Ozone Dosimetry & Uptake

- Ozone is a highly-reactive, poorly water soluble gas at room temperature, and it is a respiratory toxicant;

- Ozone is scavenged by ventilation systems and indoor surfaces, and therefore is primarily an outdoor pollutant

- ~50% reacts in the head (nose, mouth, pharynx), ~7% in the larynx/trachea and ~43% in the lungs (little in the alveolae). More in alveolae with exercise

- The respiratory tract lining fluid contains antioxidants (primarily ascorbic acid, glutathione, and uric acid) that can react with ozone and prevent it from producing damaging secondary reaction products
Ozone Reactions in the Respiratory Tract

• In the respiratory tract ozone diffuses across and reacts with constituents of the epithelial lining fluid (ELF)

Source: http://www.epa.gov/apti/ozonehealth/population.html
Ozone Mode of Action

Mode of Action/Possible Pathways

Ozone + Respiratory Tract

Formation of secondary oxidation products

- Activation of neural reflexes
- Initiation of inflammation
- Alteration of epithelial barrier function
- Sensitization of bronchial smooth muscle
- Modification of innate and adaptive immunity
- Airways remodeling

Systemic inflammation and oxidative/nitrosative stress

Extrapulmonary Effects

- Decrements in pulmonary function
- Pulmonary inflammation/oxidative stress
- Increases in airways permeability
- Airways hyperresponsiveness
- Exacerbation/induction of asthma
- Decreased host defenses
- Epithelial metaplasia and fibrotic changes
- Altered lung development

Figure 5-8 The modes of action/possible pathways underlying the health effects resulting from inhalation exposure to $O_3$. Source: US EPA ISA 2013
Summary of MOA

- Ozone is a respiratory toxicant that reacts with antioxidants, proteins, and lipids in the respiratory tract lining fluid.
- Ozone (or, more likely, its secondary reaction products) cause several respiratory effects:
  - Nervous system activation \(\rightarrow\) spirometric effects
  - Inflammation
  - Increased epithelial permeability
  - Airway hyper-responsiveness
- The mechanisms of antioxidant depletion of ozone suggest a threshold of ozone-induced respiratory effects.
- Uncertainties in the data include relating experimental doses to ambient doses.
