Safety in the use of anesthetic gases

Consensus paper from the basic German and French documentation

Working document for occupational safety and health specialists
ISSA International Section on the Prevention of Occupational Risks in Health Services

Safety in the use of anesthetic gases

Consensus paper from the basic German and French documentation

Working document for occupational safety and health specialists
Participants and authors

Dr. Marcel Jost, Chairman
Schweizerische Unfallversicherungsanstalt (Suva)
Lucerne (CH)

Dr. Rudolf Ahrens
Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege (BGW)
Hamburg (D)

Dr. Christine Breton
Caisse régionale d’assurance maladie d’Ile-de-France (CRAMIF)
Paris (F)

Georges Croatto, Chemical engineer
Caisse régionale d’assurance maladie d’Ile-de-France (CRAMIF)
Paris (F)

Dr. Udo Eickmann
Berufsgenossenschaft für Gesundheitsdienst und Wohlfahrtspflege (BGW)
Cologne (D)

Dr. Michel Falcy
Institut national de recherche et de sécurité (INRS)
Paris (F)

Dr. Martin Rüegger
Schweizerische Unfallversicherungsanstalt (Suva)
Lucerne (CH)

Martine Bloch, translator
Institut national de recherche et de sécurité (INRS)
Paris (F)

Anna-Maria Belz, translator
Institut national de recherche et de sécurité (INRS)
Paris (F)
In 1993, the International Social Security Association Health Services Section charged a Working group with a review of measures to prevent health risks related to products used in the health sector. This Working group includes R. Ahrens and U. Eickmann representing the German Institution for statutory accident insurance and prevention in the health and welfare services (BGW), M. Falcy for the French National research and safety institute (INRS), G. Croatto and C. Breton of the Paris Regional health insurance fund (CRAMIF) and M. Rüegger and M. Jost (the Working group's Chairman) for the Swiss National accident insurance fund (Suva). The Group would like to thank Martine Bloch and Anna-Maria Belz (of the INRS, Paris) who provided translation services during the Working group meetings.

This paper has been developed as a consensus statement from the basic German\textsuperscript{1} and French\textsuperscript{2} documentation on safety in the use of anesthetic gases generated by the Chemical products Working group of the ISSA Health Services Section in 1997. It summarizes the Working group's thinking on occupational risks and applicable preventive measures in the use of anesthetic gases.

The consensus document deals mainly with adverse health effects and assessment of risks related to occupational exposure to anesthetic gases (standards, hazard identification methods, exposure assessment, workplace monitoring). It also gives an overview of the experience of the organizations represented in the Working group in the field of risk assessment data. It recommends protective measures in the use of anesthetic gases such as technical measures, measures concerning anesthetic apparatus, procedures and individual behavior, organizational measures, specific recovery room aspects and specific measures concerning pregnancy. Finally, recommendations for preventive medical surveillance are given.

The Chemical products Working group of the ISSA Health Services Section has also published two documents respectively on “Safety in the Use of Disinfectants in the Health Services” and “Occupational Risk Prevention in Aerosol Therapy (pentamidine, ribavirin)”. These documents are available on the ISSA Website at: http://health.prevention.issa.int/product/publication.htm.

\textsuperscript{1} ISBN 92-843-7148-1; ISSN 1015-8022
\textsuperscript{2} ISBN 92-843-2148-4; ISSN 1015-8022
Contents

1. Adverse health effects of occupational exposure to anesthetic gases
   1.1. Toxicology of anesthetic gases
   1.2. Reproductive toxicology
   1.3. Conclusions

2. Assessment of risks related to occupational exposure to anesthetic gases
   2.1. Risk assessment approach
   2.2. Risk assessment data: experience of the organizations represented in the Working group

3. Recommended protective measures in the use of anesthetic gases
   3.1. Technical measures
   3.2. Measures concerning anesthetic apparatus
   3.3. Measures concerning procedures and individual behavior
   3.4. Maintenance and checking of technical systems
   3.5. Organizational measures
   3.6. Specific recovery room aspects
   3.7. Specific measures concerning pregnancy
   3.8. Relationship between personnel health protection and patient safety

4. Recommendations for preventive medical surveillance
1. Adverse health effects of occupational exposure to anesthetic gases

Exposure to anesthetic gases in the health sector, whether in the operating room, recovery room, or in the context of outpatient clinics, may entail a health risk for the personnel exposed. Although health care workers are exposed to much lower anesthetic concentrations than the patients, this exposure often extends over many years. Personnel often indicate fatigue and headaches, especially when occupational hygiene conditions are inadequate. More serious disorders such as reduced fertility and problems during pregnancy are mentioned. The decisive factors as concerns the adverse health effects of exposure to anesthetic gases are mainly the type of gases used, the length of exposure, and the gas concentrations.

1.1. Toxicology of anesthetic gases

1.1.1. Data from animal experiments

Animal experiments provide important data concerning the toxicology of inhaled anesthetics. These data are to be considered with care, in view of the high concentrations generally used in animal experiments, the often long exposure, and the differences between species. But animal experiments do allow us to identify effects of inhaled anesthetics that would appear only slowly or would be difficult to detect in the context of occupational exposure where the concentrations involved are generally rather small.

The main data from animal experiments can be summarized as follows:

**Nitrous oxide** causes an inhibition of the methionine synthase. High concentrations of nitrous oxide cause a peripheral leucopenia due to a bone marrow disorder. In primates, high concentrations of nitrous oxide induce neuropathy with histological degeneration of myelin sheaths and axonal cylinders. In cases of concomitant vitamin B\textsubscript{12} deficiency, nitrous oxide inhibits growth in the rat by a phenomenon of synergy.

**Halothane** causes dose-dependent hepatic alterations in the mouse, rat, and guinea pig. Prolonged exposure results in degenerative modifications of the cerebral cortex in the rat. At very high concentrations (1,000 ppm), **isoflurane** induces hepatic lesions in the mouse, rat, and guinea pig, but at a much lower incidence than in the case of halothane. A **sevoflurane** degradation product, 2-fluoromethoxy-1,1,3,3,3-pentafluoro-1-propene, also known as compound A, causes death in 50% of rats exposed to 330-420 ppm for 3 hours. **Desflurane** causes no organic disorder or induction of hepatic enzymes in the rat, even at high concentrations.

Animal experiments provide no clear conclusion concerning a possible carcinogenic risk from inhaled anesthetics.

1.1.2. Acute and chronic toxicity in humans

Occupational exposures to anesthetic gases involve concentrations much smaller than those administered to patients in surgery. However, the side effects of anesthetic gases on patients are of
interest for purposes of preventing adverse health effects on health care workers who are generally exposed to these gases over many years while working in operating rooms, recovery rooms, or in outpatient clinics.

\subsection*{Central nervous system}

The effects of sedation and analgesia sought for the patient may lead to undesirable effects in the personnel exposed, especially when the concentrations exceed current occupational exposure limits. The following symptoms have been described, among others: fatigue, headaches, dizziness, nervousness, nausea, concentration impairment and lacking fitness. Experimental and field studies have shown that concentrations of more than 500 ppm of nitrous oxide and more than 15 ppm of halothane or enflurane can alter performance, according to subjective assessments and neuropsychological tests. Recent neuropsychological tests have shown that nitrous oxide concentrations of less than 100 ppm can already cause a drop in performance. However, with such low exposure levels, the effect of other factors such as stress or poor work organization cannot be excluded.

\subsection*{Peripheral nervous system}

Peripheral neuropathy with sensitivity impairments, paresthesias, and muscular weakness has been observed after occupational exposure to nitrous oxide, but only at very high concentrations of several thousand ppm, for example in dental practices using no waste anesthetic gas scavenging system and in operating rooms equipped with inefficient air exhaust systems. Peripheral neuropathy due to nitrous oxide can also be explained by inactivation of the methionine synthase. When the concentration is less than 400 ppm, no significant inhibition of this enzyme is observed.

\subsection*{Hematopoietic system}

Nitrous oxide oxidizes the cyanocobalamin (vitamin B\textsubscript{12}) cobalt complex and thereby irreversibly inhibits the methionine synthase activity that requires vitamin B\textsubscript{12} in reduced form as coenzyme. This effect is dose-dependent. Nitrous oxide can thus cause medullary depression with megaloblastic anemia, leucopenia and thrombocytopenia. In patients, such hematological side effects are observed only for nitrous oxide concentrations at or above 20 \% by volume. They have been observed mainly in cases of prolonged or intermittent use of nitrous oxide (for example, sedation of patients suffering from tetanus with intermittent administration of nitrous oxide to facilitate physiotherapy). However, damage to the hematopoietic system from occupational exposure to nitrous oxide in the operating room is improbable. The other anesthetic gases don’t induce any hematological changes in exposed personnel.

\subsection*{Immune system}

Changes in the immune system such as a reduction in the number of B-lymphocytes and natural killer cells have been observed in exposed personnel after exposure to high concentrations of nitrous oxide (100 to 1,500 ppm) and halothane (1 to 40 ppm). This observation was not confirmed by other studies.

\subsection*{Liver}

In nearly 20 \% of patients, halothane causes an increase in hepatic enzymes that is usually not clinically apparent, but which can exceptionally evolve toward a clinically manifest toxic hepatitis. Severe cases of hepatitis with massive liver cell necrosis were even observed (with an incidence of 1:35,000). This is probably an antigen-antibody reaction involving trifluoroacetic acid (TFA) adducts and hepatocyte proteins as antigens. Cases of hepatitis due to halothane have also been described in personnel after months or years of occupational exposure.
Enflurane exceptionally prompts liver cell necroses in patients in cases of overdosing and severe hypoxia. Cases of toxic hepatitis in patients have also been attributed to exposure to isoflurane. But no hepatic disorder due to isoflurane or enflurane has been found in exposed personnel. No sign of hepatotoxicity has been observed for desflurane or sevoflurane.

**Kidneys**

Methoxyflurane has a nephrotoxic effect and is therefore no longer used in human medicine. There is no data hinting that commonly used anesthetic gases have nephrotoxic effects.

**Respiratory tract**

A case of bronchial asthma has been reported after repeated exposure to enflurane. The diagnosis could be established by specific bronchial provocation tests with enflurane.

**Skin**

A few cases of airborne allergic contact eczema have been described after occupational exposure to halothane and isoflurane.

**Metabolic effects**

Sevoflurane causes an increase in plasmatic fluorides in patients, but this effect seems to have no relevance in subjects occupationally exposed to sevoflurane.

**Genotoxic effects**

Studies on the genotoxic effects of occupational exposure to anesthetic gases (chromosome aberrations, sister chromatid exchange, micronucleus assay) yield contradictory results. Some, including recent ones, bring out a partly dose-dependent increase in sister chromatid exchange and micronuclei in the lymphocytes of exposed personnel, while others find no effect either in patients or exposed personnel.

**Carcinogenic effects**

Some epidemiological surveys bring out an increased incidence of leukemia, neoplasias of the lymphatic system, and other malignant tumors in exposed personnel. When evaluating these surveys, though, other factors such as exposure to ionizing radiation should be taken into account. Considering the methodological lacks of the older studies, the lack of data indicating an increased carcinogenic risk in the recent studies and the lack of conclusive data on any carcinogenic risk in the framework of animal experiments, a cancer risk due to occupational exposure to anesthetic gases seems unlikely, though it cannot be entirely excluded.

### 1.2. Reproductive toxicology

#### 1.2.1. Data from animal experiments

Nitrous oxide causes a reduction in the testicular weight in the male rat, with a decrease in sperm count, anomalies in spermatozoa form, and a drop in fertility. Fertility is also reduced in the female rat. Nitrous oxide is embryotoxic and increases the incidence of resorption as well as malformations of the skeleton and soft tissues. Minimum concentrations of nitrous oxide causing a significant drop in methionine synthase correspond approximately to those for which fetotoxicity (between 50 and 1,000 ppm) was observed, which seems to indicate a relationship between these two phenomena.
Halothane also has dose-dependent teratogenic effects in animal experiments. For enflurane and isoflurane, animal experiments bring out no embryo or fetotoxic effects except in cases of exposure at very high doses.

1.2.2. Effects on fertility

A retrospective study conducted in the United States on female dental assistants shows a significant relationship between high exposures to nitrous oxide and a decrease in fertility. For exposures between 200 and 7,000 ppm for more than five hours per week, the probability to become pregnant was reduced by 60% compared with persons with little or no exposure. So it is likely that high exposures to nitrous oxide will impair fertility.

1.2.3. Unfavorable effects on progress of pregnancy

A series of studies have been carried out to assess if there is an increased risk of spontaneous abortion in cases of occupational exposure to anesthetic gases. Several of those published in the 1970s concluded that the rate of spontaneous abortion is increased by a factor of 1.5 to 2, including in the spouses of exposed anesthesiologists. However, exposure to anesthetic gases in the operating room was generally higher and sometimes much higher at the time these studies were conducted than it is at present.

Recent studies meeting current requirements concerning epidemiological surveys have nonetheless shown an increased risk of spontaneous abortion. Some of these have brought out a dose-effect relationship between concentrations of anesthetic gases and the frequency of abortions in exposed female workers. A recently published meta-analysis established that, in case of exposure prior to the introduction of waste gas scavenging techniques, and therefore exposure to concentrations in excess of occupational exposure limits (mainly for nitrous oxide and halothane), the risk of spontaneous abortion should be considered as increased.

On the basis of epidemiological evidence and the data supporting the current occupational exposure limits, it can be considered that, if the recommended preventive measures are applied and the occupational exposure limits complied with, i.e., when the occupational hygiene principles are followed, there is probably no increased risk of spontaneous abortion except in cases of exposure to halothane.

1.2.4. Developmental effects

Most retrospective studies, as well as one recent prospective study, have shown no evidence of significant increase in malformations in the offspring of parents occupationally exposed to anesthetic gases. However, a small number of studies have shown a relationship between the malformation rate (mainly malformations of the cardiovascular system, osteo-articular and muscular malformations, central nervous system disorders) and exposure of the parents. Under the conditions that currently prevail in operating rooms, though, it seems that the risk of malformation in the offspring of parents occupationally exposed to anesthetic gases is not increased. Because of the neurotoxic effects of halothane and the high sensitivity of the human embryo's brain, central nervous system disorders in the case of in utero exposure to this anesthetic can nonetheless not be excluded. However, such effects cannot readily be evidenced.
1.3. Conclusions

When occupational hygiene conditions are unfavorable, personnel exposed to anesthetic gases may mainly exhibit effects on central nervous system such as mood disorders and impairment in neuropsychological performance. Rare cases of occupational diseases have been described, such as hepatitis due to halothane, bronchial asthma due to enflurane, and allergic contact eczema due to halothane or isoflurane.

Some studies have also brought out genotoxic effects of occupational exposure to certain anesthetic gases by biological monitoring on the lymphocytes (chromosome aberrations, sister chromatid exchange, micronucleus assay). However, other studies have not confirmed these data.

Similarly, on the basis of available data, it is unlikely that the risk of cancer is increased by occupational exposure to anesthetic gases.

An increase in the rate of spontaneous abortion resulting from occupational exposure to anesthetic gases under sub-standard hygiene conditions (i.e., in cases where exposure concentrations are clearly in excess of the occupational exposure limits to be complied with in the countries represented within the Working group, see section 2.1.1) may be considered as likely, especially in the case of halothane, whereas an increase in the malformation rate seems to be relatively unlikely. But it is also probable that high occupational exposure to nitrous oxide causes a reduction in fertility.

When the occupational exposure limits are complied with in the workplace, it can be considered that neither mood disorders are to be feared nor any risk for all of the exposed personnel or unfavorable effect on the progress of pregnancy.
2. Assessment of risks related to occupational exposure to anesthetic gases

The adverse health effects of occupational exposure to anesthetic gases depend on the level and length of exposure. Risk assessment therefore firstly calls for air monitoring data as well as biological monitoring data.

2.1. Risk assessment approach

Risk analysis and assessment in the workplace is an integral part of any modern occupational risk prevention system and is a legal requirement in all the countries involved in the drafting of this consensus paper. Every country has a different approach:

- In Switzerland, the employer can refer to the recommendations published by the Suva.
- In France, the Paris Regional health insurance fund (CRAMIF) has published a guide for prevention of occupational exposure to anesthetic gases and vapors. This guide includes methodological tools.
- In Germany, the “Technical rules applicable to dangerous products (TRGS)” No 525 describe the steps to be followed to assess risks related to anesthetic gases.

2.1.1. Occupational exposure limits

The main criteria for assessing exposure to anesthetic gases are the atmospheric exposure limits, which are not yet harmonized Europe-wide. In many countries (in particular, Germany and Switzerland), these values are given in the official list of occupational exposure limits. In France, a Ministry of health circular sets the exposure limits applicable for the anesthesia maintenance phase.

<table>
<thead>
<tr>
<th>Substance</th>
<th>SWITZERLAND</th>
<th>FRANCE</th>
<th>GERMANY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occupational exposure limit - Time-weighted average for 8 hours ppm</td>
<td>Short-term occupational exposure limit (4 x 15 min/shift) ppm</td>
<td>Occupational exposure limit during maintenance phase ppm</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>100</td>
<td>182</td>
<td>200</td>
</tr>
<tr>
<td>Halothane</td>
<td>5</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Enflurane</td>
<td>10</td>
<td>77</td>
<td>80</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>10</td>
<td>77</td>
<td>80</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Desflurane</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

For the biological limit values, please refer to section 2.1.2.4.
2.1.2. Methods of assessing exposure to anesthetic gases in the workplace

Various tools are used to assess the risks at an anesthesia workstation.

2.1.2.1. Analysis of data from the literature

Many studies have been published over recent years on the risks related to anesthetic gases. These data can be used to identify the risks on a case-by-case basis after checking that the working conditions described do correspond precisely enough to the situation actually encountered in the field.

It is important especially to compare the following parameters, which influence the exposure:

- The intensity of emission at the source depends on the anesthetic method used, the type of surgery practiced, the working technique, the anesthetic apparatus, the exhaust device, as well as quality assurance measures (mainly maintenance, servicing, checks).
- Gases released into the atmosphere are diluted by the fresh air introduced into the working zone. The introduction of fresh air depends on the mode of room ventilation (technical ventilation system, natural ventilation), organizational measures, and quality assurance measures.
- The concentration of anesthetic gas that develops in the room depends on the room size, the length of anesthesia, and the intensity of the ventilation.

It is impossible for all parameters to coincide with the situations described in the literature, so it is to be checked that the differences between the data from the literature used for the assessment and the field data are not essential as concerns the level of exposure.

2.1.2.2. Air monitoring

There are various techniques for measuring anesthetic gas concentrations in the air:

- Direct-reading systems
- Air sampling with equipment such as adsorbent tubes or cuffs, followed by analysis using gas chromatography or an infrared technique
- Diffusion sampler and analysis.

Considering the variation range of the parameters affecting exposure to anesthetic gases, air monitoring should be preferred to other methods of assessing exposure in the workplace. Measurements should be conducted and reviewed according to the state of the art by applying the methods recommended by national regulations in force or other validated methods.

It is nonetheless possible to do without air monitoring when the data from the literature or checklists allow adequate assessment of the workplace.

2.1.2.3. Calculation methods

Occupational exposure to anesthetic gases can be estimated by mathematical modeling of exposure in the workplace on the basis of all intervening factors. The same process can be applied for evaluating past occupational exposure (e.g., when assessing occupational diseases) or forecasting exposure at future workplaces (e.g., when planning protective measures). To do so, full information is needed concerning the product in question, the emission source, the room dimensions and ventilation conditions and work methods, and it must be possible to document the calculations precisely.

The simplest calculation method assumes that a homogeneous gas mixture forms in the room and a steady-state regime is established.
The dangerous product concentration is computed using the following formula:

\[ x_D = \frac{m_D}{V_L} \]

in which:

- \( x_D \) = concentration of dangerous product in the air \([\text{mg/m}^3]\)
- \( m_D \) = dangerous product mass flow \([\text{mg/h}]\)
- \( V_L \) = fresh air flow \([\text{m}^3/\text{h}]\)

However, to calculate the concentration more precisely, other factors need to be taken into account such as the length of anesthesia, room size and air exchange rate in the operating room. The following complex formula is then used:

\[ x_D = \left[ \frac{m_D}{V_L} + x_{D, ex} \right] \left[ 1 - \frac{1 - e^{-\lambda \Delta t}}{\lambda \Delta t} \right] + x_{D, 0} \cdot \frac{1 - e^{-\lambda \Delta t}}{\lambda \Delta t} \]

in which:

- \( x_D \) = mean concentration of dangerous product in the air \([\text{mg/m}^3]\)
- \( m_D \) = dangerous product mass flow \([\text{mg/h}]\)
- \( V_L \) = fresh air flow \([\text{m}^3/\text{h}]\)
- \( x_{D, ex} \) = concentration of dangerous product in fresh air \([\text{mg/m}^3]\)
- \( x_{D, 0} \) = concentration of dangerous product in room studied at beginning of calculation \([\text{mg/m}^3]\)
- \( \lambda \) = air exchange = \( V_L / \text{room volume} \) \([\text{l/h}]\)
- \( \Delta t \) = time interval over which the calculation is made \([\text{h}]\)

The conclusions that can be drawn from the calculation results depend essentially on the quality of the available data input on the relevant factors. Calculation methods have been published by the German BIA – Occupational safety institute of the institutions for statutory accident insurance and prevention (Report 3/2001).

### 2.1.2.4. Biological monitoring

Concentrations of anesthetic gases or their metabolites can be determined in the biological material to complement the air monitoring data, notably in cases of intermittent exposure or when establishing a cumulative exposure over several days.

Few biological limit values have been published to date for anesthetic gases. Some exist in Germany and Switzerland for halothane (total trifluoroacetic acid in the blood: 2.5 mg/l). The simplest approach is to dose inhalation anesthetics or their metabolites in a urine sample. For halothane, urinary trifluoroacetic acid can be taken (indicative value: 10 mg/g of creatinine) in order to evaluate the cumulated internal load over several days. Other inhalation anesthetics can be determined in the urine: exposure to 100 ppm of nitrous oxide corresponds to urinary concentrations of 50 to 60 µg/l, 10 ppm of enflurane to 20 µg/l, and 2 ppm of isoflurane to 4 - 6 µg/l.
2.2. Risk assessment data: experience of the organizations represented in the Working group

2.2.1. Experience of the Paris Regional health insurance fund (CRAMIF)

2.2.1.1. Study design

The study was conducted in 37 surgical units with 191 operating rooms and ancillary rooms. The following data were collected:
- Concentrations in workroom air (435 samples analyzed), essentially of nitrous oxide (N\textsubscript{2}O), which is an excellent indicator of exposure to N\textsubscript{2}O - halogenated gas mixtures;
- Data for the various parameters (type and phase of anesthesia, active or passive scavenging system, N\textsubscript{2}O flow rate, general ventilation, maintenance and servicing of facilities).

2.2.1.2. Measurement methods

Spot samples were taken in sealed cuffs (in the operating room at one meter from the mask). The different phases of anesthesia and work sequences were recorded. The samples were analyzed by gas chromatography with electron capture detection.

2.2.1.3. Overview of measurement data

The table below shows the relationships between the airborne N\textsubscript{2}O concentration during anesthetic maintenance phase, the type of anesthesia, and the N\textsubscript{2}O flow rate.

<table>
<thead>
<tr>
<th>Circuit (with/without rebreathing)</th>
<th>With rebreathing</th>
<th>Without rebreathing</th>
<th>Mask</th>
</tr>
</thead>
<tbody>
<tr>
<td>N\textsubscript{2}O flow rate (l/min)</td>
<td>&lt; 0.5 &lt; 0.5 (^{(1)})</td>
<td>&lt; 0.5 (^{(2)})</td>
<td>0.5 - 1</td>
</tr>
<tr>
<td>Waste anesthetic gas scavenging system</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Number of readings</td>
<td>6</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Median (ppm)</td>
<td>13</td>
<td>33</td>
<td>108</td>
</tr>
</tbody>
</table>

| Exposure classes \(^{(3)}\) | A | B | A | C |

(1) Intravenous induction with pure O\textsubscript{2} inhalation
(2) Induction with N\textsubscript{2}O inhalation
(3) Exposure classes:
- A: controlled exposure
- B: relatively high exposure
- C: high, uncontrolled exposure

2.2.1.4. Factors influencing measurement data

The main factors that have a favorable influence are:
- Intravenous induction with O\textsubscript{2} or a mixture of O\textsubscript{2} + N\textsubscript{2}O + halogenated gas with rebreathing circuit and/or waste anesthetic gas scavenging system;
- Maintenance with a mixture of O\textsubscript{2} + N\textsubscript{2}O + halogenated gas with rebreathing circuit, low fresh gas rate and/or waste anesthetic gas scavenging system;
- General ventilation: according to rule and well used.
2.2.1.5. Main conclusions concerning preventive measures

An action plan should be implemented in a four-phase approach based on the determination of the persons in charge to make this plan a management concern, extensive staff information and participation, the drawing up of a written policy, and support by the local gas monitoring commission and staff representatives.

1st phase: Data collection
- Technical data: premises, room ventilation, surgical activities, anesthetic products, gas circuits, anesthetic practices, inspection procedures, personnel exposed.
- Medical data: results of occupational medical examinations.
- Exposure data: activity practiced, results of air and biological monitoring, personnel exposed.

2nd phase: Assessment of environmental and individual exposures
- Identify the existence of favorable factors such as those mentioned in section 2.2.1.4.
- If these are lacking, go on to phase 3 because other measurements are needed (as a rule they are not necessary).
- If favorable factors are present, carry out a quantitative assessment (measurement plan comprising air movement, concentration of chemicals and biological monitoring). Methodological guidance documents for assessment have been developed. They include checklists relating to the various parameters and methods for measuring exposure levels and bringing together medical and biological monitoring data.

3rd phase: Drawing up of an action plan
The action plan will state the objectives and corresponding indicators in the following fields:
- Good anesthetic practices: choice of anesthetic products and equipment, adoption of low-pollution practices, use of local exhaust devices, programmed maintenance of anesthetic systems.
- Work premises: design, maintenance of facilities, local exhaust system, room ventilation.
- Personnel: training and information, medical surveillance.

4th phase: Action plan assessment and follow-up
Proper implementation of the action plan is to be checked regularly in light of the objectives set and the indicators provided.

2.2.2. Swiss Experience

Since 1984, the Swiss National accident insurance fund (Suva) has assumed an inspection mission as concerns the prevention of occupational diseases in all of the country's companies, and thus also in the health sector. The “Prevention of occupational diseases in the health sector” project lists and evaluates the risks related to chemical, biological and physical factors as well as the stresses and strains placed on the musculoskeletal system. In this framework, a campaign was conducted from 1991 to 1996 in all hospitals to assess exposures to anesthetic gases. It included the following steps: a survey by questionnaire to all hospitals, anesthetic gas concentration measurements in fifty operating units and publication of recommendations concerning safety in the use of anesthetic gases.

2.2.2.1. Project design
Surveys conducted in Swiss hospitals in 1976-77 and 1983-84 on working conditions in the anesthetic field had already revealed serious occupational hygiene problems. This is why another survey was undertaken in 1991 prior to a measurement campaign in representative surgical units throughout Switzerland. The purpose was mainly to review the status quo and formulate recommendations to improve the situation.
2.2.2.2. Measurement method

Personal sampling was performed with a photoacoustic IR multigas analyzer (Brüel & Kjær type 1302) especially equipped with filters to absorb water, ethanol and isopropanol vapors, and calibrated accordingly. This instrument measured simultaneously N\textsubscript{2}O and the halogenated anesthetic used every two minutes. It is better suited to evaluating rapidly-varying quantities than are passive samplers.

2.2.2.3. Analysis of measurement data and factors influencing the results

In all, 114 measurements were made in 50 surgical units of 25 hospitals. The data were evaluated on the basis of the occupational exposure limits currently applicable in Switzerland (see section 2.1.1). In those operating rooms with no ventilation system or with a deficient system (air exchange rate < 5 /h), 85 % of the N\textsubscript{2}O concentrations measured exceeded the occupational exposure limit of 100 ppm. In those operating rooms equipped with an efficient ventilation system (over 10 air changes per hour), this percentage fell to 30 %. When there was no anesthetic gas scavenging system, 87 % of the concentrations exceeded the occupational exposure limit compared with only 11 % when the rooms were equipped with an efficient scavenging system.

Another important factor was the fresh gas flow rate. When it was less than 3 l/min, the gas concentration in the air was reduced by 50 - 90 %. The type of anesthesia practiced also had an effect. Values often exceeded 100 ppm in mask anesthesia, especially when little attention was paid to avoiding the leaks. For this reason, the concentrations are much higher in the operating rooms of pediatric services than in services for adults.

In comparison, anesthesia by intubation and the more and more commonly used laryngeal mask gave sharply reduced values on the average. When a double mask was used, the excess anesthetic gas was recovered around the edge and it was observable that exposure was very much reduced with respect to induction using a conventional mask.

The main factors noted in this campaign were those influencing the emission of anesthetic gases (and thus the source of pollution), namely the use of a leak-free anesthetic technique, the use of an efficient anesthetic gas scavenging system, and the anesthetic gas flow rate.

2.2.2.4. Main conclusions

From a technical viewpoint, and in accordance with Switzerland's energy saving objectives, a ventilation system ensuring a fresh air inflow of 800 to 1,000 m\textsuperscript{3}/h is recommended for each operating room.

It is essential that an anesthetic gas scavenging system be installed and maintained regularly.

An effort should be made to keep the flow rates of anesthetic gases as low as possible, and preference should be given to anesthetic techniques with low leakage risk (intubation, laryngeal mask, double mask). It is essential that all necessary precautions be taken (especially for mask anesthesia) and that the apparatus be maintained regularly and checked for leakage. Lastly, it should be checked in all cases if gas anesthesia cannot be conveniently replaced by intravenous anesthesia. In Switzerland, the current trend is more and more largely toward this solution for general anesthesia.

2.2.3. German experience

The present assessment of risks related to anesthetic gases in the health sector in Germany is not based on data from one research project but on the results of several approaches, which were:

- literature review
- analysis of measurement data from different sources (inspection and insurance organizations)
- modeling of anesthetic gas emissions in the workplaces concerned
• analysis of available data on exposure, to establish a description of safe working conditions

The model established for calculating exposure brought out the importance of the following factors:
• concentration of anesthetic gases in the fresh gas supply
• apparatus leakage
• type and efficiency of gas scavenging system
• anesthetic method used
• link between patient and anesthesia system (tube, laryngeal mask, face mask)
• breathing system maintenance measures
• type of room ventilation system, ventilation efficiency
• ventilation system maintenance measures
• room size
• length of operation
• time spent in the room
• personnel position with respect to emission source

These factors have to be documented in the framework of risk analyses for comparison purposes. Many studies emphasizing organizational parameters such as type of unit (Ear, Nose and Throat, pediatric surgery, etc.) do not supply this data.

2.2.3.1. Operating rooms

Several hundred measurements were taken in workplaces in which various anesthetic techniques were applied. The results were interpreted on the basis of room characteristics and equipment used. The following conclusions can be drawn:
• When mask anesthesia predominates, excursions from the nitrous oxide occupational exposure limit can be frequently expected, even when the room is equipped with a ventilation system in conformity with standard DIN 1946, part 4.
• In cases of anesthesia mainly by intubation, with intravenous induction, in a room equipped with an efficient general ventilation system (fresh air flow $\geq 1200 \text{ m}^3/\text{h}$), the occupational exposure limits for anesthetic gases are complied with.
• When laryngeal masks are used in operating rooms equipped with a ventilation system (fresh air flow $\geq 1200 \text{ m}^3/\text{h}$), the occupational exposure limits for anesthetic gases are also complied with.
• In certain anesthetic processes (for bronchoscopy, for example, or in mask anesthesia with a poorly fitting face mask), peaks in excess of the occupational exposure limits can be observed, i.e., 15-minute time-weighted average in excess of the short-term occupational exposure limit.

2.2.3.2. Recovery rooms

On the basis of 267 measurements made in 25 recovery rooms and data from the literature, the following conclusions can be drawn:
• The available exposure data support the conclusion that the occupational exposure limits are complied with in recovery rooms when:
  - the rooms are equipped with a general ventilation system;
  - any avoidable source of anesthetic gases is excluded and quality assurance measures (checks, maintenance) are implemented and documented.
In case of natural ventilation, the concentration measurements (values too close to the occupational exposure limit, dispersion of measurements under poorly specified ventilation conditions) and data from the literature (showing excursions from occupational exposure limits) prevent any comment as concerns durable compliance with occupational exposure limits. An additional investigation must be carried out in the context of workplace analysis.
3. Recommended protective measures in the use of anesthetic gases

As for conventional dangerous products (such as organic solvents or formaldehyde), the use of anesthetic gases calls for protective measures. In accordance with the risk assessment process described in section 2.1, it is important to establish what kind of protective measures are to be implemented in the workplace. Priority usually goes to technical measures first, then organizational measures, and lastly personal protective measures. These general principles nonetheless need to be adapted to the specific conditions of anesthetic workplaces. When designing new workplaces, the employer, anesthesiologists and prevention specialists have to take due account of technical preventive measures, considering that most personal protective measures can be ineffective (face masks, for example, are ineffective against exposure to nitrous oxide) and do not correspond to the state of the art. The recommendations below are made mainly on the basis of the guidance documents published by the Paris Regional health insurance fund (CRAMIF), the recommendations from the Swiss Suva, the German technical rules (TRGS) No 525 and the recommendations from the German Institutions for statutory accident insurance and prevention (Berufsgenossenschaften) for operating and recovery room surveillance.

3.1. Technical measures

Technical preventive measures aim mainly to prevent polluting the workplace atmosphere with anesthetic gases, or to remove the gases released from ambient air. The following measures are recommended:

- It is important to use an effective waste gas scavenging system, if possible with a volumetric buffer regulation system. The exhaust rate should be adjusted in such a way that no gas is released into the room from the overpressure relief valve in the patient's breathing system. A minimum exhaust flow rate of 40 l/min is generally recommended.
- Rooms where anesthetic gases are regularly used should be equipped with a ventilation system. System performance should meet the requirements of hospital hygiene, occupational risk prevention, and environmental protection (including the viewpoint of energy savings). In order for all the routine techniques to be carried out in an operating room without exceeding the occupational exposure limits, it is recommended that the minimum fresh air supply be 800 to 1,200 m$^3$/h, or more than 15 (fresh) air changes per hour, as recommended by various national regulations.
- Activated charcoal cartridges are not an effective replacement for active scavenging of anesthetic gases.

3.2. Measures concerning anesthetic apparatus

- As far as possible, anesthetic apparatus should have little leakage and include an automatic leakage check device. If there is no such device, leakage tests should be conducted regularly by a standardized method. Please refer to standard EN 740, which limits total leakage in the anesthetic system to 150 ml/min. Commercially available leak detectors can be used routinely.
• All gases sampled for system surveillance, and the anesthetic circuit flushing gases, are to be directed to the exhaust system.
• Double mask systems effectively reduce personnel exposure to anesthetic gases, especially in mask induction.

3.3. Measures concerning procedures and individual behavior

To reduce anesthetic gas concentrations in the operating room, technical preventive measures but also the choice of anesthesia system and working techniques are decisive. Anesthesia system operation depends not only on technical factors but also on individual behavior. Special attention should be paid concerning working techniques that reduce leakage to a minimum, so it is indispensable to inform the exposed personnel of these techniques.

The following gives recommendations concerning the preparation and induction of anesthesia, the maintenance and emergence phase.

a) Preparation of anesthesia
• It is important to consider the exposure risk when choosing the anesthesia system. It is recommended that a system be chosen that has little leakage and allows scavenging of excess gases.
• From the health protection viewpoint, anesthesia apparatus that has a low or minimum flow of fresh gas makes it possible to reduce leakage to a minimum while reducing the consumption of anesthetic gases.
• Face masks must be of optimum size and should be used only when laryngeal masks cannot be used. The latter are relatively leak-proof, which reduces the concentrations of anesthetic gases in workroom air.
• For intubation without cuff, choose a tube size that induces little leakage.

b) Induction
• The induction phase is an important factor of personnel exposure to anesthetic gases during the operation. Intravenous induction or a double mask system will notably reduce total personnel exposure.
• Gas supply should only be started after the mask is placed leaktight, or after the tube is connected to the patient system.
• An anesthetic gas scavenging system should be used during induction because the internal dose during the induction phase may come to as much as half of the total dose absorbed during the entire operation.
• It is important to check that the scavenging device is correctly connected before anesthesia and whenever the apparatus is moved.

c) Maintenance
• In mask anesthesia, the mask airtightness must be checked constantly.
• When the patient is disconnected from the breathing system, contamination in workroom air should be limited by opening the exhaust gas valve and keeping the open end of the system closed, or briefly cut off the gas supply and empty the buffer balloon via the anesthetic gas scavenging system.
d) Emergence

- At the end of anesthesia, before removing the tube or mask, oxygen should be administered to the patient at a high flow rate to flush the anesthetics out of the anesthesia system and the patient's lungs.
- At the end of anesthesia, it is important to check that the fresh gas supply is fully cut off.

e) Other recommendations

- Safety devices should be used to fill the vaporizers in order to avoid spilling volatile anesthetics.
- Handling of anesthetic gases should be avoided in the recovery room (e.g., filling vaporizers).
- Anesthesia system seal should be checked regularly with leak detection apparatus.

3.4. Maintenance and checking of technical systems

The following technical systems should undergo regular maintenance:

- Anesthesia apparatus and accessories (hoses, etc.)
- Wall plugs
- Anesthetic gas piping
- Anesthetic gas scavenging devices
- Ventilation system

Systematic checks should be planned:

- Regular check of the administration system, gas supply and scavenging hoses, and gas system tightness. It is advised that apparatus with automatic integrated check be used.
- Check of anesthesia machines, piping, connections and the ventilation system at regular intervals. Maintenance and checking results are to be recorded in writing.

3.5. Organizational measures

The employer should make improvement of occupational safety and health part of the establishment's objectives. Occupational safety and health are a management job coming under the employer's responsibility.

The responsibility of protection against anesthetic gases should be entrusted to a competent working group including representatives of the employer, prevention specialists, occupational safety and health specialists, and staff representatives. The employer should make the necessary resources available to this working group so it can accomplish its task. It is recommended that an anesthesiologist well-informed of occupational safety questions be entrusted with the mission of applying the necessary measures, to promote acceptance by the staff.

3.5.1. General organizational measures

General organizational measures include the following:

- Safety instructions should be established indicating the possible risks and stating preventive measures and procedures applicable. This aspect is especially important when new machinery or processes are introduced.
- These safety instructions are the basis for personnel training – both the training prior to assuming a position, as well as the training conducted when procedures are modified and the periodic knowledge and procedure refreshers.
• It is important to make sure that these safety instructions are followed by the personnel.
• The personnel should be regularly trained and informed prior to assuming a position and all through their activity with the anesthesiology unit, especially when new equipment and processes are introduced. Training and information activities are to be documented in writing by the health care establishment. The occupational physician and/or safety specialist in charge should be called in for these actions.
• A establishment-specific risk analysis and monitoring system can be essential (see section 3.5.2)
• Employment restrictions are to be evaluated on the basis of national regulations and European directives. In some countries, these restrictions are part of medical prevention. Special precautions are needed for people suffering from diseases caused by anesthetic gases, whose assignment comes under the responsibility of the occupational physician. As concerns the employment of pregnant and breastfeeding women, see section 3.7.

3.5.2. Risk analysis and monitoring system

The protective measures implemented are to be in conformity with the state of the art and suited to the work procedures, so it is very important to set up a risk analysis and monitoring system in workplaces where there is a risk of exposure to anesthetic gases.

a) The following approach is advised:
• initial and then periodic assessment of exposure to anesthetic gases
• identification of critical points
• choice of improvement measures
• writing of an action plan and application of the corresponding protective measures
• periodic check of the measures taken and of the parameters justifying them

b) Periodic checks should be made of the following points:
• number and type of premises concerned
• layout and installation of gas supply systems
• ventilation characteristics
• surgical activities
• anesthetics used (types and quantities)
• anesthetic gas circuits
• anesthesia methods
• extent of regular maintenance actions concerning safety
• personnel concerned, number of employees and training level

c) Personnel exposure should be evaluated regularly on the basis of the latest data collected. Qualitative and quantitative methods can be applied in this respect (see section 2.1.2).
3.5.3. Implementation of measures for health protection

It is recommended that a person in the anesthesia unit be put in charge of developing directives in concert with occupational safety and health specialists, and making sure these directives are followed. Part of this person's missions should also be to inform colleagues of the hazards and the preventive measures to be applied. Generally, only duly trained personnel should perform any work that carries a risk of exposure to anesthetic gases. A regular personnel training is of special importance. In Germany, it is proposed that this mission be entrusted to a specially trained anesthesiologist in order for this process to be better accepted.

3.6. Specific recovery room aspects

The concentration of nitrous oxide in the air exhaled by a patient who has been under anesthesia for 60 - 90 minutes is still 2 to 4 % by volume 30 minutes after the end of anesthesia. When more than two or three patients are in recovery, the emission of anesthetic gases into the recovery room reaches or exceeds the emission due to leakage in operating rooms with waste gas scavenging devices. Non-negligible exposure may result from this for personnel taking care of the patients in the recovery room while the exposure depends mainly on the number of patients, their rate of arrival, the length of anesthesia they have undergone (long operations result in greater anesthetic off-gassing), room ventilation and the care the patients need. Excursions from occupational exposure limits are to be expected in recovery rooms that have only natural ventilation, both as concerns time-weighted average and short-term occupational exposure limits. Technical ventilation is therefore of special importance.

The following measures are recommended:

- The recovery room should be equipped with a ventilation system.
- This system should supply at least 100 to 200 m$^3$ of fresh air per bed and per hour.
- Pressurized anesthetic gas supply systems and anesthesia apparatus in recovery rooms should be subjected to regular maintenance. The apparatus should be checked regularly for leakage, e.g., by gas detector apparatus or sprays or other appropriate measures.
- Anesthetic gas vaporizers should not be filled in recovery rooms.
- Technical system maintenance and checking operations should be documented in a maintenance register.

3.7. Specific measures concerning pregnancy

Occupational physicians must consider the scientific data that show a relationship between exposure to anesthetic gases and the progress of a pregnancy when they have to evaluate workplaces incurring this type of exposure. However, they must also take other risk factors into account such as work schedules, work postures, exposure to ionizing radiation or to disinfectants, and the like. As many women are occupationally exposed to anesthetics, the problem of pregnancy should be considered at the outset, and the measures to be taken are to be planned with the heads of the various sectors. Generally, risk assessment should integrate the “exposure to anesthetic gases - pregnancy” situation. The preventive measures should make it so that there is no risk for the pregnant woman or the unborn child, especially at the very beginning of a pregnancy that may not yet have been identified. It is important to recall the potential risks for a pregnancy to all personnel exposed to anesthetic gases at the time of medical examinations, and to recommend that they contact the occupational...
health service in case of pregnancy or, better yet, when planning a pregnancy. It will then be important to check the workplace conditions as well as any exposure to anesthetic gases. Employment restrictions should be left to the appreciation of the occupational physician. It is reasonable to avoid employing pregnant women in operating rooms where the risk assessment (see section 2.1) shows that the anesthetic concentrations are potentially high (Ear, Nose and Throat and pediatrics, for example). In cases of fertility problems, the occupational physician should also think of the possible exposure of the partner to high concentrations of anesthetic gases. National regulations concerning the protection of employees during pregnancy must also be taken into account. Because of their lipohily, most gaseous anesthetics enter mother's milk easily. This should be kept in mind when considering the assignment of breastfeeding mothers to rooms where there is a risk of exposure to anesthetic gases. The terms of national regulations are to be applied, and it is incumbent upon the occupational physician to evaluate the hygiene conditions in the workplace.

3.8. Relationship between personnel health protection and patient safety

In matters of anesthesia, there is a strong relationship between patient and worker safety. The effectiveness and safety of the anesthetic technique should not be impaired by the safety measures implemented for the health care workers. The choice of anesthetic technique should be based both on patient safety and personnel health protection criteria. In particular, the patient should remain constantly accessible to the anesthesiologist during the operation. Health protection measures can be planned at the same time as the anesthesia itself. The purpose of the hospital's strategy should be to reconcile the health protection and patient safety aspects. In the hospital environment, anesthetic techniques that subject the personnel to least risk without altering safety for the patients are to be preferred, even if this calls for additional personnel or equipment or organizational measures. In evaluating the respective interests of patient and personnel, however, the rule is that the patient's interest comes first, especially in emergency situations. Under exceptional circumstances, short-term excursions from occupational exposure limits do not constitute a serious risk for the personnel compared with the possible risk for the patient. A number of elements underlie safety for all: choice of the least dangerous anesthetics; use of lowest doses; and choice of anesthetic technique. It should be pointed out that preventive measures aimed at reducing the risk of acute exposure to anesthetics in health care workers are usually the same measures that lead to better safety for the patient. The use of gas-less anesthetic techniques should be considered whenever possible.
4. Recommendations for preventive medical surveillance

Personnel exposed to anesthetic gases should undergo medical surveillance in compliance with national regulations. The purpose of this medical surveillance is to detect health damage that might result from exposure to anesthetic gases on the basis of physical examinations or additional investigations; to review working conditions in those workplaces where there is exposure to anesthetic gases; and to improve worker awareness concerning the measures to be implemented in the workplace.

Generally, a medical examination should be performed before hiring. The interval between two examinations depends on the regulations in force as well as the specific features of the workplace. The examination should include a medical and occupational history and a physical examination; complete blood count, hepatic enzyme and urinary analyses may also be deemed necessary. Special care is advisable for employees with hepatic disorders, especially when exposure to halothane or isoflurane is expected.

The preventive medical examination may be complemented by biological monitoring, in particular in cases of exposure to nitrous oxide or halothane.

Special attention should be paid to the reproductive effects of anesthetic gases (see section 3.7). Female health care workers having pregnancy plans or who are already in early pregnancy should undergo special surveillance; they should discuss with the occupational physician about their further assignments as soon as they discover that they are pregnant or even better at the time of planning pregnancy.

Medical surveillance of exposed personnel should also provide an opportunity to look into other aspects such as the risks of bloodborne infectious diseases, or tuberculosis, the risk of exposure to ionizing radiation, exposure to disinfectants, the ergonomic environment, mental load, and other factors.