medical physiology :: **Pulmonary Physiology in a Nutshell**

by:

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INTRODUCTION

The lungs are not the gaseous equivalent of the duodenum and rectum, there to absorb oxygen from the ambient air and to evacuate "stale, waste air" (CO_2) to the outside. In fact, CO_2 is a much more valuable gas than O_2. Its concentration in the arterial blood (24 mmol/l) is 3 times that of oxygen (8 mmol/l). A small reduction in CO_2 concentration causes tetany and death, whereas an equivalent reduction in O_2 concentration causes no abnormality, and certainly no compensatory physiological responses (e.g. hyperventilation).

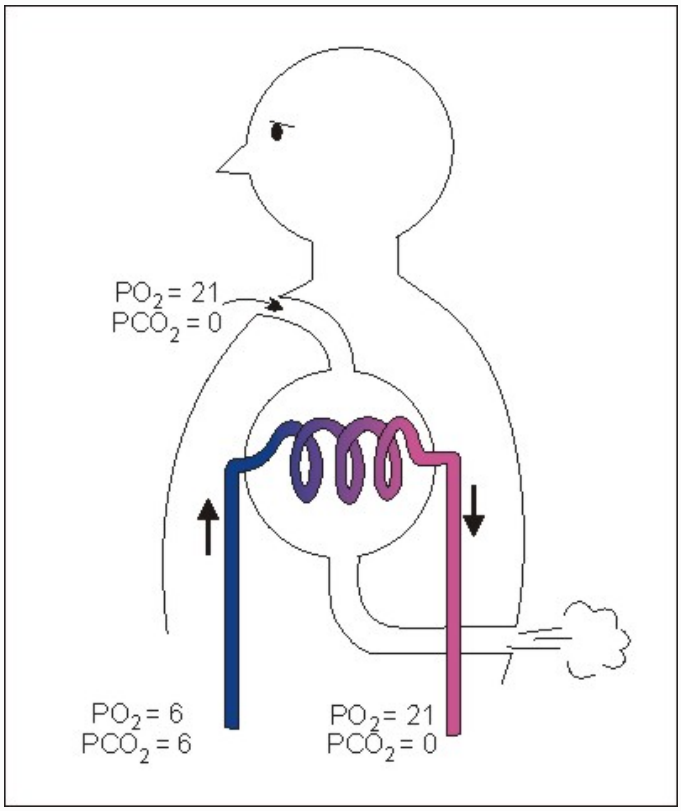
The purpose of the lungs is, in fact, to retain CO_2 and to drastically limit the body's exposure to O_2. They do so by dialysing the blood against a gaseous dialysate (i.e. the 3 litres of alveolar air), equivalent to the watery dialysate used for renal dialysis. The gaseous dialysate has a unique composition which differs markedly from that of the ambient atmosphere. Modern ambient air is highly toxic to a great many creatures including all vertebrates**.** Instead, the pulmonary dialysate resembles the earth's atmosphere of about 400 - 500 million years ago: poor in oxygen, but rich in carbon dioxide. It probably also resembles that fossil atmosphere in being warm and humid.

We dialyse our blood, therefore against a benign, relic atmosphere, whose composition is as carefully monitored and fanatically guarded against deviations from a very strict set of specifications as is the renal dialysate of the artificial kidney. Even small deviations from the specified concentrations of CO_2 and O_2 produce dramatic symptoms, and initiate powerful reflexes designed to reconstitute the relic atmosphere.

It is, therefore, a mistake to view the lungs as uptakers of oxygen and disposers of carbon dioxide. The cul-de-sac design of the respiratory airways and the ventilatory-perfusion "imbalances" of the normal lungs (of sea level residents) are designed to retain carbon dioxide (a trace gas in the ambient atmosphere), and to severely restrict the availability of oxygen in the internal environment. If our lungs did, in fact, rid the blood of carbon dioxide and load it with oxygen at, or near, ambient PO_2's, then we would die within a very short space of time. Ambient air is extremely poisonous. Fifteen to thirty seconds of voluntary hyperventilation should be enough to dispel any notion of how healthy and invigorating "fresh air" is for one's physiology.

Cul-de-sac respiratory passages

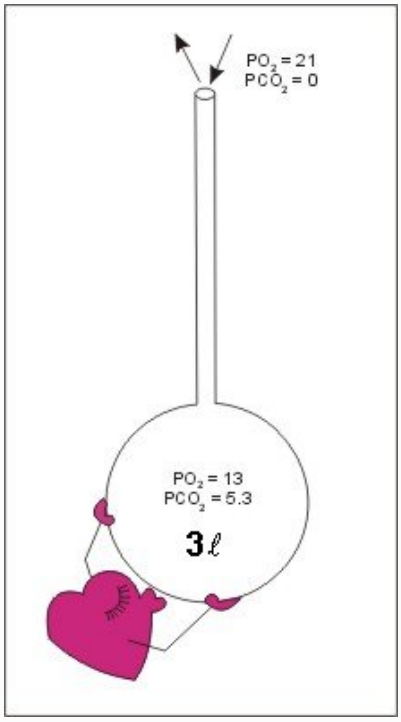
If the purpose of the lungs was to rid the blood of carbon dioxide and to load it with as much oxygen as possible, then the pulmonary system would have had a through-flow design. Ambient air would be taken in through an inlet vent, passed over a gas-exchanger, and then discharged through a separate exhaust vent. The blood would then be exposed to ambient fresh air, making the arterial PCO_2 effectively zero, and the arterial PO_2 about 21 kPa.



A through-flow ventilatory system (with separate inlet and exhaust vents, as depicted above), would ensure that the lungs clear the blood of carbon dioxide and load it with as much oxygen as possible. The fact that the lungs are not designed this way suggests that this view of the lungs' function might be erroneous.

All values in this, and all the subsequent figures, are in kilopascals (kPa). They apply to sea level residents.

The cul-de-sac construction of the respiratory passages provides the average adult with a 3 litre portable atmosphere (at the end of a very long, narrow tube) whose composition can be kept markedly different from that of the ambient atmosphere.



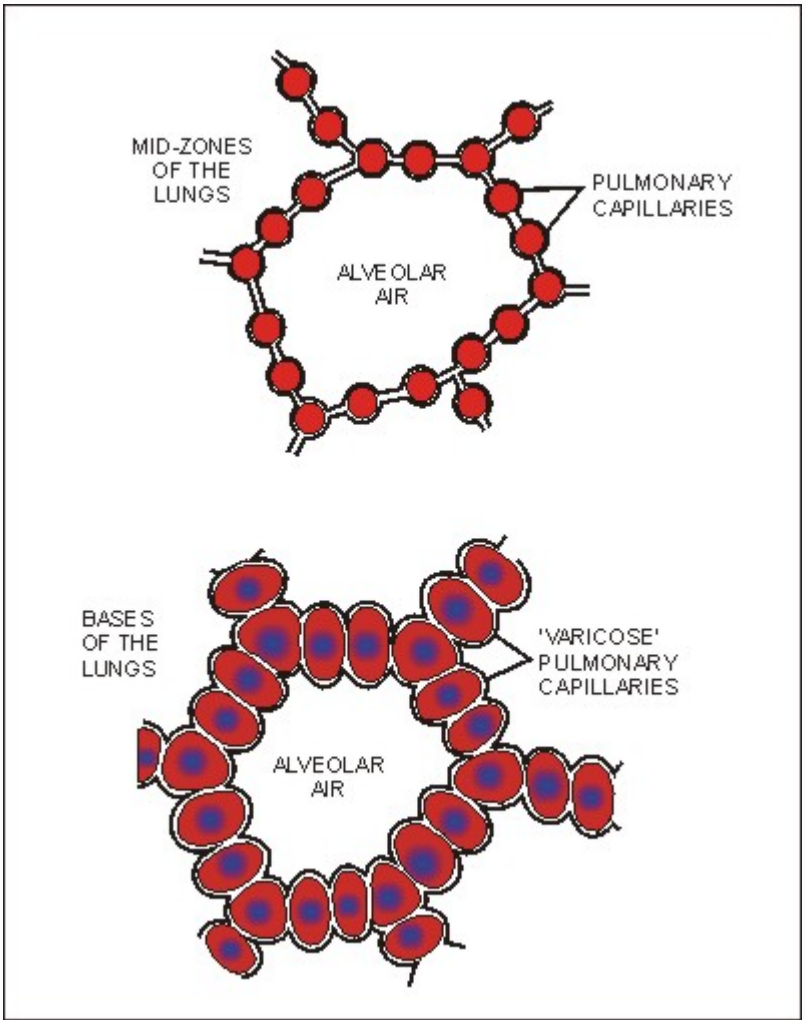
With each breath, at rest, only 10% of that portable atmosphere is very gently and carefully replaced with ambient air. That "fresh air" is immediately thoroughly mixed into the functional residual capacity, with the result that the composition of the portable atmosphere (the pulmonary dialysate) changes imperceptibly with each breath. There are CO_2 and O_2 receptors in the alveoli and arterial blood through which the process is closely monitored, ensuring that the alveolar air kept remarkably constant at a PCO_2 of 5.3 kPa, and a PO_2 of 13 kPa.

Ventilation-perfusion physiology

The cul-de-sac design of the respiratory passage allows only one of the respiratory gasses to be kept at its physiologically optimum value. Thus, if the physiologically ideal alveolar PCO_2 is 5.3 kPa, then the alveolar PO_2 is inevitably fixed at 13 kPa. If, on the other hand, the lungs were hypoventilated to reduce the alveolar PO_2 to its physiologically optimum of 11.5 kPa, then the PCO_2 would unavoidably rise to 6.5 kPa. At sea level it is therefore impossible to ventilate the lungs to keep both the PCO_2 and PO_2 at their physiologically optimum values (5.3 kPa and 11.5 kPa respectively). Yet the arterial blood gases have, in fact, this composition, even in sea level residents.

Ventilation-perfusion ratios

The optimization of both the PCO_2 and the PO_2 in the arterial blood (of sea level residents) is achieved by ventilation-perfusion mismatches in the normal lung. In a sea level resident the apices of the lungs are perfused only during peak pulmonary artery systolic pressure (the rest of the time they are ischaemic, apart from the small bronchial circulation). The bases of the lungs, on the other hand, are over-perfused, so that effectively about 6% of the total cardiac output is not dialysed against the alveolar air.

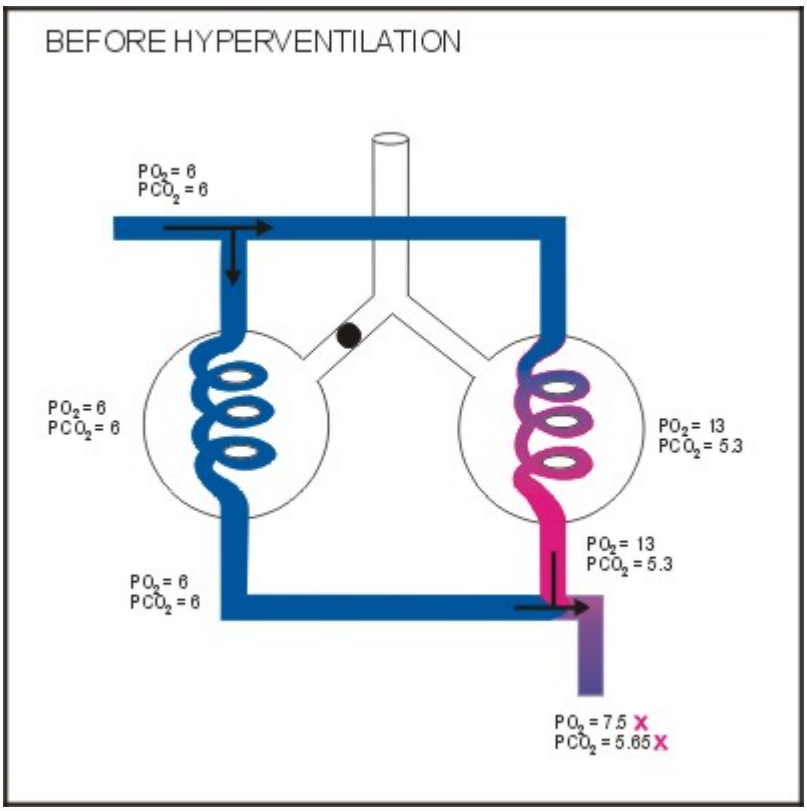


Diagrammatic histological sections through the lungs of a sea level resident. The alveolar capillaries are seen in cross-section. The top diagram represents lung tissue from the mid-zones of the lungs where the alveolar capillary blood is completely surrounded by alveolar air, with which it equilibrates. The lower diagram depicts the situation in the bases of the lungs. Here the alveolar capillaries are overdistended. Not all of the blood in the lung bases can equilibrate with alveolar air. Thus the capillary blood indicated in blue represents shunt blood, which comprises about 6% of the cardiac output of a sea level resident. (The lungs of high altitude residents have the appearance of mid-zone tissue throughout the lungs.)

These ventilation-perfusion "imbalances", which effectively occur only in sea level residents (they disappear at high altitude - indicating that they are not physically inevitable), reduce the arterial PO_2 to about 11.5 kPa, while allowing the arterial PCO_2 to be maintained at 5.3 kPa.

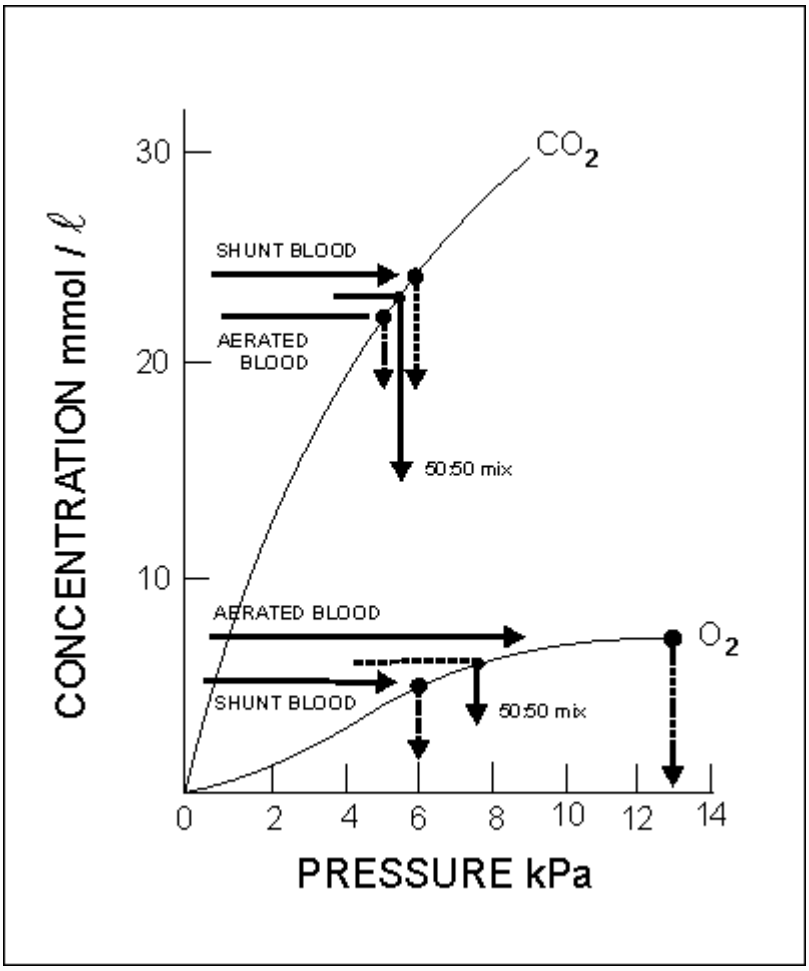
The effects of ventilation-perfusion imbalances

Instead of a 6% shunt, consider, for simplicity, a 50% shunt. Half of the right ventricular output goes to unventilated alveoli. That blood therefore arrives in the left atrium with a PCO_2 of 6 kPa, and a PO_2 also of 6 kPa (the composition of mixed systemic venous blood). The other 50% of blood is dialysed during its passage through the lungs, and arrives in the left atrium with a PCO_2 of 5.3 kPa and a PO_2 of 13 kPa (the composition of "normal" pulmonary venous blood).



The mixture (in the left atrium) produces blood whose O_2 and CO_2 concentrations (in mmol/l) is a 50:50 average of the two O_2 *concentrations* and of the two CO_2 *concentrations*.

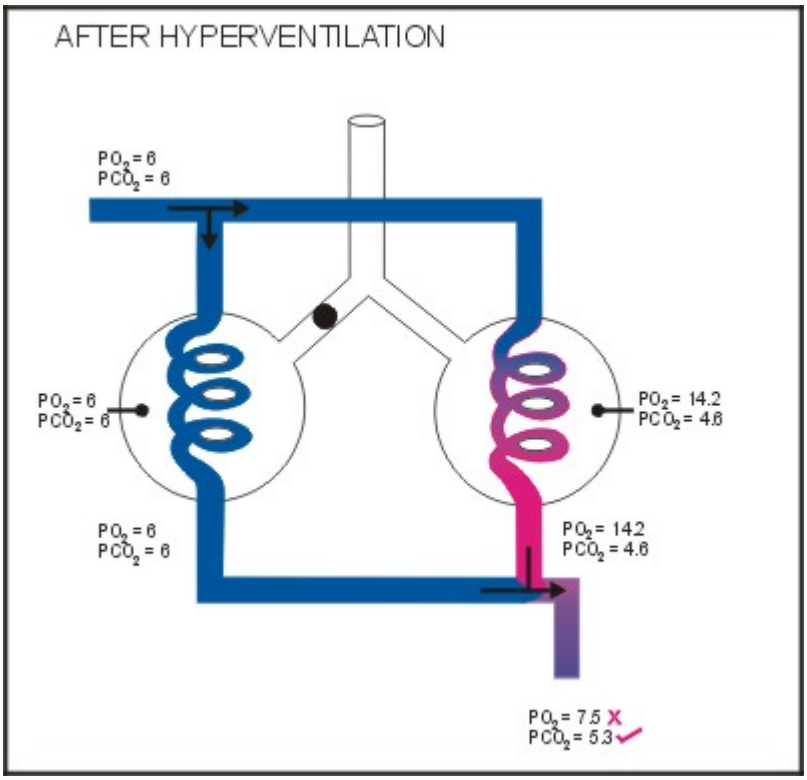
The dialysed ("aerated" or "oxygenated") blood contains 8 mmol O_2 per litre, while the undialysed ("shunt" or "deoxygenated") blood contains 6 mmol O_2 per litre. The mixture therefore contains 7 mmol O_2 per litre. The PO_2 of this mixture can be read off the oxygen-haemoglobin dissociation curve. It is about 7.5 kPa.



This PO_2 of 7.5 kPa is not the 50:50 average of the two PO_2's (13 kPa and 6 kPa) because of the non-linear relationship between PO_2 and oxygen content of the blood.

The near linear relationship between the blood's CO_2 concentration and its PCO_2 produces a simpler product when aerated and non-aerated blood are mixed. The final $[CO_2]$ and PCO_2 are approximate 50:50 averages of the two lots of blood: $[CO_2]$ = 23 mmol CO_2/l (exact average of 24 and 22 mmol/l), and PCO_2 = 5.54 kPa (approximate average of 5.3 and 5.8 kPa).

The initial effect of a 50% shunt through the lungs is, therefore, that the arterial PCO_2 = 5,54 kPa and PO_2 = 7.5 kPa. This constitutes a powerful stimulus for hyperventilation. This will, of course, not affect the shunt blood (whose composition remains unchanged). Hyperventilation will however alter the composition of dialysed (or aerated) blood.



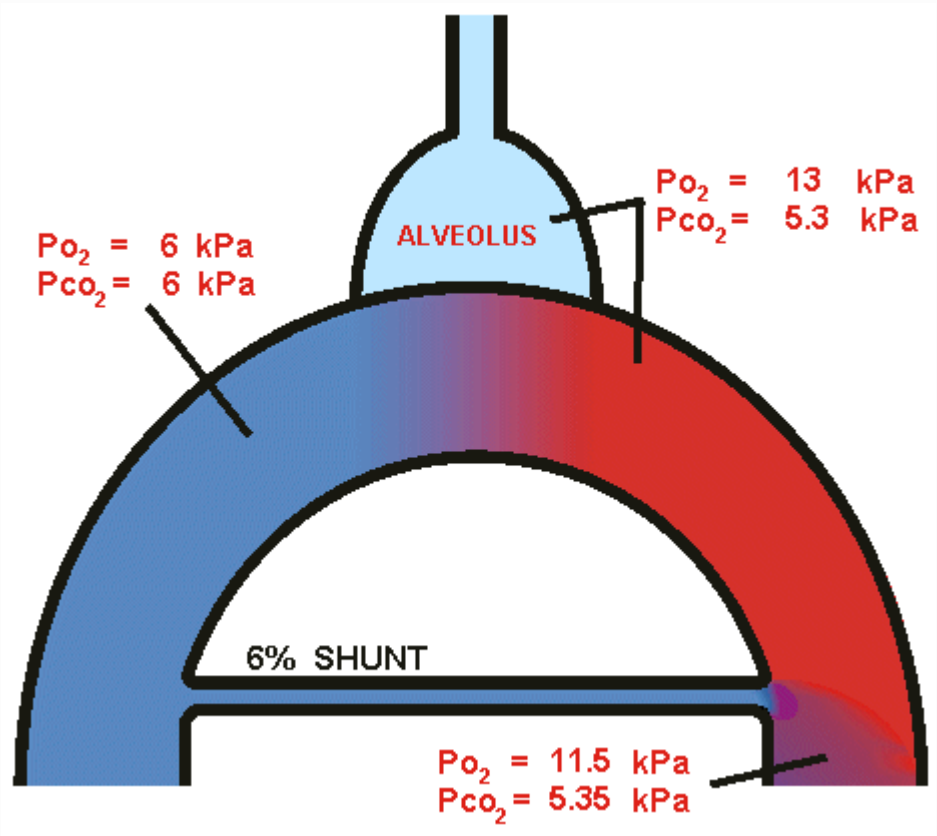
If the alveolar PCO_2 of the ventilated portion of lung is lowered to 4.6 kPa then a 50:50 mixture of dialysed and undialysed blood will have a PCO_2 of 5.3 kPa (the physiologically optimum value).

The PO_2 of the mixture, however, remains 7.5 kPa because, although the PO_2 of the dialysed blood is now 14.2 kPa, it still contains only 8 mmol O_2 per litre. Haemoglobin is saturated with oxygen above about 10 kPa, and can therefore not carry more than 8 mmol O_2 per litre, no matter how much the PO_2 is raised. Thus, when blood with a PO_2 of 14.2 kPa (8 mmol O_2/l) is mixed with blood with a PO_2 of 6 kPa (6 mmol O_2/l) the resultant oxygen concentration is 7 mmol/l which is no greater than it was before the hyperventilation took place. The PO_2 is therefore also unchanged (arterial PO_2 = 7.5 kPa).

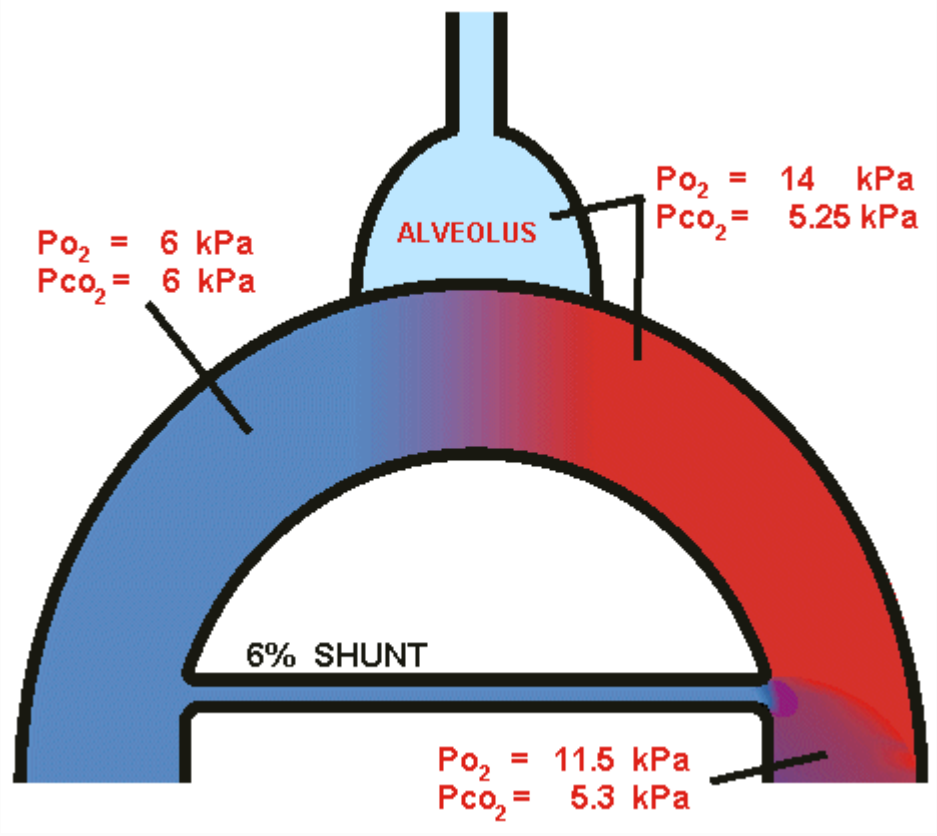
A low ventilation-perfusion ratio of part of a lung is therefore characterized by arterial hypoxaemia, combined with a normal PCO_2. The arterial hypoxaemia is resistant to hyperventilation (and oxygen administration).

A mild physiological version of this effect is used, in normal sea level residents, to reduce the arterial PO_2 from 13 to 11.5 kPa, while maintaining the arterial PCO_2 at 5.3 kPa. By over-perfusing the bases of the lungs (see 3rd diagram above) approximately 6% of the pulmonary arterial blood is not ventilated, and is thus effectively shunted from the right side of the heart to the left side without passing through the gas exchanger:

Before hyperventilation:



After mild hyperventilation:



This overcomes the problem that it is impossible to ventilate the lungs with ambient air at sea level to produce this combination of partial gas pressures (PO_2 = 11.5 kPa, and PCO_2 = 5.3 kPa) in the alveoli. The 6% right-to-left shunt, on the other hand, *produces precisely this effect*, so that the systemic arterial blood does in fact have the ideal PO_2 and PCO_2.

High altitude and other forms of pulmonary hypoxia

Consider once again the 50% shunt described above. While hyperventilation cannot correct the arterial hypoxaemia, pulmonary arteriolar constriction (in response to the low alveolar PO_2 values), sufficient to stop the blood flow through unventilated alveoli, would however eliminate the shunt, and thus effect an apparent "cure" of the ventilation-perfusion imbalance. The entire cardiac output would then flow through ventilated alveoli, and thus be dialysed in the normal way, relieving the arterial hypoxaemia.

Pulmonary arteriolar vasoconstriction is indeed the normal response to pulmonary hypoxia, and therefore the reason for the (partial) correction of the blood gas abnormalities that result from pathologically low ventilation-perfusion ratios in parts of the lungs.

In normal persons at sea level the alveolar oxygen tensions are so high that they cause pulmonary arteriolar vasodilatation. This results in low pulmonary artery pressures which are insufficient to perfuse the apices of the lungs while causing the bases to be overperfused (i.e. the physiological shunting of blood through the bases of the lungs).

At high altitude, however, the low ambient partial pressures of oxygen cause pulmonary vasoconstriction, pulmonary hypertension, and a more even distribution of blood flow throughout the lungs. Shunting is reduced to a minimum and arterial PO_2 values are very nearly equal to their alveolar equivalents.

Pathologically low ventilation-perfusion ratios

Low ventilation-perfusion ratios in patches of lungs are probably the most common cause of arterial hypoxaemia with relatively normal arterial PCO_2 values (Rhoades & Tanner, 1995). The blood gas picture in fact falsely suggests that there is a "diffusion impairment", with carbon dioxide "diffusing" through the alveolar membrane barrier more easily than oxygen. While such situations can occur (e.g. in pulmonary oedema), the majority of cases are probably caused by ventilation-perfusion defects, which are more resistant to oxygen therapy than would be expected in a diffusion defect.

However, oxygen is a highly reactive, dangerous element. It is indeed a di-radical, and at the very top of electrochemical series of elements. It is the most aggressively reactive element in the universe! Like a fat soluble vitamin, it is "healthy" and "beneficial" only when administered in small doses! Very few hypoxaemic patients (as opposed to laboratory reports!) probably benefit from its administration in mega-doses.

Illustrations by Ann Koeslag (Mail me)

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