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Keywords: inhalation anesthetics global warming, ozone depletion human health.

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Accelerated changes in climate are already affecting human health, multiplying the existing health problems and increasing the burden of medical care. In recent years, however, it has been found that health care is also an important source of greenhouse gas emissions. Anesthetic gases are greenhouse gases that contribute to global warming, which will produce greenhouse effect by absorbing infrared radiation and react with ozone to destroy the ozone layer. Anesthesia providers have a duty to minimize unnecessary anesthetic gas emissions and lower environmental impact in practice. This paper will mainly discuss the impact of climate change on various aspects of human health, explore the impact mechanism of inhaled anesthetics on climate change, and put forward four solutions for reducing anesthetic gases - reduce, remove, recycle and replace by improving the "3R" principle of waste reduction. Only by changing the way of thinking and corresponding practice to realize the sustainability of anesthesia can we truly fulfill the desire of "do no harm".

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I. INTRODUCTION

As an important part of the natural environment for human survival, climate is closely related to human activities. With the development of industry, the combustion of fossil fuels, the use of refrigerants, deforestation, the use of cars and other human activities have increased significantly, resulting in a significant increase in greenhouse gases. Greenhouse gas is any gas that can absorb infrared radiation in the atmosphere, including water vapor, carbon dioxide, methane, nitrogen oxides, chlorofluorocarbons, ozone, etc.

When short wave solar rays enter the atmosphere, about one third of the rays are directly reflected back into space, a small part is absorbed by water vapor, clouds and particles, while most of the rays are absorbed by the earth's surface, and then radiated back to the atmosphere in the form of long wave rays. The greenhouse gases in the atmosphere absorb these radiations to keep the earth warm. This process is referred to as the greenhouse effect. However, excessive greenhouse effect will lead to global warming[1]. According to the report of the World Meteorological Organization, the global mean temperature in 2020 is 1.2±0.1℃ above the 1850–1900 baseline temperature, which places 2020 as one of the three warmest years on record globally, and the mean temperature in the past five and ten years is also the highest on record[2].

Global warming affects human health, global ecosystem stability and even socio-economic development. Although some effects are beneficial, such as increasing crop yield and available water in some areas and reducing mortality caused by cold, in general, scientists believe that most of the effects of climate change on human beings are adverse[3]. The consequences of global warming, such as increased frequency of heat waves, changes in precipitation, sea-level rise, increased extreme weather events (drought, flood, hurricane, wildfire, etc.),the deterioration of air quality and environmental sanitation, have caused great harm to humans and ecosystems[4][5].

Although scholars pay more and more attention to the impact of climate change on health and its coping strategies, the global response to climate change has been muted, and fail to meet the commitment made in the Paris agreement to limit global warming to "far below 2℃"[6]. Climate change still causes millions of deaths every year.

The World Health Organization has recognized it as the number one threat to human health in the 21st century[7]. Therefore, there is an urgent need for all countries to take strong action to address climate change and jointly protect our planet and the health of present and future generations.

In the health care industry, with the increase in the amount of surgery and the use of anesthetics, people began to pay attention to the impact of inhaled anesthetics on the global climate, but their contribution to the climate is largely ignored because they are "medically essential"[8][9]. In the past decade, different authors have discussed the impact of inhalation anesthesia on the environment[8]-[12]. It has been established that all inhaled anesthetics are potent greenhouse gases and can destroy the ozone layer. Yet the solutions that will reduce their impact on the environment have not been clearly formulated. Therefore, this review mainly summarizes the impact of climate change on human health, the effects of anesthetic gases on the global environment, and the measures to reduce these effects, so as to provide suggestions for anesthesiologists' decision-making in anesthesia practice.

II. IMPACT OF GLOBAL WARMING ON HEALTH

Global warming will have a direct or indirect impact on human health. Direct impact is usually caused by extreme weather, such as death or injury caused by heat wave, flood, storm, etc.[3]. The change of disease transmission mode, air pollution, water pollution, fresh water shortage, reduction of food production and population migration caused by climate change will indirectly affect human health and bring infectious, nutritional, psychological and allergic diseases[1].

2.1 Infectious Diseases

Climate is one of the important factors affecting the spread of infectious diseases. The continuous warming of the global climate and the frequent occurrence of extreme climate will directly or indirectly aggravate the spread of most infectious diseases. Temperature is a major factor in the prevalence of vector-borne diseases. It can influence the survival, reproduction and life cycle of pathogens[13], as well as the survival, growth, reproduction and distribution of vectors and their ability to transmit pathogens[14]. Temperature, humidity and precipitation are important climatic factors affecting the incidence and transmission of malaria. Among them, climate warming provides suitable habitat for the vector Anopheles, and promotes the growth and development of them and their pathogens, so as to increase the chance of human infection[15]. Dengue virus and its vector Aedes are also sensitive to climatic conditions, especially temperature. Rising temperature can accelerate the reproduction of dengue virus[16], affect the life cycle, distribution density, range, and behavior of mosquitoes, which will lead to the epidemic of dengue fever, but the temperature above a certain threshold will reduce the incidence of dengue fever[13][17].

Higher temperatures and changes in rainfall can affect water and food-borne diseases, which is likewise the reason for the significant increase in diarrhea cases. Algae and plankton provide a habitat for Vibrio cholerae. When the sea water warms or becomes eutrophicated, marine phytoplankton multiply in large numbers (such as red tide caused by algae flooding), which will be conducive to the outbreak of cholera[13][18][19].

Similarly, the increase in temperature within a certain range will also accelerate the reproduction speed of Schistosoma japonicum, Salmonella, Escherichia coli, Shigella and typhoid bacilli[13][16]. If rainfall increases and floods break out, the water flow containing pathogens is more likely to pollute drinking water and irrigation water, greatly increasing human exposure, which often occurs in developing countries with insufficient infrastructure[14][18]. In arid areas, waterborne pathogens are concentrated in the only water, will also increase water and food-borne diseases[13][20]. As the WHO said, rainfall will affect the transportation and transmission of infectious substances, while temperature will affect their growth and survival[3].

In addition, transmission of diseases such as plague, rabbit fever, yellow fever, Kala Azar, Lyme disease, West Nile disease, tick-borne encephalitis and hantavirus lung syndrome may also be affected by climate change[13][14][16][21]. It is worth mentioning that although the incidence of extreme weather events is low, the impact on infectious diseases is fierce. For example, the famous El Nino phenomenon will lead to the outbreak of malaria, dengue fever, cholera, avian influenza, hantavirus, Rift Valley fever, plague and other diseases[13][14][17][22].

2.2 Respiratory, cardiovascular and neurological system

The increase of temperature and CO_2 concentration will affect the growth of plants and prolong the pollen season, thereby generating more pollens with enhanced allergenicity[23]-[26]. The thunderstorm will gather pollen grains and provoke the release of a large number of respirable allergic particles after they rupture, which is conducive to penetrate deeper respiratory tract[25][27][28]. Warming in winter will increase mite growth and spore formation[28].

Climate warming, increased precipitation, floods and tsunamis will lead to environmental humidity and mold growth[25][26][28]. Smoke, particulate matter and ozone produced by wildfire and sandstorm are all sources of air pollution [25][26][29]. Exposure to these allergens such as pollen, mold and particles will induce more severe asthma and allergic rhinitis[24]-[28]. Exposure to more and more allergens may also make people that do not have allergies develop allergic symptoms[26]. Ozone is generated by photochemical reaction of oxygen in the atmosphere in the presence of ultraviolet and precursor pollutants (nitrogen oxides and volatile organic compounds), which is closely related to high temperature, drought and forest fire[26][29].

Exposure to pollutants such as ozone and particulate matter can induce airway inflammation, reduce lung function, increase the morbidity and mortality of respiratory diseases such as asthma, respiratory tract infections, chronic obstructive pulmonary disease, lung cancer and so on[25][27][29], especially in children and elderly people[26]. Heat causes dehydration of the body and disrupts lung perfusion, which can increase the number of deaths and acute morbidity among respiratory patients[25][27].

Extreme heat can rapidly increase airway resistance and trigger asthma symptoms by stimulating thermosensitive bronchopulmonary C-fiber nerves[28]. Extreme heat, air pollution and air allergens act synergistically to cause excessive mortality and hospital admissions for respiratory allergic respiratory diseases[28].

In the context of global warming, cardiovascular disease accounts for the largest proportion of heat induced mortality, and coronary heart disease is the main cause of death[30]. Some studies have found that the relationship between temperature and cardiovascular disease mortality is U-shaped, meaning that too low or too high temperature will both increase the risk of death[31]-[33], and the mortality even doubled to tripled under extreme high temperature[31]. Moreover, some categories of population are more vulnerable to the adverse effects of climate changes, such as elderly, those suffering from chronic vascular diseases, and low socio - economic conditions[33]. At high temperature, due to the need of heat dissipation, the body will activate sweat glands, expand blood vessels and increase skin blood flow, resulting in increased cardiac output, accelerated heart rate and increased burden on the heart[31][33]. During decompensation, high body temperature leads to systemic inflammatory response and oxidative stress, damages the structure and function of vascular endothelium and produces cytotoxic effects, which will lead to acute coronary syndrome, trigger arrhythmia and even heart failure[31]. In addition, dehydration may result in increases in the counts of platelets, red blood cells cholesterol levels and blood viscosity, promote, thrombosis, which can easily lead to atherosclerosis, coronary heart disease and thromboembolic diseases, and also increase the risk of ischemic stroke[30][33]-[35]. Electrolyte and acid-base imbalance caused by high temperature is also considered as triggers of acute cardiovascular events[33]. Exposure to air pollutants (O_3, PM) will also increase plasma viscosity and heart rate, which is positively correlated with the morbidity and mortality of coronary artery syndrome, hypertension, arrhythmia, and cerebrovascular events[29][33][35].

The rise of global temperature increases the probability of environmental heatstroke. It is reported that 100% of patients with heatstroke presented with acute neurological symptoms, and 23.3% suffered convalescent or long-term neurological sequelae(prolonged coma, quadriplegia, ataxia, dysarthria and cognitive impairment)[35][36]. Elevated temperature will limit the storage of energy and oxygen, increase the number of free radicals and toxic substances, increase oxidative stress, damage mitochondria, destroy microvascular integrity, and induce neuronal apoptosis and necrosis, which may be the mechanism of stroke pathogenesis and aggravation[29][35]. The damage of high temperature to neurons leads to serious neurological dysfunction and exacerbates the course of neurodegenerative diseases such as dementia, Alzheimer's disease and Parkinson's disease[35]. Besides increasing the morbidity and mortality of ischemic stroke, air pollution will increase the likelihood of dementia and Alzheimer's disease through a variety of pathophysiological mechanisms[35].

2.3 Endocrine and Metabolic Diseases

Studies have shown that by controlling other relevant variables, there is a positive correlation between high temperature and the prevalence of obesity, and the impact of temperature on obesity is stronger than that of most physical activities, and almost the same as that of age and population density[37]. Temperature rise and extreme weather events may increase the morbidity and mortality of diabetes. Diabetics are more likely to experience dehydration, heatstroke and cardiovascular events than non diabetics[38]-[40], which may be related to their impaired thermoregulation mechanism and the use of certain drugs[41]. It is worth mentioning that extreme weather can bring negative influence on the stability and efficacy of insulin, the metabolic control of patients, as well as on access to healthcare, threatening the medical security for the vulnerable group of diabetes[38]-[41].

There are a large number of mitochondria containing uncoupling protein-1 (UCP-1) in brown adipose tissue(BAT) of the human body.

Uncoupling protein-1 can convert the energy generated by glucose and fat decomposition into heat energy instead of ATP, thus increasing energy consumption[42]. The lipids used in BAT will in turn increase the influx of glucose to skeletal muscles, thereby improving insulin sensitivity[40]. Under various stimuli such as cold exposure or sympathetic nerve stimulation, adipocytes expressing UCP-1 are developed in white adipose tissue, which are called beige adipocytes with thermogenic capacity[42][43]. Cold exposure can activate BAT, supplement beige adipocytes, increase thermogenic gene expression, and then improve energy consumption through adaptive thermogenesis to maintain core body temperature[43]. While long term heat exposure will lead to a decrease in the activity of brown and/or beige adipose tissue, reduce energy consumption and thermogenesis, and reduce insulin sensitivity[43]. On the other hand, the adverse effects of climate on agriculture lead to poor grain harvests and rising prices of healthy food, prompting people to consume relatively cheap, high-fat, high-sugar junk food, which are all possible causes of obesity, diabetes, and metabolic syndrome due to global warming[32][38][39][44]. Dehydration caused by global warming may stimulate the production of vasopressin and endogenous fructose. They can not only reduce water loss, but also stimulate fat accumulation and increase blood glucose, thus increasing the risk of these diseases[45]. Extreme climate leads to displacement, poor living conditions and scarcity of resources, resulting in the expansion of slums. This is also directly associated with the increased risk of obesity and diabetes[38].

In fact, the obesity epidemic will influence global warming in turn[37]. Obese patients may increase energy consumption in diet, transportation and medical treatment, such as taking more cars, eating more processed food and using more medical resources, resulting in more greenhouse gases[44]. Obesity may increase the risk of many other diseases, such as type 2 diabetes mellitus, hypertension, dyslipidemia, coronary heart disease, stroke and several cancers[44]. It also serves as a risk factor for metabolic syndrome[46].

In addition, air pollutants activate various cellular pathways and change gene expression, which may lead to decreased insulin sensitivity, increased adipose tissue deposition and β cell dysfunction, increasing incidence rate and prevalence of diabetes mellitus[41].

2.4 Skin Diseases and Eye Diseases

The increase in ultraviolet radiation caused by the depletion of the ozone layer due to greenhouse gases damages two organs that are directly exposed to sunlight, eyes and skin, which can cause sunburn, accelerate skin aging, and increase the morbidity of skin cancer, cataract and snow blindness[3][5][14][47][48]. According to relevant studies, diseases such as cancer of the cornea and conjunctiva, pterygium, macular degeneration, acute photokeratitis and photoconjunctivitis, climatic droplet keratopathy are also related to UVR irradiation[3][49]. Studies have shown that rising temperatures and ultraviolet have a synergistic effect, which will enhance the carcinogenic effects of ultraviolet[14][47][48][50].

Incidence rate of vitreous adenoviral conjunctivitis, fungal keratitis, pseudomonas keratitis, posterior vitreous detachment and retinal detachment may increase when the temperature rises[49]. Higher temperature is beneficial to the growth and reproduction of pathogens and the colonization of that on human skin, increasing the morbidity of skin infections, especially bacteria such as Staphylococcus, Streptococcus and intestinal bacteria, etc.[14][47].

Some infectious diseases caused by climate change also have clinical manifestations on the skin, such as dengue fever, cercarial dermatitis, hand-foot-and-mouth disease, Lyme disease, dracunculiasis and so on[14][48]. After hurricanes, floods, tsunamis and other disasters, the most common skin diseases are skin infections, which can be caused by various pathogens, even some rare pathogens[14]. High allergen counts and strong allergenicity will exacerbate dermatitis and pruritus in patients with atopic eczema[14]. It also exacerbates the exposure and duration of allergic conjunctivitis[49]. Global warming has also led to alterations in plants and animals, resulting in the increased incidence rate of contact dermatitis[14][24].

2.5 Mental Health

In recent years, people mainly pay attention to the impact of climate on physical health, but rarely focus on mental health. Diseases, death, migration, displacement, food insecurity and economic losses as a result of climate change and extreme climate will cause psychological panic, anxiety, sadness, loss, avoidance, emotional disorder, difficulty in concentrating, acute stress disorder, etc.[5][51][52][53]. The incidence of post-traumatic stress disorder and depression in climate related victims is higher than that in ordinary people, and there is a significant increase in suicidal ideation and suicide action among the victims[51]-[53]. Mental illness was considered to be most closely associated with death during a heat wave[51]. Studies suggest that in hot and dry weather, the morbidity, mortality and hospitalization rate of mental illness are higher. The reason may be that heat waves will exacerbate underlying mental illness and behavioral disorders[53]. The number of hospitalized patients with mania was positively correlated with temperature [16]. Depression and suicide rates are also linked to high temperature and air pollution. Extreme high temperature affects the work efficiency of workers, and they are prone to suffer dehydration, heatstroke, fatigue, work injury, kidney disease, etc.[4][51][54].

These factors will lead to psychological problems, socio-economic problems and impact physical and mental health. Climate change will also affect public health[51]. It's believed that as temperatures rise, acts of violence,crime and aggression occur more frequently[53][55]. Competition for limited resources will cause social instability and affect national and international security, which will bring about adverse mental health[51].

2.6 Other

The most direct impact of heat waves is the increase in morbidity and mortality of heat-related diseases (heat cramp, heat syncope, heat exhaustion, heatstroke)[45][56], especially for some vulnerable groups such as children, elderly, chronic patients, mental patients[56][57][58]. Under high temperature environment, human body temperature regulation disorder and excessive heat accumulation in the body will contribute to tissue damage and dysfunction of various organs and systems. Mild manifestations include dizziness, headache, thirst, sweating, panic, weakness, nausea, vomiting, etc.If not handled in time, it will develop into severe heatstroke, manifested with high fever, delirium, coma, seizures, water and electrolyte disorders and multiorgan failure including heart failure, ARDS, Liver failure and acute kidney injury, which can be life-threatening[35][36][56][58]. Rising temperature has resulted in an increase in patients with various kidney diseases, including acute kidney injury, chronic kidney disease, kidney stones and urinary tract infection[58][59][60]. Acute kidney injury is a frequent manifestation of heatstroke.

Repeated acute kidney injury can develop into chronic kidney disease, which mainly occurs in laborers who are often subjected to extreme heat conditions[58][59]. In addition, acute febrile diseases from vector-borne diseases, diarrheal and rodent-borne diseases caused by extreme weather are also well-recognized causes of acute renal injury[59]. Heat stress and dehydration predispose to urinary concentration and low urine volumes, increase the concentration of calcium and uric acid, and the acidity of urine, thus increasing the risk of kidney stones and urinary tract infection[58][59][60]. Climate change and extreme weather such as flood and drought will affect agricultural production and food transportation, resulting in food shortage and insecurity, and eventually causing malnutrition and stunting[38][52]. Insufficient intake of macronutrients and micronutrients will also affect the development of the immune system, leading to secondary immunosuppression in children[52]. Exposure to ultraviolet radiation directly or indirectly inhibits cell-mediated immune to secondary immunosuppression in children[52]. Exposure to ultraviolet radiation directly or indirectly inhibits cell-mediated immune responses through various mechanisms, which can reduce vaccine efficacy and increase the morbidity of tumors and infections, but also reduce the incidence of allergic reactions and some autoimmune diseases[3][52][61].

III. EFFECTS OF INHALED ANESTHETICS ON GLOBAL CLIMATE

At present, commonly used inhalation anesthetics include volatile liquids and gases. The former, such as halothane, isoflurane, enflurane, sevoflurane and desflurane, are halogenated organic compounds, which are evaporated and transported to patients through anesthesia machines. Desflurane and sevoflurane have the fastest onset and offset speed, and are gradually replacing isoflurane and halothane. The latter, such as N_2O, can make people laugh, also known as "laughing gas". It has potent analgesic effect and slight anesthetic effect. It is often combined with other general anesthetics and can be used in surgery and dentistry[8][10][62]. Inhalation anesthetics may exert anesthetic effects by acting on different ion channels, prolonging the activity of inhibitory postsynaptic channels, inhibiting the activity of excitatory synaptic channels, to inhibit the transmission of nerve impulses[63]. These anesthetic gases are mainly discharged through the respiratory tract in their original form and rarely metabolized in the body. Most of the time, they will be discharged into the atmosphere and remain in the atmosphere for a long time[8][9][62]. With the wide use of inhalant anesthetics, it is found that they have potential harm to the global climate. The main impact is their contribution to tropospheric greenhouse effect and stratospheric ozone depletion[10].

3.1 Absorption of Infrared Radiation

Volatile anesthetics(VAs) and N_2O are recognized greenhouse gases[8]-[11]. They will also absorb long wave infrared radiation from the surface, raising the temperature of the surface and troposphere. Radiation forcing refers to the net radiation energy obtained by the earth system due to the change of some factors (the balance between incident solar radiation and outgoing infrared radiation)[9][64]. For example, the increase of carbon dioxide concentration can increase the radiation energy obtained by the earth, which is called as positive forcing, leading to a warming[64].

Each gas absorbs infrared radiation in its own specific wavelength range, so their radiative forcing is different[9]. Radiative forcing is used to quantitatively compare the intensity of different factors in causing climate change[64]. Although the concentration of halogenated organic compounds in the atmosphere is one millionth of carbon dioxide, their total radiation forcing is about 1/6, approximately 11% of the total radiative forcing[65].

This may be explained by their strong absorption capacity in the infrared region of the electromagnetic spectrum, which is the vital spectral region where the earth emits radiation into the space to cool itself, called "atmospheric window"[11][66]. Naturally occurring gases such as CO_2 and H_2O absorb less radiation in the "atmospheric window", which makes VAs a strong greenhouse gas[67]. At present, N_2O accounts for about 6% of the total radiation forcing[8][10]. In order to more accurately express their impact on climate, many scholars calculate their radiation efficiency and global warming potential (GWP) through formulas. GWP is a measure of the contribution of a given mass of greenhouse gas to global warming over a specified time period[9].

This is a relative scale used to compares the contribution of the gas in question to that of the same mass of carbon dioxide[9]. For example, the GWP_{20} of a gas is 100, which means that its warming potential in 20 years is equivalent to 100 times that of CO_2 in the same mass. Hospitals can simply multiply the mass of discharged gas by GWP to calculate the carbon dioxide equivalent of the gas and know the impact of emitted anesthetic gas on climate[66]. Sulbaek Andersen et al.[11][66][68] calculated and corrected for many times that the GWP_{100} of isoflurane, desflurane, sevoflurane, halothane and enflurane were 510, 2540, 130, 50 and 680 respectively, and estimated that the annual impact of global inhaled anesthetic emissions on climate was equivalent to 4.4 million tons of carbon dioxide based on the assumption that 200 million anesthetic operations were performed in the world every year, which is comparable with that of the CO_2 emissions from one coal-fired power plant or approximately 1 million passenger cars. Under comparable and common clinical conditions, the potential impact of desflurane on global warming is greater than that of other VAs[9]. According to the fifth assessment report of the Intergovernmental Panel on climate change (IPCC), the GWP_{100} of N_2O is 264.8[64]. Due to the phasing out of CFC emissions by the Montreal Protocol, N_2O has exceeded CFC-12 and become the third largest source of greenhouse gas emissions, second only to carbon dioxide and methane[64]. Therefore, regardless of the fact that its GWP value is not high, it contributes greatly to climate warming[62].

3.2 Depletion of Ozone Layer

The stratospheric ozone layer can absorb the short wave ultraviolet rays in the sunlight to shields life on the earth from the harmful ultraviolet(UV) radiation. Inhalant anesthetics can be carried up into the stratosphere by the upward-moving air currents and broken down by the UV to form free radicals that can consume and destroy the ozone layer through chemical reaction[8]. Moreover, the recycling of the free radicals allows one that to destroy 10^3-10^5 ozone molecules before it is converted to a less-reactive molecule[69]. Chlorine atoms and bromine atoms decomposed by chlorine-containing anesthetics such as isoflurane, enflurane and halothane (also containing bromine atoms), as well as nitrogen oxides decomposed by N_2O are all ozone depleting substances[69], while sevoflurane and desflurane only contain fluorine atoms that may not participate in the destruction of ozone[65][66][70].

Researchers frequently use ozone depletion potential (ODP) to reflect the ability of gas to destroy ozone, and compare the effectiveness of gas in destroying ozone with that of CFC-11 of the same quality[66][69][71]. Similarly, we can estimate the impact of actual emissions on ozone by computing ODP-weighted emissions (i.e. the ODP multiplied by gas emissions)[69]. Sulbaek Andersen et al.[66] calculated the ODP of halothane, isoflurane and enflurane as 0.4, 0.01 and 0.01, and Ravishankara et al.[71] calculated the ODP of N_2O as 0.017. The contribution of bromine to ozone depletion is 35-80 times that of chlorine[72], so halothane is the most destructive to ozone.

However, the use of halothane has been reduced and is now widely used only in some developing countries[10][66]. The contribution of halothane to the total stratospheric ozone depletion is approximately 1%, and that of enflurane and isoflurane is 0.02%[62][72]. Although the ODP value of N_2O is not the highest, the ODP-weighted emission of N_2O is the largest as the consumption volumes of N_2O far exceed those of the other anesthetic gases[8][10][62][69], so it is considered the most important ozone depleting substance. The influence of these inhaled anesthetics on ozone depletion is of increasing importance because of decreasing CFCs globally.

3.3 Atmospheric Lifetime of Inhaled Anesthetics

Another important determinant in assessing the contribution of gases to ozone depletion and the greenhouse effect is the atmospheric lifetime of gases. The atmospheric lifetime of gas refers to the mean residence time before the gas is removed by chemical reaction with radicals, by photolysis, and by wet or dry deposition[72].

Langbein et al.[72] estimated that the tropospheric lifetime of volatile anesthetics is 4.0 to 21.4 years and the stratospheric lifetime is more than 100 years from observations of hydroxyl radicals reaction kinetics and UV absorption spectra. According to the data of the World Meteorological Organization, the atmospheric lifetime of desflurane, sevoflurane, isoflurane, halothane, enflurane and N_2O are 14.1, 1.9, 3.5, 1, 4.42 and 123 years[73]. Tropospheric lifetime determines the amount of gas entering the stratosphere, thus determining the extent of its destruction of ozone.

It was derived that up to 20% of the anaesthetics may enter the stratosphere and hence contribute to halogen loading[72]. With regard to the greenhouse effect, tropospheric lifetime can adjust the average concentration level of anesthetic gases that affect the infrared radiation balance of the earth[72]. As time goes by, the anesthetic gas gradually decays, resulting in a gradual decrease in the warming potential[66][67].

Therefore, the long-lived greenhouse gases in the atmosphere have a long-term impact on the climate. Desflurane not only has high GWP value, but also has the longest atmospheric lifetime among VAs, leading to a great and prolonged impact on the environment[67]. As well, N_2O has an almost constant impact on climate because of its long lifetime. This becomes even more pronounced when we consider carbon dioxide equivalent, since desflurane and N_2O are used in much higher concentrations than other anesthetics[67]. Timur et al.[67] called VAs with short lifetime as flow pollutants, considering that if the diurnal emission remains constant, the pollution created will remain constant at the maximum value. While N_2O is called stock pollutants, and the pollution will accumulate with ongoing emission. Because of the continuous use of VAs, they suggested using GWP_1 to help anesthesiologists understand its real impact on the climate.

In addition, other aspects of the whole life cycle of inhaled anesthetics can also produce greenhouse effects, such as carbon dioxide produced by the extraction of natural resources, drug production, transportation, usage and disposal[12], but the proportion is small.

IV. SOLUTIONS

The healthcare industry has become one of the main causes of global warming, accounting for 5% of global greenhouse gas emissions[74]. The waste generated in the operating room accounts for one third of the total waste of the hospital, and the anesthetic gas inhaled alone constitute 5% of hospital greenhouse gas emissions[74][75][76]. If this situation continues, public health will be at risk and will directly lead to the burden of medical care. Hospitals have the responsibility to take immediate action to avoid the significant effect of climate change and integrate sustainability into medical practice. The three basic principles of waste minimization are Reduce, Reuse and Recycle, which will also be the basis of the scheme to reduce operating room waste. Yoan kagoma et al.[77] believed that two more Rs should be added: Rethink and Research. Timur et al.[78] also proposed modified 3R approach adapted to inhalational anesthetics: Reduce, Refine, and Replace. In this article, we also formulate a strategy for the sustainable development of inhaled anesthetics, improving 3R to 4R: Reduce, Remove, Recycle and Replace.

4.1 Reduce

As we all know, desflurane and N_2O have a significant and long-term impact on the environment. Therefore, their use should be reduced or avoided as far as possible, unless there is a clinical reason to prefer them[12][65][67][74]-[76]. N_2O is often used as a carrier gas for VAs because it can reduce the necessary minimum alveolar concentration of other concomitantly used anesthetic gases[10]. Compared with the use of volatile drugs alone, when adding N_2O, a smaller amount of VAs is required to achieve the same level of anesthesia, and the patient can recover more prompt from general anesthesia[10], but at the same time it will increase the emission of N_2O.

Ryan and Nielsen's research shows that[9], using N_2O as carrier gas significantly increases the impact of sevoflurane and isoflurane, but decreases the impact of desflurane on global warming within 20 years. However, after 100 years, this improvement will be offset by the long lifetime of N_2O, eventually contributing environmental harm. Therefore, try to refrain from delivering N_2O as carrier gas.

Reasonable and effective management of fresh gas flow (FGF) can reduce the waste and pollution of anesthetic gas while achieving the same effect on the patient[79]. There is no doubt that the closed-circuit anesthesia system can maximize the use of fresh anesthetic gas, reduce the use of anesthetic gas by 80% to 90%[8], and hence eliminate virtually all of the environmental contamination. However, the conditions required for closed-circuit anesthesia such as injection of liquid anesthetic, tightly monitoring of gas concentration and evaluation of anesthetic machine volume are more challenging, making it impractical in modern practice[79]. For that reason, so-called "low flow anesthesia" (defined as less than 1L/min) is commonly used now, which can not only reduce the use of anesthetics[78] -[80], but also maintain the temperature and humidity in the breathing circuit, and increase mucociliary clearance[80]. However, because the increase in the requirement for CO_2 absorbent and its concomitant footprint at very low flow rates, there is a need to balance the environmental impact of anesthetic use and energy costs associated with absorbent use[9][79]. Nevertheless, it is unlikely to offset the benefits of reducing volatile drug and N_2O emissions[12][76]. For now, based on the research results of Ryan and Nielsen[9], reducing FGF to 2L/min with sevoflurane (the lowest value to prevent the production of nephrotoxic compound A) and reducing FGF to 0.5 to 1L/min with desflurane and isoflurane would be the best approximations of ideal FGF rates. However, subsequent studies in humans have failed to demonstrate a significant impact on renal function, in addition, the emergence of new carbon dioxide absorbers such as calcium hydroxide and lithium hydroxide may no longer produce any quantifiable levels of compound A, which may allow better acceptance of lower FGF of sevoflurane in the near future[9][74][79]. Therefore, it is recommended to use minimal FGF rates in combination with modern CO_2 absorbers[78].

In fact, the flow is not constant throughout the anesthesia process, and the management of FGF is different at each stage. Feldman[79] provided management strategies during anesthesia induction, intubation, maintenance and emergence, which can truly and effectively obtain the effect of "minimum flow anesthesia". It is worth noting that the inhaled oxygen concentration and exhaled anesthetic gas concentration must be monitored at all times to ensure the safe implementation of these strategies, and the workload may make it difficult for anesthesiologists to adhere to the idea of low flow anesthesia. The development of the automated control of end-tidal anaesthetic gases can reduce the need for anesthesiologists to continually monitor and change gas concentration, significantly decrease volatile agent consumption, and hence bring economic and environmental benefits, which will increase anesthesiologists' compliance and participation in low flow anesthesia[81].

Besides, anesthetic techniques and the anesthesia machine delivery system will also lead to the leakage and waste of anesthetic gas.

Anesthesiologists can employ the following anesthetic practices to minimize environmental contamination: use appropriate face mask, endotracheal tube and laryngeal mask airway cuff, and reduce the gas flow during the introduction of mask; carefully fill the vaporizer of anesthesia machine to reduce overflow; turn off the flow control valve and vaporizer in time after anesthesia; check of all connections along the anesthesia circuit and at the machine[10].

4.2 Remove

At present, various technologies have been developed to remove organic pollutants from waste gas stream, namely adsorption, absorption, cryogenic condensation, membrane technology, and the first three have been proved to be applicable for removing VAs[82]. Among them, adsorption is by far the most extensively investigated method. VAs can be removed by using adsorbents with strong affinity for anesthetic molecules. Among promising adsorbents, activated carbon, zeolite and metal organic framework have the potential to adsorb and capture VAs[65][82]-[85]. Many chemists have continuously changed the composition, morphology, structure and pore size of these adsorbents to improve their adsorption capacity[82][84]. Compared with VAs, N_2O is usually difficult to be adsorbed[86], and researchers are also looking for suitable adsorbents to reduce N_2O emissions[87]-[89]. The captured anesthetic is not really removed, and the adsorbed anesthetic molecules can be removed from the adsorbent's inner surface via high temperature, low pressure or vacuum and purge gas flow, which is called desorption[82]. Desorption can not only regenerate and recycle the adsorbent to save the cost, but also conduce to the recovery or further processing of anesthetic gas[82][85]. Water absorption of anesthetic gas is also a method, but it is laborious and risks gas evaporation into the atmosphere[90], which may be used when conditions are limited. Other experts have described the technology of cryogenic condensation[86] - using a cold fractionator to selectively condense nitrous oxide and halogenated anesthetics from waste anesthetic gas, and a compressor, a low-flow scavenging system and an intelligent anesthetic waste gas collection unit are used to improve its efficiency and feasibility.

The real removal of anesthetic gas is to destroy anesthetic gas through pyrolysis, catalytic reaction and photochemical reaction. Numerous methods have been proposed for the abatement of N_2O, including thermal decomposition, catalytic oxidation, catalytic reduction, direct catalytic decomposition, photocatalytic technology[91]-[94].

There are also many studies on various catalysts (metals, metal oxides, zeolite molecular sieves, etc.)[92][93][95]-[97]. Among these approaches, direct catalytic decomposition is quite promising because of its superiority in the simple achievement, high decomposition efficiency, low production of nitrogen oxides and environmental friendliness[93]. Japan has developed a system for treating waste anesthetic gas, Anesclean, which can collect volatile anesthetic from waste anesthetic gas and immediately decompose nitrous oxide (N_2O) into N_2 and O_2[98]. According to the technology of Japan, the Swedish company developed and installed a device for simply destroying N_2O in the hospital, called Anesclean SW[94], whose principle is to directly decompose N_2O with heated catalyst. After continuous updating, the new generation can destroy about 98% of the collected gas, and has the advantages of small volume, flexibility, lower energy demand and lower price. Kuroki et al.[91] investigated a system for removing high concentration N_2O by using nonthermal plasma along with an adsorbent, which had the advantages of significant reduction in overall size and total cost and without nitrogen oxides formation when compared to a conventional catalytic reduction or thermal plasma system. At present, there is a new photochemical anesthesia exhaust gas destruction system[99], which can destroy halogenated anesthetics and nitrous oxide through direct photolysis by ultraviolet light or free radicals reaction to prevent them from leaking into the atmosphere. The system is efficient and economical for removing halogenated anesthetics, but is expensive and inefficient for removing N_2O, so modifications of this current system are necessary to improve its removal efficiency of N_2O. Various methods have their own advantages and disadvantages, so appropriate methods can be selected in combination with the conditions of the hospital.

4.3 Recycle

As mentioned above, VAs can be desorbed under certain conditions after being captured by adsorbents. The trapped halogenated agents could then be reprocessed by steam extraction or fractional distillation for reuse[8][65][85]. The low cost of producing N_2O and the high cost of recycling it may make destruction more suitable for it. Blue-Zone Technology of Canada has developed a filter canister system - Deltasorb. The proprietary silica zeolite in the canister can selectively capture VAs before they are discharged into the air. Then VAs collected in the canisters are recovered through sophisticated desorption and distillation devices, and finally processed into low-cost anesthetics for resale[10][74][82], so as to prolong the life cycle of anesthetics[62]. In a five-year trial, the Deltasorb system was installed in 21 operating rooms in Toronto and prevented 634 tons of carbon dioxide equivalent emissions from entering the atmosphere[82]. But there are still some shortcomings need to be overcome. It can only trap VAs, but allows N_2O to pass through unabated[82], which may be solved by working in conjunction with the system that destroys N_2O.

When the relative humidity is high, the adsorption of water vapor by silica zeolite will displace the adsorbed anesthetic[82]. Apart from that, the system is quite labor-intensive because saturated canister must be collected and new canister must be installed regularly[82][100].

Moreover, the U.S. FDA has yet to grant approval to use salvaged anaesthetic agents for clinical purposes[74], thus alternative solutions would be to use the recovered VAs to produce other fluorinated products or decompose them[82]. This technology has just started and more work needs to be done to determine its sustainability. And it is required to promote it to more operating rooms, after all, reducing the emission of anesthetics is necessary.

One other company – Anesthetic Gas Reclamation Inc. in the United States has created a cryogenic condensation Anesthetic Gas Reclamation (AGR) system[100] to cool the VAs in the waste gas stream to a saturated liquid. It has demonstrated workable for separating and reclaiming exhaled VAs, but hasn't undergone trials in hospitals.

When it is paired with the Dynamic Gas Scavenging System(DGSS), 99% of the anesthetic gas can be collected and reused without chemical alterations in the process[10][100]. DGSS is a scavenging system designed by Vanderbilt University Medical Center[101]. It is activated only when the patient exhales and used anesthetic appears[12],which can reduce vacuum pump duty cycle and decrease energy cost[101].Moreover, it can collect and generate a concentrated stream of waste anesthetic, reduce the dilution of anesthetic gas by air, and facilitate the subsequent condensation process[101].

Although the anesthetic recovery technology is still in a fledging period and the "carbon cost" in the process has not been systematically evaluated, it is very promising. If the recovered anesthetic can be applied to clinical practice in the future, it will be a win-win situation for environmental and economic sustainability.

4.4 Replace

Technologies other than inhalation anesthetics, such as intravenous anesthesia and regional anesthesia, would be least harmful to the climate[12][65][74][76]. Evaluated in the whole life cycle, the greenhouse effect of total intravenous anesthesia (TIVA) with propofol is 4 orders of magnitude lower than that of inhaled anesthetics[12]. Nevertheless, a potential disadvantage of TIVA is that a large amount of unused propofol is wasted[12][76], and these unmetabolized propofol may have harmful influences on aquatic and terrestrial ecosystems, mainly owing to its high persistence, bioaccumulation and toxicity[65][102][103]. Compared with intravenous anesthesia, regional anesthesia seems an obvious choice to become the "green" anesthesia[102]. Most regional anesthetics use neuraxial or peripheral nerve block anesthesia along with intravenous sedation, thus reducing the use and waste of inhaled anesthetics gases[104].

Other studies have shown that regional anesthesia can bring nursing benefits, including reducing patients' adverse anesthetic reactions, earlier and improved rehabilitation, faster time to discharge, etc.[104]. However, not all surgical operations are suitable for regional anesthesia. Anesthesiologists should choose anesthesia techniques that are beneficial to both patients and environment according to the patient's condition. In some cases, it may be feasible to combine the two anesthesia techniques to reduce the consumption of harmful anesthetics. Xenon is a naturally occurring atmospheric trace gas manufactured from liquefied air, which is a byproduct of pure oxygen production[62][105]. It can exert an anesthetic effect by inhibiting cell membrane calcium pump and blocking N-methyl-D-aspartate(NMDA) receptor and acetylcholine receptor[62][106]. Xenon has many properties of an ideal anesthetic gas, including: non-inflammable and non-explosive; rapid induction of anesthesia; quick recovery from anesthesia; stronger anesthetic and analgesic effects compared to N_2O; low toxicity, devoid of teratogenicity, mutagenicity or carcinogenicity; neuroprotective effect; little effect on cardiovascular and other systems; the potential to protect organ grafts from ischemia-reperfusion injury; hemodynamic stability[8][62][105][106].

Moreover, its impact on the global climate has not been found and hence can be used as a substitute for halogenated compounds and N_2O. However, the production of xenon requires high cost and high energy[105]. Only by using closed-circuit system or adsorption separation technology to reclaim and reuse gas can it become an economically feasible method[8][62][106][107]. However, these require high-tech anesthesia workstation and anesthesia delivery system, which can not be widely used at present.

Therefore, when it is clinically feasible, utilizing other anesthesia methods instead of inhalation anesthesia can reduce environmental contamination. In spite of this, there are still some uncertainties that need to be further studied and considered, such as life cycle assessment of regional anesthesia, other environmental impacts of intravenous anesthetics, xenon recovery technology and so on.

V. CONCLUSION

Medical care can cope with the health burden brought by climate change, but it can also cause climate change and threaten human health. If global health care is a country, it will be the fifth largest carbon emitter on earth[65]. Substantive action is urgently needed to avoid the significant impact of climate change. Anesthesiologists, as professionals, have the obligation to take the lead in applying appropriate strategies and new technologies to clinical practice, reduce the harmful impact on the environment, improve the sustainability of anesthesia, and obtain the synergistic benefits of health, environment and economy. At the same time, researchers should continue to evaluate and research the uncertainty in this field and constantly update the decision-making scheme. Of course, all this needs the support of government policies and funds. As a direct consequence of the COVID-19 pandemic, greenhouse gas emissions are expected to be reduced by 8% in 2020. This may be an opportunity for the government to implement policies to mitigate climate change while restarting and restructuring the economy and rebuilding the public health system, so as to reduce the harm of the two crises to the world[6]. It is time for the whole world to unite to address the critical challenges of global health, and to promote green development of the medical industry.

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