Journal of Anesthesia (2018) 32:269–282
https://doi.org/10.1007/s00540-018-2448-1

REVIEW ARTICLE

Waste anesthetic gas exposure and strategies for solution

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Received: 2 September 2017 / Accepted: 2 January 2018 / Published online: 5 February 2018

Abstract
As inhaled anesthetics are widely used, medical staff have inevitably suffered from exposure to anesthetic waste gases (WAGs). Whether chronic exposure to WAGs has an impact on the health of medical staff has long been a common concern, but conclusions are not consistent. Many measures and equipment have been proposed to reduce the concentration of WAGs as far as possible. This review aims to dissect the current exposure to WAGs and its influence on medical staff in the workplace and the environment, and summarize strategies to reduce WAGs.

Keywords Waste anesthetic gases · Occupational exposure · Inhaled anesthetics

Introduction

With the advantage of low solubility in blood and high controllability [1], inhalation anesthetics are widely used in the operating room (OR), dental clinic, delivery room, MRI suite and intensive care unit. However, inhalation anesthetics inevitably cause waste anesthetic gases (WAGs) in the workplace. Anesthesiologists, nurse anesthetists, OR nurses, nurse aides, OR technicians, surgeons, interns, dentists and other medical staff have to face chronic exposure to WAGs. Although air-conditioning and scavenging systems are widely used, which effectively reduce the concentration of WAGs, complete elimination of WAGs is impossible [2, 3].

Studies have shown that long-term exposure to WAGs can lead to increased oxidative stress [4–6], DNA damage [7–9], genotoxicity [10] and carcinogenesis [11, 12]. Some large epidemiological investigations have also found increased risks of chronic diseases (cancer, liver dysfunction, renal insufficiency etc.), spontaneous abortion, congenital malformations, low birth rates and higher stillbirthrates in offspring [13–15]. Although there is no definite evidence to prove these side-effects, the National Institute of Occupational Safety and Health (NIOSH) set the exposure threshold limits in 1977 [16], and the Occupational Safety and Health Administration (OSHA) also recommended keeping WAG exposure to the lowest level [17].

Recently, the Health and Safety Practices Survey of healthcare workers conducted a study on practices of controlling exposure to N_2O for dentists, dental hygienists and dental assistants. It was disappointing that 13% of respondents (284 dental professionals in private practice) lacked standard procedures, and 3% were not trained on safe handling and administration of N_2O [18]. Meanwhile, another survey by the affiliates of Isfahan University of Medical Sciences assessed the risk status of WAGs in 4 hospitals (over 100 ORs) using a standard-structure checklist developed by the Emergency Care Research Institute. Only 28% of all ORs complied with predetermined standards, while 16% needed improvement and 56% had no compliance. Total mean scores of compliance of planning, training, evaluation and monitoring of WAGs were weak, with equipment and work activity at medium level [19].

In order to fully understand the status of WAGs worldwide and to improve our working environment, we here review the present emission situations of WAGs in OR in different countries, the threshold limits of WAGs in different countries and the side-effects of WAGs, and summarize the strategies to reduce WAGs.

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Materials and methods

A search in the scientific databases PubMed, Medline and Web of Science was made by an information scientist based on the following keywords: "waste anesthetic gases" or "trace anesthetic gases" or "anesthetic gases" or "volatile anesthetics" or "inhalation anesthetics" or "occupational exposure" or "occupational hazards", with no time limit. To optimize the search, the reference lists of relevant articles and narrative reviews were also included.

A study was considered not eligible if the article was a case-report with insufficient information. The review proceeded by synthesizing the exposure threshold limits, the measurement of WAGs, the influence on medical staff and environment, and finally solutions to reduce WAGs.

Results

Exposure threshold limits of WAGs in different countries

It was noticed that WAGs had potential adverse effects on the human body a long time ago, and a large number of experimental studies and epidemiological investigations were conducted. As early as 1977, the NIOSH published recommended limits for WAGs [16], and some other organizations [such as the American Conference of Governmental Industrial Hygienists (ACGIH)] and other countries also developed their own limit standards. The standards are measurable by techniques available to industries and government agencies. The occupational exposure level is based on the weight of the agent collected from a 45-L air sample by charcoal adsorption over a sampling period of 1 or 8 h. Such set levels are lower than those that cause side-effects in animal experiments and no evidence had indicated that these levels had an impact on human health. However, the recommended permissible exposure levels cannot be defined as safe levels since the potential adverse health effects of WAGs are not completely understood. In any case, compliance with all standards should control WAGs to the lowest feasible levels which minimize potential adverse effects on the health and safety of workers and their unborn children (https://www.cdc.gov/niosh/pdfs/77-140a.pdf). Several countries have established their own threshold limits of exposure to five anesthetic gases (Table 1). Large variability was present between different countries [20–22], such as 5 ppm (38 mg/m^3) in Denmark and 50 ppm (383 mg/m^3) in England or Spain for isoflurane [23], and the limit is related to use in conjunction with N_2O. Even some large associations (NOISH and ACGIH) are inconsistent [24], thus a worldwide standard for WAGs has not yet been reached. In addition, we found that many countries do not assign a limit to sevoflurane. Various limit standards in different countries may be due to frequent changes of WAG concentration during operations. Some organizations (NOISH) prescribe the limit standards by a 1-h time-weighted average, while some use an 8-h time-weighted average [21, 25]. Some countries have also developed the average concentration of WAGs for any 15-min period in a working day [23].

Additionally, the Expert Group for Chemical Hazards has set the maximum admissible concentrations of WAGs in ORs, sevoflurane [55 mg/m^3 (7 ppm)] and isoflurane [55 mg/m^3 (7 ppm)], in the belief that these exposure levels could protect the surgical staff against adverse effects on neurology, the cardiovascular system and respiratory system [26].

WAG exposure situation

WAGs may leak from the patient's anesthesia breathing circuits and anesthesia machines, and can be exhaled by patients in ORs and recovery rooms. Although WAGs are recommended to be as low as possible, the situation is not as optimistic as is supposed in our daily workplaces. Kucharska et al. conducted a five-year survey of WAGs in 117 ORs from 31 hospitals in Poland. 40% of the ORs reported that N_2O concentrations exceeded the maximum allowable value, 3% reported halothane to be over the limit and 2% reported sevoflurane to be over the limit, and in individual tests, 130 cases reported that WAG exposure exceeded the admissible level in 146 anesthesiologists and 154 nurses [27]. The same result was revealed in the survey of Asefzadeh et al. [19]. By scanning the exposure of WAGs in different countries (Table 2), we found that the exposure level in some settings was significantly above the recommended limits, which was closely related to usage of the scavenging system [28–30]. Even in the same country, study results from Mierdl et al. [31] and Krajewski et al. [21] were not uniform, which might relate to the different scavenging systems that were installed. The research from Westberg et al. [32] and Sackey et al. [33] also indicated inconsistent concentration of WAGs in different places and different hospitals. The main reason for the differences may be that the intensive care unit used anesthetic gas mainly for sedation, while the delivery room needed to adopt a higher concentration to achieve inhaled anesthesia. Interestingly, postanesthesia care units (PACUs) had a high concentration of WAGs, even higher than that in the ORs [34], which has been overlooked. After airway devices are removed, the residual WAGs would be exhaled directly into the PACU without enough laminar flow and scavenging system. On the other hand, even if the average exposure concentration is lower than the limit standard in

Table 1 Exposure threshold limits of WAGs in different countries

Country	N_2O		Halothane		Desflurane		Isoflurane		Sevoflurane	
	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3	ppm	mg/m^3
Poland [20]	–	90	–	40	–	125	–	32	–	55
Germany [21]	100	180	5	40	10	70	10	80	–	–
Italy [22]	100	–	–	–	–	–	–	–	–	–
French [22]	–	–	2	–	–	–	–		–	–
Netherlands [22]	25	–	5	–	–	–	2	–	–	–
Sweden [22]	100	180	5	40	10	70	10	80	10	80
China [25]	25*	–	2*	–	–	–	2*	–	2*	–
Canada [23]	25		2	–	–	–	2	–	–	–
Denmark [23]	50	90	5	40	5	35	5	38	5	42
Norway [23]	50	90	0.02	0.2	20	140	2	15	20	140
England [23]	100		10	82	–	–	50	383	–	–
Spain [23]	50	92	50	410	–	–	50	383	–	–
Belgium [23]	50	91	50	410	–	–	–	–	–	–
Finland [23]	100	180	1	8.2	10	70	10	77	10	83
Austria [23]	100	180	5	40	–	–	10	80	10	80
NOISH [16]	25#	45#	2#	4.0#	–	–	2#	3.8#	2#	4.2#
			0.5&				0.5&		0.5&	
ACGIH [24]	50	–	50	–	–	–	–	–	–	–

– not mentioned

ACGIH American Conference of Governmental Industrial Hygienists

*Time-weighted average (TWA) over an 8-h working shift

#Exposure level that cannot be exceeded during a 1-h period when used alone

&Exposure level that cannot be exceeded when used in conjunction with N_2O

the ORs, short-term exposure to high-level WAGs might exist when staff were in the induction and extubation periods during inhaled anesthesia [35].

Interestingly, Sarkany et al. found that the physical position could affect WAG exposure levels [36]. For example, the WAG level was higher in the sitting position than standing, and significantly lower in the corners. Looking at individual exposure levels, the patient's mouth captured the highest amount of WAGs [37, 38], and the anesthesiologist was always exposed to higher WAGs than the surgeon and nurse [39, 40].

However, the measured concentration of WAGs may not be a real situation, due to frequent usage of alcohols and disinfectants in the ORs. Such potential cross-sensitivity reactions between the gas monitors will affect the measured results [41]. Herzog-Niescery et al. found that concentrations in previous measurements may be overestimated (10–15%) because of the cross-sensitivity reaction [35]. Meanwhile, personal samplings merely reflect the WAG concentration of an individual's breathing zone, which does not necessarily represent a picture of an individual's dose. We therefore need to check the accurate concentration of WAGs inside the body. Researchers tried to combine biological and atmospheric indicators to evaluate the WAG exposure situation [42–45], such as urinary concentrations of sevoflurane, and blood concentrations of anesthetic gas and its metabolite hexafluoroisopropanol. However, these indicators are also disturbed by shift-work and metabolism, such as working hours and liver and kidney function. Some studies found no significant relationship between various biological indicators measured [46, 47]. More work is needed to identify the best biomarkers to monitor WAG exposure and the corresponding biological equivalent levels.

The influence of WAGs

Influence on the health of medical staff

Medical staff may simply inhale and exhale the prototype of the anesthetic gas, leaving only a small amount of metabolic forms inside the body, which finally discharge through the urine [48]. However, the side-effects of WAGs on staff who stay in the same environment for a long time are still controversial. Studies have shown that exposure to high concentrations of WAGs in a short time caused a series of neuropsychological symptoms such as drowsiness, headache, fatigue, irritability, nausea, poor judgment and loss of coordination, which disappeared after the person left the workplace [29, 49, 50]. It was also demonstrated that these symptoms are strongly related to WAG exposure levels [51].

Table 2 Exposure situation of different countries

Study	Country	Place	Scavenging system	Gas	The concentration of WAGs		Unit	Content
Mierdl, S [31]	Germany	OR	All install		Before/During CPB:		ppm	Exposure levels of SEV and N_2O were below the limit at all times. When DEF was used to maintain anesthesia before CPB, the NIOSH limit was exceeded by 32.0% for perfusionists and by 12.4% for surgeons respectively, while the anesthesiologist received only marginal levels
				N_2O	9.32/3.00(S)	6.67/0.46(A)		
				DEF	0.21/0.62(S)	0.02/0.02(A)		
				SEV	0.16/0.16(S)	0.03/0.04(A)		
Krajewski, W [21]	Germany	OR	15/26 install	N_2O	468.0 ± 350.3		mg/m^3	19/26 N_2O concentration exceeded the German OEL, only 5/26 conformed to ACGIH, and 3/26 conformed to NIOSH. ISO and HAL did not exceed Germany or ACGIH OEL
				SEV	4.7 ± 7.0			
				ISO	3.8 ± 8.2			
				HAL	2.2 ± 16.1			
Westberg, H [32]	Sweden	Delivery room	Part used ventilated double mask	N_2O	M	Hospital: A(220 ± 55) B(41 ± 66) C(10 ± 11) D(44 ± 36) E(120 ± 51) F(17 ± 9.9)	mg/m^3	Around 25% of the 8-h TWAs exceeded ACGIH OEL, 14% short-term samples exceeded the Swedish occupational exposure ceiling limit value
					AM	Hospital: A(150 ± 18) B(78 ± 89) D(50 ± 4.2)		
Sackey, P V [33]	Sweden	ICU	All install	ISO	0.1 ± 0.2		ppm	ISO concentration were below exposure recommended limits in all cases
Sarkany, P [36]	Hungary	OR	–	SEV	0.37(sitting) 0.55(standing) 0.14(corner) 1.2(patient)		ppm	SEV concentration is below the accepted threshold limits in all positions except patient's mouth. WAGs level was higher in the sitting position than standing, and significantly lower at the corner
Tanko, B [39]	Hungary	OR	All install	SEV	0.15 ± 0.05(S) 1.54 ± 0.55(P) 1.14 ± 0.43(A)		ppm	The exposure level of anesthesiologist was about six-fold higher than the surgeons' exposure, and the patient's mouth captured the highest amount of SEV
Gao Rui-jun [28]	China	OR	38.4% OR install	SEV	2.94		ppm	24.6% ORs were detected contamination, 52.5% concentration is over 2.0 ppm
Wronska-Nofer, T [4]	Poland	OR	–	N_2O	185-1502		mg/m^3	N_2O concentration exceed the OEL, but ISO and SEV concentration are below the OEL
				ISO	0.4–15.0			
				SEV	0.5-14.0			

Table 2 (continued)

Study	Country	Place	Scavenging system	Gas	The concentration of WAGs	Unit	Content
Sanabria, C, P [29]	Spain	OR	With/Without install	N_2O SEV	423/24.7 1.1/12	ppm	The level of exposure N_2O and SEV were obvious over the recommended limits without an extractor
Cheung, S K [34]	USA	PACU/ OR	–	SEV DEV	0.7/0.5 4.1/2.1	ppm	WAGs levels in patients' breathing zones significantly higher in the PACU compared to the OR
Braz, L. G. [30]	Brazil	OR	With/Without install	ISO SEV	1.2/10.3 3.3/16.7	ppm	The both anesthetic gases exceeded the limit without scavenged. The concentrations of SEV and ISO in the OR with scavenged is significantly reduced
Raj, N [46]	Britain	MRI Dental	Without install	SEV	4.2 (blood) 2.2 (environment)	ppm	The highest environmental levels were found in the MRI suite where the T-piece was used with no scavenging

CPB cardiopulmonary bypass, *DEF* desflurane, *SEV* sevoflurane, *ISO* isoflurane, *HAL* halothane, *S* surgeons, *A* anesthesiologis, *P* patients, *M* midwives, *AM* assistant midwives, *OEL* occupational exposure limit, – not mentioned

Individuals' description of neuropsychological symptoms are often subjective, while biological parameters may be more accurate. Yilmaz et al. found that exposure to WAGs was associated with a statistically significant increase in genotoxic damage. In addition, chronic exposure to all WAGs instead of single ones induced cumulative genotoxic effects [52]. Exposure time is also an important factor in DNA damage and genetic mutations (Table 3). Costa et al. found an increasing risk of DNA damage and oxidative stress in young professionals, and 22-month WAG exposure had a more significant influence than 8 or 16 months [53]. Turkan et al. found exposure to WAGs over 3 years significantly increased oxidative stress levels [54]. El-Ebiary et al. and Chandrasekhar found more DNA damage by WAG exposure over 10 years [55, 56]. Horasanli et al. indicated that anesthesiologists working for more than 4 years had prolonged median saccharine nasal transit time, compared with those working for less than 4 years [57]. However, Rozgaj et al. found no relationship between exposure time and sister chromosome changes, but the frequency of chromosome aberrations and micronucleus increased significantly [58]. Meanwhile, there are studies showing that long-term exposure to WAGs has little effect on human health [8, 59]. Wronska-Nofer et al. found no correlation between genotoxic effects and exposure to sevoflurane and isoflurane, but occupational exposure to N_2O was associated with increasing DNA damage [8], and the level of exposure played a critical role in this regard [4]. Wiesner et al. showed that high-level exposure (exceeding limit values) was associated with an increase in chromosome damage, whereas low-level exposure (within limits) did not [60]. Shirangi et al. concluded that long working hours and absence of a scavenger system for WAGs are important risk factors for preterm birth in female veterinarians [61]. To summarize, whether exposure to WAGs will affect human health largely depends on the concentration of WAGs and the exposure time. However, how WAGs cause DNA damage has not been fully elucidated. N_2O was considered to inactivate vitamin B_{12} and influence the activity of methionine synthase [62, 63], and it is widely believed that WAGs lead to increased oxidative stress, oxidation and antioxidant capacity imbalances. The level of antioxidant enzymes and trace elements in the body changes, and endogenous oxidative stress induces various lesions in DNA such as oxidized bases, abasic regions, strand breaks and DNA–protein cross-links, even genotoxicity [7]. Therefore, different endpoints (comet assay, micronucleus, sister chromatid exchanges or chromosome aberrations) have been used to detect systemic DNA damage and genotoxicity [64], despite providing inconsistent findings.

Some large epidemiological studies have focused on side-effects in chronic diseases (cancer, liver dysfunction, renal insufficiency etc.), spontaneous abortion, congenital malformations, low birth rate and higher stillbirth rate in offspring

Table 3 The relationship between the time of exposure and DNA damage or genetic mutations

Study	Time of exposure	Content
Turkan [54]	At least 3 years	Plasma, erythrocyte antioxidant activities and trace element levels decreased significantly in anesthesiologists and surgeons chronically exposed to WAGs
Costa [53]	8, 16 and 22 months	DNA damage and antioxidant protection increased compared with control group in young professionals, plasma thiols and GPX higher at 22 months of exposure than 8 and 16 months of exposure
El-Ebiary [55]	1–35 years, average of 19 years	The length and percentage of DNA in the tail increased but not significantly in those exposed over 10 years
Rozgaj [58]	–	No relation between exposure time and sister chromosome changes, but the frequency of chromosome aberrations and micronucleus increased significantly
Chandrasekhar [56]	1–23 years, average of 10.47 years	DNA mean tail length, micronucleus frequency and chromosome aberration frequency increased in those exposed to WAGs over 10 years, but only micronucleus frequency increased significantly
Horasanli [57]	2–20 years, average of 4 years	Anesthesiologists working for more than 4 years had prolonged median saccharine nasal transit time, compared with those working for than 4 years

of female workers and wives of male workers among staff working in a WAG environment [13–15, 65–70]. As can be seen from Table 4, there is no consistent conclusion as to whether there are side-effects or not. In addition, a higher proportion of female offspring presented in the firstborn of OR staff [65, 71, 72]. The reasons for such a skew are not clear at present: perhaps the WAGs can increase the X-bearing sperm/Y-bearing sperm ratio [73]. Nilsson et al.'s review found no evidence of an association between occupational exposure to WAGs and health risks, and that occupational exposure is harmless under modern environmental regulations [74]. Similarly, Molina et al. found no evidence of adverse effects when environmental levels were kept within legal threshold values [75]. Quansah et al. found an increasing risk of adverse pregnancy outcomes among nurses, but the strength of the association was weaker in well-designed studies [76]. It is critical to choose sensitive biological parameters to indicate various adverse health effects after exposure to WAGs. Epidemiological investigations, clinical signs and biomarkers are limited by the sample size, unclear exposure concentration and exposure time, lack of confirmation or evidence of these adverse reactions, incomplete information, various living habits (smoking, drinking and staying up late), bias in the investigators' questions and heterogeneity of the studies. OR staff face many kinds of risk factors: physical risks (noise, ionizing radiation and temperature),

Table 4 Epidemiological investigations about spontaneous abortion, congenital abnormalities and chronic disease

Study	Year	Countries	Exposed group	Control group	Spontaneous abortion	Congenital abnormalities	Chronic disease
Cohen [13]	1966–1970	California	OR Nurses, Anesthesiologists	General nurses, Physicians	Y Y	Y Y	– –
An Ad Hoc Committee [14]	1972–1974	USA	Anesthesiologists Anesthesia nurses OR nurses OR technicians	Pediatrics General nurses	Y	Y	Cancer, hepatic and renal disease increased
Pharoah [15]	1977	England	Anesthesiologists	Other doctors	N	Y	–
Rosenberg [66]	1978	Finland	Anesthesiologists	Pediatricians	N	N	N
Guirguis [67]	1981–1985	Canada	Work in OR	Other departments	Y	Y	N
Saurel-Cubizolles [68]	1987–1989	French	Work in OR	Other departments	Y	N	–
Teschke [69]	1990–2000	Britain	Mothers exposed to WAGs	Mothers not exposed to WAGs	–	Y	–
Gauger [70]	2003	Michigan	Pediatric anesthesiologists	Pediatric anesthesiologists	Y	Y	–
Nagella [65]	2015	India	Anesthesiologists, Anesthesiologists' wives	–	Y	Y	–

chemical risks (vapors, fumes and chemicals), biological risks (viruses, bacteria, blood and blood products), ergonomic risks (improper posture, monotony, repetitiveness, work shifts and situations causing stress) and work stress [77]. However, many of the above surveys only clarified the health situation of the OR staff, but could not attribute health problems entirely to WAGs. In order to understand the influence of WAGs, a baseline clinical examination of medical staff exposed to WAGs is required, including medical history, physical examination, blood tests and inhaled anesthetic agents, such as a protocol issued by the Spanish Ministry of Health in 2001 [78]. Therefore, more prospective studies are needed to assess whether long-term exposure to WAGs has an impact on human health.

The influence of WAGs on the environment

In 1975, it was first reported that halogenated anesthetics led to the destruction of the ozone layer and acceleration of global warming [79]. Chlorofluorocarbons from the degradation of halogenated anesthetics and reactive nitrogen oxides from the degradation of nitrous oxide are the main components leading to ozone depletion and damage to the ozone layer [80]. In addition, N_2O and halogenated anesthetics can absorb terrestrial radiation, which causes the greenhouse effect [81]. Isoflurane, desflurane and sevoflurane were therefore identified as greenhouse gases. Ryan and Nielsen calculated the 20-year global warming potential of desflurane, sevoflurane and isoflurane, and showed that carbon dioxide equivalent values for 1 MAC-hour at 2 L fresh gas flow were: sevoflurane 6980 g, isoflurane 15,551 g, and desflurane 187,186 g. They then concluded that desflurane exerted a greater potential impact on global warming than either isoflurane or sevoflurane, and N_2O alone produces a sizeable greenhouse gas effect relative to sevoflurane or isoflurane. It was suggested that N_2O and unnecessarily high fresh gas flow rates should be avoided to reduce the environmental impact of inhaled anesthetics [82]. Sherman et al. [83] and Ishizawa [84] also came to similar conclusions that WAGs had a significant impact on global warming.

Strategies

In spite of the controversy about the exact effect of WAGs on human health, it is important to make efforts to reduce the concentration of WAGs in the OR and other polluted areas.

Air-conditioning systems and WAG scavenging systems

As early as 1971, Whitcher et al. pointed out that WAG contamination could be caused by recirculating systems capable of providing minimal total air exchange rate and closed-system venting [85]. 'Air-conditioning system' refers to the use of air cleaning technology in the OR to achieve an appropriate environment for all kinds of surgery. A 'scavenging system' is a device directly connected to the anesthetic equipment or placed near the patient to collect or remove the WAGs in the OR, PACU or dental clinic. Table 5 shows that air-conditioning systems and scavenging systems can effectively reduce the concentration of WAGs, and even keep the concentration within the limits [30, 35, 40, 86–88]. In ORs equipped with ventilation systems alone, the N_2O levels exceeded the standard limit, and air-conditioning ventilation with a scavenging system can reduce WAGs by nearly 20-fold compared to natural/pressure ventilation [86]. Herzog-Niescery et al. showed that a laminar flow air-conditioning system is more useful for expelling WAGs than a turbulent flow air-conditioning system [35]. The highest environmental levels with high blood, urine and breath levels were found in the MRI suite where the T-piece was used with no scavenging [46]. Iso-Gard Mask is a new scavenging system placed near the patient's mouth which can effectively reduce WAGs compared to a nasal cannula [87]. Adsorbers filled with activated charcoal are devices attached to the expiratory valve of the mask or anesthesia machine vent and are used to adsorb the anesthetic gases and prepare an anesthetic workstation for malignant hyperthermia-susceptible patients [89]. Johnstone et al. reported that activated charcoal canisters can reduce the mean halothane concentration by approximately 78% compared to the simple device of the nasal mask for dental anesthesia [90]. Fay identified the effectiveness of passive scavenging with an adsorptive charcoal canister or active scavenging with a building vacuum system [91]. This effectiveness had also been pointed out in other studies [92–94]. Therefore, it is essential to reduce WAGs whether using a scavenging system, air-conditioning system, Iso-Gard Mask or passive scavenging with an activated charcoal canister.

Methods of anesthesia induction

Owing to their low blood gas distribution coefficients, volatile anesthetics have been the preferential choice for pediatric induction. However, inhalation induction increases the concentration of WAGs by more than 50-fold compared with intravenous induction [95]. Hoerauf et al. [96] evaluated the exposure concentration of anesthesiologists under four different induction techniques (sevoflurane and N_2O from a rebreathing bag, sevoflurane and N_2O from a circle circuit, propofol and thiopental sodium). The result showed that even using a breathing bag or a circle circuit system, WAG concentrations could exceed the standard limit.

The double-mask system is a new delivery system. The inner layer is a flexible soft cover for the gas transmission channel, and the outer layer is mainly used to extract exhaled gas. It can not only provide anesthetic gas, but also

Table 5 Comparison of kinds of systems

Study	System	Gas	WAGs	Unit	Content
Krajewski, W [86]	Natural/pressure ventilation	N_2O	1154.0	mg/m^3	Air conditioning or pressure/exhaust ventilation with scavenging system were sufficient to sustain the N_2O levels below or within the OEL value, but natural/pressure ventilation with scavenging was inadequate to maintain N_2O concentration below the OEL value
	Natural/pressure ventilation + Scavenging system		635.5		
	Pressure/exhaust ventilation		308.7		
	Pressure/exhaust ventilation + Scavenging system		107.1		
	Air-conditioning ventilation		339.1		
	Air-conditioning Ventilation + Scavenging system		62.4		
McGlothlin, JD [87]	Nasal Cannula (6 inches/3 feet)	N_2O	69.10/11.91	ppm	Iso-Gard Mask can better control occupational exposures to WAGs for PACU personnel
	Iso-Gard Mask (6 inches/3 feet)		23.99/7.4		
	Nasal Cannula (6 inches/3 feet)		5.04/0.92		
	Iso-Gard Mask (6 inches/3 feet)		1.89/0.69		
LIAN Ai-ling [88]	100 class laminar flow OR	SEV	1.0	ppm	The concentrations of WAGs in PACU was higher than OR
	10,000 class laminar flow OR		1.3		
	100,000 class laminar flow PACU		2.1		
Herzog-Niescery, J [35]	Laminar flow (LF)	SEV	0.29	ppm	LF air-conditioning system is more useful than TF to reduce SEV concentrations
	Turbulent flow (TF)		0.13		
Braz, L. G [30]	Without/with scavenging system	ISO	10.3/1.2	ppm	There is a significant reduction in the concentration of SEV or ISO when equipped with the scavenging system
		SEV	16.7/3.3		
Maroufi, Sh S [40]	Without ventilation system	N_2O	440.0	ppm	It shows that ventilation system can reduce the exposure ratio from 4.02 to 1.83 ppm
	With ventilation system, not operational		326.8		
	With ventilation system, operational		138.5		

remove the WAG around the patient's head. When using the double-mask system during inhalation induction in pediatric general anesthesia in dental offices, the levels of N_2O decreased from 40.0 to 3.0 ppm compared with the traditional mask, the levels of sevoflurane decreased from 4.60 to 0 ppm, and N_2O and sevoflurane were kept within limit standards in all working areas [97]. At the delivery suites in six Swedish hospitals, using the non-ventilated and simple ventilated masks, the 8-h time-weighted averages (TWAs) of N_2O were four-fold higher than those with the double mask [32]. Freilich et al. concluded that the double-mask system minimized N_2O exposure more effectively during sedation of outpatients in a variety of pediatric dental clinical procedures [98]. Panni and Corn [99] and Chessor et al. [3] also confirmed the effectiveness of the scavenging mask in heat conservation of patients. Animal models concur with these observations [2, 100]. Therefore, the double-mask system is a good choice for the inhalation induction technique.

Anesthesia airway management

In order to meet the requirements of various types of surgery, anesthesiologists often choose different airways to ensure the patient is ventilated, such as the Cobra perilaryngeal airway (CobraPLA), the cuffed oropharyngeal airway (COPA), the laryngeal mask airway (LMA), the conventional face mask (FM), the endotracheal tube (ET) and the uncuffed endotracheal tube (UET). Table 6 shows that ET is superior to UET, COPA, LMA, CobraPLA and FM in reducing the concentration of WAGs [35, 37, 38, 101, 102]. When using COPA, LMA or CobraPLA, the concentration of WAGs around patients' mouths exceeded the recommended limit value, even about 20-fold higher than that of the anesthesiologists' breathing zones [37, 38]. Comparing the breathing zones of the medical staff, anesthesiologists are always exposed to higher concentrations of WAGs than surgeons and nurses, so it is important to choose reasonable airways to reduce the concentration of WAGs.

Closed loop technology and low flow technology

Closed circuit anesthesia refers to the use of a circulating breathing circuit: the patient exhales gases which are all returned to the circulatory system, where CO_2 is removed. Low flow anesthesia refers to a fresh gas supply flow below 1 L/min, and that below 0.5 L/min is called minimal-flow anesthesia. Feldman calculated that the use of fresh gas at 1 L/min to maintain anesthesia can reduce more than

Table 6 Comparison of the different methods of airways management

Study	Airways	Gas	Concentration (ppm)	Context
Schebesta, K [37]	CobraPLA	N_2O	207.5 ± 20.8(P) 11.7 ± 7.2(A)	At the anesthesiologist' breathing zone, 4% of N_2O in the LMA patients and 14% of N_2O in the CobraPLA patients exceeded recommended thresholds. SEV and N_2O at the patient's mouth more often exceeded
	LMA		92.4 ± 14.7(P) 4.1 ± 4.3(A)	
	CobraPLA	SEV	8.9 ± 11.9(P) 0.7 ± 4.4(A)	
	LMA		4.8 ± 9.4(P) 0.6 ± 2.6(A)	
Gustorff, B [38]	COPA	N_2O	213.3 ± 289.2(P) 5.7 ± 4.8(A)	The concentrations of N_2O and SEV were significantly over limit values when FM was used for short surgical procedures, and LMA was higher than COPA, but no significant difference
	LMA		283.4 ± 361.0(P) 12.2 ± 14.3(A)	
	FM		750.7 ± 308.3(P) 37.5 ± 14.3(A)	
	COPA	SEV	8.1 ± 12.2(P) 0.5 ± 0.2(A)	
	LMA		18.5 ± 25.8(P) 1.0 ± 0.9(A)	
	FM		46.5 ± 19.6(P) 2.2 ± 0.9(A)	
Herzog-Niescery, J [35]	LMA	SEV	0.87 ± 0.39(P) 0.79 ± 0.53(A)	When using LMA, the concentration of SEV is higher than ET in both the anesthesiologist and the patient around, LMA leak increased SEV concentrations compared with LMA tight
	ET		0.38 ± 0.23(P) 0.37 ± 0.16(A)	
Hoerauf, KH [101]	LMA	ISO	0.64(N) 0.50(A) 0.36(S)	ISO concentration in patients, nurses and surgeons breath area was generally increased when using LMA than ET, but no significant difference
	ET		0.31(N) 0.35(A) 0.29(S)	
Smith, J C [102]	LMA	ISO	8.4 ± 0.6 (rabbit)	The concentrations measured for the LMA were modestly higher than ET and UET, and UET slightly higher than ET
	ET		6.7 ± 0.5 (rabbit)	
	UET		6.3 ± 0.4 (rabbit)	

CobraPLA Cobra perilaryngeal airway, *COPA* cuffed oropharyngeal airway, *LMA* laryngeal mask airway, *FM* conventional face mask, *ET* endotracheal tube, *UET* uncuffed endotracheal tubes

19,600 L of isoflurane emissions compared with 2 L/min. However, even in a closed cycle using fresh gas at 1 L/min, an anesthesiologist will produce 52,850 L of isoflurane exhaust gas in his/her career [103]. This is why Brattwall et al. suggested that with our modern anesthesia machines, it is a reassuring and safe anesthetic technique to reduce the fresh gas flow of oxygen to 0.3–0.5 L/min using third-generation inhaled anesthetics. Low-flow anesthesia improved body temperature and humidity homeostasis [104]. There are obvious economic and environmental advantages and less workplace contamination. Kennedy and French reported that isoflurane usage decreased from 47 to 4% by changing patterns in anesthetic fresh gas flow rates, which represents potential annual savings of more than USD 130,000 [105]; Weinberg and Dexter indicated the same in their results [106, 107].

Vitamin supplements

Supplementations such as vitamins are thought to be useful to protect against the harm of WAGs. In one study, after a 12-week intake of vitamin E (300 mg/day) plus vitamin C (500 mg/day), blood samples were retaken and evaluated by comet assay. Sardas et al. concluded there was a significant decrease in DNA damage induced by occupational exposure to WAGs [6]. Similarly, Kan et al.'s studies showed that taking vitamin E (600 mg/day) for 14 weeks could also reduce DNA damage [108]. However, it is unclear whether long-term intake will remain effective and whether it will cause other unnecessary complications.

Lack of critical homocysteine (Hcy) metabolic enzymes and vitamins can cause high levels of tHcy, which can increase cardiovascular risk and morbidity, coronary heart disease and cerebrovascular disease. Krajewski et al. assessed vitamin B_{12} status to understand its association with WAG exposure levels. They found that serum concentrations of vitamin B_{12} were significantly lower and tHcy was higher in subjects exposed to WAGs. In addition, the researchers found that the metabolic status of vitamin B_{12} critically depended on the level of N_2O exposure [21]. However, Uzun et al. showed that exposure to N_2O had no influence on tHcy, folic acid and vitamin B_{12} levels, but the study did not assess the exposure levels [109]. The relation between long-term exposure to WAGs and the metabolic level of vitamin B_{12} have not been fully understood. There is doubt whether vitamin B_{12} supplementation can reduce the changes in tHcy and folic acid.

Novel anesthetic gases

The ideal inhalation anesthetic should have the advantages of high anesthesia intensity, low blood solubility, high controllability, rapid induction and recovery, less metabolism in the body, and no toxicity to liver and kidney. Xenon has been studied as a general anesthetic since 1951 by Cullen and Gross. No toxic or teratogenic potential has been found [110]. Its low blood solubility contributes to rapid induction and recovery [111]. Hemodynamic stability and organ protection effects (such as ischemia and reperfusion injury) are also confirmed [112]. The feasible and safe use of xenon in general anesthesia has already been demonstrated in several randomized controlled clinical trials [113, 114]. But it has failed to become popular in the clinic because it is expensive and very rare, and its production consumes a lot of energy [115]. Rawat and Roehl have shown that closed or semi-closed recirculation techniques can be used through modern anesthesia stations to reduce xenon waste and increase utilization to reduce environmental damage [116, 117]. Therefore, xenon can be a potential and novel anesthetic gas in clinical anesthesia if the production cost of xenon can decrease. As xenon is currently not widely used in clinical practice, it is still unknown that whether long-term exposure to low concentrations of xenon will have an impact on human health.

To better understand the use of the practices recommended above, a survey was conducted in 2011 among members of professional practice organizations representing anesthesia care providers. It was found that scavenging systems were universally used; however, some recommended practices have not been in common use, including high fresh gas flow anesthesia, starting anesthetic gas flow before delivery mask or airway mask, checking the leakage of anesthesia equipment routinely, or using a funnel-fill system to fill vaporizers. In addition, there were no safe handling procedures in facilities or training about hazard awareness [118]. Therefore, some practices are recommended to protect medical staff from WAGs, such as properly fitted nasal scavenging masks, supplementary local exhaust ventilation and adequate general ventilation. In addition, it is also advised to regularly inspect the gas delivery and scavenging equipment to avoid leaks, monitor ambient air and exposure, and maintain medical surveillance with periodic training [18].

Summary and conclusions

This review indicates that previous evidence about the side-effects of WAGs is insufficient and inconsistent. Exposure to high levels of WAGs in the short term can cause a series of behavioral symptoms; whether long-term exposure to WAGs can affect personnel health largely depends on the concentration of WAGs and the exposure time. Further study is needed as to whether long-term intake of supplements is a potential treatment or whether there will be other complications induced by the supplements.

The concentration of WAGs is recommended to be as low as possible, but the situation is not as optimistic as supposed. The concentration of WAGs varies in different workplaces, physical positions, operation types and procedures. Successful control of WAG emissions should include proper scavenging systems and air conditioning systems, using the double-mask system for the inhalation induction technique, reasonable airway management, and low flow by closed circuit anesthesia. It is a huge challenge to discover new ideal anesthetic gases. Therefore, we should consider ongoing monitoring and evaluation, personnel training, modification of policy and procedures, and improvement of work activities.

Acknowledgements We would like to thank Dr. Hong-Fei Zhang and Dr. Hong-Yi Lei who assisted our manuscript preparation. The work was supported by Guangdong Science and Technology Project (2014A020213018 to Ye-Hua Cai) and National Natural Science Foundation of China, Beijing, PR China (81471272 to Shi-Yuan Xu).

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