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D-91730-2018

Low-flow, minimal-flow and metabolic-flow anesthesia

Clinical techniques for use with rebreathing systems

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ACKNOWLEDGEMENT: AHEAD OF HIS TIME

Professor Jan A. Baum (died September 13th 2009) was ahead of his time by certainly more than two decades. Long before there was any mention of anesthesia management using pure oxygen as the carrier gas, let alone before there was any talk of high doses of concentrated oxygen to avoid intra-operative infections, Professor Baum embraced the role of oxygen as carrier gas. In the article produced jointly with colleagues Professor van Aken and Professor Bohrmann, he had already established standards during the years 2001 to 2004.

Professor Baum can rightly be described as one of the pioneers of low- and minimal-flow anesthesia. He also described metabolic-flow anesthesia using pure oxygen as the carrier gas. By doing so, he simplified and perfected minimal-flow anesthesia.

In view of the enormity of the work, we found it difficult to consider all the publications by Professor Baum. It would, however, never have been possible to produce this book had Professor Jan A. Baum not carried out his outstanding preliminary work. We would therefore like to dedicate the present work to him.

In addition, we would like to extend our heartfelt thanks to Professor Jan A. Baum for his excellent instructions and training during our work in Damme.

We would also like to extend our warm thanks to Sven Olaf Maack of Drägerwerk AG & Co. KGaA for his outstanding assistance in producing this book.

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01 Introduction/Definition of terms

The various options of low- and minimal-flow anesthesia present sufficient clinical techniques for use with rebreathing systems. Only when low-flow anesthesia is performed can the advantages of rebreathing systems be realized. Therefore, in everyday clinical practice where inhalational anesthesia is performed using a rebreathing system, the fresh gas flow should always be as low as possible. This is the only way in which the emission of excess anesthesia gases can be reduced to a minimum and the advantages of improved respiratory gas conditioning achieved.

1.1 Low-flow anesthetics

Low- and minimal-flow anesthetics are characterized by the rate of fresh gas flow (L/min) which is fed into the breathing gas system of the unit. The deciding factor is for the fresh gas flow to be distinctly lower than the patient's breathing minute volume. If a lower flow of fresh gas is set, the anesthetic gases in the patient's exhalation air are returned to the patient via closed or semi-closed rebreathing systems after CO_2 has been chemically bonded. This explains the name 'rebreathing system'. As a result of this process flow, the rebreathing volume consecutively increases with a reduction in fresh gas flow and the excess gas volume is continually reduced.

Propedeutic anesthesiology features the following notable procedures, which are employed with low- and minimal-flow anesthesia:

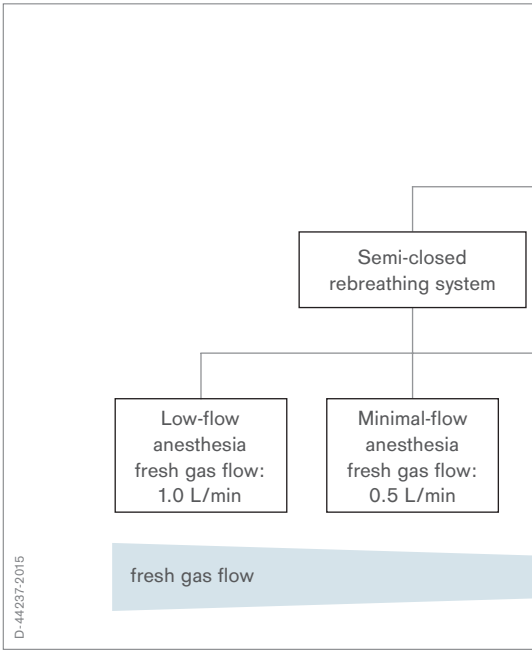
1) In low-flow anesthesia, the fresh gas flow is reduced to 1.0 L/min. This method was first described by Foldes et al. in 1952[1,2].
2) In minimal-flow anesthesia, first described by Virtue in 1974, the fresh gas flow is reduced to 0.5 L/min[3].

Provided the system is completely leakage-free, the fresh gas flow can be continuously reduced to the gas volume which the patient is absorbing and metabolizing while under anesthesia.

In the closed system, a distinction is made between non-quantitative and quantitative anesthesia.

With non-quantitative anesthesia, the anesthetist maintains a constant volume in the circuit system by adjusting the fresh gas flow so that the filling of the breathing system and the breathing pattern remain unchanged.

In contrast, when quantitative anesthesia with closed systems is performed, the anesthesia machine keeps not only the gas filling, breathing pattern and internal pressures constant, according to the anesthetist's instructions, but also the fresh gas composition in terms of the carrier gases and volatile anesthetics (if necessary, with nitrous oxide). The total gases supplied therefore always correspond to the patient's actual gas uptake[4,5].



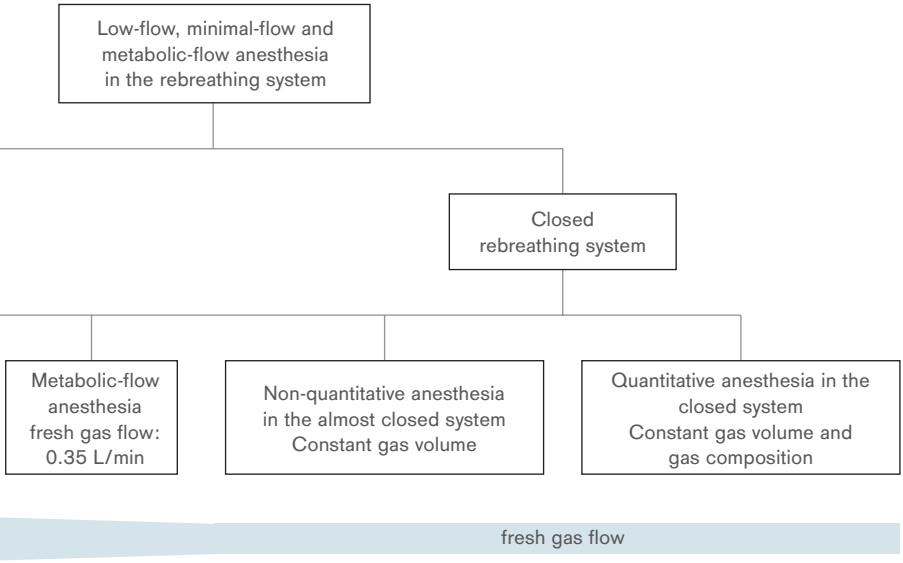


Fig. 1: Overview of low-flow, minimal-flow and metabolic-flow anesthesia in the rebreathing system (modified from Baum JA[6])

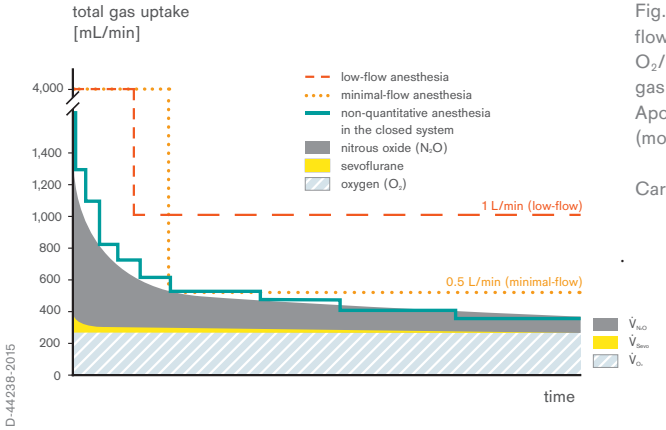


Fig. 2: Low-flow and minimal-flow anesthesia with an O_2/N_2O mixture as carrier gas in the semi-closed Apollo® breathing system (modified from Baum JA[6])

Carrier gases: O_2/N_2O

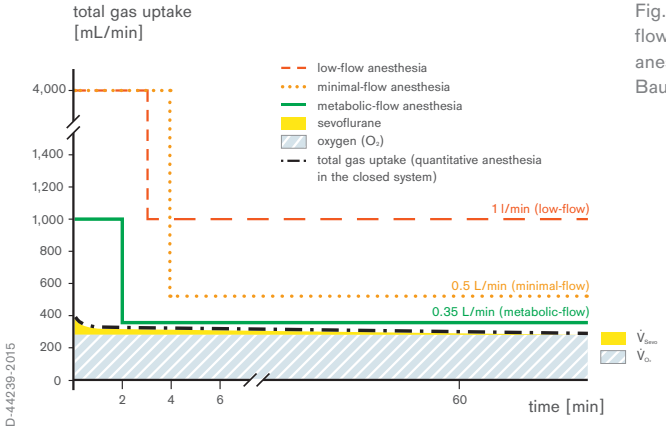


Fig. 3: Low-flow, minimal-flow and metabolic-flow anesthesia (modified from Baum JA[6])

1.2 Rebreathing systems

As already mentioned, the basic requirement for conducting anesthesia with a low fresh gas flow is the use of a rebreathing system. With this system, the unused gases and anesthetic contained in the patient's exhaled air are reused in the inhalation gas.

Rebreathing systems currently used correspond to the conventional circuit systems (for example, those of the Dräger product families Fabius®, Apollo®, and Perseus® A500).
A characteristic of these systems is a carbon dioxide absorber: it chemically removes and binds exhaled carbon dioxide from the breathing circulation system. During removal, heat (ΔT) and moisture (H_2O) are also generated, helping condition the breathing gas in the circuit system. To absorb the CO_2, soda lime is used. Today, this mainly consists of calcium hydroxide ($Ca(OH)_2$).

The absorption reaction is exothermic and calcium carbonate, water and heat are generated as end products:

$$Ca(OH)_2 + CO_2 \rightarrow CaCO_3 + H_2O + \Delta T \text{ (heat)}$$

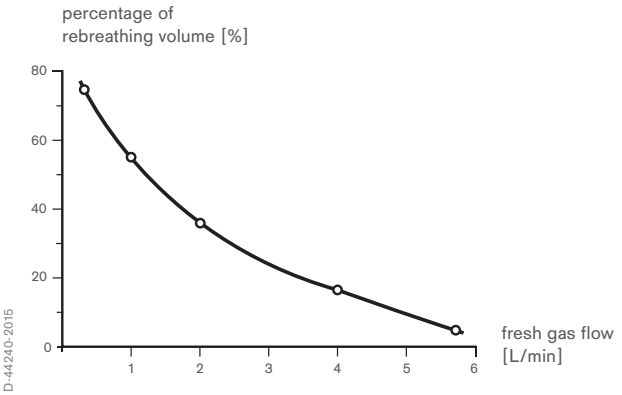


Fig. 4: Percentage of expiratory air which, depending on the flow following the addition of fresh gas and discharge of the excess gas, is returned to the patient (modified from Hönemann C[7])

The continuous loss of gas from the system—a result of oxygen consumption and enrichment of the anesthetic gases in the tissues (plus possible system leakages)—is compensated for by introducing fresh gas into the breathing system.

The absorber should be inserted into the inhalational limb of the breathing system in order to condition the breathing gas, so that the rebreathed portion of exhaled air flows through it. As heat and water are released during the chemical reaction, the absorber helps to condition the inhalation breathing gases[8].

1.3 Differentiating between anesthesia systems

In order to differentiate between the breathing systems according to technical design criteria, the terms ‘open’, ‘semi-open’, ‘semi-closed’ and ‘closed’ are used. These terms, however, are no longer adequate to properly classify anesthesia systems: subdividing them into systems with and without rebreathing appears to be more suitable[9]. Depending on the fresh gas flow, rebreathing systems may be semi-open, semi-closed or closed. The amount of rebreathing is determined by the amount of fresh gas flow.

> The lower the fresh gas flow, the higher the amount rebreathed and the smaller the excess gas portion.

SEMI-OPEN SYSTEM

With partial rebreathing, a semi-open rebreathing system is used. The fresh gas flow must be approximately two to three times the minute volume so that the expiratory volume can be flushed from the system before the next breath is taken. This corresponds to a set fresh gas flow of > 6 L/min.

SEMI-CLOSED SYSTEM

In the semi-closed system, the patient rebreathes a portion of the expired air and the gas mixture that is not re-circulated is expelled from the system as excess gas. The majority is transferred back to the patient. As a result, a functional circuit system is created.

The volume of fresh gas supplied to the anesthesia system is therefore larger than the patient’s gas uptake and at the same time lower than the minute volume. The recircuit gas volume is inversely proportional to the fresh gas flow, and the excess gas volume directly proportional.
As the rebreathing portion increases, the difference between the

composition of the volatile anesthetic and fresh gas increases.

In the semi-closed anesthesia systems, the fresh gas flow is between 0.5 and 6 L/min.

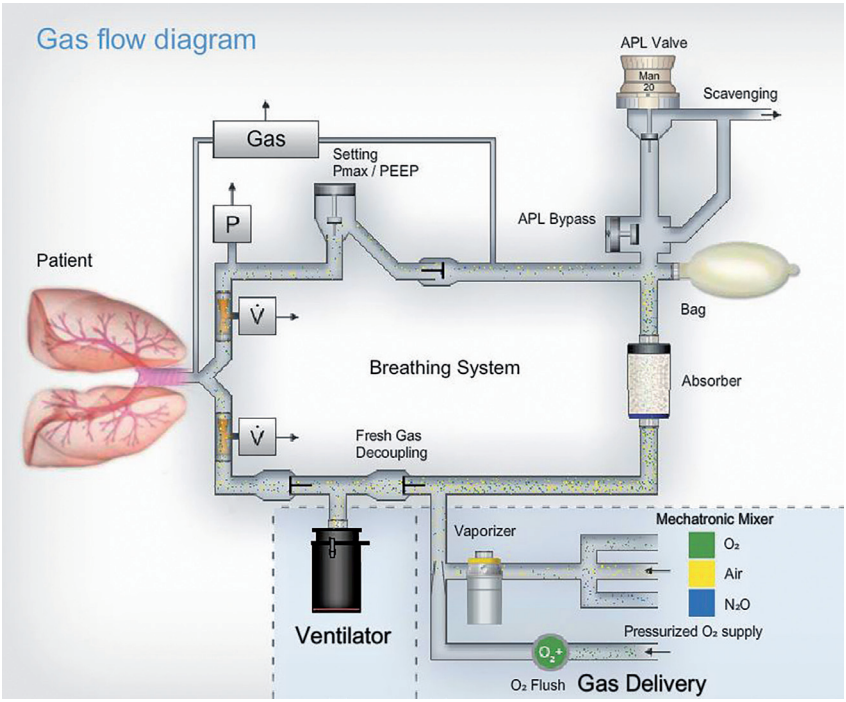


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Fig. 5: Gas flow diagram using the Apollo® rebreathing system as an example

NON-QUANTITATIVE ANESTHESIA IN THE ALMOST CLOSED SYSTEM

The closed anesthesia system feeds the total exhaled gas mixture back to the patient after carbon dioxide has been eliminated by the interposed absorber. In this way, the flow of fresh gas in the circuit system can be sufficiently reduced so that only quantities of gas that have been metabolized or have diffused have to be replaced. Excess gas no longer escapes from the system. This corresponds to the use of a closed rebreathing system (non-quantitative anesthesia). Non-quantitative anesthesia with a closed system can be performed with most anesthesia machines.

The following requirements are sufficient: the breathing systems must be sufficiently tight (no leakages). The anesthesia machines must allow a setting to even the lowest fresh gas flow. Dosing of the anesthetic gas must also be sufficiently accurate in the low flow range, and machine monitoring must guarantee comprehensive monitoring of the composition of the anesthesia gas (see also Section 3.6 Monitoring, page 48).

Any short-term imbalances between the fresh gas volume and the consumption/uptake, as well as leaks, can be compensated for by a gas reservoir, for example the bag. This is implemented in all Dräger machines with a rebreathing system (Dräger product families, Fabius, Apollo®, and Perseus® A500).

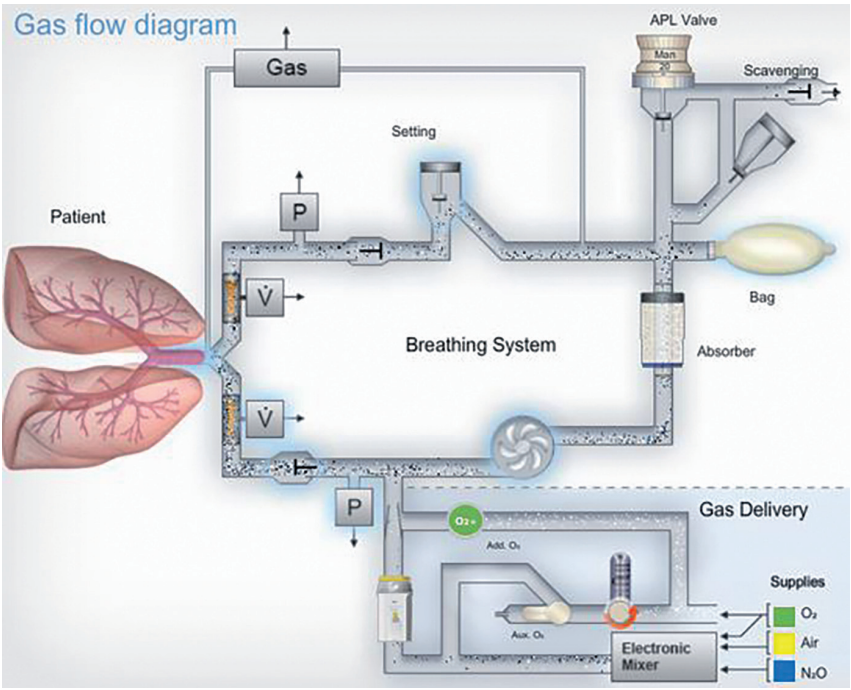

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Fig. 6: Gas flow diagram using the Perseus® A500 rebreathing system as an example

QUANTITATIVE ANESTHESIA IN THE CLOSED SYSTEM (CLOSED LOOP—AUTO—CONTROL)

Quantitative anesthesia with a closed system requires electronically-controlled gas and anesthetic dosing by means of closed-loop feedback control.

To date, this dosing principle is only common in a select few anesthesia machines.

02 Benefits of low-flow anesthesia

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2.4 Less contamination with volatile anesthetics	27

02 Benefits of low-flow anesthesia

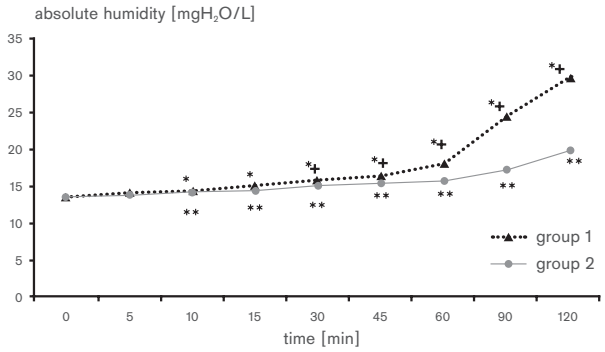
2.1 Clinical benefits—humidifying, warming, pulmonary function

The importance that breathing gas conditioning has for the anesthetized patient has been known for some time[10,11,12]. The need to condition breathing gas for intubated or tracheotomized patients in intensive care is now beyond dispute. Disabling the upper respiratory tract by a laryngeal mask or an endotracheal tube prevents it completely from performing its physiological functions (humidifying and warming the breathing gas). Inadequate breathing gas conditioning entails the risk of hampering the function of the ciliary epithelium and hence mucociliary clearance. The consequences of inadequate breathing gas conditioning may be morphological damage to the respiratory tract epithelium, resulting, for example, in secretory reflux, obstruction of the bronchioles and the encouragement of microatelectasis.

During prolonged anesthesia, therefore, an absolute humidity of between 17 and 30 mg H_2O/L with an anesthetic gas temperature of at least 28°C should be provided. These demands are met by minimal-flow anesthesia: in clinical use, for example, after only 15 minutes the desired absolute humidity is established and after one to two hours the required warming of the breathing gas is achieved (see figure 7)[13,14].

Therefore, even for relatively short procedures lasting 15 to 30 minutes, we recommend reducing the fresh gas flow in minimal-flow or metabolic-flow systems.

For cancer treatment the radiology department in Vechta (Germany) uses HDR brachytherapy with afterloading. Those high-dosage interventions last one to two hours and are performed under general anesthesia with endotracheal intubation.



*p < 0.05 values at times 10, 15, 30, 40, 60, 90 and 120 minutes after tracheal intubation compared with time 0 in group 1

**p < 0.05 values at times 10, 15, 30, 40, 60, 90 and 120 minutes after tracheal intubation compared with time 0 in group 2

+p < 0.05 values for comparison between both groups

Fig. 7: Comparison of absolute humidities of inspiratory breathing gas

Group 1: Fresh gas flow 1 L/min (0.5 L/min O_2 + 0.5 L/min N_2O) + desflurane;
Group 2: Fresh gas flow 3 L/min (1.5 L/min O_2 + 1.5 L/min N_2O) + desflurane (modified from Bilgi M et al.[15])

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The case is started with propofol (2 mg/kg), sufentanil (0.15 to 0.25 µg/kg) and rocuronium chloride (0.4 to 0.6 mg/kg). Anesthesia is then continued as inhalational anesthesia.

Three groups with different fresh gas flows were compared. 2 or 6 L/min fresh gas flow were used and retained over the course of anesthesia. In a third group, the inhalational anesthetic was introduced with a fresh gas flow of 1 L/min. Once 0.9 MAC was reached, the fresh gas flow was reduced to 0.35 L/min.

The following three figures show the measurement parameters (temperature of the breathing gas, relative and absolute breathing gas humidity). They were measured at the Y-piece in the inspiratory limb of the anesthesia machine.

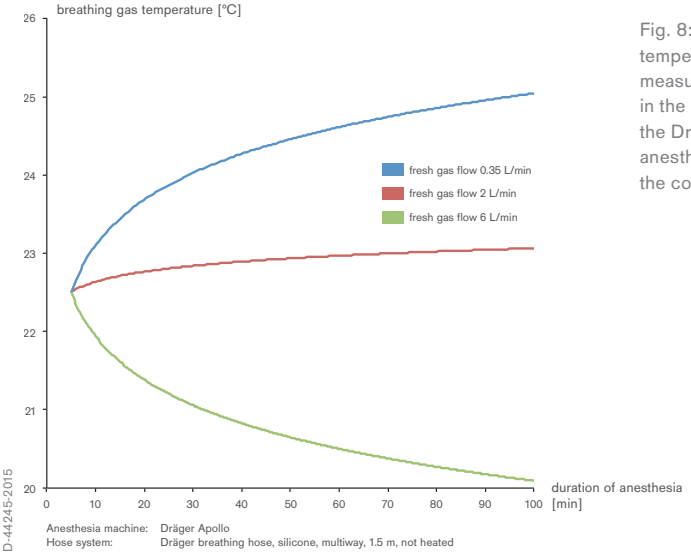

Fig. 8: Breathing gas temperature in °C measured at the Y-piece in the inspiratory arm of the Dräger Apollo® anesthesia machine over the course of anesthesia

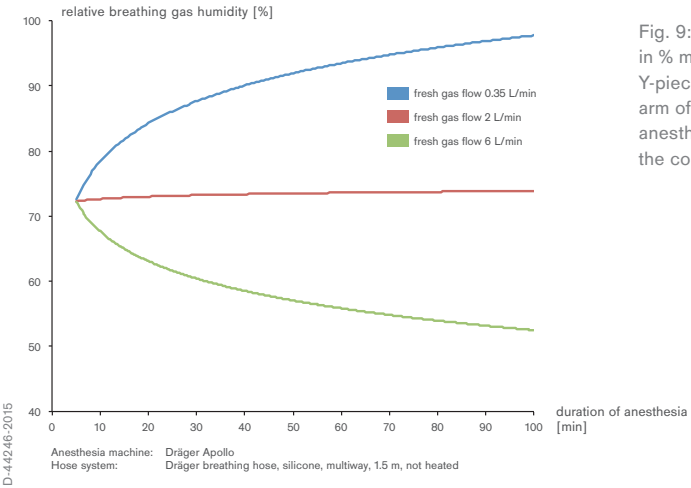

Fig. 9: Relative humidity in % measured at the Y-piece in the inspiratory arm of the Dräger Apollo® anesthesia machine over the course of anesthesia

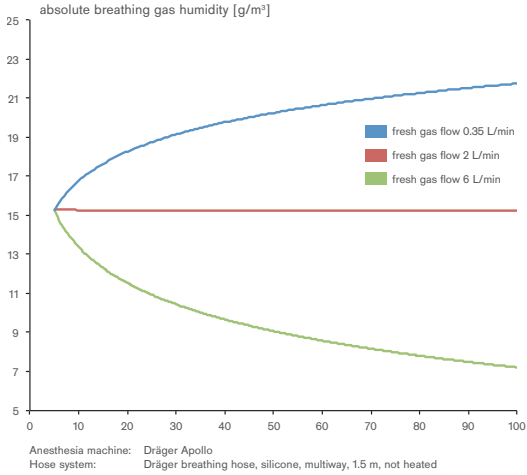

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Fig. 10: Absolute humidity in g/m³ measured at the Y-piece in the inspiratory arm of the Dräger Apollo® anesthesia machine over the course of anesthesia

Low fresh gas flows also have a positive effect on body temperature (see figure 12).

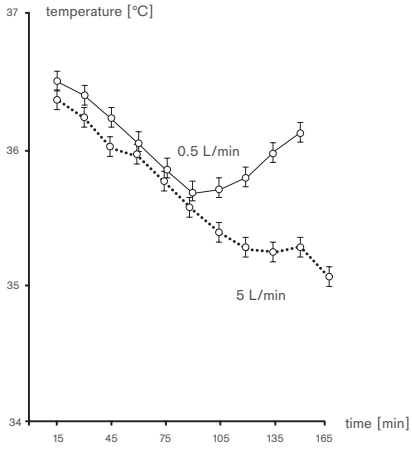

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Fig. 11: Average oesophageal body temperature with different fresh gas flows (0.5 versus 5 L/min) (modified from Aldrete A et al. [16])

2.2 Ecological benefits

A characteristic of high-flow anesthesia is that large amounts of volatile anesthetics are emitted. This not only pollutes the environment, as well as placing an extra burden on a tight budget. Growing environmental awareness, increasingly strict industrial safety regulations and, last but not least, cost considerations now require us to rethink clinical procedures relating to anesthesia. The emission of anesthesia gases should, therefore, be reduced to an unavoidable minimum and unused anesthetics should be reused. Low-flow and minimal-flow anesthesia meet these demands.

Despite these obvious advantages, clinics still express reservations to use these procedures more frequently. In order to adopt different methods, a change in thinking must be initiated and customary procedures must accordingly be changed. A commitment to this new way of thinking, however, will pay off due to the resulting ecological and economic benefits.

2.3 Cost savings—economic benefits

The use of low-flow and minimal-flow anesthesia reduces the requirement for anesthetics, particularly those that contribute to the greenhouse effect, as well as for nitrous oxide and oxygen. The ecological benefit is accompanied by notable cost savings. Not only do over 20-year-old data confirm a cost reduction between 55 and 75% if the fresh gas flow is reduced from 4 to 1 L/min; more recent data show similar potential savings of approximately 60%. The data is based on consistent use of quantitative anesthesia using a closed system, compared with the standard method using a fresh gas flow of 3 L/min [17, 18, 19]. While consistent use of the minimal-flow method results in a threefold consumption of the soda lime, the associated costs are negligibly small in the cost-to-benefit analysis.

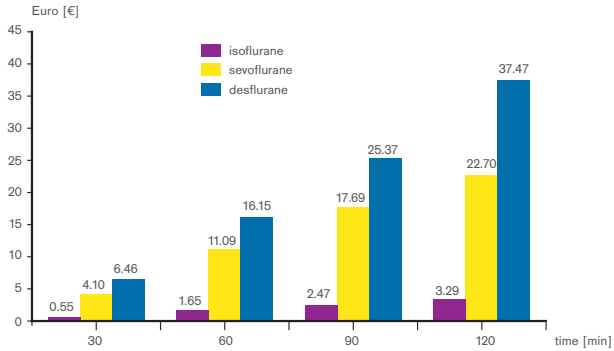

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Fig. 12: Cost savings in Euros as a result of minimal-flow anesthesia of 0.5 L/min compared with the standard method using fresh gas flow of 3 L/min

Note: The savings shown in figures. 13/14 were calculated on the basis of the underlying costs for the following anesthesia gases, including delivery, value added tax, etc. (average values, date: 10/2013):

Isoflurane 250 mL € 32.73
Sevoflurane 250 mL € 131.92
Desflurane 250 mL € 81.16

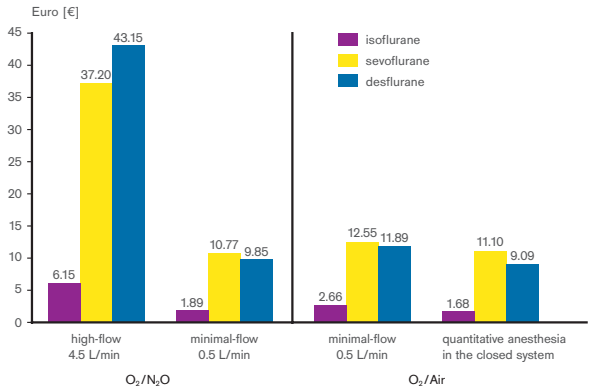

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Fig. 13: Cost of inhalational anesthetics in Euros based on 2-hour inhalational anesthesia

Comparison of the different types of anesthesia

In addition, critical comments are constantly raised that, even when the cost of inhalational anesthesia is calculated correctly, the costs of additional intravenous drugs, capital costs, depreciation and inspection and repair costs must be taken into account. These costs, however, are also incurred when using standard procedures or procedures using high fresh gas flow. Therefore, in our opinion, a clear demand must be made for the consistent use of anesthesia with low fresh gas flow in daily use. In line with this argument is the fact that the technical level of anesthesia machines allows for a low fresh gas flow and that some of the machines are even designed for low-flow anesthesia techniques.

In summary, the efficiency of the anesthesia gases used increases with reduced fresh gas flow. Only with quantitative anesthesia in a closed system can the ratio between oxygen (or nitrous oxide) and volatile anesthetics temporarily assume the maximum value of 1.

Efficiency then corresponds to the ratio between the uptake and the quantity of fresh gas and anesthesia gases that are simultaneously supplied to the breathing system.

$$\text{efficiency} = \frac{\text{VU L/min}}{\text{FGF L/min}}$$

VU = patient uptake
FGF = fresh gas flow

2.4 Less contamination with volatile anesthetics

Modern inhalational anesthetics belong to the group of partially substituted chlorofluorocarbons (CFCs) and fluorinated hydrocarbons. They have a long lifetime in the atmosphere. They therefore have an ozone-damaging potential that contributes 5 to 13% to that of the fully substituted CFCs used industrially. The annual production of volatile anesthetics amounts to roughly 1% of the annual production of fully substituted CFCs. It is, however, undisputed that the demand for the greatest possible reduction of unnecessary emission of anesthesia gases must lead to the appropriate use of rebreathing systems.

Reducing anesthesia gases by up to 90% has another beneficial effect: the exposure for staff in the anesthesia workplace drops noticeably[20].

As Virtue et al.[21] were able to show, if there is no central waste gas scavenging system, workplace contamination from nitrous oxide could be reduced to 29 or 15 ppm for a time-weighted average concentration, purely by the consistent use of rebreathing systems with a reduction in fresh gas flow for N_2O to 0.5 L/min (low-flow) or even 0.2 L/min (minimal-flow). These values not only fall below the threshold limit of 50 ppm set by the Hamburg Office for Industrial Safety in Germany, they even satisfy the more stringent recommendations by the American National Institute for Occupational Safety and Health (NIOSH), which suggest a maximum permissible concentration of 25 ppm. Lowering workplace contamination by reducing the consumption of anesthesia gas has direct effects on all areas of work.

03 Conditions for low-flow and minimal-flow anesthesia

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3.4 Control via the MAC value	37
3.5 Effects of reduced fresh gas flow	44
3.6 Monitoring	48

03 Conditions for low-flow and minimal-flow anesthesia

3.1 Oxygen consumption

Apart from maintaining a respiratory tract climate that is better adjusted to physiological conditions, the use of low-flow techniques also allows the important parameter of oxygen consumption to be monitored or at least estimated.

Patients' oxygen consumption during anesthesia corresponds to their metabolic consumption and can be assumed to be roughly constant.

As early as 1945, Samuel Brody conducted extensive studies into energy and oxygen consumption in both animals and in human beings.
From this research, he developed his formula, which is still commonly used today[22]:

$$VO_2 = 10 \times KG[kg]^{3/4}$$

VO_2 = uptake of oxygen
KG[kg] = body weight in kilograms

In subsequent years, this formula was further developed by various authors and applied to body surface, body compartments and age. However, it is well known that oxygen consumption is overestimated by 10 to 20% in anesthetised patients, particularly in those in the higher weight classes. Nevertheless, we too continue to refer to the Brody formula by including in our calculations a general overestimate of oxygen consumption as a safety margin.

The rule of thumb is that oxygen consumption in mL/min corresponds roughly to:

$$VO_2 = 3.5 \times KG \text{ [mL/min]}$$

VO_2 = uptake of oxygen in mL/min
KG = body weight in kilograms

For a patient with a weight of 100 kilograms, for example, this means that an oxygen uptake of 350 mL/min must be expected.

3.2 Anesthesia gas uptake

Anesthesia gas uptake is based on the pharmacokinetics and dynamics of the volatile anesthetic used. The uptake of inhalational anesthetic agent—assuming a constant gas composition in the anesthesia system—drops exponentially over the course of anesthesia. In accordance with the Lowe formula, it is proportional to the desired concentration and solubility of the anesthetic, and to cardiac output[23,24].

$$V_{AN} = f \times MAC \times \lambda_{B/G} \times Q \times t^{1/2} \text{ [mL/min]}$$

V_{AN} = uptake of inhalational anesthetics (anesthesia gas uptake) in mL/min
f × MAC = desired expiratory anesthetic concentration as a function of the minimal alveolar concentration of the anesthetic chosen (e.g., 0.8 × MAC)
$\lambda_{B/G}$ = coefficient of blood-gas solubility
Q = cardiac output (dL/min)

The prediction models, based on Bailey's[25] 5-compartment model, also appear valid. This allows the distribution of anesthesia gases in the human body to be calculated. In addition, calculation models for prediction

modules are now used for anesthesia gases that are based purely on empirical data relating to organ volumes, blood flows, physiological distribution patterns and solubility coefficients. These models calculate the presumed gas patterns and list gas that has already been consumed[26,27].

Of major clinical importance is that the greatest anesthesia gas uptake occurs in the first minutes—during the so-called uptake time and uptake phase/wash-in phase. In the further phase of constant anesthesia, the anesthesia gas uptake is roughly constant because the patient's compartments can be regarded as saturated. The crucial factor for determining the actual effect of the anesthesia is the target concentration in the effect compartment—the brain. Equally important is the choice of a suitable volatile anesthetic agent for which the relevant pharmacodynamics and pharmacokinetics must be taken into account. Not all agents in current use are equally suitable for performing low- and minimal-flow anesthesia. This is principally dependent on the different solubilities and associated anesthetic potencies as well as on the physiological uptake of the agent [28].

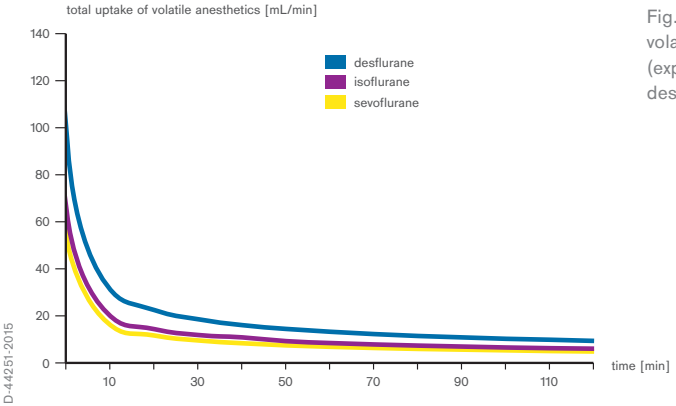

Fig. 14: Total uptake of volatile anesthetic agents (expiratory concentration—desired state: 0.9 × MAC)

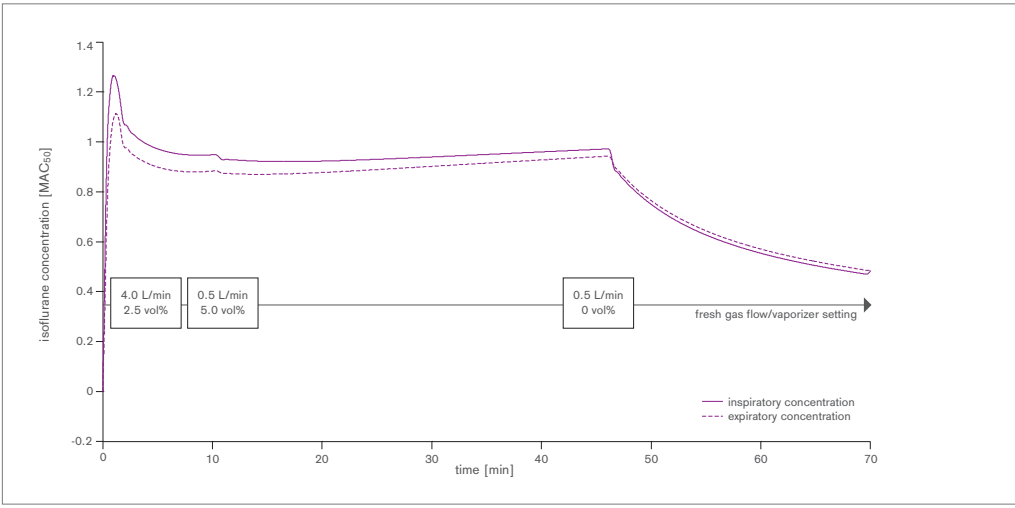

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Fig. 15: Inspiratory and expiratory isoflurane concentration over the course of inhalation anesthesia with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Desired value: expiratory concentration: 0.9 MAC
For vaporizer adjustments, see also diagram of minimal-flow anesthesia procedure with oxygen-air mixture as carrier gas.

Start with 4 L/min fresh gas flow, vaporizer setting 2.5 vol%. Once the desired value of 0.9 MAC is reached, change the fresh gas flow to 0.5 L/min and vaporizer setting to 5%. After 45 minutes, change the vaporizer setting to 0 vol%. Do not change the fresh gas flow.

Adjust the vaporizer settings to maintain the desired value, according to whether the anesthetic concentrations are increased/reduced, using the various time constants.

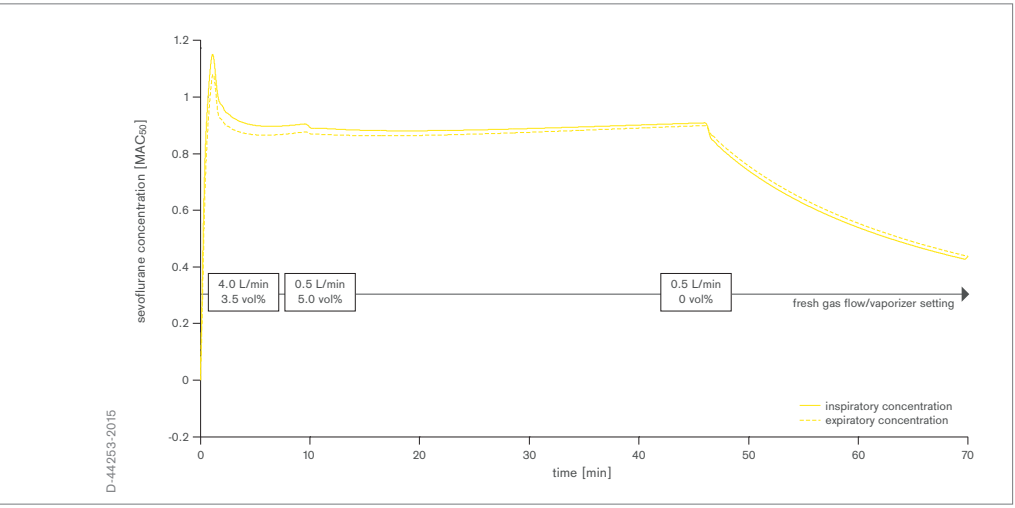

Fig. 16: Inspiratory and expiratory sevoflurane concentration over the course of inhalation anesthesia with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also diagram of minimal-flow anesthesia procedure with oxygen-air mixture as carrier gas.

Start with 4 L/min fresh gas flow, vaporizer setting 3.5 vol%. Once the desired value of 0.9 MAC is reached, change the fresh gas flow to 0.5 L/min and the vaporizer setting to 5%. After 45 minutes, change the vaporizer setting to 0 vol%. Do not change the fresh gas flow.

Adjust the vaporizer settings to maintain the desired value, according to whether the anesthetic concentrations are increased/reduced, using the various time constants.

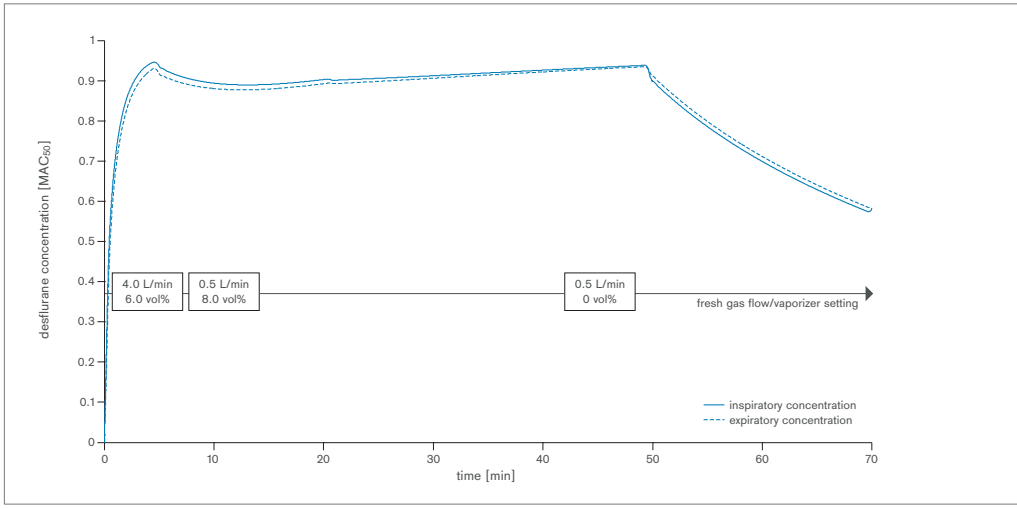

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Fig. 17: Inspiratory and expiratory desflurane concentration over the course of inhalation anesthesia with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also diagram of minimal-flow anesthesia procedure with oxygen-air mixture as carrier gas.

Start with 4 L/min fresh gas flow, vaporizer setting 6 vol%. Once the desired value of 0.9 MAC is reached, change the fresh gas flow to 0.5 L/min and the vaporizer setting to 8%. After 45 minutes, change the vaporizer setting to 0 vol%. Do not change fresh gas flow.

Adjust the vaporizer settings to maintain the desired value, according to whether the anesthetic concentrations are increased/reduced, using the various time constants.

3.3 Nitrous oxide uptake

Nitrous oxide is not metabolized in the body. Therefore, the uptake of N_2O is only determined by the alveolar-capillary partial pressure difference. At the start of anesthesia, this difference is large but over time it drops as gas saturation in the tissues increases. The approximate nitrous oxide uptake can be calculated, for a standard weight adult patient, using the indicated Severinghaus exponential function[29]:

$$V_{N_2O} = 1.000 \times t^{-1/2}$$

V_{N_2O} = uptake of nitrous oxide
t = time after anesthesia induction (min)

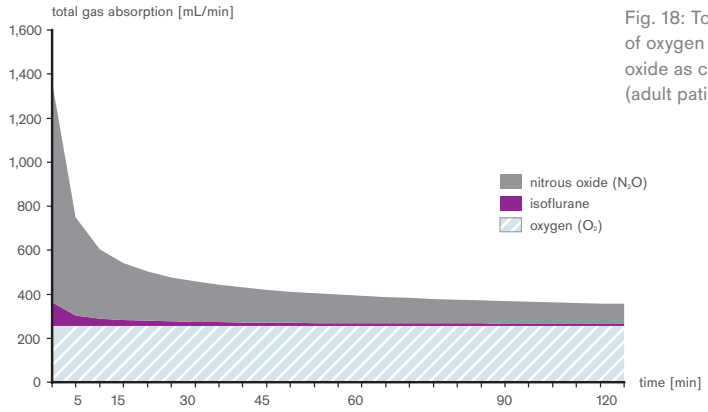

Fig. 18: Total gas uptake of oxygen with nitrous oxide as carrier gas (adult patient, 75 kg)

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3.4 Control via the MAC value

A clear distinction exists between the pharmacodynamic and pharmacokinetic behavior of volatile anesthetics. The crucial factor is the blood-gas distribution coefficient and the fat solubility of the concentrate. The anesthetic concentrate contained in the inspiratory mixture passes through the alveolar barrier, is dissolved in the blood, distributed in the various body compartments and finally reaches the target—or effect compartment—i.e. the brain.

The depth of inhalation anesthesia is determined by the concentration of anesthetics in the brain, which is directly dependent on the alveolar partial pressure as a function of the blood concentration. The depth of anesthesia is therefore established by changing the inhalation concentration of the volatile anesthetic in the expiratory breathing gas. There is a linear relationship between the potency of the anesthetic and fat solubility: the greater the fat solubility, the more potent the inhalational anesthetic and the smaller the alveolar concentration required to achieve a defined depth of anesthesia.

The MAC value is the minimal alveolar concentration of a volatile anesthetic at which 50% of patients no longer respond with a defensive reaction to an incision in the skin. The lower the MAC value of an anesthetic, the higher its potency.

The MAC value differs depending on the carrier gas used[30,31]. The MAC_{50} awake value is defined differently. This is the value at which half of patients open their eyes following anesthesia.

Thus, if we refer to the MAC value in daily use, we are referring to the MAC_{50}, which is the approximate measure for the potency of the inhalational anesthetics relative to the respective carrier gas used.

Table 1: MAC-, MAC Aware and MAC Awake values of different volatile anesthetics (modified from Heller AR et al.[30])

Anesthetic strength	MAC (vol% in O_2)	MAC AWARE (70% of MAC) (vol% in O_2)	MAC AWAKE (35% of MAC) (vol% in O_2)
Isoflurane	1.15	0.78	0.42
Sevoflurane	2.05	1.43	0.71
Desflurane	5–6	4.2	2.1

MAC values of volatile anesthetics in 40-year-old patients

FACTORS INFLUENCING THE MAC VALUE

A large number of studies show that neither the size and weight of the patient nor the duration of anesthesia have any effect on the respective MAC value. In contrast, drugs that act on the central nervous system reduce the MAC value. When using combination anesthesia on a daily basis, this is expressly desired and conceptually demanded (see balanced anesthesia, page 39). Thus, opioids and co-anesthetics, such as sedatives, reduce the MAC value. The principle of balanced anesthesia involves affecting the individual anesthesia components by combining various drugs. Ideally, this allows components (hypnosis, analgesia, muscle relaxation) to be controlled separately and, secondly, the dosage of substances used to be lowered, with the benefit of a low rate of adverse events.

Hypothermia and pregnancy, for example, also lead to a reduction in MAC values. In contrast, hyperthermia accompanied by fever, and chronic alcoholism, increase the need for inhalational anesthetics and therefore lead to higher MAC values.

BALANCED ANESTHESIA BY HÖNEMANN C.[33]

A general anesthesia that is maintained by a combination of various anesthetics with synergistic pharmacological properties is described as balanced anesthesia. Monoanesthesia, i.e. anesthesia using just one anesthetic, is virtually no longer performed in practice today.

For total intravenous anesthesia (TIVA), a hypnotic (propofol) is combined with an analgesic (e.g., remifentanil). When anesthesia is maintained by inhalation anesthesia, a combination anesthesia consisting of nitrous oxide, oxygen, air and a volatile anesthetic agent is exclusively used.

Nowadays, the term 'balanced anesthesia' is mostly associated with a combination of intravenous opioid administration (analgesia) and inhalation anesthesia (hypnosis). However, as already mentioned above, the term is not tightly defined and has already been used for other combinations of anesthetics, such as regional analgesia and inhalation anesthesia.

Balanced anesthesia is the most frequently used anesthesia procedure world-wide. General anesthesia is made up of four different basic qualities:
– Hypnosis,
– Analgesia,
– Muscle relaxation and
– Autonomic shielding.

With balanced anesthesia, this is accomplished by individual drugs based on current requirements. Anesthesia (as target or overall effect) is therefore achieved by combining different, low-dose anesthetics instead of using only one drug at a high dosage.

The individual components balance out the anesthesia. Reducing the dosages of the individual drugs causes undesirable side effects to occur more rarely and, overall, the anesthesia is subject to fewer fluctuations.

In conventional balanced anesthesia, volatile anesthetics, nitrous oxide, opioids and muscle relaxants are combined. The patient is rendered unconscious by the volatile anesthetics. Volatile anesthetics more effectively prevent the patient from experiencing phases of waking during an operation than intravenously administered hypnotics. While EEG-monitored anesthesia depth measurement appears to be essential—because of the high degree of inter-individual variability of i.v. anesthesia—for preventing the patient from waking up during the operation, it remains a subject of controversy when discussing balanced anesthesia; however, it does not seem to be necessary.

In addition, volatile anesthetics have muscle-relaxing properties and thereby enhance the effect of added muscle relaxants. Nitrous oxide and intravenously administered opioids reduce the need for volatile anesthetics by a factor of between 10 and 15%. As a result of the lower gas concentrations, the saturation of the bradytrophic tissues is also decreased. This speeds up postoperative awakening.

OTHER FACTORS INFLUENCING THE MAC VALUE

The effect of age on MAC values has been extensively described by Nickalls and Mapleson. Thus, from the 32nd week of gestation to the peak during the first year of life, the MAC value rose, then fell successively with old age [31].

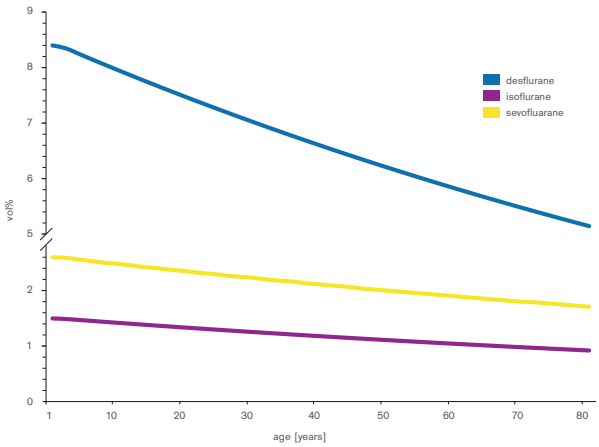

Fig. 19: Effect of age on MAC (modified from Mapleson WW et al. [34])

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The highest inhalation concentrations in the inspiration mixture are required in infants. They drop continuously with age. In order to achieve an equivalent anesthesia depth, different MAC values for the same substance in the various stages of life are required. By combining a general and a regional anesthesia procedure, volatile anesthetic agents and other hypnosis-inducing medications can be saved; the anesthetic process can be maintained at a more constant level and, with lower MAC values, can adequately isolate stimuli.

If, as is generally performed today, various groups of drugs are combined together with an i.v. opioid and a common i.v. hypnotic by pre-medicating with sedative and anesthesia induction—which is done by an volatile anesthetic agents to maintain anesthesia—MAC values of between 0.8 and 1.2 are needed to reach an adequate anesthesia depth. Exceeding these values is not reasonable neither from a pharmacological nor anesthesiological point of view.

On the contrary: Exceeding the MAC value introduces considerable risks and increases perioperative morbidity and mortality.

Current data by Eger et al. clearly document prolonged recovery time and increased mental disorder in the sense of a postoperative transitional syndrome relating to volatile anesthetic agents in the geriatric patient[32]. Correspondingly, data from large meta-analyses indicate that excessive MAC values in anesthesia during the first four years of life may be accompanied by impaired cognitive development.

> There is no rational reason to justify increasing the MAC value above 1.2.

It can be concluded from the above that the depth of anesthesia can be best controlled when using volatile anesthetics that exhibit the lowest possible solubility and thus low anesthetic potency.

As alveolar partial pressure is the deciding factor that determines the uptake of the volatile anesthetic agents, the rate at which this value increases appears to be decisive for anesthesia induction and its deepening. Alveolar pressure depends on the inspiratory concentration, alveolar ventilation, functional residual capacity and the solubility of the volatile anesthetic agents in the blood.

Therefore, we particularly recommend inhalational anesthetic agents with a low blood/gas distribution coefficient, such as exhibited by sevoflurane (0.65) and desflurane (0.45).

In contrast, isoflurane, with a comparatively high blood/gas distribution coefficient of 1.4, is not optimally suited for minimal-flow and metabolic-flow anesthesia because it leads to longer uptake and clearance.

By increasing the vaporizer setting and fresh gas flow, rapid deepening of anesthetic can be achieved with additional intravenous injection of a hypnotic drug. In addition, by closing the vaporizer, the anesthetic can be reduced if the MAC value of isoflurane is too high[28].

Table 2: Pharmacokinetic and pharmacodynamic properties of different volatile anesthetics (modified from Baum JA et al.[28])

Solubility	**Isoflurane**	**Sevoflurane**	**Desflurane**
λ Blood/gas	1.4	0.65	0.42
λ Fat/gas	64	34	12
λ Fat/blood	45	48	27
Metabolism			
Biotransformation (%)	< 1.0	3–5	< 0.1
Anesthetic strength			
MAC (vol%)	1.2	2.0	6.0
MAC Awake	0.4	0.7	2.0
MAC 3–5 years	1.6	2.5	8.6
MAC approx. 30 years	1.2	2.1	7.3
MAC approx. 70 years	1.1	1.5	5.2

3.5 Effects of reduced fresh gas flow

When a high fresh gas flow is used, the composition of the fresh gas corresponds to the one found in the circuit system (fresh gas flow > minute volume). In the case of anesthesia using a high fresh gas flow, changes in the fresh gas composition lead to rapid and similar changes in the inspiratory and expiratory anesthetics concentration in the anesthesia system. Reducing the fresh gas flow changes the composition of the gases in the circuit system compared with the composition of the fresh gas. In addition, with a low fresh gas flow, a change in gas composition in the circuit system results in a very delayed and slow change in the inspiratory and expiratory concentration of anesthetics. Accordingly, the time constant is inversely proportional to the fresh gas flow. This applies to anesthesia machines, which dose according to the fresh gas, when they are used as semi-closed systems, for example, with low-flow and minimal-flow anesthesia or with non-quantitative anesthesia in a closed system.

Particularly at the end of anesthesia, this effect can be used by stopping the anesthetic agent supply by shutting off the vaporizer approximately 10 to 15 minutes before the end of the operation. Due to the long time constant of low fresh gas flow, only a slight drop in anesthetic agent concentration in the circuit system is produced because washing out occurs slowly. Only an increase in fresh gas flow to minute volume values results in very rapid washing out of the anesthetic agent and in the recovery of the patient within a very short time.

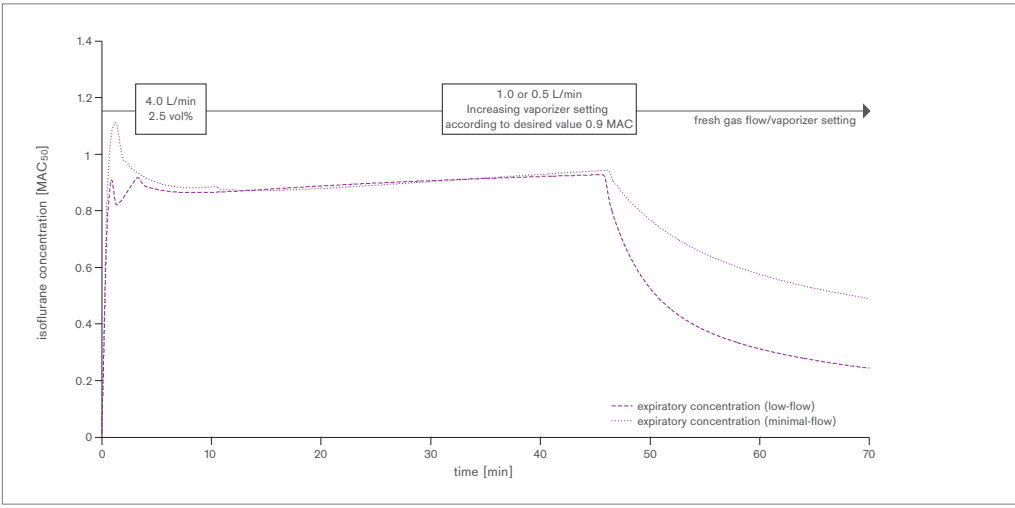

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Fig. 20: Comparison of expiratory isoflurane concentration over the course of inhalation anesthesia. Various fresh gas flows (low-flow versus minimal-flow) with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey [25]

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also procedure diagram. Minimal-flow anesthesia with oxygen/air mixture as carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 2.5 vol% isoflurane. Once the desired value of 0.9 MAC has been reached, reduce flow to 1.0 or 0.5 L/min. The lower the fresh gas flow, the higher the vaporizer settings must be in order to maintain the expiratory isoflurane concentration of 0.9 MAC.

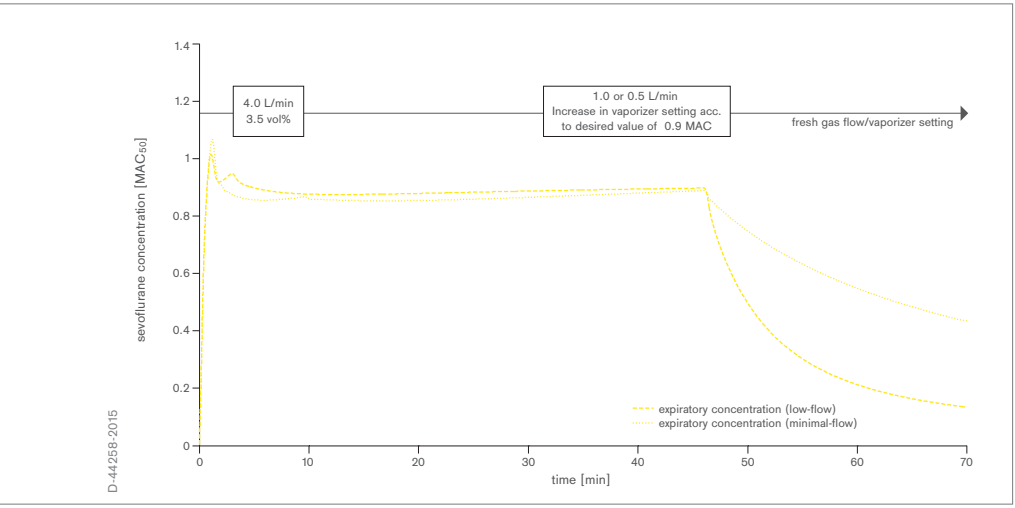

Fig. 21: Comparison of expiratory sevoflurane concentration over the course of inhalation anesthesia. Various fresh gas flows (low-flow versus minimal-flow) with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also procedure diagram. Minimal-flow anesthesia with oxygen/air mixture as carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 3.5 vol% sevoflurane. Once the desired value of 0.9 MAC has been reached, reduce flow to 1.0 or 0.5 L/min. The lower the fresh gas flow, the higher the vaporizer settings must be in order to maintain the expiratory sevoflurane concentration of 0.9 MAC.

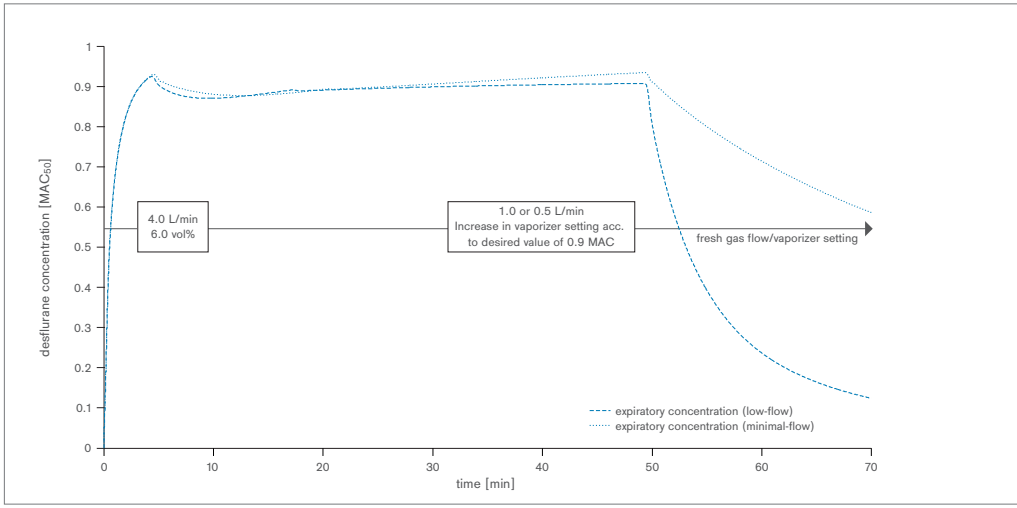

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Fig. 22: Comparison of expiratory desflurane concentration over the course of inhalation anesthesia. Various fresh gas flows (low-flow versus minimal-flow) with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey [25]

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also procedure diagram. Minimal-flow anesthesia with oxygen/air mixture as carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 6 vol% desflurane. Once the desired value of 0.9 MAC has been reached, reduce flow to 1.0 or 0.5 L/min. The lower the fresh gas flow, the higher the vaporizer settings must be in order to maintain the expiratory desflurane concentration of 0.9 MAC.

3.6 Monitoring

For monitoring purposes, we restrict ourselves to the anesthesia gas composition in the circuit system. This is mainly a function of the settings of the different gases (O_2, air, N_2O plus volatile anesthetics) and the patient's uptake. While with a high fresh gas flow in the circuit system the gas composition is similar to that of the fresh gas, with low-gas flow the composition differs considerably from that of the fresh gas. Routine monitoring of the patient hemodynamics is completely independent of the fresh gas flow chosen.

Technical mandates and recommendations by professional anesthesia organizations (DGAI, BDA)*, as well as current schools of thought, thus regulate the necessary monitoring. This includes, among others, constant presence and clinical monitoring of the patient by the anesthetist. Monitoring also includes continuous reading of the electrocardiogram, regular checks of blood circulation parameters, measurement of respiratory tract pressure and expiratory volume. For the monitoring, the regulations apply to ISO 21647 or ISO 80601-2-55. Continuous monitoring of the inspiratory oxygen concentration, of the expiratory anesthesia gas concentration and expiratory CO_2 concentration, of the respiratory tract pressure and minute volume are mandatory. For this purpose, an automated algorithm that triggers the alarms is required. In particular, the inspiratory oxygen concentration must be monitored by an alarm system. The alarm should be set to a FiO_2 of 28% in order to prevent hypoxia.

*DGAI = german association for anesthesia and intensive care
BDA = professional association of German anesthesiologists

Because of the large difference between anesthesia gases (fresh gas composition—gas concentration in the circuit system), the monitoring of inspiratiory and expiratory anesthesia gas concentration is extremely important, especially for less experienced user of low- and minimal-flow anesthesia. Concentrations of anesthetic agents, oxygen and CO_2 must be monitored—inspiratory and expiratory.

Chemical elimination of carbon dioxide from the circuit system is of vital importance. With rebreathing systems, it must always be ensured that the carbon dioxide absorber is not depleted, because an accumulation of carbon dioxide in the circuit system results in respiratory acidosis. The change of color of the state of the art soda limes does not provide adequate safety.

04 Performing minimal-flow anesthesia

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04 Performing minimal-flow anesthesia

4.1 Minimal-flow anesthesia with oxygen/air mixture as carrier gas

SCHEMATIC PROCEDURE*

Premedication

Premedication according to usual model

Induction

- Pre-oxygenation with 100% oxygen at 6 L/min for 1 to 3 minutes, with a face mask
- Intravenous administration of the hypnotic or inhalation induction
- Analgesia and relaxation (attention: There might be a need for 20'% higher dosing of induction opioid)
- Endotracheal intubation or insertion of a laryngeal mask
- Connection of patient to the circuit system

Initial phase

- Fresh gas flow settings

  Oxygen 1 L/min, air 3L/min (40% oxygen and 4 L/min fresh gas flow)
- Vaporizer settings (see also figures 21 to 23)

Isoflurane	2.5 vol%
Sevoflurane	3.5 vol%
Desflurane	6 vol%
- The inspiratory oxygen concentration will stabilize between 35 and 40 vol%.

* All values are clinically tested orientation values. However, in individual cases they must be adapted according to the individual response by the patient, the performance characteristics of the machines used and the operational requirements.

These schematic instructions are also available as a hard copy. They are available directly from Dräger.

Once the target MAC value of 0.8 to 1 has been reached

- Reduction of fresh gas flow for oxygen to 0.3 L/min, for air to 0.2 L/min (68% oxygen and 0.5 L/min fresh gas flow)
- Increase of vaporizer setting for

Isoflurane to	5 vol%
Sevoflurane to	5 vol%
Desflurane to	8 vol% (see also figures 20 to 22)

Monitoring

- Inspiratory oxygen concentration with a lower alarm threshold of at least 28 vol%.
- Minute volume: set lower alarm threshold to 0.5 L/min below the desired target value.
- Monitoring of the anesthetic agent concentration in the breathing system: set upper limits for isoflurane to 2 to 2.5 vol%, for sevoflurane to 3 to 3.5 vol% and for desflurane to 8 to 10 vol%.

Reversal

- Reduction of vaporizer setting to 0% approximately 10 minutes before end of operation.
- Maintaining low flow of 0.5 L/min.
- Switching to spontaneous breathing.
- Following completion of suture, prior to extubation: purging of the system with 100% oxygen at 6 L/min.
- Postoperative care of the patient according to the usual internal procedures of the department.

4.1.1 Practical hints

Increasing the anesthetic agent concentration using the long time constant

- Fresh gas flow remains unchanged at approximately 0.5 L/min.
- Increase the vaporizer setting by 1 to 2 vol% (sometimes even to the maximum output).
- Once the desired concentration is reached, set the vaporizer to a value of 0.5 to 1 vol% higher than the target value.

Reducing the anesthetic agent concentration using the long time constant

- The fresh gas flow remains unchanged at 0.5 L/min.
- Reduce the vaporizer setting by 1 to 3.5 vol%.
- Once the desired low concentration is achieved, reset the vaporizer to the previous setting.

Rapid change of anesthesia depth using a short time constant

- Set the vaporizer to a value of 0.5 to 1 vol% above or below the desired quantity of anesthesia gas.
- Increase the fresh gas flow to 4 L/min (1 L oxygen, 3 L air).
- Once the desired anesthetic agent concentration is reached—as a rule after approximately 5 minutes—the fresh gas flow must again be reduced to 0.5 L/min.
- For all low-flow anesthesia, measuring the expiratory end-tidal anesthetic agent concentration in the breathing system is mandatory. As an alternative to short-term deepening of the anesthesia by increasing the fresh gas flow, additional intravenous injection of the hypnotic or analgesic should be considered.

Warning—inspiratory O_2 alarm

– If with the chosen setting, the inspiratory oxygen concentration drops to less than 28 vol%, increase the fresh gas flow of oxygen from 0.3 to 0.5 L/min and reduce air to 0 L/min (100% oxygen and 0.5 L/min fresh gas flow).

Warning—fresh gas flow too low

– The minute volume drops, airway peak pressure drops, the machine sounds fresh gas alarm, the reservoir bag collapses.
– Fill the breathing system by increasing the fresh gas flow to 4 L/min (1 L oxygen, 3 L air).
– Search for leakage (hole in hose system, bag valve mask, CO_2 absorber correctly secured?). If the leakage cannot be repaired, increase the fresh gas flow by 0.5 L/min and switch to low-flow anesthesia at 1 L/min (0.3 L/min oxygen and 0.7 L/min air or 45% oxygen and 1 L/min fresh gas flow).

Fresh soda lime is essential

– Observe the inspiratory CO_2 concentration and the soda lime. If the inspiratory CO_2 concentration increases, this is an indication that the soda lime should be replaced.

4.1.2 Discussion of the use of an oxygen/air mixture

The advantages of performing minimal-flow anesthesia with an oxygen/air mixture are that the process can be simplified and accelerated. For example, not using nitrous oxide simplifies minimal-flow and metabolic-flow anesthesia drastically because any surgical contraindications (intracerebral interventions, distension of air-filled body cavities) as well as gas volume

fluctuations (for example, as a result of the second gas effect) do not have to be considered. Not using nitrous oxide also accelerates the process of shorter high-flow phases. Ensuring sufficient denitrogenation and the avoidance of volume imbalances are only of secondary importance.

As a result of this procedure and the rapid reduction to a low fresh gas flow of 0.5 L/min—once a MAC value of 0.8 has been reached—considerable cost saving can be expected. This is due to the fact that according to current investigations, 60 to 70% of volatile anesthetics consumption takes place during the first ten minutes of the wash-in phase. It must be ensured during the initial distribution phase that the fresh gas volume supplied is not lower than the gas losses caused by individual gas uptake and system leakages.

In order to alert to a fresh gas deficit in the anesthesia system, a fresh gas deficit alarm is installed, for example, in Dräger machines. In addition, the Low Flow Wizard may be useful as the preferred 'early warning system' when carrying out low- and minimal-flow anesthesia for discovering fresh gas deficits (for example, leaks). Checking the filling of the bag valve mask which is always available as a reservoir for the anesthesia machine, however, requires the user to adequately check the volume balance.

The air humidified at normal body temperature has the following partial pressures in kPa, under BTPS (body temperature pressure saturated) conditions, i.e., 37°C, barometric pressure = 100 kPa = 747 mmHg):

pO_2 = 19.6 kPa
pCO_2 = 0 kPa
pN_2 = 74.1 kPa (this also includes all noble gases under nitrogen, such as argon and xenon etc.)
pH_2O = 6.3 kPa

If we proceed according to the regime described above when carrying out anesthesia with low fresh gas flow, an inspiratory O_2 concentration of 35 to 40% is reached.

During interventions of longer duration, gases of low solubility may accumulate (nitrogen, methane, argon, hydrogen). Concentrations of these gases that were problematic or hazardous to health were not detected in any case. Only nitrogen can develop in the system in such a notable concentration that both oxygen and nitrous oxide concentrations are affected. By performing intermittent flushing phases with a fresh gas flow of 5 L/min gases with low solubility can be washed out. For each case, therefore, precise setting of the alarm thresholds is essential. In our hospitals, the alarm threshold is set at the minimum inspiratory O_2 concentration of 28%.

When oxygen is used exclusively as the carrier gas, minimal-flow anesthesia is safer with regard to risks of accidental hypoxaemia, and it is easier to perform.

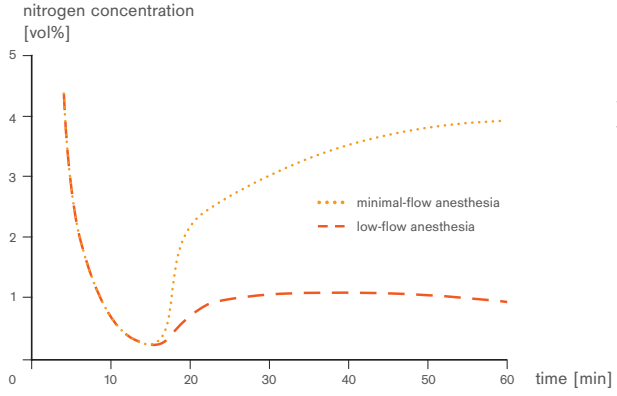

Fig. 23: Nitrogen accumulation in the breathing system, patient weight 75 kg (modified from Baum JA et al.[8])

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4.2 Minimal-flow anesthesia with oxygen as carrier gas

SCHEMATIC PROCEDURE* (FROM A PATIENT AGE OF > 6 MONTHS)

Premedication

Premedication according to usual model

Induction

- Pre-oxygenation with 100% oxygen at 6 L/min for 1 to 3 minutes, with a face mask
- Intravenous administration of the hypnotic or inhalation induction
- Analgesia and relaxation (attention: There might be a need for 20'% higher dosing of induction opioid)
- Endotracheal intubation or insertion of a laryngeal mask
- Connection of patient to the circuit system

Initial phase

- Duration 1 to 8 minutes—fresh gas flow settings
  100% oxygen 1 L/min,
- Vaporizer settings

Isoflurane	5 to 6 vol%
Sevoflurane	5 to 6 vol%
Desflurane	12 vol%

- The inspiratory oxygen concentration will stabilize between 60 and 80 vol% depending on age and weight.

* All values are clinically tested orientation values. However, in individual cases they must be adapted according to the individual response by the patient, the performance characteristics of the machines used and the operational requirements.

These schematic instructions are also available as a hard copy. They are available directly from Dräger.

Once the target MAC value of 0.8 to 1 has been reached

- Reduction of fresh gas flow for 100% oxygen to 0.25 to 0.35 L/min
- Change of anesthetic agent concentration—see practical hints (page 60)

Monitoring

- Inspiratory oxygen concentration with a lower alarm threshold of at least 28 vol%.
- Minute volume: set lower alarm threshold to 0.5 L/min below the desired target value.
- Monitoring the anesthetic agent concentration in the breathing system: set upper limits for isoflurane to 2 to 2.5 vol% for sevoflurane to 3 to 3.5 vol%, and for desflurane to 8 to 10 vol%.

Reversal

- Reduction of vaporizer setting to 0% approximately 10 to 15 minutes before end of operation.
- Maintaining low flow of 0.35 L/min.
- Switching of patient to spontaneous breathing.
- Following completion of suture, prior to extubation: purging of the system with 100% oxygen at 6 L/min.
- Postoperative care of the patient according to the usual internal procedures of the department.

4.2.1 Practical hints

Increasing the anesthetic agent concentration using the long time constant

- Fresh gas flow remains unchanged at 0.35 L/min.
- Increase the vaporizer settings to maximum output. Special feature of isoflurane: deepening of the anesthesia with isoflurane alone should only be established at maximum isoflurane vaporizer output, while simultaneously increasing the fresh gas flow.
- Once the desired concentration is reached, set the vaporizer to:

Isoflurane	maximum output: 5 or 6 vol%
Sevoflurane	5 to 7 vol%
Desflurane	12 to 14 vol%

Reducing the anesthetic agent concentration using the long time constant

- The fresh gas flow remains unchanged at 0.35 L/min.
- Close the vaporizer; shortly before the desired low concentration is reached, set the vaporizer to:

Isoflurane	4.5 vol%
Sevoflurane	4.5 to 5 vol%
Desflurane	8 to 12 vol%

Rapid change of anesthesia depth using a short time constant

- Increase the fresh gas flow to 4 L/min, 100% oxygen (Warning: adjust/reduce vaporizer setting if necessary).
- Once the desired anesthetic agent concentration is reached—as a rule after 1 to 3 minutes—reduce the fresh gas flow again to 0.35 L/min.
- Set vaporizer to:

Isoflurane	maximum output: 5 or 6 vol%
Sevoflurane	4.5 to 5 vol%
Desflurane	8 to 12 vol%

– For all low-flow anesthesia, measuring the expiratory end-tidal anesthetic agent concentration in the breathing system is mandatory. As an alternative to short-term deepening of the anesthesia by increasing fresh gas flow, additional intravenous injection of the hypnotic or analgesic should be considered.

Warning—inspiratory O_2 alarm

– If with the chosen setting, the inspiratory oxygen concentration drops to less than 28 vol%, increase the fresh gas flow of oxygen to 0.5 L/min.
– Check the system for leakages
– Check the plausibility of the oxygen measurement

Warning—fresh gas flow too low

– The minute volume drops, airway peak pressure drops, the machine sounds fresh gas alarm, the reservoir bag collapses.
– Fill the breathing system by increasing the fresh gas flow to 2 L/min for roughly one minute.
– Search for leakage (hole in hose system, bag valve mask, CO_2 absorber correctly secured?). If the leakage cannot be repaired, increase the fresh gas flow with 100% oxygen by 0.5 L/min and switch to minimal-flow or low-flow anesthesia at 1 L/min.

Fresh soda lime is essential

– Observe the inspiratory CO_2 concentration and the soda lime. If the inspiratory CO_2 concentration increases, this is an indication that the soda lime should be replaced.

4.2.2 Discussion of the use of pure oxygen

In general, the logical consequence of using minimal-flow anesthesia and omitting an oxygen/nitrous oxide or oxygen/air mixture is metabolic-flow anesthesia.

By using pure oxygen as the carrier gas, denitrogenation can be omitted at the start of inhalational anesthesia because nitrous oxide does not have to be washed in. The advantages of rebreathing systems can therefore be used right from the start. An initially high fresh gas flow is only briefly needed or not at all.

The vaporizer output for isoflurane is 5 to 6% (depending on manufacturer and model year), 8% for sevoflurane and 18% for desflurane. Following pre-oxygenation, a low fresh gas flow can be selected at the start of inhalational anesthesia. The level of fresh gas flow is dependent on the time during which an adequate anesthesia gas concentration is to be established. The higher the fresh gas flow, the more rapidly the desired anesthesia gas concentration is achieved in the rebreathing system. The lower the fresh gas flow, the slower the volatile anesthetic agent concentration increases.

From our clinical experience we recommend a fresh gas flow of 0.5 to 1 L/min in order to reach an adequate anesthetic agent concentration in the circuit system. This allows reaching a MAC value of 0.9 within 5 to 7 minutes for any modern anesthetic agent. This timeframe is indicated because by administering an intravenous hypnotic (thiopental, propofol) for 7 to 9 minutes an adequate depth of hypnosis is induced. As the plasma concentration of the hypnotics falls, the concentration of the inhalational anesthetics increases.

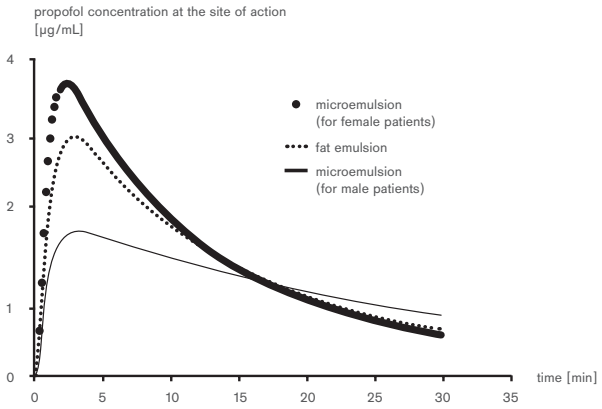

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Fig. 24: Simulation of an intravenous bolus of propofol 2 mg/kg in various emulsions (microemulsion and fat emulsion) in a person with a weight of 65 kg, a height of 170 cm, and an age of 44 years. Concentration in the effect compartment (modified from Kim KM et al.[35])

Modern anesthesia gases are metabolized to an only minor extent, have low solubility and are therefore easy to control. As a result, the time for washing in the anesthesia gases into the circuit system is defined in a simplified way by the following factors: for the most part it depends on the volume of the circuit system and the maximum vaporizer output, as well as on the patient's lung capacity and body weight.

This fact is confirmed by studies concerning the influx rates of the anesthesia gases sevoflurane and desflurane in anesthesia machines.[36] As can be seen from the following figures, the rates only differ slightly and are not clinically relevant (fresh gas flow 0.5 L/min to 1 L/min for influx in fresh gas mode). For isoflurane, on the other hand, this can only be achieved with a fresh gas flow of 1 L/min (see figure 29).

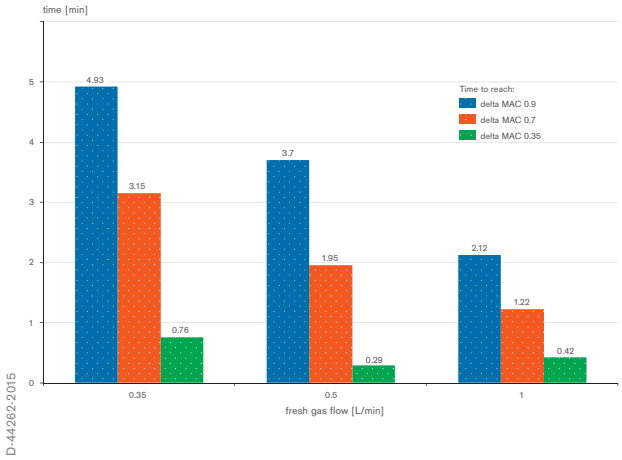

Fig. 25: Semi-closed system—sevoflurane

Maximum vaporizer output 8 vol% (this corresponds to roughly 4 × MAC)

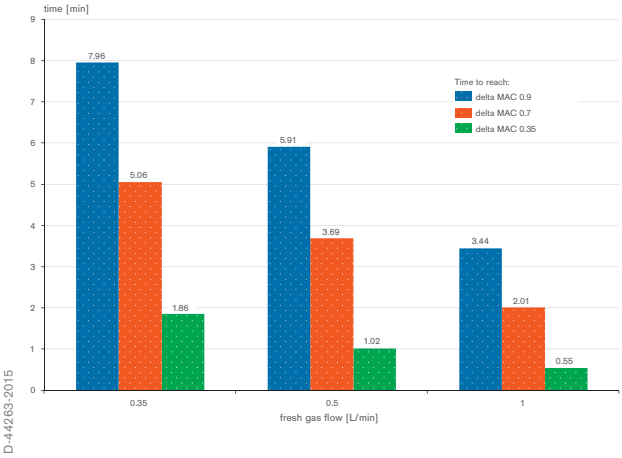

Fig. 26: Semi-closed system—desflurane

Maximum vaporizer output 18 vol% (this corresponds to roughly 3 × MAC)

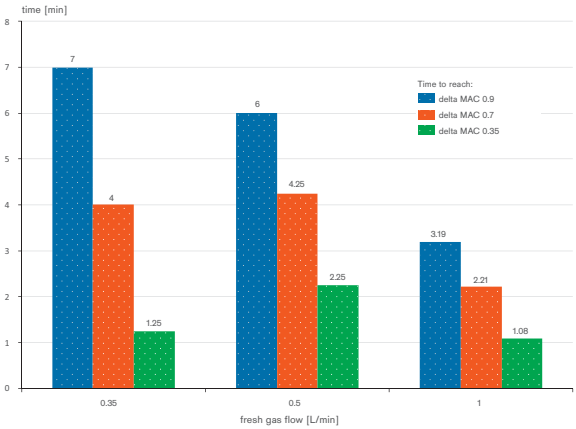

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Fig. 27: Closed System—sevoflurane—influx in fresh gas mode

Maximum vaporizer output 8 vol% (this corresponds to roughly 4 × MAC)

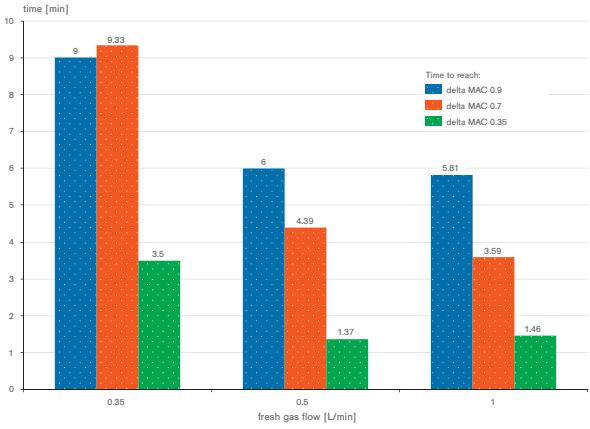

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Fig. 28: Closed System—desflurane—influx in fresh gas mode

Maximum vaporizer output 18 vol% (this corresponds to roughly 3 × MAC)

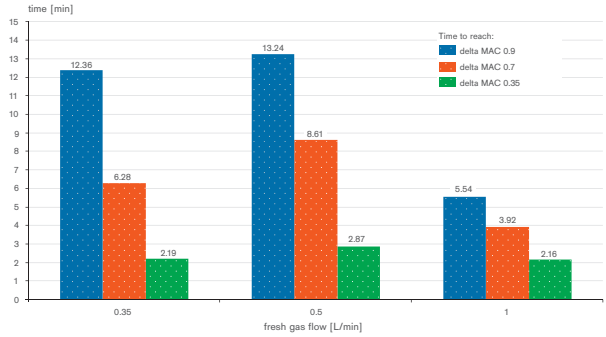

Fig. 29: Semi-closed system—isoflurane

Maximum vaporizer output 5 vol% (this corresponds to roughly 4 × MAC)

Note: All data in figures 21 to 25 originate from reference [36].

Once the anesthesia gas concentration in the circuit system has reached the desired value (e.g., MAC 0.9), the fresh gas flow can be further reduced (e.g., from 0.5 to 0.35 L/min, 100% O_2). This type of procedure enables adequate use of the rebreathing system.

As in the case of minimal-flow anesthesia, the vaporizer can be shut off roughly 10 minutes before the end of the operation.

At the same time as the last suture is performed, the fresh gas flow is increased to 4 to 6 L/min in order to wash out the anesthesia gas. An even higher fresh gas flow in the reversal phase does not wash out the anesthesia gas more rapidly because with a fresh gas flow of 4 to 6 L/min, the rebreathing portion is already below 2.5%. Increasing the fresh gas flow three-fold to 18 L/min reduces rebreathing from 2.5 to only roughly 0.75% and will clinically cause only minor acceleration of reversal.

With metabolic-flow anesthesia, despite the significant reduction in fresh gas flow, a certain excess volume of gas and maintaining a standardized fresh gas composition are not omitted. This process can be carried out during routine clinical procedure, as described by Professor Baum. This means yet another distinct simplification of low- and minimal-flow anesthesia when using pure oxygen as carrier gas compared with low- and minimal-flow anesthesia using oxygen/air mixture or oxygen/nitrous oxide mixture as carrier gas[9].

In the Vechta and Damme hospitals, more than 100,000 anesthesia procedures with oxygen as carrier gas have been documented since 2004[37, 38].

4.3 Minimal-flow anesthesia with oxygen/nitrous oxide mixture as carrier gas

SCHEMATIC PROCEDURE*

Premedication

Premedication according to usual model

Induction

- Pre-oxygenation with 100% oxygen at 6 L/min for 1 to 3 minutes, with a face mask
- Intravenous administration of the hypnotic or inhalation induction
- Analgesia and relaxation
- Endotracheal intubation or insertion of a laryngeal mask
- Connection of patient to the circuit system

Initial phase

- Fresh gas flow settings
  Oxygen 1.4 L/min, nitrous oxide 3L/min
  (32% oxygen and 4.4 L/min fresh gas flow)
- Vaporizer settings

Isoflurane	1 to 1.5 vol%
Sevoflurane	2 to 2.5 vol%
Desflurane	4 to 6 vol%

- The inspiratory oxygen concentration will settle between 30 and 40 vol%

* All values are clinically tested orientation values. However, in individual cases they must be adapted according to the individual response by the patient, the performance characteristics of the machines used and the operational requirements.

These schematic instructions are also available as a hard copy. They are available directly from Dräger.

Once the target MAC value of 0.8 to 1 has been reached

- Reduction of fresh gas flow to a total of 0.5 L/min (oxygen 0.3 L/min, nitrous oxide 0.2 L/min, 60% oxygen and 0.5 L/min fresh gas flow)
- Increase of vaporizer setting

Isoflurane to	2.5 vol%
Sevoflurane to	3 to 3.5 vol%
Desflurane to	5 to 7.5 vol%

Monitoring

- Inspiratory oxygen concentration with a lower alarm threshold of at least 28 vol%.
- Minute volume: set lower alarm threshold to 0.5 L/min below the desired value.
- Monitoring of the anesthetic concentration in the breathing system: Set upper limits for isoflurane to 2 to 2.5 vol% for sevoflurane to 3 to 3.5 vol%, and for desflurane to 8 to 10 vol%.

Reversal

- Reduction of the vaporizer setting to 0% approximately 10 to 15 minutes before end of operation.
- Maintaining the low flow of 0.5 L/min.
- Switch to spontaneous breathing.
- Following completion of suture, prior to extubation: Purging of the system with 100% oxygen at 6 L/min.
- Postoperative care of the patient according to the usual internal procedures of the department.

4.3.1 Practical hints

Increasing the anesthetic agent concentration using the long time constant

- Fresh gas flow remains unchanged at approximately 0.5 L/min.
- Increase the vaporizer setting by 1 to 2 vol% (sometimes even up to maximum output).
- Once the desired concentration is reached, set the vaporizer to a value of 0.5 to 1 vol% higher than the desired target value.

Reducing the anesthetic agent concentration using the long time constant

- The fresh gas flow remains unchanged at 0.5 L/min.
- Reduce the vaporizer setting by 1 to 3.5 vol%.
- Once the desired low concentration is reached, set the vaporizer to the previous setting.

Rapid change of anesthesia depth using a short time constant

- Set the vaporizer to a value of 0.5 vol% above or below the desired quantity of anesthesia gas.
- Increase the fresh gas flow to 4.4 L/min, (1.4 L oxygen, 3 L nitrous oxide).
- Once the desired anesthetic concentration is reached—as a rule after approximately 5 minutes—reduce the fresh gas flow again to 0.5 L/min (0.3 litres oxygen, 0.2 litres nitrous oxide).
- For all low-flow anesthesia, measuring the expiratory end-tidal anesthetic agent concentration in the breathing system is mandatory. As an alternative to short-term deepening of the anesthesia by increasing fresh gas flow, an additional intravenous injection of the hypnotic or analgesic should be considered.

Warning—inspiratory O_2 alarm

– If with the chosen setting, the inspiratory oxygen concentration drops to less than 28 vol%, increase the fresh gas flow of oxygen from 0.3 to 0.35 L/min and reduce the nitrous oxide from 0.2 to 0.15 L/min (70% oxygen and 0.5 L/min fresh gas flow).

Warning—fresh gas flow too low

– The minute volume drops, airway pressure drops, the machine sounds fresh gas alarm, the reservoir bag collapses.
– Top up the breathing system by increasing the fresh gas flow to 4.4 L/min (1.4 L oxygen, 3 L nitrous oxide).
– Search for leakage (hole in hose system, bag valve mask, CO_2 absorber correctly secured?). If the leakage cannot be repaired, increase the fresh gas flow by 0.5 L/min and switch to low-flow anesthesia at 1 L/min (0.4 L/min oxygen and 0.6 L/min nitrous oxide, 40% oxygen and 1 L/min fresh gas flow).

Fresh soda lime is essential

– Observe the inspiratory CO_2 concentration and the soda lime. If the inspiratory CO_2 concentration increases, it is an indication that the soda lime should be replaced.

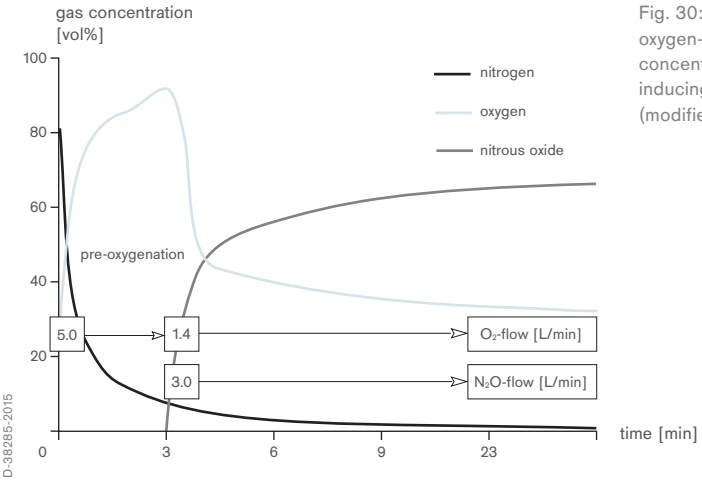

Fig. 30: Inspiratory oxygen- and nitrous oxide concentration when inducing the anesthesia (modified from Baum J [28])

4.3.2 Discussion

IS THIS PROCEDURE STILL UP-TO-DATE?

Dinitrogen monoxide or nitrous oxide (N_2O) is one of several oxides of nitrogen. This gas is also described in the literature as nitrous oxide. In 1772, the American chemist, Joseph Priestley, discovered the Colorless nitrous oxide. Humphry Davy (1778 to 1829), also an English chemist, is considered today to be the first person to describe its analgesic effect (1799). During the first half of the 19th century, however, nitrous oxide was mainly used in performances at fairs and marketplaces because of its stimulating effect. There are even reports of nitrous oxide parties. The Scottish dentist Horace Wells was the first to scientifically examine the topic. Nitrous oxide was first used for tooth extractions in 1844. Once its analgesic effect was established, nitrous oxide was the globally most frequently used of all anesthesia gases.

When the use of nitrous oxide in anesthesia is discussed, it should be remembered that the maximum additive anesthetic effect by nitrous oxide is rather insignificant. Thus, it can be replaced by increasing the concentration of volatile anesthetic by no more than the 0.1- to 0.15-fold MAC value. In order to replace the effect of nitrous oxide, opioids (e.g., sufentanyl, remifentanyl or alfentanyl) may be used as alternatives. These have not only an additive effect, but are also easy to control.

Furthermore, clearly defined contraindications must be observed when using nitrous oxide. Especially with certain risky interventions performed in neurosurgery that may lead to a reduction in compliance and an increase in brain pressure nitrous oxide has meanwhile become dispensable. New anesthetics can be used by supporting treatment with effective, modern antiemetics.

In heart surgery, it is better to omit nitrous oxide because of possible myocardial depressions and increases in pulmonary resistance. The same applies to visceral surgery because of the risk of ileus. Due to the increasing cost pressure—not only since the introduction of diagnosis-related groups (DRGs) in Germany—a cost-to-benefit ratio consideration is sensible today.

Apart from very effective antiemetics, new anesthetics can allow to completely omit nitrous oxide. In addition, given the increasing cost pressure, the cost-to-benefit analysis must be considered. Against this background, the use of nitrous oxide as an additive appears rather negligible.

Experiences from our own clinical practice, as well as from two hospitals shows that consistent omission of nitrous oxide during the performance of more than 100,000 inhalational anesthesia, as well as intravenous anesthesia, has so far shown to be entirely unproblematic.

However, the positive and negative properties are the subject of great controversy. While some still support use, others completely omit nitrous oxide. For many anesthetists nitrous oxide is a known and trusted component of the carrier gas in anesthesia rebreathing systems. The arguments mentioned are relatively easy controllability and a notable analgesic effect, among others. The sympathomimetic effect of nitrous oxide can compensate for the depressive effect of inhalational anesthesia on circulation. Anesthetics may also be saved. In addition, a second gas effect during mask inhalation induction appears to accelerate the effect of the inhalational anesthetics. Nitrous oxide actively protects against intraoperative awareness and suppresses spinal defensive reflexes caused by anesthetics.

Despite the advantages listed, many arguments against the further routine use of nitrous oxide are [39]:

- In animal experiments, nitrous oxide is embryo toxic and teratogenic compared with nitrogen.
- Nitrous oxide is ecologically harmful and contributes to the greenhouse effect.
- In the overall concept, its contribution during inhalational anesthesia is rather of minor importance.
- With prolonged use of nitrous oxide, megaloblastic changes to the bone marrow may occur.
- This leads to corresponding changes in the peripheral blood picture that can be attributed to vitamin B_{12} shortage. This may be accompanied by inhibition of DNA synthesis and result in demyelination processes in nerve cells. In the past years, there have been reports of severe neurological disorders which occurred particularly amongst strict vegetarians and vegans even after comparatively short anesthesia using nitrous oxide.
- Nitrous oxide leads to cerebral vasodilation and hence to increased intracranial pressure. This occurs particularly among patients with limited cerebral compliance. Following its concentration gradient, nitrous oxide diffuses into air-filled cavities and spaces in the body. If these spaces are compartmentalized, an increase in pressure or expansion of these spaces may occur resulting in contraindications for the use of nitrous oxide:
  - ileus,
  - pneumothorax,
  - pneumomediastinum,
  - pneumopericardium,
  - operations on the middle ear,
  - air embolisms,
  - neurosurgical and cardiosurgical interventions and operations on the open ear.

Further arguments for dispensing with the use of nitrous oxide are of rather technical nature. Thus, a central nitrous oxide supply is completely unnecessary. This results in potential savings associated with logistics and technical maintenance. The gas dosing systems in anesthesia machines can be simplified. If nitrous oxide is consistently omitted anesthesia using almost closed systems can be achieved even with conventional anesthesia machines in routine clinical practice.

The strongest argument against the use of nitrous oxide is that it is a hypoxic gas. This means that oxygen from the outside must be admixed.

05 Technical requirements of the anesthesia machine

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05 Technical requirements of the anesthesia machine

5.1 Technical requirements of the anesthesia machine

The latest-generation Dräger anesthesia machines meet all requirements to ensure safe execution of minimal-flow anesthesia. The dosage systems and vaporizers/evaporators operate with a high degree of accuracy—even in the lowest flow range. The compact breathing systems are tightly sealed. The machines are also equipped with a sophisticated monitoring system. This guarantees continuous monitoring of the inspiratory oxygen concentration, the airway pressure, the minute volume and the concentration of anesthetic agent (for a flow of less than 1 L/min). This technical safety design is a mandatory requirement by national and international standards and regulations.

5.2 Maximum vaporizer output depending on anesthesia gas

Conventional anesthesia systems consist of a breathing circuit into which fresh gas is fed. Volatile anesthetics are mixed with the fresh gas flow and also supplied to the breathing circuit. This means that, depending on the fresh gas supply and size of the breathing circuit in question, the gas composition in the fresh gas and in the circuit may be completely different (see figures 5, 6 and 7: gas flow diagrams using Apollo® and Perseus® A500 rebreathing systems as examples).

So that sufficient anesthesia gas can still be fed into the circuit when the fresh gas flow is reduced, the maximum vaporizer output is of vital importance. During the steady-state anesthesia phase, however, the vaporizer output very quickly reaches its limits when the fresh gas flow is low. Thus, the maximum vaporizer output is no longer three—to five-fold MAC of the respective anesthesia gas. For example, at a fresh gas flow of 250 L/min, vaporizers supply no more than 12.5 mL/min gaseous isoflurane, 20 mL/min sevoflurane or 45 mL/min desflurane to the fresh gas system.

Desflurane and sevoflurane best meet the requirements for establishing the required expiratory concentration of anesthesia gas. In particular, sevoflurane and desflurane are characterized by their lower solubility. A comparatively ‘high’ maximum output rate of both gases by the vaporizer using the lowest fresh gas flow is recommended for use in the closed system.

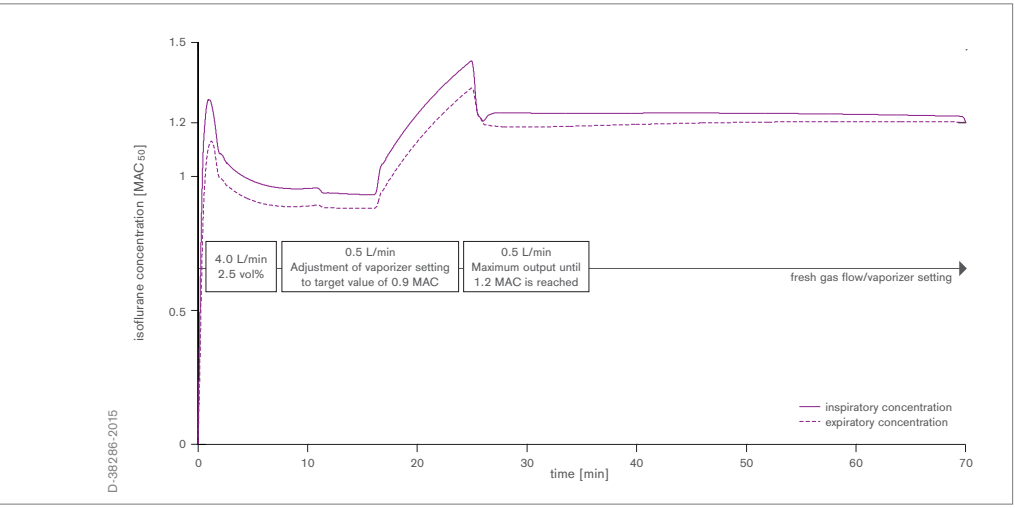

Fig. 31: Inspiratory and expiratory isoflurane concentration over the course of inhalation anesthesia. Relationship between fresh gas flow and maximum vaporizer setting with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey [25]

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anesthesia procedure with oxygen/air mixture as the carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 2.5 vol% isoflurane. Once the target value of 0.9 MAC is reached, reduce the flow to 0.5 L/min and adjust the vaporizer setting to the target value of 0.9 MAC.

Note: For longer anesthesia cases (> 90 minutes), the vaporizer setting must be accordingly corrected downwards so that the target value of 0.9 MAC is maintained.

After 15 minutes, increase the vaporizer setting to the maximum output until the expiratory concentration of 1.2 MAC is reached.

Particular feature of isoflurane: For metabolic-flow anesthesia with a fresh gas flow of 0.25 L/min to 0.35 L/min, the target isoflurane concentration of 1.2 MAC using the long time constant can only be reached by increasing the vaporizer setting to the maximum output while simultaneously increasing the fresh gas flow.

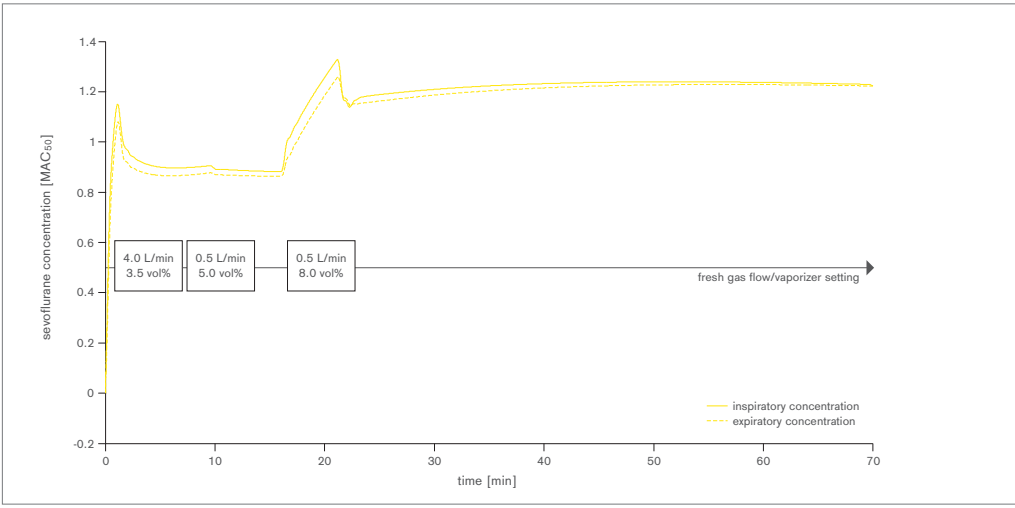

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Fig. 32: Inspiratory and expiratory sevoflurane concentration over the course of inhalation anesthesia. Relationship between fresh gas flow and maximum vaporizer setting with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anesthesia procedure with oxygen/air mixture as the carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 3.5 vol% sevoflurane. Once the target value of 0.9 MAC is reached, reduce the flow to 0.5 L/min and increase the vaporizer setting to 5 vol%. After 15 minutes, increase the vaporizer setting to maximum output (in this case 8 vol%) until the expiratory concentration of 1.2 MAC is reached.

At a constant flow of 0.5 L/min, the target sevoflurane concentration of 1.2 MAC can be reached using the long-time constant by increasing the vaporizer setting to the maximum output.

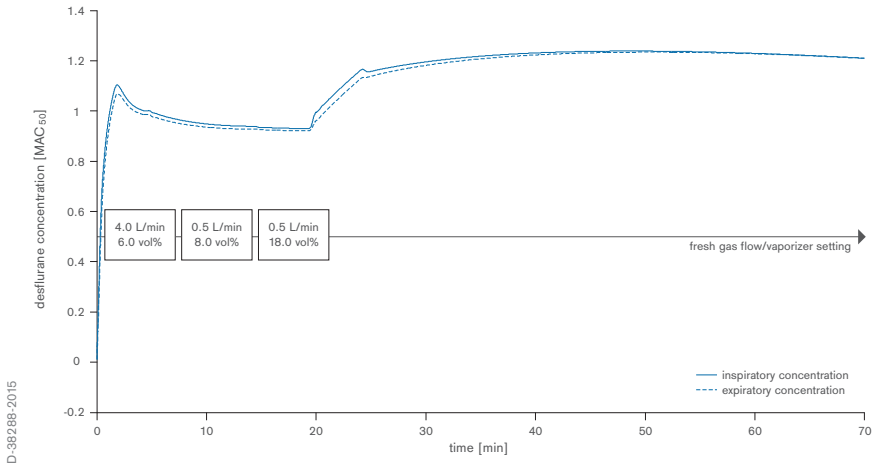

Fig. 33: Inspiratory and expiratory desflurane concentration over the course of inhalation anesthesia. Relationship between fresh gas flows and maximum vaporizer setting with O_2/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey[25]

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anesthesia procedure with oxygen/air mixture as the carrier gas (page 52/53).

Initial phase with 4.0 L/min and a vaporizer setting of 6 vol% desflurane. Once the target value of 0.9 MAC is reached, reduce the flow to 0.5 L/min and increase the vaporizer setting to 8 vol%. After 15 minutes, increase the vaporizer setting to maximum output (in this case 18 vol%) until the expiratory concentration of 1.2 MAC is reached.

At a constant flow of 0.5 L/min, the target desflurane concentration of 1.2 MAC can be reached using the long-time constant by increasing the vaporizer setting to the maximum output.

5.3 Circuit system volume and time constant

The time constant describes the time during which setting changes at the gas dosing unit lead to a corresponding change of the gas composition in the breathing system.

$$T = V_S / (V_D - V_U)$$

T = time constant
V_S = system volume
V_D = fresh gas volume fed to the system
V_U = volume that is taken up by the patient (patient uptake)

As can be seen from the Conway formula, the time constant T is proportional to the system volume V_S (machine and pulmonary volume) and inversely proportional to the fresh gas volume V_D.

It follows that the smaller the circulating volume in the circuit system and the larger the fresh gas volume supplied, the smaller the resulting time constant and the faster the patient experiences vaporizer changes.

06 Contraindications of low-flow anesthesia

6.1 Contraindications of low-flow anesthesia 86

06 Contraindications of low-flow anesthesia

6.1 Contraindications of low-flow anesthesia

If toxic gases are to be washed out or accumulations prevented by controlled respiration, minimal-flow anesthesia is contraindicated. Fresh gas flow should then not fall below 1 L/min, in order to guarantee an adequate washing out effect (approximately 50%).

Low-flow anesthesia is likewise contraindicated with smoke intoxication (carbon monoxide, cyanide intoxication). Malignant hyperthermia also counts as a contraindication if sufficient exhalation of carbon dioxide must be achieved and the supply of volatile anesthetics must be stopped immediately. The following additional indications also seem dangerous for minimal-flow anesthesia: patients in a ketoacidotic coma, diabetes mellitus, or for patients suffering from a ketoacidotic metabolic condition (for example, anorexia nervosa). When gases with high fat and water solubility are exhaled, such as by patients with alcohol or acetone poisoning, this type of anesthesia is also contraindicated.

It goes without saying that, during the doctor's pre-operative visit and the preliminary anesthesia consultation, the patient's specific risks and requirements must be discussed in the same way as the extent and nature of the impending operation. Thus, with regard to the anesthesia procedure, anesthesia administration and monitoring, an anesthesia method which is best suited to the individual can be discussed with the patient.

For routine operations, but also for spontaneous intraoperative complications, a high-flow phase for intermittent flushing (5 L/min for 1 to 5 minutes) may be necessary if there is a large leakage of gas, inadequate anesthesia depth or potentially insufficient denitrogenation. However, it must also be accepted that short-term increase of the fresh gas will interrupt or impair the breathing gas condition already achieved.

Considering the contraindications, it can be summarised that, in most cases of anesthesia, a low fresh gas flow (less than 0.25 L/min to 1 L/min) can be provided and has proven reliable under various circumstances.

07 Establishment and outlook

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7.2 Future prospect—low-flow anesthesia? 91

07 Establishment and outlook

7.1 Establishing low-flow anesthesia

Experts consider the greatest danger of anesthesia to be that patients entrusted to our care could suffer accidental hypoxia under anesthesia. This is stated as the main point of criticism against establishing and implementing low- and minimal-flow anesthesia in everyday clinical practice. Experienced anesthetists also sometimes take the position that these procedures would not be suitable for anesthetists in further training or for junior colleagues.

From our wide-ranging clinical experience, we can contradict these two points of criticism: hypoxia can be ruled out if the alarm parameters are adequately set at the machine. This means that an inspiratory O_2 concentration of 28% and continuous paO_2 measurement must be guaranteed. Furthermore, performing low- and minimal-flow anesthesia is, of course, also suitable for training purpose. If the impeding operations are thoroughly planned and the individual requirements of the patient considered, the assumed oxygen uptake by the respective patient will already be taken into account, and if anesthesia is conducted using oxygen as the carrier gas, a very safe and simple-to-perform anesthesia is provided.

We hope that with the concepts offered in this book we were able to convey to colleagues that this method of anesthesia is safe. The safety and technical capability of today's Dräger anesthesia machines make low-flow, metabolic-flow and minimal-flow anesthesia the procedures of choice.

7.2 Future prospect—low-flow anesthesia?

In order to make these anesthesia techniques even better established in future, it would be useful to install loaded algorithms in the machines, which can suggest a low-flow regime for the patient concerned after entering age, body weight and size.

At this point, we should also refer once again critically to oxygen as a carrier gas. The simplest way of performing these anesthesia techniques is based on an oxygen carrier gas. It is, of course, well known that oxygen as a carrier gas is the subject of controversial discussion. For example, reliable data indicate that a too high FiO_2 is contraindicated for patients suffering from acute cardiac insufficiency, particularly following resuscitation.

In this context, we also talk of a secondary hit, which often occurs when previously ischaemic organ systems are reperfused. In such cases, it would appear that cellular protection mechanisms against oxidative stress are exhausted and cannot withstand any increased exposure to oxygen radicals. Enzymatic and non-enzymatic radical interceptors (antioxidative protection system), in particular, become exhausted and therefore, as a secondary consequence, so do the DNA repair mechanisms. In order to further reinforce the reference literature on this problem, studies and further data collections are being carried out world-wide and also by us [40, 41, 42, 43, 44, 45, 46, 47].

On the other hand it is undisputed that the vast number of patients with elective surgery (surgical time < 8 hours) with oxygen as carrier gas are supplied with excellent low- and minimal-flow anesthesia. This allows potential benefits as less nausea, better wound healing, low risk of hypoxia and easy implementing of the procedure.

In summary, the low-flow anesthesia is an elegant, resource-efficient, economical and safe procedure for our patients.

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8.4 Color code

Color	Element
	Isoflurane
	Sevoflurane
	Desflurane
	Oxygen (O_2)
	Nitrous oxide (N_2O)
	Nitrogen (N)
	Low-flow anesthesia
	Minimal-flow anesthesia
	Metabolic-flow anesthesia
	Non-quantitative anesthesia in the closed system
	delta MAC 0.35
	delta MAC 0.9
	delta MAC 0.7
	Total gas uptake
	Fresh gas flow 0.35 L/min
	Fresh gas flow 2 L/min
	Fresh gas flow 6 L/min

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