III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Sulfuric acid is produced by the oxidation of sulfur dioxide. [1] Approximately 99% of all production is now by the contact process. It is one of the most widely used chemical compounds.

Sulfuric acid is a colorless to cloudy liquid. Fuming sulfuric acid (oleum) has a sharp, penetrating odor. Concentrated sulfuric acid has an extremely irritant, corrosive, and destructive action on all living matter, including human tissues, not by virtue of its aciarity (in concentrated form it is only slightly ionized) but because of its affinity for water. The affinity is so strong that it will remove the elements of water from even anhydrous organic matter such as carbohydrates, resulting in charring or carbonization with the liberation of heat. In sulfuric acid splashing accidents, the heat liberated by dilution of the concentrated acid with water used to flush the affected areas, can add thermal burn to chemical injury of the body.

Oleum, or fuming sulfuric acid, is a solution of sulfur anhydride (sulfur trioxide) in anhydrous sulfuric acid. The "fumes" of oleum are initially composed of sulfur trioxide which will combine with water, either present in the air or on the mucous membranes of exposed persons, to form sulfuric acid. Effectively then, exposure to sulfur trioxide is equivalent to exposure to sulfuric acid, the site of effect in the respiratory tract being largely determined by droplet size. [2] The more important strengths, properties, and characteristics of sulfuric acid and oleum are presented in Table X-1. [3]
Sulfuric acid mist, the airborne form of sulfuric acid, is an aerosol of droplets of varying diameter of aqueous sulfuric acid solution, the concentration of which will initially depend upon the concentrations of the liquid acid from which the mist is generated. However, the concentration of droplets may change as the highly hygroscopic droplets pick up more water from the atmosphere, growing in size in the process. Sulfate is one of the normal anions in the body [4]; however, the occupational hazard results not from the sulfate ion, but it is related either to the hygroscopic characteristics of the acid or to its oxidizing potential.

Among the common processes which result in the evolution of sulfuric acid mist are pickling, anodizing, and plate-forming and charging in battery manufacturing. Exposures to the mist may result whenever sulfuric acid is heated in the open air or when gas bubbles are released from a liquid surface containing the acid.

Table X-2 [5] indicates the important uses of sulfuric acid and Table X-3 [6] lists representative occupations with potential exposures to sulfuric acid. It is an active acid, with catalytic properties, a special affinity for water, and a high boiling point. Such properties, together with its low cost, make it useful for many purposes. Among these are the pickling of steel, the manufacture of halogen acids, removal of water vapor from gases, alkylation operations in the petroleum and petrochemical industries, acidulation and neutralization processes, and the manufacture of organic sulfonates used in household detergents and lubricants. The single largest use of sulfuric acid is in the manufacture
of phosphate fertilizers. [5] Sulfuric acid production in the United States in 1970 was almost 30 million tons. [7]

A small amount of sulfuric acid is available in a "dry" powdered form, composed of 80% by weight of 1.835 specific gravity sulfuric acid and 20% inert absorbent material (synthetic hydrated silicate). The particle size of the powder is approximately 0.02 to 0.07 μm. In use, the powder is dissolved in water and filtered, yielding a clear acid in strengths up to 60%. [8]

NIOSH estimates that 200,000 persons in the work force have potential exposure to sulfuric acid.

Historical Reports

Alfred Nobel, prior to the establishment of the Nobel awards, is said to have commented that the economic progress of a country might be measured in terms of how much sulfuric acid is consumed through manufacturing productivity. In view of the 200 years history of the use of sulfuric acid in industry [9] and the wide variety of industries in which it has been used, there is a remarkable dearth of reports in the early literature concerning adverse health effects of sulfuric acid in any form, including mist. Possibly the effects of concentrated sulfuric acid splashed on the skin or eyes are too well known for published comment. [10]

Greenwald [11] in 1954 reviewed occupational and experimental observations of exposure to sulfuric acid mist in conjunction with
his review of the effects of sulfur dioxide exposure upon man and animals. Dorsch [12] in 1913 presented the only historical report of adverse health effects in workers to sulfuric acid mist. He noted coughing and sneezing among exposed persons in a lead-sulfuric acid battery room of a telephone exchange. Dorsch [12] also made the following observations on himself and his colleagues: below 0.5 mg/cu m (expressed as SO2), hardly noticeable "annoyance"; between 0.5 and 2 mg/cu m, slight, from 3 to 4 mg/cu m, distinct; and from 6 to 8 mg/cu m, strong "annoyance" or "nuisance." He also personally experienced nosebleeds on occasions when exposed in the 3.12 to 8.3 mg/cu m range (again expressed as SO2). Values would be approximately 50% greater if they were calculated as sulfuric acid.

Although there is evidence, both circumstantial and direct, that sulfuric acid aerosol was a significant atmospheric pollutant in some instances of "smog" episodes in the population-at-large, [13] many other factors have undoubtedly also been present.

**Effects on Humans**

(a) Observed Effects

Concentrated sulfuric acid, by virtue of its great affinity and strong exothermic reaction with water, will effectively remove the elements of water from many organic materials with which it comes in contact, thus it can burn and char the skin. [9] It is even more rapidly injurious to the mucous membranes, and exceedingly dangerous to the eyes. Dilute sulfuric acid, while it does not possess this
charring property, irritates the skin and mucous membranes by virtue of its acidity and can cause dermatitis. [10]

Splash injuries to the eyes are in practice the most serious adverse health effect of sulfuric acid in industry, because contact with concentrated acid of any magnitude is capable of causing irreparable corneal damage resulting in blindness. [5] At the same time, acid burns of the eyelids and surrounding parts of the face will produce cicatization with disfigurement. [14]

As liquid sulfuric acid becomes progressively more dilute with water, the intensity of its dehydration/charring action gradually diminishes and it then behaves as a strong mineral acid by virtue of its complete ionization. Oleum, or fuming sulfuric acid, may be regarded as sulfuric acid of above 100% concentration, because it contains sulfur trioxide (sulfuric anhydride) in solution. As oleum combines with water, more sulfuric acid is formed until all the sulfur trioxide is consumed. Only thereafter does the sulfuric acid start to become diluted. [5]

The effects of exposure to mist of sulfuric acid in the human can be considered under two distinct headings: irritant effects on the mucous membranes, including those of the eyes, but principally the respiratory tract epithelium, [15, 16, 17, 18] and the chemical corrosive effects upon the teeth. [19, 20]

Exposure to sulfuric acid at the mist concentrations encountered in certain industries [20] (about 0.8 to 17 mg/cu m and sometimes higher) causes first, etching of the dental enamel, and then erosion of enamel and dentine with loss of tooth substance. The damage is limited to the parts
of the teeth which are exposed to direct impingement of acid mist droplets upon the surface. [19,20] This phenomenon does not seem to influence dental caries or other dental and periodontal lesions. The teeth affected are mostly the central and lateral incisors, and, to a much less extent, both the upper and lower canines. The observed effects are largely influenced by the degree of mouth-breathing and by the resting position of the lips, which effectively shield the teeth from the acid. In severe cases, which usually develop after many years of exposure, the loss of tooth substance may cause considerable cosmetic disfigurement as well as functional loss due to nonapposition of the cutting teeth. Denuding of the dentine may make the teeth sensitive to temperature extremes. [19]

Inhalation of sulfuric acid in high enough concentration causes an irritation or tickling of the nose and throat, sneezing, and coughing which is somewhat likened to the effects of breathing dusty air. At levels below those detectable by the foregoing subjective effects, sulfuric acid causes a reflex increase in the rate, and diminution of the depth, of respiration, [16] with reflex bronchoconstriction resulting in increased pulmonary air flow resistance. [17] Exposure to higher concentrations or for longer periods may result in bronchitic symptoms, [17, 21] and rhinorrhea, lacrimation, and epistaxis. [16] Over the course of many years, exposure to sulfuric acid has also been claimed to result in conjunctivitis, frequent respiratory infections, emphysema, and digestive disturbances. [21] However, other substances, including dusts, have also been associated with the effects noted. A single overexposure to sulfuric acid may lead acutely
to laryngeal, tracheobronchial, and even pulmonary edema, and chronically to pulmonary fibrosis, residual bronchiectasis, and pulmonary emphysema. [14]

Dilute sulfuric acid, as with sulfuric acid mist, is absorbed as sulfate and hydrogen ions through mucous membranes, ultimately into the bloodstream. The sulfate ion is quite stable in the body and one of the normal minor anions of the plasma. Some sulfate (6 to 8%) from the plasma pool is conjugated in the liver with such metabolites as phenol, cresol, indole, and skatole and excreted in the urine as "ethereal sulfates." Such urinary excretion of the ethereal sulfates constitutes a detoxicating mechanism. The inorganic sulfate (85 to 90%) is excreted as compounds of sulfuric acid with Na, K, Ca, and NH₃. The remainder, neutral sulfur (4 to 6%), is excreted in compounds such as sulfur-containing amino acids, thiosulfates, and thiocyanates. [22]

There is some evidence that acclimatization to the subjective effects of inhalation of sulfuric acid mist may occur in many persons who are occupationally exposed, to the extent that they may be able to tolerate 3 or 4 times the exposure levels which are intolerable to the unacclimated. [23] On the other hand, there is also limited, inadequate evidence that sensitization to the effects of sulfuric acid mist may occur. [17] Possibly both phenomena occur, and in the industrial situation, self-selection may take place. Individuals becoming acclimatized would most likely remain in an occupation involving exposure to sulfuric acid mist, whereas those with either an idiosyncratic hypersusceptibility or an acquired hypersensitivity leave such employment.
Bushtueva [24] failed to find any evidence of potentiation between sulfuric acid aerosol at 0.3 mg/cu m and 0.7 mg/cu m and sulfur dioxide at 0.65 and 3 mg/cu m, respectively, to effects on the light sensitivity of the dark adapted eye in 3 women subjects. The simultaneous administration of 0.3 mg/cu m sulfuric acid and 0.65 mg/cu m sulfur dioxide failed to produce an effect which differed from unexposed control determinations. The combination of 0.7 mg/cu m sulfuric acid and 3 mg/cu m sulfur dioxide produced simple physiological summation of effects as compared with effects produced by each substance separately. Similarly, the percent prolongation of the time required to produce a reflex optical stimulus (optical chronaxy) was also reported to be simply additive for a combination of 0.73 mg/cu m sulfuric acid and 1.5 mg/cu m sulfur dioxide. On the other hand, Amdur in 1954 [25] demonstrated potentiation between sulfuric acid and sulfur dioxide in guinea pigs with respect to growth, lung changes, and respiratory alterations (see Animal Toxicity).

(b) Human Experimental

In the past two decades a certain amount of human as well as animal experimental work has been performed with sulfuric acid aerosols, some of it at exposure levels relevant to the occupational situation, that is, in the 0.35 to 40 mg/cu m range.

In 1952, Amdur and her associates [16] reported exposing by mask a group of 15 normal subjects, men and women, to levels of 0.35 to 5 mg/cu m sulfuric acid aerosol (1.0 μm mean particle size), for periods of 5 to 15 minutes and determined subjective sensations, percent
retention of sulfuric acid, and respiratory effects from pneumotachygraph tracings indicating rate and depth of respiration. Their results are tabulated as follows:

<table>
<thead>
<tr>
<th>Concentration (mg H₂SO₄/cu m)</th>
<th>Subjective Effects</th>
<th>Respiratory Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.35</td>
<td>Not detected</td>
<td>Increased rate in 5 subjects</td>
</tr>
<tr>
<td>0.40</td>
<td>Not detected</td>
<td>Increased rate in 5 others</td>
</tr>
<tr>
<td>0.50</td>
<td>Not detected</td>
<td>Increased rate in remaining 5 subjects</td>
</tr>
<tr>
<td>1.0</td>
<td>Detected by 2 subjects</td>
<td>Increased rate, forced expiration in 1 subject</td>
</tr>
<tr>
<td>2.0</td>
<td>Not reported</td>
<td>Increased rate more rapid and marked, recovery slower</td>
</tr>
<tr>
<td>3.0</td>
<td>Detected by all</td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td>Very objectionable to some but less so to others; usually caused cough</td>
<td>More marked and varied effects on respiratory rate</td>
</tr>
</tbody>
</table>

The increase in rate of respiration was always accompanied by some decrease in depth and also by a decrease in maximum inspiratory and expiratory flow rates. Retention of sulfuric acid in the respiratory tract averaged 77% over a 0.4 to 1.0 mg/cu m exposure concentration range.

Morando, [26] in 1956 reported surprisingly similar information to that given by Amdur et al [16] which indicated that Morando was probably presenting data as exemplary of the effects resulting from exposures to low concentrations of sulfuric acid in humans under experimental conditions.
In 1957, Sim and Pattle [17] exposed healthy male volunteers by mask to 10 N acid mist concentrations ranging from 3 to 39 mg/cu m (1 μm median diameter) at 62% relative humidity. The subjects were also exposed in a chamber to 4 N acid mist of from 11.5 to 38 mg/cu m (1.5 μm median diameter) at 91% relative humidity. Mask exposures were of 10 minutes' duration and chamber exposures were up to 60 minutes in duration. In general, the sulfuric acid was much more irritating at higher humidity. The irritant effect of 20.8 mg sulfuric acid/cu m at high humidity (and larger particle size) was greater than that of 39.4 mg sulfuric acid/cu m at lower humidity (and smaller particle size). Under the conditions of high humidity, increases in airway resistance of from 43 to 150% above preexposure levels were measured and increases under the lower humidity conditions (62%) ranged from 35.5 to 100%.

A study on pulmonary airway resistance by Toyama and Nakamura in 1964 [27] reported interaction between hydrogen peroxide aerosols and sulfur dioxide. The interaction product was reported as sulfuric acid aerosol. Nine healthy male volunteers were exposed, through mouth breathing, to reported concentrations of from 0.01 to 0.1 mg/cu m sulfuric acid of 1.8 μm "count median diameter" (CMD) for a period of 5 minutes. Fifteen similar subjects were reportedly exposed to from 0.8 to 1.4 mg/cu m sulfuric acid of 4.6 μm CMD. Both exposures followed in sequence 5 minutes' exposure to similar aerosols of hydrogen peroxide alone, and 5 minutes' exposure to 1 to 60 ppm sulfur dioxide alone. The sulfuric acid exposures represented simultaneous administration of predetermined amounts of the hydrogen peroxide and sulfur dioxide.
Airway resistance was measured by an airflow interruption technique. Airway resistance was not statistically different from controls by inhalation of hydrogen peroxide aerosol alone, it was increased following inhalation of sulfur dioxide alone to an extent partly dependent upon concentration, and the airway resistance was increased more on exposure to sulfuric acid mist (hydrogen peroxide and sulfur dioxide together). The mean increase in airway resistance was 36.5% above preexposure baseline in the 15 subjects exposed to the higher sulfuric acid concentration and larger droplets (4.6 μm CMD). The mean increase in airway resistance in the 9 subjects exposed to the lower concentration and smaller droplets was 17.9%. Considerable individual variation existed in sensitivity to change in airway resistance. Furthermore, no data were given concerning how much unreacted sulfur dioxide or hydrogen peroxide was present during the sulfuric acid exposure phases of the study.

Bushtueva in 1957 [18] exposed 10 human subjects to low concentrations of sulfuric acid aerosol to determine the subjective threshold for irritation and other low level effects. The mean minimum concentration was 0.72 mg/cu m (range, 0.6 to 0.85 mg/cu m) to which the 10 subjects, averaging 33 tests per subject, detected minimal effects of throat tickling and scratching. At 1.1 to 2.4 mg/cu m, all subjects noticed considerable irritation at the base of the esophagus and 40% of the subjects noticed irritation of the eyes. At 2.4 to 6.0 mg/cu m, all subjects experienced acute irritation of the mucous membranes and a
pronounced reflex cough. All individuals experienced eye irritation at this exposure level. Pneumographic studies were performed on three of the subjects exposed to 0.6 to 2.0 mg/cu m. No respiratory changes were elicited by exposures to less than 1.0 mg/cu m. Slight changes in respiration occurred at levels of 1.0 to 1.1 mg/cu m and concentrations of 1.8 to 2.0 mg/cu m produced changes in respiratory amplitude and rhythm in all subjects. The particle size of the mists and the ambient humidity were not given.

Bushtueva [24] also studied sensory and central nervous system responses to sulfuric acid mist with and without sulfur dioxide in female volunteer subjects. The effects studied were optical chronaxy (in 1 subject) and dark adaptation (in 3 subjects). A sulfuric acid concentration of 0.73 mg/cu m was reported to elicit a threshold response, an approximately 19% prolongation of chronaxy, whereas 0.6 mg/cu m sulfuric acid was subthreshold. Similarly, 0.7 mg/cu m sulfuric acid produced an average 24% increase above control levels in sensitivity to light during the dark adaptation studies. A sulfuric acid concentration of 0.3 mg/cu m was below the sensitivity thresholds of the test subjects. Sulfuric acid aerosols given in combination with sulfur dioxide resulted in simple addition of physiological effects (see Effects on Humans).

Epidemiologic Studies

Very few epidemiologic studies of health effects resulting from sulfuric acid exposure have been carried out in industry. In recent
years, there have been some community studies of morbidity and mortality associated with "smog" episodes, but since sulfuric acid is only one of the significant constituents of most smogs, the results of such studies have little meaning to the industrial sulfuric acid exposure situation.

In 1970, Williams [28] studied sickness absence and ventilatory capacity in 461 workers exposed to sulfuric acid mist in the manufacture of lead-acid batteries. Sickness absence rates, expressed as spells of sickness per man-year of exposure, were compared in plate-forming workers who were exposed to sulfuric acid mist with workers unexposed to acid who served as controls and who worked in the pasting and assembly departments of the same battery plant. The respective sickness absence records of 157 ex-workers in plate-forming and assembly departments, prior to their leaving employment, was also determined for comparison purposes. No environmental measurements of sulfuric acid levels were made expressly for this study. Two estimates were obtained from separate environmental investigations in the same plant. One of these (3 to 16.6 mg/cu m) was obtained from determinations obtained on a single day within the epidemiologic study period, 1950-1962. [20] The second estimate was made 6 years after the end of the study and was reported as 1.4 mg/cu m (mean) with a range from 0.2 to 5.6 mg/cu m. [29] Ventilatory capacity measurements, forced vital capacity (FVC) and forced expiratory volume in the first second (FEV 1), were conducted on 29 forming workers (exposed group) and 16 plate-cutting workers (controls) at the beginning and end of the work shifts on Monday and Friday.
For all respiratory diseases, classified according to the International Classification of Diseases, [30] both younger (20 to 34 years) and older (35 to 64 years) forming workers and ex-workers had more spells of sickness absence than was expected from a calculated rate of all men. Pasting and assembly workers (controls) had fewer spells than expected. It was suggested that the increased number of spells of respiratory diseases in men exposed to sulfuric acid mist was due to an increased incidence of spells in attacked men rather than by an increased proportion of men attacked. No tests of statistical significance were made because of the variation in the number of spells of sickness absence which was contributed by different individuals. Both exposed and control workers showed a statistically significant decrease in mean FVC and FEV 1 during both Monday and Friday shifts. These decreases were somewhat larger in the exposed than in the control groups but the author considered this difference to be insignificant and attributed the decrease in both groups to circadian (presumably day-night) variation. It was suggested that the absence of statistically significant differences in FVC and FEV 1 between the exposed and control groups could have been due to the several minutes which elapsed between exposure to acid mist and observations of ventilatory capacity in the medical department. It was concluded from the study that an excess of spells of respiratory disease, especially bronchitis, occurred in the forming group. It seemed likely that there were one or more factors present in the forming operation which was
specifically associated with bronchitis and other respiratory disease in susceptible individuals. It was also suggested by Williams [28] that the absence of any considerable lower respiratory tract disease observed in this study might be due to the large size of the mist particles or droplets, thus preventing their reaching the deep lung. Although the mist particle size was not measured in this plant, it was found in the forming department of another similar factory to have a mass median diameter (MMD) of 14 μm with only 4% of the particles being less than 4 μm in diameter. The mean concentration of sulfuric acid in the air of this other forming department was 2.7 mg/cu m.

These data on particle size were cited by Williams [28] apparently as having some bearing by analogy to the conditions present in his own study. As an additional factor to particle size, the high solubility of sulfuric acid would suggest rapid absorption in the upper respiratory air passages with little effect being expected on the lower portions of the respiratory tract. In the absence of comparative data such as ambient relative humidity, temperature, and air movement, the comparisons may be uncertain.

In Egypt, El-Sadik and his associates [31] in 1972 reported on 33 workers and 20 controls "never exposed to any chemicals," in the manufacturing departments of two storage battery plants. All subjects were clinically examined, had a history taken with particular attention to respiratory symptoms, and were tested for pulmonary function (FVC and FEV 1), salivary pH, and dental anomalies. Air samples indicated
concentrations of 26 to 35 mg/cu m of sulfuric acid in one plant and 12.6 to 13.5 mg/cu m in the other. No significant difference was found in the prevalence of chronic bronchitis and/or chronic asthmatic bronchitis between exposed and control workers, based on history and examination findings. A reduction in vital capacity was found at the end of the work shift compared to the beginning of the work shift, but the group mean decrease was greater in the control than in the exposed group. On the other hand, there was a greater group mean decrease in FEV1 in the exposed group than in the controls. The authors recognized that this might be due to the inhalation of sulfuric acid mist. There was a slightly greater acidity in the salivary pH in the exposed group than in the control group during the course of the work shift. As to dental anomalies, almost 40% of the exposed workers were found to have dental erosion and more dental discoloration than the controls. Dental loss and infection rates were, however, slightly higher in the controls.

In 1961, Malcolm and Paul [20] reported on dental erosion in 160 men exposed to sulfuric acid mist in the manufacture of storage batteries. Concentrations, measured on a dry day with low relative humidity, varied from 3.0 to 16.6 mg/cu m in the forming process, and from less than 0.8 to 2.5 mg/cu m of air in the charging process. An additional 117 workers from other parts of the plant free from sulfuric acid mist were studied as controls. The prevalence and graded severity of dental erosion and decayed, missing, and filling
rates were compared in the three groups: high level sulfuric acid exposure (forming), low level exposure (charring), and unexposed controls. Etching of the dental enamel (a change in surface texture without loss of tooth substance) was found most commonly in the highest exposed group, less so in the lower exposed group, and was absent from the controls. The lowest grade of dental erosion defined, loss not exceeding 2 mm of incisal enamel, along with etching, was most prevalent in the high exposed group (55 out of 63, 87%), less so in the lower exposed group (7 out of 15, 47%), and absent in the controls. The differences were highly significant (p less than 0.01). The two higher grades of erosion, loss of 2 to 5 mm of tooth crown and loss of more than 5 mm of tooth crown, were present in the high exposed group only. Additionally, of 7 men transferred from the forming department of another factory, 6 showed advanced stages of erosion and the seventh had dentures. This small group had a mean length of exposure of 5 years, which was far less than that at the main factory. It was established that dental etching and erosion occurred only on the anterior teeth (central and lateral incisors, and to a much smaller extent, the canines) to the extent that these teeth were directly exposed to the impingement of acid droplets, as left uncovered by the lips in their customary position. Six workers from the high exposed group were unaffected by the acid. This was postulated to be due either to resistance of the enamel or to the individuals seldom parting their lips, thus preventing acid mist from reaching
the teeth. Also, it seems that time-on-the-job could have been a factor; the employment duration was not given for these workers.

In a comprehensive study of the problem of dental erosion in all those industries which involve exposure to any significant concentration of acid spray or mist, ten Bruggen Cate [19] in 1968 reported on 555 "acid workers" over a two-year observation period in Britain. The study was initiated in response to a memorandum [32] to the Industrial Injuries Advisory Council from the British Dental Association which concluded that industrial dental erosion was a hazard which existed, and that in the majority of cases severe dental damage resulting in disfigurement occurred. Of the total workers studied, 101 workers were exposed essentially to sulfuric acid alone, the other workers being exposed primarily to hydrochloric, nitric, hydrofluoric, chromic, and phosphoric acids in a wide variety of industries (48 firms) and processes. All control workers came from acid-free departments of the firms participating in the survey and all controls were found to be free from industrial dental erosion. All 555 workers studied had natural teeth, 38% having been excluded because their teeth had been extracted and descriptions of the conditions of their teeth prior to removal were unreliable. The classification of dental erosion used previously by Malcolm and Paul [20] proved unsatisfactory because it was necessary to subtract the remaining tooth substance from assumed dimensions of the original crown in order to estimate tooth loss. A
classification was therefore selected ranging from etching, loss of enamel only (Grade 1), loss of enamel with involvement of dentine (Grade 2), further exposure of secondary dentine (Grade 3), to loss resulting in pulpal exposure (Grade 4). Interestingly, no Grade 4 erosion was observed. It was suggested that pain would lead to early treatment of such an erosion, in most cases resulting in extraction. Further, pain was very rarely reported, and when present, was described as a hypersensitivity to cold. Only 5 cases reported pain for which erosion was considered to be the cause. In the storage battery industry involving almost exclusively exposure to sulfuric acid mist, nearly 20% of the forming workers showed Grade 2 or Grade 3 erosion at the first examination. Erosion was less in the charging departments, yet some of these workers had been employed for only short periods and showed progressive erosion at subsequent examinations. Erosion was also present in other acid-using industries, although the prevalence was consistently less than that observed among battery, particularly formation, workers.

A relationship was observed between the onset and advance of erosion and the length of service. Grade 1 erosion occurred in 4 to 6 months, Grade 2 erosion in 2 to 5 years, and the earliest Grade 3 cases, in 6 to 10 years. Results showing progressive erosion indicated that the battery formation process was the most likely to produce dental erosion, based on cases actually observed to advance under modern (1964) industrial environmental conditions. It was emphasized
that erosion could be greatly reduced or even eliminated by installation of effective control measures, such as efficient exhaust systems.

Functional disability and disfigurement occurred although little evidence was seen of treatment to restore function or appearance to acid-eroded natural teeth. This was believed due to the fact that many workers were not interested in the level of dental treatment required or were not aware that treatment was possible. Additionally, it was concluded that acid environments had no influence on the incidence of caries.

Animal Toxicity

Treon et al [33] in 1950 reported a comparative mortality study in guinea pigs, rabbits, rats, and mice exposed to high concentrations of sulfuric acid aerosol (87 to 1,600 mg/cu m) in which about 95% of the particles were below 2 μm in diameter. Guinea pigs succumbed after having been exposed for a brief period to 87 mg/cu m. Animals of other species survived after being exposed at this concentration for 2.75 hours, and much higher concentrations were required to produce death. Some mice died following exposure to 549 mg/cu m for 3.5 hours, exposure to 699 mg/cu m was lethal to rats, while higher concentrations were required to cause death in rabbits. Deaths occurred almost uniformly when groups of mice, rabbits, and rats were exposed to a concentration of 383 mg/cu m for 7 hours on each of five successive days. All mice, rats, and rabbits, however, survived
exposure for the same duration to 203 mg/cu m. Therefore, the order of increasing sensitivity established was rabbits, rats, mice, and guinea pigs. Concentration rather than duration was more critical in the mortality of guinea pigs. Lesions produced included degenerative changes in the epithelium of the respiratory tract, pulmonary hyperemia and edema, and focal pulmonary hemorrhages. The lungs of all animals exposed showed areas of atelectasis and emphysema.

Amdur et al [34] found the 8-hour LC50 (concentration lethal to 50% of the animals) of sulfuric acid aerosol of mass median diameter (MMD) of 1 μm to be 18 mg/cu m for 1- to 2-month old guinea pigs and 50 mg/cu m for 18-month old animals. The cause of death in the animals dying within 2 hours appeared to be asphyxia caused by bronchoconstriction and laryngeal spasm. Animals dying after longer exposures showed gross capillary engorgement and hemorrhage. When the exposure times were extended to 72 hours, there was no mortality at 8 mg/cu m; thickening of alveolar walls and areas of consolidation were found. Longer exposures at higher concentrations did not increase mortality beyond that observed at 8 hours at a given concentration, but the above-mentioned lung changes were much more marked. It was postulated that the toxicity of sulfuric acid aerosol for the guinea pig has two aspects: it promotes laryngeal spasm and bronchospasm which may be lethal depending on the concentration and, in addition, it causes parenchymal lung damage, dependent upon the total dose represented by the product of concentration and time.
Thomas et al [35] reported exposing guinea pigs for longer periods (18 to 140 days) to mean concentrations mostly from 1 to 4 mg/cu m and with 3 different particle sizes, 0.6, 0.9, and 4 μm. Of the 3 particle sizes used, 0.9 μm produced the greatest effects including slight lung edema and rare capillary hemorrhages. There was some increase in desquamated epithelial cells in the minor bronchi. Slight edema of the larynx and trachea and a decrease in mucus in the major bronchi were seen with the 4-μm particles. It was concluded that the guinea pig can tolerate levels of 2 mg/cu m for more than 3 months of continuous exposure with only minor pathological effects.

Bushtueva [36] reported exposing guinea pigs to 2 mg/cu m sulfuric acid aerosol of unspecified particle size for 5 days and found edema and thickening of the alveolar walls. One- to 2-weeks following exposures to 2 mg/cu m, a slight catarrhal reaction in the tracheal and bronchial mucosa with interstitial proliferative processes was observed accompanied by round lymphoid cell infiltration around blood vessels and bronchi. These changes seemed to progress with prolonged exposure up to 2 and 3 months.

Amdur [37] studied the effects on airway resistance in guinea pigs of sulfuric acid aerosol of 0.8-, 2.5-, and 7-μm MMD in concentrations ranging from 2 to 40 mg/cu m. The largest particles, 7 μm, even at a concentration as high as 30 mg/cu m, caused only a slight increase in airway resistance. Such particles would probably not penetrate beyond the nasal passages. The 0.8-μm particles produced a significant increase in resistance, even at 1.9 mg/cu m concentration. At 40 mg/cu m,
the 2.5-μm particles produced the greatest increase in resistance, but at concentrations below 2.0 mg/cu m, the 0.8-μm particles produced the greater effect. In general, it was concluded that large particles which reached the middle respiratory tract (trachea and bronchi) probably acted by producing mucosal swelling, secretion, and exudation of fluid which lead to obstruction of major airways, whereas the smaller particles produced simple reflex bronchoconstriction. [37]

Lewis et al [38] studied the effects of sulfuric acid mist, alone (0.755 mg/cu m) and in combination with sulfur dioxide (5.1 ppm sulfur dioxide + 0.835 mg/cu m sulfuric acid) on the diffusion capacity, pulmonary compliance and resistance, and residual volumes of purebred beagles. The duration of exposures was 21 hours daily for 225 days. Half the dogs had previously been "impaired" by exposure to 26 ppm nitrogen dioxide for 191 days. The main observed effect of sulfuric acid exposure in these experiments was a statistically significant reduction in mean diffusion capacity (measured by the single-breath carbon monoxide method) which was independent of the effect of previous nitrogen dioxide impairment or concomitant exposure to sulfur dioxide. Dogs that were exposed to sulfur dioxide and sulfuric acid without previous impairment by nitrogen dioxide had a smaller "residual volume" than any other experimental group.

In a later report, Lewis et al [39] studied the effects in beagles of exposure to 0.9 mg/cu m sulfuric acid alone and in combination with 13.4 mg/cu m sulfur dioxide on certain hematological
indices, organ weights at autopsy, and lung function indices similar to those studied earlier. [38] Exposure to sulfuric acid, with or without concomitant sulfur dioxide, for 225 or 620 days had no demonstrable effect on the white cell count or on erythropoiesis. Statistically significant decreases in both lung and heart weights in the dogs exposed to sulfuric acid aerosol were observed as compared with total body weight. It was hypothesized that this might either be an effect of elevated blood sulfate bathing those organs, or a neural or humoral response to injury to the lung. The effect of sulfuric acid exposure on lung function, as in the earlier series of experiments, was most marked in decreasing diffusion capacity. In the opinion of the authors their findings indicated that continuous chronic inhalation of 0.9 mg/cu m sulfuric acid mist had a deleterious effect, in beagles, on both the conducting airways and the lung parenchyma.

In 1954, Amdur [25] reported the effects of a combination of sulfuric acid mist at 8 mg/cu m and sulfur dioxide at 89 ppm on growth, lung pathology, and respiratory response. In 8 guinea pigs exposed for 8 hours, weight had decreased the day following exposure and growth was slower to resume than was observed for either agent administered separately. Two guinea pigs were exposed 72 hours following the initial exposure to the same concentrations for another 8 hours. In these reexposed animals, growth ceased entirely during the period of observation following reexposure. Pathologic lung changes
were also more extensive than that observed for either agent alone, consisting of large areas of complete consolidation and hepatization involving entire lobes in all cases. In the reexposed animals, extensive hemorrhage and consolidation were present. It was commented that the general ill health of the animals was very likely related to the presence of the extensive lung damage. Labored breathing was very pronounced, continuing for 24 to 48 hours after exposure. In contrast, there were no noticeable respiratory effects in guinea pigs exposed to 8 mg/cu m sulfuric acid mist alone. Restlessness and annoyance initially appeared in animals exposed to 89 ppm sulfur dioxide alone, but that disappeared after approximately 5- to 10-minutes exposure. It was therefore concluded that the effects on growth, lung changes, and respiration were much more marked than would have been predicted from the use of either agent alone.

**Correlation of Exposure and Effect**

Because of the widespread use of sulfuric acid in industry, reports appear frequently of accidental skin or eye contact with the acid. The vast majority of cases where exposures through surface contact with the acid occur, either from splash or spray, can be attributed to some type of equipment malfunction. Because of the sudden and frequently unanticipated occurrences of acute occupational exposures, concentrations are difficult to establish. The case report presented by Goldman and Hill [14] emphasizes the severe damage caused to a worker when sprayed in the face with liquid
oleum resulting from a burst valve. Even with use of a safety shower, exposure was sufficient to cause second and third degree burns of the face and body and pulmonary edema due to sulfuric acid inhalation. Chronic after-effects were manifested as pulmonary fibrosis, residual bronchitis, and pulmonary emphysema. In addition, burning and charring of the skin were sufficient to cause marked scarring and disfigurement.

The epidemiologic studies concerning the health effects resulting from sulfuric acid exposure are difficult to correlate with environmental concentrations, either because environmental sampling was not performed, because data were unavailable for inclusion in the studies, or because sampling and analytical procedures made environmental results very questionable (see Environmental Data). The 1970 study by Williams [28] for lead-acid battery workers indicated that forming process workers and ex-workers had more spells of sickness absence due to respiratory disease than was expected from a calculated absence rate for all men. Pasting and assembly workers (controls) had fewer spells than expected. Statistically significant decreases were noted in mean forced vital capacity (FVC) and forced expiratory volume at one second (FEV 1), but the differences were attributed to possibly circadian (presumably day-night) variation. However, the FVC and FEV 1 decreases were somewhat larger in the exposed than in the control groups. No environmental measurements were made expressly for this study [28]; however, estimates from other studies conducted in the same plant indicated environmental sulfuric acid levels to vary from 3 to 16.6 mg/cu m, taken on a single day and reported in the dental erosion.
study by Malcolm and Paul. [20] The second estimate, 1.4 mg/cu m (range, 0.2 to 5.6 mg/cu m), was reported by Anfield and Warner [29] 6 years after the end of Williams' [28] sickness absence study. Williams [28] concluded that an excess of spells of respiratory disease, especially bronchitis, occurred in the forming group workers manufacturing the lead-acid batteries.

El-Sadik et al [31] reported environmental concentrations of 25 to 35 mg/cu m of sulfuric acid in one storage battery plant and 12.6 to 13.5 mg/cu m in another (see Environmental Data). No significant difference was found in the incidence of chronic bronchitis or chronic asthmatic bronchitis between 33 exposed workers and 20 controls. Changes in vital capacity and FEV 1 were similar to those observed by Williams [28] and there was a greater group mean decrease in FEV 1 in the exposed group than in the controls. The authors [31] suggested that the decreased FEV 1 might be due to the inhalation of sulfuric acid mist. In addition, the sulfuric acid exposed workers showed a nearly 40% higher occurrence of dental erosion and dental discoloration than was noted in the controls.

The studies on dental erosion reported by Malcolm and Paul [20] in 1961 and by ten Bruggen Cate [19] in 1968 demonstrated a high incidence of dental damage among forming process workers and among charging workers, with dental erosion being absent in all of the controls (p less than 0.01). [20] Airborne acid concentrations varied from 3.0 to 16.6 mg/cu m in the forming process and from less than 0.8 to 2.5 mg/cu m in the charging process. [20] A positive relationship was also observed [19] between the
onset and advance of dental erosion and the length of service. In addition, functional disability and disfigurement occurred, although there appeared to be no influence of acid environments on the incidence of dental caries. [19]

Human experimental exposure studies have included changes in respiratory airway resistance [27] and changes studied by measurement of sensory and central nervous system responses from light sensitivity in the dark adapted eye or from reflex optical stimulation. [18] In addition, determinations have been made on the lower limits of detection of sulfuric acid. [12, 16, 18] Bushtueva [18] reported erratic changes in respiratory amplitude and an increase in respiratory rate at sulfuric acid concentrations of 1.8 to 2 mg/cu m. Very slight changes were noted at 1.0 to 1.1 mg/cu m and no effects were obtained at concentrations below 1 mg/cu m. Amdur et al [16] reported an increased respiratory rate in all subjects tested at 0.35, 0.40, and 0.50 mg/cu m. At 1.0 mg/cu m, forced expiration was noted and at 2 mg/cu m the increased rate was more rapid and marked. Effects were even more marked and varied at 5 mg/cu m. Morando [26] reported similar results at 0.52 to 0.7 mg/cu m. Bushtueva [24] reported prolongation of optical chronaxy at 0.73 mg/cu m sulfuric acid (0.6 mg/cu m was subthreshold) and an increase in sensitivity to light during dark adaptation at 0.7 mg/cu m (0.3 mg/cu m was subthreshold). The subjective limit of detection to sulfuric acid has been reported to be between about 0.5 and 0.7 mg/cu m by a number of investigators. [12, 16, 18]

Sulfuric acid exposures are lethal to mice, rabbits, and rats at about 400 mg/cu m of air for exposure periods of 7 hours a day for 5
days. [33] Guinea pigs are much more susceptible, however, 87 mg/cu m being lethal after only brief exposure periods accompanied by degenerative changes of the respiratory epithelium, pulmonary edema, and hemorrhages. The lungs of all animals exposed showed areas of atelectasis and emphysema. [33] Amdur et al [34] reported the 8-hour LC50 to be 18 mg/cu m for young guinea pigs (1 to 2 months old) and 50 mg/cu m for 18 month old animals. Sulfuric acid exposures of 8 mg/cu m for 72 hours produced no mortality. Further, no changes in respiratory effects were noted in guinea pigs exposed at 8 mg/cu m sulfuric acid. [25] At exposure levels of 2 mg/cu m, Thomas et al [35] reported minor pathological changes in guinea pigs after more than 3 months and Bushtueva [36] reported edema and thickening of alveolar walls after 5 days' exposure. Lewis et al [39] considered that the continuous chronic inhalation (225 days) of 0.9 mg/cu m sulfuric acid had a deleterious effect on beagles on both the conducting airways and the lung parenchyma.

Particle (droplet) size seems to interplay along with temperature and humidity to influence the toxic effects of sulfuric acid in the respiratory tract. Amdur [37] found that 2.5 μm particles produced a marked increase in pulmonary flow resistance at a concentration of 40 mg/cu m. However, median particle sizes of about 0.8 μm were more effective at concentrations below 2.0 mg/cu m. It was concluded that large particles probably exerted their effects on the middle respiratory tract (trachea and bronchi) whereas the smaller particles produced simple reflex bronchoconstriction. [37] Thomas et al [35] found
similar results in guinea pigs with particle sizes of 0.6, 0.9, and 4 μm. The animal mortality studies of Treon et al [33] and Amdur et al [34] were performed with median particle sizes of sulfuric acid mist less than 2 μm. In contrast, the human experimental study of Toyama and Nakamura [27] reported a greater mean increase in pulmonary airway resistance (36.5%) in subjects exposed to 0.8 to 1.4 mg/cu m sulfuric acid of 4.6 μm particle size. A 17.9% increase in airway resistance was found for a reported sulfuric acid concentration of from 0.01 to 0.1 mg/cu m of air at 1.8 μm particle size. These results are difficult to evaluate because of the method by which the sulfuric acid was generated. An interactive effect was indicated between hydrogen peroxide and sulfur dioxide rather than to sulfuric acid alone. A comment given by Williams [28] in his epidemiologic study may be pertinent at this point to reflect particle sizes in an occupational situation. Although mist particle size was not measured in the Williams study, a forming process department of another similar factory was reported to demonstrate acid mist having a mass median diameter of 14 μm with only 4% of the particles being less than 4 μm in diameter.

The interaction of sulfuric acid with other gases and aerosols has been reported. Amdur [25] reported that a combination of sulfuric acid mist at 8 mg/cu m in guinea pigs (which produced no noticeable respiratory effects when administered alone) and 89 ppm sulfur dioxide produced effects on growth, lung changes, and respiration which were more marked than would have been predicted from the use of either agent.
alone. Bushtueva, [24] however, reported that in humans 0.7 mg/cu m sulfuric acid (which was a threshold concentration) and 3 mg/cu m sulfur dioxide produced simple physiological summation of effects as measured by light sensitization to the dark adapted eye. Similar additive effects were noted for optical chronaxy at 0.73 mg/cu m sulfuric acid and 1.5 mg/cu m sulfur dioxide. Lewis et al [38] reported a statistically significant reduction in mean diffusion capacity in beagles exposed 21 hours a day for 225 days to a combination of 0.835 mg/cu m sulfuric acid and 5.1 ppm sulfur dioxide. The reduction was greater than that which would have been expected by either agent alone. Further studies by Lewis et al [39] showed statistically significant decreases in both lung and heart weights as compared with total body weight to exposures at 0.9 mg/cu m sulfuric acid and 13.4 mg/cu m sulfur dioxide. The human study on sulfuric acid exposure reported by Toyama and Nakamura [27] appears to resemble more closely a combination study between hydrogen peroxide and sulfur dioxide rather than sulfuric acid because of the manner in which the substances were administered.

Humidity also seems to play a role in influencing the effects of sulfuric acid exposure. Sim and Pattle [17] reported a greater increase in pulmonary airway resistance in humans exposed to 20.8 mg/cu m sulfuric acid at 91% humidity as compared with 39.4 mg/cu m at 62% relative humidity. The lower dose under conditions of high humidity was also more irritating to the respiratory tract than the higher dose under the less humid conditions.