Inhalational anaesthetics, ozone depletion, and greenhouse warming: the basics and status of our efforts in environmental mitigation

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Purpose of review
Following their use for medicinal purposes, volatile inhalational anaesthetic agents are expelled into the atmosphere where they contribute to anthropogenic climate change. We describe recent evidence examining the benefits and harms associated with their use.

Recent findings
The environmental harms associated with desflurane and nitrous oxide likely outweigh any purported clinical benefits. Life cycle analyses are beginning to address the many gaps in our understanding, and informing choices made on all aspects of anaesthetic care. There is, however, an urgent need to move beyond the debate about anaesthetic technique A vs. B, and focus also on areas such as sustainable procurement, waste management, pharmacological stewardship and joined-up solutions.

Summary
There is now compelling evidence that anaesthetists, departments and hospitals should avoid desflurane completely, and limit nitrous oxide use to settings where there is no viable alternative, as their environmental harms outweigh any perceived clinical benefit. Life cycle analyses seem supportive of total intravenous and/or regional anaesthesia. There are many other areas where choices can be made by individual anaesthetists that contribute towards reducing the environmental burden of healthcare, such as prioritising the reduction of inappropriate resource use and over-treatment. However, this all requires joined up solutions where all parts of an organisation engage.

Key points

- There is now sufficient physiochemical data for us all to be well-informed about the choices we make when selecting inhalational anaesthetic agents, as well as alternatives such as total intravenous anaesthesia.
- For individual anaesthetists and departments, it is reasonable to avoid the use of desflurane and nitrous oxide, as their cost in terms of the role they play in anthropogenic climate change exceeds any purported clinical benefit for individual patients.
- The debate must move beyond arguments about anaesthetic A vs. B and instead look at the environmental harms caused by healthcare more generally and how these might be mitigated.

Introduction

Climate change and environmental pollution threaten to disrupt the ability of health systems to provide high quality care, and undo the past 50 years of advances in public health [1]. Since the industrial revolution global temperature rises have accelerated as a consequence of anthropogenic greenhouse gas emissions, with resultant negative impacts on water availability, food supplies, and vector-borne disease. As a major industrial sector, healthcare itself makes a substantial contribution to environmental impacts.

There is an urgent need to cut the environmental impact of healthcare as part of a rapid and crucial transition to a zero-carbon economy, identified by the UN 2018 Intergovernmental Panel on Climate Change (IPCC) as a vital goal if global warming is to be limited to 1.5 degrees above pre-industrial levels [2]. Two degrees of warming may lead to sea level rises, loss of biodiversity, global health problems, food and water shortages, mass migration and geopolitical insecurity. Limiting global warming will require global net emissions of carbon dioxide to fall by approximately 45% from 2010 levels by 2030, reaching net zero around 2050 [3].

Both nitrous oxide and volatile anaesthetic agents act as 'greenhouse gases'. In the UK, it has been estimated that the emission of inhaled anaesthetic agents accounts for 5% of the carbon footprint of acute healthcare organisations [3]. Because analgesia and anaesthesia can safely be provided by other means, inhaled agents are seen by many as 'low hanging fruit', the use of which can be minimised without affecting the quality of patient care, in order that anaesthesia can be provided more sustainably.

Global emissions from hydrofluorocarbon and chlorofluorocarbon anaesthetic gases in 2014 were estimated to be equivalent to 3 million tonnes of carbon dioxide. Eighty percent of this was from desflurane alone. The Montreal Protocol aimes to gradually reduce the manufacture and use of hydrofluorocarbons. However, medicinal hydrofluorocarbons such as sevoflurane and desflurane, are exempt on the grounds of medical necessity. Nitrous oxide is responsible for approximately 6% of anthropogenic greenhouse gas, 1% of which is from medical use [4].

Meeting the net-zero target will require globally-coordinated changes in anaesthetic practice. However, decisions are rarely straightforward, and a universal comparator is required to achieve unbiased comparisons between alternative techniques. Life cycle analyses of global warming impact, which may account for the development, evaluation, manufacture, packaging, transport, storage, administration and waste management are available for many drugs and devices [2]. Sherman et al. calculated full life cycle assessments for inhaled agents [5], and Parvatker et al. have created cradle-to-gate data (i.e. not including distribution, storage, administration or waste) for 20 commonly used injectable drugs in anaesthesia including sedatives, neuromuscular blocking drugs and local anaesthetic agents [6]. It should be noted, however, that life cycle assessments only account for global warming impacts, and do not include other emissions to which anaesthetic practice may contribute such as water contamination and plastics waste [7–9].

This article aims to discuss recent data, opinion and the controversies associated with volatile anaesthetic agent use and greenhouse warming.

Atmospheric science

The earth's atmosphere is divided into five principal layers. In ascending altitude, these are: the troposphere, stratosphere, mesosphere, thermosphere and exosphere. Almost all atmospheric water vapour is located in the troposphere, which comprises 80% of the mass of the atmosphere. Between the troposphere and the stratosphere is the boundary tropopause, which is defined by the change in temperature with altitude. It can be found at approximately 8000 m at the poles and 18,000 m at the equator. With ascent through the troposphere, the temperature decreases before it stabilises to then rise with further ascent through the stratosphere. The ozone layer is found in the stratosphere at an altitude of between 20,000 and 30,000 m, accounting for 80% of atmospheric ozone, which is responsible for limiting the passage of harmful ultraviolet radiation, 280-315 nm in wavelength [10].

The earth's surface is warmed by incoming solar radiation at a mean energy density of 342 $W.m^{-2}$ and it cools by emitting infrared radiation with a peak wavelength of 10 µm at 290 K (17°C). So-called 'greenhouse gases' in the troposphere re-absorb and re-emit infrared radiation, leading to atmospheric warming as a consequence of positive energy balance. All commonly-used inhalational anaesthetic agents absorb radiation at around 10 µm wavelength, causing heat retention (Fig. 1). The carbon dioxide equivalent (CO_2e) is a metric measure employed to compare the emissions of different greenhouse gases based on their global warming potential (GWP) in comparison to the emission of an equivalent mass of CO_2. In general, GWP is expressed over the 100-year time horizon (GWP_{100}).

The GWP is dependent on radiative efficiency and atmospheric lifetime of a gas. The radiative efficiency is the change in solar energy irradiance on the earth's atmosphere that occurs with a change in the concentration (usually in parts per billion; ppb) of a particular compound. Radiative efficiency depends on the strength and position of the compound's infrared absorption bands [11]. The atmospheric lifetime of a gas refers to the estimated amount of time an anthropogenic increase in an atmospheric pollutant concentration would take to revert to its natural level. This is dependent on how quickly a molecule is broken down. Because volatile anaesthetic agents have many similarities in terms of molecular size and number of bonds, their differences in GWP are mainly due to variations in atmospheric longevity rather than radiative forcing. Key values for desflurane, isoflurane, nitrous oxide and sevoflurane are provided in Table 1.

Volatile inhalational anaesthetic agents

Only a basic level of scientific knowledge is required in order to appreciate the environmental harms caused by volatile inhalational anaesthetic agent use. Following their administration, these agents are exhaled and typically 'scavenged' away from operating theatres before being expelled to the environment unchanged. The atmospheric breakdown of volatile agents depends on their interaction with ultraviolet radiation and hydroxyl radicals, which varies dependent on their physiochemical properties. For example, neither sevoflurane nor desflurane undergo ultraviolet photolysis, however sevoflurane is highly amenable to hydroxyl decay. This means that sevoflurane has a relatively short atmospheric lifespan of 1 year, whereas desflurane has a lifespan of 14 years, the longest of any volatile agent [12].

In 1987, the Montreal Protocol aimed to discontinue the manufacturing of ozone depleting substances such as chlorofluorocarbons. Of the volatile agents, sevoflurane and desflurane have no ozone depletion potential because fluorine does not destroy ozone, whilst halothane, enflurane and isoflurane have ozone depleting activity due to the presence of bromine and chlorine. However, it is unlikely that volatile agents will reach the stratosphere in sufficient concentrations to cause significant ozone depletion, prior to their degradation.

Medicinal nitrous oxide is responsible for a significant proportion of anthropogenic climate change [13]. Because it has a sufficiently long atmospheric lifetime (110 years), it is likely to reach the stratosphere where it is capable of ozone destruction [14]: incident solar radiation causes photolysis of both ozone and nitrous oxide to generate excited oxygen atoms that react with nitrous oxide to produce nitric oxide. This then reacts with ozone, producing nitrogen dioxide and oxygen. The nitrogen dioxide then reacts with excited oxygen atoms, again producing nitric oxide and oxygen, thus perpetuating a cycle of ozone depletion [10].

In 2016, Vollmer et al. published the first study to directly measure the atmospheric concentrations of volatile anaesthetic agents, demonstrating that the atmospheric concentration of desflurane was increasing, sevoflurane was static, and halothane and isoflurane were decreasing [15]. Integrating GWP data, they calculated that desflurane alone accounts for eighty percent of the greenhouse effect due to volatile anaesthetic agents. Since it is impossible to distinguish anaesthetic and non-anaesthetic sources of nitrous oxide in the atmosphere, it was excluded from these analyses [11].

Calculations of the carbon dioxide equivalent emissions associated with anaesthetic practice based on the GWP_{100} and potency of volatile agents have been published numerous times and compared to normal daily activity, such as driving a car, to demonstrate the impact that the choice of anaesthetic vapours may have on climate change. For example, at 1 MAC (2.2% sevoflurane, 1.2% isoflurane, 6.6% desflurane) and 1 $l.min^{-1}$ fresh gas flow, using sevoflurane is equivalent to driving 4 miles in a compact car, isoflurane is equivalent to 8 miles, and desflurane is equivalent to 190 miles (Fig. 2) [11]. Furthermore, apps have been created allowing anaesthetist to calculate the impact of their practice at the bedside [16]. As this comparison demonstrates, desflurane is associated with a much higher climate impact, and yet, there is little evidence to suggest that it is associated with any clinically-relevant benefits [17–19].

The capture and destruction or reprocessing of inhaled anaesthetic agents is a developing field of interest. Capture techniques rely on the scavenging of unchanged gases exhaled by the patient, which can then be collected for processing. In the case of nitrous oxide, this can be catalytically 'cracked' into nitrogen and oxygen (neither of which have problematic environmental impacts) [20] and volatile agents can either be destroyed by photolysis or collected for reprocessing and, potentially, reused [11,21]. Though these techniques offer a potential route to make inhalational anaesthesia more sustainable, they are not 100% efficient and are unable to collect all exhaled gas. As such, it is unlikely that this technology would ever be able to fully mitigate the environmental impact of a potent greenhouse gas such as desflurane.

Other strategies
It is becoming increasingly apparent that a sole focus on inhaled anaesthetic agents during the peri-operative period fails to acknowledge many other areas where the environmental harms of anaesthetic practice can be targeted. These include: sustainable procurement; waste management; pharmacological stewardship; and joined-up solutions.

Sustainable procurement
It is estimated that 70% of healthcare-associated carbon emissions are embodied within the supply chain of drugs and devices procured by healthcare organisations [22]. For example, the environmental sequalae from personal protective equipment use during the COVID-19 pandemic is a current area of debate, with calls to invest in research and development of more suitable materials that reduce waste generation [23]. In order to make informed

choices about the products we use, more information should be made available regarding the environmental impacts of items procured for use in clinical settings. This should include, for example, a life cycle analysis of carbon emissions, and a description of environmental toxins released during the manufacture or use of the product in question. This information should be reflective of the differences in the emissions regulations in the regions of manufacture and use. These may affect, for example, the carbon intensity of energy production [24] or the extent to which toxins may be released into the environment.

Waste management: reduce, reuse and recycle

Anaesthetic practice creates a substantial amount of solid waste such as single-use equipment, drug packaging and consumables. Whilst re-use and recycling may offer a way to mitigate some of the environmental impacts of this waste, this is often not a straightforward process in terms of waste handling regulations and logistics. Reduction of resource use therefore represents a more consistently viable strategy and developing strategies to minimise resource use without patient benefit should be prioritised. Areas of focus may include opening devices in error, the use of the incorrect size or type of device which then has to be replaced, or preparing equipment and drugs 'just in case', which are then not used [25].

Pharmacological stewardship

Many drugs that are used in anaesthesia, and their metabolites, are environmental toxins in their own right. For example, propofol and its phenolic metabolites are toxic to some forms of aquatic life. Propofol has now been found in drinking water, the tissues of aquatic organisms and even floor coverings [26]. There have been calls for its disposal by incineration instead of landfill, in order to minimise the risk of environmental toxicity, though this would increase its global warming impacts when compared to other methods of disposal. Perhaps more importantly however, clinicians should be aware that drug disposal is not benign, and should therefore consider the use of pre-prepared emergency drugs, and avoid drawing up more than is necessary. Propofol, for example, is available in ampoules of multiple sizes, and usage for a case can easily be calculated, or predicted from the information available on modern target-controlled infusion pumps.

Joined up solutions

Reducing the environmental impacts of the healthcare industry is a much greater task than can be solved by the choice of anaesthetic agents. Yet there is some irony that pollution, to which healthcare is a major contributor, is a leading cause of morbidity and mortality [27]. The most powerful solutions will only be possible when all parts of an organisation engage – from clinicians all the way to hospital management, politicians, global commissions and higher-level decision makers. Whilst variation in anaesthetic technique can have a significant impact on the environmental consequences of a given anaesthetic, focussing on technique alone makes the assumption that the anaesthetic is necessary and in the best interests of the patient. Preventative healthcare, including an emphasis on promoting health rather than treating illness, only undertaking surgical management when necessary, and pre-operative optimisation, have the capacity for much greater impacts than intra-operative anaesthesia alone. Whilst individual actions are important, global goals can only be achieved through collaboration.

Unanswered questions

There remain several unanswered questions, including:

1. What are the worldwide trends in anaesthetic gas use and how are these trends changing [28]?

2. How does the environmental impact of regional anaesthesia compare with general anaesthesia?
3. How can we translate practices around sustainable anaesthesia to critical care and the rest of the hospital?
4. What is the contribution of alternative inhaled agents such as methoxyflurane [29]? Could this replace nitrous oxide for use in, for example, emergency medicine and obstetrics?
5. Can ‘gas capture’ techniques be a useful strategy to mitigate the environmental impacts of anaesthetic practice?

Conclusion

There is now sufficient physiochemical data for us all to be well-informed about the choices we make when selecting a volatile inhalational anaesthetic agent, as well as alternatives such as total intravenous anaesthesia. There is now a need to move beyond the choices we make in the intra-operative period, however, and look at the environmental harms caused by healthcare more generally and how these might be mitigated. However, for individual anaesthetists, we recommend there is now sufficient evidence to:

1. Avoid desflurane completely, as it is becoming clear that the environmental harm caused is greater than any perceived clinical benefit.
2. Avoid nitrous oxide completely in routine anaesthetic practice, as there are alterative effective methods to provide analgesia.
3. Consider the use of total intravenous and/or regional anaesthesia for all patients. Notwithstanding concerns around the potential for propofol to act as an environmental pollutant, life cycle analyses have consistently demonstrated that total intravenous anaesthesia is preferable to inhalational anaesthesia in terms of climate effects. This is especially so for nitrous oxide and desflurane [11].
4. Prioritise the reduction of inappropriate resource use, both in terms of drug and device waste, and over-treatment.

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Conflicts of interest

None to declare.

References and recommended reading
***Of special interest**
****Of outstanding interest**

1. Tennison I, Roschnik S, Ashby B et al. Health care's response to climate change: a carbon footprint assessment of the NHS in England. *The Lancet Planetary Health* 2021; **5: e84–92.

This is the latest update on estimates of the carbon footprint of the NHS in England as well as strategies for the mitigation of associated environmental harms resulting from healthcare. The services emissions totalled 25 megatonnes in 2019 of carbon dioxide equivalent emissions, which has reduced 26% since 1990. Most of this came from the supply chain, which shows the importance of sustainable procurement strategies. Only 24% was from the direct delivery of care.

*2. Shelton CL, McBain SC, Mortimer F, White SM. A new role for anaesthetists in environmentally-sustainable healthcare. *Anaesthesia* 2019; **74**: 1091–4.

This editorial reflects on the aims of the General Medical Council in the UK which are that newly qualified doctors should be able to apply the principles, methods and knowledge of sustainable healthcare to medical practice. They argue that anaesthetist may be well placed to facilitate this. They also present many of the arguments around climate change and healthcare, including the need to move beyond comparisons of anaesthetic A vs B.

3. White SM, Shelton CL. Abandoning inhalational anaesthesia. *Anaesthesia* 2020; **75: 451–4.

This landmark editorial presents arguments for anaesthetists to abandon inhalational anaesthesia and instead consider the use of total intravenous and/or regional anaesthesia. Rather than present a one-sided piece arguing for such agents to be 'banned', the authors present either side of the argument, identify common ground and the need to prioritise the patient in front of as well as the health of future generations.

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11. McGain F, Muret J, Lawson C, Sherman JD. Environmental sustainability in anaesthesia and critical care. *British Journal of Anaesthesia* 2020; **125: 680–92.

This landmark review provides an update on the science associated with life cycle analyses in healthcare, as well as translational research on the environmental footprint of anaesthesia as applied to other areas such as critical care medicine. The science of climate change is discussed as well as volatile anaesthetic agents in particular and other areas of importance such as waste prevention, energy and infrastructure, water, travel, education and advocacy. The authors argue that it is possible for anaesthetists to protect the patient and the planet and that the two aims are not mutually exclusive.

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18. Shelton CL, Sutton R, White SM. Desflurane in modern anaesthetic practice: walking on thin ice(caps)? *British Journal of Anaesthesia* 2020; **125: 852–6.

This editorial describes the problems associated with the use of desflurane as well as the environmental impacts of volatile anaesthetic agents. They enforce the key message that anaesthetists have a responsibility not just to the patient in front of them, but also to the health and welfare of future generations. Although inhalational agents may continue to play an important role in anaesthesia, desflurane in particular should be avoided. The arguments against its use now appear to be overwhelming.

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This retrospective observational study of 23,840 patients who received desflurane anaesthesia and 84,608 patients who received sevoflurane anaesthesia found no difference in the incidence of postoperative pulmonary complications between the groups (adjusted OR 0.99 95%CI 0.94-1.04, p = 0.598). The authors conclude that in light of the environmental harms associated with desflurane, these data may help individuals and departments make an informed risk:benefit assessment

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Table 1 Key physicochemical data for modern inhalational anaesthetic agents.

	Nitrous oxide	**Desflurane**	**Sevoflurane**	**Isoflurane**
Atmospheric lifetime; years	114	14	1.1	3.2
GWP_{100}	298	2540	130	510
ODP	0.017	0	0	0.03

GWP_{100}, global warming potential in relation to how much infrared radiation absorbed in the atmosphere one tonne of gas will absorb over 100 years as compared with carbon dioxide; ODP, the ozone depletion potential in relation to how much ozone is degraded in the atmosphere relative to CFC-11 (trichlorofluoromethane), which is 1.

Figure 1 Incoming radiation from the sun is of wavelength 0.1-2 µm (dashed line), with half absorbed and half reflected back to the atmosphere. The main mechanism of radiative forcing due to volatile anaesthetic agents is in the trophosphere, where they absorb infrared radiation of wavelength 3-70 µm emitted from the earth (solid line). This also occurs with carbon dioxide, water vapour and nitrous oxide. In the stratosphere, ozone depleters such as chloroflurocarbons and nitrous oxide are broken down by ultraviolet radiation, which forms radicals that destroy ozone. This in turn allows more incoming radiation from the sun.

Figure 2 A comparison of the use of desflurane, isoflurane and sevoflurane at 1 MAC (2.2% sevoflurane, 1.2% isoflurane, 6.6% desflurane) and 1 $l.min^{-1}$ fresh gas flow with 50:50 air:oxygen in terms of number of miles driven in a compact petrol car.