Low Flow Anaesthesia

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INTRODUCTION

ENIGMA Many modern anaesthetists use the circle system (with CO_2 absorption) with high fresh gas flows, thus negating all the potential advantages that this system offers.
These include improved humidification and heat conservation
significant decreases in theatre and atmospheric pollution
economy in gas and volatile agent utilisation

HISTORY

1727	**S Hales** describes a breathing device with CO_2 absorption (28 years before CO_2 was identified).
1850 and 1906	**J Snow** and **F Kühn** describe and use rudimentary total rebreathing systems.
1908	Rotameters developed (Germany).
1915	**D Jackson** (Cincinnatti, USA) uses closed circuit anaesthesia on animals, after working with CO_2 absorption in submarines.
1920 to 1926	**R Waters** uses and describes his To-and-Fro closed system with canister, and determines the advantages, disadvantages and precautions needed with closed system anaesthesia.
1926 to 1930	DRÄGER patents a closed circle system. **B Sword** develops and describes the modern circle system.
1933	Cyclopropane is introduced into anaesthesia practice. Its explosive nature and expense necessitate a closed system.

WHAT ARE LOW FLOWS?

Traditionally	HIGH- Flows	> Minute Volume of fresh gas flow e.g. Mapleson DEF (T-pieces)
	MODERATE-	1,5 L min^{-1} - Minute Volume e.g. Mapleson A
	LOW-	0,5 - 1,5 L min^{-1}
	BASAL-	Supply only what is taken up by patient

These figures do not take into account the variation in patient size, weight, age, etc., and a better classification would be to compare it to predicted basal O_2 ($\dot{V}O_2$) requirements (using a factor of 2,5 for each level).

Thus	BASAL- Flow	= 1 x $\dot{V}O_2$	± 218 mL min^{-1}	(assuming 70 kg and 36,6° C)
	MINIMAL-	= 1 - 2,5 x $\dot{V}O_2$	± 218 - 550 mL min^{-1}	
	LOW-	= 2,5 - 6 x $\dot{V}O_2$	± 0,55 - 1,3 L min^{-1}	
	MODERATE-	= 6 - 15 x $\dot{V}O_2$	± 1,3 - 3,25 L min^{-1}	
	HIGH	= > 15 x $\dot{V}O_2$	> 3,25 L min^{-1}	

Predicted basal uptake of O_2 is calculated from Brody's formula.

BASIC PHYSIOLOGICAL CONSIDERATIONS

A) O_2 Requirements at basal metabolic rate (BMR)

The minimum gas flow required in a circle system is determined by the patient's basal O_2 uptake and any leaks (zero if the circuit is 100 % "tight" and monitor sampling gasses are returned to the circuit). O_2 requirements at BMR (temperature 37,6° C) may be predicted by **Brody's formula** (1945).

$$\dot{V}_{O_2} = 10{,}15 \bullet BW^{0,73}$$

Simplified to

$$\dot{V}_{O_2} = 10 \bullet BW^{0,75}$$

or

$$\dot{V}_{O_2} = 10 \bullet kg^{¾}$$

where $\dot{V}_{O_2}$ = Basal O_2 Uptake at 37,6° C in $mL\ min^{-1}$
and BW = Body Weight in kg

For each 1° *C* below 37,6° C, reduce by 10 %
e.g. 70 kg at 36,6° C = 242 - 10 % = 218
at 35,6° C = 242 - 10 % = 218 - 10 % = 196 $mL\ min^{-1}$
at 34,6° C = 242 - 10 % = 218 - 10 % = 196 - 10 % = 176 $mL\ min^{-1}$, etc.
The converse holds true for raised temperatures.
For an **adult** the basal O_2 consumption is $\pm 3\ ml\ kg^{-1}\ min^{-1}$ ($\pm 210\ mL\ min^{-1}$). At these fresh gas flow rates, it becomes imperative to continuously monitor the F_IO_2 **in** the circuit and maintain it above 0,3.

Cardiac Output at BMR has a similar relationship to Body Weight, the formula being

$$\dot{Q} = 0{,}2 \bullet kg^{0,75}$$

where $\dot{Q}$ = Cardiac Output in $L\ min^{-1}$ at 37,6° C

B) Anaesthetic agent uptake

Vaporisers may be mounted **in circuit** (VIC) or **out of circuit** (VOC), the former is dangerous unless an agent monitor is used continuously to monitor F_IAA, (the concentration in the circuit will always be higher than the dial setting). A VIC vaporiser must be of *low* resistance and *inefficient*, e.g. Goldman.

The dial setting of a VOC vaporiser will not reflect the actual delivered concentration (it will be lower) and will change with time as the patient approaches steady state conditions (may take several hours).

The amount of anaesthetic agent vapour required to produce a given MAC is a negative exponential function and is expressed as follows by **Lowe's formula**.

$$\dot{V}_{AA} = f \bullet MAC \bullet \lambda_{B/G} \bullet \dot{Q} \bullet T^{-0,5}$$

where $\dot{V}_{AA}$ = Anaesthetic vapour uptake in $mL\ min^{-1}$
$f \bullet MAC$ = Fraction of MAC desired/delivered
$\lambda_{B/G}$ = Blood / Gas Partition Coefficient of the anaesthetic agent
$\dot{Q}$ or $0{,}2 \bullet kg^{0,75}$ = Cardiac Output in $L\ min^{-1}$
and $T^{-0,5}$ or $\sqrt{T}$ = Square Root of Time in min

The square root of time concept (Severinghaus, 1954) implies that the same amount of agent is taken up in each period, each period increasing by 2 min.

Duration of anaesth (min)	0	1	4	9	16	25	36	49	64	81	100
Period no.		1	2	3	4	5	6	7	8	9	10
Duration of period (min)		1	3	5	7	9	11	13	15	17	19

N_2O uptake follows a similar pattern and the same formula applies, but a shunt factor of 0,7 is required to compensate for the rapid saturation of richly perfused organs, displacement of N_2, etc..

$$\dot{V}_{N_2O} = 0,7 \bullet f_{N_2O} \bullet 0,46 \bullet \dot{Q} \bullet T^{-0,5}$$

or, for a normal adult

$$\approx 1\,000 \bullet T^{-0,5}$$

where $\dot{V}\ N_2O$ = N_2O uptake in $mL\ min^{-1}$
and 0,46 = $\lambda_{B/G}$ of N_2O

C) Priming dose

The first dose of volatile agent must prime the breathing system and the lungs (FRC) and may be calculated from the following

$$V_{AA} = f \bullet MAC \bullet \lambda_{B/G} \bullet \dot{Q} + V$$

Where V_{AA} = Prime Dose
and V = Volume of breathing system and lungs (FRC)

This approximates the volume of anaesthetic agent taken up in the first minute (Period 1 above) and for convenience, the first dose of anaesthetic agent is usually doubled.

D) Calculation of the unit dose of liquid anaesthetic agent

Rate of uptake of anaesthetic agents (including N_2O) is an exponential process determined by $T^{-0,5}$. Initially, very high concentrations of volatile agents are required (beyond the capability of most vaporisers), and a more convenient method is direct injection of **liquid** agent into the expiratory limb. Unit Dose = $\dot{V}_{AA}$ in the 1st minute (i.e. $T^{-0,5} = 1$) and converted to liquid mL

Prediction of anaesthetic vapour uptake is calculated in *ml* of vapour, and this must be converted to *ml* of liquid anaesthetic agent using Avogadro's Hypothesis, as follows

$$mL_{vap.}\ mL_{liq.}^{-1} = (SG\ /\ MW) \bullet 22,4 \bullet (310\ /\ 273)$$

where SG = Specific Gravity
MW = Molecular Weight
22,4 = Volume of 1 Mol of gas - Avogadro's Number
and 310 / 273 = Temperature compensation in ° K for body temperature (37° C)

Results for the various agents are
Halothane = 226, Enflurane = 196, Isoflurane = 195, Sevoflurane = 182 and Desflurane = 207
Clinically 200 mL of vapour per mL of liquid is accurate enough

E) Time constant of the breathing system

All breathing systems have a time constant which determines how soon a change in fresh gas composition is reflected in the inspiratory gas. This is short with high flows and becomes increasingly longer the lower the fresh gas flow. The relationship is

$$\tau = V_S\ /\ (\dot{V}_f - \dot{V}_u)$$

where τ = Time constant in min
V_S = Total volume of the system
$\dot{V}_f$ = Fresh gas flows in $mL\ min^{-1}$
and $\dot{V}_u$ = Total gas uptake (i.e. O_2, N_2O, Anaesthetic agent and any leaks)

If a totally closed system is kept at a constant volume, then

$$\dot{V}_f = \dot{V}_u$$

and $\dot{V}_f - \dot{V}_u = 0$

$$\tau = V_S \div 0 = \infty$$

Theoretically, a completely closed system at *steady state* and basal flows will not reflect any change in fresh gas composition at equilibrium, and the fresh gas flow must be increased to make any changes.

ADVANTAGES

i) ***Economy*** in the use of gasses and anaesthetic agents is the main driving force behind the current world-wide resurgence in the use of low flow anaesthesia.
As health budgets come under strain, the economic advantages of low flow anaesthesia become obvious.
Assuming a flow reduction from 6 $L\ min^{-1}$ to 1 $L\ min^{-1}$ fresh gas flow:
- O_2 (although relatively cheap) may be reduced by a factor of 4 (2 to 0,5 $L\ min^{-1}$)
- N_2O (an expensive gas) may be reduced by a factor of 8 (4 to 0,5 $L\ min^{-1}$)
- Volatile agents vary in cost, newer agents being costly, and huge savings may be made.

However, soda-lime is relatively expensive and needs to be taken into account.

The above estimates ignore the short periods of high flow required for initial wash-in and denitrogenation. Further savings are obtained by reducing the flow even further.

ii) Increased humidity and warming of the inspired gasses
A major advantage of low flow anaesthesia, preserving mucociliary function and maintaining normothermia.
This results in less postoperative pulmonary dysfunction.
The reaction of CO_2 absorbents with CO_2 is an exothermic reaction (i.e. producing heat) and has water vapour as a by-product.
An heat moisture exchanger (HME) placed in a low flow system will not be efficient.

iii) Less pollution and easy scavenging
Less volatile agents and N_2O, implies less theatre and global pollution.
N_2O is a greenhouse gas and also depletes the ozone layer through NO.
Volatile agents (halogenated hydrocarbons) affect the ozone layer and release Cl and F.

iv) Facilitation of measuring O_2 uptake
If the breathing system is “tight” and completely closed, it may be used as a crude physiological tool for measuring gas and agent dynamics.

DISADVANTAGES

i) It is a complex system, with many components and often bulky, heavy and initially expensive.
The many couplings are all potential leaks, which is important if low flows are used.
Monitoring gases must be returned to the system.

ii) Moisture may cause unidirectional valves to stick (esp. the expiratory valve, or valves positioned near the patient), resulting in rebreathing.
There is also increased resistance to breathing, which may be a factor in spontaneous ventilation.

iii) Exhaustion of soda-lime is not always easy to detect.

iv) Cross infection may occur if the system is non-disposable as they are difficult to sterilise.
Soda-lime is, however, a very hostile environment for bacteria and viruses and no conclusive proof exists for increased nosocomial infections or ventilator associated pneumonia.
Bacterial/viral filters may be used but must be changed between cases, otherwise cross infection risk increases.
Disposable systems overcome these problems, but have a cost premium.

v) Efficient CO_2 absorption results in hypocarbia, which can only be reversed by relative hypoventilation, and this may cause increased atelectasis. It is wiser to slow the rate of ventilation than to decrease the tidal volume in this situation (which should be 6 - 8 $ml\ kg^{-1}$).

vi) Very low flow anaesthesia may result in the accumulation of other clinically important gasses. *Any* volatile substance that is produced in the body will accumulate.

- **Methane**
  Approximately 15 to 25 % of normal people produce methane gas in their bowel from intestinal organisms. Other sources include small amounts from piped gases and the atmosphere. A methane concentration above 5,4 % is combustible in O_2, but will require > 14 hr of low flow anaesthesia to accumulate
- **Acetone**
  As most surgical patients are starved (probably beyond their glycogen reserves) fat metabolism is present and this produces ketones. The volatile ketone, acetone, is exhaled and will accumulate in the system. Diabetic and cirrhotic patients have a higher rate of production. Acetone may lead to nausea, vomiting and slow emergence.
- **Inert gases**
  The only inert gas of any consequence is **nitrogen** (N_2). N_2 is neither produced nor utilised by the body, but as we live in a N_2 rich atmosphere, every tissue in the body has a partial pressure of N_2 of 78 kPa (at sea-level).
  To obtain an O_2 concentration > 21 %, and especially if we want to use N_2O, we need to denitrogenate the body tissues. This is achieved with an initial *high* fresh gas flow for 10 - 15 min, which will flush out most of the N_2 from the system, functional residual capacity (FRC) and the vessel rich group of tissues.
  However, a continuous washout of N_2 from the other tissues occurs until equilibrium is reached and this only occurs after many hours (? days). The result is a gradual accumulation of N_2 (to a maximum of 78 %) in the system and this may be *estimated* from the gas analyser:

$$N_2 = (101,2 - 6,2) - (P_IO_2 + P_IN_2O + P_ICO_2 + P_IAA)$$

or as a *rough* estimate

$$95 - (P_IO_2 + P_IN_2O)$$

as $P_ICO_2 = 0$ if soda-lime is not exhausted and P_IAA is usually small. (N.B. at sea level!)

The other inert gases e.g. Argon, Xenon, Helium, etc. cannot accumulate above the normal levels found in the atmosphere (unless the fresh gas supply has higher levels, e.g. from an O_2 concentrator).

To minimise the possible deleterious effects of these accumulated products, it is recommended to flush the system periodically at a higher flow e.g. every 1 - 2 hr. Remember to turn down the vaporiser setting!

vii) The reaction of soda-lime with some inhalational agents may produce toxic products.

- **Trichloroethylene**
  Seldom used nowadays, but produces toxic compounds when exposed to hot soda-lime ($\pm 60°\ C$) - dichloroacytelene (C_2Cl_2), a potent neurotoxin; and phosgene (COH_2), which may be lethal. Trichlorethylene is thus contra-indicated in circle systems.
- **Halothane**
  CO_2 absorbents degrade halothane to CF_2=CBrCl. This is nephrotoxic in rats, yet nephrotoxicity from halothane at any fresh gas flow is exceedingly rare in humans.
- **Sevoflurane**
  Compound A (CH_2F-O-C[=CF_2][CF_3]) is produced by the reaction of sevoflurane with CO_2 absorbents and an increased production is associated with high minute ventilation, low fresh gas flows, high absorbent temperature, Baralyme® > soda-lime and high anaesthetic concentration. Compound A has been shown to be nephrotoxic in rats and biochemical markers of renal injury were elevated in human volunteers after 8 hr at 2 $L\ min^{-1}$ fresh gas flow and 1,25 MAC with hyperventilation. However, renal function remained normal.

Sevoflurane also releases free F ions as a result of metabolism (± 3 %) and these may also be nephrotoxic (cf. enflurane metabolised ± 2 %).

Despite this potential for nephrotoxicity (Compound A and release of free F ions) no cases of sevoflurane attributable renal failure have been identified in over 2 million anaesthetics, although most of these were at fresh gas flows > 2 $L\ min^{-1}$, and the risk would increase with low flows. Many countries instituted a minimum fresh gas flow of 2 $L\ min^{-1}$ for sevoflurane.

It could be considered wise to withhold sevoflurane in patients with pre-existing renal disease and to limit the duration of exposure if low flows are used.

- **Desflurane**
  A series of patients with acute carbon monoxide poisoning, usually occurring on a Monday morning, alerted investigators to the considerable production of CO when desflurane came into contact with desiccated CO_2 absorbents. This occurs to a small degree in all CO_2 absorbents with desflurane > enflurane > isoflurane >> halothane and sevoflurane, and Baralyme® > soda-lime.
  It takes 24 - 48 hr to desiccate CO_2 absorbents with a flow of dry O_2, hence the preponderance of cases on a Monday, presumably after the O_2 flow had been left on over the weekend and routed through the CO_2 absorber.

  CarboxyHb levels > 30 % have been recorded and may be a cause for nausea, vomiting, headache and agitation. (Levels > 60 % are fatal.)
  A clue to the presence of elevated CarboxyHb is an unexpectedly high anaesthetic agent concentration reading on the agent monitor or its giving a wrong agent warning (caused by trifluoromethane produced with the CO).
  CO will accumulate if low flows are used and aggravate the problem.
  Fatal levels of CO have been produced experimentally and are possible.
  The incidence of CO exposure with anaesthesia was found to be 5 in 1 085 cases (0,46 %) in an American study.

  Other sources of CO include smokers with elevated carboxyHb levels.

viii) Extra monitoring is required if very low flows are to be used, but as these monitors are rapidly becoming standard for all anaesthesia, this cannot be claimed as a disadvantage.

MONITORING

The most important monitor is the **F_IO_2 monitor** especially if N_2O is used.
It is possible to provide hypoxic gas mixtures if the amount of O_2 does not meet the basal requirements or if the partial pressure becomes too low.

Regardless of the initial concentrations of gases in the circuit, the gas concentrations in the circuit will eventually stabilise at the concentration of the *net* flow of *each* fresh gas into the breathing circuit.
Net = what goes in (fresh gas flow) minus what goes out (patient uptake)

If 100 % O_2 or 50 : 50 O_2 / Air is used, this becomes less likely if the volume remains constant.

Volume of the system needs to be monitored and kept constant with the aid of a bag or preferably a graduated rising bellows (falling bellows generate negative pressures and may thus entrain air, but "new" generation falling bellows which prevent this have been developed).

Monitoring of inspired and expired concentrations of the various gases is an aid in maintaining constant anaesthesia levels and may indicate the changing needs of the patient, e.g. cardiac output. Agent monitors are not essential, but are becoming a "standard of care" and are a safeguard against patient awareness.

Standard monitoring, as for any other anaesthetic, is otherwise required.

HOW TO DO IT!

Low flow Anaesthesia
A standard technique for low flow anaesthesia was popularised by **Foldes** (1954).
After initial stabilisation at high flows (4 - 6 L min^{-1} for 15 - 20 min), the gas flows are reduced to 500 mL min^{-1} each of O_2 and N_2O with the vaporiser set at 1,5 MAC.

Minimal flow Anaesthesia
Standard technique described by **Virtue** (1974).
Most modern anaesthesia machines e.g. GE Datex-Ohmeda, Dräger, Blease, etc. are equipped to deliver minimal flow techniques.
Machine requirements include:

- A tight breathing system with a leak of less than 100 mL min^{-1} at a pressure of 20 hPa
- Flow meters graduated in 50 - 100 mL steps down to 100 - 200 mL min^{-1}
- Flow compensated vaporiser
- O_2 monitor in the breathing system (preferably at the Y-piece)

Initial gas flows are O_2 at 1,5 l min^{-1} and N_2O at 3,5 L min^{-1} with the vaporiser set at 1,5 MAC
N_2 is washed out and gas flows are reduced after 10 - 15 min to

O_2 = 300 mL min^{-1} and
N_2O = 200 mL min^{-1}

with the vaporiser increased to 2 MAC, e.g. isoflurane = 2,5 enflurane = 3,5 or halothane = 1,5

With these settings the F_IO_2 tends to increase from ± 0,32 to ± 0,4 whilst the F_IN_2O drops from ± 0,65 to ± 0,5 over the next 30 - 40 min. The difference of ± 10 % is caused by the accumulation of N_2.
Volatile concentrations tend to drop from ± 0,8 MAC to ± 0,65 MAC
After the initial 60 min a very slow drop occurs in the F_IO_2 whereas there is a slow rise in F_IN_2O, F_IAA and F_IN_2 and gradual reductions in N_2O and anaesthetic agent are required in accordance with the square root of time principle.
The initial period of high flows may be reduced for the new less soluble agents
The amount of overpressure required to attain initial levels of anaesthesia will decrease as the agents become less soluble i.e. halothane > enflurane > isoflurane > sevoflurane > desflurane. Conversely, the more soluble agents may be switched off earlier and the anaesthetic "coasted" towards the end of surgery.

Closed system or basal flow Anaesthesia
Anaesthesia machine requirements are more stringent:

- Flow meters must be graduated in 10 - 20 mL steps
- Leaks must be minimal
- Tables, calculator or computers to determine gas uptake requirements

Vaporisers may be used, but in the initial stages cannot supply the concentrations required.
In circle vaporisers (VIC) would overcome the problem but are dangerous. A more logical approach is to utilise direct injection of anaesthetic agent into the expiratory limb and this may be achieved by:

i) Manually, using a calculated unit dose and the square root of time principle
ii) Programmable exponential syringe pumps
iii) Sophisticated closed-loop electronic controllers with agent injectors

After the usual high flow washout of N_2 with 100 % O_2 and a normal IV induction, O_2 flows are reduced to Basal requirements and N_2O at maximum possible untill O_2 monitor shows a F_IO_2 of 0,4 (15 - 30 s).
N_2O flows are reduced to the rate required to maintain a constant volume in the breathing system as observed at the bellows or bag with the spill valve completely closed. Direct injection of volatile agent is commenced as described.
If a TEC vaporiser is used, it is set at the maximum (5 %) for 9 min and then reduced using the Square Root of Time (this is not possible with enflurane)

The above techniques are much simplified with the use of anaesthetic agent analysers. The end-tidal concentration will reflect MAC.

References / Recommended reading

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