III. BIOLOGIC EFFECTS OF EXPOSURE

Definitions

An examination of the technical literature on nitric acid shows a lack of consistency in the interpretation and use of such terms as fumes, gases, vapors, and mists. For clarification, the following definitions, as published by the American National Standards Institute, [2] are offered:

"Fumes: Solid particles generated by condensation from the gaseous state, generally after volatilization from molten metals, etc, and often accompanied by a chemical reaction such as oxidation. Fumes flocculate and sometimes coalesce.

"Mists: Suspended liquid droplets generated by condensation from the gaseous to liquid state or by breaking up a liquid into a dispersed state, as by splashing, foaming, and atomizing.

"Vapors: The gaseous form of substances which are normally in the solid or liquid state and which can be changed to these states either by increasing the pressure or decreasing the temperature alone. Vapors diffuse.

"Gases: Normally formless fluids which occupy the space of enclosure and which can be changed to the liquid or solid state only by the combined effect of increased pressure and decreased temperature. Gases diffuse."

The term "aerosol", frequently used in the experimental literature, refers to "any system of liquid droplets or solid particles dispersed in air, of fine enough particle size, and consequent low settling velocity, to possess considerable stability as an aerial suspension." [3] As such, "fumes" and "mists" must be considered subsets of this category.

Extent of Exposure

Although the earliest mention of nitric acid dates back to the 8th century, from at least the 18th century until World War I manufacture of nitric acid was primarily accomplished by distillation of potassium or sodium nitrate with sulfuric acid. [4] In the last several decades, the distillation process has been essentially replaced by the ammonia oxidation process. With the aid of a platinum catalyst, ammonia is oxidized with air to yield nitric oxide. This is further oxidized with excess air to produce nitrogen dioxide, which is absorbed in water to form an aqueous solution of nitric acid and additional nitric oxide. [4,5]

Nitric acid is produced in a variety of strengths ranging from approximately 50 to 99%. The pure acid is a rarity. [4] Reagent grade nitric acid is, according to specifications of the American Chemical Society, approximately 70% by weight. Stronger grades are produced by dehydration with sulfuric acid. [5] According to military specifications the terms "white fuming" and "red fuming" are applied to differentiate two concentrations of fuming nitric acid. White fuming nitric acid contains about 97.5% nitric acid by weight while red fuming nitric acid contains 82.4-85.4%. [6] The percentages of nitrogen dioxide content in white fuming and red fuming nitric acid are 0.5 and 14 $\pm$ 1.0, respectively. Some physical and chemical properties of various strengths of nitric acid are given in Tables XI-1 and XI-2. [7] Data showing the comparative vapor pressures of nitric acid and nitrogen dioxide at different temperatures are presented in Table XI-3. [8]

Production of nitric acid in the United States steadily increased during the 1950-1967 era. [5,9] Between 1960 [5] and the end of 1967, [9] production almost doubled so that by the end of 1967 total production

exceeded 6 million tons. [9] According to a 1970 report, [5] nitric acid was the second most important industrial acid and its production represented the sixth largest chemical industry in the United States.

The largest use of nitric acid is in the production of fertilizers, in the form of ammonium nitrate. This accounts for about 75% of all the nitric acid produced in the United States. Almost 15% of the production goes into the manufacture of explosives, with the remaining 10% distributed among a wide variety of uses. [5,10] Most of the ammonium nitrate obtained from nitric acid is produced at the site where the acid is made. [11] Table XI-4 lists some of the potential occupational exposures to nitric acid. [12]

Exposures to nitric acid may be divided into two basic types - those involving topical contact with the liquid acid, [13,14,15] and those where the hazard is from inhalation. [17,18,19,20,21,22,23,24] In practice, the inhalation exposures invariably include exposures to such nitrogen oxides as nitrogen dioxide and nitric oxide, and these may well constitute the principal hazard involved. [8,17,20,21,22,23,25,26] NIOSH's review of the literature showed that reports of environmental measurements of occupational exposures involving nitric acid have been limited to measurements of nitrogen oxides. No published reports of airborne concentrations of nitric acid in workroom air were found. Such emphasis on measurements of exposures to nitrogen oxides is not surprising in view of the fact that in the numerous uses involving nitric acid with metals or with oxidizable substances, as well as when nitric acid is exposed to air, nitrogen oxides are released. [27] Wade et al, [25] reporting in 1950 on the composition of nitrogen oxides evolved from various industrial processes, indicated that the probable average composition of such gases

from acid dipping would be 78% nitrogen dioxide and 22% nitric oxide.

NIOSH estimates that 27,000 persons in the national work force could have potential exposure to nitric acid.

Historical Reports

One of the earliest accounts of the toxic effects of inhalation of vapors and gases from spilled nitric acid, and from the ensuing reaction between the nitric acid and organic material, is that of Desgranges [19] in 1804. Two canisters of concentrated nitric acid broke in a storeroom and reacted with a quantity of wood with the evolution of what has been translated as suffocating fumes. The merchant entered the room for two periods of approximately 5 minutes each, in close succession. He experienced an immediate suffocating sensation and his hair turned yellowish red in color. He improved for the first 4 hours following exposure, but after this time he was weak, dyspneic, and complained of a painful sensation of constriction around the epigastrium. Although the merchant felt better several hours after his exposure, he survived only for 25-26 hours. The medical report indicated that the cause of death was apparently due to the toxic effects of the "nitrous gas" on the pulmonary organs and digestive tract.

Since that early report, there have been numerous descriptions in the literature of incidents similar to the one above in which individuals or groups were exposed to the gaseous products of the reaction between spilled nitric acid and materials such as wood, woodshavings, sawdust, [19,20,21,22] or metals, [20] or from the dipping of metals in nitric acid. [23]

Effects on Humans

(a) Skin and Eye Effects

Concentrated nitric acid, including fuming nitric acid, destroys tissues because of its corrosive chemical properties. Skin contact with concentrated nitric acid produces burns, and a change in skin color from yellow to brown will occur from contact with the acid at lower concentrations. [14,28] The actions of concentrated nitric acid on the skin have been reviewed by White [13] who states that the staining process is from the formation of xanthoproteic acid due to the action of nitric acid on skin proteins. Dilute solutions of nitric acid produce a mild irritation of the skin and tend to harden the epithelium without destroying it. [28] Leymann [as cited in 29] reported that the annual incidence of nitric acid burns to the skin of workers engaged in its manufacture early in this century was almost 12%.

In contact with the eye, concentrated nitric acid causes immediate opacification of the corneal and conjunctival epithelia. [15] In severe cases, this may result in permanent corneal opacification with attendant blindness, symblepharon (fusion of the eyelids), and shrinkage of the eyeball. [30] In a clinical description of the case of a chemist who was "showered" with hot nitric acid in a laboratory mishap, McAdams and Krop [14] reported that the right cornea was "semiopaque" by the second day after the accident, while the left appeared similar but less severely burned. However, by the 28th day the right cornea had cleared, but the left became opaque. In milder cases involving a very small quantity of acid, greater dilution, or very prompt first aid irrigation, the opacified epithelium may slough after a day or two, revealing a clear underlying cornea, and complete recovery may take place with epithelial regeneration.

[16 as cited in 15]

(b) Inhalation Effects

As already discussed, reports of inhalation exposures to the vapor or mist of nitric acid, as distinct from the gases liberated from the reaction of nitric acid with certain metals or with organic material, have not been found. The term "nitric acid fumes" [20,22,23] has been used to describe what may be considered as a mixture of nitric acid vapor and oxides of nitrogen (predominantly nitrogen dioxide and nitric oxide). In addition, the less exact term "nitrous fumes" has also been used. [31]

The acute effects of inhalation of such mixtures of nitric acid and of nitrogen oxides are characterized by a variable degree of upper respiratory irritation, which may [20,21] or may not be manifested immediately. [22] The signs exhibited minutes after inhalation can include dryness of the throat and nose, cough, chest pain, and dyspnea. [20] In some individuals, similar or more severe signs may be observed after a latent period of several hours following inhalation. [20,21,22,23] Within 24 hours after inhalation, patients may exhibit moderate to severe dyspnea and cyanosis. [21,22,23] Signs of pulmonary edema may also become apparent upon medical examination. [21,23] It is noteworthy that similar adverse respiratory effects have been observed following exposures to most of the oxides of nitrogen from sources other than nitric acid. [32,33,34]

The recovery of patients exposed to mixtures of nitric acid and oxides of nitrogen appears to be unpredictable. [20,21,22,23] Apparently, the prognosis depends upon the airborne concentration of nitric acid or oxides of nitrogen as well as the duration of exposure. [23] In some cases, recovery was essentially complete within two weeks, [20,22] but in others, it took place after a much prolonged period of bronchopneumonia.

[20] In several cases, however, the patients did not recover and died after suffering from bronchopneumonia and various other illnesses. [20,21,23] In one instance, death was said to be caused by pulmonary fibrosis. [23]

Two cases have been reported [31] with yet another clinical picture, that of only minor respiratory symptoms during and after exposure, followed by severe cyanosis, dyspnea, chest pain, cough, and general malaise, and death in one patient after a delay of a week or more. One case resulted from the inhalation of the gases and vapors evolved by the reaction of nitric acid with metals, and the second from the inhalation of gases and vapors evolved by the reaction of both nitric and sulfuric acid with metals. [31] The first patient died 1 week after the onset of the severe symptoms (2 weeks after the exposure) which had been intense, although very short in duration (allegedly 30 seconds). In the second case, the patient recovered following 2 weeks' hospitalization with intensive therapy. It was clinically evident that both patients suffered from bronchiolitis. The cause of death in the first case was attributed to a generalized obliterative bronchiolitis. The term "bronchiolitis fibrosa obliterans" was coined in 1902 by Fraenkel [35] to describe the respiratory syndrome of a brassfounder who was exposed while dipping castings in a mixture of nitric and sulfuric acids.

More recently, [36] the syndrome of bronchiolitis fibrosa obliterans was described in 2 of 4 agricultural workers exposed to gases produced in farm silos. The primary contaminant was thought to be nitrogen dioxide. [36] There was no progression of pulmonary disease in two patients; however, the other two died within a few weeks after their inhalation exposure. The descriptive term "silo-filler's disease" was used by the

authors [36] to designate "any bronchial or pulmonary condition produced by the inhalation of oxides of nitrogen derived from fresh silage."

According to Fairhall, [28] continued exposure to the vapor of nitric acid may cause a chronic bronchitis and more severe exposure may cause a chemical pneumonitis. These effects are not well established because exposures to nitric acid vapor per se, as opposed to vapor and gases generated by the decomposition of nitric acid, have not been found in the literature. However, it seems very plausible that nitric acid, being highly ionized and having strong corrosive properties, would be a potent respiratory irritant.

(c) Ingestion Effects

Accidental or suicidal ingestion of liquid nitric acid, though rare in industry, has occasionally been described from nonoccupational incidents. The following reports serve to illustrate the severely corrosive and tissue-destructive effects of concentrated nitric acid when it comes into contact with mucous membranes.

In 1921, Gray [24] reported a case in which an unknown quantity of nitric acid was ingested by a young Naval fireman, who died in shock within 12 hours. At autopsy, gross pathologic changes were limited to the skin, mouth, esophagus, stomach, duodenum, and kidneys. It was evident that the acid burned, lacerated, or inflamed numerous portions of these tissues and organs. In a case of suicidal ingestion reported by Ide [37] in 1925, the patient survived for several months despite total destruction of the esophagus, and finally died apparently from lobar pneumonia. Another case of suicidal ingestion in which the patient survived was reported by Alsted [38] in 1937. The amount ingested was stated to be a "half a cup" of nitric acid. After a period of years, the patient developed classical

pernicious anemia, presumably due to the destruction of the gastric mucosa with its vital intrinsic factor secreting function. Eight years after the ingestion of the acid, X-ray examination revealed that the stomach was converted into a small sausage-shaped organ with the diameter of a normal colon. Finally, a patient studied by Holinger et al [39] in 1953 developed "corrosive esophagitis" after the inadvertent gargling with 30-40 ml of nitric acid and the swallowing of a much smaller amount, most of it having been immediately expectorated. This victim died 14 days later of gastric hemorrhage following loss of the inner lining of the esophagus on the eighth day.

(d) Dental Erosion

In 1968, tenBruggen Cate [40] published the results of an extensive survey concerned with dental erosion in workers exposed to mineral acid aerosols and mist. Out of 783 workers examined, only 32 were exposed to nitric acid alone. Of these 32, 3 (9%) were reported to have "active dental erosion," the teeth of the remaining 29 being reported as "uneffected." None of the 293 workers comprising the control group showed signs of active dental erosion. Although no environmental data were reported in this study, results indicated that nitric acid vapor and mists were not as potent a factor in causing dental erosion as sulfuric and hydrochloric acids. Two other reports on dental erosion attributed to nitric acid vapors are described under Epidemiologic Studies. [41,42]

Epidemiologic Studies

A search of the literature has revealed no epidemiologic studies of the effects of exposure to nitric acid vapor or mist on general health or on the pulmonary system.

Dettling [41] in 1935 described the occurrence of dental erosion phenomenon in male workers engaged in the manufacture of nitrocellulose where a mixture of nitric and sulfuric acids was used in what was translated as a nitriding process. Twenty-six of 31 workers examined showed traces of dental erosion. Of the 5 workers who had no dental erosion, 4 had been employed for less than 1 year. No environmental data were given. The author speculated that the dental erosion was caused by exposure to nitrous and nitric acid fumes. The formation of nitrous and nitric acids was believed to be due to the development of nitric oxide during the nitriding process which, in turn, combined with the water present in the atmosphere to form the acids.

In 1947, Lynch and Bell [42] reported the prevalence of dental erosion in female workers involved in the manufacture of guncotton and nitrocellulose. At one stage, raw materials were dipped in earthenware baths. The baths contained a solution of 70% sulfuric acid, 22% nitric acid, and 8% water. Although no environmental analysis was made, acid "fumes" were implicated in contamination of the workplace air, despite the fact that a local exhaust ventilation system was in operation. A "localized fire" would sometimes break out resulting in the liberation of "nitrous fumes" which, in turn, contaminated the working environment. Of 26 women employed in this work for 1-3 months, 6 (23%) showed evidence of dental erosion. Of 29 women employed 3-12 months, 11 (38%) showed dental erosion, and of 42 women employed from 1 - 3 1/2 years, 26 (62%) showed

dental erosion. The implication in the preceding 2 reports that dental erosion was caused by the nitric acid in the nitration mixture must be viewed with reservation since sulfuric acid alone is known to be a potent cause of dental erosion. [43]

Animal Toxicity

There are few reports on animal toxicologic studies of nitric acid. Diggle and Gage, [44] in 1954, made the simple statement that "a single exposure to 63 mg/cu m of nitric acid (approximately 25 ppm) has no apparent effect on rats." The duration of the exposure or supporting evidence was not given.

In 1966, Pham-Huu-Chanh et al [45] reported a series of experiments using isolated guinea pig lungs. The isolated lungs were kept alive by placing and maintaining them in an artificial thoracic cage. Aerosols of several acids, including fuming nitric acid (100%), were individually administered to the isolated lungs. The aerosol sprays consisted of submicronic particles, 0.2-0.5 μm in size. Under the experimental conditions, the investigators were able to determine the changes in the ventilatory capacity of the isolated preparation resulting from the action of the aerosol spray. The effect of the aerosol sprays on the lungs was presumed by the authors to take place in the alveolar region. Nitric acid caused bronchoconstriction only after several consecutive administrations, each of which was of considerable duration. Moreover, administration of a bronchodilator aerosol spray (Aerolone R--0.25% isoproterenol, 0.5% cyclopentamine, 80% propylene glycol, and 20% water) to the lungs prior to the administration of the nitric acid aerosol spray prevented

bronchoconstriction. No report was given of epithelial destruction.

The toxic effect of nitric acid on rat lung tissue as revealed by light and electron microscopy was reported by Greenberg et al. [46] A 0.15-ml suspension consisting of dilute nitric acid (1%) and india ink (a suspension of carbon particles) was injected into the bronchial tree of the experimental animals, following a tracheotomy which was performed under ether anesthesia. Animals were killed at various intervals ranging from 2 hours to 7 days after instillation of the suspension. The preparation was administered to 16 rats; 5 others were used as controls. Sections of the lungs were then processed by routine histological procedures for light and electron microscopic examination. The lungs of rats killed 2 and 4 hours after intrabronchial instillation of the nitric acid suspension apparently showed no significant histological changes as revealed by light microscopy. Lungs processed 8 hours after instillation showed evidence of alveolar cellular hyperplasia. An increase in the number of alveolar macrophages was also observed. Within 2-3 days following injection, these 2 reactions were heightened and there was evidence of bronchiolitis, some pneumonia, and obliterative bronchiolitis. However, electron-microscopic examination revealed more subtle cytological changes in the lungs after the shortest time interval. Thus, after only 2 hours, there was evidence in focal areas of marked edema of the cytoplasm of the membranous pneumonocytes. There was also marked degenerative change in the alveolar wall as well as fibrin in the alveolar space. The Type 2 cells showed regressive alteration with dissolution of the cytoplasm and nucleus, leaving only "ghosts" of cells and residual lamellar bodies. After 8 hours, there was a marked prominence of the endothelial cells of the alveolar capillaries. In addition, cytoplasmic processes of membranous pneumocytes (Type 1) covered partially,

or completely, some degenerated granular pneumocytes (Type 2). Some Type 2 cells lacked microvilli, and free lamellar bodies and cellular fragments were seen within the alveolar spaces. Four days after injection, the damaged Type 2 cells showed accumulation of osmiophilic material in a large portion of the cytoplasm. The microvilli were absent and the osmiophilic material was randomly dispersed in the cytoplasm.

A series of interrelated studies, under the broad general heading "Toxicity of the Oxides of Nitrogen," was published by Gray and his associates. [8,17,18,26] In the 1952 study, Gray et al [26] investigated toxicity to rats by exposing several groups to the vapors of red fuming nitric acid (RFNA) for 4 hours/day. The nitrogen dioxide content of RFNA to which the animals were exposed ranged between 9 and 14 ppm. Groups of rats were exposed to RFNA for 40, 56, or 96 hours. Some animals were examined shortly after the inhalation exposure. Visual examination of the respiratory tract indicated widespread inflammation, particularly in the upper portion. Rhinitis, tracheitis, and pneumonitis were diagnosed. Other animals were examined several weeks after their inhalation exposure. In many of the latter, the respiratory inflammatory process subsided; however, localized areas of what the authors described as emphysema were evident in all lobes of the examined lungs. Moreover, these findings were not a function of the duration of exposure, since rats that were exposed to the RFNA for only 40 hours showed the same pathologic changes as those that were exposed for 96 hours. The authors concluded that exposure of rats to nitrogen dioxide greater than 8 ppm may also be injurious.

During the course of their experiments on RFNA, Gray and his associates [8,17,18,26] encountered the problem of maintaining a constant level of nitrogen dioxide in the environment. [8] This problem was due to

the differences in the vapor pressures of the two components of RFNA, namely, nitric acid and nitrogen dioxide. They thus developed a new method for dispensing RFNA which made it possible to supply nitrogen dioxide from RFNA to experimental animals at a constant and reproducible rate. [8] This new dispersion method was subsequently used in two other studies. [17,18] In one of these studies, [17] acute exposures of male rats to nitrogen dioxide, RFNA, and white fuming nitric acid (WFNA) were investigated. The RFNA contained from 8 to 17% nitrogen dioxide and WFNA contained from 0.1 to 0.4% nitrogen dioxide. The animals were exposed in groups of 10 to RFNA or nitrogen dioxide, and in groups of 5 to WFNA for various periods of time. The LC50's (median lethal concentration) data reported on rats exposed to RFNA, WFNA, and nitrogen dioxide for 30 minutes are shown in Table XI-5. In terms of total concentration, the LC50 for nitrogen dioxide gas (174 ppm) was below the LC50's for RFNA and WFNA, the latter computed by NIOSH to be approximately 310 ppm and 334 ppm, respectively. The data indicated that, on an acute basis, nitric acid vapor is approximately 1/2 as toxic as nitrogen dioxide. In addition, comparison of LC50 ppm levels for WFNA (334 ppm) and RFNA (310) suggest the possibility of a synergistic toxic effect between nitric acid vapor and nitrogen dioxide since RFNA has a higher nitrogen dioxide content by weight. This latter conclusion is further supported by the authors' own evidence which showed that the LC50 for RFNA was at a lower concentration than for nitrogen dioxide when the concentration of each was expressed in ppm nitrogen dioxide. In all cases, death was due to pulmonary edema; however, burns were noted on the skin of animals exposed to the high concentrations of WFNA.

The other study [18] determined the effect of chronic exposure to low concentrations of vapors from RFNA on mice, rats, and guinea pigs. Ninety

rats, 30 mice, and 10 guinea pigs were exposed to RFNA at a concentration of 4 ppm for 4 hours/day, 5 days/week, for up to 6 months. The results indicated that animals exposed to the vapors of RFNA showed no significant increase in pathologic changes, such as pulmonary congestion, when compared with control animals. As a result of the findings of this study and of those of a previous study, [26] Gray et al [18] recommended that the MAC for the oxides of nitrogen be set at 5 ppm.

Correlation of Exposure and Effect

No laboratory or epidemiologic reports of the respiratory effects of human exposures to nitric acid vapor per se have been discovered. However, it can be inferred from the limited amount of available animal data that nitric acid vapor or mist is irritating to the respiratory tract.

It is probable that direct exposure of the teeth to nitric acid vapor or mist causes erosion of those teeth and parts of teeth most exposed in the natural oral cleft. [41, 42] There is evidence that the longer the duration of exposure the more severe the extent of the dental erosion, but, in the absence of any environmental data, it is difficult to estimate the minimal concentration of nitric acid mist or vapor necessary to produce this effect. However, in both the reports in which dental erosion was attributed to nitric acid,[21,22] there was concomitant exposure to sulfuric acid, which is well known to cause dental erosion. [42] In the mixture of acids employed in both studies [41, 42] sulfuric acid was the major acid constituent, and nitric acid the minor.

The severity of injury caused by the corrosive effects of liquid nitric acid upon the skin [13, 14], the eyes, [15] and the gastrointestinal tract [24, 37, 38, 39] is clearly dependent upon the concentration of the

acid, the duration of contact, and the absolute quantity of acid involved.

The limited animal data reported indicate that the 30-minute LC50 for WFNA in rats is approximately 334 ppm (224 ppm measured as nitrogen dioxide), and that death in these animals appeared to be due to pulmonary edema. [17] However, a single exposure of rats to 25 ppm of nitric acid vapor for an unstated duration of time had no apparent effect. [44] Toxic effects of exposure to oxides of nitrogen, particularly nitrogen dioxide, have been reported for humans and research animals at much lower concentrations (See Criteria for a Recommended Standard....Occupational Exposure to Oxides of Nitrogen). At low concentrations, therefore, the 2:1 ratio of toxicity between nitrogen dioxide and nitric acid may not exist. A small amount (0.15 ml) of a 1% solution of nitric acid instilled directly into the bronchial tree of rats caused subtle cytological changes in the alveolar epithelial cells 2 hours following instillation. These changes were detectable only by electron microscopy. Within 3-4 days after instillation, gross pulmonary complication occured as evidenced by bronchiolitis, some pneumonia, and obliterative bronchiolitis. [46] However, it is difficult to relate such instillation dosage to doses of nitric acid vapor which are inhaled.

IV. ENVIRONMENTAL DATA

Environmental Concentrations

Published data concerned with airborne exposures involving nitric acid have been limited, for the most part, to measurements of the total oxides of nitrogen. Elkins [47] reported that in 6 studies of acid dipping by the Massachusetts Department of Labor and Industries, the maximum concentration of nitrogen dioxide found was 14 ppm with an average of 5 ppm. Wade et al, [25] in another report from the same organization, presented the following data on "acid dip fumes":

TABLE IV-1

AIRBORNE LEVELS OF NITROGEN OXIDES
FROM ACID DIPPING

Acid Strength		Tests	Range of Concentration of Total Nitrogen Oxides ppm
Unknown		2	5-7
Concentrated:	Operator's exposure	4	2-6
	Over tank	1	110
Ten percent		3	3-8

Concentrations of airborne nitric acid and nitrogen dioxide associated with production of nitric acid at the Tennessee Valley Authority's National Fertilizer Development Center have been presented in an unpublished report by Myers (written communication, April 1975). The following table summarizes results of measurements made during the past 30 years:

TABLE IV-2

AIRBORNE LEVELS OF NITRIC ACID AND NITROGEN DIOXIDE
ASSOCIATED WITH FERTILIZER PRODUCTION

Date	Type of Processing	No. of Units Operating	Airborne Agent	Measurement Location	Concentration in ppm
Unknown	Atmospheric	12	NOX*	Area around absorption tower	30-75**
1945	"	12	"	Plant vicinity	Mean=10.5** Max=35
1945	"	12	NO2	Work area	0.1-12.2 Mean=2.3
1945	"	12	HNO3	"	0.7-3.2 Mean=1.2
1961	"	6	NO2	"	0.8-3.0
1966-67	Pressure	3	NOX*	"	0.6-2.6**
1975	"	1	"	"	0.5**

* Refers to a mixture of airborne nitric acid, nitrogen dioxide, and nitric oxide

** Expressed as nitrogen dioxide

Engineering Controls

Since the use of nitric acid presents potential inhalation hazards and also dangers arising from skin contact with the acid in its liquid form, careful attention must be given to engineering controls as well as to work practices.

The control of nitric acid vapor and mist, as well as nitrogen oxides evolved from operations or processes conducted in fixed locations, may generally be effected under normal situations through use of conventional enclosure or local exhaust ventilation practices. [1, 2]

It is particularly important that all equipment be adequately resistant to the strengths of nitric acid involved and constructed so that leaks cannot develop. Failure to meet such criteria can result in serious, even fatal, consequences. [48] The Manufacturing Chemists' Association [7] points out the need for electrical fixtures to be of vaporproof type, and for all wiring and other electrical equipment to be suitable for corrosive atmospheres. The Association also recommends that operations in which large scale formation of nitrogen oxides may occur should be housed in one-story buildings from which rapid escape would be possible, or if taller structures must be used, means for rapid exit from upper floors should be provided.

Buildings, floors, and other structural elements should be of such design and materials as to minimize adverse effects which could result in the event of spills, leaks, or other accidents. This should include the provision of readily accessible water supply in adequate quantity for rapid flushing away of the maximum amount of acid which could be lost.

Sampling and Analytical Methods

Chemical methods for the analysis of nitric acid fall into two general categories: acid titration and nitrate methods. Both suffer from the same problem, lack of specificity to differentiate between oxides of nitrogen and nitric acid.

Acid titration is a simple procedure which is carried out routinely in any laboratory. A sample is collected in an impinger containing a known amount of alkaline solution. The excess base is then determined by titration, and from this total, acidity can be calculated. Since total acidity is determined, the presence of any other acids in the atmosphere may yield artificially high results which would not be indicative of the true nitric acid concentration.

A number of colorimetric nitrate methods have been used for both air and water analyses. These include the phenoldisulfonic acid method, [49,50] the 2,4-xylenol method, [51] and the brucine method. [50]

The phenoldisulfonic acid method was first used for determination of nitrates in water. It has since been adapted as an air pollution method and is recommended by the Intersociety Committee [49] for determination of total nitrogen oxides including nitric oxide (NO), nitrous anhydride (N_2O_3), nitrogen dioxide (NO_2), nitrogen tetroxide (N_2O_4), vapor or mist of nitric acid (HNO_3), and nitrous acid (HNO_2). The method depends on the oxidation of these compounds to the nitrate ion by hydrogen peroxide in an acidic medium, and subsequent reaction of the nitrate with phenoldisulfonic acid to form a yellow compound which is measured spectrophotometrically at 410-420 nm. Possible interferences include nitrites, reducing compounds such as sulfur dioxide, and chlorides. It is a time-consuming method and

accuracy below 50 ppm is questionable.

For sampling and analysis of nitrates in atmospheric particulate matter, the Intersociety Committee [51] recommends the 2,4-xylenol method. As presented, it calls for collection of a 24-hour sample on an 8" by 10" glass fiber filter attached to a high-volume sampler. Although it is theoretically possible to adapt personal sampling with smaller membrane filters to shorter duration, recent experiments indicate that nitric acid vapor penetration of the filters may be a problem (L Doemeny and J Holtz, written communication, August 21, 1975). This method is subject to interference by nitrites, chlorides, and oxidizing agents.

The brucine method, [50] a colorimetric determination simpler than the phenoldisulfonic acid method, was also initially developed for the determination of nitrates in water. It has been successfully adapted to the analysis of air samples from occupational exposures. The reaction of brucine and nitrate at a controlled temperature produces a yellow color. The intensity of the color is measured spectrophotometrically at 410 nm. Among the disadvantages of this method are the facts that brucine is highly toxic and that the analysis procedure calls for heating the sample.

Another nitrate method utilizes the specific ion electrode. Nitrates must be collected in an aqueous solution into which an ionic strength adjustor (potassium fluoride) and a preservative solution (phenylmercuric acetate) are added. Interference by bicarbonate and chloride may be removed by acidification of the sample and by substitution of AgF for KF in the ionic strength adjustor, respectively. The electrode is then placed in the sample solutions, and a reading is obtained on either a pH/mV meter or a specific ion meter. [52,53,54] If a pH/mV meter is used, a calibration curve must be constructed by measurement of standard solutions (usually 10

and 100 ppm nitrate). If the specific ion meter is used, a direct reading of sample concentration is made following calibration of the meter using standard solutions. In both cases, determinations below 1 ppm are difficult. Leakage of the electrode has also been found to be a problem (L Doemeny and J Holtz, written communication, July 28, 1975).

In 1964, a spectrophotometric analytic method with good specificity for nitric acid was reported in the Russian literature. [55] It distinguishes nitric acid from other nitrates in the atmosphere and eliminates interference by sulfur dioxide under the conditions described. It is sensitive to levels well below the current workroom environmental limit. However, there has been no testing of the efficiency of the sampling method.

The recommended method for sampling is collection via an impinger containing distilled water. This is a convenient field method, but efficiency of absorption by distilled water as opposed to an alkaline solution is questionable. Current NIOSH tests, not yet complete, of a collection method using glass fiber filters indicate that the filters have poorer collection efficiency and recovery for nitric acid than the impinger.

In conjunction with the above sampling method, an ultraviolet spectrophotometric analytic method is being recommended. It is based upon a method published for analysis of nitrates in natural and treated waters. [50] This method is simpler and faster than any of the colorimetric methods and has acceptable sensitivity (0.177 ppm) and good accuracy.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The first recommended environmental limit for nitric acid was 10 ppm (about 25 mg/cu m) as an 8-hour TWA, suggested as a tentative Threshold Limit Value (TLV) by the American Conference of Governmental Industrial Hygienists (ACGIH) [56] in 1956. The following year, this tentative value was adopted as the ACGIH recommendation, although the value cited was misprinted as "5 ppm" or approximately 25 mg/cu m. [57] The following year, this misprint was corrected [58] and the ACGIH recommended that the TLV for nitric acid remain 10 ppm through 1963. In 1964, the TLV was tentatively revised downwards to 2 ppm (about 5 mg/cu m), [59] and in 1966, 2 ppm was adopted as the definite recommendation of the ACGIH. [60]

The basis for these ACGIH recommendations appears, from the ACGIH Documentation of the Threshold Limit Values, [61] to have been largely analogous to the other mineral acids. It was pointed out that the proposed value of 2 ppm for nitric acid was intermediate between the 5 ppm TLV for hydrogen chloride and the 0.25 ppm for sulfuric acid, and the opinion was expressed that 2 ppm is low enough to prevent pulmonary irritation and corrosive effects on the teeth, but possibly not low enough to prevent potentiation of the effects of nitrogen dioxide. However, the papers cited as documentation were those of Lynch and Bell [42] in 1947, Diggle and Gage [44] in 1954, and Fairhall's textbook [28] of 1957, all of which have been reviewed in this document and none of which contains any environmental data. Furthermore, the ACGIH Committee recommended a higher TLV for nitrogen dioxide than for nitric acid, although the documentation for the latter substance states that nitrogen dioxide is more toxic. Therefore,

the recommended ACGIH TLV for nitric acid must be regarded as that Committee's judgmental recommendation.

There is no American National Standard Institute (ANSI) recommended standard for nitric acid.

The current federal standard for nitric acid is 2 ppm or 5 mg/ cu m as an 8-hour TWA (29 CFR Part 1910.93 published in the Federal Register 37:22139, October 18, 1972). This is based upon the ACGIH TLV.

The Maximum Acceptable Concentration for nitric acid as of 1970 was 10 ppm in Finland, the Federal Republic of Germany, Japan, Poland, and Rumania, and 25 ppm in Yugoslavia, according to the International Labour Office. [62]

Basis for the Recommended Environmental Standard

Concentrated liquid nitric acid is corrosive and produces severe chemical burns on contact with the skin, [13,14] with the eyes, [14,15] and with the gastrointestinal tract. [24,37,38,39] Furthermore, nitric acid vapor or mist has been found to be a pulmonary irritant to man [28] and animals. [17,45]

Nitric acid vapor or mist may cause dental erosion to those parts of the incisor and canine teeth exposed in the natural oral cleft, and this effect may develop within three months of occupational exposure to levels of acid not reported as causing other symptoms. [40,42] However, in almost all occupational exposures to nitric acid, there is concomitant exposure to oxides of nitrogen, especially to the dioxide, because these gases are evolved when nitric acid decomposes or when the acid reacts with the materials with which it comes in contact, whether metal or organic

material. [14,20,21,22,23]

Very little is known quantitatively about the effects of inhalation of nitric acid vapor in experimental animals. Data on human exposure have not been found. According to Diggle and Gage, [44] single exposures of rats, for an unstated period of time, to 63 mg/cu m (about 25 ppm) had no apparent effect. Gray et al [17] exposed rats to the vapor of white fuming nitric acid, containing less than 0.5% dissolved nitrogen dioxide, and found the 30-minute LC50 to be variable, but averaging 334 ppm (244 ppm measured as nitrogen dioxide). No animal data have been found on exposures between about 25 and 244 ppm.

In parallel experiments with pure nitrogen dioxide and with red fuming nitric acid (containing from 8 to 17% of dissolved nitrogen dioxide), Gray et al [17] found that the red fuming acid vapor was slightly more toxic than acid-free nitrogen dioxide at the same measured concentration of nitrogen dioxide. At the same time, they found that nitric acid vapor alone was "much less toxic" than either the vapor of red fuming nitric acid or nitrogen dioxide. They therefore concluded that with mixtures of nitric acid vapor and nitrogen dioxide gas, the latter is the primary toxic constituent, but that nitric acid might slightly potentiate the effects of nitrogen dioxide.

At the present time, it is known that contact with concentrated liquid nitric acid has corrosive effects on the skin [13,14] and on mucous membranes. [24,37,38,39] However, only minimal quantitative data are available on the pulmonary effects resulting from inhalation of nitric acid vapor or mist as distinct from the effects of the oxides of nitrogen. In the absence of data showing toxic effects in humans and animals exposed to nitric acid at and below 2 ppm, it is recommended that the current federal

standard of 2 ppm be continued as a TWA for up to 10 hours/day and 40 hours/week. It is interesting to note that the recommended workplace limit for nitric acid is twice that recommended for nitrogen dioxide in Criteria for a Recommended Standard...Occupational Exposure to Oxides of Nitrogen, and that the relative toxicity from acute exposures, as measured by experimental animal mortality, [17] is approximately twice as great for nitrogen dioxide as for nitric acid. However, future research should be conducted to determine chronic effects of inhaling low concentrations of airborne nitric acid independent of exposure to nitrogen dioxide as well as determination of the toxic potentiation of nitrogen dioxide by nitric acid vapor or mist.

In an industrial environment, the occupational hazard associated with the production, use, and handling of nitric acid is in two forms, namely topical contact with the liquid form of nitric acid and inhalation of nitric acid vapor and mist. Available workplace data suggest that workers in some occupations are exposed to extremely low concentrations of airborne nitric acid. Under such conditions, it should not be necessary to comply with many of the provisions concerned with airborne hazards associated with nitric acid vapor and mist. Concern for worker health requires that protective measures be instituted below the airborne workplace limit in order to ensure that exposures to the vapor and mist of nitric acid do not exceed the standard. Therefore, "occupational exposure to nitric acid" has been defined as exposure to airborne nitric acid equal to or exceeding one-half of the workplace environmental (workroom air) limit. However, since a significant topical hazard exists from contact of the skin or eye with concentrated nitric acid, it is recommended that appropriate work practices and protective measures be required regardless of the airborne

concentration of nitric acid. Furthermore, since the combination of nitric acid with metals, oxidizable substances, or air results in the release of oxides of nitrogen, it is imperative that sampling for oxides of nitrogen be done concomitantly with the sampling for airborne nitric acid.

VI. RESEARCH NEEDS

Epidemiologic Studies

Available animal research indicates that exposure to nitric acid may result in the same or similar changes in the pulmonary system as exposure to the oxides of nitrogen, ie, pulmonary edema, [17] bronchiolitis, pneumonia, and obliterative bronchiolitis. [46] However, as stated in Chapters III and V, no reports have been found on chronic effects in humans resulting from long-term exposure to low concentrations of nitric acid vapor. Therefore, cross-sectional studies of pulmonary function, including measures of ventilatory mechanics and spirometry, should be conducted on selected groups of workers routinely exposed to nitric acid vapor in order to discover and evaluate any effects from such exposure. Posterior-anterior chest X-ray films should also be studied for signs of chronic obstructive pulmonary diseases.

Further research is also needed to determine the incidence of dental erosion in workers employed in the manufacture, use, and handling of nitric acid.

Acute Effects of Exposure to Nitric Acid Vapor in Humans

Reports of acute effects of exposure to nitric acid vapor in humans have been limited to industrial accidents [19,20,21,22,23] in which exposures were to unknown but presumably high concentrations of the oxides of nitrogen and nitric acid vapor. Research is needed to determine if nitric acid vapor per se at concentrations at and below the recommended environmental limit can produce acute changes in pulmonary function.

Chronic Animal Exposure Studies

Several different animal species should be exposed to concentrations of nitric acid vapor between 0.05 and 25 ppm for 8-10 hours/day, 5 days/week, for 18-24 months in order to evaluate:

(a) long-term physiologic effects with particular emphasis on macro- and microscopic changes in the pulmonary system;

(b) dose-effect relationships on selected dependent variables, and

(c) interspecies variation of effects.

Similar studies should be conducted using combined oxides of nitrogen-nitric acid vapor exposure in order to assess potentiation of the toxic effects of the oxides of nitrogen by nitric acid.

Mutagenicity and Teratogenicity

Nitrous acid has been shown to be a potent mutagenic agent. [63] Presumably, nitrates from nitric acid serve as a reservoir of nitrates via reduction. [63] However, no evidence has been found of the direct mutagenic properties of nitric acid. Therefore, studies of the possible mutagenicity of nitric acid, including microbial screens, should be conducted. In addition, research should be conducted to determine possible teratogenic effects of exposure to nitric acid vapor.

Risk of Tumor Formation Following Nitric Acid Exposure

The formation of certain carcinogenic agents such as nitrosamines from their precursors may occur in acidic environments. Laboratory studies should be undertaken to determine the kinetics and thermodynamics of nitrosamine formation from secondary amines and low concentrations of nitric acid vapor. Environmental studies should be initiated in occupations where both nitric acid and secondary amines exist in order to

determine if nitrosamines are formed in the workplace air. Furthermore, laboratory animals should be examined for neoplastic lesions following lifetime exposure to nitric acid vapor. If such changes do occur, the dose-response relationship should be determined at concentrations in the neighborhood of the proposed environmental limit. Finally, animal experiments using exposures to nitric acid vapor in combination with other occupational contaminants, such as hydrocarbons, fibrous dusts, and other pulmonary irritants should be conducted to investigate potential additive, synergistic, or inhibitory effects of nitric acid on neoplastic dose-response relationships.