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### SPECIAL ARTICLE

# Occupational hazards, DNA damage, and oxidative stress on exposure to waste anesthetic gases

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#### **KEYWORDS**

Inhaled anesthetics; Occupational exposure; Environment pollution; Genotoxicity testing; Genomic instability; Oxidative stress

#### Abstract

*Background and objectives*: The waste anesthetic gases (WAGs) present in the ambient air of operating rooms (OR), are associated with various occupational hazards. This paper intends to discuss occupational exposure to WAGs and its impact on exposed professionals, with emphasis on genetic damage and oxidative stress.

*Content:* Despite the emergence of safer inhaled anesthetics, occupational exposure to WAGs remains a current concern. Factors related to anesthetic techniques and anesthesia workstations, in addition to the absence of a scavenging system in the OR, contribute to anesthetic pollution. In order to minimize the health risks of exposed professionals, several countries have recommended legislation with maximum exposure limits. However, developing countries still require measurement of WAGs and regulation for occupational exposure to WAGs. WAGs are capable of inducing damage to the genetic material, such as DNA damage assessed using the comet assay and increased frequency of micronucleus in professionals with long-term exposure. Oxidative stress is also associated with WAGs exposure, as it induces lipid peroxidation, oxidative damage in DNA, and impairment of the antioxidant defense system in exposed professionals.

*Conclusions:* The occupational hazards related to WAGs including genotoxicity, mutagenicity and oxidative stress, stand as a public health issue and must be acknowledged by exposed personnel and responsible authorities, especially in developing countries. Thus, it is urgent to stablish maximum safe limits of concentration of WAGs in ORs and educational practices and protocols for exposed professionals.

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### PALAVRAS-CHAVE

Anestésicos inalatórios; Exposição ocupacional; Poluição ambiental; Testes de genotoxicidade; Instabilidade genômica; Estresse oxidativo

### Riscos ocupacionais, danos no material genético e estresse oxidativo frente à exposição aos resíduos de gases anestésicos

#### Resumo

*Justificativa e objetivos:* Os Resíduos de Gases Anestésicos (RGA) presentes no ar ambiente das Salas de Operação (SO) são associados a riscos ocupacionais diversos. O presente artigo propõese a discorrer sobre exposição ocupacional aos RGA e seu impacto em profissionais expostos, com ênfase em danos genéticos e estresse oxidativo.

*Conteúdo*: Apesar do surgimento de anestésicos inalatórios mais seguros, a exposição ocupacional aos RGA ainda é preocupação atual. Fatores relacionados às técnicas anestésicas e estação de anestesia, além da ausência de sistema de exaustão de gases em SO, contribuem para poluição anestésica. Para minimizar os riscos à saúde em profissionais expostos, recomendamse limites máximos de exposição. Entretanto, em países em desenvolvimento, ainda carece a mensuração de RGA e de regulamentação frente à exposição ocupacional aos RGA. Os RGA são capazes de induzir danos no material genético, como danos no DNA avaliados pelo teste do cometa e aumento na frequência de micronúcleos em profissionais com exposição prolongada. O estresse oxidativo também é associado à exposição aos RGA por induzir lipoperoxidação, danos oxidativos no DNA e comprometimento do sistema antioxidante em profissionais expostos.

*Conclusões:* Por tratar-se de questão de saúde pública, é imprescindível reconhecer os riscos ocupacionais relacionados aos RGA, inclusive genotoxicidade, mutagenicidade e estresse oxidativo. Urge a necessidade de mensuração dos RGA para conhecimento desses valores nas SO, especialmente em países em desenvolvimento, de normatização das concentrações máximas seguras de RGA nas SO, além de se adotarem práticas de educação com conscientização dos profissionais expostos.

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### Introduction

Waste anesthetic gases (WAGs) are small amounts of inhaled anesthetics present mainly in the operating room (OR) and post-anesthesia care unit (PACU) ambient air. Halogenated anesthetics, including halothane, isoflurane, sevoflurane, desflurane, and nitrous oxide ( $N_2O$ ) are the main constituents of WAGs, as they are the most frequently used anesthetics.<sup>1</sup>

According to estimates by the American Occupational Safety and Health Administration (OSHA), more than 200,000 health professionals are at risk of occupational diseases due to chronic exposure to WAGs.<sup>2</sup> Because it is a public health issue, knowledge of these risks and adoption of formal practices and regulations to reduce ambient air pollution in ORs to safe minimum levels of exposure are critical.<sup>3</sup> The aim of this article is to show the impacts of occupational exposure to WAGs on exposed professionals' health, with emphasis on topics more recently explored in the literature, as well as the definition of genotoxicity, mutagenicity, and oxidative stress applied to anesthesiology.

### Background

Inhaled anesthetics are drugs widely and routinely used in general anesthesia. The unprecedented public demonstration of diethyl ether as an inhalation anesthetic by William Morton in 1846 at the Massachusetts General Hospital in Boston in the United States enabled to perform a pain-free surgical procedure and gave rise to one of the most significant scientific discoveries in medicine.<sup>4</sup>

Since then, the practice of anesthesiology has witnessed the profound evolution in this field, as other anesthetics emerged, such as  $N_2O$ , chloroform, and trichloroethylene. However, the high toxicity and risk of explosion within the surgical environment related to these agents discontinued its use and encouraged the search for safer anesthetics.<sup>5</sup> In the 1950s, the first compound derived from fluoride ion (fluoroxene) was tested clinically, but was soon ruled out as extremely toxic. Halothane is a halogenated hydrocarbon synthesized in 1957, whose reduced flammability compared to agents available at that time consolidated it as the main inhaled anesthetic of the time, which lasts until today.<sup>6</sup> In 1960, it was followed by methoxyflurane, which had limited use due to its high nephrotoxicity.<sup>7</sup> At the same time, reports of rare cases of halothane-related fatal hepatitis led to the search for newer and safer volatile anesthetics synthesized in the 1960s, such as enflurane in 1963 and its structural isomer isoflurane in 1965, in addition to sevoflurane and desflurane (popularized in the mid-1990s).<sup>7,8</sup> Xenon, recognized as an inert, odorless gas, has rapid absorption and elimination through the lungs, no hepatic and renal metabolism, and minimal cardiovascular effects. However, its use is still restricted due to its high cost and limited availability.<sup>5</sup> Thus, the optimal inhaled anesthetic is still missing, being an important research topic.4,7

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