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In Defense of Desflurane: Is There a Specific Role for Desflurane in Neuroanesthesia?

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Abstract

It is challenging to counter the widespread criticism of desflurane as the volatile anesthetic agent with the most significant greenhouse gas effect, one which is likely to exacerbate global warming. In 2022, the journal "*Anaesthesia*" published guidelines for minimizing the impact of anesthetic gases on global warming, which the anesthetic community has largely embraced. One of its recommendations was the removal of desflurane from drug formularies. However, this review underlines the likely benefits of desflurane in the context of actual and potential neurological injuries. With an estimated 13.8 million neurosurgical operations performed annually, desflurane could offer advantages to some of these patients. Therefore, it is imperative to develop an environmentally safe approach for its use rather than remove it from formularies. We discuss desflurane's environmental impact, its unique anesthetic and chemical properties, and its specific application in neuroanesthesia practice. Based on existing evidence, we argue that desflurane could hasten the wake-up of neurosurgical patients. We propose switching to desflurane toward the end of surgery for patients at risk of, or with, neurological injuries. Predictable, early, and monitorable wake-up in these cases could prevent surgical delays, avoid additional investigations, or enable early detection of new deficits. Instead of a blanket ban, desflurane's use should be investigated—systematically and carefully. With education, well-defined indications, limited use, intelligent vaporizers, scavenging, and recycling systems, the use of desflurane could be justified under specific circumstances. Moreover, the problem of environmental damage from inhaled anesthetics must be comprehensively evaluated. Minimizing the use of desflurane is a positive step to protect the environment, but anesthesiologists should enforce other measures to protect the environment with equal urgency.

Keywords
- desflurane
- inhaled anesthetic gases
- greenhouse gases
- medical
- pollution
- climate change

Introduction

The December 1970 issue of *National Geographic* pictorially highlighted the perils of global pollution. It warned, "*Unless we stop abusing our vital life support systems, they will fail. We must maintain them or pay the penalty. The penalty is death.*"[1] One of the significant risks to this planet's health is global warming due to pollution by greenhouse gases (GHGs). Rising levels of carbon dioxide, methane, nitrous oxide, sulfur hexafluoride, and halogenated hydrocarbons can trap heat in the Earth's atmosphere, which could profoundly impact the global climate.[2,3] The scorching and hellish atmosphere of our companion planet, Venus, is often depicted as the result of runaway greenhouse warming.[4]

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The literature clearly shows that desflurane is a potent GHG. It is also chemically stable, which significantly amplifies its harmful environmental impact.[5–10] The recent call for restricting the use of desflurane has led to its removal from many hospital pharmacies.[11,12] However, desflurane has many unique properties that are particularly relevant during the emergence from anesthesia after neurological surgeries. For those who have used it effectively for this purpose, the ban left a void that has been hard to fill.[13]

In this review, we highlight the unique properties of desflurane. The injured brain is fundamentally different, which alters the risks versus benefits of desflurane use. The defense of desflurane is not seeking its unrestricted use as a sole anesthetic throughout the case but very narrowly using it during the waking of patients at risk of, or with, neurological injuries. In our experience, banning desflurane could significantly impact patient care in high-risk neurosurgical cases. Furthermore, banning desflurane will be of little consequence unless we see it in the context of other environmental assaults. If we, as anesthesiologists, care about the environment, then our efforts should be directed elsewhere as well, not just on a feel-good ban on a drug. What is needed is the intelligent use of desflurane to mitigate environmental risk rather than banning it from formularies.

The Discovery of Desflurane

The fires caused by ether and cyclopropane led to the search for noncombustible anesthetic agents. Halogenated compounds such as chloroform had many desirable properties, such as potency, a pleasant taste and smell, and reduced vomiting compared with ether. It was realized by 1930 that the addition of fluorine to hydrocarbons decreased their boiling point, increased their stability, and decreased their toxicity. This led to the discovery of Freon, which, until recently, was a widely used refrigerant. However, the synthesis of fluorinated hydrocarbons remained a technological challenge, as they were explosive during their manufacture. During the Manhattan Project, the purification of uranium-235 required the production of uranium hexafluoride and the synthesis of fluoride compounds.[14] Earl McBee synthesized these compounds and developed fluorinated ethers for anesthetic purposes. Between 1930 and 1951, several halogenated compounds were tested for anesthetic purposes. Consequently, halothane was introduced in 1951 and methoxyflurane in 1960. In the 1960s, Ross Terrell's team synthesized some 700 halogenated compounds specifically for their anesthetic properties.[15] Although enflurane was synthesized in 1963, its cardiovascular depressant and proconvulsive effects delayed clinical testing. Similarly, isoflurane was synthesized in 1965, but due to problems with purification, it was not tested until 1971.[16] By the early 1990s, all available volatile anesthetics raised concerns. Halothane could cause hepatitis, methoxyflurane high-output renal failure, enflurane seizure, and nephrotoxicity, while isoflurane could cause coronary steal. These limitations led to the continued search for better volatile agents.[15]

Desflurane (I-653) was among Terrell et al's 700 compounds. However, the compound's vapor pressure was close to 1 atmosphere, and its synthesis posed an explosive risk. Consequently, the testing of the compound was delayed until 1988. It was approved in the United States in 1992, 10 years earlier than sevoflurane. The clinical use of the compound also awaited the development of a suitable vaporizer capable of tolerating its high vapor pressure. Desflurane, with its low solubility, offered rapid induction and recovery from anesthesia. Although the induction was quick, it was associated with airway irritation that limited its use. Less than 0.02% of desflurane was metabolized; hence, it was eliminated primarily by expiration. Whether desflurane shortens the time to discharge or is cost-effective during routine surgery is somewhat controversial.[15]

The Environmental Concerns with Desflurane

The greenhouse effect refers to the trapping of heat in the atmosphere. GHGs include anesthetic gases and several industrial compounds.[17,18] Chlorofluorocarbons (CFCs), such as isoflurane and enflurane, have both the greenhouse effect and deplete the ozone layer. In contrast, desflurane lacks chlorine and primarily acts as a potent GHG.[8] Depletion of the ozone layer increases the amount of harmful ultraviolet light reaching the Earth's surface and contributes to an approximate 2% temperature rise.[19] Due to the rapid depletion of the ozone layer, efforts were made to protect it under the Montreal Treaty of 1987. In 2016, the Kigali amendment to the treaty aimed to phase out CFCs.[18,20] The greenhouse effect of fluorocarbons depends on three properties[2,8]:

- The amount of infrared light absorbed by the molecule and its radiative efficiency.
- The survival time of the molecule in the atmosphere and its atmospheric lifetime.
- The effect of competing molecules, such as water, carbon dioxide, or even nitrous oxide, that absorb the same wavelength. For example, the harmful GHG effects of desflurane are mitigated when it is used with nitrous oxide. However, they remain significantly higher than sevoflurane or isoflurane, with or without nitrous oxide.[9]

To calculate the relative impact of anesthetic gases on the environment, Özelsel et al used the parameters in ►**Table 1** to derive the equivalent amount of CO_2 emitted while driving a car.[15] The Environmental Protection Agency (EPA) estimates that a passenger car generates 8.8 kg of CO_2 per gallon of gasoline. The driving distances are based on the 1-year global warming potential. The table shows that the detrimental effect of desflurane is due to its high concentrations during clinical use and its long atmospheric life compared with other anesthetic agents.[3] The simulations by Özelsel et al clearly showed the cumulative effects of desflurane use on global warming potential and their CO_2 equivalent effects over 100 years. Furthermore, the cumulative greenhouse effects of desflurane and nitrous oxide over time are significantly greater than that of sevoflurane, as the latter has a shorter atmospheric half-life

Table 1 Properties of anesthetic gases and their environmental impact as judged by driving distances[8]

Anesthetic agent	FGF (L/min)	Concentration (%)	Molecular weight (g/mol)	Atmospheric lifetime (y)	Radiative efficiency ($W/m^2/ppb$)	Driving equivalents/d assuming 7-h use (km)		
						0.5 L/m	1.0 L/m	2.0 L/m
Isoflurane	0.5	1.2	184.5	3.5	0.42	667	1,334	2,668
Sevoflurane	0.5	2	200.055	2.2	0.32	783	1,566	3,132
Nitrous oxide	0.5	66	44.013	121	$3.0e^{-3}$	279	558	1,116
Desflurane	0.5	6	168.038	10.8	0.45	3,924	7,849	15,698

Abbreviation: FGF, fresh gas flow.

compared with the other agents.[8,9] Assessing the environmental impact of volatile anesthetic agents is challenging, and typical GHG models predict impact over 20 or 100 years. Furthermore, anesthetic gases exist in very low concentrations (in parts per billion range), and the amounts produced globally are very small relative to other pollutants. It is estimated that ~13% of GHG warming is due to fluorocarbons.[19] While the volatile anesthetics contribute to 0.1 to 0.01% of the GHG warming effect.[12] It is estimated that the GHG effect of volatile anesthetics is several orders of magnitude greater than that of propofol.[10]

ASA Recommendations for Desflurane Use

In 2022, evidence-based recommendations provided by the American Society of Anesthesiologists (ASA) were as follows[12]:

- Providers should avoid inhaled anesthetics, such as desflurane and nitrous oxide, which have disproportionately high climate impacts.
- The lowest possible fresh gas flow (FGF) should be selected when using inhaled anesthetics.
- Regional and intravenous anesthesia should be prioritized and used when appropriate since they have less negative environmental impact.
- Nitrous oxide is mainly lost before use and released into the air through leaks in central piping systems. The pipelines should no longer be used. Portable canisters should be substituted and closed between uses to avoid continuous leaks.
- More research is needed before recommending investment in technological solutions for capturing or destroying inhaled anesthetic waste, and these should not be considered high mitigation priorities.

These guidelines led to the removal of desflurane from many medical centers in the United States, which resulted in substantial cost savings.[21]

Desflurane Use Worldwide

A recent correspondence in the *British Journal of Anesthesia* summarized global desflurane use.[22] In Scotland, it was eliminated in 2023. In England, its use will phase out in 2024. In the European Union, it will be eliminated by 2026. In Australia and New Zealand, it has been effectively eliminated. However, desflurane continues to be used in Japan, Taiwan, and Singapore. No data were available from China, and there was no mention of India, the two most populous countries in the world.[22] The British National Health Services (NHS) issued guidance in 2024, considering two exceptions for desflurane decommissioning: morbidly obese (body mass index [BMI] >30) patients and neurological operations.[23] An estimated 600 million people have a BMI >30, and millions of neurosurgical operations will qualify for the NHS's exemption criteria globally, challenging the effectiveness of the desflurane ban.[24,25]

Neuropathology Alters the Risk–Benefit Paradigm for Desflurane Use

In 2018, it was estimated that 13.8 million people required neurosurgery worldwide. These included 6.1 million surgeries for traumatic brain injury, 2.7 million surgeries for stroke, and 735,180 brain tumor operations.[25] ►**Fig. 1** shows the potential structural and functional changes in the brain in the presence of brain pathology. Neuropathology can result in adaptive changes in the synapse, axons, and neurons; neuroplasticity could alter the neurocircuitry and even result in structural changes in the brain.[26,27] The neuroplasticity of the brain in tumors and stroke patients is an area of intense research, and understanding this mechanism will have a profound impact on understanding clinical features and functional outcomes.[28–30] What is significant here is that an injured brain is uniquely susceptible to the effects of anesthetic drugs. Clinical studies on patients with brain tumors and stroke revealed the unmasking of neurological deficits with minimal exposure to sedative drugs.[31–33] For example, in 30% of patients undergoing carotid endarterectomy or intracranial tumor surgery who were asymptomatic at baseline, sedative doses of midazolam and fentanyl could lead to clinical symptoms. In 73% of these patients, sedation resulted in the unmasking of a resolved deficit or a worsening of the deficit.[33] The functional vulnerability of the injured brain to low concentrations of anesthetic and sedative drugs makes a case for drugs that are rapidly cleared from the body, and therein lies the value of desflurane.

There is ample clinical evidence that the emergence of anesthesia from desflurane is significantly more rapid than other anesthetic agents.[34] This is not unexpected, as

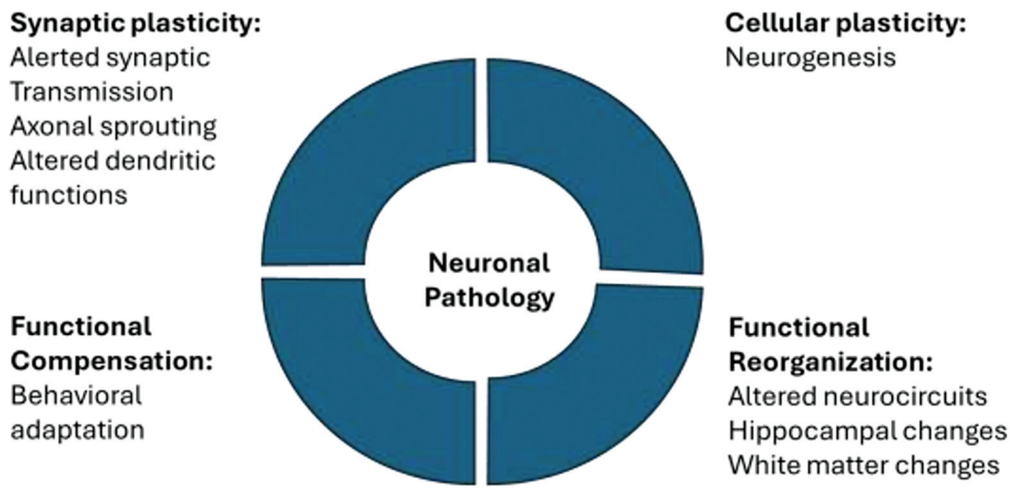

Fig. 1 Neuropathology can alter neuronal pharmacodynamics.

desflurane has a lower brain–blood partition coefficient. Therefore, it is rapidly eliminated from the brain and the body during emergence. However, it is often overlooked that significant amounts of anesthetic agents remain in the body after waking from surgery with prolonged exposure. The context-sensitive half-life of volatile anesthetics is usually not taken into consideration. Lockwood assessed the residual amount of anesthetic after 4 hours of 1-MAC anesthesia with isoflurane, sevoflurane, desflurane, and 50% nitrous oxide. A significant amount of anesthetics remains in the body for days after anesthetic exposure. The 99.9% elimination time for anesthetics ranges from 9 hours for nitrous oxide, 33 hours for desflurane, 52 hours for sevoflurane, and 71 hours for isoflurane.[35] It is unlikely that such trace concentrations would impair neurological functions in healthy individuals, but residual volatile anesthetics could affect neurological functions when the neural tissue is substantially disturbed.

Emergence from neuroanesthesia, specifically after an intracranial procedure, fundamentally differs from other anesthetics. It also has enormous clinical significance. Delayed emergence could lead to unnecessary investigations after surgery; it affects operating room functions, but most significantly, it can delay the detection of ongoing injuries such as a bleed or a stroke.[36,37] During intracranial neurosurgery, brain functions could be altered due to anatomical, physiological, and pharmacological changes that are compounded by surgical intervention to enhance the sensitivity to sedative and anesthetic drugs. Rapid and monitorable elimination of anesthetic drugs, such as desflurane, is clinically significant. Yet, the ASA and anesthesia recommendations do not provide exemptions for the use of desflurane in neurosurgical cases.[11,12,23,38]

Altered Regional Drug Clearance: An Unexplored Consideration

It is well known that independent of the anesthetic drugs used, the size (>3.5 cm) and location of brain pathology can delay the emergence from anesthesia.[39] Operative intervention, such as pressure under the retractors, can affect tissue perfusion. Surgery can directly affect healthy brain tissue through local inflammatory and microcirculatory changes, changes in regional perfusion, the draining of cerebrospinal fluid, and displacement of brain structures over time. Thus, it is reasonable to assume that intracranial surgery could also have local and remote microcirculatory effects. If we accept that peripathology perfusion could be impaired during surgery, it is safe to assume that regional clearance from the perioperative tissues could be delayed. Pharmacokinetic models have described regional trapping of drugs in brain tumors with decreased regional blood flow.[40] However, to our best knowledge, no experimental or modeling data describe the regional drug clearance from brain pathologies or peritumor tissue during or after intracranial neurosurgery (►**Fig. 2**). Thus, altered regional pharmacokinetic factors might play a significant role during wake-up after neurosurgery.

Evidence Showing Shorter Recovery from Desflurane Anesthesia after Intracranial Surgery

A recent review of the use of desflurane as the sole anesthetic after supratentorial craniotomy found early recovery and no adverse side effects of desflurane anesthesia.[41] Five of the studies that addressed recovery were after 2015. Haldar et al (2020) found that the wake-up with sevoflurane and desflurane was faster than that with propofol, although intraoperative bispectral index (BIS) values were between 40 and 60 for all three agents.[42] Paul et al (2017) compared isoflurane and desflurane anesthesia. They found a significantly shortened median time to eye-opening, response to verbal commands, and time to orientation by 30 to 35%.[43] Furthermore, they encountered fewer transient neurological deficits; when they occurred, they resolved quicker than isoflurane.[43] Gökçek et al (2016) found that the times to respond to painful stimuli, hand-squeezing, extubation,

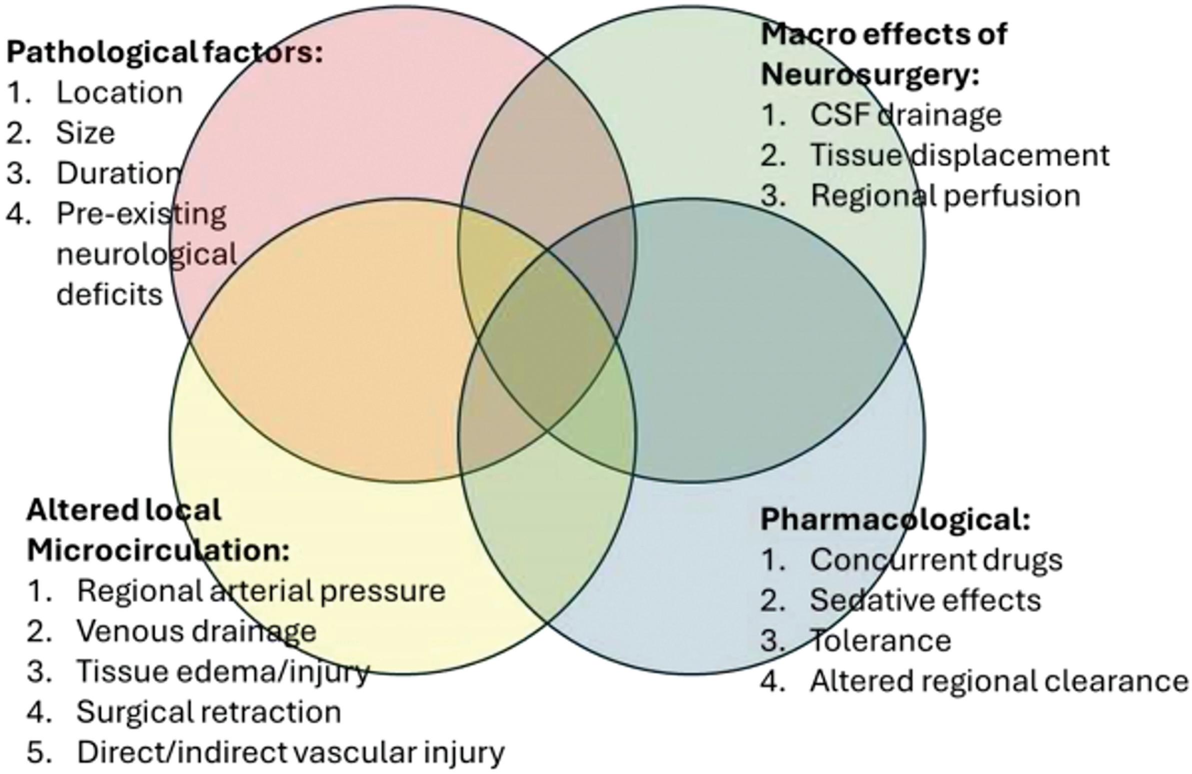

Fig. 2 Factors that could impact emergence after intracranial neurosurgery. CSF, cerebrospinal fluid.

orientation, and achieving an Aldrete score of 9 to 10 were significantly shorter with desflurane than sevoflurane-based anesthesia.[44] While Bastola et al (2015) found shorter recovery with desflurane than with sevoflurane, Dube et al (2015) found no difference between the two anesthetics.[45,46] Thus, there is evidence that desflurane anesthesia affects recovery after intracranial neurosurgery.

Switching to Desflurane toward the End of Surgery

We are making a very narrow case for the use of desflurane during wake-up—only for the last 30 minutes in patients at risk of, or with, neurological injuries. We could not identify any publication that addressed that specific issue. Four publications (►**Table 2**) assessed the effect of switching to desflurane on wake-up in nonneurosurgical cases.[47–50] None of these patients had neurological deficits. Neumann et al assessed switchover in five human volunteers. They found early recovery with desflurane alone but no benefit in switching to it from isoflurane.[50] Given the small sample size, the reliability of psychometric tests can be challenging. The most relevant study for us was the one conducted by Kim et al, who switched from sevoflurane to desflurane 30 minutes before the end of surgery.[48] They found that switching to desflurane shortened the time to eye-opening and extubation by one-third. Kang et al found that the psychrometric scores with the switch were comparable to solo desflurane anesthesia and shorter than those with isoflurane.[49] However, none of these studies was in patients with neurological deficits, which is our core argument. A search of PubMed and National Clinical Trial Web sites revealed no reports or ongoing research to address the benefits of switching to desflurane at the end of neurosurgery.

Fresh Gas Flows Used during Switchovers

Fresh Gas Flows (FGFs) from 2 to 4 L/min were used during switchovers to desflurane (►**Table 2**). Additionally, FGF was further increased to 6 L/min at extubation and wake-up. However, at that point, desflurane is no longer administered. The washout of sevoflurane and desflurane plateaus at ~4 L/min of FGF.[51] Our approach to switchover was substantially different. We aimed to slowly rid all sevoflurane with the least FGF by the end of the case. We used the circle system, kept the air/oxygen flows low by ~1 L/min or as required by the anesthesia machine, maintained the fractional inspired oxygen, and monitored the age-appropriate MAC values. Thirty minutes before waking up, we shut off sevoflurane and adjusted the inspired desflurane concentration to maintain a total 1-MAC concentration of sevoflurane and desflurane combined. After head wrapping, desflurane was shut off, and FGF increased to 6 L/min. With this approach, we believe we can significantly decrease desflurane use and ensure near-perfect scavenging.[13]

Advantages of Desflurane Compared with Other Anesthetics

- With desflurane, emergence from anesthesia can be expected *within 3 minutes*, the shortest of all volatile anesthetics. Desflurane *has the lowest context-sensitive*

Table 2 Studies describing the impact of switchover to desflurane

Author (year)	Cohort size	Patient profile	Critical differences in intervention	Outcome
Neumann et al (1998)[50]	$N = 5 \times 3$ challenges	ASA = I, male volunteers	Intubated and ventilated Gp 1: Des (1.25 MAC × 2 h) Gp 2: Iso (1.25 MAC × 2 h) Gp 3: Iso (1.25 MAC × 1.5 h) + Des 1.25 MAC (1.5–2 h) FGF = 2.0 L/min, semiclosed system	No effect of crossover Gp 1 has a shorter wake-up time and early cognitive test return than Gps 2 and 3
Kang et al (2010)[49]	82 patients	ASA = I and II, patients for laparotomy	Gp D: $n = 27$, 12% Des initially, later 6% Gp I: $n = 29$, 2.4% Iso initially, 1.2% after Gp X: $n = 26$, 2.4% iso initially and 1.2% after. Replaced for last 60 min with 6% Des. All Gps were treated with 50% nitrous oxide/oxygen. FGF = 3.0 L/min	Crossover to desflurane effective: Gps D and X showed no difference in wake-up but earlier than Gp I. Psychometric test scores were significantly better in Gps D and X compared with Gp I
Mikuni et al (2016)[47]	52 adults	ASA = I–III, nonneurologic general surgery patients	Gp 1: ($n = 25$) Sevo alone Gp 2: ($n = 25$) Sevo within 5 min crossover to Des. Two excluded FGF = air/oxygen 1:1 = 2 L/min	The crossover to desflurane is effective: recovery is quicker and shorter with desflurane, and it takes less time to orient to name, time, and place
Kim et al (2022)[48]	71 adults	ASA = I and II, nonobese, 18–65 y. For thyroid and breast surgery	Gp 1: ($n = 30$) Sevo alone Gp 2: ($n = 30$) Sevo with crossover to Des 30 min at the end of surgery 11 excluded/refused FGF = FiO_2 50%, 4 L/min	The crossover to desflurane is effective: compared with sevoflurane, the time to eye-opening and extubation was reduced by a third

Abbreviations: ASA, American Society of Anesthesiologists; Des, desflurane; FGF, fresh gas flow; FiO_2, fractional inspired oxygen; Gp, group; Sev, sevoflurane.

prolongation of recovery time. Yet, the emergence time will be shortened in sub-1-MAC concentrations with under 30 minutes of use.[34] A recent meta-analysis comparing total intravenous anesthesia (TIVA) with inhalational anesthetics from 1985 to 2023 revealed that the time to respond to verbal commands was shorter with desflurane than with TIVA, but not with sevoflurane and isoflurane.[52]

- Less than 0.02% of desflurane is metabolized in the body; *its uptake and elimination from the body depend on physical parameters*, not the metabolic functions of a given subject.
- Desflurane has much lower blood–gas, oil–gas, and blood–brain partition coefficients. *Thus, it is less likely to be retained regionally if tissue perfusion is impaired during surgery.*
- Infrared measurements in volume% of volatile agents are comparable after custom calibration across volatile anesthetics.[53] However, due to a much higher MAC value for desflurane, the wider spread of volume% measurements can provide a finer assessment of anesthetic depth (MAC values) than with sevoflurane or isoflurane.
- End-tidal desflurane concentrations could be more advantageous for wake-up from anesthesia than processed electroencephalogram (EEG)/BIS that is used for monitoring propofol infusion for the following reasons:
  - It is not often possible to satisfactorily place BIS leads during craniotomies, while end-tidal desflurane concentrations can be easily monitored in all cases.
  - BIS reduces the dose of anesthetic drugs during supratentorial neurosurgery. However, its impact on decreasing recovery time from TIVA remains debatable.[54] While end-tidal concentrations of volatile agents are reliable for monitoring anesthetic recovery.
  - With desflurane pharmacological recovery (end-tidal concentrations), functional recovery (EEG activity) can be monitored separately.

The Rationale for Using Desflurane during Emergence after Intracranial Surgery

- Desflurane hastens emergence from anesthesia after supratentorial surgery.[43] Delayed recovery could lead to additional imaging investigations to rule out surgical complications such as hematoma, pneumoencephalus, or stroke.[41] Similar benefits of early recovery with desflurane anesthesia have also been reported for spine surgery.[55,56]
- Desflurane could be associated with less transient neurological deficits.[43]
- If transient deficits are encountered, they resolve quicker with desflurane.[43]
- Elimination of anesthetic by end-tidal gas monitoring is more reliable than monitoring recovery from propofol anesthesia with processed EEG. Injury and residual anesthetic could confound the latter observations.
- The merits of propofol-based TIVA as an alternative to desflurane can be debated. TIVA is at an obvious

advantage due to its beneficial effects on cerebral circulation, less postoperative agitation, and less nausea and vomiting, but at higher pharmaceutical costs.[52,57] However, the most significant disadvantage of propofol use is that its elimination from the body cannot be confidently monitored when there is delayed wake-up after a neurosurgical operation.

Strategy to Optimize Desflurane Use in Neuroanesthesia in the Environmental Context

Currently Feasible

- Education regarding the environmental risk of desflurane is essential, and it could have a considerable impact, both on the environment and result in cost savings.[21]
- Safe handling of vaporizers and desflurane bottles:
  - Limiting access to vaporizers, so they are available only at sites of use.
  - Careful disposal of desflurane bottles that might contain residual anesthetic.[58]
  - Avoid leaks and spills during refilling and handling of vaporizers.[59]
- Developing a comprehensive desflurane-based wake-up plan: Supplementing desflurane with short-acting narcotics, intravenous and tracheal local anesthetics, and intravenous acetaminophen. Correcting hypothermia and hypocapnia as soon as permissible.[13]
- Timely switching to desflurane at the end of the case (►**Table 2**). Switching further enhances rapid emergence due to a shortened context-sensitive half-life of the drug.[34]
- The lowest possible FGF (around 1 L/min) should be used. Modern machines that provide FGF requirements can immensely assist in setting minimal FGFs.
- When used only for wake-up, desflurane will be entirely contained in the breathing system during use. If waste gases are adequately scavenged, the risk of environmental pollution will be significantly reduced.[60]

Future Strategies

- Scavenging volatile agents is eminently possible, significantly reducing environmental harm. It is estimated that only 5% of administered desflurane is used during anesthesia, and 95% is wasted. Thus, scavenging and collecting waste gases is essential.[60,61]
- Design compact desflurane scavenging and recycling systems built into anesthesia machines that scavenge and reuse all volatile anesthetic agents. Zeolites are used to scavenge nitrogen in oxygen concentrators[61] and CO_2 absorbers in the International Space Station.[62] Zeolites can also scavenge volatile agents such as isoflurane[63] and desflurane.[60] Heat and vacuum can reverse zeolites' absorption. Thus, it may theoretically be possible to scavenge and even recycle volatile agents.[64]
- Design intelligent vaporizers that warn against excessive use, have preset dose alerts, and even smart controls to limit the use. Desflurane vaporizers are electrically powered, so developing additional smart components should not be a problem.

Funding Research

Support efforts to capture and eventually recycle all inhalational agents as they cannot be financially justified.[65] Cost justification is a weak argument when, in 2023, Medicare in the United States spent $12.6 billion on Eliquis alone.[66] Investing in environmental protection from low-cost volatile agents seems to have few supporters when discarding the drug reaps immediate financial benefits.[21]

Desflurane Ban in the Totality of Climate Problem

Neither the ASA nor the NHS advocates an absolute prohibition on desflurane use.[12,23] However, others have suggested removing it from formularies.[11] No publications have assessed the effect of switching to desflurane at the end of intracranial surgeries. If desflurane is banned, the benefits we hypothesize will remain unproven. Ironically, the lack of proof could be used to justify the ban. All inhalation agents harm the atmosphere, but desflurane and nitrous oxide stand out.[2] Nitrous oxide's environmental and clinical hazards have been known for over a decade.[67,68] However, the lack of urgency in banning nitrous oxide compared with desflurane defies logic. It could be that removing desflurane from the formularies is financially beneficial. Desflurane anesthesia costs 5 times that of sevoflurane and 20 times that of isoflurane.[69] Furthermore, the online listed price for a desflurane vaporizer ($9,995) is about three times the cost of sevoflurane and isoflurane vaporizers ($3,699). A facility may have 100 or more anesthesia machines, so avoiding desflurane use substantially reduces hospital expenses. In one teaching hospital, such savings amounted to about half a million dollars annually.[21]

The expeditious removal of desflurane is even more inexplicable when other global warming contributors are ignored. For example, medical facilities are constantly being torn down and rebuilt. Concrete used in construction has a substantial environmental footprint. Not many hospitals are enthusiastic about greening their supply chain, energy use, and employee and patient transport, all of which have a far greater carbon footprint. Fabrication, supply, and disposal of single-use plastics and devices also have a significant carbon footprint.[5,70,71] The efforts to protect the environment[72] contrast sharply with rising market projections.[73] The global anesthesia market for disposal equipment amounted to $1.07 billion in 2023. It was projected to be $1.14 billion in 2024 and $1.43 billion in 2028. It is likely to grow at 6% annually.[73] Large quantities of medical-use plastic are shipped from the United States for disposal in developing countries.[74] Yet, we never question our drive to decrease disposable goods seriously. Similarly, it has been shown that robotic surgery has a much greater carbon footprint than conventional surgery.[75] Yet, medical centers are insatiable about using robotic technology even when conventional surgery might yield similar results. It is reasonable to assume that curtailing other sources of GHGs has been less urgent than the expeditious banning of desflurane, which raises the concern that the expeditious banning of desflurane is partly—if not primarily—due to cost considerations.

Global warming is an undeniable global concern with profound and catastrophic implications. There should not be any dispute about the matter. However, ►**Fig. 3** looks at the total impact of desflurane on global warming. It is estimated that the net effect of desflurane on total GHG emissions is 0.01 to 0.1%.[12] Let us first acknowledge that this warming began at the end of the last ice age, so some long-duration cycles might affect global warming irrespective of human activity.[76] A second significant variable we cannot control is planetary events such as volcanoes, spontaneous release of methane from subterranean sources, uncontrolled burns in coal mines, and forest fires. Unfortunately, human activity today exceeds the natural release of carbon dioxide and other GHGs.[77]

Environmental predictions, even from human activities, are challenging; some are based on robust science, while others are frank speculations that lead one to question their projections.[78] Technology changes rapidly and new threats may emerge over a 20- to 100-year time frame. These threats are yet unknown or are hard to quantify. Climate models cannot include the environmental impact of unforeseen elements such as wars[79] or, more recently, rocket launches. Rockets deposit carbon and moisture in the upper stratosphere as we enter a new space race. Hitherto, the pollution from spacecraft was minor compared with that from aviation. However, with increased privatization and numerous launches, there is a growing concern about space vehicles.[80] Similarly, it is estimated that the war in Ukraine generated 150 million tons of GHG in 18 months due to increased fuel consumption (25%), fires (15%), reconstruction (33%), refugee movements, and flight path alterations.[81] Projected over 20 or 100 years, as was done for volatile agents, it would have a staggering carbon footprint. Thus, accurately predicting GHG emissions over long time scales is challenging, and an honest, comprehensive, and apolitical approach is needed to address the problem.[82]

In the more actionable realm, if we look into GHG emissions from human activities, the significant sources of GHGs are energy generation, transportation, industrial activities, construction, and agriculture. Health care accounts for 5 to 10% of the GHG from human activities.[83] Hospitals account for one-third of those emissions, of which volatile anesthetics account for ~5%.[59] Most of this is due to the production and delivery of medical supplies, transportation, and energy use.[84] Only a small amount of human GHG production is due to inhaled anesthetics combined.[12] Curtailing desflurane use is a step in the right direction,[5,71] but given that patients at risk of, or with, neurological injury could benefit from its use, banishing desflurane is not the best solution. The effort should be directed toward developing technology that does not impact the environment when desflurane is used under specific circumstances and ultimately protects the planet from all inhalational agents.

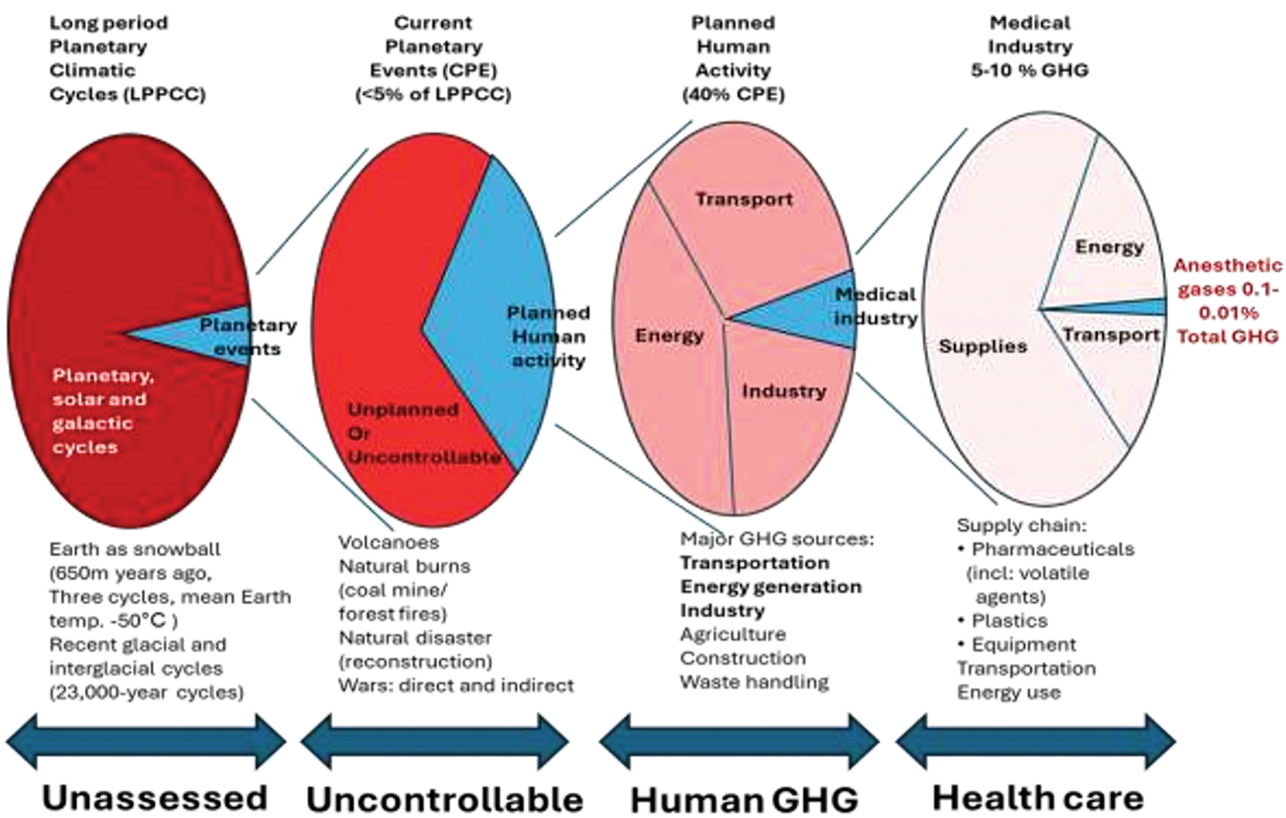

Fig. 3 A holistic look at global warming and greenhouse gas (GHG) emissions.

Conclusion

In 1942, thiopental was blamed for the deaths of marines after the Pearl Harbor bombing. A case report and an editorial in *Anesthesiology* advocating careful dosing saved the drug for generations to come.[85] The case being made here is simple: Trace anesthetics can affect cognition in the setting of neurological injuries. Switching to desflurane could provide rapid, monitorable elimination of the anesthetic agent from the body. Knowing that an anesthetic agent is not responsible for delayed wake-up could enhance the safety of supratentorial neurosurgery. Early detection of neurological deficits is critical in such a setting. However, no study has assessed whether switching to desflurane is effective in patients with neurological injuries. We believe denying desflurane use in such settings is premature and ill-justified. Desflurane has a specific role in neuroanesthesia. When used narrowly for wake-up purposes in sub-MAC concentrations, for a short time, with low flows, desflurane's environmental effects can be significantly mitigated. The extent to which the emergent banning of desflurane is financially motivated can be debated. However, in neuroanesthesiology practice, the ban risks potential patient harm. Using desflurane intelligently while avoiding any environmental impact is the right solution to the problem, not removing it from the formularies altogether.

Conflict of Interest
None declared.

References

1 Young G. Pollution threat to man's only home. Natl Geogr Mag 1970;138(06):738–780
2 Campbell M, Pierce JT. Atmospheric science, anaesthesia, and the environment. BJA Educ 2015;15(04):173–179
3 Sulbaek Andersen MP, Nielsen OJ, Karpichev B, Wallington TJ, Sander SP. Atmospheric chemistry of isoflurane, desflurane, and sevoflurane: kinetics and mechanisms of reactions with chlorine atoms and OH radicals and global warming potentials. J Phys Chem A 2012;116(24):5806–5820
4 Rasool SI, De Bergh C. The runaway greenhouse and the accumulation of CO2 in the Venus atmosphere. Nature 1970;226(5250):1037–1039
5 Alexander R, Poznikoff A, Malherbe S. Greenhouse gases: the choice of volatile anesthetic does matter. Can J Anaesth 2018;65(02):221–222
6 Andersen MPS, Nielsen OJ, Sherman JD. The global warming potentials for anesthetic gas sevoflurane need significant corrections. Environ Sci Technol 2021;55(15):10189–10191
7 Shine KP. Climate effect of inhaled anaesthetics. Br J Anaesth 2010;105(06):731–733
8 Özelsel TJ-P, Sondekoppam RV, Buro K. The future is now-it's time to rethink the application of the Global Warming Potential to anesthesia. Can J Anaesth 2019;66(11):1291–1295
9 Ryan SM, Nielsen CJ. Global warming potential of inhaled anesthetics: application to clinical use. Anesth Analg 2010;111(01):92–98
10 Sherman J, Le C, Lamers V, Eckelman M. Life cycle greenhouse gas emissions of anesthetic drugs. Anesth Analg 2012;114(05):1086–1090
11 Devlin-Hegedus JA, McGain F, Harris RD, Sherman JD. Action guidance for addressing pollution from inhalational anaesthetics. Anaesthesia 2022;77(09):1023–1029
12 Reduce Carbon Footprint from Inhaled Anesthesia with New Guidance Published. Accessed July 31, 2024 at: https://www.asahq.org/about-asa/newsroom/news-releases/2022/06/reduce-carbon-footprint-from-inhaled-anesthesia-with-new-guidance-published
13 Joshi S. Appendix 18: Approach to Fast Track Wakeup After Craniotomy and Its Assessment. In: Neuroanesthesiology Case Companion. Jaypee Publisher: Delhi; 2023:620–622
14 Eger EI, Westhorpe RN, Saidman LJ. 1910–1950: Anesthesia Before, During, and After Two World Wars. In: Eger Ii EI, Saidman LJ, Westhorpe RN, editors. The Wondrous Story of Anesthesia. New York, NY: Springer New York; 2014:51–70
15 Whalen FX, Bacon DR, Smith HM. Inhaled anesthetics: an historical overview. Best Pract Res Clin Anaesthesiol 2005;19(03):323–330
16 Terrell RC, Speers L, Szur AJ, Treadwell J, Ucciardi TR. General anesthetics. 1. Halogenated methyl ethyl ethers as anesthetic agents. J Med Chem 1971;14(06):517–519
17 Andersen MPS, Nielsen OJ, Sherman JD. Assessing the potential climate impact of anaesthetic gases. Lancet Planet Health 2023;7(07):e622–e629
18 Purohit P, Höglund-Isaksson L. Global emissions of fluorinated greenhouse gases 2005–2050 with abatement potentials and costs. Atmos Chem Phys 2017;17(04):27952816
19 NASA. Are Ozone Hole and Global Warming Related. National Aeronautics and Space Administration. Accessed July 31, 2024, at: https://earthobservatory.nasa.gov/blogs/climateqa/category/global-warming/
20 Son S-W, Tandon NF, Polvani LM, Waugh DW. Ozone hole and Southern Hemisphere climate change. Geophys Res Lett 2009;36(15):1–5
21 Kelleher D, Fouts-Palmer E, Yu S, Malhotra V. Greening the operating room and your budget by reducing desflurane use. ASRA Pain Medicine News. 2022
22 Hu EP, Yap A, Davies JF, Goyagi T, McGain F. Global practices in desflurane use. Br J Anaesth 2023;•••:S0007-0912(23)00471-3
23 Anonymous. Guidance: Desflurane decommissioning and clinical use. NHS England. Updated 27 March 2024. Accessed August 27, 2024 at: https://www.england.nhs.uk/longread/guidance-desflurane-decommissioning-and-clinical-use
24 Kamal FA, Fernet LY, Da Silva NK, et al. Comparing perioperative outcomes of total intravenous anesthesia (TIVA) with volatile anesthesia in patients with obesity: a systematic review. Cureus 2024;16(02):e54094
25 Dewan MC, Rattani A, Fieggen G, et al; Executive Summary of the Global Neurosurgery Initiative at the Program in Global Surgery and Social Change. Global neurosurgery: the current capacity and deficit in the provision of essential neurosurgical care. J Neurosurg 2018;130(04):1055–1064
26 Falcó-Roget J, Cacciola A, Sambataro F, Crimi A. Functional and structural reorganization in brain tumors: a machine learning approach using desynchronized functional oscillations. Commun Biol 2024;7(01):419
27 Zotey V, Andhale A, Shegekar T, Juganavar A. Adaptive neuroplasticity in brain injury recovery: strategies and insights. Cureus 2023;15(09):e45873
28 Yuan B, Xie H, Gong F, et al. Dynamic network reorganization underlying neuroplasticity: the deficits-severity-related language network dynamics in patients with left hemispheric gliomas involving language network. Cereb Cortex 2023;33(13):8273–8285
29 Lv K, Cao X, Wang R, et al. Neuroplasticity of glioma patients: brain structure and topological network. Front Neurol 2022;13:871613
30 Guidotti R, Del Gratta C, Perrucci MG, Romani GL, Raffone A. Neuroplasticity within and between functional brain networks in mental training based on long-term meditation. Brain Sci 2021;11(08):1086
31 Lin N, Han R, Zhou J, Gelb AW. Mild sedation exacerbates or unmasks focal neurologic dysfunction in neurosurgical patients

with supratentorial brain mass lesions in a drug-specific manner. Anesthesiology 2016;124(03):598–607
32 Vlisides PE, Mashour GA. Pharmacologic unmasking of neurologic deficits: a stress test for the brain. Anesthesiology 2019;131(01): 5–6
33 Thal GD, Szabo MD, Lopez-Bresnahan M, Crosby G. Exacerbation or unmasking of focal neurologic deficits by sedatives. Anesthesiology 1996;85(01):21–25, discussion 29A–30A
34 Anonymous. Inhaled Anesthetics. NYSORA. Accessed July 30, 2024, at: https://www.nysora.com/anesthesia/inhaled-anesthetics/
35 Lockwood G. Theoretical context-sensitive elimination times for inhalation anaesthetics. Br J Anaesth 2010;104(05):648–655
36 Black S, Enneking FK, Cucchiara RF. Failure to awaken after general anesthesia due to cerebrovascular events. J Neurosurg Anesthesiol 1998;10(01):10–15
37 Kim JH, Jin Y, Hong SW. Failure to awaken from general anesthesia due to infratentorial hemorrhage after cervical spine surgery: a case report. Medicine (Baltimore) 2019;98(44):e17678
38 Bennetts FE. Thiopentone anaesthesia at Pearl Harbor. Br J Anaesth 1995;75(03):366–368
39 Schubert A, Mascha EJ, Bloomfield EL, DeBoer GE, Gupta MK, Ebrahim ZY. Effect of cranial surgery and brain tumor size on emergence from anesthesia. Anesthesiology 1996;85(03): 513–521
40 Dedrick RL. Arterial drug infusion: pharmacokinetic problems and pitfalls. J Natl Cancer Inst 1988;80(02):84–89
41 Gkantinas G, Tataki EI, Lykoudis PM, Lelekaki E, Kouki P. Clinical effects and adverse events associated with desflurane use in adult patients undergoing supratentorial craniotomy: a systematic review. J Neurosurg Anesthesiol 2024;36(01):20–28
42 Haldar R, Kannaujia AK, Verma R, et al. Randomized trial to compare plasma glucose trends in patients undergoing surgery for supratentorial gliomas under maintenance of sevoflurane, desflurane, and propofol. Asian J Neurosurg 2020;15(03): 579–586
43 Paul AP, Vedantam A, Korula G, Chacko AG. A comparison of the recovery profiles of desflurane and isoflurane anesthesia in patients undergoing elective supratentorial craniotomy: a randomized controlled trial. Neurol India 2017;65(05): 1053–1058
44 Gökçek E, Kaydu A, Akdemir MS, Akil F, Akıncı IO. Early postoperative recovery after intracranial surgical procedures. Comparison of the effects of sevoflurane and desflurane. Acta Cir Bras 2016;31 (09):638–644
45 Bastola P, Bhagat H, Wig J. Comparative evaluation of propofol, sevoflurane and desflurane for neuroanaesthesia: a prospective randomised study in patients undergoing elective supratentorial craniotomy. Indian J Anaesth 2015;59(05):287–294
46 Dube SK, Pandia MP, Chaturvedi A, Bithal P, Dash HH. Comparison of intraoperative brain condition, hemodynamics and postoperative recovery between desflurane and sevoflurane in patients undergoing supratentorial craniotomy. Saudi J Anaesth 2015;9 (02):167–173
47 Mikuni I, Harada S, Yakushiji R, Iwasaki H. Effects of changing from sevoflurane to desflurane on the recovery profile after sevoflurane induction: a randomized controlled study. Can J Anaesth 2016;63(03):290–297
48 Kim JW, Lee JY, Hwang SW, et al. The effects of switching from sevoflurane to short-term desflurane prior to the end of general anesthesia on patient emergence and recovery: a randomized controlled trial. BioMed Res Int 2022;2022:1812728
49 Kang H, Cha SM, Park SG, et al. The effects of changing from isoflurane to desflurane on the recovery profile during the latter part of anesthesia. Acta Med Okayama 2010;64(05):307–316
50 Neumann MA, Weiskopf RB, Gong DH, Eger EI II, Ionescu P. Changing from isoflurane to desflurane toward the end of anesthesia does not accelerate recovery in humans. Anesthesiology 1998;88(04):914–921
51 Leijonhufvud F, Jöneby F, Jakobsson JG. The impact of fresh gas flow on wash-in, wash-out time and gas consumption for sevoflurane and desflurane, comparing two anaesthesia machines, a test-lung study. F1000 Res 2017;6:1997
52 Kampman JM, Hermanides J, Hollmann MW, et al. Mortality and morbidity after total intravenous anaesthesia versus inhalational anaesthesia: a systematic review and meta-analysis. EClinicalMedicine 2024;72:102636
53 Rudolff AS, Moens YP, Driessen B, Ambrisko TD. Comparison of an infrared anaesthetic agent analyser (Datex-Ohmeda) with refractometry for measurement of isoflurane, sevoflurane and desflurane concentrations. Vet Anaesth Analg 2014;41(04):386–392
54 Boztuğ N, Bigat Z, Akyuz M, Demir S, Ertok E. Does using the bispectral index (BIS) during craniotomy affect the quality of recovery? J Neurosurg Anesthesiol 2006;18(01):1–4
55 Hirata N. Efficacy of desflurane for early recovery and early detection of neurological abnormality in spinal surgery. J Jpn Soc Clin Anesth 2015;35(03):393–398
56 Ting CK, Hu JS, Teng YH, Chang YY, Tsou MY, Tsai SK. Desflurane accelerates patient response during the wake-up test for scoliosis surgery. Can J Anaesth 2004;51(04):393–397
57 Alnemri A, Sussman S, Estephan L, et al. Cost of total intravenous anesthesia versus inhalation anesthesia in obstructive sleep apnea surgery. Laryngoscope 2022;132(07):1487–1494
58 Cleland J, Bill V, Williams E, Shelton C. Retained desflurane in decommissioned vaporisers: a national problem? Anaesthesia 2023;78(05):651–652
59 O'Brien O, Conlon N. Anaesthetic gases and the environment: is it time for a rethink? Surgeon 2024;22(04):200–202
60 Jänchen J, Brückner JB, Stach H. Adsorption of desflurane from the scavenging system during high-flow and minimal-flow anaesthesia by zeolites. Eur J Anaesthesiol 1998;15(03):324–329
61 Yadav VK, Choudhary N, Inwati GK, et al. Recent trends in the nanozeolites-based oxygen concentrators and their application in respiratory disorders. Front Med (Lausanne) 2023;10; 1147373
62 El Sherif D, Knox JC. International Space Station Carbon Dioxide Removal Assembly (ISS CDRA) Concepts and Advancements. SAE Technical Paper 2005-01-2892, 2005
63 Doyle DJ, Byrick R, Filipovic D, Cashin F. Silica zeolite scavenging of exhaled isoflurane: a preliminary report. Can J Anaesth 2002;49 (08):799–804
64 Fulton B. Combating the Negative Impacts of Volatile Anesthetic on the Environment by Embracing New Technology. The Sensor 2023(04):9–15
65 Gandhi J, Barker K, Cross S, Goddard A, Vaghela M, Cooper A. Volatile capture technology in sustainable anaesthetic practice: a narrative review. Anaesthesia 2024;79(03):261–269
66 Cubanski J, Neuman T A Small Number of Drugs Account for a Large Share of Medicare Part D Spending. Updated August 27, 2024, at: https://www.kff.org/medicare/issue-brief/a-small-numberof-drugs-account-for-a-large-share-of-medicare-part-d-spending/
67 Pasternak JJ, Lanier WL. Is nitrous oxide use appropriate in neurosurgical and neurologically at-risk patients? Curr Opin Anaesthesiol 2010;23(05):544–550
68 Culley DJ, Crosby G. Nitrous oxide in neuroanesthesia: tried and true or toxin? Anesthesiology 2008;108(04):553–554
69 Moody AE, Beutler BD, Moody CE. Predicting cost of inhalational anesthesia at low fresh gas flows: impact of a new generation carbon dioxide absorbent. Med Gas Res 2020;10(02):64–66
70 Smith M, Singh H, Sherman JD. Infection prevention, planetary health, and single-use plastics. JAMA 2023;330(20):1947–1948
71 Özelsel TJ-P, Sondekoppam RV, Ip VHY, Tsui BCH. Re-defining the 3R's (reduce, refine, and replace) of sustainability to minimize the environmental impact of inhalational anesthetic agents. Can J Anaesth 2019;66(03):249–254

72 Gonzalez-Pizarro P, Brazzi L, Koch S, et al; Sustainability National Representatives. European Society of Anaesthesiology and Intensive Care consensus document on sustainability: 4 scopes to achieve a more sustainable practice. Eur J Anaesthesiol 2024;41(04):260–277
73 Anonymous. Anesthesia Disposable Global Market Report 2024 by The Business Research Company, Accessed August 27, 2024 at: https://www.thebusinessresearchcompany.com/report/anesthesia-disposables-globalmarket-report
74 Jain N, LaBeaud D. How should US health care lead global change in plastic waste disposal? AMA J Ethics 2022;24(10):E986–E993
75 Papadopoulou A, Kumar NS, Vanhoestenberghe A, Francis NK. Environmental sustainability in robotic and laparoscopic surgery: systematic review. Br J Surg 2022;109(10):921–932
76 Fairbridge RW. Climatology of a glacial cycle. Quat Res 1972;2(03):283–302
77 Yue X-L, Gao Q-X. Contributions of natural systems and human activity to greenhouse gas emissions. Adv Clim Chang Res 2018;9(04):243–252
78 Voosen P. 'Hot' climate models exaggerate Earth impacts. Science 2022;376(6594):685
79 Anonymous. How does war contribute to climate change? Conflict and Environment Observatory. 2024, Accessed August 27, 2024 at: https://ceobs.org/how-does-war-contribute-to-climate-change/
80 Hall S The New Space Race Is Causing New Pollution Problems. New York Times. 2024, Accessed August 27, 2024 at: https://www.nytimes.com/2024/01/09/science/rocket-pollution-space-xsatellites.html?smid=url-share
81 Anonymous. Ukraine war responsible for 150 million tons of CO2 emissions. Japan Times. 2023, Accessed August 27, 2024 at: https://www.japantimes.co.jp/environment/2023/12/05/climatechange/ukraine-war-co2emissions/#:~:text=The%20experts%20also%20took%20into,in%20ruins%20by%20the%20war
82 Bun R, Marland G, Oda T, et al. Tracking unaccounted greenhouse gas emissions due to the war in Ukraine since 2022. Sci Total Environ 2024;914:169879
83 Weller M. A general review of the environmental impact of health care, hospitals, operating rooms, and anesthetic care. Int Anesthesiol Clin 2020;58(04):64–69
84 Tomson C. Reducing the carbon footprint of hospital-based care. Future Hosp J 2015;2(01):57–62
85 Editorial. The question of intravenous anesthesia in war surgery. Anesthesiology 1943;4(01):74–77

