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GASEOUS POLLUTANTS: 1- OZONE

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REVIEW ARTICLE

INTRODUCTION :

Community air pollution is a problem that is as old as civilization, and may date back to prehistoric cultures. Investigation of the effects of air pollutants on human health has followed a multidisciplinary approach using animal toxicology, epidemiology, controlled human exposure studies and, more recently, molecular and cellular biology. Air pollutants may, in addition to other responses, cause lung damage, inflammatory responses, impairment of pulmonary host defenses, acute changes in lung function and respiratory symptoms as well as chronic changes in lung cells and air ways. The focus of this review is on the human health hazards of pollutants as determined through controlled human exposure studies and emphasizes the deleterious responses that have been shown with ozone.

Ozone (O_3), a reactive species of oxygen, is an important natural constituent of the atmosphere (Cadle and Allen, 1970). Background levels of ozone in the lower atmosphere may reach 0.1 ppm and are modified by geographic elevation, solar radiation and climatic conditions (National Research Council, 1977). Since some effects of ozone are radiomimetic (Brinkman and Lambert, 1958; Brinkman et al., 1964), its action may be enhanced in the presence of ionizing radiation from background and or man-made sources (Borek and Mehlman,

1983). While stratospheric ozone spares the earth from excess solar ultraviolet radiation (National Research Council, 1977); high levels of ozone in the environment are toxic and result in health hazards to man (WHO, 1979 and Lee et al., 1983).

Ozone is one of the most powerful oxidizing substances. It is formed in the troposphere by the action of sunlight on nitrogen dioxide. Direct emission of ozone into the atmosphere as a result of industrial activity is only very limited. Ozone is an important component of photochemical smog and its formation in the atmosphere depends to a large extent on the absolute and relative concentrations of volatile organic substances on the one hand and nitrogen oxides on the other. The maximum natural background concentration, expressed as the average over a period of 24 hours, is 120 μgm^{-3} (0.06 ppm), the 50% values lying between 40 And 60 μgm^{-3} (Feron et al., 1996).

On a global level, the main concern with ozone is the reduction in its concentration in the upper atmosphere. The well-publicized ozone "hole" which occurs over the Antarctic (but now detected at high latitudes in the Northern Hemisphere), is caused by the degradative effects of Chlorofluorocarbons (CFCs) on ozone molecules. CFCs are released from aerosol containers, from the coolants in domestic refrigerators when they are broken up or leaked, and from foam packaging. The ozone layer absorbs ultraviolet light so that one hazard associated with the thinning of this ozone layer, is an increase in the rates of skin cancer. Environmentally, it has been suggested that the increased radiation could decrease photosynthesis of phytoplankton in the Antarctic (Walker et al., 1996).

TOXICOLOGY :

Ozone is an extremely reactive oxidant molecule. Its toxicity is complex because of the large number of biological systems that can be affected and the variety of effects that can result from ozone interactions with cellular components (Lee et al., 1983). The toxic effects of ozone are manifested upon its inhalation and absorption in the lungs. The pulmonary system is therefore the primary target for ozone toxicity though extrapulmonary effects have been recognized and documented (Stockinger, 1965; Goldstein, 1979; Borek and Mehlman, 1983).

The levels at which ozone toxicity becomes evident are influenced by variety of parameters. These include; genetic factors, (species, airway anatomy, stage of development) as well as host factors such as pre-existing disease state, age, dietary and hormonal status and cellular protective systems. The latter, which directly or indirectly suppress the oxidative damage induced by ozone , serve as important determinants in establishing the consequences of ozone health effects (WHO, 1979; Borek and Mehlman, 1983).

While the exact molecular mechanisms of ozone toxicity are unknown; a number of pathways have been proposed which suggest that ozone damage is in part produced via free

radical mechanisms (Pryor, 1976; Borek and Mehlman, 1983). The peroxidation of polyunsaturated fatty acids (Chow et al., 1981; Goldstein et al., 1969) and oxidation of thiols, amines and proteins (Mudd et al., 1969; Mudd and Freeman, 1977) which produce free radicals have been implicated in ozone-induced damage in pulmonary and extrapulmonary sites (Borek and Mehlman, 1983).

(A) PULMONARY EFFECTS OF OZONE :

Ozone is an air pollutant and a major component of photochemical smog. It is a respiratory irritant producing irritation of the upper airways and high concentration may even produce fatal pulmonary edema in both humans and experimental animals.

In rodents, approximately 50% of the ozone present is removed from the inhaled air in the nose. The highest tissue concentrations, in both man and experimental animals, are found in the transitional area between the bronchioles and the alveoli. Exposure to ozone causes damage to all parts of the respiratory tract. The effects exerted are dependent mainly on the concentration. At relatively low concentrations (400 μgm^{-3}), effects are observed mainly in the lung, while at higher concentrations (800-1600 μgm^{-3}) the nasal mucosa is also affected. The effects range from reversible interference with pulmonary function, increased enzymatic activity, reduced resistance to pulmonary infections, proliferation of type II pneumocytes, hyperplasia and metaplasia of the respiratory epithelium in the nose, to permanent pulmonary fibrosis. Clinical and epidemiological studies in man have suggested that exposure to concentrations between 160 and 340 μgm^{-3} resulted in respiratory complaints such as coughing, dry throat, chest pain and tightness of the chest (Feron et al., 1996).

1- Morphology:

Toxicological research on the effects of ozone in laboratory animals indicated that the types and distribution of lesions in the respiratory tract following short- or long-term ozone exposure largely depend on the following variables: (1) Lung morphometry which differs among species (American Thoracic Society, 1983), (2) Location of sensitive cells (Stephens et al., 1974a, b) and (3) Junction between conducting airway and gaseous exchange areas (Schrieder and Raabe, 1981).

Scheel et al (1959) reported that short term exposure to ozone resulted in pulmonary edema, hemorrhage and inflammation. Damage to respiratory tract epithelia can be seen in various species exposed to 0.2 ppm ozone and higher. The sites of damage include the trachea (Cavender et al., 1977; Schwartz et al., 1976), bronchi (Castleman et al., 1973), bronchioles (Castleman et al., 1980), alveolar ducts and alveoli (Stephens et al., 1974b; Schwartz et al., 1976). Fibrosis and enhanced collagen synthesis have been observed following long-term exposure to ozone at doses of 0.1 ppm and higher (Boorman et al., 1980; Last et al., 1979; Moore and Schwartz, 1981; Plopper et al., 1978).

The sensitivity of lung tissue to ozone-induced damage varies with cell type and location. The ciliated cells in the airway passages and the squamous alveolar epithelial cells (type I cells) are the most sensitive to ozone (Stephens et al., 1974a, b; Schwartz et al., 1976; Mellick et al., 1977; Castleman et al., 1980). Type II alveolar epithelial cells are more resistant to ozone and in fact serve as progenitor cells which differentiate into type I cells during the process of repair of ozone lesions (Evans et al., 1976). Morphological changes following ozone exposure also differ with the state of the animal and are modified by an altered nutritional or immunological status (U.S. Environmental Protection Agency, 1978). For example, rats maintained on vitamin E-deficient diets tend to develop more morphological lesions as compared to those maintained on vitamin E-supplemented diets (Plopper et al., 1978; Chow et al., 1981).

2- Pulmonary function:

Changes in the pulmonary function have been observed in a variety of species following short- and long-term exposure to ozone (National Research Council, 1977; Lee et al., 1983). Short-term exposure (1-2 hr) in experimental animals produces rapid, shallow breathing, increasing pulmonary resistance (Lee et al., 1977, 1979) and increases in residual volume, closing volume, closing capacity (Inoue et al., 1979). Long-term exposure (0.2 ppm for 4-6 weeks) resulted in an increased lung distensibility at high lung volumes (Raub et al., 1983; Bartlett et al., 1974). A longer period of ozone exposure (up to 0.8 ppm for 3-12 months) shows more severe consequences resulting in increased pulmonary resistance, impaired airway stability and lung distensibility suggesting a development of lung fibrosis (Wegner et al., 1982).

Studies of airway reactivity following ozone exposure indicate a hyperactive state resulting from a disruption of the respiratory epithelium and a sensitization of the underlying nerves to chemical and mechanical stimuli (Nadel, 1977; Lee et al., 1979). This sensitization may be an underlying factor in the reflex broncho-constriction and the rapid shallow breathing observed following ozone exposure; conditions which are enhanced if exposure takes place during exercises (Lee et al., 1979; Folinsbee et al., 1978). Epithelial damage induced by ozone has also been implicated in the enhanced allergic reactions to inhaled foreign proteins (Osebold et al., 1980).

Chronic exposure to ozone causes pulmonary arterial lesions that result in thickening of the arterial walls. Ultrastructural changes in the alveolar capillaries have also been found (Van Vleet et al., 1991).

3- Inhibition of enzymatic systems:

A large number of enzymes are inhibited following ozone exposure. The cytochrome P-450 enzyme system, important in carcinogen and drug metabolism, is inhibited in hamsters (Palmer et al., 1971) and rabbits (Goldstein et al., 1975) following short exposure to ozone

(0.75 - 1.0 ppm). The inhibition of cytochrome P-450 activity increases the hazard of ozone exposure due to the decrease in detoxification of inhaled chemicals including pneumotoxicants and carcinogens. The inhibition of prostaglandin synthetase, a membrane bound enzyme, has also been reported (Menzel et al., 1976). The decreased lung cholinesterase activity which has been observed following ozone exposure (Gordon et al., 1981) could result in elevated acetylcholine concentration in the bronchial muscle that end by enhancement of bronchial concentrations following a given stimulus.

4- Lung protein synthesis:

The action of ozone on pulmonary protein synthesis falls into two general categories: (a) an effect on the synthesis of collagen and structurally related proteins, which is directly related to ozone-associated lung fibrosis; (b) an action on glycoprotein synthesis and mucous secretion, which affects their role in protecting underlying cells from ozone toxicity and in removing adventitiously inhaled particles (Mehlman and Borek, 1987).

Continuous exposure to ozone for 7 days (0.5 - 0.8 ppm) results in a significant enhancement of collagen synthesis and precursor protein, but a negligible effect is observed when animals are exposed to 0.2 ppm (Hussain et al., 1976). Exposure of rats to 0.5 ppm ozone for 1-3 weeks results in a linear dose-response relationship for pulmonary biochemical and histological responses (Last et al., 1979). The inhibitory effect of ozone on the synthesis and secretion of mucus glycoprotein synthesis in tracheal explants varied with the species studied (Last and Kaizu, 1980).

5- Tolerance:

Many studies indicated that preexposure to low concentrations of ozone renders animals less sensitive to the damaging action of a second dose of exposure (Matzen, 1957; Mendenhall and Stockinger, 1959; Fairchild, 1967; U.S. Environmental Protection Agency, 1978). Frager et al (1979) showed that the protective effect of preexposure to ozone exerts its action on mucociliary clearance of foreign particles. Preexposure of animals to 0.8 ppm ozone for 3 days resulted in a marked reduction in the delay of mucociliary clearance, which lasted for 1 week.

Tolerance does not impart protection from all forms of lung injury (U.S. Environmental Protection Agency, 1978). Preexposure of animals to ozone at levels of 0.3 ppm prevents edema but affords only a partial protection from infection upon challenge with infectious agents (Coffin and Gardner, 1972a) and has little effect on cell renewal upon a second exposure (Evans et al., 1976).

At a cellular level, tolerance induced by preexposure to 0.5 ppm ozone protects against pulmonary edema, but has little effect on the cytotoxic effects caused by a second exposure to ozone as measured by a reduction of enzyme activity, enhanced inflammation and altered macrophages (Alpert and Lewis, 1971; Gardner et al., 1972). Rats preexposed to 0.75 ppm ozone for 3 days followed by secondary

challenge to 4.0 ppm ozone for 8 hours, showed no dramatic effects on a variety of biochemical parameters in lung tissue (Chow et al., 1976).

(B) EXTRAPULMONARY EFFECTS OF OZONE :

1-Central nervous system and behavioral effects :

Rats and mice exposed to low levels of ozone (0.5 ppm) suffered from a depression of motor activities . Limited data on the effects of ozone on the enzymes in the central nervous system indicate variability depending on the studied enzyme. For example, catechol-O-methyl transferase is decreased while the levels of monoamine oxidase are increased (Trams et al., 1972). Despite reports of dizziness, throat and nose irritations and visual impairment in humans exposed to ozone; there is limited information on ozone-induced changes on animal behavior (Tepper et al., 1983).

2- Effects of ozone on the immune system :

The immunotoxicological data on ozone indicate marked impairment of the pulmonary host defense mechanisms (Graham and Gardner, 1985). Mice exposed to 0.1 ppm ozone show decreased host resistance to bacterial challenge (Coffin and Gardner, 1972b). Additionally, ozone has been shown to increase the incidence of pulmonary infections induced by a number of other pathogenic organisms, including streptococcus sp., Pasteurella haemolytica and Mycobacterium tuberculosis (Graham and Gardner, 1985). The increased susecptibility may relate to ozone induced impairment in alveolar macrophage function. Studies supporting this assumption demonstrated that exposure to ozone can significantly decreases the number of alveolar macrophages (Gardner and Graham, 1976), impairs the phagocytic ability of alveolar macrophages (Devans et al., 1985) and decreases the ability of macrophages to secret reactive oxygen intermediates (Amoruso et al., 1981) and interferon (Shingu et al., 1980). Ozone-induced systemic immune dysfunction has also been demonstrated (Aranyi et al., 1983) and cannot be ruled out as an addition ional factor which impairs host defense. Alterations in rabbit alveolar macrophage production of arachidonic acid metabolites (increased prostaglandin E2, PGE2) following in vitro and in vivo ozone exposure have been also reported (Driscoll, 1986; Schleshinger and Driscoll, 1987). These authors suggested that increased PGE2 production represents a potential mechanism for the impaired alveolar macrophage function consistently observed in ozone-exposed animals. Non immunological mechanisms may contribute to decreased host resistance. Ozone-induced impairment in mucuciliary clearance and increased mucous secretion could result in an accumulation of pathogenic organisms (Kenoyer et al., 1981; Last et al., 1977). Lung inflammation occurs in humans exposed to extremely low level of ozone (Koren et al., 1989).

3- Hematological effects:

The effects of ozone exposure on hematological endpoints has been investigated in many in vivo and in vitro studies (U. S. Environmental Protection Agency, 1978; Borek and Mehlman, 1983). The morphological and biochemical parameters observed in hematological studies serve as useful indicator for ozone in different species (Chow et al., 1975). Exposure of red blood cells (RBCs) to ozone resulted in some changes including increased fragility, potentiation of complement-dependent membrane damage (Goldstein et al., 1974), formation of Heinz bodies (Menzel et al., 1975), inhibition of Na^+/K^+-ATPase and spherocytosis (Koontz and Heath, 1979) RBCs from humans exposed to 0.5 ppm ozone for 2 hrs showed enhanced glutathione and glucose-6-phosphate dehydrogenase activity (Buckley et al., 1975), while that from rats and monkeys at the same dose and conditions failed to show such changes (Chow et al., 1975). Oxidation of intracellular glutathione has been observed in human RBCs exposed to 0.84 ppm ozone for 2 hr (Freeman and Mudd, 1981) supporting earlier studies by Menzel et al., (1972) which showed a decrease in RBCs glutathione following long-term exposure of rats to 0.5 ppm ozone for 23 days.

In addition to the effect of ozone on RBCs, other changes have been detected in serum of animals to ozone. These include decreased albumin and enhanced levels of globulins in rabbits (P›an and Jegier, 1976) and increased lysozyme activity (Chow et al., 1974) and prostaglandin levels in rats (Giri et al., 1980).

4- Endocrine effects:

The endocrine system is adversely affected by ozone inhalation. Morphological changes are observed in the parathyroid after a single exposure to ozone (Atwal, 1974). Reduced levels of thyrotropin and thyroid hormones were shown in rats exposed to 1 ppm ozone for 24 hr (Clemons and Garcia, 1980), suggesting changes in hypothalamic function. Hormones have been recognized as playing a role in modulating ozone toxicity (Stockinger, 1965; Borek and Mehlman, 1983). A protective effect has been observed by removing the thyroid, hypophyseal or adrenal glands (Fairchild, 1963; Fairchild and Graham, 1963), suggesting that hormones such as thyroxin may potentiate the toxic action of ozone (Fairchild and Graham, 1963).

5- Reproductive effects:

The reproductive and teratogenic effects of ozone have been investigated. Brinkman et al., (1964) reported from his studies on mice, that prenatal exposure of mice to 0.2 ppm ozone can reduce infant survival. Progeny of dams exposed to 1 ppm ozone during late gestation showed slower growth rate and retarded early reflex development (Kavllock et al., 1980).

6- Genotoxic effects:

The genotoxic effects of ozone have been predicted from its radiomimetic character. Free radicals produced upon decomposition of ozone in water, such as OH^- radical, are similar to those produced by ionizing radiation and thought to play a role in some of its

genotoxic actions (Borek, 1982; Borek and Troll, 1983).

Fenter (1962) showed an induced chromosomal aberrations in human fibroblasts due to exposure to 1960 μg ozone m^{-3}. Different results were obtained when human lymphocytes were exposed to ozone both in vivo and in vitro (Gooch et al., 1976). No effect was shown in hamster and mouse peripheral lymphocytes exposed in vitro to 1 ppm ozone or less than 5 hr (Gooch et al., 1976). In contrast, significant chromosomal aberrations were found in hamster peripheral lymphocytes when exposed to ozone under similar previous conditions (Tice et al., 1978; Zelac et al., 1971a).

Data on sister-chromatid exchange (SCE) induced in human cells by ozone at 1 ppm or less are also conflicting. A dose-related increase in SCE was observed in WI-38 diploid cells exposed in vitro; but exposure of human subjects to ozone showed no significant enhanced SCE in their blood lymphocytes (Guerrero et al., 1979).

7- Carcinogenic effects of ozone:

The role of ozone in carcinogenesis is unclear (Stockinger, 1965). Some of its actions as a powerful oxidant and producer of free radical might render it suspect in playing a role in carcinogenesis and mutagenesis (Borek and Mehlman, 1983). Radiation, a complete carcinogen (Borek, 1982), produces chromosomal aberrations in synergistic fashion with ozone (Zelac et al., 1971b). These may play a role in the neoplastic process. Free radicals produced by oxidants damage to DNA (Lesko et al., 1980) and modify cellular genetic integrity, could lead to carcinogenic events.

The role of free radicals in carcinogenesis is seen by the fact that scavengers of free radicals, such as catalase, inhibit oncogenic transformation in vitro by radiation and chemicals (Borek and Troll, 1983). In addition, dietary factors such as selenium enhance the breakdown of peroxides in the cells exposed to radiation and chemicals and prevent oncogenic transformations (Borek and Biaglow, 1984).

MECHANISMS OF OZONE TOXICITY :

The toxicity of ozone depends upon its oxidative properties.

(1) Ozone acts by initiating peroxidation of polyunsaturated fatty acids (PUFAs) present in the cell membrane. The peroxides and secondary reactive oxygen species which ensue produce their toxicity by damaging the integrity of the cell membrane and other cellular molecules, Fig.(1) (Goldstein et al., 1969; Chow and Tappel, 1973; Mudd and Freeman, 1977; Borek and Mehlman, 1983; Pryor et al., 1983; Witz et al., 1983; Mehlman and Borek,1987).

(2) Ozone exerts its toxicity by oxidation of compounds of low-molecular weight like those containing thiol, amine, aldehyde and alcohol functional groups and by oxidation of proteins. Both soluble peptides, such as glutathione and

protein in lipid bilayers provide potential targets for ozone action. Protein modification takes place via oxidation of amino acid side groups (Mudd et al., 1969; Freeman and Mudd, 1981). So, the two mechanisms of ozone toxicity may be interrelated. Peroxidation of PUFAs gives rise to water-soluble products such as aldehydes, peroxides and hydroxy radicals (Pryor, 1976; Pryor et al., 1983,) which diffuse into the cytosol and initiate oxidation of amino acids and proteins, Fig. (2) (Borek and Mehlman, 1983; Mehlman and Borek, 1987).

Direct oxidation of amino acids and proteins by high ozone levels or oxidation by secondary reaction products of PUFAs peroxidation can inhibit a variety of cellular protective systems. These include glutathione, a scavenging thiol, glutathione peroxidase, superoxide dismutase and catalase, which detoxify peroxides (Mustafa et al., 1983), enzymes which supply reducing cofactors such as glucose-6-phosphate dehydrogenase (DeLucia et al., 1972) and antiproteases (Johnson, 1980), which play a role in the inhibition of ozone-mediated leakage and edema (Borek and Mehlman, 1983). Both thiols and enzymes may be restored metabolically to control levels or rebound to higher protective levels following intermittent or continuous ozone exposure (Chow and Tappel, 1972, 1973; DeLucia et al., 1972; Mustafa and Lee, 1976).

The degree to which ozone reacts with proteins is determined by the presence of ozone-susceptible amino acids at their active sites (Mudd et al., 1969; Mudd and Freeman, 1977; Freeman and Mudd, 1981) and the location of the amino acids in the tertiary structure of the protein (Boyer, 1972). For example, cystein, methionine and tryptophan are very susceptible to ozone (Mudd et al., 1969) and the oxidation of tryptophan produces peroxides (Meiners et al., 1977) which are toxic and give rise to other reactive toxic oxygen species (McCord and Fridovich, 1978).

The hypothesis that lipid peroxidation is the primary factor in ozone-mediated toxicity has its strongest support in the findings that vitamin E, a dietary antioxidant, is a powerful protective agent against ozone toxicity (Chow et al., 1981; Chow, 1983; Mustafa, 1975). Its effectiveness is further enhanced by other antioxidants such as ascorbic acid and butylated hydroxytoluene (Fletcher and tappel, 1973).

Peroxidation of PUFAs by ozone results in the generation of fatty acid hydroperoxides. These are destroyed by glutathione peroxidase-consuming glutathione. Oxidized glutathione is reduced by glutathione-reductase consuming NADPH. Thus, the loss of glutathione following ozone exposure (Freeman and Mudd, 1981) promotes lipid peroxidation indirectly through the inhibition of glutathione peroxidase or by direct oxidation and depletion of glutathione. Chow and Tappel (1973) suggested that peroxides formed via lipid peroxidation induce glutathione peroxides and this in turn induces enhanced levels of the enzymes required to supply reducing factors such as NADPH to

glutathione peroxidase. Vitamin E suppresses spontaneous formation of lipid peroxides. The supplementation of vitamin E in the diet would therefore decrease the utilization of glutathione peroxidase and maintain a high level of protection in the cell. There is a cross function between various antioxidants. Selenium, an essential factor in selenium-dependent glutathione peroxidase and an inducer of the enzyme (Borek and Biaglow, 1984), prevents vitamin E deficiency and increases the transport and utilization of the vitamin (Menzel, 1970; Borek and Mehlman, 1983).

Following exposure to high levels of ozone, the relative importance of PUFAs peroxidation and the oxidation of proteins and compounds of low molecular weight depends on many factors. These include (a) membrane composition of PUFAs and proteins, which determine ozone accessibility and degree of interaction and damage, (b) enzymatic pathways to decompose peroxides, (c) pathways to generate thiols and (d) the presence of antioxidants (vitamin E, vitamin C and selenium) to prevent peroxide formation and to partake in scavenging free radicals arising from secondary reactions (Pryor et al., 1983; Borek and Mehlman, 1983).

CONCLUSION :

Ozone, a potent toxic agent, exerts its effects in a rapid fashion and only a small amount of ozone is needed in each lung cell to intiate damage and cytotoxicity. The lipid peroxidation theory is an attractive one to explain ozone action. The reaction is rapid and is propagated through cascading events mediated via free radicals (Pryor et al., 1983; Borek and Mehlman, 1983). Direct oxidation of proteins which regulate membrane functions could alternatively produce some forms of cytotoxicity through cell leakage and edema. The powerful protective effect of vitamin E and other antioxidants supports lipid peroxidation as a primary toxic action of ozone.

In vitro studies suggested that ozone toxicity is due to oxidative damage of membrane lipids and cellular sulfhydryls and by inactivation of key enzymes involved in cellular metabolism. Ozone affects the respiratory epithelium from the nasal cavity to the alveoli. Ciliated and type I epithelial cells are injured, while mucous production and mucous cell membranes are increased, Fig. (3) (Haschek and Witschi, 1991).

Ozone is a toxic potent oxidant. In the body ozone reacts to produce reactive free radicals. These species become involved in destructive oxidative processes, particularly reaction with SH groups and lipid per-oxidation. This is a process in which the C = C double bonds in unsaturated lipids are attacked by free radicals and undergo chain reactions in the presence of O_2, resulting in their oxidative destruction. Species rich in sulfhydryl groups, such as metallothionine acts as antidotes to ozone poisoning (Manahan, 1992).

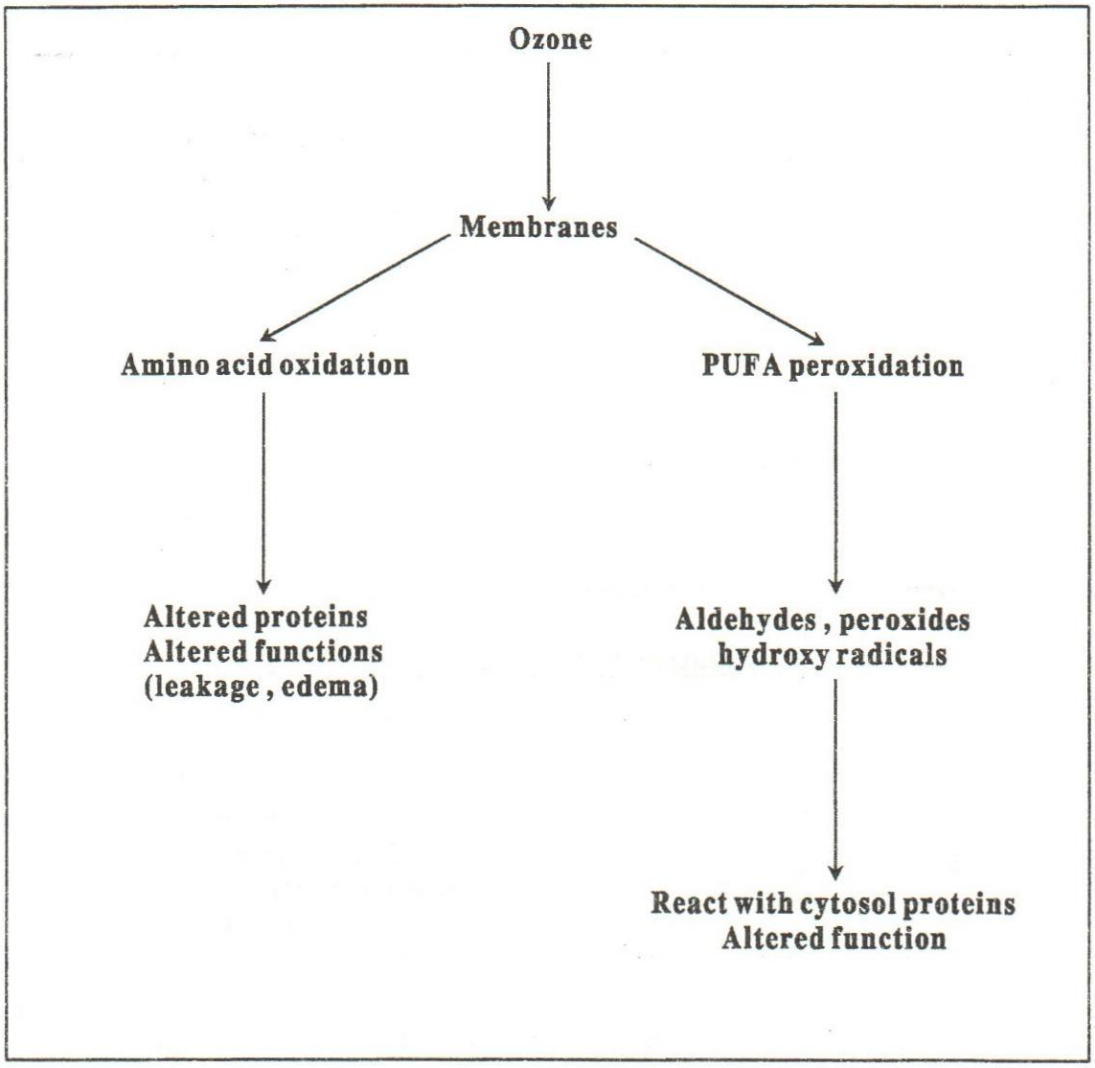

Fig.(1): The effects of ozone on the cell membrane as a primary site of its toxicity which suggest that ozone damage to membranes is in part induced via free radical processes (Mehlman and Borek, 1987).

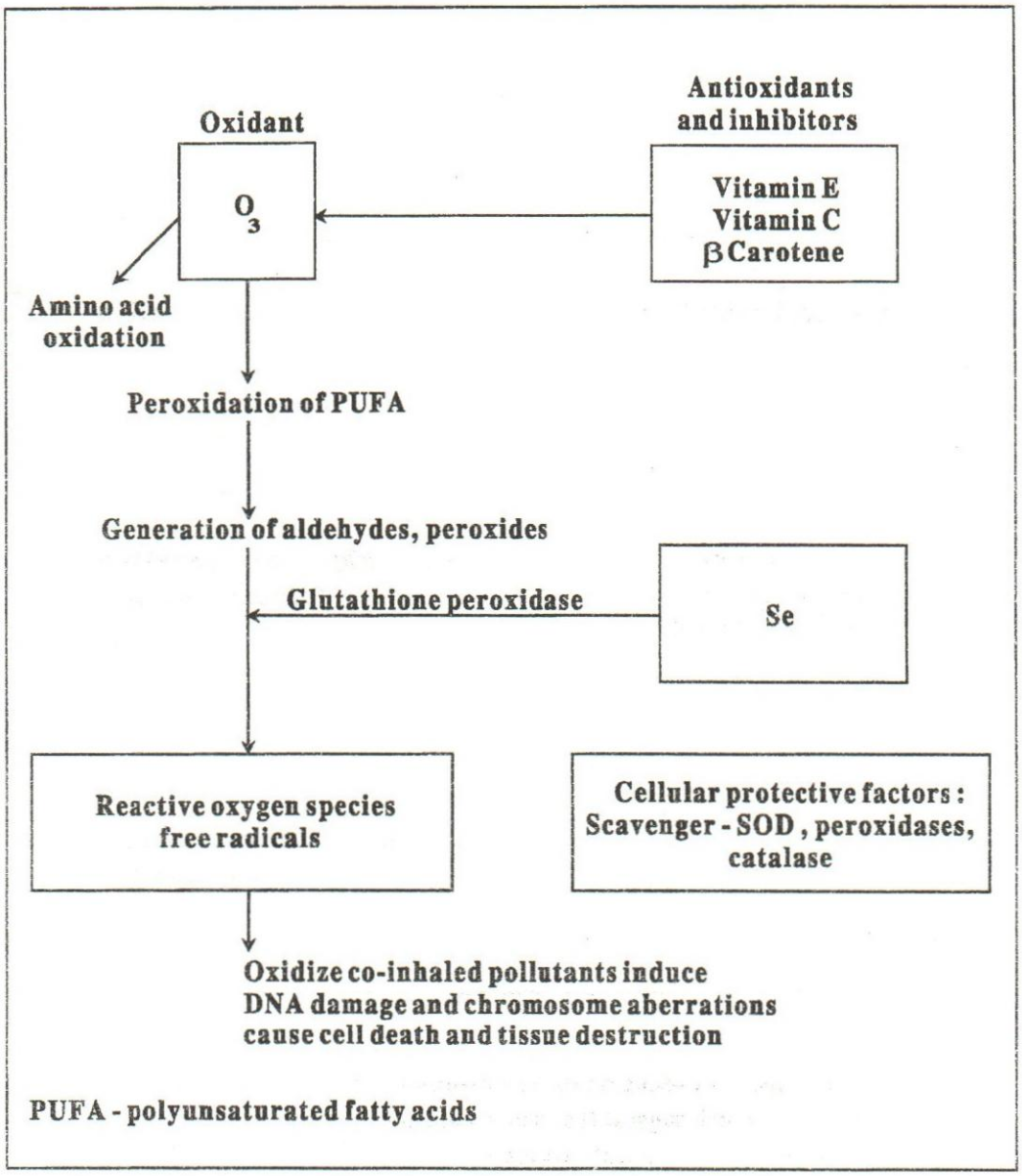

Fig.(2): Mechanisms of ozone toxicity (1) Initiation peroxidation of polyunsaturated fatty acids which present mainly in the cell membrane. (2) Oxidation of proteins via oxidation of amino acid side groups (Mehlman and Borek, 1987).

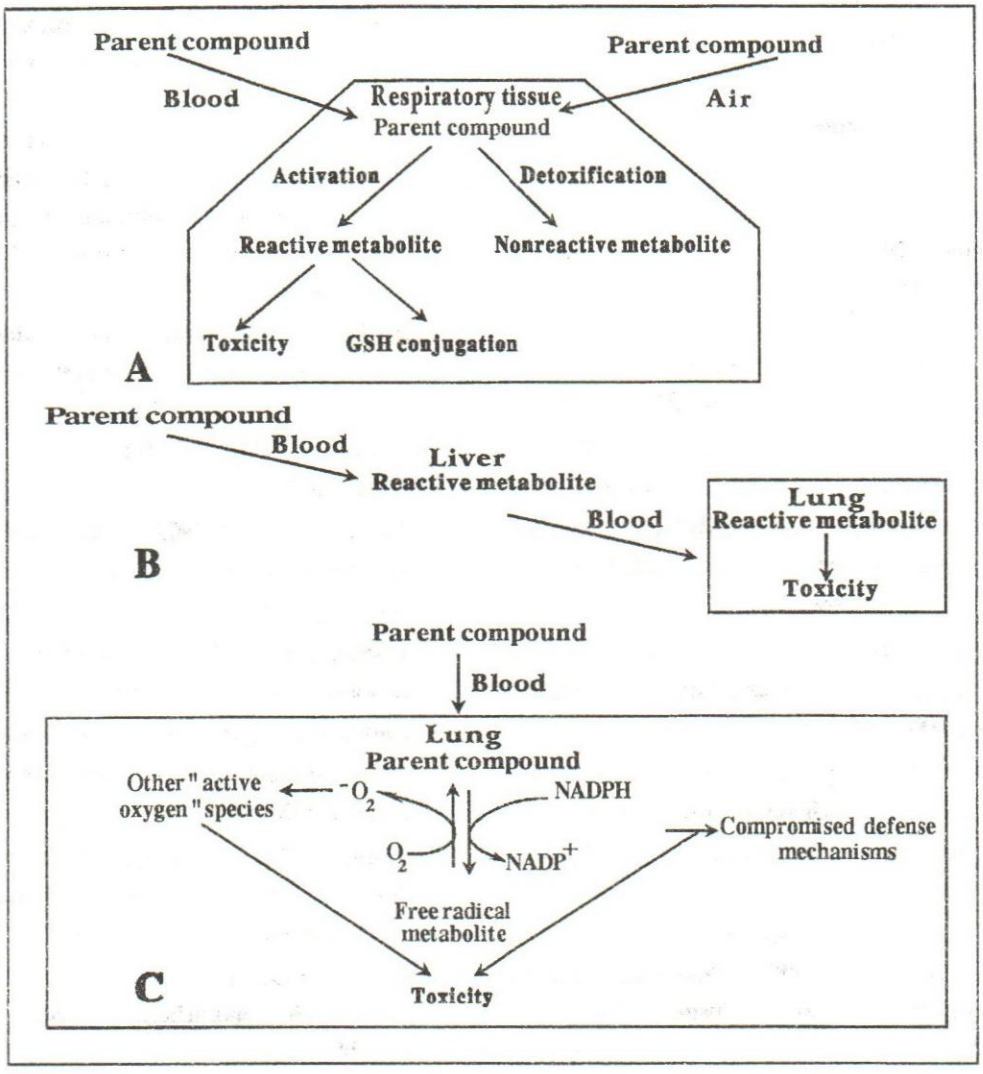

Fig.(3): Mechanisms of respiratory injury involving metabolic activation. (A) In situ metabolic activation of parent compound. (B) Activation of parent compound in liver, metabolite produces toxicity in lung. (C) Parent compound undergoes cyclic reduction/oxidation, indirectly inducing toxicity (Haschek and Witschi, 1991).

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الملوثات الغازية : ١ - الأوزون

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قسم الطب الشرعى والسموم - كلية الطب البيطرى - جامعة أسيوط

يعد التلوث من أهم المشاكل البيئية التى تواجه العالم اليوم . ويعتبر الأوزون واحداً من أهم الملوثات الغازية إذ أنه أحد مركبات الأكسجين النشطة ، والذى إذا زادت نسبته فى الهواء الجوى عن ٠,١ جزء فى المليون يحدث بعضاً من الآثار السامة .

وقد تم فى هذه المقالة إظهار تأثيرات الزيادة فى تركيزات الأوزون فى الهواء المحيط بنا على أجهزة الجسم المختلفة كما يلى :

أولاً - تأثيرات الأوزون على الجهاز التنفسى :

مثل : تأثير على الشكل الظاهرى للجهاز التنفسى ، تأثير على وظائف الجهاز التنفسى ، تثبيط بعض انزيمات الجهاز التنفسى ، تثبيط تكوين البروتين داخل أنسجة الرئتين .

ثانياً - تأثيرات الأوزون على الأجهزة الأخرى :

مثل : الجهاز العصبى ، الجهاز المناعى ، الجهاز الدموى ، الغدد الصماء ، الجهاز التناسلى ، تأثير على الكروموسومات ، تأثيرات مسببة للسرطان .

ومما لا يفوتنا أن الأوزون يعمل عن طريق :

١- تنبيه أكسدة الأحماض الدهنية المتعددة الغير مشبعة التى توجد فى جدر الخلايا .

٢- أكسدة المركبات الخلوية ذات الوزن الجزيئى البسيط والتى تحتوى على المجموعات الوظيفية.

مما سبق يتبين لنا أن الأوزون من الملوثات السامة التى تعمل عن طريقة الأكسدة ، ولذلك يجب أن نتوخى الحذر من التعرض لمثل هذه المواد ، وأن نعمل جاهدين بكل ما أوتينا لتلاشى جميع الأخطار التى قد تنجم عن انتشار مثل هذه الملوثات فى بيئتنا ، من خلال تقنيات علمية .