Ozone effects on the respiratory system

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ABSTRACT

Ground level (tropospheric) ozone, an air pollutant and key ingredient of urban smog, has a negative impact on human health worldwide. Many studies have reported increases in emergency-room visits, hospital admissions, and mortality for patients with these conditions, associated with days of increased ozone. Short-term exposures to ozone irritate the respiratory system and may cause health problems by damaging lung tissue, reducing lung function, increased airway inflammation and making the lungs more sensitive to other irritants. It not only affects people with existing breathing problems, but also can affect healthy children and adults. Persons especially sensitive to ozone exposure are the elderly, infants, children, persons with existing respiratory issues such as diabetes mellitus, asthma or allergies, asthmatics, chronic respiratory patients, pregnant women, smokers, and persons with lung cancer, cardiovascular disease or immune system deficiency.

Furthermore, recent research studies suggest that long-term exposure to ozone may be associated with lung cancer. This possibility is expected to be further explored.

Key words: ozone, respiratory system, health effects of ozone, inflammation

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Ground level ozone as a global pollutant

Ozone is a natural constituent of the atmosphere and is present in the stratosphere (at abundances of a few ppm) and throughout the troposphere down to the earth's surface. In the stratosphere, ozone provides protection from potentially harmful UV radiation. In the troposphere, ozone is a greenhouse gas, and especially at the ground level, is a harmful pollutant; it is generated by sunlight driven chemical reactions between NO_X and volatile organic compounds (VOC) including methane (CH_4), CO and other more complex organic compounds. These ozone precursors may be of natural origin (e.g. may be produced naturally by vegetation, soil, forest fires or lightning), or may be emitted as a consequence of human activities, especially those that involve combustion of fossil fuels (power plants or internal combustion engines) and biomass.

The average lifetime of ozone in the troposphere is approximately three weeks but varies with altitude, and is determined by the processes which remove ozone from the atmosphere. This relatively long tropospheric life-time means that ozone can be transported large distances. This, in combination with the potential for ozone to be produced from precursors long after they have been emitted, makes ozone a global pollutant [1].

Ozone is also water-insoluble and is a strong oxidant. It is adsorbed in proximal and peripheral areas of the respiratory system and causes oxidative damage to the epithelium. At levels of environmental exposure, though, the most significant effects are found in the terminal bronchioles [2]. One of the main goals of the declaration by the Forum of International Respiratory Societies that 2010 be the "Year of the Lung" was to reaffirm the right of all people to live in unpolluted areas. The highest concentrations of ozone are found in areas of greatest population densities, such as in Central Europe, Eastern China, North eastern India, Southern Africa, and the Eastern USA [1,3] where it has the potential to affect the greatest numbers of people. Background levels of ozone have been increasing worldwide over the past three decades, with increases of as great as 2%/year measured over the mid-latitudes of the northern hemisphere [4].

Ambient ozone was highlighted as an important ambient air pollutant in human health in the Clean Air Act of 1970 by the U.S. Environmental Protection Agency (EPA). In 1997, the EPA reduced the ozone standard from 120 to 80 ppb based on evidence that supported detrimental health effects. Since that time, multiple epidemiologic studies have supported the health-related benefits of adherence to established regulatory standards. Environmental exposure to ambient ozone has a significant impact on human health, which can lead to a significant economic burden. It has been estimated that each year strict adherence to the established 8-hour ozone standard would result in reductions in the 800 premature deaths, 4,500 hospital admissions, 900,000 school absences, and more than 1 million restricted activity days with an estimated $5 billion annual economic burden [5] Children [6,7] and adults older than 65 years of age [8] are particularly vulnerable to low levels of inhaled ozone. However, population-based studies support a global impact on minimal increases in ambient levels of ozone. One study found a 4% increase in mortality for each 25-ppb measured increase in the level of ambient ozone [9]. Recent estimates suggest that, for each 10-ppb increase in 1-hour daily maximum of ozone, there is an increase in mortality between 0.39 and 0.87 % [10-13]. The association with increased mortality persists even at levels of ambient ozone of 15 ppb, which is well below the current EPA standard [14]. Increased levels of ozone can lead to increased severity of respiratory illness, but it remains unclear whether this is secondary to primary alterations in airway mechanics or dysregulation of immune function [15].

Ozone is the most widespread and one of the most dangerous air pollutants. The American Lung Association recommends EPA adopt the most protective level in the proposed range: 60 ppb. [16].

Why is ozone harmful?

Ozone reacts chemically ("oxidizes") with internal body tissues, such as those in the lung. Some have described the inflammation that ozone causes in the airways as similar to "sunburn" on the lungs. It acts as a powerful respiratory irritant at the levels frequently found across the nation during the summer months. Breathing ozone may lead to:

• Shortness of breath, chest pain;
• Inflammation of the lung lining, wheezing and coughing;
• Increased risk of asthma attacks, need for medical treatment and for hospitalization for people with lung diseases, such as asthma or chronic obstructive pulmonary disease (COPD) [17] and
• Premature death. [12,13,18]

Mechanisms of ozone effects – how does ozone cause damage to human health?

Ozone has been associated with a wide spectrum of human health effects most of which relate to the respiratory system [19].

Ozone can cause direct oxidative damage to cells or secondary damage by diverting energy away from primary cell functions to the production of defence mechanisms such as antioxidants.

Ozone reacts with antioxidants, such as ascorbate within the lung lining fluid (LLF), which

protect the lungs from oxidative damage. In those instances when ozone reacts with other substrates in the LLF such as protein or lipid, secondary oxidation products arise which lead to a number of cellular responses within the lung including an influx of inflammatory cells. As a consequence, the delicate blood/air barrier is damaged and the lung does not function as efficiently as it should.

Individuals react differently to ozone exposure and many factors affect the amount of ozone taken up by an organism, i.e. the dose. This makes the determination of a dose–response relationship for the assessment of human health impacts extremely complex.

The mechanisms that control the balance between beneficial and detrimental interactions in the LLF compartment are not well established but these may contribute, in part, to an individual's varying sensitivity to ozone.

Adverse effects range from small effects on lung tissue through to respiratory symptoms and exacerbations of pre-existing diseases, such as asthma or chronic obstructive pulmonary disease, sufficient to cause hospitalization or death. In the latter instance, ozone acts as one of a number of factors leading to disease exacerbation in patients with reduced lung function. The strongest evidence for effects on human health relates to acute effects but there is growing evidence that ozone may also cause chronic effects by causing permanent damage to the lung (Table 1) [1].

Table 1. Human health and pathophysiological effects of ozone.

Experimental studies	**Epidemiological studies**	
Acute effects	Reduced lung function Respiratory symptoms Airway inflammation Airway hyperactivity Increased airway permeability LLF antioxidant depletion	Reduced lung function Respiratory symptoms Increased asthma medication School absence Daily mortality – all cause, respiratory, cardiovascular Daily emergency hospital outpatient visits – respiratory Daily hospital emergency room attendance for respiratory diseases
Chronic effects	Morphological changes in the airways	Reduced lung function in children and young adults Increased incidence of asthma? Increased prevalence of asthma?

Who are most at risk?

People at greatest risk include:

- People with lung disease, especially chronic lung diseases such as asthma and Chronic Obstructive Pulmonary Disease [20,21]
- Children, because their airways are smaller, their respiratory defences are not fully developed, and their higher breathing rates increase their exposure [22]
- People who work or exercise outdoors [23]
- Senior citizens [24]
- "responders"—otherwise healthy individuals who experience health effects at lower levels of exposure than the average person.[25]

There is evidence to suggest that children, asthmatics, and the elderly are populations that may be more susceptible or vulnerable to the effects of ozone. Ozone also affects women more than men [26,30] and can even harm the unborn child [31-33].The most pronounced adverse effects of ozone, however, are seen in the ever-growing population of those with predisposing conditions, such as obesity, diabetes mellitus (DM), asthma, chronic obstructive pulmonary disease (COPD), pneumonia, and other cardio respiratory diseases [16,27,30-31,34-43]. Children who grow up in areas of high ozone pollution may never develop their full lung capacity as adults.

That can put them at greater risk of lung disease throughout their lives. However, not all individuals, either healthy or predisposed, exhibit the same level of susceptibility to ozone [43,45].

Some individuals are sensitive to ozone (even at ambient levels) [43], and remarkable variability in ozone susceptibility is observed among healthy non-smokers engaging in moderate to heavy exercise [46-48]. Various factors appear to influence an individual's susceptibility to ozone, such as: genetic susceptibility, age and pre-existing cardio respiratory disease. Ozone induced differential responses in lung function and airways hyperreactivity in people with allergic rhinitis suggests that asthmatics have greater responses than healthy people with exposure to ozone, which increase with disease severity. In addition, repeated ozone exposure over several days has been shown to increase responsiveness to bronchial allergen challenge in subjects with pre-existing allergic airway disease, with or without asthma. Asthmatics

responses than similarly-exposed healthy individuals [49].

Controlled human exposure studies have shown that lung function responses to O_3 vary with age, with responsiveness generally diminishing after about 18 to 20 years of age. As the size and surface area of the airway's changes with age, this is most likely due to higher O_3 absorption in children. [50]

Genetic and molecular characterization studies in laboratory animals identified regions of the genome responsible for both sensitivity and resistance. Recent human clinical and epidemiologic studies also have shown that genetic variations for antioxidant enzymes and inflammatory genes (GSTM1, NQO1 and TNF-a) may modulate the effect of O_3 exposure on pulmonary function and airway inflammation [51].

Ozone effects on the respiratory system

Ozone is a powerful oxidizing agent which causes many adverse effects in the respiratory system, including:

- Reduction of lung function, making it more difficult to breathe.
- Aggravation of asthma. (In reality, ozone is one of the most common trigger mechanisms of asthma.)
- Aggravation of chronic lung diseases such as chronic obstructive pulmonary disease (COPD).
- Inflammation of the respiratory airway.
- The cause of permanent lung damage in children and adults through repeated short-term exposures.
- Irritation of the respiratory system, causing coughing, throat irritation, and/or an unpleasant sensation in the chest.
- Increased hospitalizations and mortality in Europe and in the USA.
- Increased sensititivity to allergens **[**52,53].

People who are affected by ozone will experience symptoms. But that's not always the case. Some damage can occur without any noticeable signs, and lung damage can continue to occur even after symptoms go away [54].

The results of a study showed that exposure to 0.08 ppm ozone for 6.6 h induced increased airway neutrophils, monocytes, and dendritic cells and modified the expression of CD14, HLA-DR, CD80, and CD86 on monocytes 18 h following exposure. Exposure to 0.08 parts per million ozone is associated with increased airways inflammation and promotion of antigen-presenting cell phenotypes 18 hours following exposure [55].

Elevated levels of ozone (80 - 400 ppb) cause airway inflammation. After the entry of neutrophils, there is a big production or pre-inflammatory cytokines and other factors to increase the levels of tissue factors, albumin, lactate dehydrogenase of IL -6, the IL -8 and prostaglandin E_2 in broncoalveolar secretions. Bronchial mucosal biopsies confirmed the process of inflammation and showed that mast cells were the main mediators of inflammation, caused by an increased amount of vascular adhesive molecules in the surface vessels of bronchial mucosa. The bronchospasm observed in healthy subjects after exposure to ozone is transient, but the tissue damage persists [56].

Ozone causes persistent airway hyperactivity in humans and animals. One day after ozone exposure, airway hyperactivity is mediated by release of eosinophil major basic protein that inhibits neuronal M (2) muscarinic receptors, resulting in increased acetylcholine release and increased smooth muscle contraction in guinea pigs. Three days after ozone, IL-1β, not eosinophils, mediates ozone-induced airway hyperactivity, but the mechanism at this time point is largely unknown. IL-1β increases NGF and the tachykinin substance P, both of which are involved in neural plasticity [57].

Many previous studies suggest that preexposure to O_3 can reduce host antibacterial defense. Altered host vulnerability to live pathogens after O_3 exposure is supported by multiple previous rodent studies that demonstrate impaired clearance of live microbial organisms, including *Streptococcus zooepidemicus* [58**],** *Streptococcus pyogenes*, [59**]** *Staphylococcus aureus***,** [60] *Klebsiella pneumonia*, **[**61**]** *Mycobacterium tuberculosis*, [62**]** and *Listeria monocytogenes* [63]. The mechanisms that alter host vulnerability to each of these bacterial pathogens remain poorly understood. O_3 susceptibility seems, in part, dependent on genetic background in humans [64,65] and mice [66-69]. Current literature supports a complex interaction between O_3 and host response [70,71].

Animal toxicological studies provide extensive evidence that acute (1–3 h) low dose O_3 exposures can cause lung inflammatory responses, damage to epithelial airway tissues, increases in permeability of both the lung endothelium and epithelium and increases in susceptibility to infectious diseases due to the modulation of lung host defences [72,73]. Inflammatory responses have been observed in the airway in some individuals following O_3 exposures even in the absence of O_3 induced reductions in lung function. There is also evidence that repeated O_3 exposures over several days' results in a reduction in inflammation.

However, evidence suggests that lung tissue damage continue during repeated exposure [74]. Controlled human exposure studies have found that acute O_3 exposure causes an increase in non-specific airway responsiveness. Ozone has also been shown to further increase the airway responsiveness in allergic asthmatic subjects, in response to allergen challenges. These effects are supported by studies on laboratory animals. The

lung lining fluid antioxidant status is compromised in asthma and although the cause of the decreased complement of antioxidant defenses on the surface of the lung is unknown, it is likely that as a consequence these individuals will be more susceptible to an oxidative challenge. It has also been shown that O_3 induced exacerbation of airway responsiveness persists longer and decreases more slowly than the effects on lung function and respiratory symptom responses [1].

A study of nonsmoking adult Seven-Day Adventists in California, found that long-term exposure to O_3 was associated with the incidence of doctor diagnosed asthma [75]. There is little evidence for an independent long-term O_3 effect on lung cancer or total mortality [76]. According to a large US study, researchers concluded that the risk of dying from lung disease (due to ozone exposure) is three times higher in large cities compared to smaller urban areas, where pollution concentrations are lower [77], It is estimated that there will be 1,500 more ozone-related deaths annually by the year 2020, in the UK alone [78].

What are the main health hazards associated with breathing in ozone?

Even very low concentrations of ozone can be harmful to the upper respiratory tract and the lungs. The severity of injury depends on both by the concentration of ozone and the duration of exposure. Severe and permanent lung injury or death could result from even a very short-term exposure to relatively low concentrations.

Exposure to extremely low concentrations of ozone initially increases the reactivity of the airways to other inhaled substances (bronchial hyper responsiveness) and causes an inflammatory response in the respiratory tissue. Exposure to ozone during exercise or work increases susceptibility to this effect. Increased bronchial responsiveness has been observed following 7-hour exposures to 0.08, 0.1 or 0.12 ppm (with moderate exercise), or a 1-hour exposure to 0.35 ppm. This response occurs almost immediately following exposure to ozone and persists for at least 18 hours.

Other symptoms observed following acute exposures to 0.25-0.75 ppm include cough, shortness of breath, and tightness of the chest, a feeling of an inability to breathe (dyspnea), dry throat, wheezing, headache and nausea.

More severe symptoms have been seen following exposure to higher concentrations (greater than 1 ppm) and have included reduced lung function, extreme fatigue, dizziness, inability to sleep and to concentrate and a bluish discoloration of the skin (cyanosis). Intermittent exposure to 9 ppm for 3-14 days has produced inflammation of the bronchi and lungs.

Animal studies indicate that ozone can also cause a potentially fatal accumulation of fluid in the lungs (pulmonary edema). Symptoms of pulmonary edema, such as shortness of breath, may not appear for 24 hours after exposure and are aggravated by physical exertion.

The severity respiratory responses to ozone become reduced following repeated daily exposures. This "functional adaptation" to the effects of ozone may persist for several days after exposure stops. Decreases in respiratory function do not appear to be more pronounced in cigarette smokers or people with pre-existing lung disorders [79].

Health Effect of Ozone in children

Children are at special risk during high ozone alert days because they breathe more rapidly than adults, taking in more pollution per pound of body weight. Because their airways are smaller, they are more likely to become blocked when irritated. Children with asthma are even more likely to experience the harmful impact of high ozone levels. It is estimated that 5 million children suffer from asthma, making it the leading chronic illness of children in the U.S.[80].

The average adult breathes 13,000 liters of air per day. Children breathe even more air per pound of body weight than adults. Because children's respiratory systems are still developing, they are more susceptible than adults to environmental threats. Ground-level ozone is a summertime problem, and children are at risk when they are outside playing and exercising during the summer months at summer camps, playgrounds, neighborhood parks and in backyards [81].

The study of Southern California children referred to above followed children without evidence of asthma over five years and found no increase in risk was in relation to long-term O_3 exposure. However, in a subgroup analysis, an increase in incidence was observed in both boys and girls living in high O_3 areas who played three or more team sports, suggesting that exercise rate are an important factor [82]. The evidence that long-term O_3 exposure is associated with reductions in lung function is somewhat inconsistent. Cross-sectional studies of children in Austria and Southern Germany [83-85] have observed reductions but there was some evidence that these effects could be reversed over several years. In Southern California, however, there was no evidence that O_3 exposure was associated with reduction in the expected rate of lung function growth [86].

Health Effects of Ozone in Patients with Asthma

People with asthma are the only segment of the population that has been identified to be the most acutely responsive to ozone exposure. Although younger adults (teens to thirties) experience larger lung function changes than do

older adults (fifties to eighties), the limited data available do not suggest that children have larger responses than young adults for a given exposure. Children are generally at risk of higher exposure. However, and therefore, at risk of larger acute responses because they tend to be more active and spend more time playing outdoors than most adults. In particular, following respiratory exposure to ozone, people with asthma experience:

- Increased frequency of asthma attacks
- Increased use of health care services

Furthermore, based upon non-human primate data, very young children may be at special risk of effects upon respiratory system development, the long-term effects of which are not known. Furthermore, those exposed early in life have the potential for the greatest lifetime exposures. Individuals with chronic lung diseases characterized by impaired lung function may theoretically be at higher risk since even small additional decrements in lung function could result in disproportionate effects. The extent to which this is true is not known.

How does ozone affect people with asthma? There are two major mechanisms by which people with asthma might be more severely affected by ozone than those without asthma. The first is that those with asthma might be more responsive or sensitive to ozone and therefore, experience the lung function changes and respiratory symptoms common to all, but either at lower concentrations or with greater magnitude. There is evidence that this may be true, but it is likely to play a small role in the response of people with asthma. By far, the greater concern is that the injury, inflammation, and increased airway reactivity induced by ozone exposure may result in a worsening of a person's underlying asthma status, increasing the probability of an asthma attack or requiring more treatment.

Epidemiologic studies indicate that there is a relationship between ambient ozone concentration and medication use among children with asthma, and ER visits and hospital admissions for asthma. In a camp for children with asthma in New York, it was observed that on days when ozone concentrations were high, children in camp used their asthma inhalers more frequently than on days when ozone levels were low.

Presumably, this was due to a perception that their asthma was worse on those days. Measures of peak expiratory flows in these children were lower on days when ozone levels were high, supporting this hypothesis.

The validity of these epidemiologic observations has been supported by the results of controlled experimental ozone exposures in human volunteers in which markers of asthma status were measured after ozone and after clean air exposures. In these studies, ozone has been demonstrated to worsen airway inflammation, to increase the airway response to inhaled allergen, and to increase nonspecific airway responsiveness, each of which is likely to indicate worsening asthma. In one study, people with asthma exposed to 0.16 ppm ozone were observed to have larger changes in PMNs and BAL protein than individuals without asthma, suggesting a more intense inflammatory response. Exposure to 0.20 ppm ozone increased the numbers of eosinophils found in the BAL fluid of people with asthma. In contrast, eosinophils are not found in the BAL of individuals without asthma as a result of ozone exposure.

In another study, house dust mite (HDM) sensitive individuals underwent airway challenge with HDM antigen after ozone exposure and after air exposure. As seen in Figure 11, after ozone exposure, the concentration of HDM needed to cause a 20% fall in FEV_1 was reduced compared to the air exposure, suggesting that people with asthma would have a greater response to environmental levels of HDM following ozone exposure.

Many studies have demonstrated that nonspecific airway responsiveness is greater following ozone exposure. These findings are consistent with ozone causing an increase in asthma severity and, taken together, provide a plausible biological mechanism for the epidemiological observations that ambient ozone exposure results in a higher probability of experiencing an asthma attack and other manifestations of worsening asthma [87].

Health Effects of Ozone in Healthy Adults:

Even moderately exercising healthy adults can experience 15 to over 20 percent reductions in lung function from exposure to low levels of ozone over several hours. Damage to lung tissue may be caused by repeated exposures to ozone - something like repeated sunburns of the lungs, and this could result in a reduced quality of life as people age. Results of animal studies indicate that repeated exposure to high levels of ozone for several months or more can produce permanent structural damage in the lungs. Among those most at risk to ozone are people who are outdoors and moderately exercising during the summer months. This includes construction workers and other outdoor workers [88].

Ozone air quality guideline and interim target

The second edition of the WHO AQG (WHO 2000) set the guideline value for ozone at 120 $\mu g/m^3$ for an 8-h our daily average. Since the mid-1990s there has been no major addition to the evidence from chamber studies or field studies. There has however been a marked increase in health effects evidence from epidemiological time-series studies combined evidence from those studies show convincing, though small, positive

associations between daily mortality and ozone levels, independent of the effects of particulate matter. Similar associations have been observed in both North America and Europe. These time-series studies have shown effects at ozone concentrations below the previous guideline of 120 μg /m^3 without clear evidence of a threshold. Evidence from both chamber and field studies also indicate that there is considerable individual variation in response to ozone. In view of these considerations, there is a good case for reducing the WHO AQG from the existing level of 120 μg/m^3. It is recommended that the air quality guideline for ozone is set at the level of: ozone: 100 μg/m^3 for daily maximum 8-hour mean.

It is possible that health effects will occur below this level in some sensitive individuals. Based on time-series studies, the number of attributable deaths brought forward can be estimated at 1-2% on days when ozone concentration reaches this guideline level as compared with the background ozone level.

There is some evidence that ozone also represents unmeasured toxic oxidants arising from similar sources. Measures to control ozone are also likely to control the effects of these pollutants.

Hemispheric background concentrations of tropospheric ozone vary in time and space but can reach average levels of around 80 μg/m^3. These arise from both anthropogenic and biogenic emissions of ozone precursors and downward intrusion of stratospheric ozone into the troposphere. The proposed guideline value may occasionally be exceeded due to natural causes.

There is some evidence that long-term exposure to ozone may have chronic effects, but it is not sufficient to recommend an annual guideline. As concentrations increase above the guideline value, health effects at the population level become increasingly numerous and severe. Such effects can occur in places where concentrations are currently high due to human activities or during episodes of very hot weather.

The 8-hour interim target-1 level has been set at 160 μg/m^3 at which measurable, though transient, changes in lung function and lung inflammation among healthy young adults have been shown in the presence of intermittent exercise in controlled chamber tests. Although some would argue that these responses may not be adverse, and that they were seen only with vigorous exercise, these views are counterbalanced by the possibility that there are substantial numbers of persons in the general population, including persons of different ages, pre-existing health status, and co-exposures that might be more susceptible than the relatively young and generally healthy subjects who were studied. Furthermore, chamber studies provide little evidence about repeated exposure. The exposure to 160 μg/m^3 is also likely to be associated with the same effects noted at 100 μg/m^3. Based on time-series evidence, the number of attributable deaths brought forward can be estimated at 3-5% for daily exposures above the estimated background.

At concentrations exceeding 240 μg/m^3, important health effects are likely. This is based on findings from a large number of clinical inhalation and field studies. Both healthy adults and asthmatics would experience significant reductions in lung function as well as airway inflammation that would cause symptoms and alter performance. There are additional concerns about increased respiratory morbidity in children. Based on time-series evidence, the number of attributable deaths brought forward can be estimated at 5-9% for daily exposures above the estimated background [89].

Ozone Linked to Lung Cancer

Also, recent research studies suggest that long-term exposure to ozone may be associated with lung cancer. This possibility is expected to be further explored [90] Ozone was the pollutant that best correlated with the incidence of lung neoplasms in 12 São Paulo City districts. This study, however, does not allow us to conclude that there is a causal relationship [91].

According to the research effort, ozone can trigger genetic modifications in human cells that are exposed to the gas, according to observations made of the four "letters" or chemical bases, in DNA sequences. In the genes of cells exposed to ozone, these pairs are switched, or appear in a different order, similar to the cases of non-smokers [92].

Occupational exposure to ozone

Acute exposure to high levels of ozone increases the risk of noninfectious rhinitis [93]

When the mills were using ozone, there was an increased incidence rate of wheezing among the workers in the bleachery [94].

An acute occupational exposure to approximately 11 ppm for 15 minutes caused severe respiratory irritation and almost caused unconsciousness. A 30-minute exposure to 50 ppm is considered potentially lethal.

A small number of studies examining the potential effects of long-term occupational exposures to ozone have reported headache, irritation of the nose and throat, chest constriction and lung congestion in exposed workers. Human population studies indicate that people living in communities with high background ozone levels have experienced a greater decrease in lung function over 5 years than people living in communities with lower background levels.

These studies suggest that long-term exposures to ozone may result in impaired lung function. These reports are consistent with animal studies which also indicate that long-term exposure

to ozone can impair lung function and cause structural changes to the lungs.

Based on animal evidence, exposure to ozone may increase susceptibility to bacterial infections of the respiratory system [95].

CONCLUSIONS

The respiratory system is the primary target of this oxidant pollutant. Respiratory tract responses induced by ozone include reduction in lung function, aggravation of preexisting respiratory disease (such as asthma), increased daily hospital admissions and emergency department visits for respiratory causes, and excess mortality. The degree of adverse respiratory effects produced by ozone depends on several factors, including concentration and duration of exposure, climate characteristics, individual sensitivity, preexistent respiratory disease, and socioeconomic status [96].

Severe reactions to even brief exposure to ozone unfortunately include death and impaired lung functioning as individuals lose their ability to exhale particles, which have now become "stickier". Milder or more transient symptoms include coughing or wheezing, headaches or dizziness, vomiting or nausea, inability to concentrate, shortness or tightness of breath [97].

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