Air Pollution and the Upper Airways

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Introduction

Environmental pollution represents a major health problem. Because of the large populations exposed to ambient levels of toxic gases and particles, the number of adverse health effects of air pollutants, a considerable health burden is experienced by many individuals, mainly those with a prevailing health condition. Nasal passages represent a preferential target of air pollution. The turbulent flow that occurs in the nasal structures acts as an efficient filter to prevent the access of toxic species to deeper segments of the respiratory tract. However, the retention of toxic species by the nasal filter implies that nasal epithelium receives a high load of inhaled pollutants.

Several studies reported that ambient levels of air pollution induce inflammatory lesions of nasal passages in rodents as well as in humans. In studies conducted in Mexico, Calderón-Garcidueñas et al (2001), reported that children living in areas with high levels of air pollution exhibit ciliary abnormalities and increased transepithelial permeability of the nasal epithelium. In São Paulo, children living in areas with high levels of air pollution exhibit higher frequency of upper respiratory symptoms (Sih, 1999). Coherently with the above mentioned clinical findings, rodents maintained for prolonged periods in São Paulo, downtown, develop secretory cell hyperplasia and foci of squamous metaplasia of nasal epithelium in comparison with matched controls (Lemos et al, 1994; Camargo-Pires Neto et al, 2006)

The aforementioned studies clearly point out that air contaminants present in the atmosphere of the large urban conglomerates, mainly those located in developing countries, induce inflammatory changes of the upper respiratory tract. However, ambient air pollution represents a situation where a biological target - in our case, the nasal epithelium - is continuously exposed to a complex mixture of gases and particles, whose composition varies along season, hour of the day and weather conditions. In such scenario, it is very difficult to ascribe to a single agent the responsibility of determining a given adverse health effect. As a general rule, particles and ozone represent the most significant air pollutants in terms of health effects, especially in developing countries. Because of space limitations, this text will focus on these two components.

Particles

Air pollution due to particles refers to the mixture of solid or liquid aerosol suspension in the air. These particles exhibit a wide variation of size, shape, and chemical composition depending upon their source as well as weather conditions (wind, temperature and height of the inversion layer, for instance). Particles are usually classified in terms of their aerodynamic diameter in fraction as coarse, fine and ultrafines. The coarse fraction is composed by particles with an aerodynamic diameter below 2.5 micrometers, and is usually produced from crustal processes (such as erosion) or resuspension, In cities with high traffic, a significant fraction of coarse particles is produced by the friction of tires with asphalt, containing elements of tire rubber. The fine mode (PM 2.5) is produced by combustion processes (car and industrial emissions and burning of biomass). The fine mode contains elements produced primarily by the pollution source (such as metals, hydrocarbons and elemental carbon), but also contains secondary particles (mainly sulfates and nitrates) produced by gas-to-particle conversion. Ultrafine particles are defined as those having an aerodynamic diameter under 0.1 micrometers, and are the result of primary emissions of the air pollution sources. The ultrafine mode has a short life in the atmosphere, since particles within this size range rapidly aggregate among themselves.

In general terms, particles in the ultrafine and coarse modes are those with higher rate of deposition in the upper airways. Because of the variety of toxic species that may be contained in the urban aerosol, particles represent a well established agent to harm the respiratory epithelium. Recent studies in mice have demonstrated that selective filtering of particles (but not gases), significantly reduces the inflammatory alterations induced by prolonged exposure to ambient levels of air pollution (Camargo-Pires Neto et al, 2006).

Ozone

Ozone and photochemical oxidants are pollutants not directly emitted by primary sources, but encompass a group of chemical species formed through a series of complex reactions in the atmosphere driven by the energy transferred to molecules (precursors) when they absorb photons under solar radiation. The precursors that contribute most for the formation of oxidant species in the atmosphere are NO_2 and volatile organic compounds (VOCs).

Most of ambient ozone absorption occurs in the upper respiratory tract and conducting intrathoracic airways (Bush et al, 1996; Sarangapani et al, 2003). Diffusion of ozone across the airway epithelial lining fluid (ELF) is determined by its reactivity. In fact, the direct contact of ozone with airway epithelium seems to be small (Pryor, 1992). Indeed, the process by which retained along the respiratory tract may be characterized as “reactive absorption”, whose rate is determined by the equilibrium constant of the chemical reactions between ozone and the constituents of ELF (Postlethwait et al, 1994). ELF contains substrates, e.g., ascorbic acid (AH2), uric acid (UA), glutathione (GSH), proteins, and unsaturated lipids, which may undergo oxidation mediated by ozone (Ballinger et al, 2005), preventing (or minimizing) damage to the underlying epithelium. ELF is constantly renovated by the mechanical input provided by the coordinated

movement of airway ciliated cell, producing new biological substrates to react with ozone, thus acting as a chemical barrier against this pollutant.

Ozone is a potent oxidant may induce either direct or indirect oxidative stress to respiratory epithelium. Direct oxidative stress occurs when ozone contacts with cells located in areas not entirely covered by ELF, or in cells that may protrude above ELF, such as macrophages. The interaction between lipids with ozone may trigger an autocatalytic process that impairs the integrity of cell and organelle membranes. Interaction of ozone with components of ELF may generate chemical species capable to triggering inflammation and cell damage (Postlethwait et al, 1998). In a series of studies in rodents, Harkema et al (1989, 1997, 1999) demonstrated that ozone exposure near ambient levels induces secretory hyperplasia of the nasal epithelium.

DNA-reactive aldehydes from lipid peroxidation may deregulate cellular homeostasis and can drive normal cells to malignancy Bartsch and Nair, 2004), suggesting that ozone may play a role in the development of neoplasms respiratory tract (Pereira et al, 2005).

Final considerations

The foregoing considerations indicate that physicians should pay more attention to the role of outdoor air pollution in determining airway inflammation. Because of their role in conditioning and filtering inspired air, nasal passages pay a high tribute to air deterioration due to automotive and industrial emissions.

Recommended readings

1. Ballinger CA, Cueto R, Squadrito G, Coffin JF, Velsor LW, Pryor WA, Postlethwait EM. Antioxidant-mediated augmentation of ozone-induced membrane oxidation. Free Radic Biol Med Feb 15;38(4):515-26, 2005.
2. Bartsch H, Nair J. Oxidative stress and lipid peroxidation-derived DNA-lesions in inflammation driven carcinogenesis. Cancer Detect Prev 28(6):385-91, 2004.
3. Bush ML, Asplund PT, Miles KA, Ben-Jebria A, Ultman JS. Longitudinal distribution of O_3 absorption in the lung: gender differences and intersubject variability. J Appl Physiol 81(4): 1651-1657, 1996.
4. Calderón-Garcidueñas L, Salazar GV, Alcazar AR, Gambling TM, Garcia R, Osnaya N, Calderón AV, Devlin RB, Carlson JL. Ultrastructural pathology in children chronically and sequentially exposed to air pollutants. Am J Respir Cell Mol Biol 24:132-138, 2001.
5. Camargo Pires-Neto R, Julia Lichtenfels A, Regina Soares S, Macchione M, Hilário Nascimento Saldiva P, Dolhnikoff M. Effects of Sao Paulo air pollution on the upper airways of mice. Environ Res. 2006;101(3):356-61.
6. Harkema JR, Hotchkiss JA, Henderson RF. Effects of 0.12 and 0.8 ppm ozone on rat nasal and nasopharyngeal epithelial mucosubstances: quantitative histochemistry. Toxicol Pathol 17:525-535, 1989.

7. Harkema JR, Hotchkiss JA, Griffith WC. Mucous cell metaplasia in rat nasal epithelium after a 20-month exposure to ozone: a morphometric study of epithelial differentiation. Am J Respir Cell Mol Biol 16:521-530, 1997.
8. Harkema J, Hotchkiss JA, Barr EB, Benett CB, Gallup M, Lee JK, Bausbaum C. Long-lasting effects of chronic ozone exposure on rat epithelium. Am J Respir Cell Mol Biol 20: 517-529, 1999.
9. Lemos M, Lichtenfels AJF, Amaro Jr E, Macchione M, Martins MA, King M, Bohm GM, Saldiva PHN. Quantitative pathology of nasal passages in rats exposed to urban levels or air pollution. Environ Res 66:87-95, 1994
10. Madden MC, Friedman M, Nancy Hanley N, Siegler E, Quay J, Becker S, Devlin R, Koren HS. Chemical Nature and Immunotoxicological Properties of Arachidonic Acid Degradation Products Formed by Exposure to Ozone. Environ Health Perspect 101:154-164, 1993.
11. Mudway IS, Blomberg A, Frew AJ, Holgate ST, Sandstrom T, Kelly FJ. Antioxidant consumption and repletion kinetics in nasal lavage fluid following exposure of healthy human volunteers to ozone. Eur Respir J Jun;13(6):1429-38, 1999.
12. Pereira FA, de Assuncao JV, Saldiva PH, Pereira LA, Mirra AP, Braga AL. Influence of air pollution on the incidence of respiratory tract neoplasm. J Air Waste Manag Assoc. 2005 Jan;55(1):83-7.
13. Postlethwait EM, Langford SD, Bidani A. Determinants of inhaled ozone absorption in isolated rat lungs. Toxicol Appl Pharmacol Mar 125(1):77-89, 1994.
14. Pryor WA. How far does ozone penetrate into pulmonary air/tissue boundary before it reacts? Free Radic Biol Med 12:83-88, 1992.
15. Sarangapani, R, Gentry PR, Covington TR, Teeguarden JG, Clewell III HJ. Evaluation of the potential impact of age- and gender-specific lung morphology and ventilation rate on the dosimetry of vapors. Inhal Toxicol 15:987-1016, 2003.
16. Sih T. Correlation between respiratory alterations and respiratory diseases due to urban pollution. Int J Pediatr Otorhinology. 1999; 49 Suppl 1:S261-7.
17. Slade R, Crissman K, Norwood J, Hatch G. Comparison of antioxidant substances in bronchoalveolar lavage cells and fluid from humans, guinea pigs and rats. Exp Lung Res 19:469-484, 1993.
18. Vallyathan, V and Shi, X**.** The role of oxygen free radicals in environmental and occupational lung disease. Environ Health Perspect 105(Suppl1):165-177,1997.
19. van Aalst R, Air pollution by ozone in Europe in summer 2003, European Environment Agency, topic report 3/2003.