Ventilation/blood flow and gas exchange

JOHN B. WEST

FOURTH EDITION

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Preface to First Edition

This monograph arose out of lectures given at the Postgraduate Medical School, and particularly three invited lectures at the Westminster Hospital Medical School in the autumn of 1964. Presenting clinical respiratory physiology today is not easy because the advances have been so fast in the last 20 years that many doctors have elected to wait until the subject settles down and the terminology sorts itself out. Thus some degree of immunity has often been developed.

However the relations between ventilation, blood flow and gas exchange are of great practical importance because ventilation–perfusion ratio inequality is the chief cause of hypoxaemia in the medical wards. The subject is not an easy one and any serious attempt to understand it must take advantage of the oxygen–carbon dioxide diagram which has proved to be such a powerful tool. This monograph begins at an elementary level and aims to bridge the gap between the simple review article and the original papers on ventilation–perfusion ratio inequality. This restricted field has been deliberately chosen because it is the most important aspect of gas exchange and the most difficult to understand. It is hoped that this monograph will be a painless introduction to the ventilation–perfusion ratio for the resident and consultant physician who are interested in lung function as well as for the physiologist.

To this end, equations have been omitted almost entirely from the text because they invariably provoke resistance in many people. However there are a great many diagrams and graphs which contain the same ingredients in a more palatable form. For the same reason the text contains relatively few references because these distract the reader, although those who talk the $\dot{V}_A/\dot{Q}$ language will immediately realize that this book contains virtually nothing that is new.

Many colleagues and friends have read the manuscript and suggested improvements. These include Dr G. Brandi, Dr E.J.M. Campbell, Dr J.E. Cotes, Dr. L.E. Farhi, Dr. C.M. Fletcher, Dr B.E. Heard, Dr M.C.F. Pain, Dr H. Rahn and Dr M.K. Sykes. I wish to express my gratitude to all these. The experimental work described in Chapter 2 was done in conjunction with Dr C.T. Dollery, Dr P. Hugh-Jones and others, and it owes much to the constant support of Sir John McMichael F.R.S., and to Mr. D.D. Vonberg and the M.R.C. Cyclotron Unit of facilities. The work was supported by the Medical Research Council.

Preface to Fourth Edition

Important advances have been made in the area of ventilation–perfusion relationships in the last few years. In this new edition, the material has been brought up to date, and a new chapter has been added on recent work on distributions of ventilation–perfusion ratios. These studies were carried out with Dr Peter D. Wagner.

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Introduction

This small monograph attempts to answer the question: how does inequality of blood flow and ventilation in the lung interfere with gas exchange, that is the ability of the lung to take up oxygen and put out carbon dioxide. Because this mechanism is the chief cause of arterial hypoxaemia in the medical wards, the question is important to the physician as well as to the physiologist. The problem is approached by first looking at the normal lung because its inequality of blood flow and ventilation follow a simple topographical pattern. For this reason, the regional differences of gas exchange can be set out like a map, and although the abnormal lung is not so amenable, the same principles apply. Overall gas exchange is approached through the oxygen–carbon dioxide diagram because in a simple form this is an invaluable tool in this field. Just as a diagram is useful in understanding acid-base balance in the body, so the oxygen–carbon dioxide diagram allows the impairment of gas exchange in the diseased lung to be easily grasped.

The plan of the book is as follows. Chapter 1 takes a bird's eye view of the movement of oxygen from the atmosphere to the blood by the lung and thus introduces the various causes of arterial hypoxaemia. Chapter 2 examines the distribution of blood flow and ventilation in the normal upright lung and derives the pattern of ventilation–perfusion ratio inequality. Chapter 3 takes this pattern of ventilation–perfusion ratio inequality and by means of the oxygen–carbon dioxide diagram, deduces differences in regional gas exchange. In Chapter 4, the resulting impairment of overall gas transfer is examined, and the normal lung is compared with the abnormal lung where the pattern is less orderly but the effects are far more dramatic. Chapter 5 deals with ways of measuring ventilation–perfusion ratio inequality, and shows how this mechanism can be distinguished from other causes of arterial hypoxaemia. Chapter 6 describes recent work on determining various patterns of ventilation–perfusion inequality which occur in common lung diseases.

Contents

Chapter 1
Oxygen transport from air to tissues

The lung unit

The prime function of the lung is to exchange gas or, in other words, to arterialize venous blood. A logical starting point for a discussion of lung physiology is therefore the alveolar membrane through which the gas exchange occurs. This is shown in Fig. 1 as a single thin line. In practice, the gas–blood interface is some 100 m^2 in area with a mean thickness of less than 1 μm. If its thickness were increased to 1 cm and its relative dimensions remained the same, the membrane would cover the whole of Wales (or Connecticut) so that its shape is well suited to its gas-exchanging function.

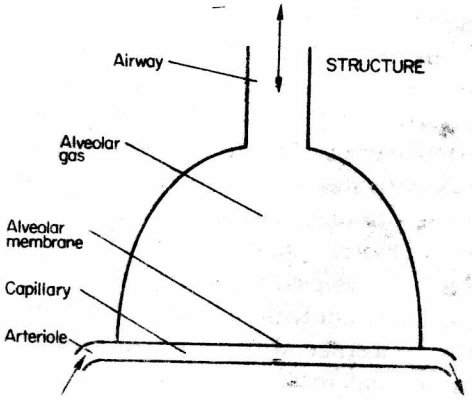

Fig. 1. The functional lung unit. The alveolar membrane, across which gas exchange occurs, has alveolar gas on one side and pulmonary capillary blood on the other. Gas is brought to the alveoli by the bronchi and blood to the capillaries by arterioles.

Air is brought to one side of the interface and blood to the other. Fig. 1 shows the alveolar gas volume, that is the gas which is

actively engaged in exchanging oxygen and carbon dioxide. This space is connected to the outside air by a system of conducting airways, the bronchi and bronchioles. This volume is called the anatomic dead space because the gas within it does not take part in gas exchange. On the other side of the alveolar membrane is the pulmonary capillary fed by a pulmonary arteriole and draining into a venule. As blood passes along the capillary, it takes up oxygen and gives off carbon dioxide.

This, then, is the unit of lung function analogous to the nephron, for example, which is the function unit of the kidney. Two features of the lung unit may be emphasized at this stage. One is its symmetry, that is the fact that gas and blood are equally important in its function. This simple fact is not always appreciated in that sometimes the lung is regarded chiefly as a pump which moves air in and out of the chest. It certainly does this, but only as a means to an end which is gas exchange, and for this prime function gas and blood are equally important.

The other feature of the lung unit is its simplicity. Compare it, for example, with the nephron with its glomerulus, proximal convoluted tubule, descending and ascending loops of Henle, distal convoluted tubule and collecting tubule. Each part is lined with a special cell and there are brush borders, cell inclusions and exotic staining reactions. In addition the kidney consumes a considerable amount of oxygen doing its job. By contrast, the structure of the lung unit is remarkably simple (Fig. 1) and the reasons for these differences in structure are the differences in function. The kidney is concerned with regulating the concentration of a variety of substances in the blood—many ions, urea and other solutes, and as part of this job it uses energy to pump sodium ions against concentration gradients. On the other hand, the lung as a gas exchanger is chiefly concerned with only two substances, oxygen and carbon dioxide, and these move by passive physical diffusion. This means that they move from a region of high partial pressure to a region of low partial pressure just as water runs downhill. For this reason, the lung tissue does no work on these gases and it consumes little oxygen itself. Thus the structure of the lung unit is simple because its function is simple: it merely brings blood and air very close together so that gases can exchange by passive diffusion.

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To all this, the pathologist may retort that the structure of the lung is not at all like Fig. 1 in that the large bronchi divide into smaller bronchioles which lead into terminal and respiratory bronchioles and finally into alveolar ducts from which the alveoli bud. This is true, but from a functional standpoint, the lung can be divided into two volumes: the conducting airways where no gas exchange with blood occurs, and the 'alveolar gas' volume where gas is continually exchanging with blood. The precise division in anatomical terms between these two functional compartments is not yet known but the 'alveolar gas' volume includes the alveoli themselves, the alveolar ducts and probably the respiratory bronchioles.

Now let us put some figures for the volumes and flow of gas and blood on this lung unit. If we assume that all the units are the same, Fig. 1 can be used to denote the whole organ as well as a single unit. Fig. 2 shows that the total volume of the conducting airways is about 150 ml. (These and the following numbers are typical values only and there is considerable variation.) The total lung gas volume at the end of a normal expiration (functional residual capacity) is about 2500–3000 ml. Thus the conducting volume is a remarkably small proportion of the active gas exchanging volume but nevertheless as we shall see, a considerable proportion of inspired gas is wasted in the bronchi. By contrast with the large alveolar gas volume, the volume of blood undergoing gas exchange in the pulmonary capillaries is only about 70 ml.

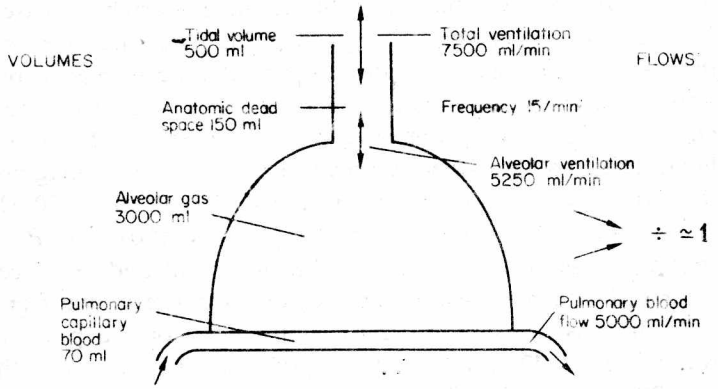

Fig. 2. Lung unit with the volumes of gas and blood for the whole organ (both lungs). Numbers are typical values only and there is considerable variation. Note that the normal ratio of ventilation to blood flow is about 1.

Turning now to the movement of gas and blood, suppose the tidal volume is 500 ml and the number of breaths each minute is 15. The total volume of air passing the lips each minute (in one direction) is therefore $500 \times 15 = 7500$ ml/min; this is called the total ventilation or minute volume. Of this 500 ml of inspired air, 150 ml remains in the airways (anatomic dead space) and takes no part in gas exchange; this volume can therefore be disregarded in the ensuing discussion. The remainder of the 500 ml, that is 350 ml, enters the alveolar volume. This is the volume which matters for gas exchange; the volume per minute $350 \times 15 = 5250$ ml/min is called the alveolar ventilation. (Conventionally, the alveolar ventilation is strictly the volume of this gas when it leaves the alveoli whicl. is usually slightly smaller because less carbon dioxide is given out than oxygen is taken in.) On the blood side of the alveolar membrane, the total pulmonary capillary flow is the same as the cardiac output, say 5000 ml/min. Note the important fact that the total volume of fresh gas (alveolar ventilation) and the total volume of fresh blood brought to the alveolar membrane each minute are approximately the same. Thus the normal ventilation–perfusion ratio is about 1.

Perfect lung

A convenient way of approaching the normal transport of oxygen in the body and disturbances of this normal pattern by disease is to look at the gradual fall in oxygen partial pressure from air to tissues. In this way, we can compare the performance of the normal lung and the diseased lung with that of a perfect gas exchanger. Fig. 3 shows the oxygen partial pressures for a perfect lung. The total atmospheric pressure is about 760 mmHg and of this 20·9% is due to oxygen. Thus the P_{O_2} of air is 20·9% of $760 = 159$ mmHg. (P_{O_2} means partial pressure of oxygen, P representing pressure.) Actually as the air is inhaled, it becomes saturated with water vapour at body temperature so that from the total dry gas pressure we must subtract the partial pressure of water vapour (47 mmHg). The P_{O_2} of moist inspired gas is therefore 20·9% of $(760-47) = 149$ mmHg (say 150 mmHg).

Fig. 3 shows that in the perfect lung, the P_{O_2} in alveolar gas is much less than in inspired gas. This is because oxygen is continually

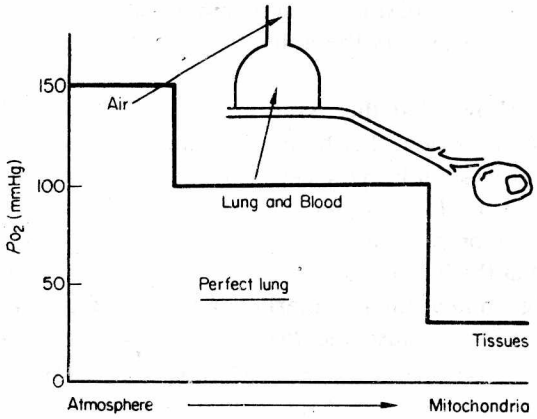

Fig. 3. The perfect lung. Note that alveolar gas and arterial blood have the same oxygen partial pressure. The large 'step' of some 50 mmHg between inspired and alveolar gas is determined by the balance between oxygen removal from alveolar gas by the blood and its replenishment by ventilation.

being removed from this gas by the blood and carbon dioxide added. Indeed if it were not for the fact that alveolar ventilation continually replenishes the oxygen and removes carbon dioxide, the P_{O_2} would become lower and lower. As it is, a balance is struck between the rate at which oxygen is removed and the rate at which it is replenished giving an alveolar P_{O_2} of about 100 mmHg. If alveolar ventilation is reduced for the same oxygen consumption, the alveolar P_{O_2} falls, and similarly if the alveolar ventilation is increased (oxygen uptake constant), the alveolar P_{O_2} rises.

Note that even in this perfect oxygen transport system, one-third of the inspired P_{O_2} is lost before the oxygen reaches the arterial blood. It is worth pausing for a moment to compare the mammalian lung in this respect with the gill of the fish. It has been shown that the flows of inspired water and blood are in opposite directions in fish gills so that blood leaving a gill capillary is brought very close to fresh water entering the gill. The result is that, in principle, arterial blood can have the same P_{O_2} as the inspired water. Thus the large fall of P_{O_2} between inspired air and arterial blood which exists even in a perfect mammalian lung (Fig. 3) is avoided. A disadvantage of the arrangement in the fish is the vulnerability to brief exposure to a hypoxic environment because if the inspired P_{O_2} falls, the arterial P_{O_2} follows closely. By contrast,

the alveolar gas volume in the mammalian lung is a useful store of oxygen which buffers the animal against short periods of breath-holding.

Fig. 3 shows that the tissue P_{O_2} is much less than the arterial blood P_{O_2}. When the blood reaches the systemic capillaries, oxygen moves out into the cells and eventually to the mitochondria where it is used. Again movement is by diffusion from an area of high partial pressure to one of low partial pressure and there is evidence that the intracellular P_{O_2} may be very low, possibly less than 1 mmHg. In fact, the line marked 'tissues' in Fig. 3 is a great over-simplification because the P_{O_2} varies between different types of tissue and between adjacent part of the same tissue. However it serves as a reminder that the arterial blood P_{O_2} is one link in the chain which eventually connects the air to the mitochondria.

Hypoventilation

Fig. 4 introduces the first important cause of hypoxaemia, that is hypoventilation. We have seen that the alveolar P_{O_2} depends on a balance between the rate at which oxygen is removed from the lung by the blood and the rate at which it is replenished by alveolar ventilation. If ventilation is reduced, alveolar hypoxia and therefore

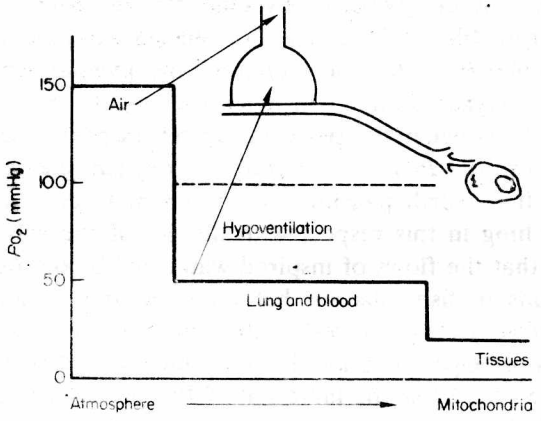

Fig. 4. Hypoventilation. The difference between the oxygen partial pressures of inspired and alveolar gas is abnormally large because the rate of replenishment of the oxygen in alveolar gas has been reduced, while the rate at which it is removed by the blood remains unchanged.

arterial hypoxaemia must follow. It is clear that hypoxaemia due to hypoventilation may occur although the lung itself is normal. Causes include depression of the respiratory centre by drugs or anaesthesia, damage to the medulla by disease, diseases affecting the nerve supply to the muscles of the thorax or the muscles themselves, injury to the chest wall and obstruction to the upper airways. An important feature of hypoventilation as a cause of hypoxia is that because the lung itself is often normal, the prognosis is excellent if the participating cause can be removed. The defective gas exchange which occurs in hypoventilation is dealt with in more detail on p. 93.

In practice, the normal lung falls short of the perfect lung shown in Fig. 3 in three respects each of which may become a cause of hypoxaemia in disease. These are diffusion, shunt and ventilation–perfusion ratio inequality. These defects show as discrete falls in the P_{O_2} so that the net result is that a lower P_{O_2} is available to the tissues. In the normal lung, these defects are small and their contributions to arterial hypoxaemia barely measurable, but in the diseased lung they may result in profound hypoxaemia.

Diffusion

Oxygen moves across the gas–blood interface by passive diffusion because the partial pressure in the alveolar gas is higher than that in the blood. Fig. 5a shows the way in which the P_{O_2} rises in the blood as it flows along a pulmonary capillary when the lung is breathing air. The P_{O_2} of alveolar gas is about 100 mmHg; the P_{O_2} of mixed venous blood (blood in the pulmonary artery) is about 40 mmHg. When a corpuscle enters the capillary, it 'sees' a P_{O_2} of 100 mmHg on the other side of the alveolar membrane less than 1 μm away. Thus there is a driving pressure of $(100-40) = 60$ mmHg between gas and blood with the result that oxygen moves rapidly across the thin interface, and the P_{O_2} in the blood rises quickly. This rise in blood P_{O_2} now reduces the driving pressure so the rate at which oxygen moves across the membrane becomes less. The result is that the blood P_{O_2} rises in a curve.

The precise shape of this curve is difficult to determine but is unimportant in the present context. The shape of the oxygen dissociation curve (Fig. 27a) has a large effect. It is also known that

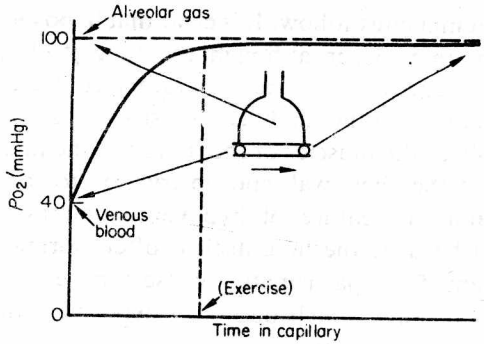

Fig. 5a. Diagram of the way in which P_{O_2} rises as the blood flows along the pulmonary capillary. Blood enters the capillary with a P_{O_2} of 40 mmHg and this rises rapidly until it is very close to the P_{O_2} of alveolar gas, 100 mmHg (typical values only). Note that when the lung breathes air, equilibration between gas and blood is nearly complete after one-third of the time available, and that the P_{O_2} difference between alveolar gas and blood at the end of the capillary is exceedingly small. During exercise, the available time may be reduced to a third (dashed line) but equilibration is still almost complete. The alveolar P_{O_2} may rise on exercise.

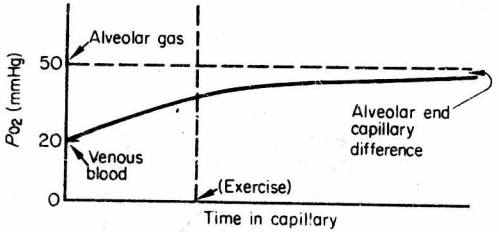

Fig. 5b. Changes in capillary P_{O_2} when the lung breathes a low oxygen mixture which reduces the alveolar gas P_{O_2} to 50 mmHg. Now the rate of rise of blood P_{O_2} is much slower and there is an appreciable P_{O_2} difference between gas and blood at the end of the capillary. This difference is exaggerated on exercise because the time available for equilibration is reduced.

the rate at which oxygen moves into the blood depends not only on the diffusion properties of the interface itself but also on the rate of chemical combination of oxygen with haemoglobin which itself varies with the P_{O_2} of the blood. In addition, the larger the volume of blood in the pulmonary capillaries, the faster the oxygen can move across.

Such complicating factors do not affect the present argument and two features of Fig. 5a should be emphasized. One is that the

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