A Clinical Perspective on Ozone in the Healthcare Setting

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Introduction

Ozone is a molecule that is comprised of three oxygen molecules, with the chemical symbol O3. Present in trace amounts in Earth's surface atmosphere, it is faintly blue in color and has a pungent odor. The molecule is formed when ultraviolet (UV) light or electricity interact with O2. In addition to its function of blocking much UV radiation from striking the earth (the so-called 'Ozone Layer'), ozone is also a potent oxidizer. This property makes ozone a useful chemical in industrial applications, and also makes ozone potentially damaging to humans and animals. The World Health Organization (WHO) guideline is to keep 8-hour exposure below 100 ug/m3. The US Environmental Protection Agency (EPA) recommends 8-hour levels below 0.070 ppm (equivalent to 70 ug/m3). For clarity, in the remainder of this report, all units will be converted to ppm (parts per million).

Antimicrobial effects

The mechanism of ozone as an antimicrobial is that it oxidizes organic compounds to carbon dioxide and water. Upon exposure to ozone, airborne and surface bacteria are killed because their organic material is destroyed. These effects have been known for over 100 years.

Ozone generators for rooms are widely available and marketed as air purifiers, deodorizers, and sterilizers. A search on amazon.com reveals over 300 hits. The EPA reviewed the utility of these devices and concluded, **"if used at concentrations that do not exceed public health standards, ozone applied to indoor air does not effectively remove viruses, bacteria, mold, or other biological pollutants."**

The killing of bacteria on surfaces with gaseous ozone has also been studied. When looking at heavy loads of manure-based pathogens (e.g. e. coli), gaseous ozone at concentrations as low as 4 ppm (note: this is 50 times the EPA's recommended level) can reduce bacterial loads to safe levels after 4 minutes of exposure on surfaces like plastic or metal. However, surfaces such as rubber, nylon, and wood do not experience sufficient reduction to be considered safe. In fact, for rubber and wood, the point estimate of the probability of reducing bacteria to safe levels approaches zero. Exposure times of 2- and 8- minutes show similar results. This means that it is extraordinarily unlikely that exposure to high levels of ozone for several minutes would result in sterilization of these surfaces. Concentrations as high as 1000 ppm and exposure times as high as 24 hours were studied. A separate study showed the effectiveness of gaseous ozone + hydrogen peroxide at concentrations of 80 ppm for 30-90 minutes. This proved to be effective at disinfecting cotton swabs. Unsurprisingly, higher concentrations, and longer exposure times are more effective. Such exposures are well above safe levels and would be toxic and possibly lethal to humans.

> OZONE IMPACT ON LUNG HEALTH
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> **THE [EPA CONCLUSION] IS BASED ON A CONVINCING BODY OF HIGH-QUALITY HUMAN AND ANIMAL EVIDENCE THAT SHORT-TERM OZONE EXPOSURE TRIGGERS 'LUNG FUNCTION DECREMENTS, DECREASED AIRWAY RESPONSIVENESS, RESPIRATORY SYMPTOMS, AND RESPIRATORY TRACT INFLAMMATION."**

Effects of Ozone on the Human Respiratory Tract

The EPA released a 1500-page report in April 2020 (Integrated Science Assessment (ISA) for Ozone and Related Photochemical Oxidants) that covers the many health risks of ozone. When inhaled, ozone reacts with various components of the cells of the respiratory tract, creating oxidation byproducts. Short-term exposure to toxic levels was determined to be "causal" for respiratory problems in humans. This conclusion is based on a convincing body of high-quality human and animal evidence that short-term ozone exposure triggers, "lung function decrements, decreased airway responsiveness, respiratory symptoms, and respiratory tract inflammation" which leads to, "asthma exacerbation, chronic obstructive pulmonary disease (COPD) exacerbation, respiratory infection, and hospital admissions and emergency department (ED) visits for combined respiratory diseases." Negative lung effects can be observed in healthy adults when exposed to concentrations as low as .06 ppm for 6.6 hours. Other studies document effects at even lower concentrations. People with pre-existing lung conditions, as well as children, seem to be at increased risk for these deleterious effects.

Conclusion: **There is a substantial amount of evidence that ozone reduces lung function in all populations. The effects are greater in children, the elderly, and in people with underlying lung disease.**

Ozone in Confined Spaces

The aforementioned association of the presence of ozone and decreases in lung function is described in multiple studies across multiple populations for indoor-specific exposure as well. The median concentration of indoor ozone in schools and offices has been found to be 0.008-0.009 ppm with some exceeding 0.01 ppm or more. Much indoor ozone comes from outdoor sources. In the summer months, when ambient outdoor ozone is higher, indoor ozone will increase.

Indoor ozone can come from multiple sources including photocopiers, laser printers, electrostatic air filters, and antimicrobial ozone generators. Medical devices can also generate ozone, either inadvertently or by design. In the words of Hubbard et. al., "Explicit ozone generators should be a concern with respect to elevated inhalation exposure of building occupants to ozone."[Hubbard, H.F., *Indoor Air* , 15(6), 432–444.]

Elevated ozone levels present risk indoors

Medical devices can also generate ozone, either inadvertently or by design. "Explicit ozone generators should be a concern with respect to elevated inhalation exposure of building occupants to ozone."
- Hubbard, HF. *Indoor Air*, 15(6), 432-444

Conclusion: **Generating ozone indoors increases ozone levels and should be avoided.**

Ozone in the Healthcare Setting

High concentrations of ozone have been used to sterilize reusable surgical instruments as well as in the processing of hospital laundry. Notably, neither of these activities take place where there are patients or other hospital personnel. In fact, the levels of ozone used in these applications are extremely dangerous to humans.

One of the most common sources of ozone in patient care environments is from UV light room sterilizing devices. In this instance, ozone is an unintentional byproduct. There are case reports of healthcare workers with asthma having asthma attacks when working near one of these devices. There are ozone-generating devices marketed to consumers to clean home CPAP machines. The FDA has received reports of users who have experienced cough, difficulty breathing, and, asthma attacks and other breathing problems when using one of these machines. Multiple well-designed studies demonstrate the need to minimize various patient population's exposure to ozone.

Because of cases like these and the overwhelming evidence of a lack of efficacy in patient care, the US Food and Drug Administration (FDA) has addressed the issue and established a maximum level of ozone generation of 0.05 ppm for medical devices and that these devices may not cause an accumulation of ozone in a room to be greater than 0.05 ppm. In the same regulation, the FDA declares that devices that "generate ozone and release it into the atmosphere in hospitals or other establishments occupied by the ill or infirm" are not compliant with its branding regulations.

Conclusion: **In concentrations that are toxic to humans, ozone can be used for the sterilization of the environment with varying degrees of efficacy. Because of its toxicity, the generation of ozone (whether intentional or unintentional) in areas where humans are present should be avoided. This is especially true in healthcare settings where vulnerable populations reside.**

Bibliography

Weschler C. J. Ozone's impact on public health: contributions from indoor exposures to ozone and products of ozone-initiated chemistry. Environmental health perspectives, 2006;114(10), 1489–1496. https://doi.org/10.1289/ehp.9256

Young CJ, Zhou S, Siegel JA, Kahan TF. Illuminating the dark side of indoor oxidants. Environ Sci Process Impacts. 2019;21(8):1229-1239. doi:10.1039/c9em00111e

Weschler CJ. Ozone in indoor environments: concentration and chemistry. Indoor Air. 2000;10(4):269-288. doi:10.1034/j.1600-0668.2000.010004269.x

Hwang SH, Park WM. Indoor air concentrations of carbon dioxide (CO2), nitrogen dioxide (NO2), and ozone (O3) in multiple healthcare facilities. Environ Geochem Health. 2020;42(5):1487-1496. doi:10.1007/s10653-019-00441-0

Salonen, H., Salthammer, T., & Morawska, L. (2018). Human exposure to ozone in school and office indoor environments. Environment International, 119, 503-514. doi:10.1016/j.envint.2018.07.012

U.S. EPA. Integrated Science Assessment (ISA) for Ozone and Related Photochemical Oxidants (Final Report). U.S. Environmental Protection Agency, Washington, DC, EP-A/600/R-20/012, 2020. ** CITED **

Boeniger, M. F. (1995). Use of ozone-generating devices to improve indoor air quality. American Industrial Hygiene Association Journal, 56(6), 590. Retrieved from http://echo.louisville.edu/login?url=https://search-proquest-com.echo.louisville.edu/docview/236303453?accountid=14665

Megahed, A., Aldridge, B., & Lowe, J. (2018). The microbial killing capacity of aqueous and gaseous ozone on different surfaces contaminated with dairy cattle manure. PloS one, 13(5), e0196555. https://doi.org/10.1371/journal.pone.0196555

Code of Federal Regulations Title 21, § 801.415 Maximum acceptable level of ozone. (2019).

Sheffield, P. E., Zhou, J., Shmool, J. L., & Clougherty, J. E. (2015). Ambient ozone exposure and children's acute asthma in New York City: a case-crossover analysis. Environmental health : a global access science source, 14, 25. https://doi.org/10.1186/s12940-015-0010-2

Tian, Y., Xiang, X., Juan, J., Song, J., Cao, Y., Huang, C., Li, M., & Hu, Y. (2018). Short-term Effect of Ambient Ozone on Daily Emergency Room Visits in Beijing, China. Scientific reports, 8(1), 2775. https://doi.org/10.1038/s41598-018-21154-x

Kurai, J., Noma, H., Sano, H., Iwat, K., Tohda, Y., & Watanabe, M. (2018). Association of short-term ozone exposure with pulmonary function and respiratory symptoms in schoolchildren:A panel study in a western Japanese city. The journal of medical investigation : JMI, 65(3.4), 236–241. https://doi.org/10.2152/jmi.65.236

Chang, L. T., Hong, G. B., Weng, S. P., Chuang, H. C., Chang, T. Y., Liu, C. W., Chuang, W. Y., & Chuang, K. J. (2019). Indoor ozone levels, houseplants and peak expiratory flow rates among healthy adults in Taipei, Taiwan. Environment international, 122, 231–236. https://doi.org/10.1016/j.envint.2018.11.010

He, L., Li, Z., Teng, Y., Cui, X., Barkjohn, K. K., Norris, C., Fang, L., Lin, L., Wang, Q., Zhou, X., Hong, J., Li, F., Zhang, Y., Schauer, J. J., Black, M., Bergin, M. H., & Zhang, J. J. (2020). Associations of personal exposure to air pollutants with airway mechanics in children with asthma. Environment international, 138, 105647. https://doi.org/10.1016/j.envint.2020.105647

Peden, D. B., Boehlecke, B., Horstman, D., & Devlin, R. (1997). Prolonged acute exposure to 0.16 ppm ozone induces eosinophilic airway inflammation in asthmatic subjects with allergies. The Journal of allergy and clinical immunology, 100(6 Pt 1), 802–808. https://doi.org/10.1016

Christian, D. L., Chen, L. L., Scannell, C. H., Ferrando, R. E., Welch, B. S., & Balmes, J. R. (1998). Ozone-induced inflammation is attenuated with multiday exposure. American journal of respiratory and critical care medicine, 158(2), 532–537. https://doi.org/10.1164/ajrccm.158.2.9709023
Huang, J., Song, Y., Chu, M., Dong, W., Miller, M. R., Loh, M., Xu, J., Yang, D., Chi, R., Yang, X., Wu, S., Guo, X., & Deng, F. (2019). Cardiorespiratory responses to low-level ozone exposure: The inDoor Ozone Study in childrEn (DOSE). Environment international, 131, 105021. https://doi.org/10.1016/j.envint.2019.105021

Chen, C. H., Chan, C. C., Chen, B. Y., Cheng, T. J., & Leon Guo, Y. (2015). Effects of particulate air pollution and ozone on lung function in non-asthmatic children. Environmental research, 137, 40–48. https://doi.org/10.1016/j.envres.2014.11.021

Yoda, Y., Tamura, K., Adachi, S., Otani, N., Nakayama, S. F., & Shima, M. (2020). Effects of the Use of Air Purifier on Indoor Environment and Respiratory System among Healthy Adults. International journal of environmental research and public health, 17(10), 3687. https://doi.org/10.3390/ijerph17103687

Bernstein, J. A., Alexis, N., Bacchus, H., Bernstein, I. L., Fritz, P., Horner, E., Li, N., Mason, S., Nel, A., Oullette, J., Reijula, K., Reponen, T., Seltzer, J., Smith, A., & Tarlo, S. M. (2008). The health effects of non-industrial indoor air pollution. The Journal of allergy and clinical immunology, 121(3), 585–591. https://doi.org/10.1016/j.jaci.2007.10.045

Hubbard, H. F., Coleman, B. K., Sarwar, G., & Corsi, R. L. (2005). Effects of an ozone-generating air purifier on indoor secondary particles in three residential dwellings. Indoor air, 15(6), 432–444. https://doi.org/10.1111/j.1600-0668.2005.00388.x

Foarde, K., & Eaton, C. (2007, December). Ozone Antimicrobial Efficacy. Retrieved September 05, 2020, from https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P1002X3S.TXT

Zoutman, D., Shannon, M., & Brown, K. (2011). Effectiveness of a novel ozone and hydrogen peroxide gas-vapour system for the rapid high level disinfection of surfaces and healthcare spaces. BMC Proceedings, 5(S6). doi:10.1186/1753-6561-5-s6-o38

CDC - Immediately Dangerous to Life or Health Concentrations (IDLH): Ozone - NIOSH Publications and Products. (2014, December 04). Retrieved September 06, 2020, from https://www.cdc.gov/niosh/idlh/10028156.html

Vrablik, Kevin A. MD, MPH, FACOEM; Green-McKenzie, Judith MD, MPH, FACOEM What Is a Potential Source of Ozone in the Health Care Environment?, Journal of Occupational and Environmental Medicine: February 2016 - Volume 58 - Issue 2 - p e54-e55
doi: 10.1097/JOM.0000000000000626

Center for Devices and Radiological Health. (2020, February 27). Potential Risks of Ozone, Ultraviolet Light for Cleaning CPAP Machines. Retrieved September 23, 2020, from https://www.fda.gov/medical-devices/safety-communications/potential-risks-associated-use-ozone-and-ultraviolet-uv-light-products-cleaning-cpap-machines-and

Other Sterilization Methods. (2016, September 18). Retrieved September 23, 2020, from https://www.cdc.gov/infectioncontrol/guidelines/disinfection/sterilization/other-methods.html