Altitude and Anaesthesia

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Inhalational pharmacology is the backbone of clinical anaesthetic practice. The delivery of respiratory gases, together with inhaled anaesthetic agents, is the sine qua non of anaesthesia. An understanding of how gases behave under conditions of altered barometric pressure is, therefore, essential for all anaesthetists, particularly those practising in a country like South Africa where there are wide variations in altitude between major cities.

Oxygen and Altitude

While the proportional composition of the atmosphere remains remarkably consistent, ambient pressure decreases logarithmically with ascent, causing a corresponding decrease in the partial pressure of all atmospheric gases, but, most importantly, that of oxygen (PO_2). The physiological effects of altitude are predominantly due to the resultant hypoxia and hypobaria. High altitude is defined as >1 500 m above sea level, where the physiological effects of altitude may first be consistently observed, but pathological consequences are very rare. At this level, the alveolar partial pressure of oxygen (PaO_2) is ~10 kPa, compared with the sea level value of 13 kPa(Figure 1) [1]. It is worth noting that large areas of SA, including the extensive metropolitan areas in Gauteng, therefore qualify as high altitude.

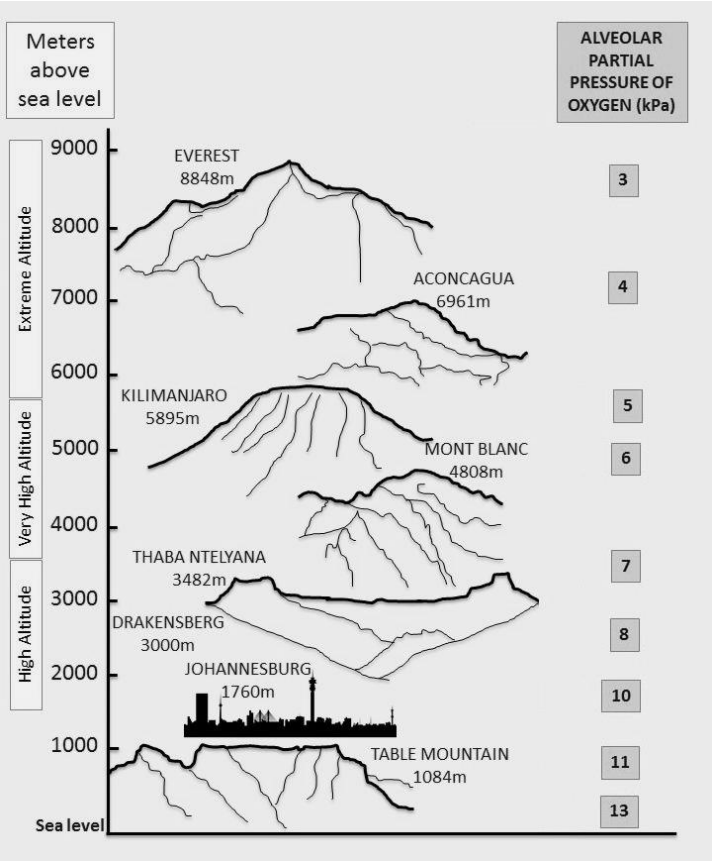

Figure 1. Changes Alveolar PO2 with altitude. Adapted with permission from reference 1.

The partial pressure of oxygen in the lung is given by the alveolar gas equation:

$$P_A0_2 = F_i0_2(P_B\text{-}PH_20) - PaCO_2/R$$

At sea level	$P_A0_2 = 0.21(101\text{-}6.2)\text{-}5.3/0.8$	=	13.3 kPa
In Johannesburg	$P_A0_2 = 0.21(80\text{-}6.2)\text{-}4.3/0.8$	=	10.13 kPa
Summit of Everest	$P_A0_2 = 0.21(34\text{-}6.2)\text{-}1.5/0.8$	=	3.9 kPa

Gas volumes are absolutely dependent on the barometric pressure to which the gasses are exposed (Boyle's Law) and thus fractional concentration does not adequately express the active component of any gas within a mixture. For example, 21% oxygen at sea level represents a partial pressure of 21 kPa at sea level. However, the same fractional concentration at the top of Mount Everest represents a partial pressure only approximately 7 kPa (see Figure 1). Since physiology entirely depends on the solution of these gases in the tissues, which is partial pressure dependent, the use of fractional concentration or percentage is profoundly misleading. Thus a person living in Johannesburg has a persistently lower P_A02 than the same individual at sea level and a mountaineer on Everest is profoundly hypoxic – all at 21% oxygen!

To understand the physiological impact of this issue properly, it is necessary to revisit some basic laws of physics. Dalton's law of partial pressure states that the partial pressure (PP) of one gas in a mixture of gases is the pressure that gas would exert if it alone occupied the whole space. Thus if all gasses other than oxygen are removed from a container of air at sea level while keeping the volume constant, the remaining gas would be 100% oxygen, but the pressure in the container would be only 21 kPa. The second important physical principle is expressed in Henry's Law which states that, at constant temperature, the amount of a given gas that dissolves in a given liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid. The implication of this is that the number of gas molecules entering the blood stream from the alveolus is dependent on the PP (not the concentration) of that gas in the alveolus. Finally, Ostwald's solubility coefficient is the volume of gas dissolved per milliliter of liquid and per unit PP of the gas at any given temperature, with the solubility increasing as the liquid temperature decreases. The corollary of this is that the tendency of a gas to leave a solution is also driven by its partial pressure and the temperature of the liquid. This is why a carbonated drink bubbles when opened as the CO_2, dissolved under pressure, escapes from the liquid when that pressure is released (especially if the liquid is warmed).

The gradient between PaO_2 and the oxygen PP in the tissues provides the driving force for oxygen to reach the mitochondria resulting in the oxygen cascade (Figure 2).

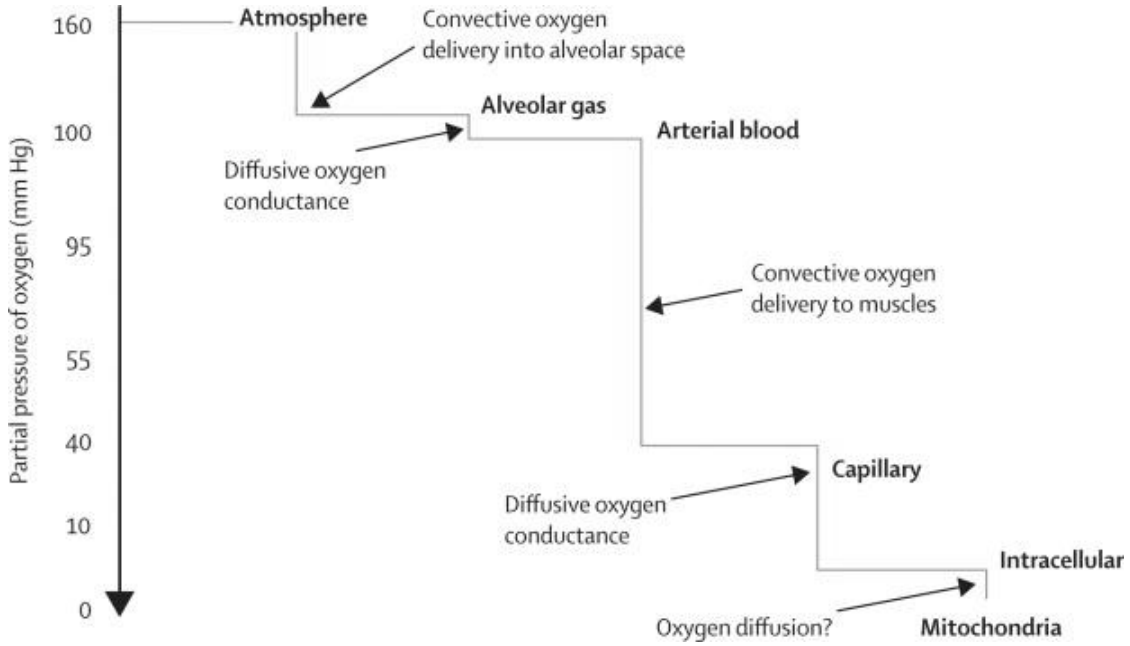

Figure 2. Oxygen cascade illustrating the partial pressure gradients that drive oxygen across the various tissue components to reach the mitochondria.

A quarter of the world's population live at more than 500m above sea level and nearly 10% reside over 1500m [2] including heavily populated cities such as Denver, Nairobi, Bogota, Mexico City and Johannesburg. Inhalational anaesthesia at such altitudes is common. South Africa is a country with widely varying altitudes and therefore it is imperative that anaesthetists understand the influence of altitude on the accuracy and reliability of their delivery and measurement systems.

Inhalational Agents

Anaesthetic gases and vapours exert their effects in proportion to the partial pressure that can be established within the brain. The driving force for an anaesthetic agent to enter the brain from the blood is the partial pressure of the anaesthetic in the blood, not its concentration. This explains the apparent anomaly of agents such as ether, which are very soluble in blood, and thus develop a high concentration rapidly, but act very slowly. The high solubility of ether means that the partial pressure in the alveolus falls rapidly, resulting in a low partial pressure in the alveolus and thus in the blood. The driving force for the agent to enter the brain is thus low until such time as the blood is saturated with ether and the partial pressure begins to rise. The same phenomenon explains why relatively insoluble agents such as desflurane exert their effects rapidly, but require a high alveolar partial pressure to dissolve sufficient gas molecules in the blood to exert the pharmacological effect. The reverse is true when it comes to removal of the gases, meaning that insoluble gases with high partial pressures have a high driving force to leave the blood when the gas is removed from the alveolus resulting in more rapid recovery than that seen with soluble agents.

The potency of an anaesthetic agent is classically described in terms of the minimal alveolar concentration (MAC) defined as the concentration of an inhaled agent that will prevent movement to a surgical stimulus in 50% of subjects. Note that concentration is specified; this means that, for precision, the atmospheric pressure should be quoted when stating a MAC value. If the pressure departs significantly from 1 atm, then this becomes essential. The difficulty is avoided by expressing MAC as a partial pressure (MAP).[3] At sea level, 1 MAC of isoflurane is 1.15 vol %. This corresponds to an end-tidal partial pressure of 101.3 kPa X 0.0115 = 1.16 kPa. To achieve an end-tidal isoflurane partial pressure of 1.16 kPa in Mexico City (barometric pressure 76.4 kPa), one should aim for an end-tidal concentration of 1.16 kPa/76.4 kPa = 1.5%. Consequently, when using isoflurane in Mexico City, its MAC is 1.5 vol%[4], not the standard 1.15%. It is far more logical, therefore, to use the concept that is independent of altitude, and thus applicable throughout the world, minimal alveolar partial pressure (MAPP). In SI unit terms this conversion is simple as the kPa MAPP value and the sea level MAC value are essentially the same [5]. The correct measure of potency that is independent of altitude is the minimum alveolar partial pressure (MAPP), first described in 1984[6] and now accepted as standard in the major anaesthetic textbooks.[7]

Nitrous oxide, although a vapour at normal room temperature, behaves like a gas with a MAPP of 105 kPA (about 105% MAC at sea level). As it behaves like a gas, not a vapour, the partial pressure of any given concentration decreases as barometric pressure falls. Consequently, the value of nitrous oxide as an anaesthetic agent diminishes with increasing altitude. At sea level, N_2O has a considerable analgesic potential, approximately equivalent to 10 mg IV morphine. However, at the altitude of Johannesburg, the 20% reduction in partial pressure of the agent reduces its analgesic effect by half and at 3 000 m there is no detectable analgesic effect at all (Figure 3).[8]

These results have been widely confirmed. The reduced effectiveness of N2O at the altitude of Johannesburg was noted as long ago as 1913 [9]. Powell[10] concluded that the efficacy of N2O was decreased at an altitude of 5280 feet (1670 m). Cleaton-Jones and colleagues[11] reported that there were only marginal differences between a group studied at sea level and a different group studied at 1670 m. However, they did not measure objective end points and there were strong trends suggesting a lower potency of N2O at altitude, particularly in conscious level, at 60 and 70% concentrations between the two altitudes. A study of anaesthesia using volatile agents and N_2O in combination at sea level and at altitudes >1300 m showed a significantly greater consumption of volatile agents at higher altitudes, suggesting a diminished effect of N2O [12]. Furthermore, a comparative trial of i.v. anaesthesia in conjunction with 66% N_2O at high and low altitudes demonstrated significantly higher propofol requirements at altitude [13]. It can be safely concluded that the efficacy of N_2O is entirely dependent on the partial pressure of the agent and not the concentration.

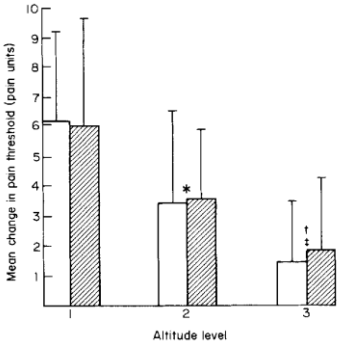

Figure 3. Effect of 50% nitrous oxide on the analgesic threshold in volunteers at sea level (level 1), 1 700 m (level 2, equivalent to Johanesburg) and at 3 000 m (level 3) in either pure oxygen (open bars) or an air/oxygen mixture (hatched bars). At 3 000 m there was no detectable analgesic effect.[8]

Vaporisers

Variable bypass anaesthetic vaporisers function on the basis of diluting a saturated vapour of the agent into a bypass flow stream. The mass of anaesthetic agent delivered from the vaporiser is determined by the SVP of the agent within the vaporising chamber at a fixed temperature and a variable splitting ratio, which dilutes the SVP to the desired value. Since SVP is solely determined by temperature and virtually unaffected by barometric pressure, temperature compensation measures are used within the vaporiser to minimise temperature fluctuations and to adjust the splitting ratio should the temperature vary from the calibrated value (usually 20°C). These vaporisers deliver a partial pressure, not a concentration of the agent and continue to be reasonably accurate with fluctuations in barometric pressure.[7,14] Thus, a variable bypass vaporiser set to deliver 2% at sea level will deliver a partial pressure of approximately 2 kPa regardless of the barometric pressure. The same vaporizer in Johannesburg or Denver, Colorado (at an altitude of approximately 1700m (5500 feet) and a barometric pressure of approximately 80 kPa will continue to deliver the same partial pressure of 2 kPa, but at a concentration of 2.5%. At a higher altitude where the barometric pressure is half that at sea level, the proportion of isoflurane vapour output increases due to the lower barometric pressure. Therefore, the dial setting that delivered 2% isoflurane at sea level will now deliver 4% isoflurane. However, according to Dalton's law, the partial pressure of isoflurane delivered would be approximately the same at both altitudes since 2% isoflurane at 760mm Hg (15.2 mm Hg) is the same as 4% isoflurane at 380mm Hg (15.2 mm Hg).[1] If the anaesthetist were to titrate anaesthetic agent dosage to end-tidal volatile concentration, the partial pressure would be half that delivered at sea level and the risk of under-dosing (and thus accidental awareness under anaesthesia) would be substantial. The desflurane vaporiser functions on a different principle, more akin to a nitrous oxide cylinder, and delivers a concentration of vapour which requires adjusting upwards for increasing altitude.[15] Cassette-type vaporisers for most volatiles behave like a computer-controlled variable bypass vaporiser. However, the cassette for desflurane injects a known mass of volatile into the system (similar to a carburettor) and thus should also deliver a partial pressure, not a concentration, so similar considerations could apply although this has never been scientifically tested.

Gas Analysers

In gas analysis, volumetric measurement was historically the standard technique used for establishing the fractional concentration of different gases in a mixture using such equipment as the Haldane and Van Slyke devices. Hence the universal use of concentration as the standard descriptor of gas mixtures. These are clumsy, time-consuming techniques that are not amenable to the rapid gas analysis required in current clinical practice. Modern gas analytical techniques all measure gas composition using a specific property of each gas, ignoring other gases in the mixture.

It is obviously vital to know and understand how we measure the delivery of oxygen and removal of carbon dioxide as errors in this area may be life-threatening. In addition, anaesthetic vapour analysis is an essential element of monitoring during inhalational general anaesthesia [16] and recent publications have re-emphasised the importance of monitoring end-tidal anaesthetic concentrations as a means of minimising the risks of awareness in this setting [17,18]. Consequently the question arises as to whether exhaled vapour concentration is a valid measure of the dose of volatile anaesthetic gases in all circumstances [5]. In particular, are such measures misleading under conditions of altered barometric pressure occurring with increasing altitude?

Oxygen Analysers

There are four main types of analysers currently in common use for measurement of the oxygen content of gas mixtures. They are paramagnetic, fuel cell, oxygen electrode, and mass spectrometer devices. All respond to the partial pressure of oxygen alone, and the output changes as the barometric pressure changes. At an altitude of 5000 ft an oxygen analyzer set to measure 21% oxygen at sea level will give a reading of 17.4% unless it is recalibrated to read 21% in air at the new pressure (Table 1)[5].

[1] In actual fact, the splitting ratios vary slightly with altitude, so variable bypass vaporisers at altitude actually deliver a slightly higher partial pressure than that marked on the dial, but the error is much smaller (and in a safer direction) than the concentration error.

TABLE 1. INFLUENCE OF BAROMETRIC PRESSURE ON OXYGEN CONTENT OF AIR AS MEASURED BY PARAMAGNETIC OXYGEN ANALYSER

	Barometric Pressure			Partial Pressure of Oxygen	
Altitude (ft)	(kPa)	(mm Hg)	Scale Reading (% oxygen)	(kPa)	(mm Hg)
0	101.5	760	21.0	20.9	165
5000	83.2	624	17.4	17.4	122
10000	69.0	518	14.2	14.2	110

If the device were to be calibrated in terms of partial pressure the scale readings would reflect the true state of oxygen availability to the patient. This effect is of relatively minor importance unless accurate research work is being performed or the changes in barometric pressure are extreme. At altitudes of 10,000 ft and above, 21% oxygen becomes a relatively hypoxic mixture, and measurements of partial pressure are the only sensible ones to follow. It is worth noting that breathing air at this altitude is equivalent to breathing 14% oxygen at sea level. As a practical point, the gain controls on some models of oxygen analysers do not permit resetting of the scale to read 21% in air at such low partial pressures of oxygen. These devices will, however, continue to reflect the reduced partial pressure. Under hyperbaric conditions, it is again important to know the partial pressure of oxygen in the mixture inhaled, because 21% oxygen at 5 atmospheres pressure will exert a partial pressure greater than that of 100% oxygen at sea level, with the consequent risks of oxygen toxicity. Hence, divers operating at depths of 200 metres (a pressure of +20 atm), such as in the North Sea oil fields use gas mixtures of 1% oxygen in helium, which results in a partial pressure of 20 kPa of oxygen under 20 atm pressure.

Carbon Dioxide Analysers

Carbon dioxide is most commonly measured by absorption of infrared radiation by the gas. Such instruments are often produced commercially with an internal calibration device that is supposed to read in percentages. Because the instrument actually responds to partial pressure, this is misleading, and reliance on the internal calibration device will introduce errors of clinical importance when such equipment is used at altitude. A device with an internal calibration nominally set at 7% will, in fact, be calibrated to 7 kPa (53 mmHg), which is actually 8.2% of barometric pressure at 5000 ft altitude. For such equipment to function correctly, it must be either recalibrated against known concentrations of carbon dioxide at the correct barometric pressure or the scale converted to read partial pressure. If kilopascals are used, this conversion is simple because sea level percentages and kilopascals are, for practical purposes, the same. Fortunately, many CO_2 analysers now available display the transducer output in pressure units and not as percentages and these should be used wherever possible. The effect of varying barometric pressures on the output of an infrared analyzer using a fixed concentration of carbon dioxide is shown in Table 2. At an altitude of 5000 ft, the concentration of carbon dioxide in alveolar gas is 5.5%. If a device calibrated in percentages is used to monitor end tidal CO_2; to maintain normocapnoea, the use of the percentage figure will result in the patient being rendered significantly hypercapnic, because the partial pressure of expired CO_2 will be 5.5 kPa (42 mmHg), the normal at this altitude being 4.6 kPa (35mmHg). A more subtle error may also be introduced if a machine of this nature is used to monitor a patient being ventilated inside a one-man hyperbaric chamber in, for example, the management of carbon monoxide poisoning. If the analyser is placed outside the chamber and the patient's expired gas led outside the chamber before measurement, the gas will expand. The concentration of carbon dioxide in the mixture will remain unchanged, but the partial pressure will decrease, thus giving a falsely low reading.

TABLE 2. INFLUENCE OF BAROMETRIC PRESSURE ON 4.5% MIXTURE OF CO_2 AS MEASURED BY INFRARED ANALYSER

	Barometric Pressure			Partial Pressure of Oxygen	
Altitude (ft)	(kPa)	(mm Hg)	Scale Reading (% CO_2)	(kPa)	(mm Hg)
0	101.5	760	4.5	4.5	34.2
5000	83.2	624	3.7	3.74	28.5
10000	69.0	518	3.1	3.18	24.3

The same principle applies to all modern gas measurement devices including those measuring oxygen and anaesthetic agents (Table 2).

Vapour Analysers
Similar arguments apply to the use of vapour analysers, all of which in modern practice respond to partial pressure, although they are almost invariably calibrated in percentages (the latest Dräger analyser can be set to return measurements in partial pressure). These devices are almost all based on infrared absorption technology (as is used in capnography) and thus the same considerations apply. This situation can be confirmed by producing a gas mixture of known composition by vapourising a known mass of a volatile anaesthetic liquid into a closed vessel of known volume. Reduction of the ambient pressure to which the flask and its contents are subjected will result in a fall in the partial pressure of the vapour in the flask, with a consequent reduction in the reading of the analyzer, even though the concentration of the vapour is unchanged. Alternatively, a fresh vapour mixture can be prepared at different ambient pressures by adding the same mass of liquid to the cleaned flask after the pressure had been altered. In this way, a constant mass of anaesthetic vapour would be contained within the flask and the partial pressure of the vapour should be the same at each level of pressure, although the concentration would be different. The output of the analyzer remains constant despite the altered concentration.

The standard device used to calibrate the output of vaporisers is the Rayleigh refractometer. This instrument compares the refractive index of the gas under investigation with that of a standard gas mixture and produces an accurate measure of the number of gas molecules in the sample. Again such devices respond to partial pressure not concentration, meaning that vaporiser output is calibrated in terms of partial pressure (even though expressed as a concentration).

As with other gas analysers, the use of percentage measures on an agent analyser to guide the use of anaesthetic vapours at altitude can lead to serious dosing errors. It must be remembered that vapour analysers measure partial pressure not concentration. The use of percentage units to describe anaesthetic agent dosing is simply wrong and can lead to serious errors in dosages, particularly at altitude.

Gas density and flow

Changes in barometric pressure produce changes in the density of gases. As a result, an apparatus whose function is partly or wholly dependent on gas density will not behave as it would at the altitude at which the device was calibrated (almost invariably sea level). Consequently, equipment used by anaesthesiologists in the operating room, critical care area, and laboratory may not function in the expected manner.

Flowmeters
Most flowmeters use the decrease in pressure that occurs when a gas passes through a resistance as a measure of gas flow. The magnitude of the decrease in pressure depends on the density and viscosity of the gas. In situations where the resistance represents an orifice, resistance depends primarily on the density of the gas. Where the resistance is tubular, viscosity becomes the prime determinant of the magnitude of the decrease in pressure provided that the flow remains laminar. Most flowmeters use a floating ball or bobbin supported by the stream of gas in a tapered tube. At low flow rates, the device depends primarily on tubular flow, and as the float moves up the tube the resistance behaves progressively more like an orifice. The density of a gas changes, of course, with changes in barometric pressure, but the viscosity changes relatively little, as it is primarily dependent on temperature. Gas flow through an orifice is inversely proportional to the square root of the density of the gas. As the density of the gas falls, therefore, the flow through an orifice of given size will increase. Thus at altitude the actual flow delivered by a flowmeter will be greater than that indicated by flowmeter. The actual flow delivered by a flowmeter under conditions of altered barometric pressure can be described by Equation 1:

$$\text{Equation 1: } F_1 = F_0 \sqrt{\frac{\rho_0}{\rho_1}}$$

where F_1 is the flow delivered at the new pressure,
Fo is the flow delivered at the original pressure,
ρ_0 is the original density of the gas,
ρ_1 is the density of the gas at the new pressure.

As density is directly proportional to pressure, values for barometric pressure may be substituted for density. The relative contributions of density and viscosity to the behaviour of a floating bobbin flowmeter are unpredictable, as each flowmeter has its own characteristics determined by the relationship between the shape of the bobbin and the taper of the tube. Thus, the exact role of viscosity in the determination of the position of the float has not been well established. Viscosity has been shown to exert an important effect in clinically used flows, and at flow rates at which viscosity is the predominant factor, Equation 1 will not apply. Little if any error in measured flow will occur with changes in altitude at the lower settings of the flowmeter where viscosity is the main determinant of the pressure drop.

If accurate measurements are to be made, the only practical approach is to recalibrate the flowmeter at the altitude at which it is to be used. These comments do not apply to fixed orifice flowmeters, in which turbulent flow is probable at all flow rates, and the error should be accurately described by Equation 1 at any flow. Various other flow-measuring devices will also perform inaccurately at altitude. The manufacturers of the Wright respirometer include a guide to the inaccuracy of the instrument at altitude. Devices that depend on other physical properties of the gas, such as katharometers and electronic flowmeters, will also tend to under-read, because the number of gas molecules per unit volume, and hence the thermal or electrical capacity, will be reduced. Pneumotachographs, on the other hand, use laminar flow to generate a pressure drop, and therefore viscosity, not density, will be the prime determinant of the measurement obtained. These devices should, therefore, continue to perform well regardless of changes in barometric pressure but may be sensitive to temperature fluctuations.

High Air Flow Oxygen Enrichment Devices
The importance of administering known concentrations of oxygen at flows exceeding peak inspiratory flow in the management of patients with respiratory disease has often been stressed. High airflow oxygen enrichment equipment usually consist of a fixed orifice Venturi device for which a specified minimum gas flow must be provided in order to produce adequate flow rates. Changes in barometric pressure might be expected to exert profound effects on such devices, because the driving force that accelerates air along the breathing pathway is the pressure gradient between the atmosphere and the negative pressure area created by the jet of oxygen emerging from the nozzle. Under conditions of reduced barometric pressure, these devices might be expected to "run rich," that is, to produce higher oxygen concentrations than those set but at a lower flow rate than that delivered at sea level. When tested, however, these devices performed better than might have been anticipated. In virtually every case, there was a small but consistent increase in the oxygen percentage and a similar decrease in the total flow produced by the device. The magnitude of these errors, however, was smaller than had been anticipated when a standard flowmeter, not corrected for altitude, was used. When a fresh gas flow is set on a standard flowmeter, it appears that the increased flow delivered by the flowmeter at altitude largely offsets the errors in delivered flow and oxygen concentration that would otherwise occur with decreases in barometric pressure. When flows corrected for altitude are used, the performance of the device deteriorates to the point where the flow delivered by the mask may well decrease below the patient's peak inspiratory flow, and higher than expected percentages of oxygen are produced. This is unlikely to be of major importance at altitudes of 5000 ft or less but may be problematic at higher altitudes. It should be noted that although the oxygen percentage may have remained more or less constant, there is a reduction in its partial pressure, and this effect must be allowed for when prescribing such a device for patient use.

Minimal Alveolar Partial Pressure

These considerations have a major import for the outdated concept of minimum alveolar concentration (MAC).

Since all gaseous agents exert their physiological effects in proportion to their partial pressure, the instruments that measure the amount of gaseous agent in any gas mixture measure partial pressure and anaesthetic vaporises deliver only partial pressures of the agents, it is quite simply absurd to persist with percentage expressions of these agents. Using percentages may lead to serious clinical errors. Particularly at altitude the use of percentages as a descriptor of the dose of gases in the clinical situation will inevitably lead to serious clinical errors including possible hypoxia and awareness. This inappropriate terminology should be abandoned. This is clearly illustrated by the so-called “universal definition of ARDS”: P_aO_2/FiO_2 [19]. This is anything but universal as alveolar oxygen PP will be substantially lower at altitude for the same FiO_2 leading to many more patients being wrongly diagnosed with ARDS at altitude.

The only rational solution is to express all medical units of measurement in terms that actually describe the clinically relevant amount. Thus gases should be described in terms of partial pressures and drugs in solution should only be described in terms of the mass of drug per unit of solvent. Anything else will inevitably result in errors in drug dosage and the literature is replete with descriptions of such errors with profound clinical consequences.

Partial pressure is the factor determining the effectiveness of the volatile agents as well as of the inhaled gases. Consequently, because the concentration of an agent required to produce a given effect increases with reductions in barometric pressure, the concept of MAC does not apply accurately at altitude and should be converted to minimal alveolar partial pressure (MAPP). The idea has much to recommend it; using this concept would eliminate many of the problems described herein. For ease of reference, the MAC and MAPP values of the commonly used anaesthetic agents are listed in Table 5.

TABLE 5. EQUIVALENT VALUES OF MAC AND MAPP AT VARIOUS BAROMETRIC PRESSURES

	MAC			**MAPP**	
Agent	Sea Level	5000 ft	10 000ft	kPa	mm Hg
Nitrous Oxide	101.5	126.5	152.2	106.1	798
Halothane	0.75	0.9	1.09	0.76	5.7
Isoflurane	1.2	1.45	1.73	1.22	9.1
Sevoflurane	2.0	2.4	3.2	2.12	15.9
	6.0	7.25	9.6	6.36	47.7

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