Respiratory physiology: VQ mismatch and shunt

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INTRODUCTION

Ventilation-perfusion (VQ) mismatch and shunt are two of the causes of hypoxemia. The other three causes are hypoventilation, diffusion limitation and a decreased partial pressure of O_2 in inspired gas (PIO_2). Ventilation-perfusion relationships in the lung is a very broad topic and therefore this refresher will focus on ventilation-perfusion (VQ) mismatch and shunt.

VQ MISMATCH

Gas exchange in the lung is dependent on the interplay between perfusion and ventilation. If there is a mismatch between ventilation and perfusion it results in impairment of both O_2 and CO_2 transfer. Both the rate at which O_2 is added to the alveolar compartment via ventilation and the rate at which O_2 is removed via blood flow will affect the concentration of O_2 in the alveolar compartment. More importantly the concentration of O_2, CO_2 and N_2 are determined by the ratio of these rates. In the ideal lung this ratio will be one, but this situation is not attainable in the normal lung.

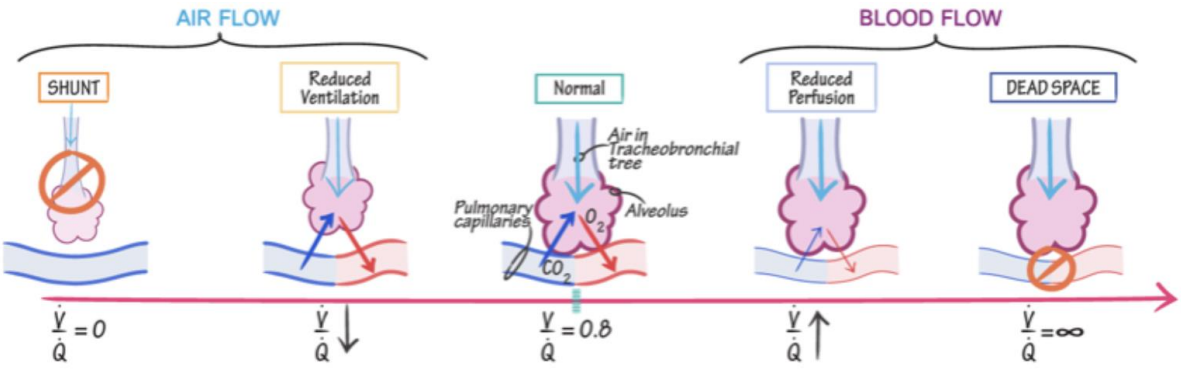

Figure 1 (from Ventilation to perfusion ratios, drawittoknowit.com)

The consequence of VQ mismatch on a lung unit

Figure 2 depicts the effect of altering the ventilation-perfusion ratio on the PO_2 and PCO_2 in the lung unit. Inspired air has a PO_2 of 150 mmHg and PCO_2 of zero; the mixed venous blood entering the unit has a PO_2 of 40 mmHg and PCO_2 of 45 mmHg. In the normal lung unit, the alveolar PO_2 of 100 mmHg and alveolar PCO_2 of 40 mmHg are determined by the balance between the addition of O_2 and removal of CO_2 via ventilation and the removal of O_2 and addition of CO_2 via blood flow.

The lung unit with a V/Q ratio of zero (units with no ventilation) will have an alveolar and end-capillary blood PO_2 and PCO_2 that are the same as that of mixed venous blood.

The lung unit with a V/Q ratio of ∞ (units with no blood flow) will have an alveolar PO_2 and PCO_2 of inspired gas.

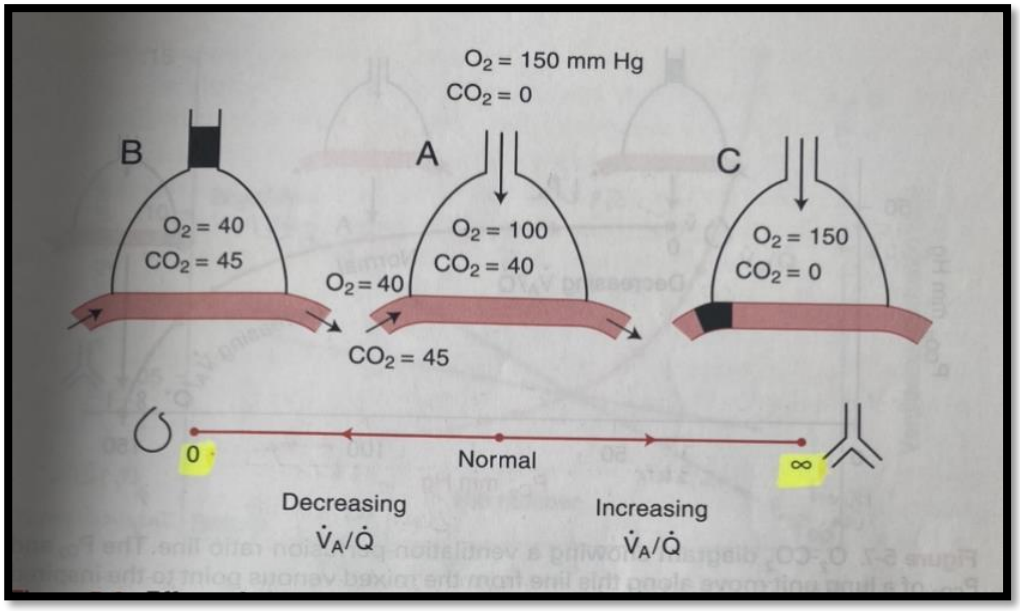

Figure 2: Effect of altering the ventilation-perfusion ratio on the PO_2 and PCO_2 in a lung unit (West 8th edition)

Regional gas exchange in the lung

Figure 3 illustrates that in the upright lung ventilation increases slowly from the top to the bottom of the lung whereas blood flow increases more rapidly towards the bottom of the lung. The consequence hereof is an abnormally high V/Q ratio at the top of the lung (where there is little blood flow) and a much lower V/Q ratio at the bottom (where blood flow is more due to gravity).

Above it is stated that the O_2 concentration is determined by the VQ ratio. Figures 3 and 4 beautifully illustrate this concept. Although there is higher ventilation at the bottom of the lung, PO_2 decreases from the top of the lung to the bottom due to the lower VQ ratio at the bottom of the lung. Note that the PO_2 of the alveoli (horizontal axis) decreases substantially down the lung, whereas the PCO_2 (vertical axis) increases much less.

Figure 4 also illustrates why PTB predominantly involves the upper lobes; probably due to the higher O_2 tension in this area creating a more favourable environment for this organism.

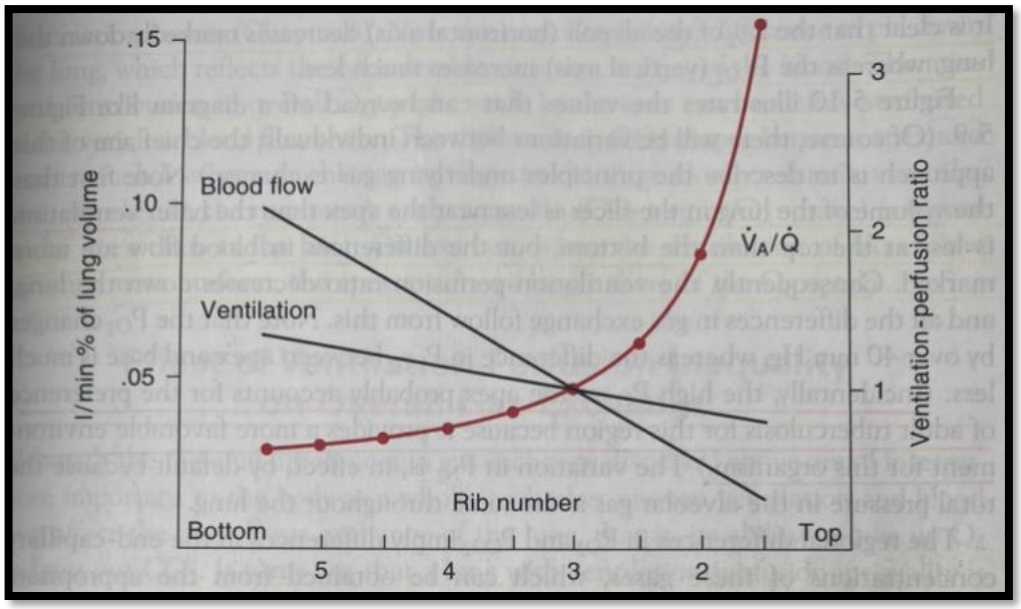

Figure 3: Distribution of ventilation and blood flow down the upright lung (West 8th edition)

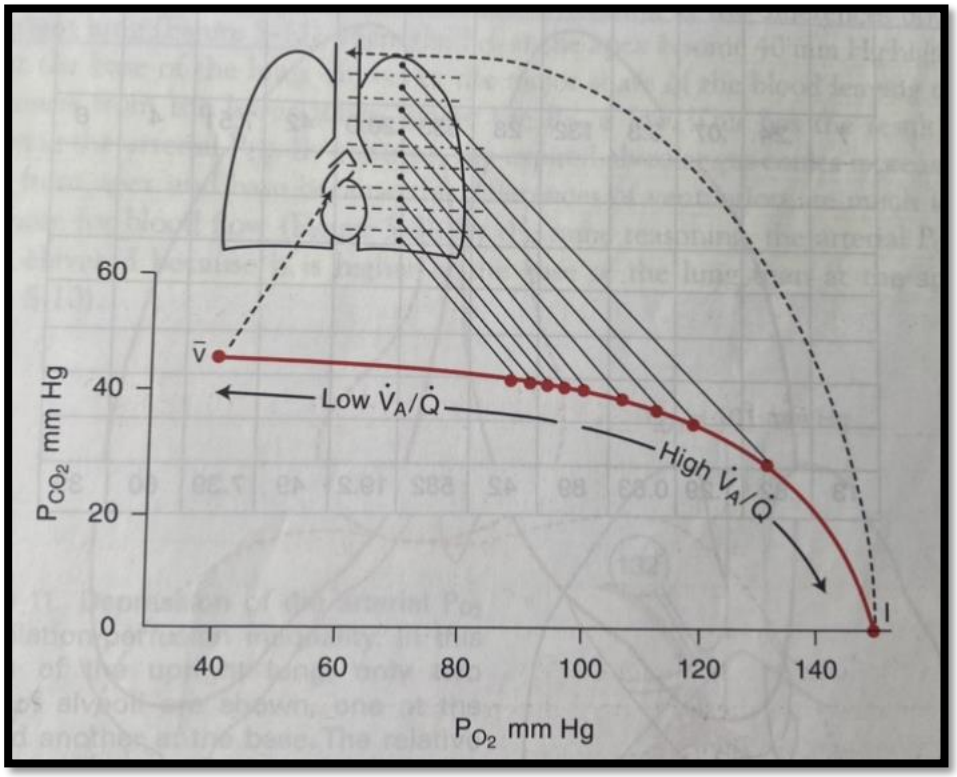

Figure 4: The result of combining ventilation-perfusion ratio inequality with the effects of this on gas exchange (West 8th edition)

The consequence of V/Q mismatch on overall gas exchange

Although regional differences in V/Q matching affect gas exchange it is more important to understand what the consequence of V/Q mismatch is on overall gas exchange of the whole lung. A lung with V/Q mismatch is not able to transfer as much O_2 and CO_2 as a homogenous lung (uniformly ventilated and perfused lung).

The reasons that a lung with uneven ventilation and blood flow have lower PaO_2 and higher $PaCO_2$ levels are:

1. Figure 4 shows that PO_2 at the apex of the upright lung is higher than at the base of the lung, but most of the blood leaving the lung comes from the lower zones where the PO_2 is low and therefore the net effect is depression of the arterial PO_2. The same reasoning can be used to explain the higher arterial PCO_2 levels.

2. Figure 5 illustrates another reason for depression of PaO_2 in the instance of V/Q mismatch. Lung units with high V/Q ratios add relatively little O_2 to blood when compared with the reduction in O_2 caused by alveoli with low V/Q ratios. The result is mixed capillary blood with a lower O_2 concentration than that of lung units with normal V/Q ratios. This phenomenon is explained by the nonlinear shape of the oxygen dissociation curve, see figure 6. Units with high V/Q ratios have relatively high PO_2, but due to the nonlinear shape of the curve, blood oxygen concentration does not increase a lot. The same reasoning can't be used for the elevation of PCO_2, because the CO_2 dissociation curve is almost linear.

The net result of V/Q mismatch on overall gas exchange, via these mechanisms is depression of the arterial PO_2 below that of the mixed alveolar PO_2 and it can be quantified via the alveolar-arterial O_2 difference which will be discussed below.

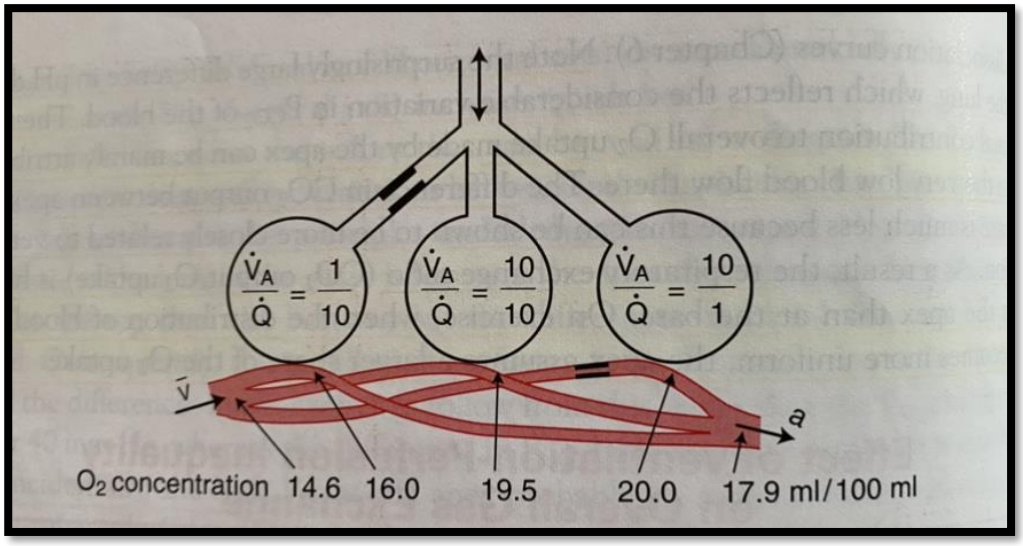

Figure 5: Additional reason for the depression of arterial PO_2 by mismatching of ventilation and blood flow (West 8th edition)

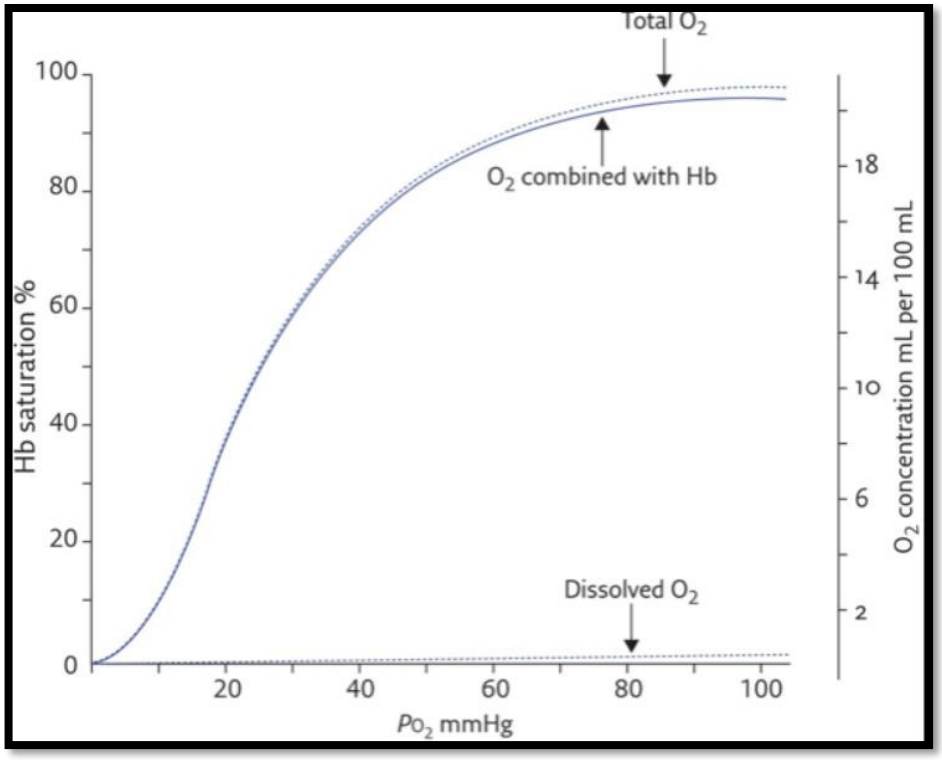

Figure 6: The haemoglobin-oxygen dissociation curve (Breathe, J Collins et al)

THE EXTREME ENDS ON THE V/Q MISMATCH SPECTRUM

Dead space ventilation

Dead space ventilation is the extreme end of the high V/Q range that is units that are ventilated but not perfused. High V/Q units are units that are overventilated in proportion to blood flow. Ventilation in excess of blood flow (high V/Q units) causes less CO_2 to be removed by ventilation if compared to ventilation of areas that are better perfused (V/Q units closer to 1). In scenarios where there are dead space or high V/Q units a higher minute ventilation is needed to maintain adequate gas exchange and $PaCO_2$ levels. The first consequence of dead space ventilation is usually not an increase in $PaCO_2$,

but rather a change in minute ventilation and thus the work of breathing. In situations of chronic hypercapnia CO_2 removal is maintained with a lower minute ventilation and therefore the work of breathing is reduced. In normal subjects the PCO_2 of alveolar gas ($PACO_2$) and arterial blood are nearly identical and thus $PaCO_2$ is inversely related to alveolar ventilation according to the alveolar ventilation equation (figure 7).

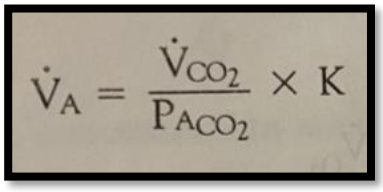

Figure 7: Alveolar ventilation equation

(V_{CO2} is CO_2 production in ml/min (STPD), V_A is alveolar ventilation in L/min (BTPS) and k is a constant which converts fractional concentration to partial pressure and corrects to standard conditions)

Alveolar minute ventilation = respiratory rate x (tidal volume – physiological dead space volume)

Thus, an elevated $PaCO_2$ can arise from a decrease in respiratory rate, a decrease in tidal volume or an increase in dead space.

Physiological dead space volume (ventilation that does not participate in gas exchange) consists of airway dead space and alveolar dead space.

Airway dead space = conducting airways (+/- 2-3ml/kg or 1/3 of a normal tidal volume)
Alveolar dead space = alveoli that is ventilated, but not perfused (V/Q = ∞)

Measurement of physiological dead space: Bohr equation

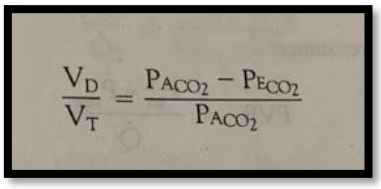

Figure 8: Bohr equation

(V_D is physiological dead space, V_T is tidal volume, $PACO_2$ is alveolar CO_2 and can be replaced by arterial PCO_2, $PECO_2$ is mixed expired CO_2 measured via volumetric capnography)

Shunt

This refers to desaturated blood from the right heart that returns to the left heart without going through ventilated areas of lung. Shunt refers to the extreme end of the low V/Q range. The V/Q ratio in shunt is not merely less than 1 but has reached 0.

Sources of shunt:

1. Bronchial artery blood that has perfused the bronchi and then drains into the pulmonary veins
2. Coronary venous blood that drains into the left ventricle via the thebesian veins
3. Pulmonary arteriovenous fistula
4. A defect between the right and left side of the heart leading to the addition of venous blood to arterial blood

Measurement of amount of shunt flow: Shunt equation

The amount of shunt flow can be calculated via the shunt equation if the shunt is caused by the addition of mixed venous blood ($C\bar{v}O_2$) to blood draining from the capillaries. The total amount of O_2 leaving a system is the total blood flow (Q_T) multiplied by the O_2 concentration in the arterial blood

(CaO_2). This must equal the amount of O_2 in shunted blood (Q_S x CvO_2) plus the amount of O_2 in end-capillary blood {(Q_T – Q_S) x $Cc'O_2$}. Via the principle of mass conservation, the shunt equation as depicted in figure 9 is derived.

$$\frac{\dot{Q}_S}{\dot{Q}_T} = \frac{Cc'_{O_2} - Ca_{O_2}}{Cc'_{O_2} - C\bar{v}_{O_2}}$$

Figure 9: Shunt equation

CaO_2 obtained from arterial blood sample, $C\bar{v}O_2$ obtained from mixed venous blood sample via a pulmonary artery catheter, $Cc'O_2$ is calculated from the alveolar PO_2 and the oxygen dissociation curve

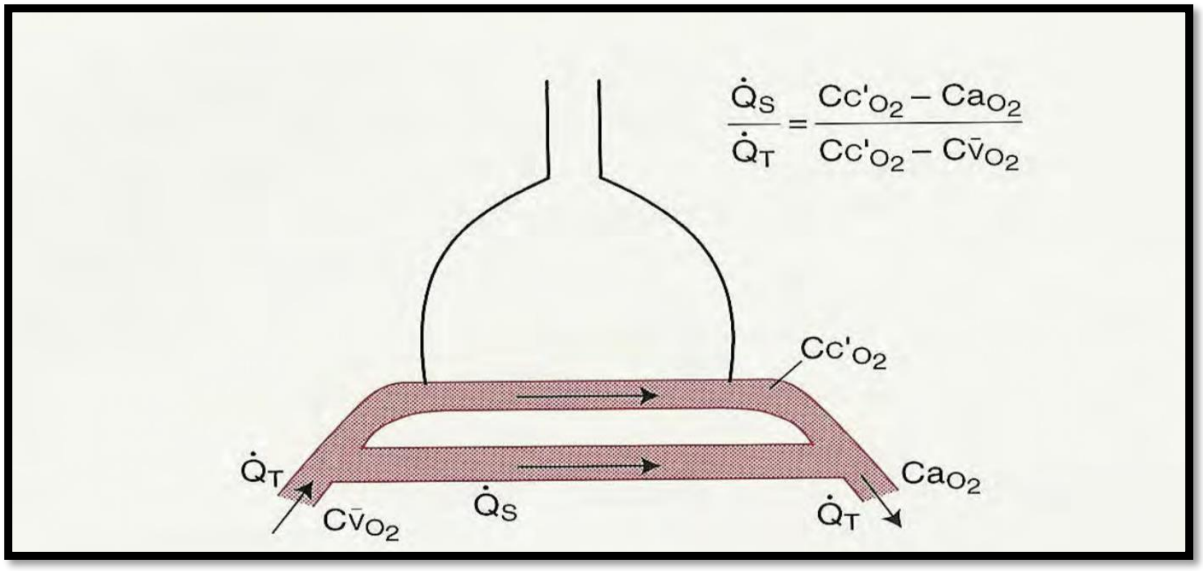

Figure 10: Measurement of shunt flow (West 8th edition)

It is usually not possible to calculate the true shunt magnitude when the shunt is caused by blood that does not have the same O_2 concentration as mixed venous blood.

In shunt a FiO_2 of 1.0 will not abolish hypoxaemia, because shunted blood is never exposed to the higher alveolar PO_2. There may, however, be some increase in the arterial PO_2, because of the O_2 added to the capillary blood of ventilated lung. Blood that is perfusing ventilated alveoli is nearly fully saturated and thus most of the added O_2 is in the dissolved form.

Figure 11 illustrates why giving a subject 100% O_2 to breathe is a very sensitive measurement of shunt. When 100% O_2 is inspired the PaO_2 does not rise to the expected level. Due to the almost flat slope of the O2 dissociation curve when the PO_2 is high a small depression of arterial O_2 concentration will cause a relatively large drop in PO_2.

A shunt usually does not result in a raised PCO_2 in arterial blood. The shunted blood will have a higher CO_2 concentration but the chemoreceptors will sense the elevation in $PaCO_2$ and respond by increasing ventilation. This will lead to a reduction in the PCO_2 of the unshunted blood until the arterial PCO_2 is normal.

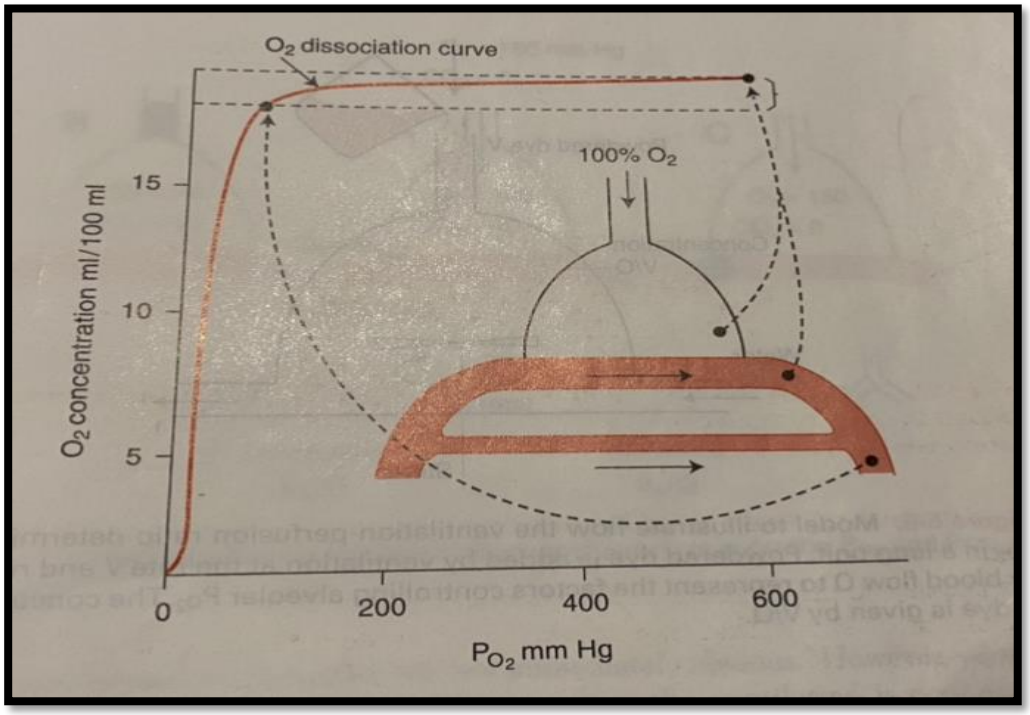

Figure 11: Depression of arterial PO_2 by shunt during 100% O2 breathing (West 8th edition)

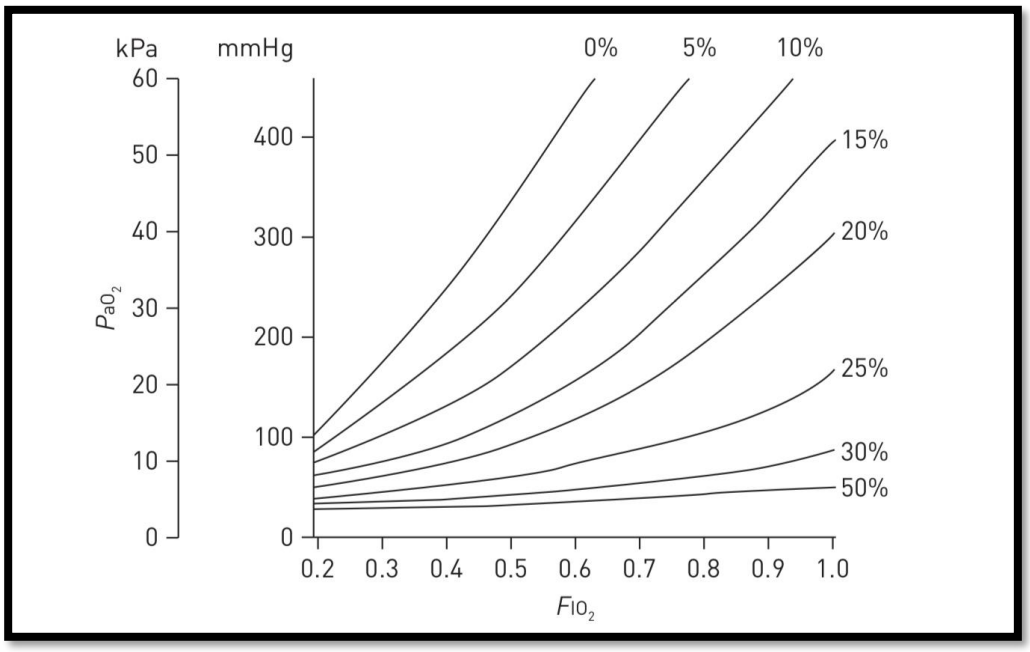

Figure 12: Iso-shunt diagram (Physiology in respiratory medicine, J Petersson and RW Glenny)

The diagram illustrates the relationship between PaO_2 and FiO_2 in the presence of different shunt fractions. There is a near linear relationship between PaO_2 and FiO_2 in the absence of shunt. The change in PaO_2 with increasing FiO_2 is flatter with an increase in shunt fraction. A shunt more than 30% of cardiac output fails to attain a PaO_2 of 100mmHg (13,3kPa) with even a FiO_2 of 1.0. Modelling is based on a haemoglobin concentration of 14g/dL, $PaCO_2$ of 40mmHg (5,3kPa) and an arterial-mixed venous oxygen content difference of mL/dL

MEASUREMENT OF V/Q MISMATCH

Alveolar-arterial PO_2 difference (A-a gradient)

V/Q mismatch can be measured by obtaining the alveolar-arterial PO_2 difference (subtracting the arterial PO_2 from the alveolar PO_2). The alveolar PO_2 is the PO_2 that the lung would have if there were no V/Q mismatch and the respiratory exchange ratio was the same as the real lung. It is derived from the alveolar gas equation, see figure 13. Normally the A-a gradient is less than 15 mmHg, but it can increase with age up to 20 to 30 mmHg. An abnormally high A-a gradient indicates that there is V/Q mismatch.

The partial pressure of oxygen in the alveolus (PAO_2) is a determining factor of arterial oxygen tension (PaO_2). The alveolar gas equation highlights the three conditions that can cause a decrease in PAO_2: low altitude, hypoxic gas mixture (low FiO_2) and hypoventilation (high $PACO_2$).

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{A_{CO_2}}}{R} + F$$

Figure 13: Alveolar gas equation

PIO_2 = FiO_2 x (atmospheric pressure minus saturated vapour pressure of water at body temperature)
$PACO_2$ = arterial PCO_2 is used for the partial pressure of CO_2 in the alveolus
R = respiratory exchange ratio (CO_2 production/O_2 consumption), normal value of 0,8
F = small correction factor, typically about 2 mmHg

SUMMARY

There are 5 causes for hypoxaemia: decreased partial pressure of O_2 in inspired gas, hypoventilation, diffusion limitation, low V/Q ratios and shunt.

The two causes for hypercapnia or CO_2 retention are: hypoventilation and V/Q mismatch.

The following table summarizes how low V/Q ratios and shunt affect PAO_2, the PA-aO_2 gradient and the PaO_2 response to an increase in FiO_2 in comparison to the other three causes of hypoxaemia.

Cause of hypoxaemia	P_{AO_2}	P_{A-aO_2}	P_{aO_2} response to increased F_{IO_2}
Diffusion limitation	Normal	Increased	Improved
Hypoventilation	Reduced	Normal	Improved
Decreased P_{IO_2}	Reduced	Normal	Improved
Low V'_A/Q'	Reduced locally	Increased	Improved
Shunt	Reduced locally	Increased	Minimal improvement

P_{AO_2}: alveolar partial pressure of O_2; P_{A-aO_2}: alveolar–arterial O_2 tension difference; P_{aO_2}: arterial partial pressure of O_2; F_{IO_2}: inspiratory O_2 fraction; P_{IO_2}: partial pressure of O_2 in inspired gas; V'_A/Q': ratio of alveolar ventilation to perfusion.

Table 1: Five causes of hypoxaemia (Physiology in respiratory medicine, J Petersson and RW Glenny)

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