced by gravity. Hence, in normal erect man there is much greater blood flow through the dependent zones of the lungs than through the apical regions. The present findings indicate that when pulmonary blood flow increases, as it does in patients with left-to-right cardiac shunts, this difference in flow between the upper and lower pulmonary zones decreases, even if the pulmonary artery pressure remains normal. Patients with left-to-right shunts with pulmonary arterial hypertension and without pulmonary venous hypertension show a further reduction of the difference in flows between the apical and dependent zones of the lungs, so that the blood flow per unit of lung volume in the upper third of the lung is approximately 70% of that in the lower third. In this regard, in several patients with transposition of the great arteries in whom the pulmonary artery could not be entered at cardiac catheterization, lung scanning was helpful in distinguishing normal from elevated pulmonary arterial pressures. When both pulmonary arterial and venous pressure rise, blood flow to the apices of the lung increases while flow to the bases diminishes; the
result is in an inversion of the pattern observed in normal erect subjects.\textsuperscript{2, 25, 26} Although pulmonary arterial hypertension alone results in elevated levels of U/L, the latter has never been found to exceed 1.00 in the absence of pulmonary venous hypertension. Hence, while relatively increased blood flow to the apices was found in our patients with left-to-right shunts, the Eisenmenger syndrome, and primary pulmonary hypertension, lung scanning may be of diagnostic value, since at elevated levels of pulmonary arterial pressure the shift of blood flow to the apices is always significantly greater in patients with both pulmonary arterial and venous hypertension than in patients with pulmonary arterial hypertension alone. For this reason the technique has been helpful in screening patients with known severe pulmonary arterial hypertension for potentially correctable lesions such as cor triatriatum or mitral stenosis which are also associated with pulmonary venous hypertension.

References

Bicentenary of Classic Description of Angina
Correlation with Coronary Disease

It may seem surprising that Heberden did not take any active part in the pathological investigations and the controversy over the cause of angina which was already arising in his lifetime. Jenner and Parry had both adopted the coronary theory by 1778, but delayed its publication for fear of alarming John Hunter in whom Jenner had diagnosed angina in 1777, at Bath, and had written to Heberden about the case though apparently the letter was not received; it was published in Baron’s *Life of Jenner*. Fothergill had published a case of fatal angina pectoris, in which Hunter found ossified coronary arteries at necropsy in 1776, and Samuel Black of Newry had reported ossified coronaries in anginal cases in 1794.—D. Evan Bedford: *William Heberden's Contribution to Cardiology*. J Roy Coll Physicians (Lond) 2:132, 1968.
Alterations in Regional Pulmonary Blood Flow in Patients with Congenital Heart Disease Studied by Radioisotope Scanning

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