



Low-flow, minimal-flow and metabolic-flow anaesthesia

Clinical techniques for use with rebreathing systems

Christian Hönemann
Bert Mierke

IMPORTANT NOTES

Medical expertise is continually undergoing change due to research and clinical experience. The authors of this book intend to ensure that the views, opinions and assumptions in this book, especially those concerning applications and effects, correspond to the current state of knowledge. But this does not relieve the reader from the duty to personally carry the responsibilities for clinical measures. The use of registered names, trademarks, etc. in this publication does not mean that such names are exempt from the applicable protection laws and regulations, even if there are no related specific statements. All rights to this book, especially the rights to reproduce and copy, are reserved by Drägerwerk AG & Co. KGaA. No part of this book may be reproduced or stored mechanically, electronically or photographically without prior written authorization by Drägerwerk AG & Co. KGaA.

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AUTHORS



Christian Hönemann
PhD, MD

Vice Medical Director

Chief physician in the collegiate system of the department of Anaesthesia and Operative Intensive Care, St. Marienhospital Vechta Catholic Clinics Oldenburger Münsterland, Marienstraße 6–8, 49377 Vechta, Germany



Bert Mierke
PhD, MD

Medical Director

Chief physician of the Clinic for Anesthesiology and Intensive Care St. Elisabeth GmbH, Lindenstraße 3–7, 49401 Damme, Germany

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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 anaesthesia 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 anaesthesia. He also described metabolic-flow anaesthesia using pure oxygen as the carrier gas. By doing so, he simplified and perfected minimal-flow anaesthesia.

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.

Priv. Doz. Dr. med. Christian Hönemann

Dr. med. Bert Mierke

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01 Introduction/Definition of terms

The various options of low- and minimal-flow anaesthesia present sufficient clinical techniques for use with rebreathing systems. Only when low-flow anaesthesia is performed can the advantages of rebreathing systems be realised. Therefore, in everyday clinical practice where inhalational anaesthesia 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 anaesthesia gases can be reduced to a minimum and the advantages of improved respiratory gas conditioning achieved.

1.1 Low-flow anaesthetics

Low- and minimal-flow anaesthetics are characterised 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 anaesthetic gases in the patient's exhalation air are returned to the patient via closed or semi-closed rebreathing systems after CO₂ 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 anaesthesiology features the following notable procedures, which are employed with low- and minimal-flow anaesthesia:

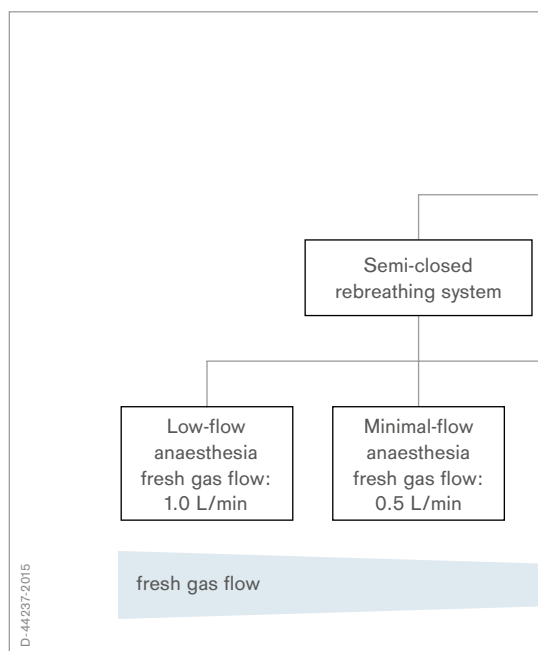
- 1) In low-flow anaesthesia, the fresh gas flow is reduced to 1.0 L/min. This method was first described by Foldes et al. in 1952^{1,2}.
- 2) In minimal-flow anaesthesia, first described by Virtue in 1974, the fresh gas flow is reduced to 0.5 L/min³.

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 metabolising while under anaesthesia.

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

With non-quantitative anaesthesia, the anaesthetist 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 anaesthesia with closed systems is performed, the anaesthesia machine keeps not only the gas filling, breathing pattern and internal pressures constant, according to the anaesthetist's instructions, but also the fresh gas composition in terms of the carrier gases and volatile anaesthetics (if necessary, with nitrous oxide). The total gases supplied therefore always correspond to the patient's actual gas uptake^{4,5}. This type of quantitative anaesthesia can be performed using Dräger's Zeus IE anaesthesia machine.



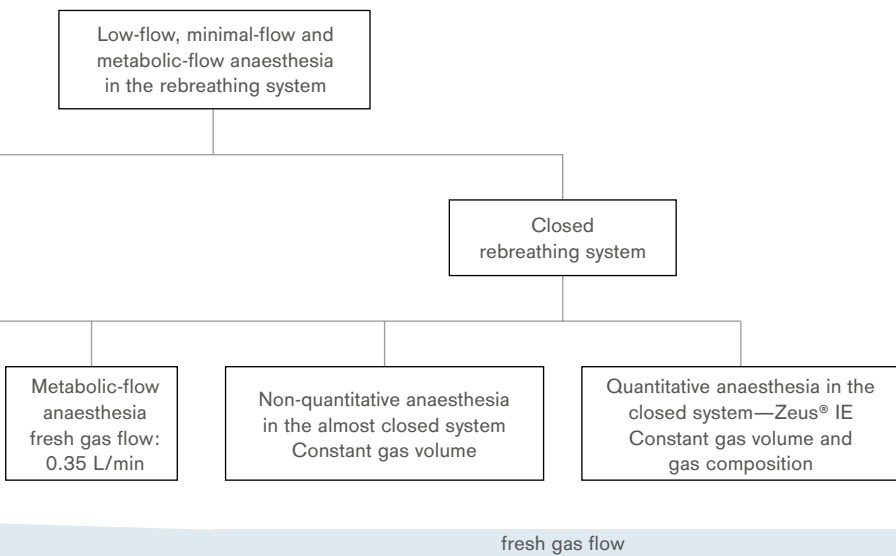


Fig. 1: Overview of low-flow, minimal-flow and metabolic-flow anaesthesia in the rebreathing system (modified from Baum JA ⁶)

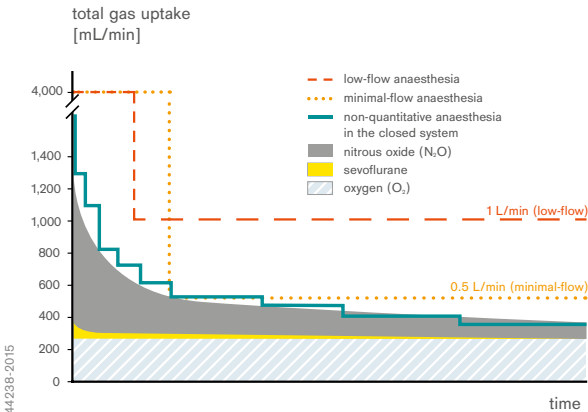


Fig. 2: Low-flow and minimal-flow anaesthesia with an O₂/N₂O mixture as carrier gas in the semi-closed Primus breathing system (modified from Baum JA⁶)

Carrier gases: O₂/N₂O

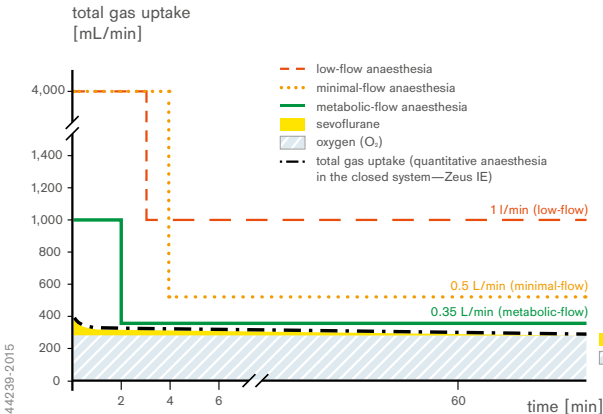


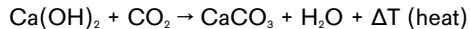
Fig. 3: Low-flow, minimal-flow and metabolic-flow anaesthesia (modified from Baum JA⁶)

1.2 Rebreathing systems

As already mentioned, the basic requirement for conducting anaesthesia with a low fresh gas flow is the use of a rebreathing system. With this system, the unused gases and anaesthetic 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®, Primus®/Primus® Infinity® Empowered (IE), Zeus®/Zeus® Infinity® Empowered (IE), 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:



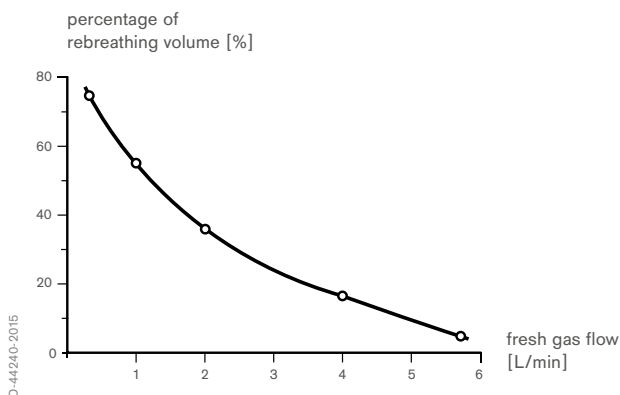


Fig. 4: Percentage of expiratory air which, depending on the flow following the addition of fresh gas and discharge of the excess gas, is returned to the patient (modified from Hönemann C⁷)

The continuous loss of gas from the system—a result of oxygen consumption and enrichment of the anaesthetic 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 gases⁸.

1.3 Differentiating between anaesthesia 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 anaesthesia systems: subdividing them into systems with and without rebreathing appears to be more suitable⁹. 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 anaesthesia 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 anaesthetic and fresh gas increases.

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

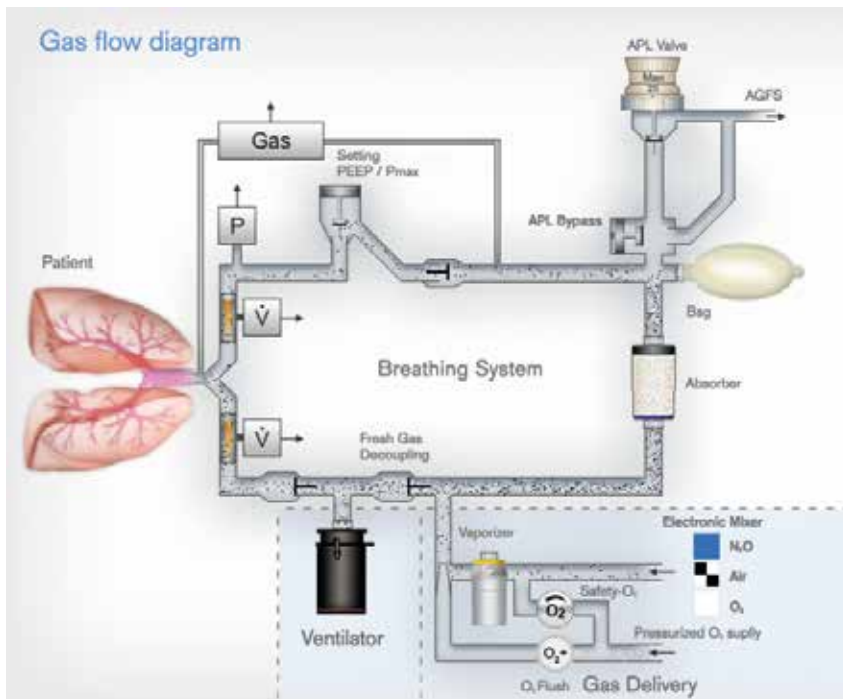


Fig. 5: Gas flow diagram using the Primus/Primus IE rebreathing system as an example

NON-QUANTITATIVE ANAESTHESIA IN THE ALMOST CLOSED SYSTEM

The closed anaesthesia 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 metabolised 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 anaesthesia). Non-quantitative anaesthesia with a closed system can be performed with most anaesthesia machines.

The following requirements are sufficient: the breathing systems must be sufficiently tight (no leakages). The anaesthesia machines must allow a setting to even the lowest fresh gas flow. Dosing of the anaesthetic gas must also be sufficiently accurate in the low flow range, and machine monitoring must guarantee comprehensive monitoring of the composition of the anaesthesia 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, Primus/Primus IE, Zeus/Zeus IE, and Perseus A500).

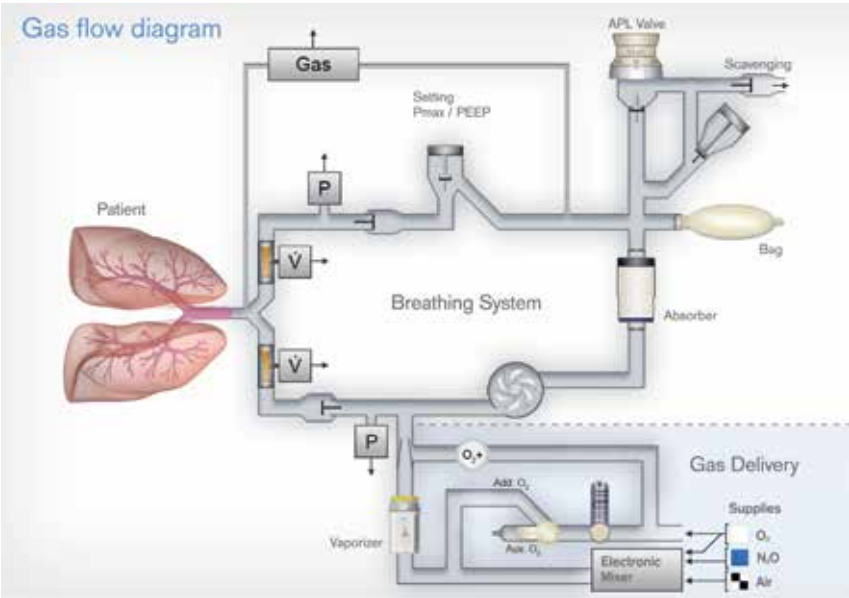


Fig. 6: Gas flow diagram using the Perseus A500 rebreathing system as an example

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

To date, this dosing principle is only common in a select few anaesthesia machines. This type of control system can be found, for example, in the Zeus/Zeus IE.

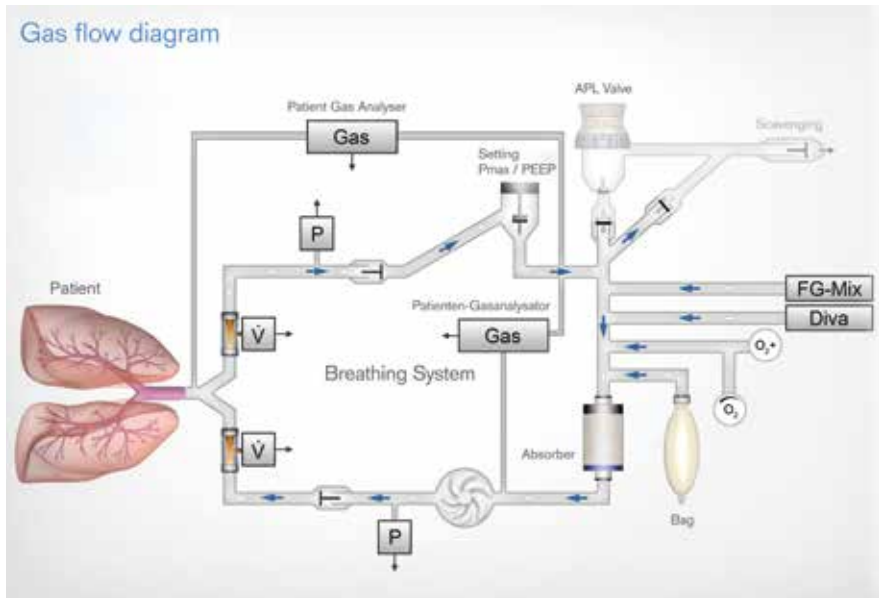


Fig. 7: Gas flow diagram using the Zeus/Zeus IE rebreathing system as an example

02 Benefits of low-flow anaesthesia

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02 Benefits of low-flow anaesthesia

2.1 Clinical benefits—humidifying, warming, pulmonary function

The importance that breathing gas conditioning has for the anaesthetised patient has been known for some time^{10,11,12}. The need to condition breathing gas for intubated or tracheotomised 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 microatelectases.

During prolonged anaesthesia, therefore, an absolute humidity of between 17 and 30 mg H₂O/L with an anaesthetic gas temperature of at least 28°C should be provided. These demands are met by minimal-flow anaesthesia: 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 8)^{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 anaesthesia with endotracheal intubation.

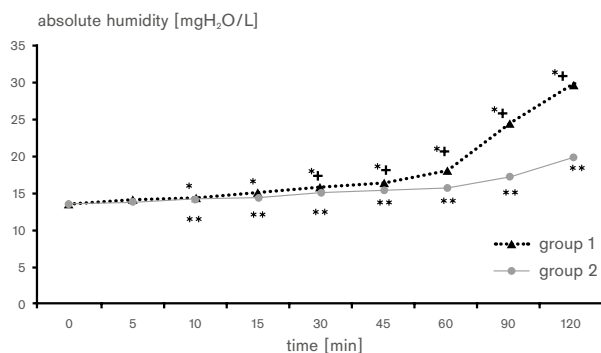


Fig. 8: Comparison of absolute humidities of inspiratory breathing gas

Group 1: Fresh gas flow 1 L/min (0.5 L/min O₂ + 0.5 L/min N₂O) + desflurane;
 Group 2: Fresh gas flow 3 L/min (1.5 L/min O₂ + 1.5 L/min N₂O) + desflurane (modified from Bilgi M et al.¹⁵)

- *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

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). Anaesthesia is then continued as inhalational anaesthesia.

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 anaesthesia. In a third group, the inhalational anaesthetic 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 anaesthesia machine.

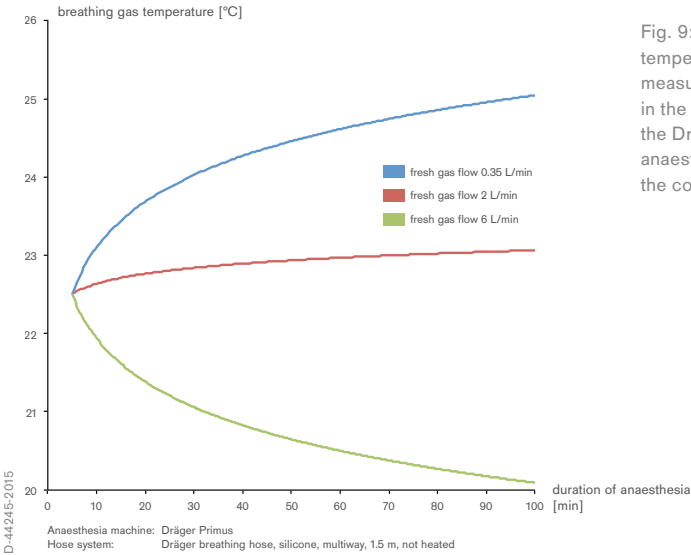


Fig. 9: Breathing gas temperature in °C measured at the Y-piece in the inspiratory arm of the Dräger Primus anaesthesia machine over the course of anaesthesia

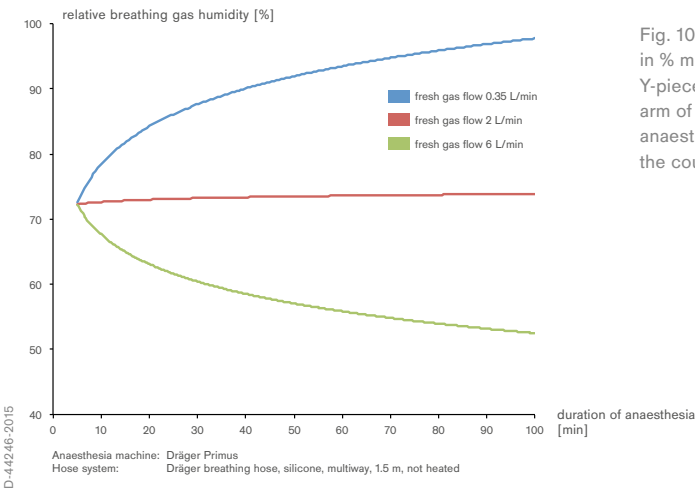


Fig. 10: Relative humidity in % measured at the Y-piece in the inspiratory arm of the Dräger Primus anaesthesia machine over the course of anaesthesia

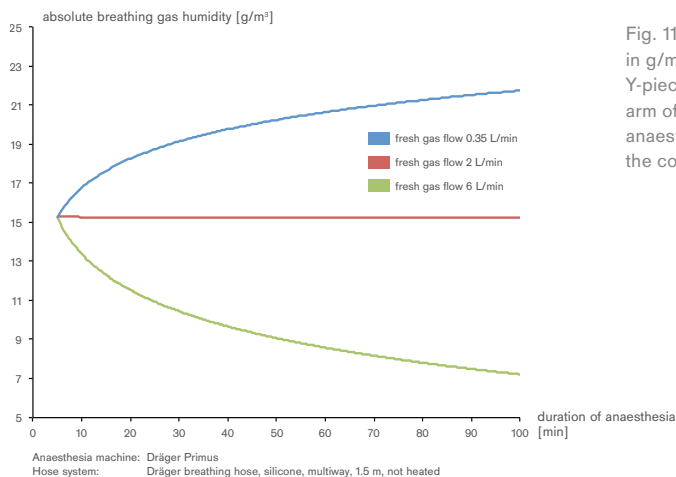


Fig. 11: Absolute humidity in g/m³ measured at the Y-piece in the inspiratory arm of the Dräger Primus anaesthesia machine over the course of anaesthesia

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

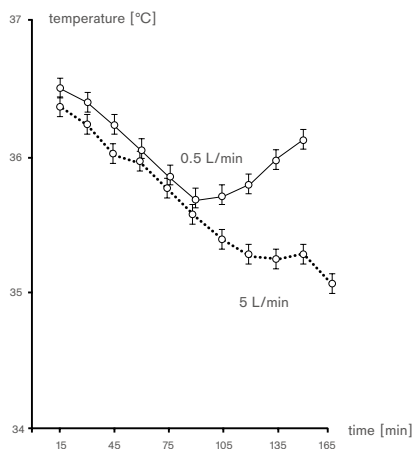


Fig. 12: Average oesophageal body temperature with different fresh gas flows (0.5 versus 5 L/min) (modified from Aldrete A et al.¹⁶)

2.2 Ecological benefits

A characteristic of high-flow anaesthesia is that large amounts of volatile anaesthetics 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 anaesthesia. The emission of anaesthesia gases should, therefore, be reduced to an unavoidable minimum and unused anaesthetics should be reused. Low-flow and minimal-flow anaesthesia 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 anaesthesia reduces the requirement for anaesthetics, 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 anaesthesia 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.

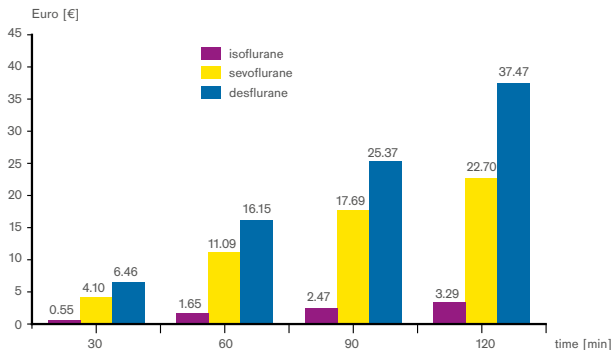


Fig. 13: Cost savings in Euros as a result of minimal-flow anaesthesia of 0.5 L/min compared with the standard method using fresh gas flow of 3 L/min

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

Isoflurane 250 mL (Forene, Abbvie) € 32.73

Sevoflurane 250 mL (Sevorane/Sevoflurane, Abbvie/Baxter) € 131.92

Desflurane 250 mL (Suprane, Baxter) € 81.16

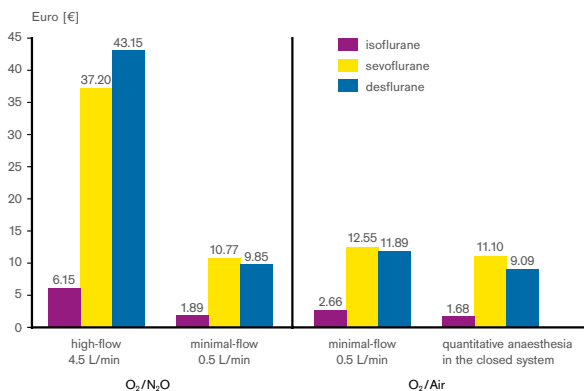


Fig. 14: Cost of inhalational anaesthetics in Euros based on 2-hour inhalational anaesthesia

Comparison of the different types of anaesthesia

In addition, critical comments are constantly raised that, even when the cost of inhalational anaesthesia 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 anaesthesia with low fresh gas flow in daily use. In line with this argument is the fact that the technical level of anaesthesia machines allows for a low fresh gas flow and that some of the machines are even designed for low-flow anaesthesia techniques.

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

Efficiency then corresponds to the ratio between the uptake and the quantity of fresh gas and anaesthesia 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 anaesthetics

Modern inhalational anaesthetics 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 anaesthetics 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 anaesthesia gases must lead to the appropriate use of rebreathing systems.

Reducing anaesthesia gases by up to 90% has another beneficial effect: the exposure for staff in the anaesthesia workplace drops noticeably²⁰.

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 N₂O 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 anaesthesia gas has direct effects on all areas of work.

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03 Conditions for low-flow and minimal-flow anaesthesia

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 anaesthesia 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 today²²:

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

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 anaesthetised 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:

$$\text{VO}_2 = 3.5 \times \text{KG} \text{ [mL/min]}$$

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 Anaesthesia gas uptake

Anaesthesia gas uptake is based on the pharmacokinetics and dynamics of the volatile anaesthetic used. The uptake of inhalational anaesthetic agent—assuming a constant gas composition in the anaesthesia system—drops exponentially over the course of anaesthesia. In accordance with the Lowe formula, it is proportional to the desired concentration and solubility of the anaesthetic, and to cardiac output^{23,24}.

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

V_{AN} = uptake of inhalational anaesthetics (anaesthesia gas uptake) in mL/min

$f \times \text{MAC}$ = desired expiratory anaesthetic concentration as a function of the minimal alveolar concentration of the anaesthetic chosen (e.g., $0.8 \times \text{MAC}$)

$\bar{\lambda}_{B/G}$ = coefficient of blood-gas solubility

Q = cardiac output (dL/min)

The prediction models, based on Bailey's²⁵ 5-compartment model, also appear valid. This allows the distribution of anaesthesia gases in the human body to be calculated. In addition, calculation models for prediction

modules are now used for anaesthesia 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 anaesthesia 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 anaesthesia, the anaesthesia 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 anaesthesia is the target concentration in the effect compartment—the brain. Equally important is the choice of a suitable volatile anaesthetic 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 anaesthesia. This is principally dependent on the different solubilities and associated anaesthetic potencies as well as on the physiological uptake of the agent²⁸.

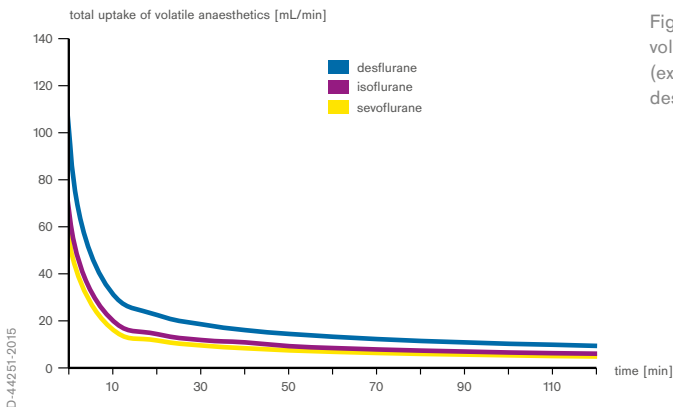


Fig. 15: Total uptake of volatile anaesthetic agents (expiratory concentration—desired state: $0.9 \times \text{MAC}$)

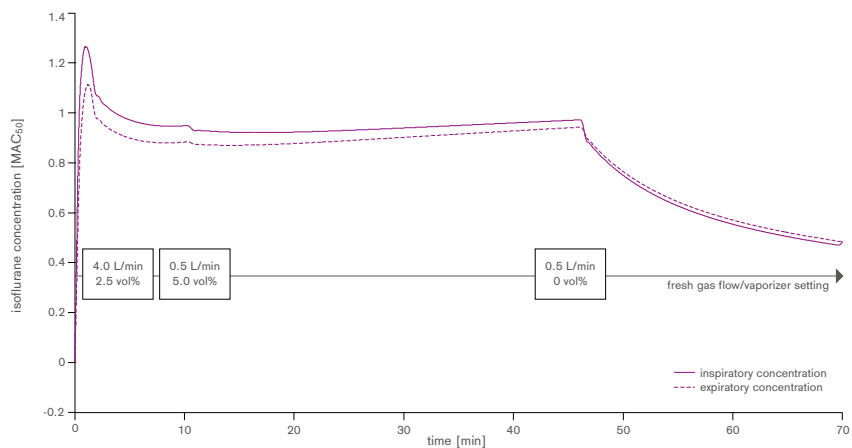


Fig. 16: Inspiratory and expiratory isoflurane concentration over the course of inhalation anaesthesia with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC

For vaporizer adjustments, see also diagram of minimal-flow anaesthesia 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 anaesthetic concentrations are increased/reduced, using the various time constants.

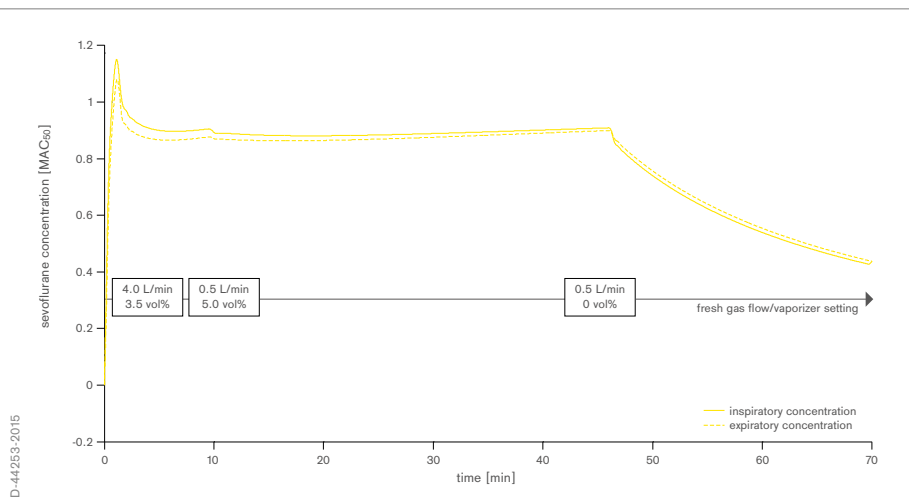


Fig. 17: Inspiratory and expiratory sevoflurane concentration over the course of inhalation anaesthesia with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC

Vaporizer settings: see also diagram of minimal-flow anaesthesia 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 anaesthetic concentrations are increased/reduced, using the various time constants.

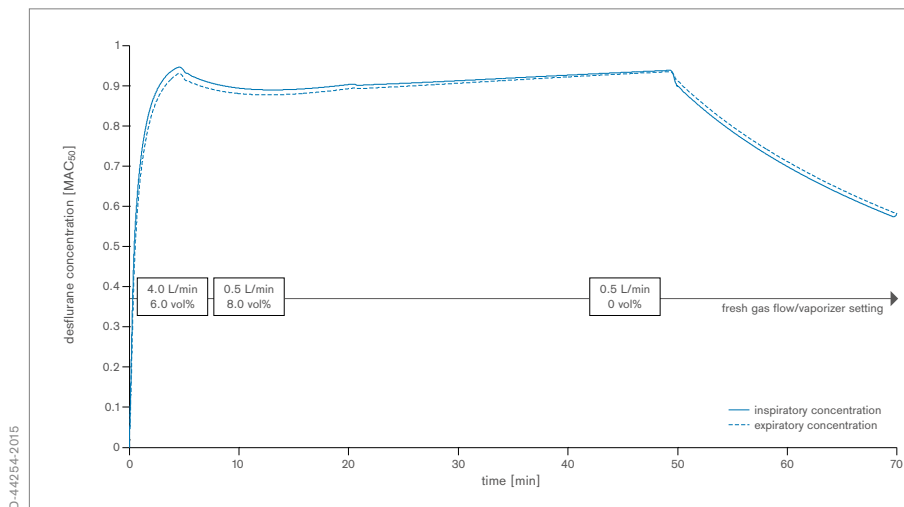


Fig.18: Inspiratory and expiratory desflurane concentration over the course of inhalation anaesthesia with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also diagram of minimal-flow anaesthesia 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 anaesthetic concentrations are increased/reduced, using the various time constants.

3.3 Nitrous oxide uptake

Nitrous oxide is not metabolised in the body. Therefore, the uptake of N₂O is only determined by the alveolar-capillary partial pressure difference. At the start of anaesthesia, 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 function²⁹:

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

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

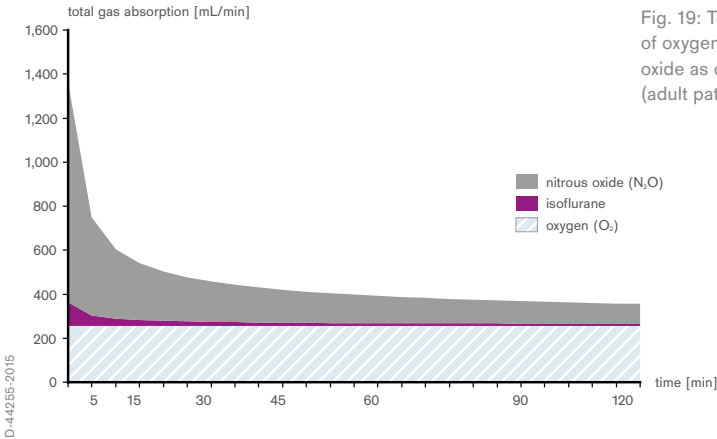


Fig. 19: Total gas uptake of oxygen with nitrous oxide as carrier gas (adult patient, 75 kg)

3.4 Control via the MAC value

A clear distinction exists between the pharmacodynamic and pharmacokinetic behaviour of volatile anaesthetics. The crucial factor is the blood-gas distribution coefficient and the fat solubility of the concentrate. The anaesthetic 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 anaesthesia is determined by the concentration of anaesthetics in the brain, which is directly dependent on the alveolar partial pressure as a function of the blood concentration. The depth of anaesthesia is therefore established by changing the inhalation concentration of the volatile anaesthetic in the expiratory breathing gas. There is a linear relationship between the potency of the anaesthetic and fat solubility: the greater the fat solubility, the more potent the inhalational anaesthetic and the smaller the alveolar concentration required to achieve a defined depth of anaesthesia.

The MAC value is the minimal alveolar concentration of a volatile anaesthetic 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 anaesthetic, the higher its potency.

The MAC value differs depending on the carrier gas used^{30,31}. The MAC₅₀ awake value is defined differently. This is the value at which half of patients open their eyes following anaesthesia.

Thus, if we refer to the MAC value in daily use, we are referring to the MAC₅₀, which is the approximate measure for the potency of the inhalational anaesthetics relative to the respective carrier gas used.

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

Anaesthetic 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 anaesthetics 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 anaesthesia 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 anaesthesia on a daily basis, this is expressly desired and conceptually demanded (see balanced anaesthesia, page 39). Thus, opioids and co-anaesthetics, such as sedatives, reduce the MAC value. The principle of balanced anaesthesia involves affecting the individual anaesthesia 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 anaesthetics and therefore lead to higher MAC values.

The use of the Dräger SmartPilot® View can meaningfully support minimal-flow techniques.

BALANCED ANAESTHESIA BY HÖNEMANN C.³³

A general anaesthesia that is maintained by a combination of various anaesthetics with synergistic pharmacological properties is described as balanced anaesthesia. Monoanaesthesia, i.e. anaesthesia using just one anaesthetic, is virtually no longer performed in practice today.

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

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

Balanced anaesthesia is the most frequently used anaesthesia procedure world-wide. General anaesthesia is made up of four different basic qualities:

- Hypnosis,
- Analgesia,
- Muscle relaxation and
- Autonomic shielding.

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

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

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

In addition, volatile anaesthetics have muscle-relaxing properties and thereby enhance the effect of added muscle relaxants. Nitrous oxide and intravenously administered opioids reduce the need for volatile anaesthetics 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 age³¹.

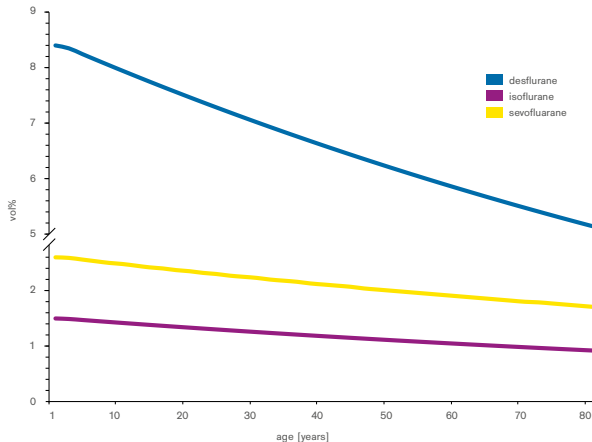


Fig. 20: Effect of age on MAC (modified from Mapleson WW et al.³⁴)

The highest inhalation concentrations in the inspiration mixture are required in infants. They drop continuously with age. In order to achieve an equivalent anaesthesia depth, different MAC values for the same substance in the various stages of life are required. By combining a general and a regional anaesthesia procedure, volatile anaesthetic agents and other hypnosis-inducing medications can be saved; the anaesthetic 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 anaesthesia induction—which is done by an volatile anaesthetic agents to maintain anaesthesia—MAC values of between 0.8 and 1.2 are needed to reach an adequate anaesthesia depth. Exceeding these values is not reasonable neither from a pharmacological nor anaesthesiological 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 anaesthetic agents in the geriatric patient³². Correspondingly, data from large meta-analyses indicate that excessive MAC values in anaesthesia 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 anaesthesia can be best controlled when using volatile anaesthetics that exhibit the lowest possible solubility and thus low anaesthetic potency.

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

Therefore, we particularly recommend inhalational anaesthetic 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 anaesthesia because it leads to longer uptake and clearance.

By increasing the vaporizer setting and fresh gas flow, rapid deepening of anaesthetic can be achieved with additional intravenous injection of a hypnotic drug. In addition, by closing the vaporizer, the anaesthetic can be reduced if the MAC value of isoflurane is too high²⁸.

Table 2: Pharmacokinetic and pharmacodynamic properties of different volatile anaesthetics (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
Anaesthetic 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 anaesthesia using a high fresh gas flow, changes in the fresh gas composition lead to rapid and similar changes in the inspiratory and expiratory anaesthetics concentration in the anaesthesia 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 anaesthetics. Accordingly, the time constant is inversely proportional to the fresh gas flow. This applies to anaesthesia machines, which dose according to the fresh gas, when they are used as semi-closed systems, for example, with low-flow and minimal-flow anaesthesia or with non-quantitative anaesthesia in a closed system.

Particularly at the end of anaesthesia, this effect can be used by stopping the anaesthetic 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 anaesthetic 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 anaesthetic agent and in the recovery of the patient within a very short time.

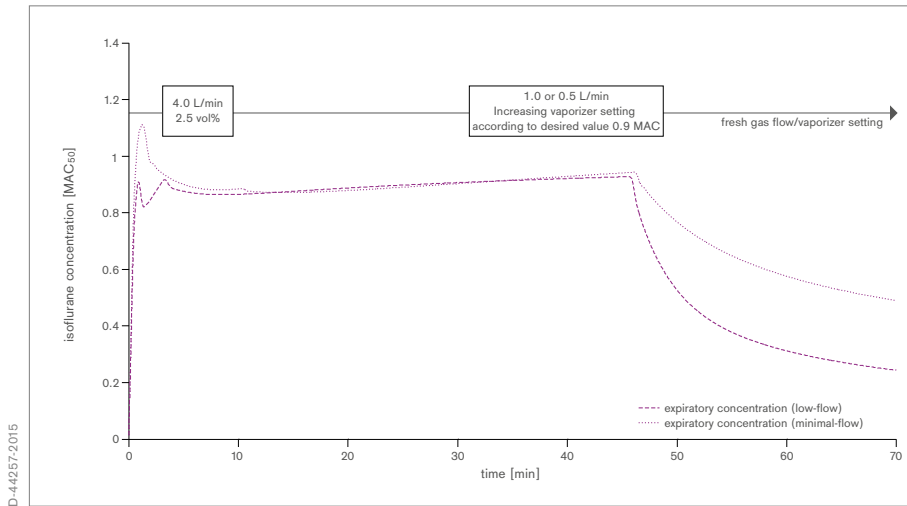


Fig. 21: Comparison of expiratory isoflurane concentration over the course of inhalation anaesthesia. Various fresh gas flows (low-flow versus minimal-flow) with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also procedure diagram. Minimal-flow anaesthesia 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.

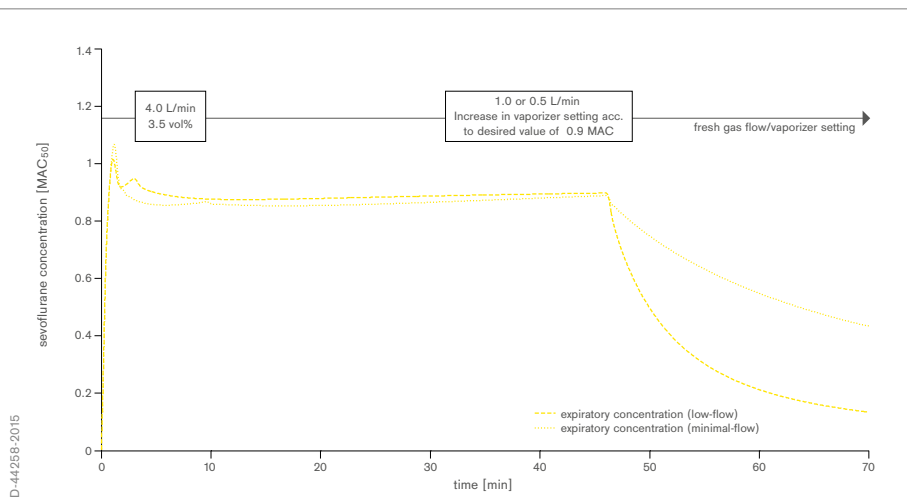


Fig. 22: Comparison of expiratory sevoflurane concentration over the course of inhalation anaesthesia.

Various fresh gas flows (low-flow versus minimal-flow) with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC

Vaporizer settings: see also procedure diagram. Minimal-flow anaesthesia 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.

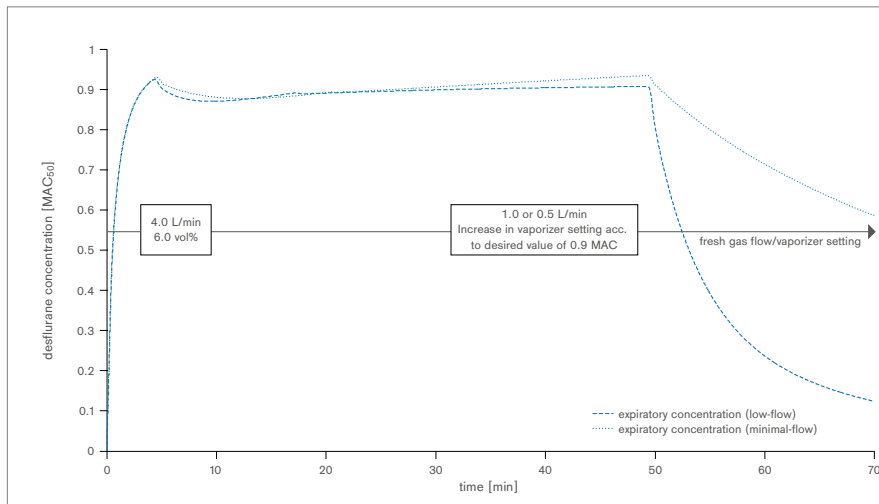


Fig. 23: Comparison of expiratory desflurane concentration over the course of inhalation anaesthesia. Various fresh gas flows (low-flow versus minimal-flow) with O₂/air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Desired value: expiratory concentration: 0.9 MAC
Vaporizer settings: see also procedure diagram. Minimal-flow anaesthesia 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 anaesthesia 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 anaesthetics) 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 haemodynamics is completely independent of the fresh gas flow chosen.

Technical mandates and recommendations by professional anaesthesia organisations (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 anaesthetist. 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 anaesthesia 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 anaesthesia and intensive care
BDA = professional association of German anesthesiologists

Because of the large difference between anaesthesia gases (fresh gas composition—gas concentration in the circuit system), the monitoring of inspiratory and expiratory anaesthesia gas concentration is extremely important, especially for less experienced users of low- and minimal-flow anaesthesia. Concentrations of anaesthetic 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.

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04 Performing minimal-flow anaesthesia

4.1 Minimal-flow anaesthesia 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 larynx 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 21 to 23)

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 anaesthetic 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%.
- Use of the Dräger SmartPilot View can meaningfully support minimal-flow techniques.

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 anaesthetic 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 anaesthetic 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 anaesthesia 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 anaesthesia gas.
- Increase the fresh gas flow to 4 L/min (1 litre oxygen, 3 litres air).
- Once the desired anaesthetic 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 anaesthesia, measuring the expiratory end-tidal anaesthetic agent concentration in the breathing system is mandatory. As an alternative to short-term deepening of the anaesthesia by increasing the fresh gas flow, additional intravenous injection of the hypnotic or analgesic should be considered.

Warning—inspiratory O₂ 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 litre oxygen, 3 litres air).
- Search for leakage (hole in hose system, bag valve mask, CO₂ absorber correctly secured?). If the leakage cannot be repaired, increase the fresh gas flow by 0.5 L/min and switch to low-flow anaesthesia 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 CO₂ concentration and the soda lime. If the inspiratory CO₂ 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 anaesthesia 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 anaesthesia 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 anaesthetics 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 anaesthesia system, a fresh gas deficit alarm is installed, for example, in Dräger machines. In addition, an econometer may be useful as the preferred 'early warning system' when carrying out low- and minimal-flow anaesthesia 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 anaesthesia 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):

$p_{O_2} = 19.6 \text{ kPa}$

$p_{CO_2} = 0 \text{ kPa}$

$p_{N_2} = 74.1 \text{ kPa}$ (this also includes all noble gases under nitrogen, such as argon and xenon etc.)

$p_{H_2O} = 6.3 \text{ kPa}$

If we proceed according to the regime described above when carrying out anaesthesia 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 anaesthesia is safer with regard to risks of accidental hypoxaemia, and it is easier to perform.

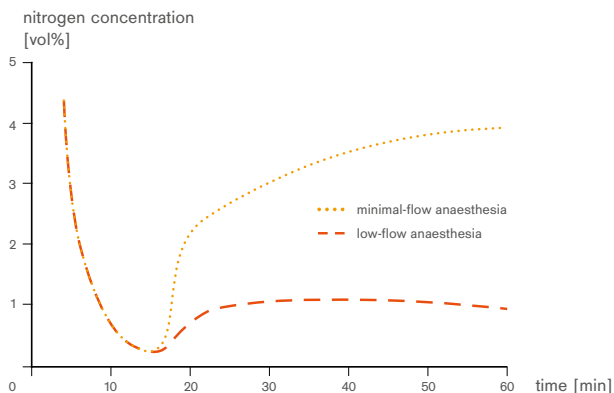


Fig. 24: Nitrogen accumulation in the breathing system, patient weight 75 kg (modified from Baum JA et al.⁸⁾)

4.2 Minimal-flow anaesthesia 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 larynx 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.

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 anaesthetic 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 anaesthetic 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%.
- Use of the Dräger SmartPilot View can meaningfully support minimal-flow techniques.

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

Warning—inspiratory O₂ 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, CO₂ 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 anaesthesia at 1 L/min.

Fresh soda lime is essential

- Observe the inspiratory CO₂ concentration and the soda lime. If the inspiratory CO₂ 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 anaesthesia and omitting an oxygen/nitrous oxide or oxygen/air mixture is metabolic-flow anaesthesia.

By using pure oxygen as the carrier gas, denitrogenation can be omitted at the start of inhalational anaesthesia 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 anaesthesia. The level of fresh gas flow is dependent on the time during which an adequate anaesthesia gas concentration is to be established. The higher the fresh gas flow, the more rapidly the desired anaesthesia gas concentration is achieved in the rebreathing system. The lower the fresh gas flow, the slower the volatile anaesthetic 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 anaesthetic agent concentration in the circuit system. This allows reaching a MAC value of 0.9 within 5 to 7 minutes for any modern anaesthetic 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 anaesthetics increases.

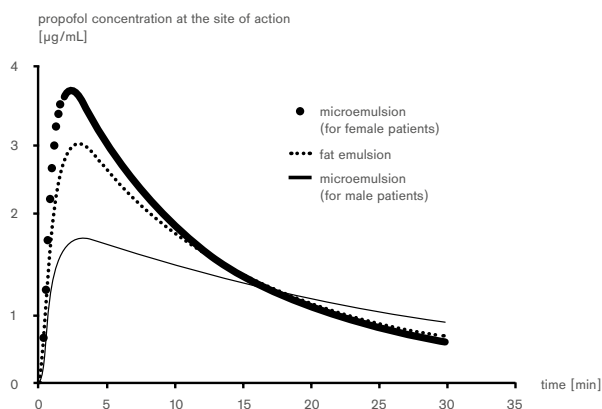


Fig. 25: Simulation of an intravenous bolus of propofol 2 mg/kg in various emulsions (microemulsion and fat emulsion) in a person with a weight of 65 kg, a height of 170 cm, and an age of 44 years. Concentration in the effect compartment (modified from Kim KM et al.³⁵)

Modern anaesthesia gases are metabolised to an only minor extent, have low solubility and are therefore easy to control. As a result, the time for washing in the anaesthesia 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 anaesthesia gases sevoflurane and desflurane in Dräger anaesthesia machines Primus and Zeus.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 30).

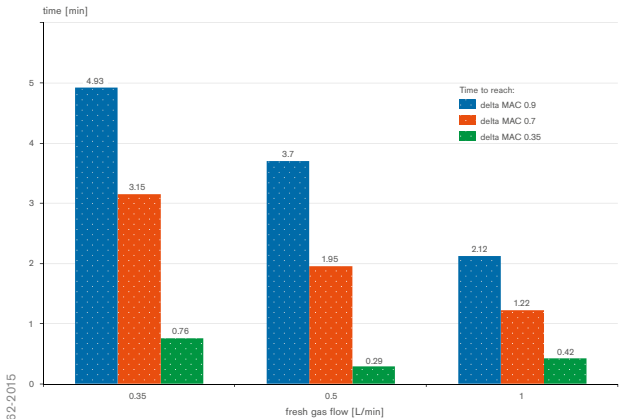


Fig. 26: Primus data—sevoflurane

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

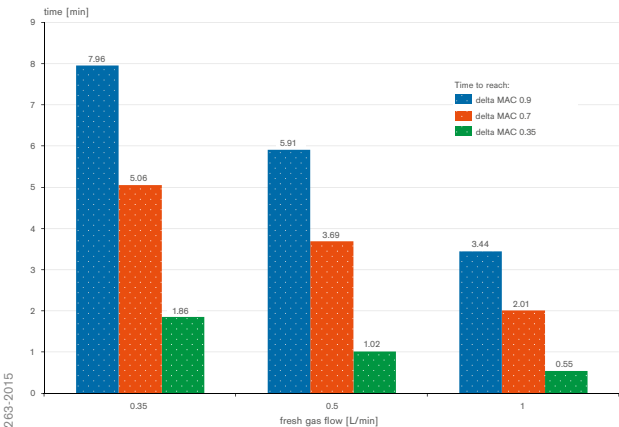


Fig. 27: Primus data—desflurane

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

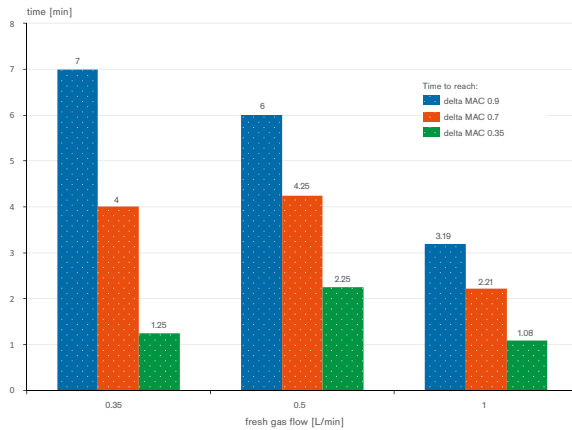


Fig. 28: Zeus data—sevoflurane—influx in fresh gas mode

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

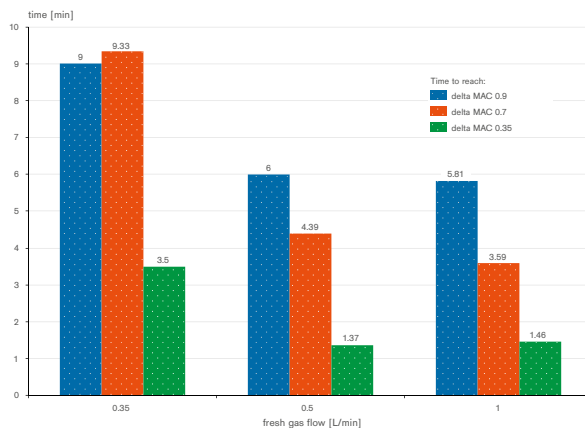


Fig. 29: Zeus data—desflurane—influx in fresh gas mode

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

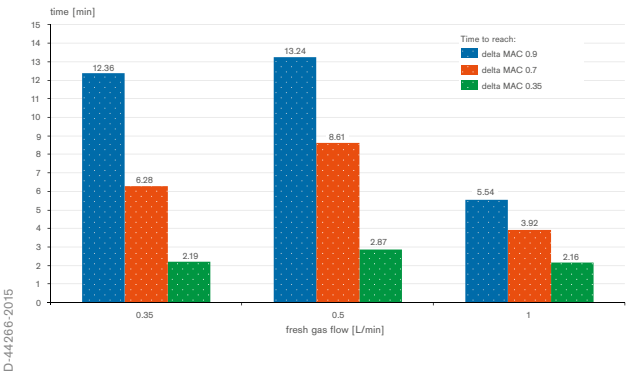


Fig. 30: Primus data—
isoflurane

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

Note: All data in figures 21 to 25 originate from reference³⁶.

Once the anaesthesia 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% O₂). This type of procedure enables adequate use of the rebreathing system.

As in the case of minimal-flow anaesthesia, 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 anaesthesia gas. An even higher fresh gas flow in the reversal phase does not wash out the anaesthesia 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 anaesthesia, despite the significant reduction in fresh gas flow, a certain excess volume of gas and maintaining a standardised 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 anaesthesia when using pure oxygen as carrier gas compared with low- and minimal-flow anaesthesia using oxygen/air mixture or oxygen/nitrous oxide mixture as carrier gas⁹.

In the Vechta and Damme hospitals, more than 100,000 anaesthesia procedures with oxygen as carrier gas have been documented since 2004^{37, 38}.

4.3 Minimal-flow anaesthesia 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 larynx 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.

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 anaesthetic 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%.
- Use of the Dräger SmartPilot View can meaningfully support minimal-flow techniques.

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 anaesthetic 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 anaesthetic 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 anaesthesia depth using a short time constant

- Set the vaporizer to a value of 0.5 vol% above or below the desired quantity of anaesthesia gas.
- Increase the fresh gas flow to 4.4 L/min, (1.4 litres oxygen, 3 litres nitrous oxide).
- Once the desired anaesthetic 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 anaesthesia, measuring the expiratory end-tidal anaesthetic agent concentration in the breathing system is mandatory. As an alternative to short-term deepening of the anaesthesia by increasing fresh gas flow, an additional intravenous injection of the hypnotic or analgesic should be considered.

Warning—inspiratory O₂ 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 litres oxygen, 3 litres nitrous oxide).
- Search for leakage (hole in hose system, bag valve mask, CO₂ absorber correctly secured?). If the leakage cannot be repaired, increase the fresh gas flow by 0.5 L/min and switch to low-flow anaesthesia 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 CO₂ concentration and the soda lime. If the inspiratory CO₂ concentration increases, it is an indication that the soda lime should be replaced.

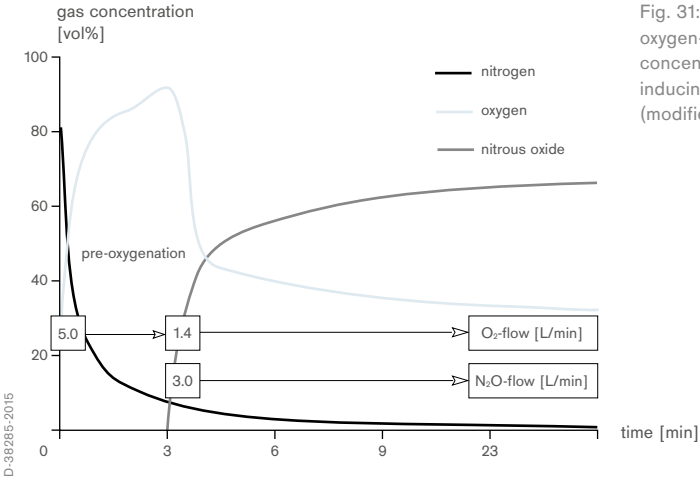


Fig. 31: Inspiratory oxygen- and nitrous oxide concentration when inducing the anaesthesia (modified from Baum J²⁸)

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 colourless 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 anaesthesia gases.

When the use of nitrous oxide in anaesthesia is discussed, it should be remembered that the maximum additive anaesthetic effect by nitrous oxide is rather insignificant. Thus, it can be replaced by increasing the concentration of volatile anaesthetic 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 anaesthetics 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 anaesthetics 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 anaesthesia, as well as intravenous anaesthesia, 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 anaesthetists nitrous oxide is a known and trusted component of the carrier gas in anaesthesia 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 anaesthesia on circulation. Anaesthetics may also be saved. In addition, a second gas effect during mask inhalation induction appears to accelerate the effect of the inhalational anaesthetics. Nitrous oxide actively protects against intraoperative awareness and suppresses spinal defensive reflexes caused by anaesthetics.

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 anaesthesia 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 B₁₂ 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 anaesthesia 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 anaesthesia machines can be simplified. If nitrous oxide is consistently omitted anaesthesia using almost closed systems can be achieved even with conventional anaesthesia 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 anaesthesia machine

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05 Technical requirements of the anaesthesia machine

5.1 Technical requirements of the anaesthesia machine

The latest-generation anaesthesia machines meet all requirements to ensure safe execution of minimal-flow anaesthesia. 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 anaesthetic 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. Moreover, this type of monitoring is a requirement per the guidelines governing quality assurance in anaesthesiology of the Deutsche Gesellschaft für Anästhesie- und Intensivmedizin (DGAI)⁴⁰.

5.2 Maximum vaporizer output depending on anaesthesia gas

Conventional anaesthesia systems consist of a breathing circuit into which fresh gas is fed. Volatile anaesthetics 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 Primus, Perseus A500 and Zeus IE rebreathing systems as examples).

So that sufficient anaesthesia 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 anaesthesia 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 anaesthesia 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 anaesthesia gas. In particular, sevoflurane and desflurane are characterised 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.

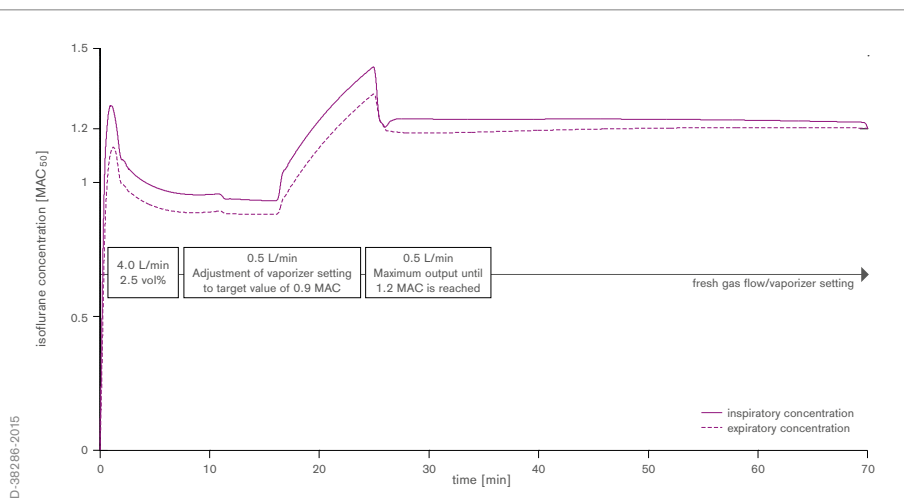


Fig. 32: Inspiratory and expiratory isoflurane concentration over the course of inhalation anaesthesia. Relationship between fresh gas flow and maximum vaporizer setting with O_2 /air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anaesthesia 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 anaesthetics (> 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 anaesthesia 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.

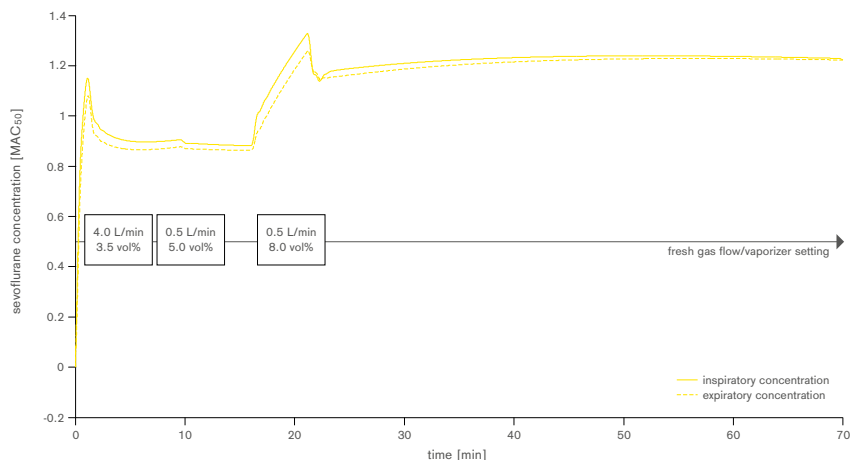


Fig. 33: Inspiratory and expiratory sevoflurane concentration over the course of inhalation anaesthesia. Relationship between fresh gas flow and maximum vaporizer setting with O_2 /air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anaesthesia 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.

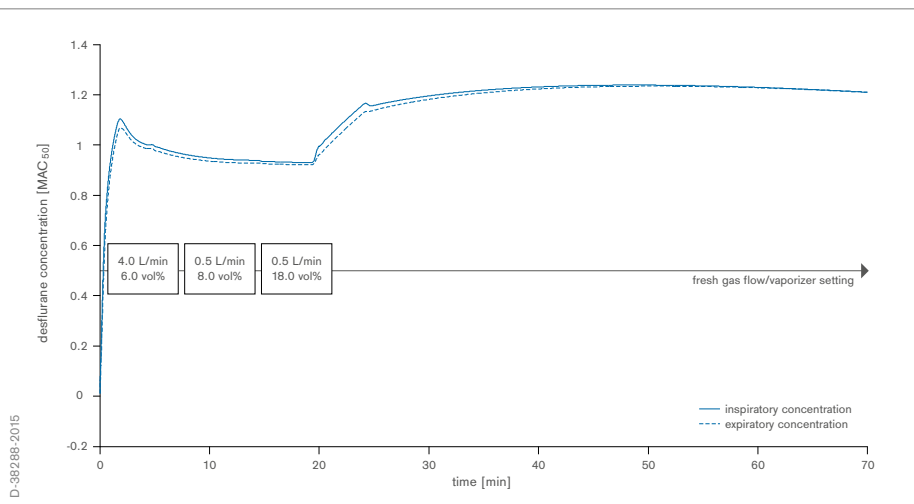


Fig. 34: Inspiratory and expiratory desflurane concentration over the course of inhalation anaesthesia. Relationship between fresh gas flows and maximum vaporizer setting with O_2 /air as carrier gases

Illustrative graph based on the 5-compartment model according to Bailey²⁵

Target value: expiratory concentration: 0.9 MAC, followed by an increase to 1.2 MAC. Vaporizer settings: see also diagram of minimal-flow anaesthesia 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_o .

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 anaesthesia

6.1 Contraindications of low-flow anaesthesia

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06 Contraindications of low-flow anaesthesia

6.1 Contraindications of low-flow anaesthesia

If toxic gases are to be washed out or accumulations prevented by controlled respiration, minimal-flow anaesthesia 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 anaesthesia 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 anaesthetics must be stopped immediately. The following additional indications also seem dangerous for minimal-flow anaesthesia: 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 anaesthesia is also contraindicated.

It goes without saying that, during the doctor's pre-operative visit and the preliminary anaesthesia 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 anaesthesia procedure, anaesthesia administration and monitoring, an anaesthesia 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 anaesthesia 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 anaesthesia, 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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07 Establishment and outlook

7.1 Establishing low-flow anaesthesia

Experts consider the greatest danger of anaesthesia to be that patients entrusted to our care could suffer accidental hypoxia under anaesthesia. This is stated as the main point of criticism against establishing and implementing low- and minimal-flow anaesthesia in everyday clinical practice. Experienced anaesthetists also sometimes take the position that these procedures would not be suitable for anaesthetists 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 anaesthesia is, of course, also suitable for training purpose. If the impending 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 anaesthesia is conducted using oxygen as the carrier gas, a very safe and simple-to-perform anaesthesia is provided.

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

7.2 Future prospect—low-flow anaesthesia?

In order to make these anaesthesia 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. The use of the Dräger SmartPilot View can meaningfully support minimal-flow techniques.

At this point, we should also refer once again critically to oxygen as a carrier gas. The simplest way of performing these anaesthesia 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^{41, 42, 43, 44, 45, 46, 47, 48}.

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 anaesthesia. 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 anaesthesia is an elegant, resource-efficient, economical and safe procedure for our patients.

08 Bibliography/References

8.1 References

- 1 Onishchuk JL. The early History of Low-Flow Anaesthesia. In Fink, B.R., L.E. Morris, C.R. Stephen, eds. The History of Anesthesia. Third International Symposium, Proceedings. Park Ridge, Illinois: Wood Library-Museum of Anesthesiology, 1992:308-313
- 2 Foldes F, Ceravolo A, Carpenter S. The administration of nitrous oxide – oxygen anesthesia in closed systems. *Ann Surg.* 1952;136:978-81
- 3 Virtue R. Minimal flow nitrous oxide anesthesia. *Anesthesiology* 1974;40:196-8
- 4 Baum JA, Enzenauer J, Krausse T, Sachs G. Soda lime – service, consumption and costs in relation to fresh gas flow. *Anaesthesiologie Reanimation* 1993;18(4):108-13 191
- 5 Baum JA, Aitkenhead AR. Low flow anaesthesia. *Anaesthesia* 1995; 50 Suppl: 37-44
- 6 Baum JA. Narkosesysteme. *Anaesthesist* 1987;36:393-399
- 7 Hönemann C, Hagemann O. Anaesthesie mit niedrigem Frischgasflow unter <http://kath-kliniken.de/images/Abteilungen/anaesthesie/Anaesthesie-mit-niedrigem-Gasfluss.pdf> (abgerufen am 01.07.2015).
- 8 Baum JA, Sachs G, v. d. Driesch C, Stanke HG. Carbon monoxide generation in carbon dioxide absorbents. *Anesth Analg* 1995;81:144-146
- 9 Baum JA: Die Anästhesie mit niedrigem Frischgasfluß: Darstellung des Verfahrens in Frage und Antwort / von Jan Baum, – Melsungen: Bibliomed, Med. Verl.-Ges., 1993, ISBN 3-921958-90-3
- 10 Ballard K, Cheesemann W, Ripiner T, Wells S. Humidification for ventilated patients. *Intensiv. Crit. Care. Nurs.* 1992;8:2-9
- 11 Chalon J, Loew D, Malebranche J. Effect of dry anaesthetic gases on tracheobronchial epithelium. *Anesthesiology* 1972;37:338-343
- 12 Hönemann C, Hagemann O, Doll D. Inhalational anaesthesia with low fresh gas flow. *Indian J Anaesth* 2013;57:345-50

- 13 Kleemann PP. Humidity of anaesthetic gases with respect to low flow anaesthesia. *Anaesth Intensive Care*. 1994;22:396-408
- 14 Aldrete JA, Cubillos P, Sherrill D. Humidity and temperature changes during low flow and closed system anaesthesia. *Acta Anaesthesiol Scand*. 1981;25:312-4
- 15 Bilgi M, Goksu S, Mizrak A, et al. Comparison of the effects of low-flow and high-flow inhalational anaesthesia with nitrous oxide and desflurane on mucociliary activity and pulmonary function tests. *Eur J Anaesthesiol*. 2011;28(4):279-83
- 16 Aldrete JA. Closed circuit anesthesia prevents moderate hypothermia occurring in patients having extremity surgery. *Circular* 1987;4:3-4
- 17 Suttner S, Boldt J. Low-flow anaesthesia. Does it have potential pharmacoeconomic consequences? *Pharmacoeconomics*. 2000;17:585-90
- 18 Baum JA. Low Flow Anaesthesia with Dräger Machines. 2004
- 19 Lortat-Jacob B, Billard V, Buschke W, Servin F. Assessing the clinical or pharmacoeconomical benefit of target controlled desflurane delivery in surgical patients using the Zeus anesthesia machine. *Anaesthesia*. 2009;64(11):1229-1235
- 20 Baum JA. Low-flow anesthesia: Theory, practice, technical preconditions, advantages, and foreign gas accumulation. *J Anesth*. 1999;13:166-74
- 21 Virtue RW. Low flow anesthesia: advantages in its clinical application, cost, and ecology. In: Aldrete JA, Lowe HJ, Virtue RW, eds. *Low Flow and Closed System Anesthesia*. New York: Grune & Stratton 1979;103-109
- 22 Brody JS. New York: Reinhold; 1945. *Bioenergetics and Growth, with Special Reference to the Efficiency Complex in Domestic Animals*
- 23 Goldberg IS, Mostert JW, Lanzl EF, Lowe HJ. A pharmacokinetic model of closed-circuit inhalation anesthesia. *Ann Biomed Eng*. 1978;6:231-49
- 24 Lowe HJ, Mostert JW. Quantitative closed circuit anaesthesia. *Anaesthesia*. 1974;29:110-1
- 25 Bailey JM. The pharmacokinetics of volatile anesthetic agent elimination: a theoretical study. *J. Pharmacokinet Biopharm* 1989;17(1):109-23

- 26 Kreuer S, Bruhn J, Wilhelm W, Bouillon T. Pharmakokinetische/pharmakodynamische Modelle für Inhalationsanästhetika, *Anaesthesist* 2007;56:538-556
- 27 Eger EI. et al., Consumption of Volatile Agents under Low Flow and Metabolic Flow Conditions, *Anesthesiology* 2004;101:A485
- 28 Baum JA. Low Flow Anaesthesia with Dräger Machines, *Dräger Medical* 2008; 15-17
- 29 Severinghaus JW. The rate of uptake of nitrous oxide in man. *J Clin Invest.* 1954;33:1183-9
- 30 Heller AR, Brückner JB. Update Inhalationsanästhesie. (2009) unter http://www.ai-online.info/abstracts/pdf/dacAbstracts/2009/01_Heller-Brueckner.pdf
- 31 Nickalls RW, Mapleson WW. Age-related iso-MAC charts for isoflurane, sevoflurane and desflurane in man. *Br J Anaesth.* 2003;91(2):170-4
- 32 Eger EI. Age, minimum alveolar anesthetic concentration, and minimum alveolar anesthetic concentration-awake. *Anesthesia and Analgesia.* 2001;93:947-953
- 33 Hönemann C. Balancierte Anästhesie. In Tonner, PH, Hein L. *Pharmakotherapie in der Anästhesie und Intensivmedizin. Grundlagen und klinische Konzepte.* Springer-Verlag 2011, 291-302
- 34 Mapleson WW. Effect of age on MAC in humans: a meta-analysis. *Br J Anaesth.* 1996;76(2):179-85
- 35 Kim KM, Choi BM, Park SW et al. Pharmacokinetics and pharmacodynamics of propofol microemulsion and lipid emulsion after an intravenous bolus and variable rate infusion. *Anesthesiology.* 2007;106(5):924-34
- 36 Cand. med. Y. Dietzler, Marienhospital Vechta, Dissertationsarbeit, Data not published
- 37 Baum JA, von Bormann B, Meyer J, van Aken H. Sauerstoff als Trägergas in der klinischen Anästhesie. *Anästhesiologie und Intensivmedizin* 2004; 45: 124-135
- 38 Baum JA. The carrier gas in anaesthesia: nitrous oxide/oxygen, medical air/oxygen and pure oxygen. *Curr Opin Anaesthesiol.* 2004;17(6):513-6.

- 39 Onody P, Gil P, Hennequin M. Safety of inhalation of a 50 % nitrous oxide/oxygen premix: a prospective survey of 35.828 administrations. *Drug Saf* 2006;29:633-40
- 40 Leitlinien zur Qualitätssicherung in der Anästhesiologie der Deutschen Gesellschaft für Anästhesie- und Intensivmedizin (DGAI) unter <http://www.dgai.de/publikationen/leitlinien>
- 41 Joshua D, Koch. Brief exposure to hyperoxia depletes the glial progenitor pool and impairs functional recovery after hypoxic-ischemic brain injury! *J Cereb Blood Flow Metab.* 2008 July
- 42 Greif R, Akca O, Horn EP, Kurz A, Sessler DI. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000;342:161-167
- 43 Greif R, Laciny S, Rapf B, Hickie RS, Sessler DI. Supplemental oxygen reduces the incidence of postoperative nausea and vomiting *Anesthesiology* 1999;91:1246-1252
- 44 Akca O, Podolski A, Eisenhuber E, Panzer O, Hetz H, Lampl K, Lachner FX, Wittmann K, Grabenwoeger F, Kurz A, Schultz AM, Negishi C, Sessler DI. Comparable postoperative pulmonary atelectasis in patients given 30 % or 80 % oxygen during and for two hours after colon resection. *Anesthesiology* 1999;91:991-998
- 45 Meier J, Habler O. Rationaler Einsatz von Sauerstoff in der Anästhesie und Intensivmedizin. *Anaesthsist* 2011;4:292-302
- 46 Habre W, Peták F. Perioperative use of oxygen: variabilities across age. *Br. J. Anaesth.* 2014;113(suppl 2):ii26-ii36
- 47 Kopp VJ. Might hyperoxia during surgical anaesthesia contribute to older patients' higher dementia risk? *Br J Psychiatry.* 2014;204(2):163
- 48 Decalmer S, O'Driscoll BR. Oxygen: friend or foe in peri-operative care? *Anaesthesia.* 2013;68(1):8-12. Epub 2012 Nov 7

ADDITIONAL REFERENCES

CME artikel: Low and Minimal flow inhalation anaesthesia, Alan D. Baxter, *Canadian Journal of Anaesthesia*, 1997

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8.4 Colour code

Colour	Element
	Isoflurane
	Sevoflurane
	Desflurane
	Oxygen (O ₂)
	Nitrous oxide (N ₂ O)
	Nitrogen (N)
	Low-flow anaesthesia
	Minimal-flow anaesthesia
	Metabolic-flow anaesthesia
	Non-quantitative anaesthesia 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

CORPORATE HEADQUARTERS

Drägerwerk AG & Co. KGaA
Moislinger Allee 53–55
23558 Lübeck, Germany

www.draeger.com

EDITOR

Drägerwerk AG & Co. KGaA
Moislinger Allee 53–55
23558 Lübeck, Germany