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# Standard Practice for SAFETY AND HEALTH REQUIREMENTS RELATING TO OCCUPATIONAL EXPOSURE TO OZONE[1]

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## INTRODUCTION

Ozone, one of the more active forms of oxygen, is found in the atmosphere in varying proportions (about 0.05 ppm (0.1 mg/m$^3$) at sea level). It is produced continuously in the outer layers of the atmosphere by the action of solar ultraviolet radiation on the oxygen of the air. Ultraviolet lamps commercially sold as "sterilizing lamps" produce ozone in a similar manner. In the laboratory, ozone can be prepared by passing dry air between two plate electrodes connected to an alternating current source of several thousand volts. The reaction is reversible, and after a little ozone has been produced, it is decomposed at the same rate as it is generated ($O_2 \rightleftharpoons O_3$).

Ozone, a strong oxidizing agent, is used as disinfectant for air and water; for bleaching waxes, textiles, and oils; and in organic syntheses. It forms ozonides, which are sometimes useful oxidizing compounds.

## 1. Scope

1.1 This practice is designed to help protect the safety and health of workers where there may be occupational exposure to ozone.

1.2 The various actions recommended in the subsequent sections of this practice apply when occupational exposure limits are at, or in excess of, the limits defined in 5.1.

1.3 When outside ambient ozone levels exceed the limits of 5.1, this practice is not applicable.

NOTE 1—This exemption is intended for intermittent or transient air pollution incidents and does not apply in situations where the outside ambient ozone concentrations exceed the limits of 5.1, such as at high altitude.

## 2. Applicable Documents

2.1 *ASTM Standard:*

D 2912 Test for Oxidant Content of the Atmosphere (Neutral KI)[2]

2.2 *ANSI Standards:*

Z9.2 Fundamentals Governing Design and Operation of Local Exhaust Systems[3]

Z88.2 Practices for Respiratory Protection[3]

2.3 NIOSH Analytical Method P&CAM 153[4]

## 3. Significance

3.1 These criteria were not developed for the population-at-large, and any extrapolation beyond general occupational exposures is not warranted. They are intended to assure that the results of practices based thereon will: (*a*) protect against development of acute and chronic ozone poisoning; (*b*) be measurable by techniques that are valid, reproducible, and available to industry and official agencies; and (*c*) be attainable with existing technology.

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[1] This standard practice is under the jurisdiction of ASTM Committee E-34 on Occupational Health and Safety.

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[2] *Annual Book of ASTM Standards*, Parts 26 and 41.

[3] Available from American National Standards Institute, 1430 Broadway, New York, N.Y. 10018.

[4] Method P&CAM 153, Jan. 15, 1974, revision, *NIOSH Manual of Analytical Methods.*

## 4. Definitions

4.1 *occupational exposure*—that level or concentration of chemical agent to which a worker is exposed determined either as a time-weighted average (TWA), or as a ceiling limit for a shorter period of time, which is at or in excess of those stated in 5.1.

4.2 *ceiling limit*—a concentration of chemical agent that shall not be exceeded for a specified period of time.

4.3 *time-weighted average (TWA)*—the concentration (ppm or mg/m$^3$) of chemical agent determined in each individual sample taken, multiplied by the duration of the individual sampling period, summed for all the samples taken during an interval, and divided by the total sampling time.

$$\text{TWA} = \frac{\Sigma C_i T_i}{\Sigma T_i}$$

where:

TWA = time-weighted average,
$C_i$ = concentration (ppm) of ozone in air in the $i$th sample,
$T_i$ = time period over which the $i$th sample was collected, and
$i$ = subscript denoting any one particular sample taken during the interval of time to which the TWA applies.

## 5. General Requirements

5.1 *Environmental:*

5.1.1 Occupational exposure to ozone shall be controlled so that workers will not be exposed to ozone at a concentration in excess of 0.1 ppm (0.2 mg/m$^3$) determined as a time-weighted average (TWA) exposure for an 8-h or more workday, as measured by minimum sampling times of 10 min (see Appendix X1).

5.1.2 No worker shall be exposed to a ceiling concentration of ozone in excess of 0.2 ppm (0.4 mg/m$^3$) as measured by a sampling time of 10 min (see Appendix X2).

NOTE 2—The number of studies in which comprehensive environmental surveys have been supplemented with a well-planned surveillance program for adequate numbers of workers exposed to ozone are so few that it is difficult to establish an environmental standard based upon unequivocal scientific data.[5]

5.2 *Medical*—Medical surveillance as specified in this section shall be made available to workers where there is occupational exposure to ozone. A preplacement examination, which is required of all workers who will be exposed to ozone, shall consist of the following:

5.2.1 A comprehensive medical and occupational history.

5.2.2 A comprehensive physical examination oriented towards defects traceable to ozone, such as pulmonary function tests, in order to ascertain any predisposing factors that may lead to injury or illness; and periodic follow-up using clinical procedures or bio-assay evaluations to ensure the effectiveness of the control measures in force.

5.3 *Labeling (Posting):*

5.3.1 The following warning sign shall be affixed in a readily visible location on processing and other equipment, or near entrances to areas where excessive exposure to ozone may occur:

OZONE
WARNING! IRRITANT GAS
ADEQUATE VENTILATION REQUIRED
AVOID PROLONGED OR REPEATED
BREATHING OF OZONE

5.3.2 If environmental levels are at or greater than the occupational standard, add pertinent information to the label or placard describing the location of the respirators, and state the mandatory use of this equipment.

5.4 *Personal Protective Equipment*—When the limits of exposure specified in 5.1.1 cannot be met by limiting the concentration of ozone in the work environment, an employer shall establish and enforce (see 5.4.2) a program of respiratory protection to provide the required protection of every worker exposed using NIOSH- or MESA-approved equipment whenever approval exists. Engineering controls shall be used whenever feasible to maintain ozone concentrations below the specified limits.

5.4.1 *Respiratory Protection:*

5.4.1.1 Only appropriate respirators, such as described in Table 1, shall be provided and used when the use of respirators is the only means of controlling exposure for routine operations, or during an emergency. Employees must be trained in their proper use and appropriate measures shall be instituted to ensure that respirators are correctly worn.

[5] The American Conference of Governmental Industrial Hygienists (ACGIH) recommended threshold limit value (TLV) for ozone is 0.1 ppm (parts of gas per million parts of contaminated air by volume at 25°C and 760 mm Hg pressure) (0.2 mg/m$^3$) (approximate milligrams of substance per cubic metre of air) in air and is the basis for this practice.

5.4.1.2 The requirements set forth in this section shall apply for nonroutine operations such as a brief exposure to concentrations in excess of the occupational standard as a result of maintenance or repair activities or in emergency situations.

5.4.2 *Respiratory Protection Program*—A respiratory protection program meeting the general requirements outlined in Section 3.5 of ANSI Z88.2 shall be established and enforced by the employer. This program shall include instructions on the selection, fitting, use, testing for leakage, cleaning, and maintenance of the respiratory protective devices.

5.4.2.1 For the purpose of determining the class of respirator to be used, the employer shall measure the atmospheric concentration of ozone in the workplace, and thereafter whenever process, worksite, climate, or control changes occur that are likely to affect the concentrations of airborne ozone. Only appropriate respirators specified in Table 1 shall be used.

5.4.2.2 Employees who are routinely required to wear a respirator shall be medically examined to determine their fitness to wear the respirator. When an employee is found medically unfit to wear a properly fitted respirator satisfactorily, he shall not be assigned duties within the scope of 5.4.1.

5.5 *Apprisal of Employees of Hazards from Ozone:*

5.5.1 Each employee exposed or potentially exposed to ozone shall be apprised of its hazards, the consequences of overexposure, appropriate emergency procedures, proper conditions for safe use, and precautions to minimize exposure.

5.5.2 Each employee shall be informed as to the location of the information described in 5.5.1. This information shall be kept on file and shall be readily accessible to all employees at each area where exposure to ozone occurs.

5.6 *Work Practices:*

5.6.1 *Emergency Procedures*—Emergency procedures shall be established (see Table 1).

5.6.2 *Exhaust or Other Systems*—Engineering design of equipment and facilities shall include provisions to reduce exposure of employees to ozone through implementation of adequate ventilation or other methods. Where a local exhaust ventilation system is used, it shall be designed and maintained to prevent the accumulation or recirculation of ozone into the workroom. Suitable preventive or filtration systems may also be employed.

5.6.3 *General Maintenance*—Emphasis shall be placed upon periodic inspection and servicing of equipment.

5.6.4 *Engineering Controls*[6]—Industrial or commercial operations that are concerned with ozone have one or more methods available to control the exposure in the general work environment. The strategy of controlling the levels of ozone includes the following:

5.6.4.1 *Equipment Design*—Careful and proper design of equipment or appliances is the most practical method for controlling dangerous gaseous emissions, for example, the use of arc shields and automatic shutoff when ventilation fails, or other "fail safe" devices.

5.6.4.2 *Process Location*—Process location is an effective method for minimizing exposure to dangerous ozone levels in the work environment. For example, operations shall be performed in rooms with limited personnel access and adequate general area ventilation wherein the entire work area is constantly flushed with sufficient uncontaminated air to control airborne ozone concentrations below the limit.

5.6.4.3 *Positive Ventilation*—Positive ventilation, either mechanical or natural, is by far the most common engineering method for controlling ozone exposures. ANSI Z9.2 and Ref **(1)**[7] provide appropriate information on ventilation.

5.6.4.4 *Proper Operating and Maintenance Procedures*—Ozone-contaminated air can be minimized by compliance with proper operating procedures and careful supervision.

5.7 *Monitoring and Recordkeeping Requirements*—Workroom areas shall not be considered to have a known hazardous ozone exposure, where it has been determined, on the basis of an industrial hygiene survey that environmental levels of ozone are less than the TWA limit as described in 5.1. Records of these surveys, including the basis for concluding that air

[6] Previous engineering control standards have been published: "Requirements for Control of Ozone Emission from Devices Designed to Produce Ozone," *Electrical Bulletin*, No. 750 to 750 C, Canadian Standards Association; and "Proposed Test Procedure for Measurement of Ozone Concentration in Office Appliances and Business Equipment," UL Subject 114, Appendix A, Nov. 5, 1973.

[7] The boldface numbers in parentheses refer to the list of references at the end of this practice.

levels of ozone are below the TWA limit, shall be kept. The following requirements apply to ozone exposures:

5.7.1 Employers shall maintain records of environmental exposures of workers to ozone based upon the sampling and recording schedule as follows:

5.7.1.1 *Semiannual Requirements*—Representative samples shall be collected, at least semiannually, for reliable evaluations of employee exposure to ozone at all work operations. Sampling shall also be executed whenever the process, worksite, climate, or control changes occur that may significantly increase the concentrations of ozone. Samples shall be collected and evaluated for both time-weighted average and ceiling values.

5.7.1.2 *Thirty-Day Requirements*—The sampling regimen shall be conducted at least every 30 days for work areas or job activities for which the time-weighted average or ceiling concentrations are in excess of the environmental standard. Sampling, monitoring, and record-keeping provisions of the 30-day schedule shall be required until two consecutive 30-day sampling periods have indicated that the concentrations of ozone are within the limits specified in 5.1.

5.7.2 Records of all sampling schedules shall be maintained for 10 years, which include the sampling methods, analytical methods, type of respiratory protection in use (if applicable), and the concentrations of ozone in each work area. Records of employees' exposure shall also be maintained.

5.7.3 Each worker shall have access to the results of samplings and be informed of his occupational exposure.

5.7.4 Medical records shall include information on all pertinent, required medical examinations. These records shall be kept for at least 10 years following the last occupational exposure to ozone.

## 6. Physical and Chemical Properties

6.1 The physical and chemical properties of ozone are as follows (2):

| | |
|---|---|
| Molecular formula | $O_3$ |
| Boiling point (760 torr (101 kPa)) | −112°C (−169.6°F) |
| Melting point | −192°C (−313°F) |
| Solubility in water by weight at 20°C (68°F) | 0.003 g/litre (3 ppm) |
| Vapor density (air = 1) | 1.65 |
| Appearance and odor | colorless at all concentrations experienced in industry. Very pungent characteristic odor usually associated with electrical sparks. Detectable at a few parts per hundred million (pphm). |

6.2 *Reactivity*—Ozone spontaneously decomposes under all ordinary conditions so that it is not normally encountered except in the vicinity of where it was formed. The decomposition is speeded by solid nonsterile surfaces and by many chemical substances. Ozone is a powerful oxidizing agent and reacts with all oxidizable materials, both organic and inorganic. Some reaction products are highly explosive. There are no hazardous decomposition products.

## 7. Sampling for Ozone

7.1 *General Requirements:*

7.1.1 The measurement of air concentrations shall be within the worker's breathing zone and shall meet the criteria of this section in order to evaluate conformance with the standard.

7.1.2 Samples collected shall be representative of the individual worker's exposure.

7.1.3 Sampling data sheets shall include a log of the date and time of sample collection, sampling duration, volumetric flowrate of sampling, a description of the sampling location, and any other pertinent information.

7.2 *Breathing Zone Sampling:*

7.2.1 Breathing zone samples shall be collected as near as practicable to the worker's face without interfering with his freedom of movement, and shall characterize the exposure from each job or specific operation in each production area.

7.2.2 The sampler shall be operated at a flowrate of 0.2 to 1 litre/min. Sampling times may vary depending on whether the sample is taken to determine a ceiling concentration or TWA concentration.

7.2.2.1 Ceiling concentrations of ozone shall be measured during periods of maximum *expected* concentrations during the work shift. Each measurement should consist of a 10-min employee's breathing zone sample (or a series of consecutive samples totaling 10 min). A minimum of three measurements should be taken on one work shift; the highest of all measurements obtained is a good estimate of the employee's upper exposure for that shift.

7.2.2.2 TWA concentrations of ozone should be measured for the total duration of exposure (typically 8 h or more). If samples are taken at *random* intervals, biased results could occur if cycles in the operations were in phase with sampling periods. **(113, 114)**

7.2.3 Breathing zone samples shall be collected in sufficient numbers to express the variability of the work situation and to permit calculations of a time-weighted average exposure for every operation involving exposure to ozone. The frequency of evaluation is defined in 5.7.

## 8. Analytical Method for Ozone[8]

8.1 Analyze for ozone in accordance with Method D 2912.[9]

[8] Other methods to be considered are: *Federal Register*, Vol 36, No. 84, April 30, 1971, Part II, Part 410.11, Appendix D, p. 8195, or other equivalent methods.

[9] This method does not presently provide for standardization of the iodine solution. NIOSH Method P&CAM 153 does provide the necessary procedure.

**TABLE 1 Requirements for Respirator Usage at Concentrations of Ozone Above the Standard[A]**

| Condition | Permissible Respiratory Protection |
|---|---|
| Gas concentration: | |
| Equal to or less than 1 ppm | Any chemical cartridge respirator with organic vapor cartridge(s).<br>Any supplied air respirator. |
| Equal to or less than 5 ppm | A chemical cartridge respirator with a full facepiece and organic vapor cartridge(s).<br>A gas mask with a chin-style or front- or back-mounted organic vapor canister.<br>Any supplied-air respirator with a full facepiece, helmet, or hood.<br>Any self-contained breathing apparatus with a full facepiece. |
| Equal to or less than 10 ppm | A Type C supplied-air respirator with full facepiece operated in pressure-demand (positive pressure) mode or with a full facepiece, helmet, or hood operated in continuous-flow mode. |
| Greater than 10 ppm, or entry and escape from unknown concentrations | Self-contained breathing apparatus. A full facepiece operated in pressure-demand (positive-pressure) mode.<br>A combination respirator which includes a Type C supplied-air respirator with a full facepiece operated in pressure-demand (positive-pressure) mode or continuous-flow mode and an auxilliary self-contained air supply operated in the pressure-demand (positive-pressure) mode. |
| Fire fighting | Self-contained breathing apparatus with a full facepiece operated in pressure-demand (positive-pressure) mode. |
| Escape | Any gas mask providing protection against organic vapors. Any escape self-contained breathing apparatus. |

[A] *Federal Register*, Vol 40, No. 196, Oct. 8, 1975.

# APPENDIXES

## X1. BIOLOGICAL EFFECTS OF EXPOSURE TO OZONE

### X1.1 Threshold Limit Values

X1.1.1 The recommended ACGIH value is 0.1 ppm (0.2 mg/m$^3$) in air.

### X1.2 Toxicology

X1.2.1 In discussing the toxicity of ozone, articles relating to ozone exposure during arc welding have not been included herein because of the potential for synergistic effects resulting from heavy metal oxide fumes. Furthermore, responses resulting from exposure to mixtures of ozone and other gases have been treated similarly. Although the information indicated in X1.3 through X1.4 represents a good portion of the literature on ozone toxicity, it is by no means complete. Several good review articles (**5, 9, 19, 20, 30, 86, 115, 123**) are available for further study.

### X1.3 Human Exposure

X1.3.1 *Symptomatology*:

X1.3.1.1 Exposure of a single human subject to 1.5 to 2.0 ppm (2.9 to 3.9 mg/m$^3$) for 2 h was carried out by Griswold et al (**122**). Symptomatology included dry throat and mouth, lessening of ability to concentrate, substernal constriction and chest pains. No eye irritation or nausea was noted. The subject also expressed the following symptoms: a marked effect on coordination and articulation, hands and feet seem to "fall asleep," loss of appetite, food did not taste good, a sleepless night after exposure, cough/clear mucous after 2 to 3 days and continuing for 2 weeks and fatigue for about 2 weeks. Spirometry indicated a 13 % decrement in total vital capacity which returned to normal after 22 h and a decrease of 16.8 % in forced expiratory volume at 3 s which was still 7 % below normal after 22 days.

X1.3.1.2 According to Nasr (**86**), symptoms of acute ozone poisoning included severe headache, dizziness, burning sensation in the eyes and throat, acrid taste and smell, shortness of breath, choking sensation, substernal pressure and nonproductive cough.

X1.3.2 *Pulmonary Function*:

X1.3.2.1 *Definitions*:

(*a*) FEV—forced expiratory volume for a given time frame. This is sometimes referred to as timed vital capacity. Thus, $FEV_{1.0}$ is the volume expired in 1 s.

(*b*) FVC—forced vital capacity. This is the maximum volume of air that can be expired after a maximum inspiration.

(*c*) MMFR—midmaximal expiratory flow rate. This is the average flow over the mid 50 % of the FVC curve. It may also be referred to as $FEF_{25-50\%vc}$ (forced expiratory flow).

(*d*) $\dot{V}_{60\%vc}$—flow rate of expired air at 50 % vital capacity. Other points on the vital capacity curve may also be designated, for example, $\dot{V}_{25\%vc}$.

X1.3.2.2 Two out of four human male subjects demonstrated small but significant increases in airways resistance after exposure to 0.1 ppm (0.2 mg/m$^3$) of ozone for 5 min, while all four showed this effect at 1 ppm (2.0 mg/m$^3$). The authors consider the effect at the lower level no more than would be produced by inhaling the smoke from a single cigarette (**94**).

X1.3.2.3 In a heretofore unpublished study, VonNieding and Wagner (**124**) studied the effects of 2-h exposure of healthy West German men to 0.1 ppm (0.2 mg/m$^3$) of ozone with intermittent exercise. Most respiratory function parameters were unchanged after ozone exposure; however, airway resistance increased and oxygen pressure of "arterialized" capillary blood decreased. The latter may reflect a disruption of the blood oxygenation process or merely small changes in peripheral blood circulation. This study requires confirmation.

X1.3.2.4 DeLucia and Adams (**125**), under a variety of exercise conditions, exposed six healthy nonsmoking males to 0.15 and 0.30 ppm (0.30 and 0.59 mg/m$^3$) ozone for 1 h. Generally, maximum oxygen intake, ventilation volume, vital capacity, $FEV_{1.0}$, and MMFR were unaffected by ozone exposure with the exception of the most severe protocol (0.3 ppm at 65 % maximum oxygen intake) after which the last two parameters showed decrements of 14 and 21 %, respectively. In addition, this protocol also resulted in shallower breathing, a 25 % increase in respiratory frequency, a 30 % decrease in mean tidal volume and the usual subjective symptomatology.

X1.3.2.5 Exposure of six male volunteers to 0.2 and 0.5 ppm (0.4 and 1.0 mg/m$^3$) ozone, 3 h per day for 12 weeks was carried out by Bennett (**126**). As a result of this study, Bennett reported that there was no increase in upper respiratory infection of exposed volunteers versus controls, but at the higher level of exposure, a decrement in $FEV_{1.0}$ was statistically significant. This observation in combination with an insignificant change in FVC is suggestive of obstruction in the terminal bronchi and bronchioles, according to the author.

X1.3.2.6 In an effort to demonstrate "adaptation" to ozone, Hackney and his coworkers (**127**) exposed matched groups of four subjects from the Los Angeles area and four from Canada (where ambient ozone is less concentrated), to 0.37 ppm (0.74 mg/m$^3$) ozone for 2 h with intermittent exercise. These workers observed that under the same exposure protocol, the Canadians demonstrated statistically significant decrements in FVC, total lung capacity (nitrogen washout) $FEV_{1.0}$. Furthermore, while both groups dem-

onstrated decreased erythrocyte acetylcholinesterase activity, a significant increase in cell fragility was noted in the Canadian group relative to the Los Angeles group. The authors claim an adaptive response in the latter.

X1.3.2.7 Human exposure under mild exercise conditions to 0.37 to 0.75 ppm (0.73 to 1.5 mg/m$^3$) ozone is reported not to effect total lung capacity, but residual volume was increased which suggests early effects in the small airways. The author concludes that 0.37 ppm (0.75 mg/m$^3$) ozone exposure for 2 h is unacceptably high if impairment of pulmonary function is to be avoided **(74)**. Another study of human exposure to 0.9 ppm (1.8 mg/m$^3$) for 5 min during exercise reports a significant decrease in specific airways conductance **(75)**.

X1.3.2.8 Silverman et al **(128)** studied exposure of 28 subjects to ozone for 2 h at concentrations ranging from 0.37 to 0.75 ppm (0.73 to 1.5 mg/m$^3$) and included intermittent exercise in his experiment. The usual symptoms were observed (dry nose and throat, cough, chest discomfort, and mild nausea) to increase with dose. Comparison of pre- and post-exposure (2 h) maximum expiratory flow-volume curves failed to demonstrate any significant effect of exposure at 0.37 and 0.5 ppm. However, under mild exercise, exposure at the 0.37 ppm resulted in a statistically significant decrease in flow at 50 % and 25 % of vital capacity ($\dot{V}_{50\%vc}$ and $\dot{V}_{25\%vc}$), respectively. The FVC at 0.37 ppm was unaffected but $FEV_{1.0}$ was decreased slightly at that same level. Both measurements were made under exercise conditions.

X1.3.2.9 Folinsbee et al **(129)** exposed 28 randomly selected human volunteers to 0.37, 0.50, or 0.75 ppm (0.73, 0.98 or 1.5 mg/m$^3$) ozone for 2 h under both resting and intermittent heavy exercise. Major responses included increased respiratory frequency and decreased tital volume but these changes were noticed only after exercise. FVC was reduced in subjects exposed to 0.75 ppm (1.5 mg/m$^3$) at rest and concentrations greater than 0.5 ppm (0.98 mg/m$^3$) after exercise. Expiratory flow at $V_{50\%vc}$ was reduced in all cases except 0.37 ppm under resting conditions. The authors conclude that the observed effects are most probably due to bronchoconstriction (airway narrowing).

X1.3.2.10 Four healthy male subjects and four males having a history of respiratory problems were exposed to various concentrations of ozone and an extensive series of pulmonary function tests were performed as responses. One week exposure to 0.5 ppm (1.0 mg/m$^3$) ozone produced minimal or no response in normal subjects, but exposure of the group with respiratory problems to 0.37 ppm (0.73 mg/m$^3$) ozone resulted in observations of definite responses as measured by pulmonary function tests. These responses became more obvious at 0.5 ppm (0.98 mg/m$^3$) but disappeared at 0.25 ppm (0.49 mg/m$^3$) **(102)**.

X1.3.2.11 Another study by the same authors makes use of the data indicated above and additional data on 13 human subjects to calculate dose – response curves for ozone exposure. Using $FEV_{1.0}$, delta nitrogen, erythrocyte fragility, and acetylcholinesterase level as responses, it is reported that one can extrapolate "no effect" levels of about 0.15 ppm (0.29 mg/m$^3$) for maximum responses to about 0.25 ppm (0.49 mg/m$^3$) for mean responses **(104)**. Protocol for both of the above studies is discussed in a prior publication **(105)**.

X1.3.2.12 In another study, Hackney et al **(130)** exposed Los Angeles residents and new arrivals to 0.4 ppm (0.8 mg/m$^3$) for 2 h at 31°C and reported mean respiratory responses essentially unchanged in residents but significantly changed in new arrivals. These changes included decrements in FVC, $FEV_{1.0}$, and MMFR. The MMFR differences between residents and nonresidents were most pronounced. Increased erythrocyte fragility, reduced erythrocyte acetylcholinesterase activity and increased pentose shunt enzyme activity were demonstrable with both exposed groups, but only new arrivals showed increased lactate dehydrogenase activity. In addition, the latter group also reported respiratory symptoms more frequently, again suggesting adaptation to ozone exposure.

X1.3.2.13 In a heretofore unpublished study of 22 nonsmoking male subjects exposed to 0.4 ppm (0.8 mg/m$^3$) for 4 h, Rummo and coworkers **(131)** included two 15-min exercise periods and measured changes in pulmonary function and heart rate. Significant decreases in flow parameters were observed including 14 to 19 % decreases in MMFR, $\dot{V}_{25-50\%vc}$, and peak flow. In addition, 7 to 11 % decreases in $FEV_{1.0}$ and FVC were also observed. The usual subjective symptomatology was evident including dyspnea, but no significant effect on heart rate was measured. Residual volume (RV), and functional residual capacity (FRC) were not affected in a significant manner under these conditions.

X1.3.2.14 In another study demonstrating human adaptation, Parent **(132)** demonstrated that preexposure to 0.4 ppm (0.8 mg/m$^3$) of ozone produced less pronounced decrements in pulmonary function tests when individuals were exposed to 0.6 ppm (1.2 mg/m$^3$) than those not previously exposed. A preexposure of 0.2 ppm (0.4 mg/m$^3$) ozone, however, did not afford protection against the higher level of exposure.

X1.3.2.15 In a study of 20 adult smokers and nonsmokers exposed to 0.5 ppm (0.98 mg/m$^3$) ozone for 6 h with intermittent exercise, Kerr et al **(133)** observed that smokers were less susceptible to subjective responses than nonsmokers. Cough was problematic in only one out of ten smokers but seven out of ten nonsmokers. Chest discomfort was observed in four; and nine out of ten for the respective groups. Pulmonary function testing showed significant changes in FVC, $FEV_{3.0}$, specific airway conductance and pulmonary resistance for nonsmokers, but changes in these parameters were not obvious for smokers.

X1.3.2.16 Human exposure to 0.75 ppm (1.5 mg/m$^3$) ozone for 2 h resulted in a decrease in the transpulmonary pressure maximum and $\dot{V}_{max}$ at 50 % vital capacity and increased pulmonary resistance. In addition, cough, pharyngitis, and dyspnea were observed in test subjects **(77)**.

X1.3.2.17 Again demonstrating an adaptive response, Hackney et al **(134)** exposed a group of six

hyperactive subjects to 0.5 ppm (1.0 mg/m$^3$) ozone for 2 h per day for 4 successive days. These investigators reported adverse responses which were maximal on day 1 or 2 for FVC, $FEV_{1.0}$, $\Delta N_2$, respiratory resistance, and symptomatology but had returned to normal on day 4, while $\dot{V}_{25-50\%vc}$ remained slightly lower than controls. These investigators indicate that the results are consistant with an adaptive response.

X1.3.2.18 Using a similar protocol as in the Rummo study **(131)**, 20 nonsmoking males were exposed to 0.6 ppm (1.2 mg/m$^3$) ozone for 2 h (B. Ketcham, et al) **(135)**. The MMFR, peak expiratory flow rate (PEFR), and $\dot{V}_{25-50\%vc}$ were significantly reduced after both 1 and 2 h of exposure as was the FVC, $FEV_1$, and the ratio of $FEV_{1.0}$ to FVC. Inspiration capacity was also decreased. The authors suggest that MMFR is the most sensitive and reliable flow-rate parameter to measure the effects of ozone. This parameter was reduced by 26.4 % after 1 h and 35.1 % after 2 h of exposure. The usual symptomatology was noted.

X1.3.2.19 Three nonsmoking healthy human males were exposed for 90 min to 0.6 to 0.8 ppm (1.2 to 1.6 mg/m$^3$), and pulmonary function was measured using spirometry and plethysmography. Although symptomatic complaints were noted, no changes in vital capacity, flow rate, or specific conductance were reported **(96)**.

X1.3.2.20 Under resting conditions Young et al **(8)** exposed 11 human subjects, through a mouthpiece, to 0.6 to 0.8 ppm (1.2 to 1.6 mg/m$^3$) ozone for 2 h and measured changes in pulmonary function as a result of this exposure. The following observations were made as a result of ozone exposure: diffusion capacity (steady state) of carbon monoxide was significantly reduced but returned to normal at 4 h post exposure; $FEV_{0.75}$ and FVC fell by about 10 % while the MMFR decreased but 15 % (the latter was not considered statistically significant); gas mixing efficiency (helium dilution) and dynamic compliance both were unaffected. The authors conclude that, edema and fluid build up in the alveolar region appears to be the most logical explanation for the decrements in diffusion capacity and, further, that other parameters are affected by the subjects inability to mount a maximal inspiration effort after ozone exposure.

X1.3.2.21 Hallett **(136)** exposed 11 volunteers, smokers and nonsmokers, to from 1 to 3 ppm (2 to 6 mg/m$^3$) ozone for up to 30 min. Analytical uncertainties cast considerable doubt as to the exact exposure level of ozone. Decrements in FVC, $FEV_{1.0}$, maximum expiratory flow rate, diffusion capacity and other pulmonary function parameters were observed in the range of 10 to 20 %. The usual symptomatology was also observed.

X1.3.2.22 In the periods described in X2.10, Linn and coworkers **(137)** studied respiratory function of office workers in Los Angeles and San Francisco to determine if there was any difference in the existence or development of chronic obstructive pulmonary disease between the two test groups. Measurement of forced expiratory parameters and single breath nitrogen inhalation failed to result in any obvious differences in the two test groups. Subjective symptoms in women appeared more pronounced in the Los Angeles group.

X1.3.2.23 In a pulmonary function study of 181 male general aviation pilots, Lategola et al **(138)** were able to show moderate degrees of respiratory impairment in 12.7 % of the population studied. Although all spirometric parameters were measured, $FEV_{1.0}$ and $\dot{V}_{25-50\%vc}$ appeared most sensitive. Smoking habits and age were considered in assessing these documents.

X1.3.2.24 Folinsbee et al **(212)** exposed fourteen nonsmoking males to 0.5 ppm (1.0 mg/m$^3$) ozone with and without exercise and at various temperatures. These investigators were able to demonstrate that decrements in vital capacity were related to decreased maximum inspiration. The reduced vital capacity and maximum expiratory flow parameters were most obvious immediately after exercise. Flow parameters were not obviously affected by temperature, but decreases in vital capacity were found at higher temperatures. The authors conclude that decreases in flow parameters are probably due to increased large and small airway resistance as a result of reflex bronchoconstriction secondary to tracheobronchial irritation.

X1.3.2.25 Studying the effect of ozone on ability to do work, Folinsbee et al **(226)** exposed 13 adult males to 0.75 ppm (1.5 mg/m$^3$) ozone for 2 h with alternating periods of exercise and rest (15-min periods). These authors compared various parameters during ozone exposure and exposure to filtered air and made the following observations following ozone exposure: oxygen uptake decreased by 15 %; maximum work decreased by 10 %; maximum ventilation decreased by 16 % and maximum heart rate dropped 6 %. Following the highest common work load, respiration rate increased by 45 % and vital volume fell by 29 % following ozone exposure. Decreases in vital capacity and $FEV_{1.0}$ were also noted. The authors concluded that the reduced oxygen uptake was related to limitation of ventilatory capability due to respiratory discomfort, but did not dismiss pulmonary edema as a probable cause of the effects noted.

X1.3.2.26 Bell and coworkers **(239)** exposed four human subjects who were sensitive to respiratory irritation to 0.37 ppm (0.73 mg/m$^3$) ozone, 2 h per day for 2 days with intermittent exercise and found a 4.7 % decrement $FEV_{1.0}$, FVC, and gas distribution ($\Delta N_2$) were unaffected by this ozone level relative to sham exposures. The authors suggest that TLVs for sulfur dioxide and ozone should be revised to account for the interactive effects.

X1.3.2.27 In a study of fourteen athletes exposed for 20 min to 0.3 ppm (0.6 mg/m$^3$) or less under heavy exercise, Veld and Zeedijk **(225)** failed to demonstrate any effects of ozone on pulmonary or heart function.

X1.3.3 *Biochemical Effects*:

X1.3.3.1 Six nonsmoking healthy male subjects were exposed to 0.15 to 0.3 ppm (0.30 to 0.6 mg/m$^3$) ozone for 1 h under conditions which included heavy

exercise; and blood biochemical parameters were studied by DeLucia and Adams **(125)**. Assays of lysed red blood cells for glucose-6-phosphate dehydrogenase (G6PD) 6-phosphogluconate dehydrogenase (6PGD); glutathione reductase, nonprotein sulfhydryl content (whole blood) failed to show significant differences from preexposure values.

X1.3.3.2 Short term exposure (2¾ h) of young adult male subjects to 0.5 ppm (1 mg/m$^3$) ozone was investigated by Buckely et al **(76)**. Erythrocyte membrane fragility, G-6-PD, lactate dehydrogenase (LDH) increased while erythrocyte acetylcholinesterase and reduced glutathione levels decreased as a result of exposure and the effects were still detectable 2 weeks post exposure. The authors suggest that most of the effects are related to maintenance of the erythrocyte redox levels through the glutathione conversion described above. Acetylcholinesterase levels are explained on the basis of reaction of a sulfhydryl function necessary for activity. This clearly indicates passage of ozone or some metabolite through the blood-air barrier **(76)**.

X1.3.3.3 Brinkman and Lamberts **(18)** studied oxygen consumption in tied-off digits of human volunteers who had been exposed to 1 ppm (2 mg/m$^3$) ozone for 10 min and found that the rate of oxyhemoglobin deoxygenation decreased in exposed individuals. They concluded that deactivation of relevant enzymes by ozone or its reactants was responsible and went further to label ozone as a radiomimetric gas.

X1.3.3.4 A theoretical study by Calabrese et al **(238)** relates reduced glutathione levels to erythrocyte membrane stability and suggests that individuals who are deficient in glucose-6-phosphate dehydrogenase may be at high risk relative to acute hemolysis when exposed to levels of ozone as low as 0.5 ppm (1.0 mg/m$^3$).

X1.3.4 *Cytogenetic Effects*:

X1.3.4.1 Using pre-exposure levels for self controls, two humans were exposed to 0.5 ppm (1.0 mg/m$^3$) ozone for 6 h and chromosomal aberrations from cultured circulating lymphocytes at metaphase were investigated **(32)** immediately after exposure, 2 weeks post-exposure and 6 weeks post-exposure. Except for one instance, no chromosome-type aberrations or chromatid exchanges were observed in circulating lymphocytes. Most lesions were classified as single strand breaks. Chromatid deletions were observed prior to treatment but definitely increased after exposure, even 2 weeks thereafter. The author points out that these results are less severe than Zelac's **(25)** and "the assumption that low-level chronic doses and short-term high concentration doses are related to each other on a linear scale is, at present, without support." He further states that we may still be at risk to effects of ozone **(32)**.

X1.3.4.2 McKenzie and coworkers **(139)** exposed 30 male nonsmoking human subjects to a concentration of 0.4 ppm (0.8 mg/m$^3$) ozone for 4 h. All subjects rested during exposure with the exception of two 15-min exercise periods. Using 100 metaphase spreads per subject, chromosomal aberrations were scored on cultured circulating lymphocytes from blood samples taken at pre-exposure, immediate post-exposure, 3 days post-exposure, 2 weeks post-exposure, and 4 weeks post-exposure. Chromosome number, breaks, gaps, deletions, fragments, rings, dicentrics, translocations, inversions, triradials and quadriradials were scored, and Q banding was used for identification of specific chromosomes and regions. The results of these studies are indicated as follows:

*(a) Percent of cells with 46 chromosomes:*

| | |
|---|---|
| Pre-exposure | 93.0 % |
| Post-exposure | 93.6 % |
| 3 days | 91.7 % |
| 2 weeks | 94.5 % |
| 4 weeks | 94.2 % |

*(b) Mean cells per 100 with breaks:*

| | |
|---|---|
| Pre-exposure | 0.96 % |
| Post-exposure | 0.85 % |
| 3 days | 1.00 % |
| 2 weeks | 0.88 % |
| 4 weeks | 0.81 % |

*(c) Mean cells per 100 with gaps:*

| | |
|---|---|
| Pre-exposure | 1.35 % |
| Post-exposure | 0.96 % |
| 3 days | 1.35 % |
| 2 weeks | 0.81 % |
| 4 weeks | 0.77 % |

The authors conclude from this data and the data relating to complex aberrations that there was no statistical relationship between ozone treatment under these conditions and chromosomal aberrations. This study was based on the examination of 13 000 cells.

X1.3.5 *Other Effects*:

X1.3.5.1 Performance on intelligence tests of 99 university students was measured in response to ozone exposure in the range of 0.2 to 0.3 ppm (0.4 to 0.6 mg/m$^3$). After 70-min exposure periods, Hore and Gibson **(140)** failed to observe any effects on the results of these tests after ozone exposure.

X1.3.5.2 In a study of human exposure (22 males, 6 females) from 0.2 ppm to 0.5 ppm (0.4 to 1.0 mg/m$^3$) ozone for 3 h, Lagerwerff **(7)** observed decrements in visual acuity, night vision, and increased convergence. Increases in peripheral vision were also observed after exposure.

X1.3.5.3 Pederson and his co-workers **(141)** exposed 13 male subjects to 0.5 ppm (1.0 mg/m$^3$) ozone for 4 to 5 h and failed to find any effect on peripheral vision when performing multiple divided tasks.

X1.3.5.4 The olfactory threshold for ozone in human subjects is reported by Feldman **(142)** to be 0.0075 ppm (0.015 mg/m$^3$).

**X1.4 Animal Exposure**

X1.4.1 *Morphological Changes Greater than 1 ppm* (2.0 mg/m$^3$):

X1.4.1.1 Rats exposed to 4 ppm (7.8 mg/m$^3$) ozone for 4 h showed lung edema and increased glycogen depletion **(34)**.

X1.4.1.2 Rats exposed to 3 ppm (5.9 mg/m$^3$)

ozone for 4 h demonstrated a doubling of alveolar macrophages 12 h after exposure. In addition to the normal macrophage population, approximately an equal number of macrophages contained larger granular cytoplasmic inclusions resulting, apparently, from extensive phagocytic activity. No ultrastructural damage to pulmonary alveolar macrophages was in evidence **(46)**. In addition, microscopic investigation revealed that the volume fraction of nonparenchymal tissue was larger than controls and that the lumina of large vessels had decreased immediately after exposure. Twelve hours later the former remained greater than control values, but the latter returned to normal. Also, the thickness of the air-blood barrier had increased as a result of intracellular edema with some recovery 12 h after insult **(47)**. Further, a histologic and ultrastructural study revealed necrosis of bronchiolar epithelium and membranous pneumonocytes and a gradation of epithelial damage in acini, the most severe occurring centrally **(48)**.

X1.4.1.3 Dogs exposed to 1 to 3 ppm (2.0 to 5.9 $mg/m^3$) ozone, 8 to 24 h per day for 18 months produced the following responses: fibrous elements deposited increasingly with increased dose but only rarely at the lowest exposure; at higher exposures: thickening of the terminal and respiratory bronchiolar walls, infiltration by lymphocytes, plasma cells and fibroblasts that formed peribronchiolar collars, connective tissue obstruction, increase in mucous forming cells and squamous metaplasia of columnar and cuboidal cells of the bronchial epithelium with occasional hyperplasia. The authors noted that the macrophage population was lower in animals exposed to 1 ppm/24 h (2 $mg/m^3$) daily than those exposed to the same dose (concentration multiplied by time) at 3 ppm/h (5.9 $mg/m^3$) daily. When continuously exposed to 1 ppm, connective tissue elements where more prominent, epithelial hyperplasia was observed sporatically and thickening of the alveolar septa was obvious. At 3 ppm for various exposure periods, the effects seen were much more severe **(36)**.

X1.4.1.4 Squirrel monkeys exposed for 3 h to 3 ppm (5.9 $mg/m^3$) ozone showed degeneration of epithelial lining and depletion in some foci. In addition, the thickness of the blood air barrier had increased and was still greater than normal 7 days after exposure **(33)**.

X1.4.1.5 Mice exposed to 3 ppm (5.9 $mg/m^3$) ozone for 15 h or 1 ppm (2.0 $mg/m^3$) 10 min daily for 90 days, showed pulmonary congestion, dilated heart cavities, microvesicular stenosis of the liver, marked capillary vasodilation in the kidneys, and slight changes in the pancreas **(44)**.

X1.4.1.6 Tumor-resistant mice exposed to 2.5 ppm (4.9 $mg/m^3$), 2 h daily for 120 days, and serially sacrificed, showed progressive metaplasia of squamoid epithelium, abnormal cilia and micronodular hyperplasia of Clara-like cells. The tracheal and bronchial changes appeared reversible 120 days after the final insult but effects on Clara-like cells remained unchanged **(45)**.

X1.4.1.7 A cytologic study of beagle dogs exposed to 3 ppm (5.9 $mg/m^3$) ozone 8 h daily for 18 months resulted in dilation of endoplasmic reticulum of Type II alveolar epithelial cells in the proximal alveoli, substantial reduction in the lamellar membranes in lamellar bodies of Type II cells, and paracrystalline arrays of cytoplasmic membranes in endothelial cells. The author suggests that these observations are consistent with a sequestering of protein in the endoplasmic reticulum **(49)**.

X1.4.1.8 Another study on tumor-resistant mice exposed to 4.5 ppm (8.8 $mg/m^3$) ozone, 2 h every third day for 75 days and serially sacrificed demonstrated progressive edema, congestion, scattered hemorrhage, bronchiectasis, bronchopneumonia, and microabscesses **(51)**.

X1.4.1.9 Mice exposed to 2.5 ppm (4.9 $mg/m^3$) ozone for 2-h periods, 5 days per week for 5 weeks demonstrated significant edema, confluent necrotic bronchopneumonia, and a typical broncho-alveolar adenomatous change **(92)**.

X1.4.1.10 Tumor-resistant mice exposed to 4.5 ppm (8.9 $mg/m^3$) for 2 h every third day for 75 days were reported to demonstrate epithelial changes, hyperplasia, squamous metaplasia, and pulmonary adenomas. The author concludes "... even low-level exposure over extended periods of time may represent unrealized hazards" **(93)**.

X1.4.1.11 Exposure of rats and guinea pigs to 1 and 2 ppm (2.0 and 3.9 $mg/m^3$) ozone for 2 and 7 days was carried out by Cavender et al **(217)**. Resulting lesions were primarily confined to the terminal bronchioles and proximal alveoli and included bronchiolar epithelial hypertrophy and hyperplasia, alveolitis, thickening of the alveolar wall, and accumulation of macrophages in the proximal alveolae. Some pulmonary edema was also noted and a marked loss of bronchial cilia was observed at 2 ppm (3.9 $mg/m^3$). At 1 ppm (2.0 $mg/m^3$) the lesions became less severe at 7 days while the severity was the same at the higher concentrations.

X1.4.1.12 Kruysse and Feron **(215)** exposed albino rats (SPF) to ozone under acute (5 to 15 ppm; 9.8 to 29.4 $mg/m^3$, 4 h) and subacute (0.06, 0.3 and 1.2 ppm; 0.12, 0.59 and 2.4 $mg/m^3$, 6 h per day, 5 days per week for 4 weeks). They determined the 4 h $LC_{50}$ to be 8 ppm but could not find treatment-related effects in rats exposed to the two lower ozone concentrations under subacute exposure conditions. The highest level of exposure (1.2 ppm, 2.4 $mg/m^3$) did, however, produce the following changes in the bronchiolar-alveolar regions: hypertrophy, hyperplasia and metaplasia of bronchiole-alveolar epithelium and infiltration of inflammatory cells and fibroblast proliferation in the underlying interstitium. The authors conclude that up to 0.3 ppm (0.59 $mg/m^3$) ozone is a "no-toxic-effect level."

X1.4.1.13 In a study of the effect of ozone on bronchial reactivity to inhaled histamine diphosphate aerosol, a known bronchioconstrictor, 5 mongrel dogs were anesthetized and mechanically ventilated by Lee et al **(213)**. Pretreatment with ozone (0.7 to 1.2 ppm, 1.4 to 2.4 $mg/m^3$, 2 h) followed by histidine, produced increases in pulmonary resistance over animals treated only with histidine. This effect peaked at 1 day post ozone exposure. Prior inhalation of

atropine sulfate, a bronchodilator, decreased the effects with and without ozone as did cooling of both cervical vagus nerves. Although the results are not considered definitive, the production of bronchoconstriction by ozone appears to involve the vagal cholinergic pathway.

X1.4.1.14 Chronic exposure of rabbits to 15 to 50 ppm (29.4 to 98 mg/m$^3$) ozone for 49 weeks (1 h per week) and hamsters to 1 ppm (2 mg/m$^3$) for 433 days (268, 6-h exposures) was carried out by Gross et al **(224)**. Chronic pneumonitis and contraction of the alveolar septa were the major effects reported. The effects are thought to represent a pre-emphysematous condition.

X1.4.1.15 Stokinger **(237)** reports 4-h $LC_{50}$ values of 3.8, 4.8, and 10.5 ppm (7.4, 9.4 and 20.6 mg/m$^3$) for albino mice, albino rats, and male hamsters, respectively. He further demonstrated that the product of concentration multiplied by time was linear in the range of ozone concentration from 2.5 to 5.0 ppm (4.9 to 9.8 mg/m$^3$). He was also able to show that vitamin C given prior to ozone exposure exerted a protective effect, older mice were less sensitive to ozone, pre-exposure produced a tolerance development and physical exercise potentiated the effects of ozone.

X1.4.1.16 Stokinger et al **(236)** studied the effect of 1 ppm (2 mg/m$^3$) ozone on mortality in rats, mice and hamsters. Using a motor-driven activity cage, these investigators were able to show that rats can tolerate this ozone concentration for over 200 6-h exposures when not exercised but when activity cages were used, high mortality occurred within the first 6 h. Similar results were found in mice but hamsters were found to be resistant to the effects of ozone. Prior exposure without exercise followed by exposure with exercise did not produce high mortality thereby demonstrating tolerance as a result of as little as 6-h pre-exposure to ozone.

X1.4.1.17 Matsumura **(231)** studied the effect of ozone exposure on sensitization to antigens administered to guinea pigs by various routes. Repeated pre-exposures to 5 ppm (9.8 mg/m$^3$) ozone for 30 min produce an enhanced sensitization when the antigens were administered by inhalation but not by other routes. A subsequent study **(232)** using radioactive egg albumin, did, however, demonstrate increased antigen absorption when guinea pigs were pre-treated with 8 ppm (15.7 mg/m$^3$) ozone for 30 min. When pre-treated with 2 ppm ozone (3.9 mg/m$^3$) or more for 30 min, anaphylatic dyspnea was observed **(233)** to be severe when a mixture of egg and serum bovine albumins was injected intraperitoneally then inhaled prior to ozone exposure.

X1.4.2 *Morphological Changes of 1 ppm (2 mg/m$^3$) or Less*:

X1.4.2.1 Exposure of cats (4.5 h) and rabbits (3 h) to a range of ozone concentrations (0.25 to 1.0 ppm (0.5 to 2 mg/m$^3$)) produced considerable desquamation in airways measuring from 2.7 to 0.15 mm at ozone concentrations ranging from 0.25 to 1.0 ppm for 3 to 4.5 h. Ciliated cells were most affected and generally were vacuolated and contained swollen mitochondria. Observations in the alveolar region included intraalveolar hemorrhage and accumulations of inflammatory cells. At both 0.5 and 0.26 ppm (1.0 mg/m$^3$ and 0.5 mg/m$^3$), Type 1 cells were intact but showed focal swelling of the cytoplasm. The effects observed were generally more severe with increasing concentration. In addition, rabbits exhibited a decreased pulmonary volume to pressure ratio which was considerably less pronounced at the lower level of exposure **(55)**.

X1.4.2.2 Another study by the same author involving exposure of cats to 0.26, 0.5, and 1 ppm (0.5, 1.0, and 2.0 mg/m$^3$) ozone from 4.6 to 6.6 h generally produced cellular changes proportional to the concentration of ozone employed. These included cytoplasmic vacuolization of ciliated cells, swelling or denudation of cytoplasm of Type 1 cells, swelling or breakage of capillary endothelium, and lysis of red blood cells, all of which occurred at the three concentrations indicated. Desquamation of ciliated epithelium occurred only at the two highest concentrations indicated. Further, diffusion capacity was decreased in all exposure groups while pulmonary resistance was increased in only a few animals at the lower concentration level **(56)**.

X1.4.2.3 A study in rats exposed to 0.2 ppm (0.4 mg/m$^3$) ozone for 30 days resulted in no change in lung weight but a 16 % increase in lung volume as a result of overdistended lungs at high transpulmonary pressure. This observation is thought to be a result of decreased lung elasticity **(54)**.

X1.4.2.4 Mice exposed to 0.1 to 0.13 ppm (0.2 to 0.26 mg/m$^3$) ozone for 5 h reportedly produced detectable levels of edema and cytotoxic damage to lymphoid cells within the lung lumen, particularly to pulmonary alveolar macrophages **(91)**.

X1.4.2.5 Schwartz and coworkers **(145)** exposed rats to ozone (0.2, 0.5, and 0.8 ppm) (0.39, 0.96, and 1.57 mg/m$^3$) continuously and intermittently (8 h/day) for 7 days and investigated the effect of these exposures on lung morphology. Although changes in the trachea and bronchi were not very obvious at the lower concentration, the two higher levels resulted in the presence of granular debris on the epithelial surface of the vessels particularly at bifurcations and foci of cilia of reduced density, variable diameter and length. In the terminal bronchiolar region, changes were most evident in the distal region. Variations in surface characteristics of Clara cells seemed to be the most sensititive indicator of damage. These changes included reduction in height and cytoplasmic projections and increased granularity. At 0.8 ppm eosinophilic granular debris was also in evidence. Again, foci of cilia having variable length and population were in evidence, although at 0.2 ppm the changes were more subtle (swelling of cilia and some shortening).

(*a*) The most extensive damage was observed to occur in the proximal alveoli and interalveolar septa of alveolar ducts. Alveolar ducts were "paved" with macrophages and sporatic neutrophils at the higher concentrations. At 0.2 ppm this "paving" was not observed, but a maximum of 2 to 3 macrophages could be seen in the individual alveolus. This "paving," mainly observed in the proximal alveolar duct, consisted of clusters of infiltrating alveolar cells hav-