# *Assessment of Ultrasonic Nebulization*

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**For assessment of delivery of moisture to the lower airway, a water vapor transducer was constructed of sufficiently small size to permit introduction into the tracheobronchial tree. Changes in moisture content were reflected in changes in conductivity across a sodium chloride crystal within an electrical circuit. The resultant responses were measured via a d.-c. recorder. Conventional air-activated nebulizers produced a mean increase of 0.18 humidity units/second in the lower airway, whereas ultrasonic generators effected a mean increase of 0.71 and 4.03 units/second, respectively, for no. 1 and no. 2 settings. Furthermore, duration of response was more prolonged following use of ultrasonic generators. Thus, ultrasonic nebulization appears to afford a definite advance in the field of inhalation therapy for transport of aerosols to the lower respiratory tract.**

ULTRASONIC nebulization represents a new approach to an old problem of delivery of aerosols. The motive force for dispersion is high frequency vibrational energy which yields uniform densely suspended particles of relative stability. These characteristics appear attractive for augmenting airway humidification in inhalational therapy and in endotracheal anesthesia circuits, particularly of nonrebreathing design. The type of aerosol produced by ultrasonic nebulization may be useful when tracheostomy or endotracheal tubes bypass the nasopharynx which normally provides and conserves considerable humidification for the airway.[1]

Although the output of nebulized water from ultrasonic generators has been measured repeatedly, distribution within the respiratory tract is a matter of conjecture.[2,3] The mass of particles produced is within the theoretically ideal range of 0.8–1.0 u which should approach 80 per cent deposition within the lung.[4,5] The experiments reported in this paper were designed to demonstrate whether or not, and to what extent, ultrasonically nebulized water is delivered to the lower airways. This was done by monitoring changes in moisture content within the primary bronchi when water vapor was introduced via the upper airway of the experimental animal.

## Methods

To measure relative changes in the moisture content of gases, a water vapor transducer was constructed as suggested by Krobath and Reid.[6] Basically, this unit employs a sodium chloride crystal* incorporated in a Wheatstone bridge circuit. Sodium chloride salts are, of course, hygroscopic and the electrical conductivity of a sodium chloride crystal varies directly with the quantity of moisture that the salt absorbs from the surrounding atmosphere. Therefore assessment of moisture content of water vapor is possible with this unit.

Although the NaCl crystal was originally incorporated in a Wheatstone bridge circuit, more stable results were obtained by simplifying the circuit to measure directly the voltage drop across a load resistor as shown in figure 1. Changes in moisture content were reflected in changes in conductivity across the crystal and recorded with a d.-c. recorder.†

The advantages of this transducer over the better known moisture indicators such as the hair hygrometer and the wet-and-dry bulb psychrometer include instantaneous response, compactness and linear output.

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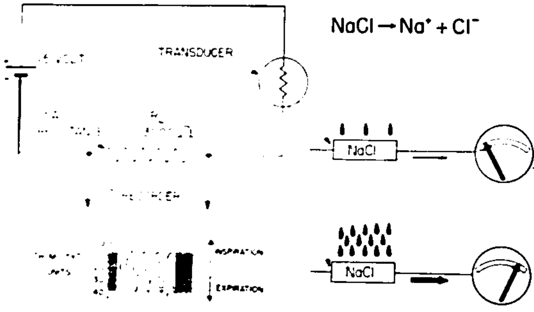


FIG. 1. Circuit diagram.

In order to measure humidity inside the tracheobronchial tree, a compact flexible detector was devised by interposing a NaCl crystal, 1.5 × 1.5 × 3 mm., between two contact electrodes, and connecting it to a bipolar pacemaker catheter.‡ Crystal size was selected because of convenience; responses proportional to change in humidity were obtained irrespective of size.

The transducer was calibrated as follows: it was placed for three seconds alternately in a stream of dry air, and air with nebulized water from the ultrasonic generator at no. 1 setting at 37° C. both at a flow rate of 10 liters per minute. The crystal was then immersed in water. In all three situations, end-deflections of electropotential were recorded and three distinct reproducible levels were obtained.

Calibration was also carried out with the transducer in the respiratory tract of the experimental animal. The transducer transmitted changes in electropotential synchronous with respiration (fig. 2). Expiration across the transducer with attendant increase in net moisture resulted in increased conductivity across the crystal in comparison to that associated with the net moisture of inspiration. The magnitude of the electrical responses was then related to moisture content by measuring the millimeters of deflection from the baseline. This quantity was denoted in terms of "humidity units" wherein one unit is equivalent to 1 mm. deflection on the recording. Time of application of various nebulizers to the system was measured in seconds. Duration of response in seconds was measured as that time required for return to basal humidity levels following removal of the nebulizer.

The ultrasonic generator in this study was the DeVilbiss Model No. 880 Ultrasonic Nebulizer. This model has settings from 1 to 4 which regulate power supply to the generator transducer and thereby determine aerosol output. To compare the respiratory distribution of aerosol of the ultrasonic nebulizer with that of a nonultrasonic instrument, a commonly used air-activated nebulizer § was selected.

Forty experiments were carried out in 13 dogs. Anesthesia was established by intravenous injection of sodium thiopental (15–20 mg./kg.) in unpremedicated animals after in-

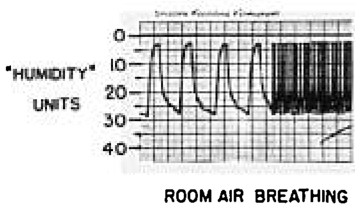


FIG. 2. Sample recording showing change in airway moisture content synchronous with respiratory cycle.

‡ U. S. Catheter and Instrument Corporation, Glens Falls, New York.

§ The Ohio Chemical "Jet" model.

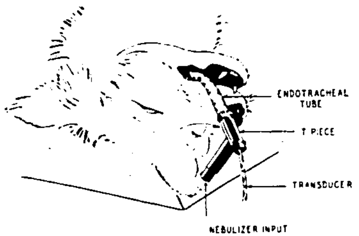


FIG. 3. Endotracheal tube with transducer and side-arm for introduction of aerosol.

sertion of an 18 gauge Rochester cannula in an extremity vein. Anesthesia was maintained by subsequent small intravenous injections of thiopental. Respiration was spontaneous in all cases.

An endotracheal tube was inserted (fig. 3) and a T-piece attached to facilitate direct introduction of the transducer into the respiratory tract to the primary bronchial level. Transducers were also placed in the pharynx in several cases and simultaneous recordings of humidity levels were obtained in order to assess the relation of humidification and depth within the airway as shown in figure 4.

After placement of the transducers, the animals were allowed to stabilize until spontaneous regular breathing occurred. Humidity values were then successively obtained when the animal was allowed to inspire the following samples via side-arm of the T-tube: (1) room air, (2) room air mixed with water aerosol delivered from the air-activated nebulizer, and (3) room air mixed with water aerosol from the ultrasonic nebulizer. The ultrasonic generator was tuned to both no. 1 and no. 2 settings. In each instance, the flow rate via the side-arm was 10 liters per minute. Time of administration of samples was varied in several experiments to determine its effect upon duration of response. After each trial the transducer was dried of excessive moisture by momentary removal to permit blotting and evaporating. The animal was permitted to return to a steady basal state prior to the next step.

## Results

Before experimental studies were undertaken, certain control procedures were evaluated. It was thought inadvisable to measure "relative humidity" because of its great variation with changes in body temperature and pressure.[1] Instead, relative changes in absolute moisture were measured and recorded. Temperature at various levels within the airway was monitored in several experiments to assess the net effect upon recordings obtained. Pressure changes when breathing with and without the side-arm of the T-tube in place were compared. The results conclusively demonstrated that changes in respiratory recordings were related to net change in moisture within the airway rather than to changes in temperature and pressure.

The results of forty experiments on dogs were analyzed with respect to degree and duration of response when the transducer was placed at the primary bronchial level. The relation of magnitude of response to time was assessed as "Slope" in humidity units per second. The data are tabulated in tables 1–3 and the mean results are plotted graphically in figure 5. The mean values for humidification were: 0.18 units per second for air-acti-

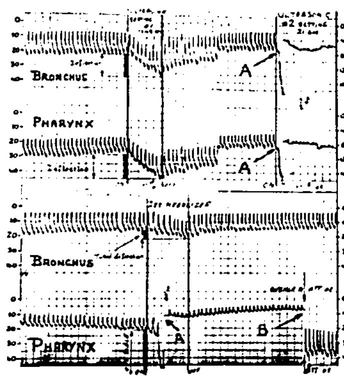


FIG. 4. Simultaneous tracings at pharyngeal and bronchial levels of moisture content within the airway. A represents change to attentuation no. 4. B denotes change to attenuation no. 1.

TABLE 1. Air Activated (Jet) Nebulizer
(Flow 10 Liters/Minute)

| Basal Humidity Units | Response Units | Net Increase Units | Time of Introduction Seconds | Slope Units/Second |
|---|---|---|---|---|
| 16 | 22 | 6 | 56 | 0.11 |
| 14 | 37 | 23 | 186 | 0.12 |
| 7 | 32 | 25 | 336 | 0.07 |
| 11 | 26 | 15 | 190 | 0.08 |
| 25 | 34 | 9 | 44 | 0.20 |
| 22 | 39 | 17 | 54 | 0.31 |
| 39 | 48 | 9 | 41 | 0.22 |
| 18 | 24 | 6 | 26 | 0.23 |
| 32 | 41 | 9 | 30 | 0.30 |
| 23 | 26 | 3 | 18 | 0.17 |
| 26 | 29 | 3 | 18 | 0.17 |
| 34 | 37 | 3 | 18 | 0.17 |
| 32 | 35 | 3 | 18 | 0.17 |
| 18 | 23 | 5 | 20 | 0.25 |
| 18 | 22 | 4 | 20 | 0.20 |
| 16 | 18 | 2 | 20 | 0.10 |
| 16 | 19 | 3 | 24 | 0.13 |
| 17 | 29 | 3 | 20 | 0.15 |
| 17 | 21 | 4 | 20 | 0.20 |
| 18 | 26 | 8 | 30 | 0.27 |
| 23 | 35 | 12 | 52 | 0.23 |
| 10 | 28 | 18 | 180 | 0.10 |

Mean slope 0.18 units/second.

TABLE 2. Ultrasonic Nebulizer No. 1 Setting
(Flow 10/Liters/minute)

| Basal Humidity Units | Response Units | Net Increase Units | Time of Introduction Seconds | Slope Units/Second |
|---|---|---|---|---|
| 24 | 38 | 14 | 54 | 0.26 |
| 21 | 39 | 18 | 36 | 0.50 |
| 43 | 68 | 25 | 24 | 1.04 |
| 20 | 35 | 15 | 34 | 0.44 |
| 36 | 61 | 25 | 26 | 0.96 |
| 14 | 20 | 6 | 20 | 0.30 |
| 24 | 68 | 44 | 50 | 0.88 |
| 22 | 60 | 38 | 50 | 0.76 |
| 30 | 68 | 38 | 50 | 0.76 |
| 13 | 88 | 75 | 180 | 0.42 |

Mean slope 0.71 units/second.

vated nebulizers, 0.71 units per second for ultrasonic nebulizers at no. 1 setting of the generator, 4.03 units per second for ultrasonic nebulizers at no. 2 setting of the generator.

These values show that the no. 1 setting of the generator resulted in some increase in aerosol output and density at the primary bronchial level in comparison to that produced by conventional air-activated nebulizers. At the no. 2 setting, a marked increase in aerosol output and density occurred. Higher output settings produce an increase in aerosol output and density which rapidly saturated the transducer.

Figure 5 shows the differences in depth of penetration of aerosols from ultrasonic and air-activated nebulizers. The air-activated nebulizers produced a great increase in moisture at the pharyngeal level whereas little increase in electropotential was recorded at the bronchial level. The ultrasonic nebulizer delivered moisture more uniformly to the

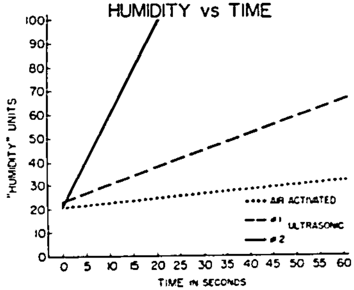


FIG. 5. Mean results for the three methods of aerosol delivery.

TABLE 3. Ultrasonic Nebulizer No. 2 Setting
(Flow 10 Liters/Minute)

| Basal Humidity Units | Response Units | Net Increase Units | Time of Introduction Seconds | Slope Units/Second |
|---|---|---|---|---|
| 29 | 88 | 59 | 14 | 4.21 |
| 32 | 100 | 68 | 30 | 2.30 |
| 12 | 112 | 100 | 15 | 6.7 |
| 9 | 88 | 79 | 29 | 2.72 |
| 15 | 88 | 73 | 32 | 2.28 |
| 8 | 80 | 72 | 38 | 1.90 |
| 27 | 140 | 113 | 19 | 5.95 |
| 23 | 100 | 77 | 8 | 9.63 |
| 43 | 100 | 57 | 19 | 3.0 |
| 16 | 40 | 24 | 20 | 1.2 |
| 20 | 112 | 92 | 20 | 4.60 |
| 26 | 104 | 78 | 20 | 3.90 |

Mean slope 4.03 units/second.

TABLE 4

| Ultrasonic Nebulizer No. 1 | | Ultrasonic Nebulizer No. 2 | | Air Activated Nebulizer (Jet) | |
|---|---|---|---|---|---|
| Introduction Seconds | Duration of Response, Seconds | Introduction Seconds | Duration of Response, Seconds | Introduction Seconds | Duration of Response Seconds |
| 16 | 96 | 14 | 480 | 16 | 88 |
| 36 | 96 | 15 | 300 | 56 | 140 |
| 24 | 230 | 32 | 252 | 44 | 35 |
| 20 | 74 | 19 | 760 | 26 | 54 |
| 24 | 250 | 19 | 340 | 18 | 16 |
| 20 | 240 | 20 | 208 | 18 | 20 |
| 40 | 500 | 20 | 650 | 18 | 20 |
| 20 | 169 | | | 20 | 14 |
| 20 | 359 | | | 20 | 8 |
| 20 | 196 | | | 20 | 20 |
| 20 | 210 | | | 24 | 10 |
| 20 | 246 | | | 20 | 18 |
| 20 | 350 | | | 20 | 30 |
| 50 | 390 | | | 30 | 36 |
| 50 | 400 | | | 52 | 140 |
| 50 | 426 | | | | |
| Mean value 8.6 seconds duration of response/second introduction | | Mean value 22 seconds duration of response/second introduction | | Mean value 1.6 seconds duration of response/second introduction | |

lower levels of the tracheobronchial tree as denoted in the upper half of figure 4. Thus greater depth of penetration occurred with ultrasonic nebulization.

When nebulized water was introduced into the respiratory tree, a consistent increase in net moisture was noted, persisting for a variable period of time following removal of the nebulizer. The time, however, varied with the type of nebulizer used (table 4). For each second of nebulization, the duration of increase in moisture following cessation of nebulization was 1.6 seconds for air-activated nebulizer as compared with 8.6 and 22 seconds, respectively, for the no. 1 and no. 2 settings of the ultrasonic nebulizer. Thus, the duration of effective increase in moisture was greatly prolonged with ultrasonic nebulizers in comparison to conventional air-activated nebulizers.

## Discussion

Conventional air-activated nebulizers in use in most hospitals effect a small transient increase in net moisture within the upper airway; very little increase in moisture is detectable at the level of the primary bronchi. Ultrasonic nebulization, however, results in a marked increase in moisture within the respiratory tract both in the upper airway and at the primary bronchial level. Following discontinuation of nebulization, this increase persists for a longer period of time. This retentive quality of ultrasonic nebulization perhaps lends validity to the practice of intermittent administration of inhalation therapy by this method.

While settings no. 3 and no. 4 of the ultrasonic generator produce an increase in aerosol output and density above that of lower settings, their measurement is beyond the scope of the detection system employed in this study. It is conceivable, therefore, that the higher settings result in a state of "supersaturation" related to a marked increase in liberation of free water. Thus, adjustment of aerosol output over a wider range than that observed in the experiments is readily achieved.

## Summary

Experiments were conducted in dogs to compare the efficacy of conventional and ultrasonic nebulizers in delivering moisture to the lower respiratory tract. To facilitate comparison, a water vapor transducer was constructed

of sufficiently small size to permit introduction into the tracheobronchial tree of dogs. Using this instrument, changes in moisture content were reflected in changes in conductivity across a sodium chloride crystal within an electrical circuit. The resultant responses were measured with a d.-c. recorder. The results of these experiments revealed that conventional air-activated nebulizers effect a mean increase of 0.18 humidity units per second in the lower airway. Ultrasonic generators produce a mean increase of 0.71 and 4.03 units per second, respectively, for no. 1 and no. 2 settings. Thus there is a marked increase in deposition of moisture in the lower tracheobronchial tree using ultrasonic generators as compared to conventional air-activated nebulizers.

## References

1. Tovell, R. M., and D'Ambruoso, D. C.: Humidity in inhalational therapy, ANESTHESIOLOGY 23: 452, 1962.
2. Mataushek, J.: Einführung in die Ultrashall-Technik, VEB Verlag, Techn., Berlin, August 1964.
3. Gauthier, W.: Aerosol output characteristics of ultrasonic generator. Toledo, DeVilbiss Res. Bull, 1964.
4. Dautreband, L.: Microaerosols. New York, Academic Press, 1962.
5. Landahl, H. O., Tracewell, T. M., and Lassen, W. W.: On the retention of airborn particles in the human lung, Arch. Indust. H and G 3: 359, 1951.
6. Krobath, H., and Reid, C.: Continuous recording of inspiraiton and expiration, Amer. J. Med. Electr. 3: 105, 1964.
7. Ruskin, Robert E.: Humidity and Moisture, vol. 1. New York, Reinhold, 1965.

**FULMINATING HEPATITIS** Since acute massive hepatic necrosis usually runs a short course and the liver cells do not have the opportunity to regenerate and resume function, the chances of survival might be increased if the patient could be maintained beyond the acute destructive phase. Exchange transfusion was successfully carried out on two successive days on a patient apparently suffering from fatal acute hepatitis. The patient survived; however, several other modes of therapy were also employed. (*Berger, R. L., and others: Exchange Transfusion in the Treatment of Fulminating Hepatitis, New Eng. J. Med. 274: 497 (Mar. 3) 1966.*) EDITOR'S COMMENT: Treatment of this condition has run a wide array of therapeutic techniques and modalities, including steroids, intestinal nonabsorbable antibiotics, homologous crosscirculation, heterologous liver perfusion and hemodialysis. This new report of exchange transfusion deserves recognition but, as the authors recognize, further evaluation of the efficacy of this procedure is indicated.

**SEPTICEMIA** Septicemia is an increasingly serious problem in surgery. During the past 10 years, the incidence has tripled. Most of the increase has been due to Gram-negative bacilli, a lesser amount to *Staphylococcus aureus*. The mortality rate has not been greatly improved. The ages of highest incidence are the first year of life and the seventh and eighth decades. (*Altemeier, W. A., Todd, J. C., and Inge, W. W.: Newer Aspects of Septicemia in Surgical Patients, Arch. Surg. 92: 566 (Apr.) 1966.*)