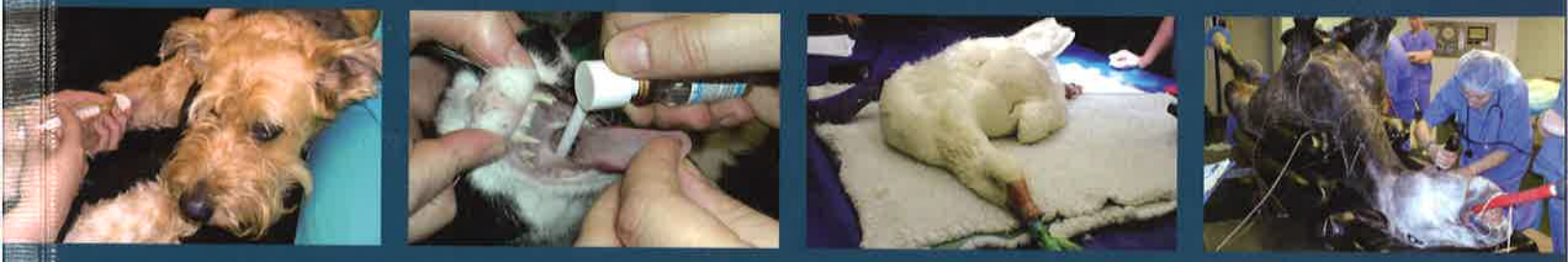
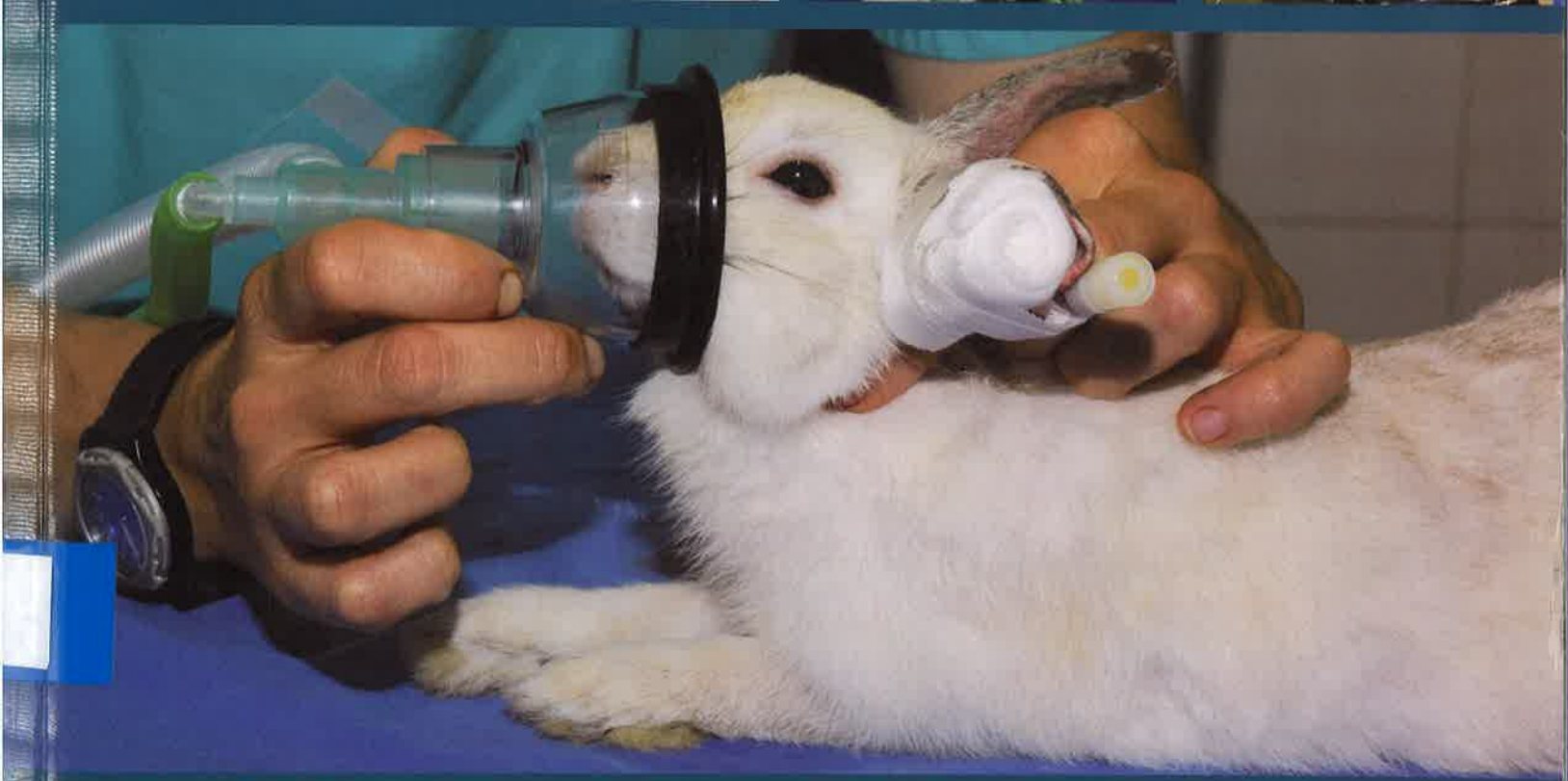
ALEX DUGDALE

VETERINARY ANAESTHESIA

PRINCIPLES TO PRACTICE





WILEY-BLACKWELL

8

Inhalation anaesthetic agents

Learning objectives

- To be able to discuss the basic pharmacology of the volatile agents.
- To be able to list the properties of an ideal inhalation agent.
- To be able to define MAC.
- To be able to discuss the factors affecting agent choice.

Introduction

Inhalation agents, commonly volatile liquids or compressed gases (strictly 'vapours'), can be administered, by inhalation, for induction and/or maintenance of anaesthesia. Although all their actions remain to be determined, it appears that most enhance inhibitory activity at $GABA_A$ receptors (in the brain) and glycine receptors (in the spinal cord), whilst also possibly inhibiting excitatory effects at cholinergic (muscarinic and nicotinic) and glutamate receptors. The volatile agents also depress activity at various types of calcium channels; and may inhibit some types of sodium and potassium channel activities.

Properties of an ideal inhalation agent

- Easily vaporised at or near room temperature.
- Non-flammable/non-explosive.
- Stable on storage (not degraded by heat or light).
- Does not react with materials of anaesthetic breathing system or vaporiser.
- Does not readily diffuse through materials of anaesthetic breathing system to pollute the operating environment.
- Compatible with soda lime.
- Non-toxic to tissues.
- Minimally metabolised; any metabolites should be non-toxic and inactive.
- Environmentally friendly; easily scavengeable.
- Non-irritant to mucous membranes; non-pungent, so that inhalation induction is not unpleasant.
- Induction of anaesthesia and recovery from anaesthesia should be excitement-free.
- Allows rapid control of anaesthetic depth (low blood solubility).
- Some analgesia would be an advantage.
- Some muscle relaxation would be an advantage.
- Few cardiorespiratory side effects.
- No renal or hepatic toxicity.
- Inexpensive.
- Not requiring expensive vaporiser.

Table 8.1 gives some physicochemical properties of inhalation agents for man. For comparison, the blood gas partition coefficient for nitrogen (N_2) is 0.0147. There are species differences, for example for the horse, the blood gas partition coefficients for halothane, isoflurane and sevoflurane are 1.66, 0.92 and 0.46, respectively.

MAC

MAC (or MAC-incision) is defined as the minimal alveolar concentration of agent at which 50% of patients fail to respond, by gross purposeful movement (i.e. a motor response), to a standard supramaximal noxious stimulus (skin incision). It is defined in terms of percentage of 1 atmosphere pressure. (Be aware of altitude.)

MAC values allow a comparison of inhalation agents by their potency, whereby potency is inversely proportional to the MAC value. Potency is directly proportional to the brain lipid solubility of the agents, which is reflected by the oil-gas partition coefficient. Table 8.2 shows MAC values for the commonly used inhalation agents in man and some of the domestic animal species.

Table 8.1 Some properties of actual inhalation agents (based on man).

Agent	B.Pt. °C	SVP mmHg at 20°C	MWt	B/G	O/G	F/B	MAC (%)	Metab.
Ether	34.6	442	74	12	65		1.92	some
Methoxyflurane	104.7	23	165	13	825		0.16	20–80%
Halothane	50.2	243	197	2.4	224	60	0.8	c. 20%
Isoflurane	48.5	238	184	1.4	98	45	1.3–1.6	0.2%
Sevoflurane	58.5	170	200	0.65	45	48	2.05+	c. 2%
Desflurane	23.5	664	168	0.45	18.7	27	5.7+	0.02%
N_2O	–89	44Atmos. Cylinder pressure	44	0.44–0.47	20	2.3	100–200	Inert
Xenon	–108.1		131	0.115	1.9	<10	60–71	Inert

The figures in this table may vary slightly from other reference sources.
B.Pt., boiling point at standard atmospheric pressure; Atmos., atmospheres; SVP, saturated vapour pressure at 20°C in mmHg (except N_2O); MWt, molecular weight; B/G, blood/gas partition coefficient; O/G, oil/gas partition coefficient; F/B, fat/blood partition coefficient; Metab., metabolism.

Table 8.2 Some MAC values.

Species	Halothane	Isoflurane	Sevoflurane	Desflurane	Nitrous oxide
Man	0.76%	1.2%	1.93%	6.99%	105%
Dog	0.87%	1.3%	2.3%	7.2%	188–297%
Cat	1.1%	1.6%	2.6%	9.8%	255%
Horse	0.9%	1.3%	2.3%	7.6%	190–205%

These values may vary slightly according to source.

As a basic rule of thumb, **if a patient has an end tidal anaesthetic agent concentration of 1.2–1.5 × MAC, it is highly unlikely to move at skin incision.**

Several different MAC values are described for man, such as MAC-BAR (where BAR means blockade of autonomic response), which refers to the minimal alveolar concentration of agent at which the increase in heart rate and/or blood pressure provoked by skin incision is prevented in 50% of subjects. MAC-BAR is usually around 1–1.7 MAC-incision.

There is also MAC-awake (usually 0.3–0.5 MAC-incision), which refers to the minimal alveolar concentration of agent at which 50% of subjects stop voluntarily responding to verbal commands (i.e. cessation of perceptive awareness) during induction of anaesthesia with that agent, or when 50% of subjects begin responding to verbal commands upon recovering from anaesthesia under that agent.

MAC is not affected by

- Duration of anaesthesia (unless patient becomes hypothermic, hypoxaemic or hypercapnic).
- Gender.
- Blood pH.
- $PaCO_2$ between 10 and 90 mmHg.
- PaO_2 between 40 and 500 mmHg.
- Moderate anaemia.
- Moderate hypotension (not below 50 mmHg mean arterial pressure).
- Hypertension.

MAC is affected by

- Species (body size, i.e. MAC increases as the relative surface area increases).
- Age. MAC is lower in the very young (neonates) and very old (geriatrics); but higher in young, growing and fit animals.
- $PaO_2 < 40$ mmHg (arterial hypoxaemia); and $PaCO_2 > 90$ mmHg (hypercapnia); both decrease MAC.
- Hypotension (mean arterial pressure <50 mmHg) decreases MAC.
- Change in body temperature (for every one degree Celsius change in body temperature, MAC changes by 2–5% of its value; it decreases with hypothermia, and increases with hyperthermia).
- Other CNS depressant drugs will reduce MAC.
- CNS stimulant drugs will increase MAC.
- Hyperthyroidism, and high levels of circulating catecholamines (excited or nervous animals; phaeochromocytoma) will increase MAC.
- Pregnancy reduces MAC.
- Hypernatraemia and hyperosmolality increase MAC.

There is **controversy** about the MAC concept because the definition of MAC is highly dependent upon spinal reflex activity and spinal sites of action of anaesthetic agents. For this reason, claims that drugs have analgesic properties because they can cause MAC reduction may not necessarily be valid.

Administration of inhalation agents

Inhalation agents may be administered for induction and/or maintenance of anaesthesia. Administration may be via:

- Face/nose mask.
- Nasopharyngeal tube (insufflation).
- Nasotracheal tube.
- Orotracheal tube (see Chapter 9 for potential problems associated with endotracheal tube use).
- Laryngeal mask airway.
- Induction chambers can be used for anaesthetic induction, but do not allow access to the patient during maintenance.

Inhalation induction

Inhalation induction may be accomplished by:

- Step-wise method, starting with just oxygen, and then slowly increasing the delivered inspired anaesthetic agent concentration, e.g. by a quarter to half a percent every three or four breaths.
- Delivering a high inspired concentration of agent from the outset (often called a 'crash induction').

Induction is said to be smoother if the first method is used; but induction is faster with the second. Most patients, especially if not premedicated, seem to traverse the 'involuntary movement/excitement stage' (Stage II) of anaesthesia as depth of anaesthesia increases towards a deeper, more surgical, plane, so be prepared for some 'struggling'. This period of struggling should be shorter when a high concentration is delivered from the outset. Inclusion of nitrous oxide may also speed the rate of induction through the second gas effect (see later).

Uptake and elimination of anaesthetic agents

Inhalation agents produce anaesthesia via their effects in the CNS. **Depth of anaesthesia depends upon the 'concentration' of the agent in the brain.** A better term than 'concentration' would be 'partial pressure' or 'tension', because these agents are gaseous, and we usually measure their 'concentration' in units of pressure.

When a patient breathes a mixture of oxygen and anaesthetic gas/vapour from a non-rebreathing system (so that each inhaled breath has the same composition), then the partial pressures of the agent in the alveoli, blood and tissues (including brain), increases over time towards those of the inspired mixture.

Rate of induction and recovery from inhalation anaesthesia is governed by the rate of change of anaesthetic agent partial pressure in the brain, which follows, with a slight delay, the change in its partial pressure in the alveoli.

We cannot measure the 'brain concentration' of these agents, but we can measure the alveolar tensions, or, at least the end tidal anaesthetic agent concentration can be measured as a guide to the alveolar anaesthetic agent concentration. See Chapter 18 on monitoring.

Let us now consider the factors which affect the rate of change of the alveolar tension of anaesthetic agents, and therefore the uptake and elimination of these agents. **Kety curves** can be constructed, which are mathematical descriptions of anaesthetic uptake under defined conditions (Figure 8.1).

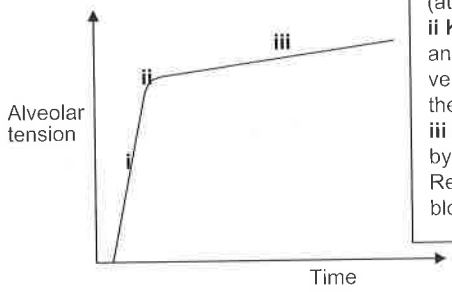
Factors affecting alveolar anaesthetic agent uptake/induction of anaesthesia

- Inspired anaesthetic agent concentration.
- Loss of agent (e.g. via diffusion through anaesthetic breathing system).
- Alveolar ventilation rate.
- Uptake by blood and tissues.

Inspired anaesthetic concentration

Depends upon the **volatility of the agent** and its **boiling point** compared to room temperature. Its **saturated vapour pressure** at room or standard temperature will give you a clue, for example ether is very volatile (SVP = 442 mmHg), methoxyflurane is much less volatile (SVP = 23 mmHg). The temperature at which the saturated vapour pressure equals atmospheric pressure is the agent's boiling point.

Increasing the **vaporiser setting** should increase anaesthetic agent delivery to the anaesthetic breathing system, and thereby to the alveoli, to hasten induction of anaesthesia. This is called the



i Initial rise: represents anaesthetic agent delivery to the lungs with alveolar ventilation. The gradient will be steeper with increased alveolar ventilation (at the same inspired concentration).
ii Knee: represents initial equilibration between anaesthetic agent delivery to the alveoli by ventilation and removal of anaesthetic agent from the alveoli by pulmonary capillary blood flow.
iii Slowly rising plateau: may also be represented by a series of knees and changing gradients. Represents equilibration between other tissues, blood and alveolar concentrations.

Figure 8.1 Kety curve.

over-pressure technique, when much more anaesthetic agent than is really required is initially delivered to the patient, but induction of anaesthesia is hastened. The vaporiser setting is turned down as soon as the patient is anaesthetised to avoid an excessive depth of anaesthesia being achieved.

The **design of the vaporiser** used may have some influence upon the achievable inspired anaesthetic agent concentration, for example:

- Temperature changes affect vaporisation, so **t**emperature **c**ompensated (e.g. **Tec**™) vaporisers will give a more consistent output.
- Incorporation of wicks to increase the surface area for evaporation may also help to increase the delivered anaesthetic agent concentration, as may increasing the operating temperature of the vaporiser. Thymol (a poorly volatile 'stabiliser' included with halothane), may affect vaporiser performance by clogging up wicks etc.
- Some vaporisers may be calibrated to deliver higher concentrations of agent than others. Most halothane and isoflurane vaporisers have a maximum calibrated output concentration of 5%, whereas some have a maximum output of 8%.

The inspired anaesthetic agent concentration cannot, however, be indefinitely increased because sufficient oxygen (usually a minimum of 33% is suggested for humans) must also be supplied to the patient.

If a circle (rebreathing) system is being used with an out-of-circuit vaporiser (**VOC**), at the beginning of an anaesthetic, then increasing the fresh gas flow into the circle will help to maintain the inspired anaesthetic agent concentration better (especially for agents which are relatively highly soluble in the blood). It is fairly standard practice to denitrogenate both the circle and the patient (via its lung functional residual capacity; FRC), such that relatively high fresh gas flows are often employed for the first 10–20 min anyway. Using the smallest possible rebreathing bag (about 2 times the patient's tidal volume), to minimise the circle's volume will also help to maintain a higher anaesthetic agent concentration delivered to the patient by reducing the **time constant of the system** (see Chapter 9).

If using a vaporiser-in-circuit (**VIC**), then increasing the fresh gas flow will tend to dilute the anaesthetic agent concentration in the circle. Higher flows through the vaporiser result in cooling and a reduction in evaporation; and higher flows do not become fully saturated during their passage through the vaporiser.

The **higher the blood solubility** of the agent, the **more pronounced** is the **effect of increasing the inspired anaesthetic agent concentration** on **hastening the speed of induction** (see below).

Loss of anaesthetic agent

This can be a loss from the anaesthetic breathing system or the patient. Fresh soda lime can ad/bsorb some of the agent from the anaesthetic breathing system and also different agents have different solubilities in the rubber or plastic hoses of the anaesthetic breathing systems, so this route could be another potential route for loss of agent from the breathing system. 'Loss' of anaesthetic agent from the patient's lungs into the blood and tissues is considered below; but loss from open body cavities or wounds, and to a small extent intact skin, can also occur to the atmosphere.

Alveolar ventilation

- Minute ventilation = breathing rate × tidal volume
- Tidal volume = alveolar volume + dead space volume
- Alveolar ventilation = breathing rate × alveolar volume
- Alveolar ventilation = breathing rate × (tidal volume − dead space volume)

The term dead space volume refers to the total, or physiological, dead space. This includes the anatomical dead space (the upper respiratory tract down to the respiratory bronchioles; i.e. where gaseous exchange does not normally occur), and the alveolar dead space (the relatively under-perfused or over-ventilated alveoli). Normally the physiological dead space is about one-third of the tidal volume; or the alveolar volume is about two-thirds of the tidal volume. So, alveolar ventilation is about two-thirds of minute ventilation.

Alveolar ventilation therefore depends upon breathing rate and depth (and also the dead space volume). Anything which increases minute ventilation and/or decreases dead space, results in increased alveolar ventilation and should facilitate an increase in the uptake of anaesthetic agent by enhancing the delivery of anaesthetic agent to the alveoli. Hyperventilation, either in an excited patient during inhalation induction, or by applying rapid or deep intermittent positive pressure ventilation (IPPV), can hasten anaesthetic induction or depth change, especially for the more highly blood-soluble agents.

Apparatus dead space should also be kept to a minimum, because this acts like an extension of the patient's own dead space. Lower patient FRC also helps to hasten anaesthetic uptake, so in pregnant or bloated animals where the chest volume is reduced, slightly quicker anaesthetic agent uptake can be expected. Such patients also have smaller oxygen reserves in their smaller FRC, so pre-oxygenation might be warranted.

The **higher the blood solubility** of the agent, the **more pronounced** is the **effect of increasing alveolar ventilation** on **hastening the speed of induction**.

Uptake by the blood and tissues

Blood uptake depends on:

- **Solubility of agent in blood** (B/G partition coefficient).
- Pulmonary blood flow/perfusion (depends on **cardiac output**).
- **Concentration gradient** between alveoli and blood.
- **Diffusing capacity** of the lung (but this rarely causes problems unless there is severe lung disease).

Tissue uptake depends on:

- **Solubility of agent in tissues**.
- Tissue blood flow/perfusion (**cardiac output**).
- **Concentration gradient** between blood and tissue (equivalent to the arterio-venous concentration gradient).

The more soluble the agent is in blood, the more is required to increase its partial pressure in the alveoli, and hence the slower the induction of anaesthesia remembering that 'anaesthetic concentration in the brain follows, with a slight delay, that in the alveoli'. Brain is in the 'vessel rich' tissue group, so has one of the first opportunities to receive anaesthetic agent delivered in the blood. Brain contains a lot of lipid, and most of these agents have high lipid solubilities.

Compared with an agent of high blood (and tissue), solubility, an agent of low blood (and tissue), solubility is associated with a more rapid equilibration, because only a small amount of anaesthetic agent need be dissolved in blood (and tissues), before equilibrium (with the delivered concentration) is reached. **Low blood solubility is usually more desirable because induction and recovery are more rapid**, and **intraoperative anaesthetic depth changes can be achieved more rapidly**. Methoxyflurane (no longer commonly available), is poorly volatile, yet very soluble in blood and fat, so that inhalation induction is very slow, as is change of anaesthetic depth, but this does make it difficult to get patients too deep very quickly. Therefore, despite its high potency (low MAC value), methoxyflurane's low volatility reduces the risks of overdose.

For rapid anaesthetic induction, theoretically we need to slow down the removal or absorption of anaesthetic agent from the alveoli, thereby promoting a rapid rise in alveolar concentration of the agent (and therefore promoting a rapid rise of brain anaesthetic agent concentration). For agents of **low blood solubility**, the rate of rise of the alveolar anaesthetic agent tension is more rapid.

The alveolar anaesthetic agent tension may also be increased by the **'second gas effect'**, sometimes called the **'concentration effect'**, because it is only noticeable when the second gas is present at high concentration. For example, if nitrous oxide (the 'second gas') and a vapour (e.g. halothane) are both delivered to the patient in a stream of oxygen then because nitrous oxide is less soluble in blood (compared to halothane), and because it is administered at a much higher inspired concentration than the volatile agent (i.e. 50–66% compared to 2–5%), its uptake by blood and brain occurs (is 'completed') more rapidly. Although nitrous oxide's solubility in blood is poor, some will dissolve; and at such high delivered concentrations, even though only relatively little becomes dissolved in blood, this small proportion of the large delivered concentration is still substantial enough to have an effect. The consequence, at this early stage of the induction, is that the initial rapid 'absorption' (removal) of nitrous oxide from the alveoli results in a relative increase in concentration of the gases left behind in the alveoli, i.e. halothane (and also oxygen). This in turn enhances the rate of rise of alveolar, and then brain, anaesthetic agent concentration, to hasten anaesthetic induction. The effect, however, is much less noticeable for volatile agents of lower blood solubility.

Anything which slows the rate of increase of alveolar anaesthetic agent tension will delay induction of anaesthesia. For example, if an **excited animal** is undergoing induction of inhalation anaesthesia, then its faster cardiac output (and pulmonary perfusion), will result in more rapid depletion of alveolar anaesthetic agent tension; and this delay in increase in alveolar anaesthetic agent tension can be thought of as reflected in a delay in increase in brain anaesthetic agent tension, and so induction of anaesthesia is also seen to be delayed. However, this is partly offset by a faster delivery of anaesthetic agent to the tissues (including brain) because of the greater cardiac output. In reality, the alveolar ventilation rate is also increased by excitement, and this also offsets the effects of increased cardiac output, so that induction may in fact be hastened.

In **shocky animals**, the lower cardiac output speeds induction of anaesthesia, because alveolar anaesthetic agent concentration rises faster when alveolar perfusion is slow.

Changes in **cardiac output** and **alveolar ventilation** have **more effect** on the speed of induction with volatile anaesthetic agents of **higher blood (and tissue) solubilities** than those of lower blood solubilities.

Alveolar-to-blood, and blood-to-tissue **concentration gradients** are greatest at the beginning of induction, and reduce with time. Different body compartments equilibrate at different rates, according to their size and perfusion (see Chapter 5 on injectable agents where the concept of **different compartmental time constants** is discussed).

Equilibration between all body compartments takes time. The fat compartment can be huge and poorly perfused and therefore can take a long time to equilibrate, perhaps longer than the actual length of anaesthesia in clinical cases. Most agents are very soluble in fat, but interestingly, N_2O and xenon are not. This equilibration time thus depends upon the fat perfusion; how fat-soluble the agent is; how obese the patient is; and whether the agent is metabolised to any extent, which will delay this slow equilibration process further.

Factors affecting elimination of inhalation agents/recovery from anaesthesia

Such 'recovery' is sometimes referred to as 'eduction'. Recovery after an intravenous infusion of anaesthetic agent is stopped depends on drug redistribution and metabolism; both of which might be affected by the duration of the drug infusion, as well as the characteristics of the drug (its solubility, especially in fat), and of the patient, for example in terms of tissues available for redistribution (e.g. absolute muscle and fat mass), and metabolic capacity (liver and kidney function). The **context-sensitive half time** helps us to be better able to predict patient 'recovery' after varying durations of infusions. The context-sensitive half time is the time taken for the plasma concentration of the drug to halve after termination of drug infusion. The 'context' refers to the duration of the infusion.

A similar concept can be applied to inhaled anaesthetics, where we talk of **context-sensitive decrement times**. Again, the context refers to the duration of the anaesthetic, so context-sensitive decrement times vary according to the duration of anaesthesia, but are also affected by the solubility of the agent (especially in fat), the adiposity of the patient and whether the agent can be metabolised or is inert and requires exhalation.

Recovery depends upon reduction of alveolar anaesthetic agent tension (by reduction of administered anaesthetic agent

concentration), and anaesthetic agent exhalation and some metabolism.

Following reduction of delivered (and therefore, alveolar) anaesthetic agent concentration, anaesthetic agent moves down the concentration gradients from the blood to the alveoli and from the tissues to the blood, and so exhalation can continue (so long as alveolar ventilation continues). Therefore, recovery is influenced by:

- Inspired anaesthetic agent concentration.
- Loss of agent from anaesthetic breathing system/patient (open wounds/body cavities).
- Alveolar ventilation.
- Tissue/blood and blood/gas solubilities (and patient adiposity).
- Tissue perfusion.
- Metabolism.

It is important to reduce the inspired anaesthetic agent concentration if you require 'reversal' of anaesthesia. Switching off the vaporiser will rapidly reduce the delivered anaesthetic agent concentration if a non-rebreathing system is used. If a rebreathing system is used, however, the delivered anaesthetic agent concentration is much slower to change, even if the vaporiser is switched off, unless the fresh gas flow is increased and the rebreathing bag is emptied ('dumped') through the pop-off valve several times (and the system is re-filled with oxygen), to increase the rate of change of anaesthetic agent concentration circulating within the system. However, the inspired anaesthetic agent concentration cannot be reduced to below zero, so there is only a limited amount you can do to reverse the concentration gradient between alveoli and blood/tissues/brain.

Alveolar ventilation is **important**, but again, more so for the **more soluble agents**.

Some anaesthetic agent will be **lost through the patient's wounds and any open body cavities**, and to a small extent, intact skin. Some agents may continue to be lost through the **anaesthetic breathing system tubing**.

The more tissue- and blood-soluble the agent, the slower its release back into the blood (and then the alveoli), and thus the slower the recovery. Tissue perfusion and cardiac output are again important. However, any **metabolism** of the agent is also important as it can accelerate the recovery.

Duration of anaesthesia potentially has a large influence, **especially for volatile agents with higher blood and tissue (especially fat), solubility**, because the longer the anaesthetic duration, the more time these agents have to (attempt to) reach equilibrium with these tissues. The larger the body 'stores' that are built up (especially in the adipose tissues of obese patients), the longer it takes for the agent to be eliminated from those stores. This was especially noticeable for methoxyflurane which is highly fat-soluble (see oil-gas or fat-blood partition coefficients). Methoxyflurane is no longer available in the UK, but is still available in some countries, most notably Australia.

When using nitrous oxide, beware of the **Fink effect**, whereby **diffusion hypoxia** may occur. In this situation, the effect is **analogous to the second gas effect, but in reverse**. At the end of an anaesthetic, when the delivered concentration of N_2O and, for example halothane, are reduced, N_2O being least soluble, most quickly leaves the blood and enters the alveoli, thereby diluting the other gases present. Dilution of oxygen in the alveoli may reduce oxygen uptake, and so result in hypoxaemia and the so-called diffusion hypoxia; whereas dilution of halothane in the alveoli steepens the blood–alveolar concentration gradient, thus enhancing its elimination.

After short anaesthetics, recovery depends mainly upon exhalation, redistribution and may be some metabolism. **After long anaesthesia, recovery depends more upon the fat solubility of the agent, and how near saturation (equilibrium), the tissues (esp. fat), have become.** Obese patients will have much more prolonged recoveries after anaesthesia (especially if lengthy), with the more fat-soluble agents, such as halothane and sevoflurane, than non-obese patients. Any **metabolism of the agent, however, helps hasten recovery**.

Elimination curves do not always exactly mirror uptake curves, because of the effects of duration of anaesthesia, fat solubility and metabolism.

Sometimes halothane recoveries do not seem very different in length to isoflurane recoveries, possibly because metabolism plays a more important role in elimination of halothane than isoflurane. Methoxyflurane recoveries were very prolonged (highly fat soluble), despite considerable metabolism; but the quality of recovery was usually excellent, as methoxyflurane also added analgesia into the post-operative recovery period. We now have to think of other methods of analgesia, as halothane and isoflurane are not analgesic to the same degree as methoxyflurane. Sevoflurane is slightly more soluble in fat than isoflurane, so after long anaesthetics, even though sevoflurane has a lower blood solubility than isoflurane, the recovery times may not be that different.

Various equations have been described to calculate uptake and elimination, or rather the rate of change of alveolar anaesthetic agent concentration. One is **Lowe's equation**, one version of which is:

$$\text{Rate of uptake of agent from alveoli} = \lambda BG \times CO \times P(a-v)$$

Where λBG is blood gas partition coefficient (measure of solubility), CO is cardiac output, and P(a–v) is the arterio-venous concentration (partial pressure) gradient.

The rate of uptake of the anaesthetic agent from the alveoli is inversely related to the rate of induction/recovery or anaesthetic depth change.

The faster the anaesthetic agent is absorbed from the alveoli, the slower the alveolar concentration of the agent rises, the slower the brain concentration rises, and therefore the slower the anaesthetic induction.

Uptake and elimination curves can be represented as in Figures 8.2 and 8.3.

Effects of the volatile agents

All agents cause dose-dependent cardiovascular depression, for example they reduce blood pressure (all agents produce

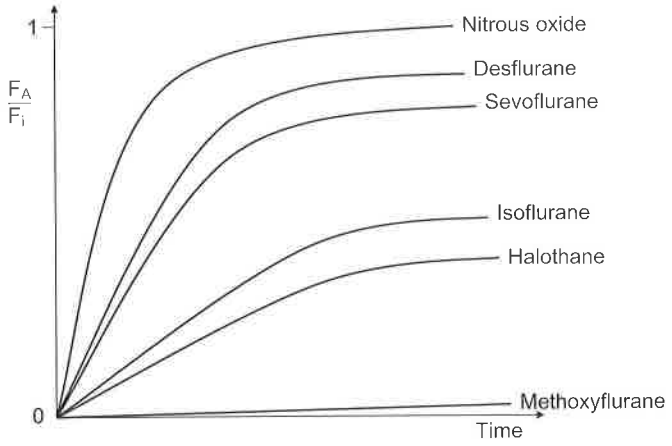


Figure 8.2 'Wash-in' of anaesthetic agent (uptake).
F_A/F_i, alveolar concentration of anaesthetic agent/inspired concentration of anaesthetic agent.

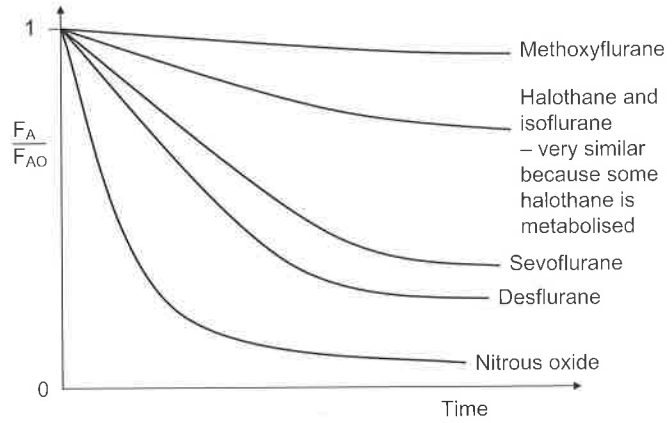


Figure 8.3 'Wash-out' of anaesthetic agent (elimination).
F_A/F_{AO}, alveolar concentration of anaesthetic agent/alveolar concentration of anaesthetic agent just before vaporiser is turned off.

similar mean arterial pressure reduction at equi-MAC doses); and they reduce cardiac output (halothane = methoxyflurane > isoflurane ≥ sevoflurane > desflurane):

- By direct myocardial depression (negative inotropy) (halothane ≫ isoflurane, sevoflurane > desflurane).
- By causing peripheral vasodilation (isoflurane, sevoflurane and desflurane ≫ halothane).
- By decreasing vascular reactivity and impairing tissue autoregulation, so that tissue perfusion becomes more dependent upon the 'driving' (systemic arterial) blood pressure. Coronary autoregulation is suggested not to be affected.
- Via CNS depression and reducing autonomic tone. These agents have sympatholytic and parasympatholytic properties, but sympathetic tone is generally reduced more than parasympathetic tone. Halothane is least parasympatholytic, desflurane is most.

Some reflex tachycardia occurs with methoxyflurane, isoflurane, sevoflurane and desflurane and this partly compensates for the reduction in blood pressure; however, this may not occur with halothane (due to relatively little vagolysis, although this is species-dependent), and thus there may be a slightly greater reduction in cardiac output seen with halothane compared with isoflurane, sevoflurane and desflurane. In addition, the peripheral vasodilation caused by isoflurane, sevoflurane and desflurane reduces the cardiac 'afterload', which may allow a relatively better maintained cardiac output with these agents compared with halothane. Greater respiratory depression (see below) tends to occur with isoflurane, sevoflurane and desflurane, leading to the development of respiratory acidosis (if ventilation is not supported), which itself results in sympathetic stimulation, which helps to offset the decrease in cardiac output and arterial blood pressure. The institution of IPPV to maintain normocapnia would then result in removal of this extra sympathetic tone and a reduction in cardiac output and blood pressure; but the physical effects of IPPV, in addition to the chemical effect (on $PaCO_2$), can also reduce venous return and cardiac output. Nevertheless, it appears that there is greater cardiovascular depression induced by halothane (even though it causes slightly less respiratory depression) than with the other agents at equi-potent doses greater than 1MAC.

Isoflurane and sevoflurane (and the other halo-ethers), do not sensitise the myocardium to the arrhythmogenic effects of catecholamines; whereas halothane does (as do the other halohydrocarbons). Paroxysmal atrio-ventricular (A-V) dissociation may occur in cats.

All agents cause some dose-dependent respiratory depression (isoflurane > methoxyflurane > halothane and sevoflurane). In some patients, however, sevoflurane appears to cause similar respiratory depression to isoflurane. Isoflurane and methoxyflurane possibly have a more pungent smell and are more irritant to the respiratory mucosa. Desflurane is also very pungent (see below). Overall, it is said that minute ventilation decreases due to a reduction in tidal volume, with a slight, non-compensatory, increase in rate; at higher 'doses', breathing rate then also tends to decrease (but the exact effects are species- and drug-dependent). The volatile agents:

- Depress the ventilatory response to CO_2.
- Depress hypoxic pulmonary vasoconstriction.
- Almost abolish the ventilatory response to hypoxia.
- Cause bronchodilation (which increases dead space); halothane > all others.

Hepatic and renal blood flow may be reduced because cardiac output and mean arterial blood pressure are reduced, and /or because splanchnic vasoconstriction occurs. Halothane hepatitis may occur in man (see below). Most volatile agents cause some inhibition of hepatic cytochrome P450 enzyme systems. Halothane reduces blood flow in the hepatic portal vein and the hepatic artery; whereas isoflurane reduces flow in the hepatic portal vein but may slightly increase flow through the hepatic artery so that little overall change in hepatic perfusion occurs but an improvement in hepatic oxygenation may result.

All volatile inhalation agents appear to inhibit insulin secretion.

Cerebral blood flow is increased (due to vasodilation) (halothane > all others), but cerebral metabolic rate is reduced (which would normally result in some vasoconstriction due to autoregulation of cerebral blood flow, but the volatile agents depress this to some extent). Intracranial pressure therefore tends to increase (dose-related), because of the overriding vasodilation. This can be offset by hyperventilation, as hypocapnia promotes cerebral vasoconstriction, at least in the short term, but cerebral autoregulation is also depressed by the volatile agents. The volatile agents may afford some cerebroprotection against ischaemia, at least partly via activating adenosine receptors and thereby modulating K_{ATP} channel activity. Sevoflurane produces less cerebral vasodilation than the other agents at equi-MAC doses, and interferes less with cerebral autoregulation than the other agents. It also produces greater protection against cerebral ischaemia than all the other agents, both acutely and more chronically after any ischaemic insult. The more chronic protective effect appears to be due to a reduction in cell apoptosis, but the mechanism of this is unclear although it may include a reduction in intracellular calcium accumulation.

All volatile agents may trigger malignant hyperthermia (in pigs, dogs, horses, cats, man).

The volatile agents produce poor analgesia except for methoxyflurane (and the most pungent ones, isoflurane and desflurane, may even cause hyperalgesia). Although methoxyflurane produces similar cardiorespiratory depression to halothane, it is a good analgesic and because of this, patients can often be adequately anaesthetised under lighter planes of anaesthesia, so relatively less methoxyflurane is required, with consequently relatively fewer cardiorespiratory side effects.

Some muscle relaxation occurs, especially with methoxyflurane; but all the volatile agents potentiate the neuromuscular block produced by non-depolarising neuromuscular blocking agents (possibly due to calcium channel blocking effects).

All the volatile agents reduce lower oesophageal sphincter tone and potentially increase the risk of gastro-oesophageal reflux, but there may be species differences due to differences in the anatomy and physiology of the lower oesophageal sphincter (i.e. smooth muscle/skeletal muscle components and muscle fibre configuration at the gastro-oesophageal junction).

All agents cause a degree of uterine relaxation, and vasodilation, but halothane may slow uterine involution more.

Isoflurane is less soluble in blood than halothane, therefore anaesthetic induction, recovery and anaesthetic depth change should be more rapid. Recovery is not always noticeably quicker after isoflurane, however, because halothane is more metabolised, which hastens an otherwise slower recovery. Methoxyflurane has a low saturated vapour pressure, and a high blood solubility, so despite being very potent (low MAC), it takes a long time to achieve induction, and recoveries are also slow, but with good analgesia and usually of good quality. Sevoflurane is less soluble than isoflurane, so faster induction, recovery and anaesthetic depth change can be expected. Recovery, however, is not always that much quicker, especially after long anaesthetics in obese patients, as sevoflurane is more fat soluble than isoflurane, so cumulates in the fat; and, despite being slightly more metabolised than isoflurane, build up of sevoflurane in the adipose tissues can still slow the recovery so that there is not often much difference between isoflurane and sevoflurane.

All the volatile agents are calcium channel (L, T and possibly N type) blockers, and their muscle relaxation effects (on cardiac, striated and vascular and other smooth muscle), may stem from reduced calcium entry into muscle cells and initial depletion of intracellular calcium stores, followed by reduced release from sarcoplasmic reticulum. The affinity of troponin C for calcium may also be affected.

In addition to the $GABA_A$mimetic effects of the volatile agents, they are likely to have other actions, and, for example, isoflurane has been shown to have NMDA antagonist actions (so potentially provides some analgesia).

Halothane requires inclusion of 0.01% poorly volatile **thymol** as a stabiliser/preservative. Methoxyflurane has **butylated hydroxytoluene** added as an antioxidant. Sevoflurane may degrade to acidic products in the presence of Lewis acids (usually metal oxides or halides, but thought to be primarily aluminium oxide impurities in glass), to form for example hydrofluoric acid, which is a toxic volatile acid with a pungent smell even at sub-toxic doses. This can further react with glass (silicon dioxide) to form silicon fluorides (e.g. SiF_4 which is volatile, pungent and highly toxic). Sevoflurane is now supplied in special plastic bottles or lacquer-coated aluminium bottles and **water** is added as its 'preservative' (a Lewis base (or Lewis acid inhibitor)) to prevent this degradation.

Agents undergo hepatic metabolism: methoxyflurane > halothane >> sevoflurane > isoflurane > desflurane. Metabolic products from methoxyflurane breakdown include free fluoride and oxalic acid, both of which can be nephrotoxic (so beware patients with pre-existing renal disease). Halothane can be metabolised to trifluoroacetic acid (see later under potential toxicities).

Desflurane has some special physical properties. Its saturated vapour pressure (SVP) is high at room temperature, which alongside its low boiling point (23.5°C), means that very high concentrations can be delivered to the patient. It requires a special temperature-controlled vaporiser (see Chapter 10 on vaporisers). Its low blood solubility means that induction, recovery and anaesthetic depth change can be very rapid. Its low oil/gas solubility means that desflurane has a low potency, and therefore a high MAC. Desflurane is also very pungent, so is not suitable for inhalation inductions, at least in man, where pulmonary (and other) 'pungent' receptors are stimulated by rapid increases in inspired desflurane concentrations and can result in 'sympathetic storms'. Desflurane may prove to be more suitable in veterinary species, but it is not yet licensed.

Nitrous oxide

Nitrous oxide is produced by thermal decomposition of ammonium nitrate at 240°C. It is supplied in pale blue painted cylinders, as a **saturated vapour above liquid**.

A substance present in the gaseous phase is referred to as a **gas** when at a temperature above its critical temperature; and a **vapour** when at a temperature below its critical temperature.

The **critical temperature** is the temperature above which a 'gas' cannot be liquefied, no matter how much pressure is applied.

Cylinder pressure is 4400 kPa. The **critical temperature for nitrous oxide is 36.5°C.** However, at room temperature (which is below this critical temperature), N_2O can be liquefied by compression, so that cylinders are filled with saturated vapour above a liquid. At constant temperature, the cylinder saturated vapour pressure (and therefore the **cylinder pressure gauge reading**), **does not decrease until** all the **liquid has evaporated**. Therefore estimation of cylinder content is made by weighing the cylinder and comparing to empty weight. The empty weight (tare weight) of the cylinder should be stamped onto its neck. The density of N_2O is also stamped on the cylinder neck (0.0018726 kg/l). Density equals mass/volume; so volume remaining equals mass/density. (It is often easier to multiply the weight of the cylinder contents by 534; (534 = 1/density).) Alternatively, because 1 mole of gas occupies 22.4 litres at standard temperature and pressure (Avogadro's law), and as the molecular weight of nitrous oxide is 44; the cylinder contents (in grammes) divided by the molecular weight, multiplied by 22.4, also gives an estimate of the number of litres remaining.

The **filling ratio** for N_2O cylinders in temperate climates like the UK is 0.75; whereas it is 0.67 in the tropics. The filling ratio is the ratio of the maximum weight of N_2O vapour and liquid that the cylinder should be filled with, compared to the weight of water the cylinder could hold, at around 16°C. It is less in hotter climates because the relative under-filling reduces the potential for pressure build up (and potential cylinder rupture) with modest increases in temperature.

If nitrous oxide is withdrawn rapidly from the cylinder, then adiabatic (rather than isothermal) cooling occurs as liquid agent evaporates (i.e. there is little time for heat energy to be transferred from the environment via the cylinder wall to the liquid agent within the cylinder). This can result in frosting of the cylinder (up to the level of remaining liquid within) and perhaps on the cylinder outlet too.

The **MAC of N_2O in man is 105%**, however, when administered at subanaesthetic doses, it affords useful analgesia. In man, inspired concentrations above 20% provide some analgesia, but animals generally need more than this. In animals its MAC value is so high (**188% in dogs**, and **255% in cats**), that in order to deliver it at sufficient dose to even contemplate any sort of anaesthesia, and without causing hypoxia, it would have to be given under hyperbaric conditions. However, it is often administered to provide some analgesia when delivered at concentrations of 50–66%.

Mechanisms of analgesic effects

- N_2O activates the endogenous opioid system (which in turn activates descending monoaminergic, cholinergic and purinergic pathways).
- N_2O has NMDA antagonist activities.

Systemic effects

Nitrous oxide causes minimal overall cardiorespiratory depression, and may even cause some mild cardiovascular stimulation. Although it is a direct negative inotrope, it also stimulates the sympathetic nervous system, reminiscent of ketamine The small rise in peripheral vascular resistance often documented has also been shown to occur with increased inspired oxygen fractions (possibly reflecting increased tissue oxygen delivery, and thence autoregulatory vasoconstriction). Some references suggest pulmonary vascular resistance increases, whereas others suggest it decreases. High inspired oxygen concentrations tend to lower pulmonary vascular resistance (through offsetting hypoxic pulmonary vasoconstriction); but if apnoea occurs (due to the relative oxygen oversufficiency), and hypercapnia follows, then hypercapnia can itself promote pulmonary vasoconstriction. Despite some texts suggesting caution with pre-existing pulmonary hypertension, if attention is paid to blood oxygenation, CO_2 tension, and FRC (lung volume can affect the pulmonary vascular resistance too), then the effects are minimal.

Nitrous oxide administration reduces the requirement for other anaesthetic agents, and therefore the side effects associated with larger doses of those agents too.

In man, its use may be associated with an increase in postoperative nausea and vomiting.

The blood/gas partition coefficient (solubility) of N_2 is 0.0147; thus it is much less soluble than N_2O (blood/gas partition coefficient of 0.47).N_2O partitions into 'insoluble gas'-filled spaces, and increases their volume or pressure, depending upon whether that compartment is distensible or not. That is, N_2O can enter such spaces faster than the already present, and even more insoluble gases, can leave. Such insoluble gases include nitrogen (so beware air-filled spaces), hydrogen and methane (so beware rumens and large intestines in herbivorous creatures with fermentation occurring at various portions of their GI tracts). This may cause problems, for example with pneumothorax, gastric dilation/volvulus and equine colics if the distended viscus is not first decompressed; and if venous air emboli are likely it can enhance their size. Nitrous oxide can also partition into air-filled endotracheal tube cuffs, so their volume and pressure can increase if not initially inflated with a mixture of gases including nitrous oxide at the concentration to be administered. Some people prefer to inflate the cuff with sterile water or saline.

The use of N_2O is equivocal in healthy horses, rabbits and ruminants, as although one study documented an increase in the volume of the large intestine in healthy horses during anaesthesia which included N_2O, no untoward adverse effects (e.g. postoperative colic) were documented. This author would still suggest caution however.

Nitrous oxide can be used to encourage uptake of other inhalation agents at the beginning of an anaesthetic (i.e. by the **second gas effect**), or during the changeover from intravenous induction to inhalation maintenance; but there is the potential for **diffusion hypoxia** at the end of the anaesthetic. Although the duration of this effect is probably only 2–5 min, most references advocate turning off the N_2O, and turning up the O_2 flow about 10 min before turning off the volatile inhalation agent to try to prevent this.

The use of N_2O is often cautioned in anaemic patients because its use limits the inspired oxygen percentage that can be delivered.

9

Anaesthetic breathing systems

Learning objectives

- Be familiar with the commonly used non-rebreathing and rebreathing systems.
- To determine the 'fresh gas flow' required to prevent rebreathing of carbon dioxide-rich exhaled gases for the commonly used non-rebreathing systems during spontaneous ventilation.
- To discuss the factors affecting choice of anaesthetic breathing system.
- To list the ways in which workplace pollution with anaesthetic gases can be reduced.
- Be familiar with the common problems associated with endotracheal tube use.

Introduction

Anaesthetic breathing systems deliver oxygen and anaesthetic gases and vapours to the patient, and allow elimination of carbon dioxide by means of one way valves, 'washout', or chemical absorption. Anaesthetic breathing systems are broadly divided into:

- **Non-rebreathing systems.**
- **Rebreathing systems.**

Rebreathing

The **clinical definition of rebreathing (Nunn)** is that: 'Rebreathing occurs when the inspired gas/es reaching the alveoli contain more carbon dioxide than can be accounted for by mere re-inhalation from/of the patient's dead space gas (which should contain negligible carbon dioxide)'.

The concept of rebreathing has been subdefined as follows:

- **Total** rebreathing: the simple re-inhalation of exhaled air, which results in re-inhalation of CO_2-laden gas.
- **Partial** rebreathing: describes the possibility for some re-inhalation of exhaled breath from which the CO_2 should have been removed (either absorbed by soda lime, or flushed out of the anaesthetic breathing system by the incoming fresh gas flow).
- **Complete** rebreathing: where the whole of the exhaled breath is available for re-inhalation, once the CO_2 has been absorbed by soda lime.

Types of breathing systems

With the above in mind, non-rebreathing systems are those systems which use no chemical absorbent for CO_2 removal, but instead depend upon a high fresh gas flow (entering the system from the anaesthetic machine), to flush out all the exhaled CO_2 from the system. Such systems are '**flow**-controlled'. There are also '**valve**-controlled' systems, in which the exhaled gases are discharged to the atmosphere via a one way non-rebreathing valve, which is positioned close to the endotracheal tube connector/the patient's incisor arcade. Some resuscitation breathing systems use these one way valves.

Anaesthetic breathing systems have several classification systems applied to them. For example, the Mapleson system for non-rebreathing systems (A to F, according to their efficiency with respect to the fresh gas flow necessary to prevent rebreathing of CO_2) and the Miller system, which describes the systems in terms of the position of the bag: whether on the efferent or afferent limb (i.e. 'efferent reservoir system' would describe the Mapleson D system; 'afferent reservoir system' would describe the Mapleson A system), or whether it could serve to store both fresh gases and expired gases ('junctional reservoir system' as used in some resuscitation systems). However, division into rebreathing and non-rebreathing is the simplest classification and serves our purposes well. The systems are then further subdivided into different 'models', but the ones we commonly use are listed below.

Common non-rebreathing systems:

- T-piece (Mapleson E (without bag); Mapleson F (with bag)).
- Bain (Mapleson D).

Table 9.1 Types of breathing systems in the UK.

In UK	Reservoir bag	Rebreathing	Examples
Open	No	No	'Open drop' e.g. chloroform mask
Semi-open	No	No	Ayre's T-piece at correct fresh gas flow
		Partial	Ayre's T-piece at too low fresh gas flow (some CO_2 re-breathed)
Semi-closed without CO_2 absorption	Yes	No	Jackson Rees T-piece, Bain at normal fresh gas flows
		Partial	J/R T-piece, Bain if too low fresh gas flow (some CO_2 re-breathed)
		Partial	Magill and Lack at correct, normal fresh gas flows
Semi-closed with CO_2 absorption	Yes	Partial	Circle, To and Fro at high fresh gas flows
Closed	Yes	Complete	Circle, To and Fro at low fresh gas flows

Table 9.2 Types of breathing systems in the USA.

In USA	Reservoir bag	Rebreathing	Examples
Open	No	No	Ayre's T-piece (at correct, normal fresh gas flow)
Semi-open	Yes	No	Jackson Rees T-piece and Bain, (at normal fresh gas flow)
		No	Magill and Lack (at higher than normal fresh gas flows)
Semi-closed	Yes	Partial	Magill and Lack at normal fresh gas flows
		Partial	Jackson Rees T-piece and Bain if inadequate fresh gas flow (some CO_2 re-breathed)
Closed	Yes	Complete	Circle, To and Fro (with CO_2 absorbers used)

- Magill (Mapleson A).
- Lack (Mapleson A).

Common rebreathing systems:

- To and Fro.
- Circle.

Terminology

Other terms applied to anaesthetic breathing systems include **open**, **semi-open**, **semi-closed**, **closed** and also **low-flow**, **medium-flow** and **high-flow**.

In the UK, the term 'open' is used to describe the situation where air can be entrained into the respiratory tract during inhalation, or even where the O_2 supply is from the air (e.g. chloroform mask). 'Semi-open' implies that some rebreathing is possible, and again, ambient air can be entrained. 'Closed' and 'semi-closed' are applied to systems where no entrainment of ambient air is possible (Table 9.1). In the USA, there are slight differences of opinion as to the meanings of the terms 'open', 'semi-open', and 'semi-closed' (Table 9.2) Although it is common to refer to 'gas flow rates', such an expression is an unnecessary repetition of words with the same meaning (in this case 'flow' and 'rate').

Low flow is the situation when **O_2 flow rate equals the metabolic oxygen demand** (i.e. around 4–10 ml/kg/min). It is used for rebreathing systems in closed mode (e.g. circles).

Medium flow is the situation when **the fresh gas flow (FGF) supplies more than the metabolic O_2 demand, but FGF is less than minute ventilation**. Used for rebreathing systems (circles, To and Fro), in semi-closed (rather than closed) mode. Can be used for non-rebreathing systems in semi-closed mode, but care must be taken to avoid excessive rebreathing.

High flow is the situation when **FGF** exceeds **minute ventilation**. Used for non-rebreathing systems in semi-open/semi-closed mode.

There is also some overlap between the use of terms, such that 'low flow' and 'closed' are often used interchangeably; 'medium flow' can be used to mean 'semi-closed' (in the USA and the UK); and 'high flow' can be used to mean 'semi-open' (in the USA) or 'semi-closed' (in the UK).

The correct method for determining if carbon dioxide rebreathing is as follows (see also Chapter 18 on monitoring). Remember that increased CO_2 will normally tend to stimulate ventilation. Rebreathing occurs when:

- Inspired CO_2 increases by 1.5 mmHg; and/or
- End tidal carbon dioxide ($ETCO_2$) tension increases by 5 mmHg (or more) without any decrease in minute ventilation that could otherwise have caused this; and/or
- Minute ventilation increases by 10% (or more) without any resultant decrease in $ETCO_2$ tension; and/or
- $ETCO_2$ tension increases by 2.3 mmHg (or more) **and** minute ventilation increases by 5% (or more).

Fresh Gas Flow (FGF)

FGF refers to those gases that emerge from the common gas outlet (CGO) of the anaesthetic machine. They usually consist of oxygen ± air ± nitrous oxide and may also pass through a vaporiser to 'pick up' volatile anaesthetic agent.

Oxygen is historically administered at 33% of the inspired mixture as a minimum. In humans under anaesthesia, due to pulmonary atelectasis and ventilation perfusion mismatching, a shunt of up to 10–15% of cardiac output may develop and in order to overcome the venous admixture (and therefore arterial desaturation) that this causes, administration of c. 30% inspired oxygen is generally sufficient. This figure of c. 30% inspired oxygen has therefore been borrowed from humans. Note, in horses where shunts of >20–30% of cardiac output may develop, even 100% inspired oxygen may be insufficient to overcome the ensuing desaturation.

In non-rebreathing systems, the nitrous oxide:oxygen ratio can be 2:1. In rebreathing systems, where there is more danger of supplying insufficient oxygen to the patient, nitrous oxide is either omitted (this is the safest thing to do if you have minimal monitoring), or the nitrous oxide:oxygen ratio can be 1:1.

Minute ventilation

Minute ventilation is usually estimated at around 200 ml/kg/min. Although often an over-estimate, using this figure should minimise the risk of rebreathing when **calculating the fresh gas flows required with non-rebreathing systems**.

Minute ventilation, or minute respiratory volume, is the volume of air moved into (or out of) the lungs in 1 min. This volume can be calculated as the product of tidal volume and breathing rate:

Minute ventilation = Tidal volume × Breathing rate

The tidal volume is usually approximated to 10–20 ml/kg. The breathing rate will depend upon species and the presence of disease, but can be approximated to 10–20 breaths/min.

Minute ventilation = 10–20 ml/kg × 10–20 breaths/min

MV = 100–400 ml/kg/min.

Most texts, however, quote **200 ml/kg/min** as the best mid-range approximation, but minute ventilation will be higher in panting animals.

The first part (about one-third) of exhaled breath consists of dead space gases (which are now warm and moist, but have not undergone any gaseous exchange); and the last part (about two-thirds) is from the alveoli and therefore contains carbon dioxide (Figure 9.1).

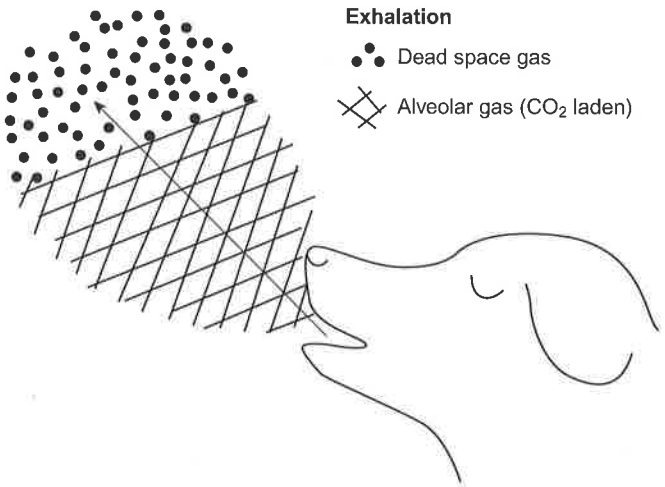


Figure 9.1 Exhaled gases.

Factors to consider when choosing a breathing system

- Patient size and respiratory capability; consider the resistance offered by the system.
- Mode of ventilation; spontaneous or IPPV.
- Requirement for economy of use of oxygen and anaesthetic gases and vapours.
- Particularly if you want to use a circle, do you want to use vaporiser out of circuit (VOC) or vaporiser in circuit (VIC)?
- If you want to use low flow in a rebreathing system, are your flowmeters and vaporisers sufficiently accurate at these low flows?
- It is 'usual' to denitrogenate rebreathing systems at the start of the anaesthetic.
- Which inhalation agent/s do you want to use? N_2O, halothane, isoflurane, sevoflurane, desflurane (probably not yet xenon)?
- Be careful with the use of N_2O in rebreathing systems; ideally you should be able to measure the inspired oxygen concentration.
- Expected length of procedure.
- Requirement for heat and moisture preservation (may partly depend upon length of procedure and size of patient).
- Necessity for sterilisation of equipment after procedure (you may wish to use a disposable breathing system).
- 'Circuit drag' (location of surgery e.g. head/mouth surgery), because anaesthetic breathing systems may affect surgical access too.
- Ease of scavenging (e.g. where is pop-off valve located?).

Non-rebreathing systems

Magill and Lack (Mapleson A)

These function similarly; the Lack in its coaxial or parallel forms is basically like a coaxial or parallel Magill.

Magill

The Magill system is shown in Figure 9.2. The corrugated tube volume should be greater than the patient's tidal volume to ensure no rebreathing. The length of the tube in a standard Magill system is around 1.1 m. The valve increases the system's resistance, therefore it is not generally used for animals <10 kg.

The characteristics of the Magill system are:

- **Modest apparatus dead space.**
- **Simple design, easy to use.**
- Easy to clean and sterilise.

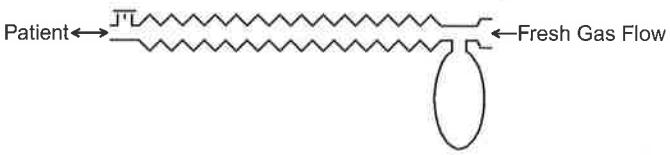


Figure 9.2 A Magill system.

- **Modest 'circuit drag'** (heavy valve near animal's mouth).
- **Can be easily scavenged from, but scavenging tubing increases 'circuit drag'.**
- **Cumbersome for head/dental surgery.**
- **Not ideal for prolonged IPPV because rebreathing is encouraged;** unless the FGF is increased to 2 times minute ventilation (i.e. doubled), adequate end-expiratory pauses are allowed, and nifty operation of the pop-off valve is carried out.
- **Generally used for animals >10 kg** and **up to around 80 kg.**
- **FGF need only be 1 (–2) times minute ventilation during spontaneous breathing in order to prevent rebreathing of CO_2.** Animals which pant or have high breathing rates have a higher minute ventilation and may also require a relatively higher FGF to prevent rebreathing because of the shortened end-expiratory pause.
- **Quite an efficient system, conserving some of the dead space gases (warm and moist) for re-use.**

Lack

Figure 9.3 shows the coaxial Lack system and Figure 9.4 the parallel Lack system.

The characteristics of the Lack system are:

- **Very similar to the Magill,** so **FGF should be 1 (–2) times minute ventilation.** This system is **possibly slightly more efficient than the Magill for spontaneous breathing,** so **FGF need only be about 0.8 times minute ventilation, but** FGF requirements do seem to be inversely dependent upon the size of the animal, so that relatively larger animals cope better with relatively smaller FGF. Also animals which pant or have high breathing rates may require higher FGF to prevent rebreathing.
- **Minimal apparatus dead space (especially the coaxial form).**
- **Resistance seems to be less (especially the parallel from), than that of the Magill,** perhaps because two-way gas flow down one tube does not occur to any great extent.
- **Slightly less 'circuit drag' (valve away from animal's head), although there is a Y piece in the parallel version, and a more bulky patient end in the coaxial form too** (inner tube is for exhalation, so must be relatively large diameter to reduce resistance; therefore outer tube is even bigger).
- **Beware prolonged IPPV; must increase FGF to about 2 times minute ventilation, and allow long end-expiratory pauses to prevent rebreathing. (It is best to monitor $ETCO_2$ if IPPV is necessary for more than the occasional breath).**
- **To test the intactness of the inner tube in the coaxial Lack:** insert, as snugly as possible, the tip of an endotracheal tube into the patient end of the inner (expiratory) tube; close the pop-off valve (which is located at the 'far' end of this expiratory limb), and then attempt to blow down the endotracheal tube. If the inner tube is intact, there should be resistance to your exhalation, and the bag (on the inspiratory limb), should not move. If there is any bag movement, then there is probably a leak in the inner tube.

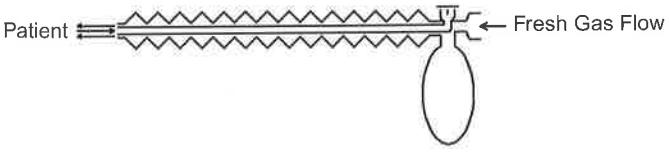


Figure 9.3 The coaxial Lack system.

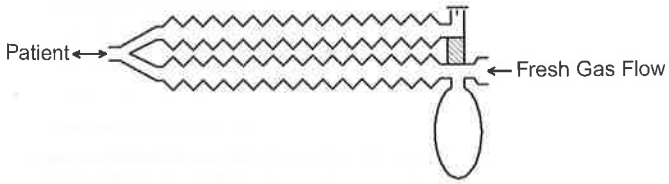


Figure 9.4 The parallel form of the Lack system.

Mini Lack

Burton's now produce a mini parallel Lack, which can be used in patients down to about 2–3 kg. This system is supplied with an extremely low resistance valve and smooth bore tubing (to reduce resistance to breathing), and the tubing is also narrower, with a special Y piece with a small septum/shelf in it, to reduce apparatus dead space. The narrower tubing also reduces some of the inevitable mixing of gases, thus reducing the potential for rebreathing of CO_2-laden gases; and it reduces the consequent turbulence, inertia and therefore resistance of the system.

Movement of gases within the Magill system during spontaneous breathing

Figure 9.5 shows how rebreathing of carbon dioxide is avoided during spontaneous breathing. Figure 9.5a represents the situation during early inspiration when some dead space gases from the previous exhalation are inhaled. Figure 9.5b depicts the situation during late inspiration. Figure 9.5c shows the situation during early exhalation. Towards the end of exhalation and during the end-expiratory pause, most of the CO_2-laden exhaled gas is pushed out through the valve, i.e. the 'pop-off' valve is 'popped open' when the pressure in the system builds up again as FGF continues to fill the bag and then the tubing (**Figures 9.5d and 9.5e**).

Movement of gases within the Magill system during IPPV

During IPPV there is a risk of causing the patient to rebreathe carbon dioxide. Imagine we are at the start of ventilating the patient's lungs, and the system is full of fresh gases from the anaesthetic machine. In order to get a reasonable chest inflation, we have to close the pop-off valve. Now we can squeeze the bag (but we all tend to be a bit over-zealous) so a lot of gas enters the patient, and we can appreciably empty the reservoir bag (Figure 9.6a). We now let the patient's chest deflate, i.e. let the patient exhale (we need to open the valve again too). The bag was so empty that both the exhaled gases from the patient and the fresh gases from the anaesthetic machine can enter the reservoir bag (Figure 9.6b).

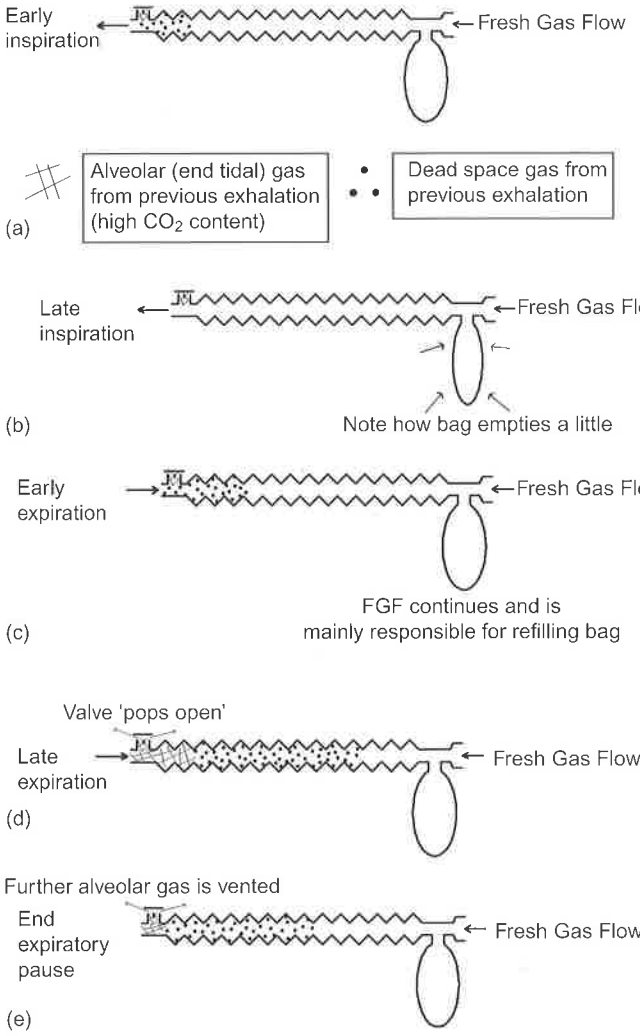


Figure 9.5 Movement of gases within the Magill system during spontaneous breathing.

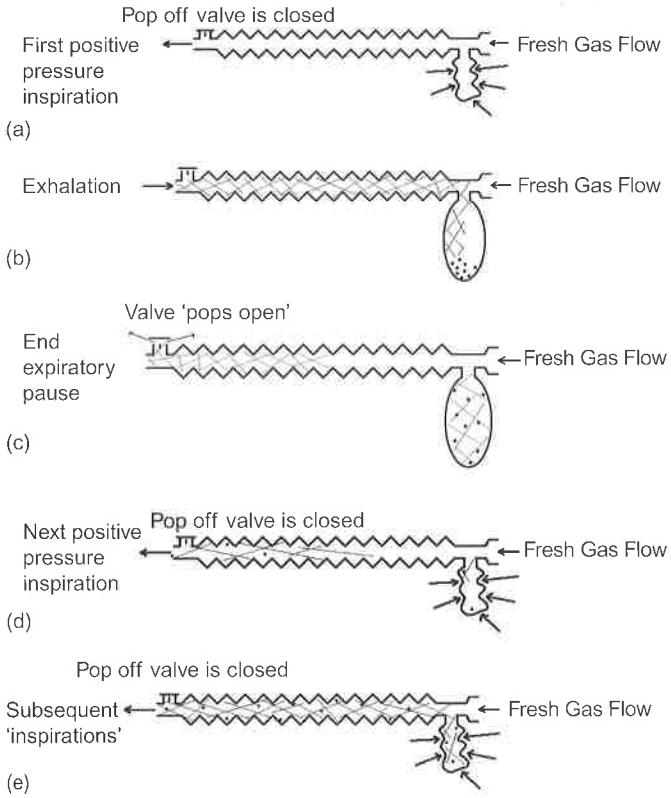


Figure 9.6 Movement of gases within the Magill system during IPPV.

After the first breath by IPPV, the FGF will purge much of the CO_2-laden gas from the tubing and out through the valve (if we remembered to open it again, and if we leave a long-ish end-expiratory pause). However, the tubing tends not to be fully purged of CO_2-laden gas between breaths, because it takes more FGF to refill the 'more empty' bag, so it takes longer to reach the breathing system pressure at which the valve 'pops open'. Some FGF, however, does enter the bag to dilute the CO_2 within it somewhat. The situation during the end-expiratory pause is shown in Figure 9.6c. Now imagine it is time for another inspiration. We need to close the pop-off valve again, and squeeze the bag again, but this time the tube and bag contain some CO_2 (Figure 9.6d). Imagine that we now give several more breaths by IPPV. Breath by breath (of IPPV), as the patient's alveolar gas (CO_2-laden end tidal gas) continues to reach the reservoir bag, the concentration of CO_2 in the reservoir bag increases. Also the tube is incompletely purged of CO_2-laden gas, especially if we allow only a relatively short end-expiratory pause. We can now see how the patient is forced to rebreathe much of its previously exhaled, and CO_2-laden, gases. Therefore the Magill, and Lack (because it works in a similar fashion), are not very good for prolonged IPPV (Figure 9.6e).

However, if we:

- Increase the FGF (to c. 2 times minute ventilation (compared with 1 times minute ventilation for spontaneous breathing); and
- Remember to allow a **long** end-expiratory pause (i.e. do not ventilate too rapidly; we should not need to ventilate too rapidly anyway, because we more than compensate for a slow rate by tending to give a larger tidal volume). This allows a long time for FGF to purge the tubing of CO_2 and further dilute what is in the bag.

Then there is less potential for causing rebreathing. So, it is possible to use the Magill and Lack for more prolonged IPPV, but you must heed these rules. It also helps if you monitor with capnography, as this will tell you whether the amount of inspired CO_2 is increasing from the normal negligible amount.

The T-piece

The original design (Ayre's T-piece), consisted of a T-shaped connector attached to a length of tube, and also to a fresh gas supply hose (which connects to the common gas outlet on the anaesthetic machine) (Figure 9.7).

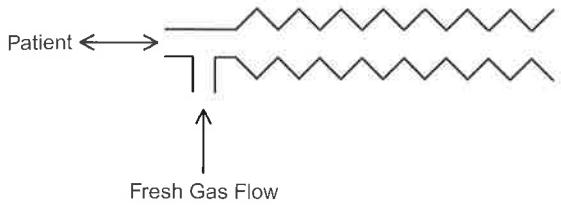


Figure 9.7 Ayre's T-piece (Mapleson E).

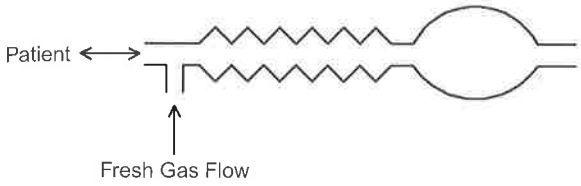


Figure 9.8 Jackson Rees modification of Ayre's T-piece (Mapleson F).

The volume of the corrugated limb should be greater than the patient's tidal volume, or else outside air will be entrained during inspiration, and will dilute the O_2/N_2O and anaesthetic vapour being delivered to the patient. Normally the fresh gas flow (FGF), is at right angles to the direction of gas flowing into and out of the patient, but other configurations are possible (see later).

Using the Ayre's T-piece, the patient's lungs can only be ventilated (i.e. IPPV can be applied), by intermittent occlusion of the open end of the expiratory limb until the chest inflates, and then releasing the occlusion to allow exhalation, none of which allows for a very good pattern of ventilation (i.e. inflation tends to be too slow). The Jackson Rees modification of the Ayre's T-piece, in which an open-ended bag is placed at the end of the expiratory limb, allows much easier application of IPPV, because the open end of the bag can be occluded, and once the bag has filled sufficiently, it can be squeezed gently to create a much better (more rapid, more physiological) lung inflation (Figure 9.8). Squeezing the bag allows some assessment of the compliance of the lungs too. Bag movements can also be observed during spontaneous ventilation to allow some assessment of the patient's spontaneous breathing.

Characteristics of T-pieces

- **Minimal apparatus dead space:** apparatus (or mechanical) dead space is defined as an extension of the patient's own anatomical dead space. Anatomical dead space is the volume of the respiratory tree where no gas exchange occurs, i.e. the upper respiratory tract from the nares down to the respiratory bronchioles; but gases are still warmed and humidified. **Apparatus dead space** is recognised as the volume within the anaesthetic breathing system, between the incisor arcade and that part of the anaesthetic breathing system where the inspired and expired gas streams divide.
- **Low resistance**, especially in the Ayre's T-piece form. Once a bag is added, the resistance of the system may be increased slightly. To minimise this, a small 'cage' is often placed in the neck of the bag, which ensures that the bag cannot flatten or deflate completely, because complete deflation increases the resistance to exhalation.
- **Simple design; easy to use.**
- **Easy to clean** and sterilise.
- Cheap disposable versions available.
- **Modest 'drag'** because two (small) tubes are near the patient's mouth.
- **Can apply prolonged IPPV (J/R modification best).**
- Used for **animals <10 kg.**
- **FGF needs to be 2–4 times minute ventilation to ensure no rebreathing.** If the animal is panting, there may be insufficient time for the FGF to purge the system of CO_2 between breaths, so you may need to increase the FGF further.
- **Not easy to scavenge from open ended bag** without kinking the bag neck or outlet, and risking a build up of gases, and subsequent volutrauma to the lungs.

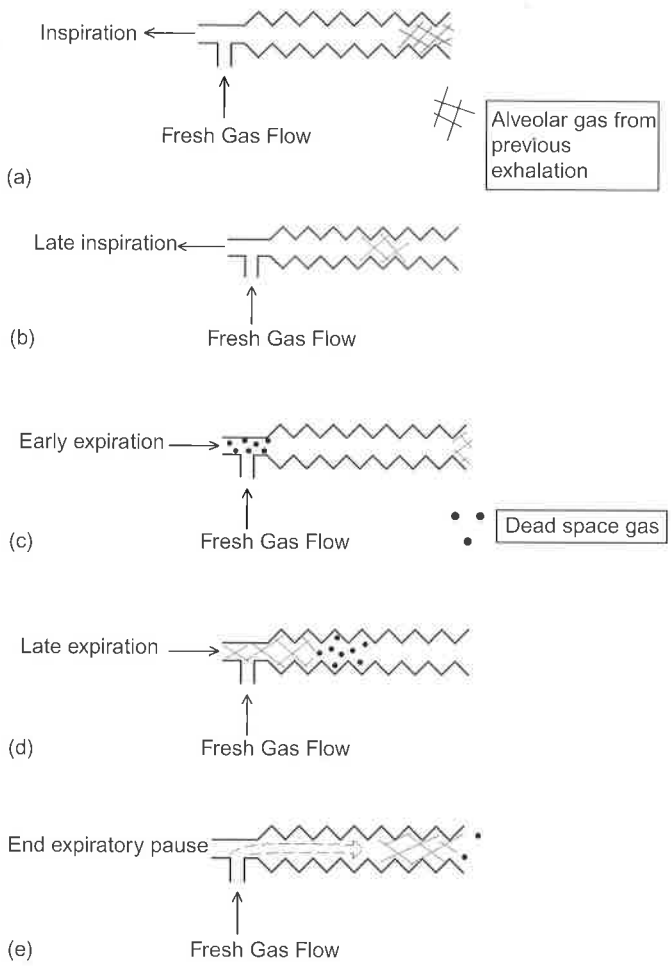


Figure 9.9 Movement of gases within a T-piece during spontaneous breathing.

How a T-piece works

The movement of gases within a T-piece during spontaneous breathing is shown in Figure 9.9.

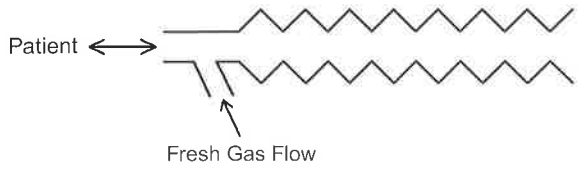


Figure 9.10 Modification at patient connector (Y piece).

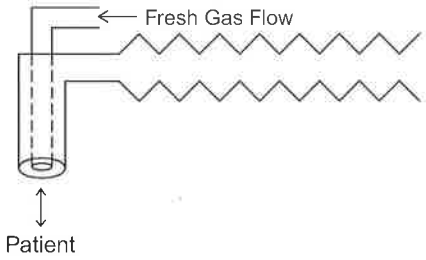


Figure 9.11 Cape Town arrangement.

T-piece modifications

The Y piece

The Y piece allows the fresh gas inlet to be angled towards the patient (Figure 9.10). This increases the resistance to exhalation (because exhalation is directly into the face of the oncoming FGF), and adds a slight positive pressure to inhalation, assisting inhalation. This continuous positive airway pressure (CPAP) is favoured in many human neonatal clinics because it reduces the tendency of the neonatal lungs to collapse. The Y piece also reduces the functional apparatus dead space slightly, by a flushing effect (during the end-expiratory pause), when fresh gases are still flowing (see below). Minimising the dead space minimises the risk of rebreathing.

The Cape Town arrangement

This design brings the FGF entry point as close to the patient's mouth as possible, thus minimising apparatus dead space (which minimises the potential for rebreathing), and also provides CPAP (Figure 9.11).

Apparatus dead space and functional apparatus dead space

Functional apparatus dead space is greater with the original T-piece configuration (Figure 9.12a) than with the Y-piece configuration (Figure 9.12b).

Mapleson D system

One anaesthetic breathing system often sold as a T-piece can be thought of as a miniature parallel modified Bain, but its true classification is as a Mapleson D system (Figure 9.13). It can be used in animals between about 3 kg and 10 kg because it has a low resistance valve and small bore corrugated tubing.

Bain (Mapleson D) system

The original Bain (unmodified version), had no bag or valve. It is like a giant co-axial Ayre's T-piece, and functions with similar

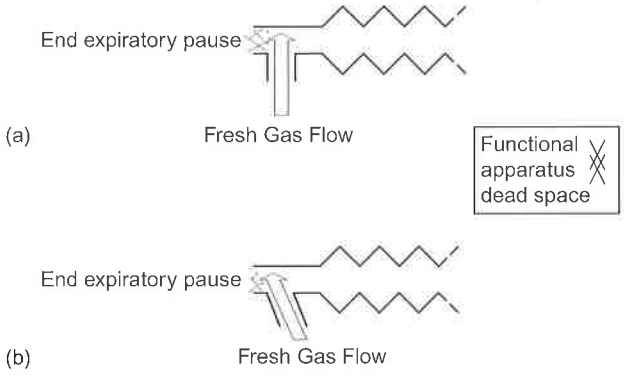


Figure 9.12 Functional apparatus dead space is greater with (a) the original T-piece configuration than (b) the Y-piece configuration.

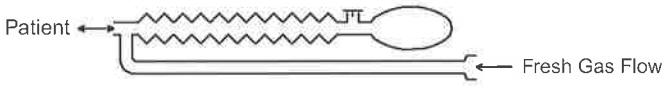


Figure 9.13 Mapleson D system.

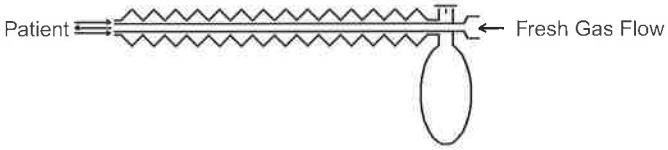


Figure 9.14 Modified Bain system.

efficiency. The (modified) Bain has the added bag and 'pop-off valve', and it still functions like a T-piece (Figure 9.14). The fresh gas **in**flow is through the **in**ner tube in a Ba**in**.

The **addition of valves usually adds resistance to a system**, which requires the animal to be able to generate higher pressures during breathing, which usually means more of a problem for smaller patients.

The volume of the corrugated tube and bag should be greater than the tidal volume of the patient. Bain (modified Bain) systems are available in three lengths: 1.8, 2.7 and 5.4 m. The longer the tube, the more the resistance to gas flows. However, animals >10 kg and up to about 80 kg can usually cope with these systems.

Very large dogs have enormous peak inspiratory flow requirements, and the relatively narrow tubing creates a higher resistance under these circumstances; also the very high fresh gas flows required for these large animals cause some of the CO_2-laden exhaled gases to be 'sucked' back towards the patient (the Venturi effect) to cause some rebreathing. Other possible problems for very large patients are that: some flowmeters do not provide high enough flows for larger animals, especially if using only oxygen and not O_2/N_2O mixtures; and at very high FGF (e.g. >15 l/min), most vaporisers no longer deliver the concentration 'dialled up'.

The characteristics of the modified Bain system are:

- **Relatively low resistance (but greater than the T-piece).**
- **Minimal apparatus dead space.**

- Fairly simple design, but **beware disconnection or leakage of inner tube** which facilitates rebreathing. Test the intactness of the inner tube by attaching the system to the common gas outlet of the anaesthetic machine; then turn on say 2 l/min O_2 flow. Now occlude the patient end of the inner tube with a pen or pencil, and watch the O_2 flowmeter bobbin; it should 'fall'. If it does not, the inner fresh gas delivery tube is broken or disconnected. An alternative test is the Pethick test: use oxygen (either turn on the oxygen flow or use the oxygen flush facility) so as to 'fill' the system, especially the bag; then, with the patient end unoccluded, activate the oxygen flush valve. If the inner tube is intact, the fast oxygen flow through the inner tube should produce a Venturi effect at the patient end which draws gases from the outer tube and bag, so the bag should deflate. If the bag does not deflate, or even inflates, then the inner tube is not intact. Of both these tests, the inner tube occlusion test seems to be most sensitive and most preferred.
- **Minimal 'circuit drag'.**
- **Easy to scavenge.**
- Disposable versions available.
- **Can be used for prolonged IPPV.**
- Used for **animals >10 kg** and **up to 70–80 kg.**
- **FGF needs to be 2–4 times minute ventilation to prevent rebreathing during spontaneous breathing. Panting animals may require higher FGF.**
- **FGF can be reduced** to nearer 1 times minute ventilation **for IPPV if** you aim to **hyper-ventilate slightly** (and thus blow off a bit too much CO_2), because this hyperventilation potentially causes hypocapnia/respiratory alkalosis which is then 'offset' by the CO_2 rebreathing that follows the reduction in FGF. This is called **deliberate functional rebreathing; or** you aim to provide IPPV with a largeish tidal volume and with a relatively slower rate, so the extra long end-expiratory pause allows FGF to purge the system of CO_2-laden gases. **However, it** is advisable to use capnography to monitor during IPPV (see Chapter 18).
- **Inhaled fresh gases are thought to be warmed slightly by heat transfer from the warm exhaled gases in the surrounding tube (counter current system).**

Non-rebreathing systems compared with rebreathing systems

Advantages

- Simple construction; easy to use; generally easy to clean.
- No soda lime necessary (cheaper? (but use higher gas flows); less resistance).
- Minimal apparatus dead space.
- Make the best use of precision vaporisers (i.e. the inspired vapour concentration should be that which is dialled up on the vaporiser).
- Lowish resistance (especially systems without valves; none have soda lime).
- No need for denitrogenation of the system.
- Can use N_2O safely.
- Cheap disposable versions available.
- Can scavenge easily from most of the systems.

Disadvantages

- Poor economy because high FGF wastes lots of O_2 and N_2O; and high FGF also leads to high consumption of volatile inhalation agent, therefore much wastage.
- Must scavenge (lots of 'waste' gases to dispose of).
- Consider mode of ventilation (spontaneous versus IPPV; remember problems associated with IPPV with Magill and Lack).
- The loss of rebreathable humidified and warmed gases with most systems promotes hypothermia and dehydration, especially in small patients; and results in reduced function of the respiratory mucociliary escalator, with increased potential for obstruction of the airways with drying secretions.
- High gas flows also increase the risk of barotrauma/volutrauma to the lungs (causing pneumothorax), should there be an obstruction to the anaesthetic breathing system outflow.

Heat and moisture exchangers (HMEs)

HMEs are available which help conserve the warmth and humidity of exhaled gases. These are often used with non-rebreathing systems, and in small patients undergoing long procedures. It may take up to 10–20 min of continued use for HMEs to reach their best performance. HMEs usually add little in the way of resistance, although they may add some apparatus dead space depending upon the size used, but they are available in several sizes to suit different patient sizes.

Bag terminology

The term **reservoir bag** is usually used for the bag in any breathing system where none of the patient's exhaled gases ever pass back into the bag. Strictly this means only the bags in the Mapleson A systems (e.g. the Magill and Lack) where the bag is on the inspiratory limb, but beware IPPV with these systems. However, some people include the bags in the Jackson Rees modified Ayre's T-piece and Bain systems, saying that if none of the exhaled gases are actually rebreathed by the animal (i.e. they should all be flushed far enough downstream by the FGF) then the bags act only as reservoir bags.

The term **rebreathing bag** is used for the bag in any breathing system where the patient's exhaled gases can/do pass into the bag. Therefore this is strictly the correct term for the bags in the Jackson Rees modified Ayre's T-piece, the Bain and also the rebreathing systems like the Waters' To and Fro and the circle.

The chosen bag should be of such a size that the capacity to which it may be easily distended must exceed the patient's tidal volume. Although larger bags are safer (they more easily absorb pressure increases), they increase the time constant in rebreathing systems (i.e. they slow down the rate of change of anaesthetic agent concentration when the vaporiser setting is altered).

Hybrid systems

The Humphrey ADE system and circle

Some of you may come across this system in practice. It is 'one' system that by switching the position of a lever, the bag, and

adding a soda lime canister with inspiratory and expiratory valves, can be converted between:

- A Magill/Lack type system (the Mapleson A) for efficient spontaneous breathing.
- A Bain/T-piece type system (Mapleson D/E) for most efficient IPPV.
- A circle with soda lime absorber.

The system used to be available in coaxial and parallel forms, but now is marketed most commonly in the parallel form. In the A configuration it acts just like a parallel Lack; in the D/E configuration it acts like a Bain/T-piece and is designed to allow IPPV in this mode. Therefore you can switch between A (spontaneous breathing) and D/E configurations (IPPV) without changing the FGF, because the efficiency of the Mapleson A system for spontaneous breathing equals that of the Mapleson D system for IPPV. A soda lime canister can be added, which incorporates inspiratory and expiratory valves, so converting the system into a circle. The system requires a lot of maintenance and regular servicing and replacement of all its moving parts, but it is a very neat piece of engineering. It is supplied with narrow smooth bore hoses, and a low resistance pop-off valve. It can be used for any patient size by choosing the configuration most appropriate for the patient's size and needs. It can be used for patients down to 2–3 kg in the A and D/E modes.

Rebreathing systems

These include a canister containing soda lime which absorbs carbon dioxide from the gases in the system. They also tend to be used with FGF rates less than the patient's minute ventilation; but for the first 20 min or so of their use, the FGF is often higher. This allows the system (and the patient's lung functional residual capacity (FRC)), to be purged of 'air' (78% nitrogen), and allows a quicker increase in oxygen and anaesthetic vapour concentration to build up in the system. This 'nitrogen washout' or **'denitrogenation'** also reduces the chance of delivering an oxygen-poor gas mixture to the patient, for example nitrogen can dilute out the gases that you are delivering to the breathing system from the anaesthetic machine. After this initial denitrogenation phase, the FGF can be reduced so that the 'pop off valve' (a safety release valve should the pressure of gases within the system exceed 'safe' levels), should not need to vent gases (and could even be closed) if the oxygen and anaesthetic inflows are reduced to become exactly equivalent to the patient's uptake; all exhaled carbon dioxide being absorbed.

Because the patient's oxygen and anaesthetic demands can vary from minute to minute (**oxygen demand is normally 4–10 ml/kg/min**; but depends on factors such as patient size, metabolic rate, temperature, depth of anaesthesia), it is very difficult to perform true 'closed system' anaesthesia. Instead, we tend to supply a little extra oxygen and anaesthetic, and allow the excess 'gases' to vent through the 'pop-off' valve, which is therefore left 'open'; we tend to use these systems in 'semi-closed' mode.

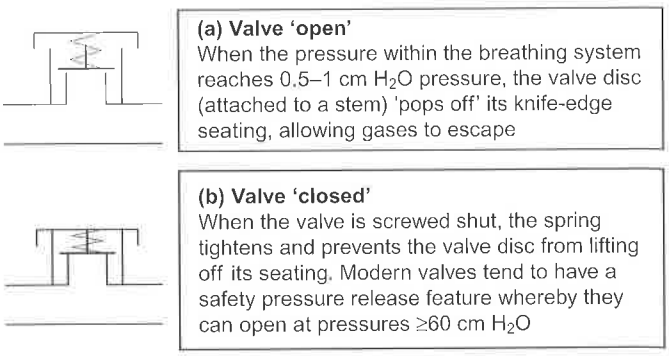


Figure 9.15 Valves in (a) the open and (b) the closed position.

Pop-off or APL (adjustable pressure limiting) valves

A valve may be partly or fully open (Figure 9.15a). The valve leaflet/disc rests on the valve seating; and depending how 'open' the valve is, variable tension is applied to a spring which acts on the valve disc. Now, when pressure within the system builds up and reaches the set 'pop-off' pressure (determined by how tightly the spring holds the disc down onto the seating), then the valve leaflet lifts from the seating, and gases can escape, ideally into the scavenging system. When the valve is closed (Figure 9.15b), the valve leaflet is held tight against the valve seating by the spring. With old fashioned valves, even very high pressures within the system could not open the valve. However, modern valves now do have a safety relief at higher pressures (usually c. 60 cmH_2O).

Anaesthetic agent concentration

With rebreathing systems, because each new inhaled breath is not mostly 'fresh gases', as delivered from the anaesthetic machine (therefore different to non-rebreathing systems), it is difficult to know exactly what concentrations of oxygen, nitrous oxide and inhalation agent the animal does inspire with each breath, because the incoming FGF from the anaesthetic machine is diluted by exhaled gases and the other gases within the system (e.g. air at the start of the anaesthetic, unless the system is first flushed with 'fresh gases' from the anaesthetic machine).

Time constants

The rate of change of anaesthetic agent concentration in rebreathing systems is proportional to the fresh gas inflow from the anaesthetic machine, and inversely proportional to the volume of the system.

$$\text{Time constant of the system} = \frac{\text{Volume of breathing system}}{\text{Fresh gas inflow}}$$

If we change the vaporiser setting (in order to change the anaesthetic concentration in the system):

- After **one** time constant, the change in anaesthetic agent concentration in the system can be expected to be 63.2% complete.
- After **two** time constants, the change is 86.7% complete.
- After **three** time constants, the change is 95% complete.