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The blood–gas partition coefficient

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Summary

A partition coefficient (λ) describes the relative affinity of a volatile anaesthetic for two phases and how that anaesthetic distributes itself between the two phases when equilibrium has been achieved. The blood–gas partition coefficient ($\lambda_{B/G}$), or Ostwald coefficient for blood–gas, is a pharmacological term used to describe the solubility of a volatile anaesthetic agent. Volatile agents with a low blood–gas partition coefficient (less soluble) will exert a high partial pressure and produce a more rapid onset and offset of anaesthetic action.

Keywords: blood–gas partition coefficient, Ostwald coefficient, volatile anaesthetic, solubility

Introduction

Volatile anaesthetic agents produce their effect through their action on the brain. The depth of anaesthesia is therefore determined by the concentration of volatile anaesthetic agent in the brain. The speed of induction and recovery from anaesthesia is governed by the speed at which this concentration in the brain changes. For a volatile anaesthetic agent to reach the brain it must be distributed throughout the body. The extent to which the volatile anaesthetic gets taken up by the body tissues will have an influence on the speed of uptake and elimination by the brain.[1]

Gas laws and gas exchange

Inhalational anaesthetics are administered as gases or vapours, therefore a specific set of physical principles applies to the delivery of these agents. Dalton's law of partial pressures states that in a mixture of non-reacting gases, the total pressure exerted is equal to the sum of the partial pressures of the individual gases.[2]

Partial pressure is the pressure a gas exerts proportional to its fractional mass (Figure 1); this is the same pressure each gas would have if it alone occupied the same volume:

$$P_{tot} = P_1 + P_2 + P_3 \ldots + P_n$$

Henry's law states that at a constant temperature, the amount of a given gas that dissolves into a given type and volume of liquid is directly proportional to the partial pressure of the gas in equilibrium with that liquid.[3,4] An equivalent way of stating the law is that the solubility of a gas in a liquid is directly proportional to the partial pressure of the gas above the liquid:[2]

$$C = kP$$

C – Concentration of dissolved gas (mol/l)

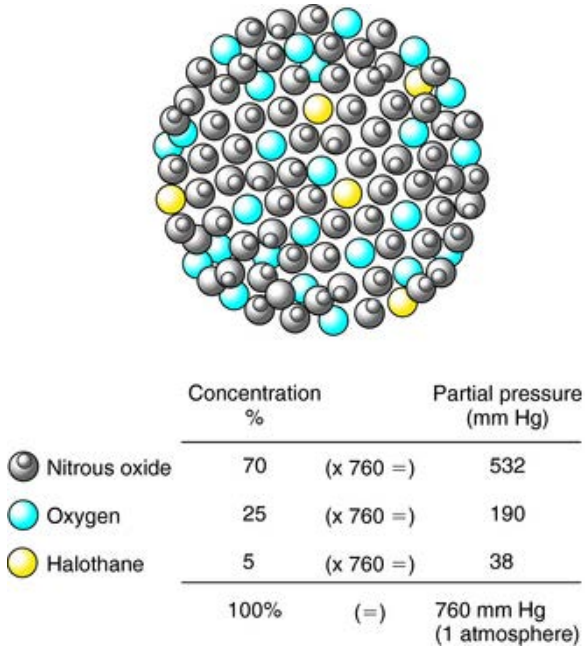

Figure 1: Partial pressure of a gas is proportional to its fractional concentration[2]

k – Henry's proportionality constant (specific to solute, solvent and temperature)

P – Partial pressure of the gas above the solution (kPa)

Volatile anaesthetics or gases equilibrate throughout the body based on their respective partial pressures and not concentrations (Figure 2). Once a volatile anaesthetic agent reaches steady state, the partial pressure of the agent within the alveoli (P_A) is in equilibrium with the partial pressure in arterial blood (P_a) as well as partial pressure within the brain (P_B). The alveolar partial pressure (P_A) is therefore an indirect measure of brain partial pressure (P_B).[5]

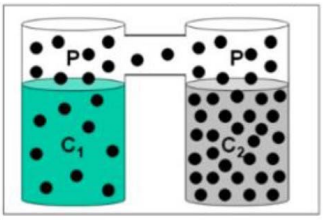

Figure 2: Partial pressure (P) of the gas is equal between the two phases even though concentration of the gas in solution (C1 and C2) differs

How long it takes for each volatile anaesthetic agent to reach steady state conditions depends on the individual properties of the agent and numerous physiological factors.[6] Kety[6] determined that the alveolar partial pressure curves for all inert gases (volatile anaesthetics are considered to behave as inert gases) have the same characteristics.

When an inert gas is introduced at a constant partial pressure in the inspired air, it takes time for the tissues in the body to obtain the gas at this partial pressure. Pulmonary ventilation carries the gas to the alveolar membrane where it diffuses to the pulmonary blood and gets distributed via the systemic circulation to the tissues. Diffusion across the capillary membranes, interstitial fluid and cellular membrane takes place so that venous blood leaving the capillary is in equilibrium with the tissue. The blood returning to the lungs carries a fraction of the inspired gas concentration and is again equilibrated with the alveolar gas. In this way the alveolar (or arterial) and venous (or tissue) partial pressures of the inhaled anaesthetic gradually rise towards equilibrium with the partial pressure of the inspired gas.[7] If this rise in partial pressure is plotted against time, it produces a curve that is similar for every inert gas or volatile anaesthetic (Figure 3).[6]

This curve has an initial rise, a knee and a tail. The steep initial rise represents the phase where ventilation moves the inhaled agent rapidly into the lungs. Following this, the knee stage arrives where lung washout gives place to tissue saturation. The slope of the knee is determined by the rate of uptake by the vessel-rich tissues such as the heart, liver and brain. Lastly, the slope of the tail is determined by the more gradual rate of uptake of volatile anaesthetic by the vessel-poor tissues such as the muscles and fat. The difference in slopes between the volatile anaesthetic agents is mainly determined by the difference in their solubilities in tissue and blood (Figure 4).

Recovery from volatile anaesthesia results from the elimination of anaesthetic from the brain. This process is simply the reversal (or wash-out) of the uptake process so the principal factors determining induction and recovery are the same.[7]

Blood-gas partition coefficients and volatile anaesthetic solubility

A partition coefficient describes the relative affinity of an anaesthetic for two phases and how

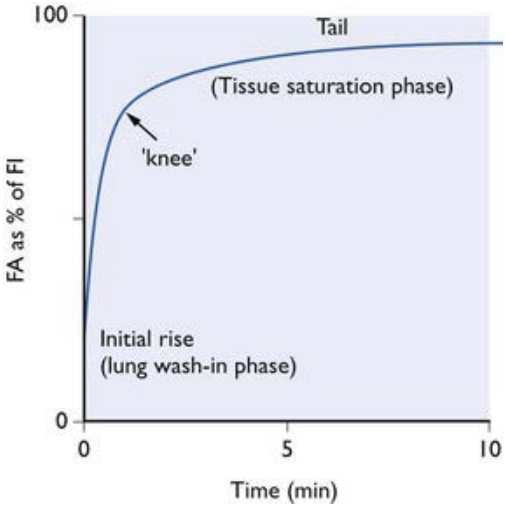

Figure 3: Kety's alveolar partial pressure curve of inhalant during uptake[6]

that anaesthetic partitions itself between the two phases when equilibrium has been achieved.[3,8,9] The blood gas partition coefficient is defined as the ratio of the amount of anaesthetic in blood and gas when the two phases are of equal volume and pressure and in equilibrium at 37 °C.[3]

A partition coefficient is simply the ratio of the concentration of anaesthetic in one phase compared to another and therefore has no units (Table I).[8,9] For example, halothane has a $\lambda_{B/G}$ of 2.3; if we had an equal volume of air in contact with an equal volume of blood and halothane is allowed to move freely between these compartments until the pressure is equal in each compartment, we have the equivalent of 1 molecule of halothane in the air to every 2.3 molecules dissolved in the blood (Figure 5).

Partition coefficients are used to describe the solubility of volatile anaesthetics in a number of different solvents. The blood–gas partition coefficient is an important determinant of the speed of

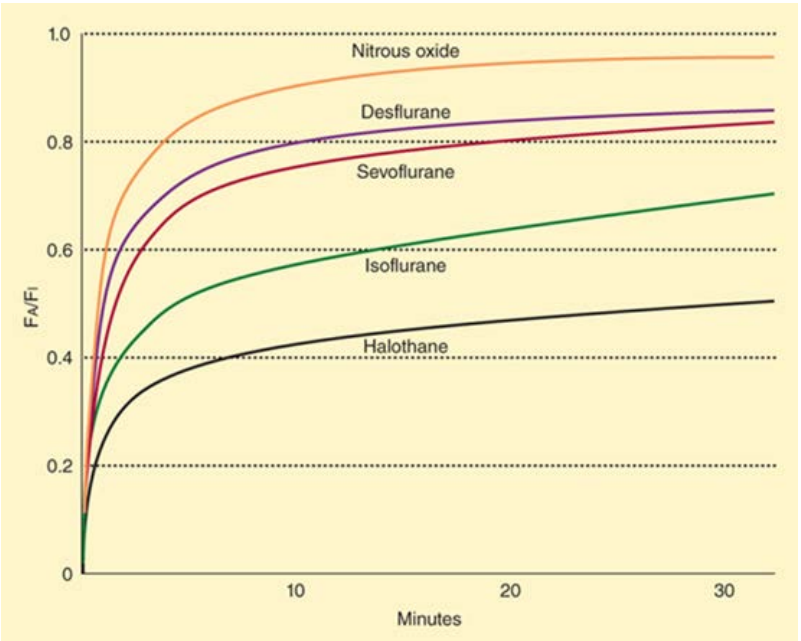

Figure 4: The rise of alveolar partial pressure (P_A) towards inspired partial pressure (P_I) in different volatile anaesthetics[8]

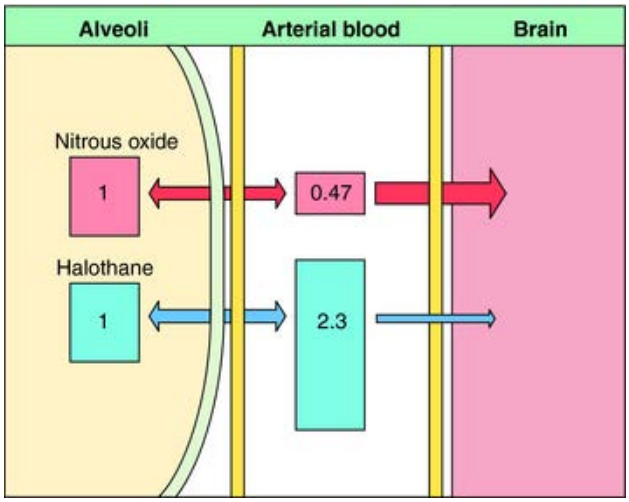

Figure 5: Blood–gas partition coefficients for halothane and nitrous oxide[2]

anaesthetic induction and recovery. It describes the distribution of an inhalational agent between a gaseous phase (alveolar air) and the blood. The greater the blood–gas partition coefficient, the greater the solubility in blood.[4,9]

Table I: Partition coefficients of volatile anaesthetic at 37 °C [8]

Agent	Blood/ Gas	Brain/ Blood	Muscle/ Blood	Fat/ Blood	MAC (%)
Nitrous oxide	0.47	1.1	1.2	2.3	104
Desflurane	0.42	1.3	2.0	27	6
Sevoflurane	0.65	1.7	3.1	48	2
Isoflurane	1.4	2.6	4.0	45	1.4
Halothane	2.4	2.9	3.5	60	0.75

Poorly soluble agents ($\lambda_{B/G} < 1$) generate a high partial pressure, which creates a steep gradient between P_a and P_B. Volatile anaesthetic agents with a low blood–gas partition coefficient will therefore exert a high partial pressure and produce a more rapid onset and offset of action.[9]

Conversely, soluble volatile anaesthetic agents with a low blood–gas partition coefficient ($\lambda_{B/G} > 1$) dissolve easily into pulmonary blood without substantially increasing the partial pressure (P_a). This leads to a slow onset of anaesthesia due to a large fall in P_A as the agent leaves the alveolus, decreasing the gradient for further diffusion and a small gradient between P_A and P_B.[9]

Uptake of volatile anaesthetic agents

The rate of uptake of anaesthetic agent by the bloodstream is predicted by the Fick equation:[10]

$V_B = \lambda_{B/G} * Q ((P_A-P_V)/P_B)$

V_B – uptake by blood

$\lambda_{B/G}$ – blood–gas partition coefficient (solubility of the volatile anaesthetic)

Q – cardiac output

P_A – alveolar partial pressure of anaesthetic

P_v – venous partial pressure of anaesthetic

P_B – barometric pressure

Factors affecting the blood–gas partition coefficient

Temperature

Hypothermia increases the solubility of volatile anaesthetics in blood. The $\lambda_{B/G}$ therefore increases as temperature decreases and vice versa.[11-13]

Haematocrit

Haemodilution or a reduction in haematocrit will generally decrease the solubility ($\lambda_{B/G}$) of volatile anaesthetics in blood.[11,13,14] The extent to which the $\lambda_{B/G}$ changes is variable and depends on the particular agent's affinity for red cells. An agent that is less soluble in red cells, e.g. isoflurane, will have a decreased blood–gas partition coefficient in anaemia. The $\lambda_{B/G}$ for sevoflurane and desflurane are mostly unaffected by changes in haemoglobin or haematocrit.[14]

Serum constituents

Concentrations of serum constituents such as albumin, globulin, triglycerides, and cholesterol can influence the $\lambda_{B/G}$.[15] These serum molecules effectively act as molecular sinks to bind anaesthetic agents, thereby increasing their blood solubility. Serum triglyceride concentrations have an important effect on the blood–gas partition coefficient for halothane because of its much higher solubility compared to the other volatile anaesthetics.[16]

Obesity

An increase in BMI causes a modest increase in F_I/F_A and $\lambda_{B/G}$ of volatile anaesthetic agents; this effect is more pronounced in those agents with a higher solubility. An increased BMI increases anaesthetic uptake and the need for the delivered anaesthetic to sustain a constant alveolar concentration.[17]

Age

Lower blood–gas partition coefficients in children explain in part the more rapid rise of alveolar anaesthetic partial pressure in this age group.[18,19] $\lambda_{B/G}$ in neonates were found to be 18% lower than in adults, and for children and the elderly 12% lower than in adults.[18] Halothane, isoflurane and nitrous oxide are significantly less soluble in fetal compared to maternal blood; this finding is independent of the known differences in lipid concentration, protein and haemoglobin content of fetal blood.[20,21]

Conclusion

The blood–gas partition coefficient is a ratio of the concentration of volatile anaesthetic in blood compared to alveolar gas once the partial pressure has equilibrated. It is a pharmacological term used to describe the solubility of a volatile anaesthetic agent. Volatile agents with a low blood–gas partition coefficient ($\lambda_{B/G} < 1$) are poorly soluble with subsequent rapid rise in partial pressure and onset of anaesthetic action.

Conflict of interest

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