Effect of heart disease on the pulmonary circulation

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The pulmonary circulation differs from other vascular beds in at least three notable ways. Since it is a relatively low-pressure system the effects of gravity are prominent; it must transmit the entire cardiac output each minute and, most importantly, the patency of the pulmonary capillaries is influenced by the pressure within the surrounding alveolar space.

The classic model divides the lung into three zones.[1] In the first zone, the apical zone of an upright subject, the alveolar pressure exceeds both pulmonary arterial and left atrial pressures so that there is no pulmonary blood flow. In the middle zone, pulmonary arterial pressure exceeds alveolar pressure, but flow is not continuous because the alveolar pressure exceeds the left atrial pressure during some part of the respiratory cycle. Pulmonary blood flow here depends on the difference between the left atrial and intraalveolar pressures. In the third zone, which is gravitationally dependent, both pulmonary arterial and left atrial pressures exceed alveolar pressure throughout the respiratory cycle and pulmonary blood flow continues without interruption, governed by the difference between the two intravascular pressures and uninfluenced during spontaneous ventilation by the intraalveolar pressure.

The model is a simple one and makes no allowance for pulmonary vasomotor tone, but it does provide a suitable framework on which to consider at least some of the effects of cardiac disease on the pulmonary circulation. These can be discussed under four headings: (1) transitory or sustained pulmonary venous hypertension; (2) increase in pulmonary blood flow; (3) decrease in pulmonary blood flow; and (4) changes in the metabolic functions of the pulmonary endothelium as a result of hemodynamic abnormalities.

Left atrial hypertension

A transitory increase in left atrial pressure without a corresponding increase in pulmonary arterial pressure would reduce the gradient across the pulmonary circulation in the third zone and so decrease basal flow. Higher in the lung, an increase in left atrial pressure allows the collapsible pulmonary capillaries to remain open throughout a greater proportion of the respiratory cycle, and pulmonary blood flow is directed away from the bases and towards the apices. Left atrial hypertension is soon matched by a corresponding rise in pulmonary arterial pressure and so apical blood flow increases and the size of the first zone decreases. Because the intravascular pressures are higher, a greater proportion of the pulmonary capillary bed remains patent and the pulmonary capillary blood volume rises. Transudation through the capillary wall is favored by the increase in left atrial above alveolar pressure, especially at the lung bases, where the gradient is highest. As a result, pulmonary lymphatic flow increases and there is also an increase in extravascular lung water, again most marked at the lung bases. This too may contribute to the redistribution of pulmonary blood flow toward the apices by raising the interstitial pressure around the basal capillaries. Alveolar edema and basal atelectasis occur as the volume of extravascular lung water rises still further.

A feature not apparent from the model is that sustained left atrial hypertension soon provokes an increase in pulmonary arterial tone, particularly at the lung bases. This too favors redistribution of pulmonary blood flow away from the bases and toward the apices. This increase in vascular tone can be relieved initially by pulmonary vasodilators but eventually structural changes develop that are largely irreversible. These anatomic changes affect the arterial, venous, and lymphatic vessels. The main pulmonary arteries are dilated and atheromatous; infarction is common as a result of either thrombosis or embolism. Medial thickening and intimal proliferation occur in the small muscular arteries and in the pulmonary arterioles, markedly in the basal vessels but less toward the apices. This is another important factor responsible for the reversal of the normal flow gradient so that the apices of the lung are perfused in preference to the bases in the upright subject. Pulmonary hemosiderosis occurs in advanced mitral stenosis, but necrotizing arteritis is rare and dilatation lesions are not seen. The pulmonary lymphatics are tortuous and dilated and their walls are thickened. Kerley B lines are usually attributed to these prominent lymphatic vessels, seen most readily on chest roentgenogram in the lower zones as horizontal lines at the outer edge of the lung shadow. Pulmonary venules and small pulmonary veins show intimal fibrosis and some medial thickening in chronic mitral valve disease; the alveolar walls are thickened but the increase in fibrous tissue is not striking.

Brief elevation of the left atrial pressure occurs in normal subjects during strenuous exercise, and the stimulation of pressure-sensitive J-receptors that results is probably one of the factors limiting exercise by contributing to the sensation of dyspnea. Elevation of the left atrial pressure is common during attacks of anginal pain, and repeated episodes of left atrial hypertension occur in patients with ischemic heart disease even though conventional tests of left ventricular function, done while symptoms are absent, demonstrate little or no impairment.

Extensive anatomic changes in the pulmonary circulation do not occur as a result of ischemic heart disease, but functional disturbances are probably more common than was realized at one time. Arterial hypoxemia and elevation of the alveolar-arterial oxygen tension difference are usual soon after myocardial infarction, especially if there are signs of pulmonary congestion or the systemic pressure is low. Such changes are to be expected from the foregoing discussion on the consequences of left atrial hypertension and the known effect on the arterial oxygen tension of a reduction in cardiac output. However, the changes can persist for 6 to 12 months or more after the infarction,[2] and abnormal values for the alveolar-arterial oxygen tension difference, the shunt fraction, and the ratio of dead space to tidal volume have been reported during exercise in 10 of 29 patients studied to 30 months after myocardial infarction.[3] None had any clinical evidence of left ventricular failure and the cardiac output was within the normal range; inappropriate elevation of the left atrial pressure appears the most likely explanation.

More surprising are the findings of the Framingham study in which vital capacity was found to be lower in symptom-free subjects in whom a first myocardial infarct subsequently developed or who died suddenly.[4] A comparable association was demonstrated in another investigation, which compared the vital capacity in subjects who subsequently had a myocardial infarct with controls, matched for age and risk factor, who remained healthy.[5] The relation between a low vital capacity and subsequent myocardial infarction or sudden death was independent of other risk factors such as cigarette smoking, hypertension, or elevated serum cholesterol and, although the forced expired volume in one second was also lower in those who subsequently had an ischemic incident, the ratio of forced expired volume in one second to forced vital capacity did not differ between subjects and controls.

Latent left ventricular failure has been suggested as the cause of this reduction in vital capacity, but such an explanation seems unlikely in view of the prolonged period of symptom-free follow-up in some of the subjects. Exercise-induced elevation of the left atrial pressure that is unusually severe, prolonged, or frequent because of early ischemic heart disease is another possibility, an increase in extravascular lung water secondary to left atrial hypertension being postulated as the immediate cause of the reduced vital capacity.

In the context of the surgical management of patients with ischemic heart disease, these early changes are of little practical significance, but the tendency to arterial hypoxemia many months after myocardial infarction is obviously important.

Pulmonary plethora

The pulmonary circulation develops abnormally when pulmonary plethora

is present from birth as a result of a left to right shunt. Pulmonary hypertension is inevitable if there is a ventricular septal defect or aortopulmonary communication, but there may be little or no increase in pulmonary arterial pressure, at least early in life, if the communication is at atrial level.

Progressive changes in the pulmonary circulation are usual with both types of shunt, but they occur more rapidly when pressure as well as flow is high from birth. Experimental studies in pigs, animals in which postnatal development of the lung resembles that of humans,[6] have shown that pulmonary vascular disease is more severe when an aortopulmonary shunt is created in young animals while postnatal remodelling of the pulmonary vasculature is occurring.[7]

The anatomic changes that develop in pulmonary hypertension associated with congenital heart disease were described as long ago as 1958 (*Table*), and this basis for staging has been retained to the present time. Although similar to the pulmonary vascular disease of mitral stenosis, there are some interesting differences. It is also important to note that the distribution of the lesions is more uniform in congenital heart disease.

The grade I lesion of pulmonary vascular disease complicating pulmonary plethora is characteristic of posttricuspid shunts in which the pulmonary arterial pressure is elevated from the outset. Pulmonary arterial pressure is normal or nearly normal in young patients with a pretricuspid shunt and, as pulmonary vascular disease develops, intimal proliferation in arterioles and the smallest muscular pulmonary arteries is the first feature, followed soon by medial hypertrophy and an extension of the muscular layer into the arterioles. Thus, the grade II lesion is the first pattern common to both pretricuspid and posttricuspid shunts. In either situation, the pulmonary vascular tone may be labile initially, but irreversible pulmonary hypertension develops eventually, often quickly in patients with a posttricuspid shunt.

Table. Pathology of the pulmonary circulation in pulmonary hypertension secondary to congenital heart disease

Grade I	Retention of fetal type pulmonary arteries with a muscular media in arterioles of 100 μ and less.
Grade II	Medial hypertrophy and cellular intimal proliferation
Grade III	Progressive fibrous vascular occlusion with replacement of muscle by fibrous tissue in the media
Grade IV	Progressive generalized arterial dilatation with the formation of complex 'dilatation lesions'
	Plexiform lesions
	Veinlike branches of hypertrophied, usually occluded, muscular pulmonary arteries
	Angiomatoid lesions
Grade V	Chronic dilatation with formation of numerous dilatation lesions and pulmonary hemosiderosis
Grade VI	Necrotizing arteritis

From Harris P, Heath D. The Human Pulmonary Circulation; Its Form and Function in Health and Disease 2nd ed. Edinburgh: Churchill-Livingstone, 1977.

Shunt reversal and right ventricular failure are the well-known consequences of these pulmonary vascular changes but pulmonary function is disturbed too. Pulmonary edema is a complication of large left to right shunts in infancy, whereas airways obstruction is frequently associated with pulmonary vascular disease in later life.

Pulmonary oligemia

Muscular and elastic tissues in the pulmonary arteries are less well developed than normal if the pulmonary

blood flow is low from birth as a result of a right to left shunt. Atrophy and luminal dilatation occur in the muscular pulmonary arteries, but the main pulmonary arteries are sometimes small.

Obliteration of parts of the pulmonary vascular bed by thrombosis occurs in patients with pulmonary oligemia, especially if they suffer from polycythemia too, but this is only common in the second decade and beyond. The ductus arteriosus remains patent in a number of these patients and the blood supply to the lungs is also increased by bronchopulmonary collateral vessels, which are large and numerous in cyanotic children. Damage and even disruption of the atrophied vessels can result when a normal pulmonary blood flow is restored by correction of the cardiac lesion, and pulmonary edema sometimes complicates postoperative management. A large palliative shunt can create such a high flow that edema develops; this is often unilateral if a Blalock rather than a Waterston shunt has been created, or if there are pulmonary arterial stenoses on one side. Edema after total correction can occur if the total pulmonary blood flow (pulmonary arterial plus bronchopulmonary collateral flow) is high and the vessels are atrophic and dilated, or if there is pulmonary venous hypertension as a consequence of left ventricular failure.

Metabolic functions of the lungs

Only in the relatively recent past have the extent and importance of the nonrespiratory or metabolic functions of the lungs been appreciated, and as yet there is little information on how they are influenced by cardiac disease.

Gillis et al,[8] in 1974, reported increased extraction of 5-hydroxytryptamine and norepinephrine by the lungs in patients with pulmonary hypertension secondary to valvular disease. Extraction fell after valve replacement if the pulmonary pressure fell too, but rose in two patients in whom the pulmonary arterial pressure remained unaltered. Amine extraction by the lung also rose after bypass in patients who did not have preoperative pulmonary hypertension. In a subsequent study of patients who had normal pulmonary arterial presssures preoperatively, Gillis et al[9] were unable to demonstrate a change in 5-hydroxytryptamine extraction after operation, but they point out that the duration of bypass was shorter and the anesthetic technique differed in their second study.

Claremont and Branthwaite[10] have studied serum angiotensin-converting enzyme activity in patients with valvular and ischemic heart disease. Preoperatively, the activity of angiotensin-converting enzyme was higher in patients with mitral valve disease than in a control group requiring thoracotomy for pulmonary surgery; those with ischemic heart disease occupied an intermediate position. Even after allowing for the effects of hemodilution, the activity of angiotensin-converting enzyme was lower postoperatively in the cardiac patients but was unchanged by thoracotomy. Preoperative pulmonary hypertension, subsequently relieved by surgery, may be a factor contributing to the higher values found preoperatively in patients with mitral valve disease. The reduction in angiotensin-converting enzyme activity after bypass might reflect some effect of the procedure on the pulmonary endothelium, or it could be a response to the high blood angiotensin II levels that are present at that time.[11]

Changes in pulmonary endothelial cell function as a consequence of cardiac disease are likely to be of practical as

well as of academic interest. Thus, Geddes et al[12] have demonstrated that propranolol is taken up by the human lung during a single passage through the pulmonary circulation. Clearance is reduced in patients using the oral preparation regularly, indicating that the mechanism responsible for uptake is saturable. This has obvious implications for the control of intravenous medication during anesthesia and cardiac surgery, and it is apparent that the effects of disease on pulmonary endothelial cell function merit further study.

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