INHALATION OF SULFURIC ACID MIST BY HUMAN SUBJECTS

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A PREVIOUS communication from our laboratory[1] reported the results of studies on the toxicity of sulfuric acid mist in which the guinea pig was used as an experimental animal. The present paper presents the results of studies of the respiratory response of normal human subjects to the inhalation of sulfuric acid mist. The tests made included determination of the per cent retention of inhaled acid, of the level at which the acid was detected by most persons, and of the pattern of respiration as studied with the pneumotachograph. The concentrations used in this work ranged from 0.35 to 5 mg. per cubic meter (mg./m.^{3}). The exposure times were from 5 to 15 minutes.

EXPERIMENTAL PROCEDURE

The method of generating sulfuric acid mist was the same as that used previously.[1] Compressed air swept the vapors from an electrically heated flask containing concentrated sulfuric acid into the main air stream which entered a 2-cu.-ft. lucite® mixing chamber.

For determination of the concentration of sulfuric acid mist in the mixing chamber, a sample of air was passed through an electrostatic precipitator. The acid thus collected was rinsed into a conductivity cell previously calibrated with standard sulfuric acid.

The subjects were at rest during all experiments and breathed through a face mask. A large wooden panel hid the apparatus from their view. A slide valve mounted on the back of the panel connected the mask to the mixing chamber so that they could not tell when the acid mist exposures began.

The per cent retention of inhaled sulfuric acid was determined by measuring the total volume of air breathed, the concentration in the mixing chamber, and the concentration in exhaled air. All these experimental inhalations were of comparatively short duration, and the total quantity of acid mist exhaled was always small. It could not be collected and estimated reliably by an electrostatic precipitator, as the latter, in small samples collected at low gas flows,[2] induces per se increased acidity and hence conductivity. This factor does not assume importance in sampling from the mixing chamber, since samples of any desired size may then be taken at uniform flow rate, thus rendering the blank insignificant.

From the Department of Industrial Hygiene, Harvard University School of Public Health.

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1. Amdur, M. O.; Schulz, R. Z., and Drinker, P.: The Toxicity of Sulfuric Acid Mist to Guinea Pigs, A. M. A. Arch. Indust. Hyg. **5**:318-329, 1952.

2. Drinker, P.; Hazard, W. G., and Ishikawa, T.: Alternating Current Precipitators for Sanitary Air Analysis: Acid Formation in Electric Precipitation, J. Indust. Hyg. & Toxicol. **14**:364-370, 1932.

Therefore, the acid mist in aliquot portions of exhaled air was collected on molecular filter papers [3] made of nitrocellulose polymers of very uniform and very small pore size.[4] The papers used were about 5 cm. in diameter, had a very high resistance to air flow, and were supported on porous carborundum discs. Sampling was done continuously at a rate of 2 liters per minute from the exhaled air stream before it entered the spirometer. The mist thus caught was removed by soaking the paper in a known volume of distilled water and then determining the acid by conductivity. The papers had no conductivity themselves and were fully as efficient for mist collection as was the precipitator.

The effect of the acid mist on respiration was studied by means of a pneumotachograph,[5] a device for instantaneous recording of air flow during breathing. It consists of a fine monel® wire screen mounted in a face mask. The screen measures air movement by measuring the velocity of air (and volume) through the screen by pressure loss or resistance of the screen which is linear with flow. The pressure corresponding to the flow is measured by a thin membrane whose movement is transmitted to an electrical recording device. From the direct tracing of the whole breathing pattern, inspiratory and expiratory flow rates and other breathing characteristics can be obtained.

RESULTS

Twenty-two determinations of retention of inhaled acid mist gave an average value of 77%. Of these, 10 were 80 to 87%, 8 were 65 to 75%, and 5 were 50 to 60%. Three of the four values between 50 and 60% were obtained on one particular subject. The exposure concentrations were from 0.4 to 1 mg./m.^{3} Within this range, per cent retention was not affected by concentration. Beyond the average figure of 77% and the range of 50 to 87%, nothing conclusive regarding the retention of sulfuric acid can be stated from our data.

No direct conclusions can be drawn as to the per cent of retained acid which reached the alveoli and the per cent removed in the upper respiratory tract. We know, however, that the mist particle size averaged 1 μ. Wilson and LaMer [6] have shown that particles of this size can penetrate to the alveoli. According to these workers, maximum "alveolar retention" is on the order of 45%.

With guinea pigs breathing sulfuric acid in this particle-size range, marked pulmonary pathology resulted, suggesting penetration to the alveoli. Accurate evaluation of this penetration could best be obtained by the use of radioactively tagged sulfuric acid in further animal experiments.

The relatively high retention figures are not surprising, since sulfuric acid droplets have a strong affinity for moist surfaces, such as would be encountered in the mucous membranes of the respiratory tract. Our figures are in the range of those reported by Wilson and LaMer for glycerin aerosols of this particle size.

In the same paper these authors showed that the retention of inhaled aerosol particles decreases with increase of respiration rate. It might then be expected

3. Millipore filters made by Lovell Chemical Company, Watertown, Mass.

4. First, M. W., and Silverman, L.: Air Sampling with Molecular Filters, presented at Atomic Energy Industrial Health Meeting, Cincinnati, April 25, 1952, to be published.

5. Silverman, L., and Whittenberger, J. L.: The Clinical Pneumotachograph, in Methods in Medical Research, Vol. 2, edited by J. H. Comroe Jr., Chicago, Year Book Publishers, Inc., 1949, pp. 104-112.

6. Wilson, I. B., and LaMer, V. K.: The Retention of Aerosol Particles in the Human Respiratory Tract as a Function of Particle Radius, J. Indust. Hyg. & Toxicol. **30**:265-280, 1948.

that in the case of men engaged in active work the retention of sulfuric acid mist would be much less than that observed in our sedentary experimental subjects. Another possible significance of this fact will be referred to later.

In the determinations of the sensory response to sulfuric acid, we found that concentrations below the maximum allowable range[7] of 1 mg./m.³ could not be detected by odor, taste, or irritation. For two persons the threshold of detection was at 1 mg./m.³ This concentration was not detectable by the other subjects. A concentration of 3 mg./m.³ was noticed by all. The most general comment was that it felt like breathing dusty air. A concentration of 5 mg./m.³ was very objectionable to some but less so to others. A deep breath at this concentration usually produced coughing.

Our studies with the pneumotachograph showed that in all subjects the inhalation of sulfuric acid mist caused changes in respiration. This occurs at 0.35 mg./m.³

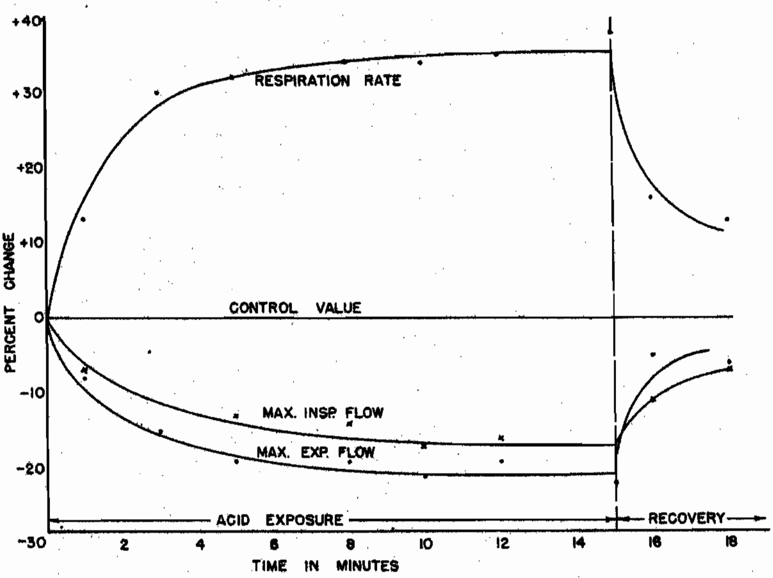

Fig. 1.—Effect of sulfuric acid mist on respiration rate and maximum inspiratory and expiratory flow rates.

as well as at 5 mg./m.³ At the lower concentrations the subjects were not aware of the presence of the acid by any sensory response. Therefore we can only conclude that the changes observed are reflex reactions to an irritant stimulant. The fact that the apparatus was hidden from the subjects' view, so that they could not tell when the exposure began or ended, ruled out any major psychological factor.

The average of respiratory changes occurring in 15 subjects, 5 at 0.35 mg./m.³, 5 at 0.4 mg./m.³, and 5 at 0.5 mg./m.³, are shown in Figure 1. Changes in respiration rate per minute and maximum inspiratory and expiratory air flow are expressed as per cent change from control values. Preexposure values for each individual

7. Threshold Limit Values for 1951 Adopted at Meeting of American Conference of Governmental Industrial Hygienists in Atlantic City, N. J., April 1951, A. M. A. Arch. Indust. Hyg. 4:398-400, 1951.

subject were averaged to give a base line from which to compute per cent change. These changes at a given time were then averaged to prepare the curve shown. The respiration rate rose at once when the inhalation of acid was started, quite steeply at first, then leveling off at about 35% above the control value. When the acid exposure was stopped, the respiration rate dropped back to within 13% above the control value by three minutes after the end of the exposure. The inspiratory and expiratory maximum flow rates fell below the control value, steeply at first, then leveling off at about 20% below normal. They returned to nearly the previous values within three minutes after exposure ceased.

Figure 2 shows the effect of sulfuric acid on tidal volume in five subjects breathing a concentration of 0.4 mg./m.[3] The curve presents the average values during the control, exposure, and recovery periods. Tidal volume drops from control values of around 900 ml. to about 650 ml. after only two minutes of acid inhalation. This level is maintained throughout the acid exposure. The first minute after the exposure period ended, the tidal volume rises higher than the control and then returns to preexposure values.

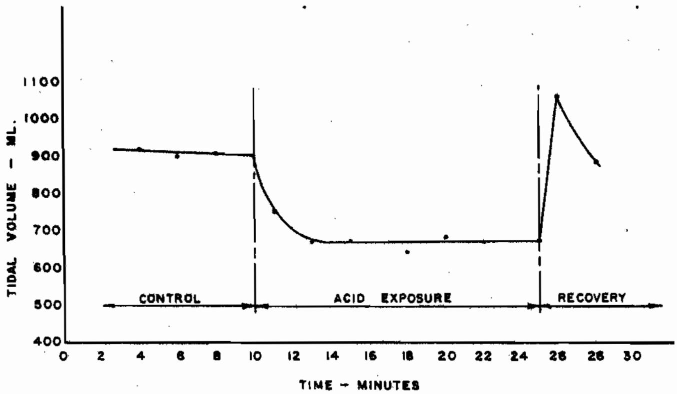

Fig. 2.—Effect of sulfuric acid mist on tidal volume.

The pattern for any given exposure followed the same shape as these average curves. The obvious control of breathing through the same apparatus with the omission of the acid mist was done, and no such changes were observed.

As has been pointed out previously, retention of inhaled acid mist decreases when the respiration rate increases. It would then appear possible that the more rapid, shallower breathing observed is a reflex protective mechanism to prevent retention of the acid mist.

In some subjects increase in respiratory rate was the predominant response, while in others shallower breathing was more marked than the change in respiration rate. In still others a very forced expiration was observed.

Figure 3 shows the pneumotachograph tracing from a subject exposed for 15 minutes to 0.5 mg./m.[3] The respiration rate increases from a control value of 8.9 respirations per minute to 11.3 at the end of 15 minutes' exposure. This tracing also shows an effect frequently observed, a change in the per cent of the total cycle occupied by expiration. The total breathing cycle occupies a shorter

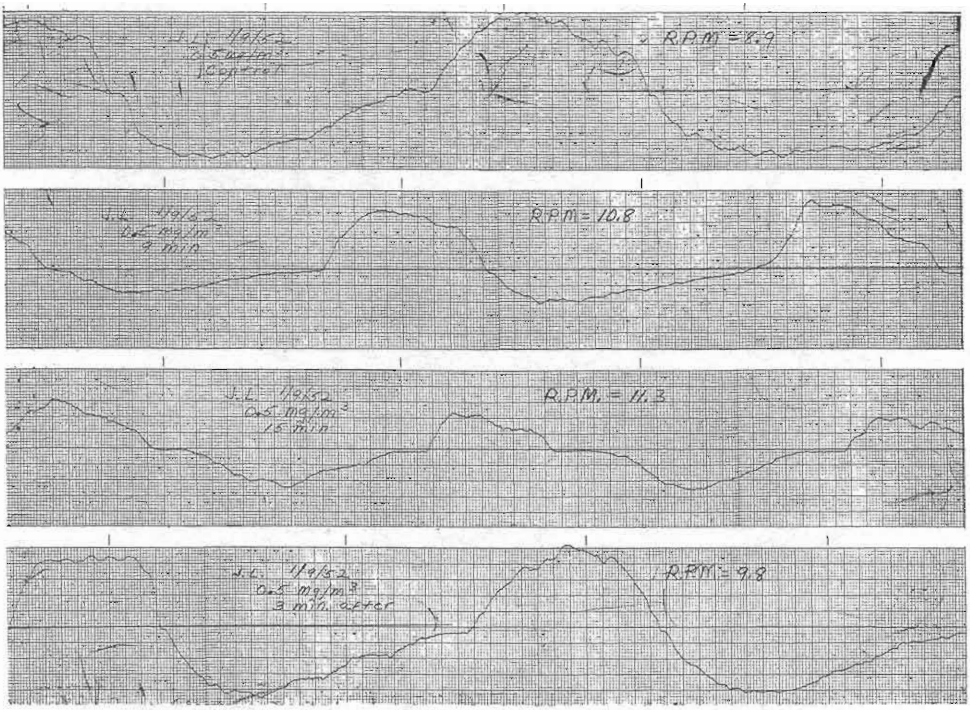

Fig. 3.—Pneumotachograph tracing. Subject exposed to 0.5 mg./m.³ In this and all other tracings shown the portion of the curve above the base line represents inspiration and that below represents expiration.

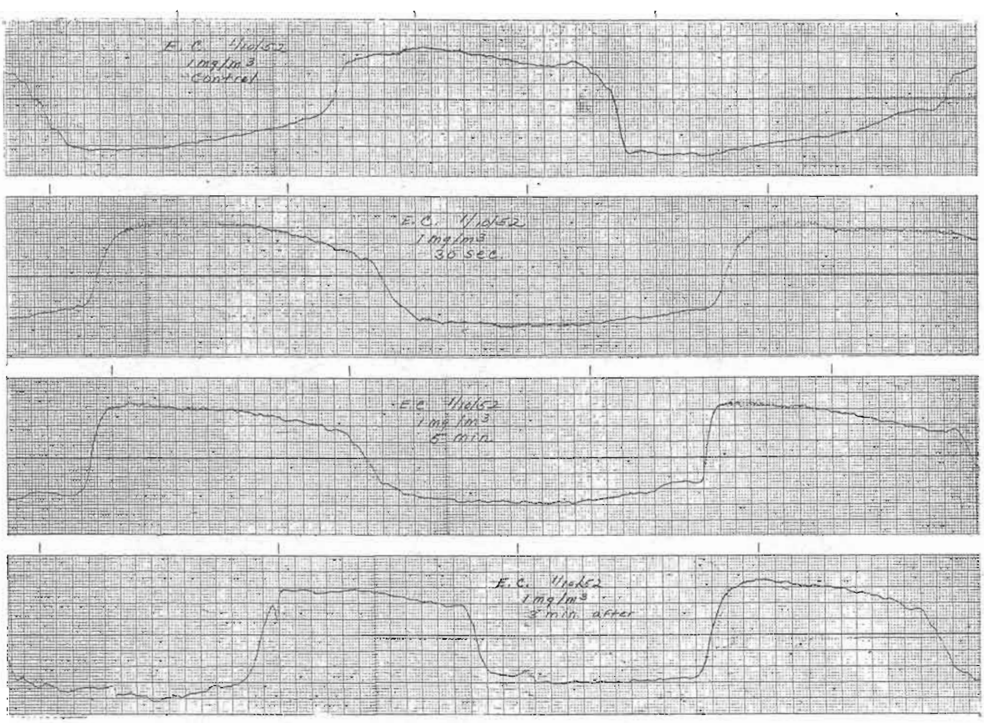

Fig. 4.—Pneumotachograph tracing. Subject exposed to 1 mg./m.³

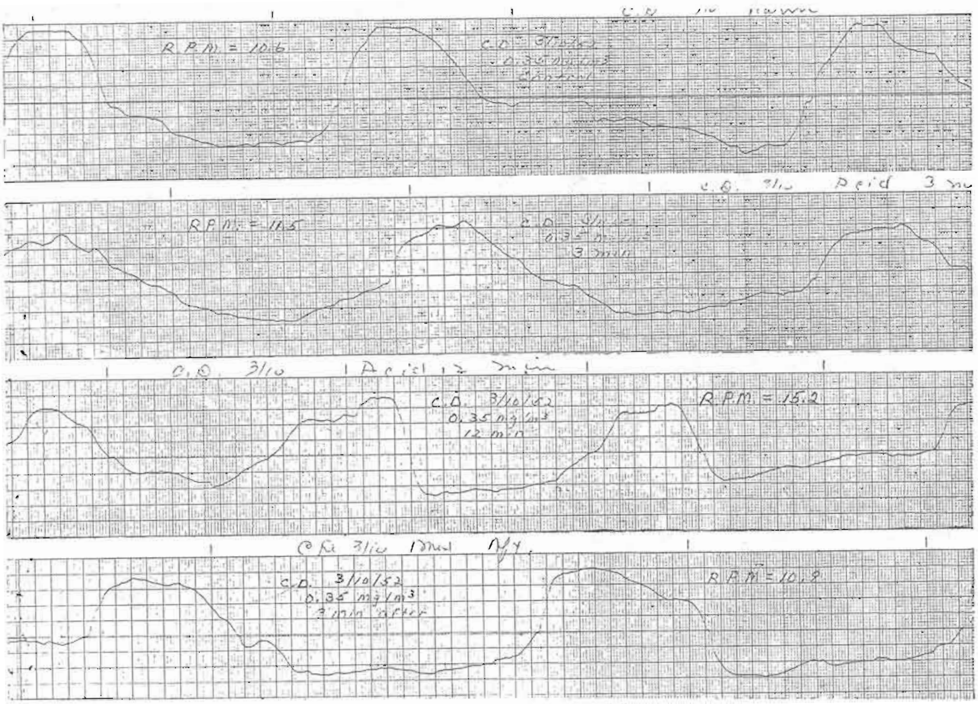

Fig. 5.—Pneumotachograph tracing. Subject exposed to 0.35 mg./m.^{3}

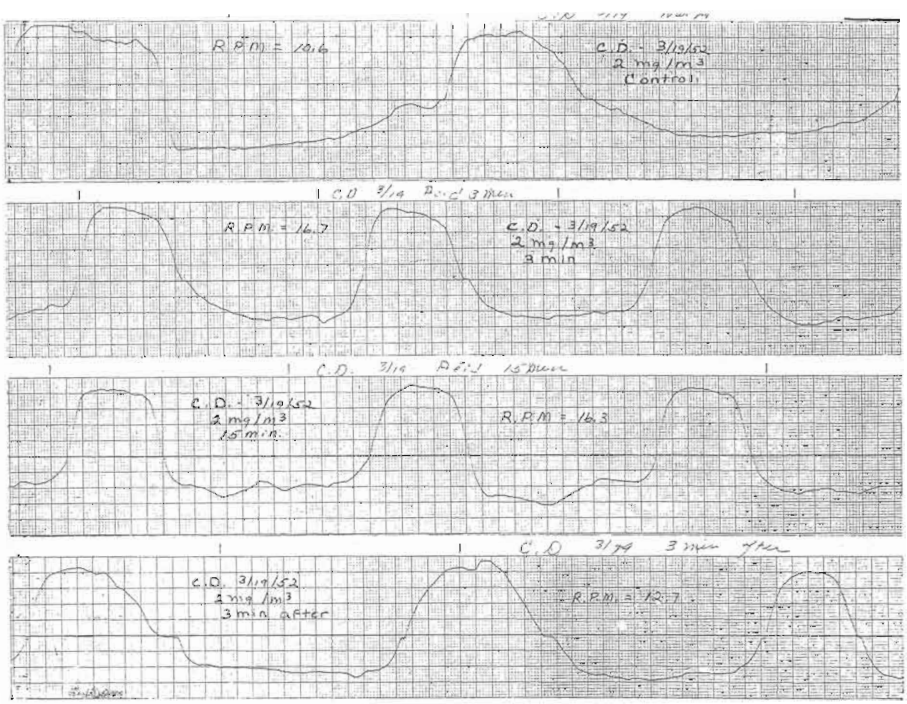

Fig. 6.—Pneumotachograph tracing. Subject exposed to 2 mg./m.^{3}

time interval, but within this, expiration is prolonged. An examination of Figure 3 shows that in the control period expiration occupies 59.6% of the total cycle, whereas after 15 minutes of acid inhalation, expiration is 69.3% of the total cycle and inspiration only 30.7%.

The tracing from a person exposed for five minutes to 1 mg./m.³ is shown in Figure 4. There is little change in respiration rate or depth of breathing. The main response is the very forced expiration which is sometimes observed.

Figures 5 and 6 at concentrations of 0.35 and 2 mg./m.³ show the tracings from a subject whose main response is increased respiration rate. In the case of expo-

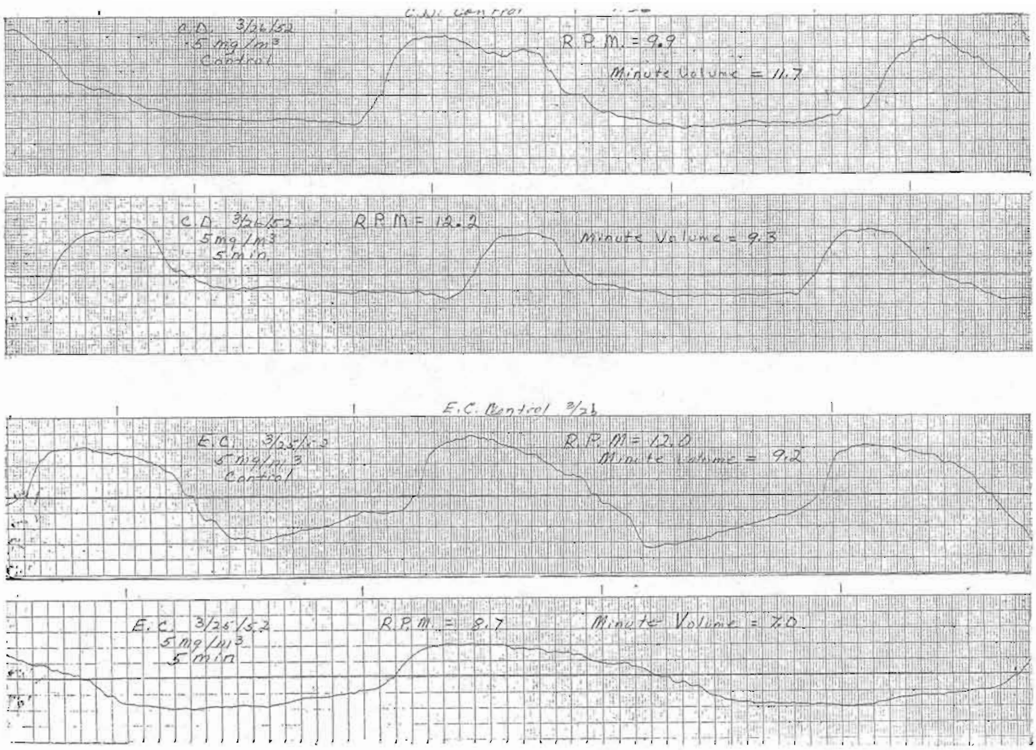

Fig. 7.—Pneumotachograph tracing. Two subjects exposed to 5 mg./m.³

sure to 0.35 mg./m.³ the respiration increases from a control level of 10.6 respirations per minute to 11.5 at the end of 3 minutes and to 15.2 at the end of 12 minutes. One minute after the end of exposure it has returned to 10.8. In the case of exposure to 2 mg./m.³ the response is more rapid and more marked, and the return to normal is slower. Starting from the same control value of 10.6, the rate rises to 16.7 respirations per minute in 3 minutes, is 16.3 at 15 minutes, and has dropped back only to 12.7 3 minutes after the end of the exposure. The type of response in the two cases is the same, but the effect is greater with the higher concentration of acid mist.

A few studies were made of exposures to concentrations of 5 mg./m.³ At this level the acid mist was perceptible to all, and so changes which occurred were not entirely reflex. Some subjects showed a very marked reaction. The response, however, was much more varied in character than that obtained on concentrations which could not be detected. The most marked effect at these concentrations was a decrease in minute volume.

Figure 7 shows the pneumotachograph tracings from two subjects exposed for five minutes to 5 mg./m.[3] The minute volume in both cases is greatly reduced, but this effect has been obtained by the two subjects in a different way. The first subject shows an increase in respiratory rate accompanied by a marked decrease in depth of breathing. The respiration rate has been increased from 9.9 respirations per minute to 12.2. The minute volume has been decreased from 11.7 to 9.3 liters per minute. This is the same subject whose response to lower concentrations has been shown in Figures 5 and 6. At those two concentrations there was little change in depth of breathing or minute volume, whereas the decrease in this case is very marked.

The second subject of Figure 7 has also decreased his minute volume. The control value of 9.2 fell to 7 liters per minute after five minutes of exposure. In his case this has been achieved by a decrease in both respiration rate and amplitude of breathing.

COMMENT

We always noted marked effects upon respiration in normal men who had no regular exposure or adaptation to sulfuric acid. Changes were produced by concentrations as low as 0.35 mg./m.[3] These were of a purely reflex nature, not under the control of the subject, since he was unable to detect the presence of the acid mist.

As has been pointed out previously, retention of inhaled particles is lower when the respiration rate is increased. Possibly, the shallower, more rapid breathing which we observed is a reflex protective mechanism to decrease the retention of acid mist particles.

Whether or not the altered breathing would continue over an extended period of exposure is a conjecture, the truth of which we have not attempted to determine. Several things, however, suggest that for some time at least it would probably continue. One evidence for this is shown by the shape of the curves in Figures 1 and 2. The changes commence at once when the acid exposure starts and reach the maximum within the first five minutes; then the curves flatten out, and there is no return to control values during acid exposure. The subject apparently reaches adjustment with the physiological problem that has been presented to his respiratory system.

Another indirect evidence in favor of the continuation of altered breathing was noted earlier in the behavior of our guinea pigs exposed to sulfuric acid mist.[1] The lowest concentrations used were 8 mg./m.[3] Above that level respiration was very rapid and labored. This type of respiration commenced soon after the acid mist entered the exposure chamber and continued an hour or so after the animals had been removed. In 72-hour exposures, the more sensitive animals died from laryngeal spasm within the first 8 hours, and the survivors continued labored breathing for the full exposure period. In a 72-hour period at least, the guinea pigs showed no return to normal breathing.

It seems most unlikely that the changes we noted for sulfuric acid mist are peculiar to this substance. Work is in progress to determine effects from a few other common irritants when breathed at subsensory levels.

It is to be noted that all our subjects were healthy men of various ages. We have made no studies on asthmatics, on persons with cardiac disease, or on any other persons somewhat below par, and we know of no convincing analogue in animal experimentation to the aging patients with asthma or cardiac disease. It is these groups to which the acute smog incidents of the past, those in the Meuse Valley in Belgium and at Donora, Pa., pointed especially.

SUMMARY

Normal human subjects inhaled concentrations of sulfuric acid mist from 0.35 to 5 mg./m.^{3} The retention of inhaled sulfuric acid averaged 77%. In all subjects changes in respiration were observed and measured by pneumotachograph. The changes were of a reflex nature and were indicative of shallower and more rapid breathing. At concentrations of 5 mg./m.^{3}, levels at which the acid mist was easily detected by all, changes were more pronounced but also more varied in nature. The main response at this concentration was a decrease in minute volume. The possible significance of these findings is discussed.