SPECIAL ARTICLE

The Main Functions of the Pulmonary Circulation

By Julius H. Comroe, Jr., M.D.

I HAVE chosen the title of this lecture to correct the belief of some that the pulmonary circulation has only one function; some later Conner Lecturer, however, will surely correct the assumption in my title that in 1965 we know all of the main functions of the pulmonary circulation.*

We do know several important functions: The first—participating in pulmonary gas exchange—has long been known. The second—serving as a blood reservoir for the left ventricle—has been known for some years but could be demonstrated quantitatively only recently. The third—providing the nutrition of the alveoli and alveolar ducts—has been uncovered in the past 2 years. The fourth—filtering particles from the mixed venous blood—sometimes results in dysfunction, but I propose to consider it instead a function that is sometimes abused. The fifth—removing excess fluid from the alveoli—has been known since 1873, when Colin poured 25 liters of fluid down the trachea of a horse in a 6-hour period.

Gas Exchange

The alveoli and the alveolar capillaries are magnificently designed to exchange gases; no artificial lung ever made approaches them in capacity, speed, efficiency, compactness, or

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*There is now a vast literature on the pulmonary circulation, which includes several recent books, reports of symposia, and scholarly review articles. Fishman's "Dynamics of the Pulmonary Circulation" (in the Handbook of Physiology, Section 2, Circulation, Volume 2, pp. 1667-1743) contains 446 references for those readers who wish further details and documentation. This Conner Lecture is not intended to be another review, but more of a personal account of recent and current work by my colleagues in the Cardiovascular Research Institute.
durability. For teaching purposes, I have often pictured the lung by a greatly simplified schema (Fig. 1). Actually it is a vast, complicated and marvelous system of branching tubes that is in itself a superb engineering job. The air tubes begin at the nose and mouth and then join to become the trachea. The trachea divides into bronchi and the bronchi divide and subdivide into bronchioles. After 18 branchings, there are several hundred thousand respiratory bronchioles and after 24 branchings the air tubes end in about 300,000,000 alveoli, where most of the gas exchange occurs. The blood tubes begin as the pulmonary trunk, divide into the right and left pulmonary arteries, which then divide into arterioles, and these in turn into hundreds of millions of alveolar capillaries. The volume of blood in these capillaries at any one time is only about 75 ml, but the total surface area of the capillaries is 70 m²; the alveoli have a similar area for gas exchange.

If the gas exchanger is an ideal one, all of the inspired gas and mixed venous blood should be distributed uniformly to these millions of gas-blood interfaces. In the systemic circulation there is need for both regional regulation (to shift blood from nonvital organs to vital organs during stress, or from inactive to active organs) and for over-all regulation (to maintain a proper pressure head to drive blood through the cerebral and coronary arteries). Is there any need for regional or over-all regulation of blood flow through the pulmonary circulation? Because all of the right ventricular output must flow through the pulmonary blood tubes, these tubes, theoretically, should always offer minimal resistance to blood flow so that the work of the right ventricle is minimal. And yet we now know that there is both regional and over-all regulation of pulmonary vascular resistance.

Regional (local) regulation seems to serve the purpose of matching gas and blood flow. If gas distribution is not uniform but blood distribution is uniform, the gas exchanger is not an ideal one; if gas distribution is uniform and the blood distribution is not, again the gas exchanger is not an ideal one. When both are nonuniform, the gas exchanger will

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Figure 2

Sections of cat lung frozen by the ultra-rapid freeze technique of Staub and Storey. The lung on the left received a mixture of gas low in oxygen and high in CO₂; the lung on the right pure oxygen. Compare the narrowed arteriole (arrow) in the "hypoventilated" lung on the left with the wide arteriole (arrow) in the oxygenated lung on the right.

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*This is not true of the fetal circulation. In the fetus, gas exchange occurs in the placenta and it is to the advantage of the fetus to reduce pulmonary blood flow to the minimum required for maturation of the lungs; this can be achieved by general pulmonary vasoconstriction.*
still function well if the alveoli that have little ventilation also have little blood flow, and if the alveoli with more ventilation also have more blood flow. The matching of blood and gas is, therefore, crucial to good gas exchange.

Two mechanisms are known which help to achieve matching:

1. Regional alveolar hypoventilation results in pulmonary arteriolar constriction in the same region. This was demonstrated first by Liljestrand. Recently, Staub and associates in our Institute have been able to see and identify the vessels that constrict. They provided a low oxygen-high carbon dioxide mixture to one lung of an anesthetized cat and pure oxygen to the other lung; in this way they mimicked severe regional hypoventilation without significantly changing the oxygen content or tension of arterial blood and (because of the local vasoconstriction) without changing the arterial PCO2 or pH. They then inundated both lungs simultaneously with liquid propane, freezing the lungs almost as they were in life: Sections of the still-frozen lungs clearly demonstrated constriction of arterioles in the "hypoventilated" lung and not in the other (fig. 2). This constriction reduces pulmonary blood flow to regions with reduced air flow and helps to match air and blood flow throughout both lungs. The mechanism is a local one and does not depend on nerves or reflexes.

2. Regional ischemia results in airway constriction in the same region. Severinghaus, Swenson, and associates inflated a balloon at the tip of a catheter to occlude one pulmonary artery in both dog and man. Within a few breaths, air flow decreased to the lung with its pulmonary artery occluded and increased to the other lung. Such a regional increase in airway resistance serves to direct more of the inspired air to alveoli with normal or increased blood flow and so helps to match air and blood flow to the alveoli. It is partly for this reason that some patients who have complete obstruction of some pulmonary arteries by emboli have little or no unsaturation of their arterial blood.

Because alveoli with no pulmonary capillary blood flow receive no carbon dioxide from mixed venous blood, it seemed reasonable that the bronchoconstriction might be related to low alveolar PCO2. This was the case, because addition of 5% carbon dioxide to the inspired gas at the moment of inflating the balloon and occluding the pulmonary artery prevented the increased airway resistance, the shift of alveolar ventilation, and the matching of gas and blood. Several years ago Severinghaus and Stupfel and later Robin and associates believed that a low PCO2 in mixed alveolar gas—relative to the PCO2 of simultaneously measured arterial blood—might serve as a sensitive diagnostic test of

![Diagram](image-url)
pulmonary embolism and might even provide a quantitative measure of the proportion of the pulmonary circulation that was obstructed by emboli. Unfortunately, it is not so useful as predicted, probably because of this compensatory increase in airway resistance, which leads to a partial correction of mismatching of blood and gas that would otherwise instantaneously follow pulmonary embolism (fig. 3). The decrease in wasted ventilation helps the patient but hinders the physician in diagnosis. However, if the bronchoconstriction is severe enough to be measured, it, instead of the difference in carbon dioxide tensions, can become the clue to pulmonary embolism.9

**Blood Reservoir**

The pulmonary vessels normally contain about 600 ml of blood; most of this is in readily distensible vessels. This blood and that in the left atrium together serve as a reservoir that supplies blood to fill the left ventricle and maintain its output, even when the right ventricular output falls behind for a few beats. Guz and associates have demonstrated this nicely; they placed one electromagnetic flowmeter on a pulmonary trunk and another on the ascending aorta so that they could simultaneously measure pulmonary artery flow (the inflow to the pulmonary circulation) and aortic flow (which in a steady state is the output from the pulmonary circulation). In this way they could calculate beat-by-beat the change in pulmonary blood volume. Figure 4 shows the response to completely blocking the inflow to the pulmonary circulation. The stroke volume of the left ventricle continued unchanged for two beats and then gradually declined; when the pulmonary circulation was congested and its blood volume considerably increased, left ventricular output was maintained even longer without any blood added to the pulmonary circulation.

**Nutrition**

Many physiologists think of the pulmonary circulation as a set of pipes, delivering blood to the alveolar capillaries, collecting it, and sending it on to the left atrium and left ventricle, but having nothing to do with nourishing the tissue through which it passes. This view was strengthened by clinical observations: Surgeons had sometimes found it necessary to tie off one pulmonary artery but still leave the lung in place. A year or two later the tissues in such lungs appeared to be healthy. There was, of course, little uptake of oxygen because there was no pulmonary

![Figure 4](#)

**Figure 4**

Response to occlusion of the main pulmonary artery by inflation of a balloon; the left ventricular output remains unchanged for two beats and then gradually decreases.
circulation but the ventilation of the ischemic lung appeared to be normal. The obvious conclusion was that the pulmonary circulation is not essential for the nutrition of the pulmonary tissues, and, since it is not, the bronchial circulation must be. We assume that the anatomists knew better, but they were silent. Several years ago we got a rude shock. Finley, Tooley, and associates in our Institute wanted to see how long compensatory bronchoconstriction lasted after one pulmonary artery was occluded. To the surprise of no one, occlusion of one pulmonary artery for 24, 48, or 72 hours led to a decrease in ventilation to that lung, but to the surprise of everyone, this lung was atelectatic and markedly congested. Grossly and microscopically, it resembled the atelectatic lung of the newborn. But still the lung did not die and, with continued occlusion of the pulmonary artery, the ventilation of that lung increased, its appearance improved, and in 6 to 8 months it was reasonably normal in both ventilation and appearance, although somewhat scarred. The time required for its recovery seemed to be similar to the time required for the establishment of connections between the bronchial artery and the alveolar capillaries and it is a reasonable assumption that the bronchial circulation, by enlargement of existing channels or growth of new vessels, comes to the rescue of the pulmonary tissues.

The anatomists are correct that the bronchial arteries supply the airways down to and including the terminal bronchioles and that the pulmonary artery supplies the alveoli, alveolar ducts, and respiratory bronchioles. Nadel and his associates confirmed this in their experiments which showed that drugs that constrict smooth muscle affected only the alveolar ducts when injected into a pulmonary artery, and affected only the bronchioles when injected into the bronchial arteries.

To function properly, the alveoli and alveolar ducts require a minimal amount of blood flow per minute whether it comes from the pulmonary artery or the bronchial circulation. In the dog with unilateral pulmonary artery ligation, Tooley and associates (personal communication) have estimated that this minimal flow is about 10 ml per kg of body weight per minute. If these estimates are transferred to adult man, the minimal flow would be 700 ml per minute or only about one seventh of the normal pulmonary blood flow. It is unlikely that total pulmonary blood flow could ever be low enough during adult life to produce bilateral pulmonary ischemia and collapse, but regional blood flow can be too little to sustain cell function.

When an organ becomes ischemic, those cells with a high metabolic rate suffer first. The alveolar cells of the lung have many mitochondria (fig. 5) and a high metabolic rate. They are unusually active in the synthesis of phospholipids and have a high content of phospholipids, particularly of the saturated phospholipids and of dipalmitoyl lecithin. The alveolar cells contain intracellular structures unique in human tissues—the lamellar inclusion bodies. It appears at present that these contain dipalmitoyl lecithin or a chemical closely related to it; in some way, not yet understood, this substance reaches the alveoli and lines them with a monomolecular layer. In this form it has the unique property of decreasing surface tension and preventing collapse of alveoli during expiration.*

*Why does the surface active material, which lowers surface tension, prevent collapse of alveoli? We are accustomed to think that the elastic recoil of the lungs is due solely to recoil of stretched elastic fibers. Actually, it is also due to the surface properties of liquid—air interfaces in the 300,000,000 alveoli. Von Neergaard showed in 1929 that fluid-filled lungs, which have a fluid-fluid interface, enlarge more for a unit increase in transpulmonary pressure than air-filled lungs, which have a fluid-air interface. Since elastic fibers recoil the same amount whether alveoli are filled with fluid or filled with air, the additional recoil of air-filled lungs must be due to the surface tension effects—the tendency of tiny bubbles to become smaller. The surfactant which normally lines the alveoli is remarkable in this respect:—As the alveoli get smaller and their surface film is compressed, the surface tension decreases almost to zero and the recoil due to surface forces almost vanishes. The surfactant produced by alveolar cells is, therefore, an anti-atelectatic factor.

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When alveolar cells receive less than the minimal blood flow necessary for nutrition, two things can happen: (1) the quality or quantity of surfactant formed is not proper, or (2) pulmonary capillaries become leaky, plasma enters the air spaces, and plasma fibrinogen interacts with pulmonary surfactant to cause both an inactivation of surfactant and an inhibition of fibrinolysis. The result is that alveoli collapse and are filled with fibrin threads, the so-called hyaline membranes.

Although a total pulmonary blood flow less than the minimal required for nutrition is virtually impossible during adult life, it is possible in the newborn because there is a large bypass, the ductus arteriosus, which can accept all of the right ventricular output if it is not able to go through the pulmonary circulation. Ischemia of the newborn lung might, therefore, be a cause of atelectasis or respiratory distress syndrome.

In 1964, Drs. Clements, Tooley and Klaus were convinced that the pulmonary surfactant was dipalmitoyl lecithin or a chemical very similar to it. Because of mounting evidence that loss or inactivation of dipalmitoyl lecithin was a major factor in respiratory distress syndrome of the newborn, they and five associates spent six months studying this
disease at the Kandang Kerbau Hospital at the University of Singapore. This hospital was chosen because it is by far the largest maternity hospital in the world and because it is affiliated with the University of California through its International Center for Medical Research and Training. At first the group tried to propel additional dipalmitoyl lecithin into the lungs of the newborn with respiratory distress syndrome after aerosolizing it. This replacement-type of therapy helped some infants but not all. The failures were probably due to inability to propel enough material into alveoli that were already collapsed, to the inability to obtain a suitable Freon propellant that was free from mild anesthetic properties, and to the presence of material in the alveoli (probably plasma fibrinogen) which inactivated some or all of the dipalmitoyl lecithin that did reach the alveolar surfaces. When they studied babies who died of respiratory distress syndrome, they found that the pulmonary circulation offered unusually great resistance to the flow of fluids through it. They then measured pulmonary blood flow in living babies and found that in those with respiratory distress syndrome it was only one third of that in healthy babies. The increased resistance to pulmonary blood flow was not due to thrombi because it returned toward normal values when pulmonary vasodilators were infused intravenously. Intravenous acetylcholine often led to an outpouring of previously retained CO2, a decrease in arterial Pco2, an increase in arterial blood pH and P02, and a marked decrease in wasted ventilation. But in some babies, sustained pulmonary vasodilatation was obtained only by intravenous administration of sodium bicarbonate, thus confirming and findings of Liljestrand, and Enson and associates that acidosis is a potent pulmonary vasoconstrictor. The same combination of pulmonary ischemia, atelectasis, and hyaline membranes occurs in babies with respiratory distress syndrome and in dogs following experimental pulmonary artery occlusion.

No one knows yet whether the pulmonary ischemia in babies comes first and is causative or whether it comes later as a result of hypoventilation, hypoxia, and acidosis. And no one knows whether, if it comes first, it is due to episodes of fetal asphyxia or fetal hypotension or whether it is due to a failure of fetal pulmonary vessels to relax normally at birth. We still have to learn much about the mechanisms which, at the birth of a baby, simultaneously cause the pulmonary arterioles to dilate but the ductus arteriosus and the umbilical arteries to constrict. High oxygen concentrations are known to dilate pulmonary arterioles in the fetus and to constrict the ductus arteriosus and umbilical arteries even in vitro, but reflexes may also be involved.

Injection of nicotine (which stimulates both the aortic and carotid bodies) into the ascending aorta of man causes pulmonary vasoconstriction (Burgess, personal communication). In the dog, stimulation of only the aortic body leads to reflex pulmonary vasoconstriction; presumably lack of stimulation leads to pulmonary vasodilatation. It is of interest that although stimulation of either the carotid or the aortic bodies increases respiration, stimulation of the carotid body in the dog produces bradycardia and hypotension while similar stimulation of the aortic body produces tachycardia and hypertension (fig. 6). The aortic bodies of adult animals receive their blood supply from a branch of a coronary artery or of the aortic arch. In the fetus this vessel communicates with a small branch of the pulmonary artery; this vascular system is similar to the ductus arteriosus in that it connects the pulmonary artery and the aorta (though the diameter of the channel is far smaller) and it closes shortly after birth. We do not know whether this unusual blood supply has some significance in the reflex control of pulmonary vascular resistance or resistance to flow through the ductus arteriosus in the fetus.

We do not believe that there is a separate pulmonary body in the adult which receives blood from a branch of the pulmonary artery because we have never been able to find, beyond the newborn period, a patent artery to chemoreceptor tissue that arises from the.
Temporal separation of aortic and carotid body stimulation. Above: Nicotine injected through a catheter placed in the aorta just beyond the aortic valves reaches the aortic bodies within 1 sec, but because it must pass through long delay paths (coil made of plastic tubing) inserted in the common carotids, does not reach the carotid bodies until 75 sec later. Below: Nicotine injected at 2 stimulates aortic bodies and causes tachycardia and hypertension; later (at 4) it reaches carotid bodies and causes bradycardia and hypotension. A neuromuscular blocking agent (succinylcholine) was injected at 1 to produce apnea and eliminate any effects of hyperventilation. Top tracing is respiratory air flow; bottom tracing is blood pressure on the cardiac side of the delay coils. A portion of the record was deleted at 3 to save space. (From Comroe, J. H., Jr., and Mortimer, L.: J. Pharmacol Exp Therap 146: 33, 1964.)

Hughes has presented anatomic evidence that the blood supply of the adult aortic body comes from the aorta in a roundabout way. Figure 7 shows that a branch of the left coronary artery first becomes the vasa vasorum of the wall of the pulmonary artery; these recombine to form a venous portal system which then breaks up into a second set of capillaries which supply the chemoreceptor cells that we call the aortic bodies. Can the composition of blood flowing through the pulmonary artery affect significantly the $P_{O_2}$ and pH of blood flowing through these vasa vasorum in the wall of the pulmonary artery? Theoretically, it is possible if the diffusion path is very short and if the blood flow through the vasa vasorum is very slow; practically, it has not yet been possible to stimulate these chemoreceptors by changing the chemical composition of pulmonary arterial blood in intact animal.

Filtration

The pulmonary circulation, located as it
is between the mixed venous blood and the systemic circulation, serves the important function of retaining fine particles present in mixed venous blood and preventing these from entering the systemic circulation and lodging in the end-arteries in other, potentially more troublesome, sites such as the coronary or cerebral circulation. There are many more pulmonary capillaries than are needed for effective gas exchange in resting man and some of these can be sacrificed to protect other vascular beds; one lung and some of the other lung can be removed without producing anoxemia. It is now possible to estimate the size of the functioning pulmonary capillary bed by special tests that measure uptake of carbon monoxide at normal, high, and low oxygen tensions in inspired gas; if there is no primary alveolar disease, low carbon monoxide uptake means that there are fewer blood-filled alveolar capillaries in contact with ventilated alveoli (fig. 8). Recently, Gold and McCormack (personal communication) have measured pulmonary capillary blood volume in 12 patients before and 1 hour after injecting radioactive iodinated macro-aggregated serum albumin into an antecubital vein for the purpose of diagnostic lung scanning, as proposed by Wagner and associates. This test depends upon the plugging of some of the previously open pulmonary vessels by the macro-aggregates of albumin. The maximal amount of albumin injected was 1 mg; assuming that the average diameter of aggregates was 30 microns, the maximal number of emboli would be 70,000, enough to occlude about 5% of the precapillary vessels in the lung, if each entered a different vessel. As one might predict, the injection of these aggregates did not lead to measurable change in the uptake of carbon monoxide in any of the patients. However, in another group of patients, Gold and associates injected 20 ml of iodized oil (Ethiodol) into the dorsal pedal lymphatic vessels for diagnostic lymphangiography. This material eventually enters the venous blood and goes to the pulmonary circulation where the oil micro-emboli lodge in the pulmonary capillaries. Assuming that the average diameter of the Ethiodol droplets is 10 microns, 20 ml would produce 40 billion emboli—more than enough to block every pulmonary capillary. Gold and his associates

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found that the uptake of carbon monoxide diminished after the injection of Ethiodol; on the average, the pulmonary diffusing capacity decreased by 32% of control values and pulmonary capillary blood volume by 42% of the initial figure. Yet at this time these patients had no symptoms of breathlessness* and no changes from control values in lung volumes or arterial blood gas tensions.

Of great interest is the fact that the diffusing capacity for carbon monoxide and pulmonary capillary blood volume returned to control values within 4 days. Obviously the pulmonary circulation possesses mechanisms for passing or disposing of macro- or micro-emboli and reestablishing the full number of open capillaries. These mechanisms deserve more study because it is likely that mixed venous blood often contains micro-emboli of tissue cells, fat globules, agglutinated red blood cells, sickle cells, white blood cells, platelets, or parasites that occur normally, follow minor trauma, or occur in disease.†

Nadel and associates (personal communication) have recently studied a group of patients whose main pulmonary abnormalities were a decrease in carbon monoxide (presumably owing to obstruction of small pulmonary vessels) and an increased pulmonary compliance at all lung volumes. Because such a change in compliance has been reported previously only in patients with emphysema, they wondered whether prolonged block of capillaries (in such a way that they can be supplied neither by pulmonary nor by bronchial arterioles) precedes and causes loss of alveolar septal tissue. If so, the mechanism for opening plugged capillaries must be inoperative in these patients.

This means that the factors which inhibit the normal scavenging of emboli also deserve study.

I have labeled the filtering of particles from the mixed venous blood as a function of the pulmonary circulation—made possible by the large reserve in pulmonary vascular bed and the apparent harmlessness of some emboli. We have noted that block of a small percentage of precapillary vessels with macro-aggregates of albumin or of a large percentage of the capillaries with Ethiodol causes few if any measurable changes in respiration or systemic circulation. Yet sometimes, pulmonary emboli cause dysfunction and indeed can be fatal. The events occurring after pulmonary emboli are not necessarily related to the fraction of the vascular bed that is occluded. Block of one pulmonary artery by inflating a balloon at the tip of a catheter causes no symptoms and no important disturbances in ventilation or in the systemic circulation if the other lung is normal. But certain types of pulmonary emboli can cause reflex rapid and shallow breathing, constriction of alveolar ducts owing to release of histamine from mast cells, constriction of bronchioles owing to liberation of serotonin from blood clots, or systemic effects. Further, there is a well-defined pulmonary chemoreflex in some animals which, when stimulated by body constituents such as serotonin or adenosine triphosphate, can cause marked systemic hypotension, bradycardia and apnea. And strangely enough, some mechanoreceptors in the lungs can be stimulated by certain chemical substances when these are injected into the pulmonary artery.

Much more remains to be learned about why some micro-emboli do and some do not cause effects in addition to local mechanical circulatory obstruction. Is the clue in their physical or chemical nature, in the point of their impaction, or in secondary chemical changes that occur locally after impaction? Even with more animal experimentation, there still will be the problem of species difference. Figure 9 shows that serotonin injected into the pulmonary artery of a cat produces apnea—
hypotension—bradycardia (from activation of the pulmonary chemoreflex) and into a
dog produces hyperpnea—hypertension—tachycardia (from stimulation of the aortic and
carotid bodies); in man, it produces variable changes.81, 82

The variability of the clinical and laboratory
manifestations of pulmonary embolism in
man have long been puzzling and have led to
disagreement. Some radiologists believe that the
typical roentgenogram of the chest after pul-
monary embolism shows an ischemic lung.
Others have stated that the typical film shows
sharp demarcated or wedge-shaped densi-
ties (infarcts), often associated with pleural
effusion. Some radiologists who have reported
these densities have seen them in the first 24
hours after the onset of symptoms, but others
not until several days have passed. Clinicians
have been puzzled by the fact that one pa-
tient can have occlusion of the right or left
pulmonary artery with no effects but another
may have occlusion of finer vessels and be
seriously ill with dyspnea, substernal oppres-
sion, cough, hemoptysis, or shock. If we knew
the precise moment of impaction of an em-
bolus in man (rather than the moment at
which symptoms occur), we might see the
sequence of bronchoconstriction, ventilatory
changes, ischemia, congestive atelectasis, and
then recovery that would be predicted from
studies of experimental pulmonary vascular
occlusion. But we would not expect this se-
quence to occur if the patient’s lung contained
pre-existing bronchopulmonary anastomoses
of any magnitude.

**Figure 9**

*Effects of serotonin on respiration and blood pressure in the cat (left) and dog (right). Serotonin
injected at arrows.*

**Removal of Alveolar Fluid**

The pulmonary circulation is designed so
that it can rapidly remove water from the
alveoli. The pulmonary capillary pressure of
a healthy man (8 to 10 mm Hg), which tends
to filter fluid from the blood to the alveoli, is
normally far less than the colloidal osmotic
pressure of the plasma proteins (25 to 30 mm
Hg), which tends to pull alveolar fluid into
the blood. This imbalance prevents trans-
udation of fluid from blood to alveoli and
hastens the reabsorption of alveolar fluid into
blood. When tagged small molecules are dis-
solved in water and introduced into the
alveoli, either by injection through a catheter
or by inhalation as an aerosol, they enter the
circulation almost as rapidly and completely
as would an intravenous injection. This is
why administration of procaine or isopro-
teranol into the lower airways can be hazar-
dous.

It is widely believed that large molecules
such as the plasma proteins leave alveoli
slowly and only through lymphatic channels.
Recently, it has been shown by Schultz and
his co-workers33 that labeled proteins placed
in alveoli enter the pulmonary circulation of
perfused, isolated lungs. The particles could
not have reached there through the usual
lymphatic channels draining into the jugular
veins and must have entered the pulmonary
capillaries directly. This has been confirmed
by Lee in our Institute (personal com-
munication). The mechanism of the uptake of
large molecules by pulmonary capillaries re-
quires further study.
PULMONARY CIRCULATION

Comment

In concluding, I have discussed the major known functions of the pulmonary circulation. I predict that important new functions will be uncovered in the future. The pancreas has an exocrine function (long known) and an endocrine function, discovered many years later; the kidney has a filtration-reabsorption function (long known) and an endocrine function (formation of renin and hematopoietin) discovered much later. We may find unsuspected functions of the lung and the pulmonary circulation. Why is the lung rich in histamine, heparin, adenosine deaminase, and in certain proteolytic enzymes? Why are leukocytes, separated briefly from blood and then reinjected, trapped preferentially in the pulmonary circulation? Why do certain bacteria, given intravenously, stay in fine pulmonary vessels although they are small enough to pass through any capillary bed? Why do certain diseases of the lung lead to inappropriate secretion of antidiuretic hormone? Why is bronchial carcinoma often associated with clubbing of the fingers although there is no arterial hypoxemia? The answers to these questions will be interesting, I hope that you will find them.

References


A Thought Twister

... In rational problem solving, goals will change not only in detail but in a more fundamental sense through experience with a succession of means-ends and ends-means adjustments. ... In an important sense a rational problem solver wants what he can get and does not try to get what he wants except after identifying what he wants by examining what he can get.—Albert O. Hirschman and Charles E. Lindblom. Economic Development, Research and Development, Policy Making: Some Converging Views. In: Behavioral Science 7: 218, 1962.
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