May 1991
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RESPIRATORY CARE

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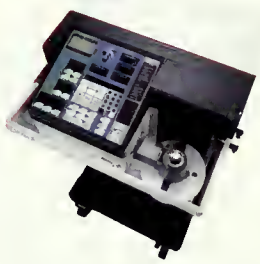

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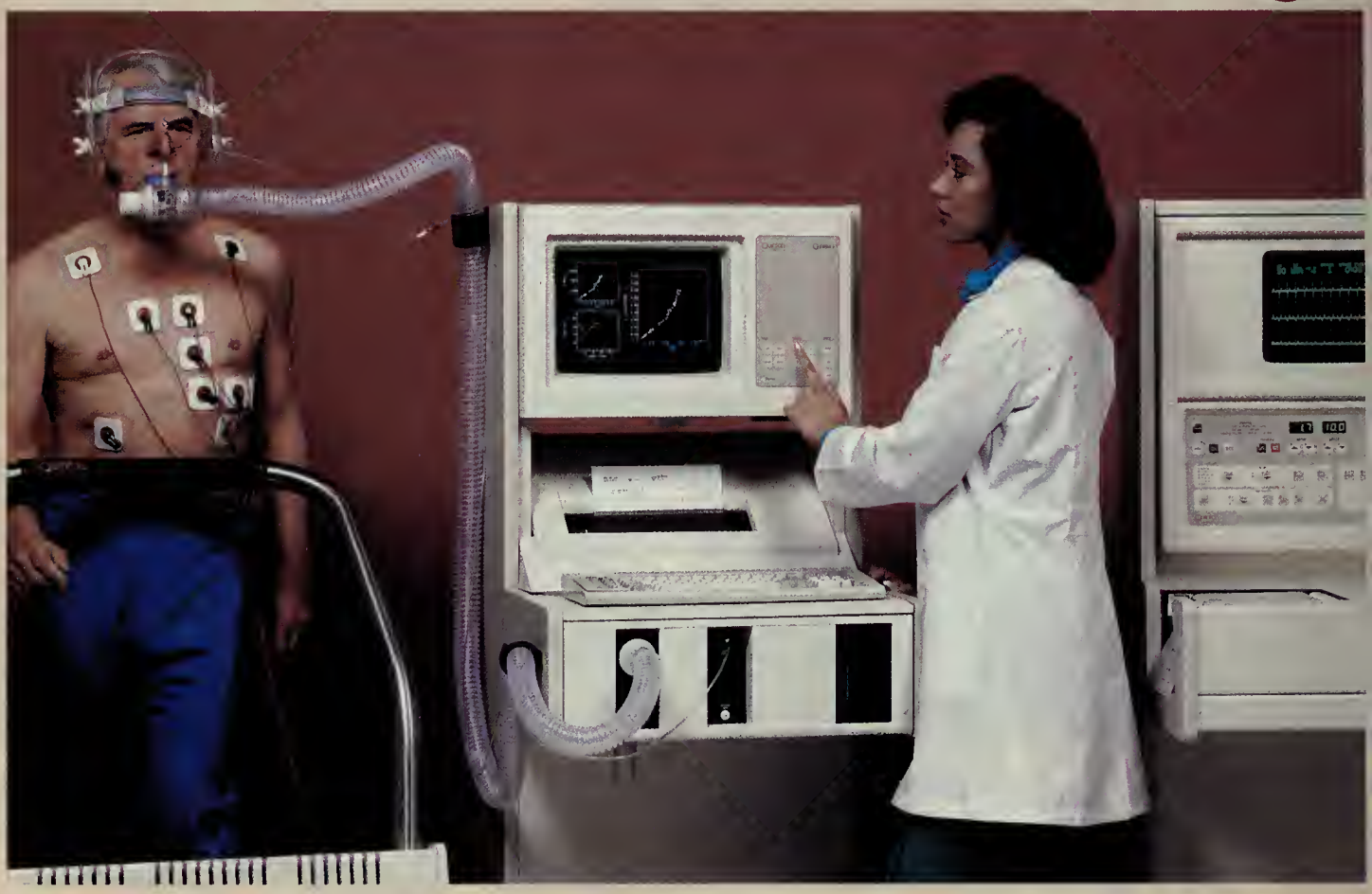

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RESPIRATORY CARE

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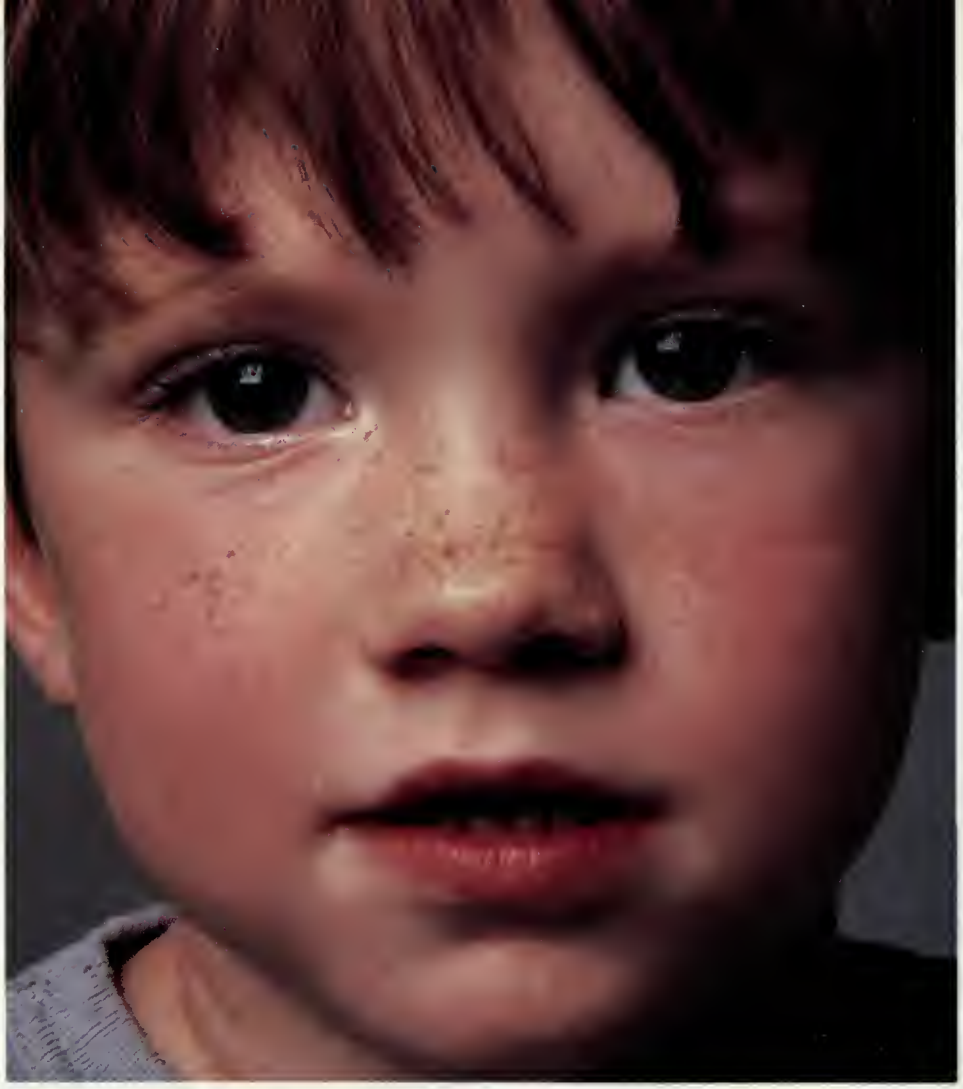

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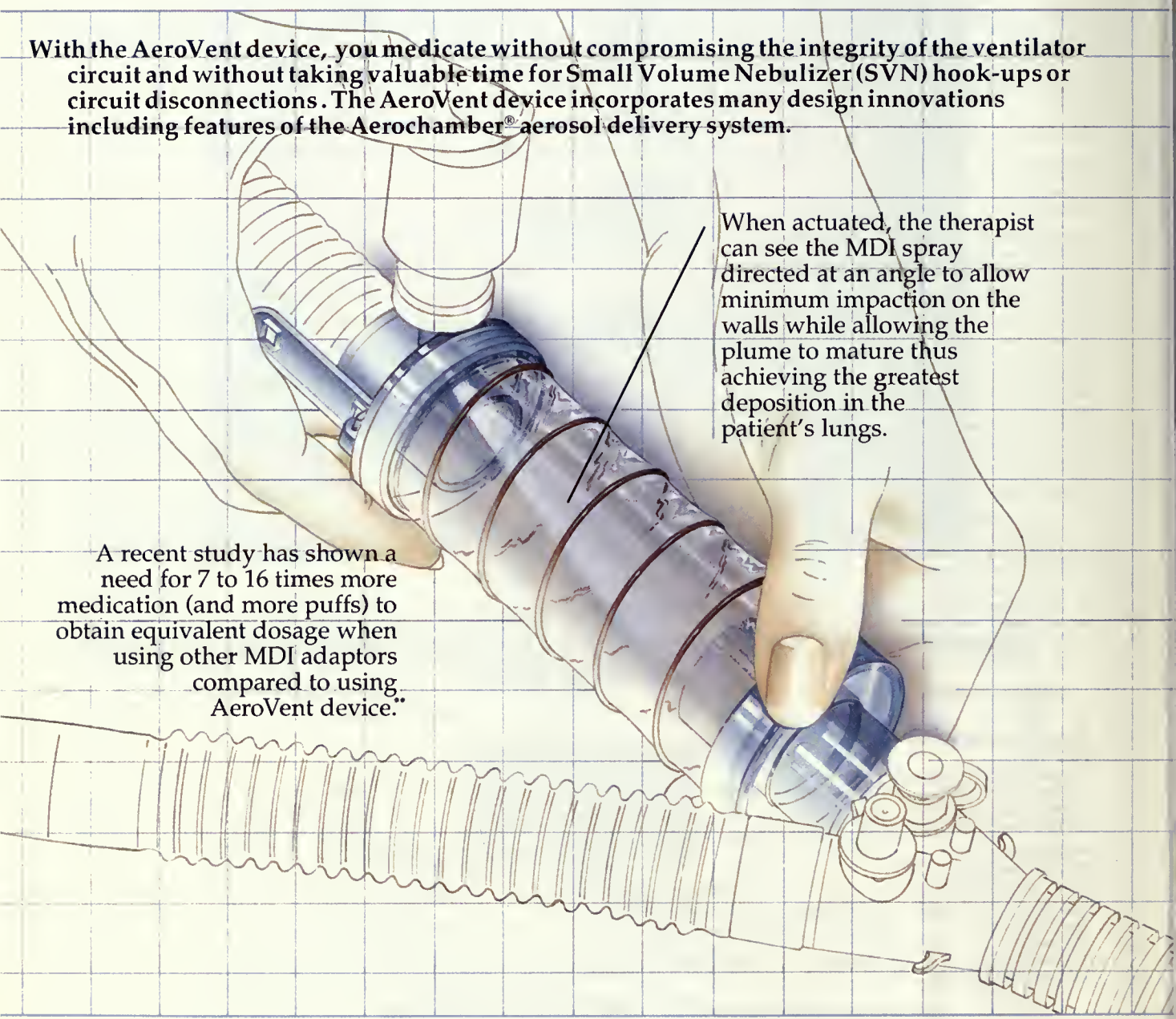

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** Metered Dose Inhaler Actuator-Adapters: A Comparison of Particle Size and Drug Delivery Through an Endotracheal Tube - Richard P. Larson, RRT et all - Resp. Care. Nov '89 Vol 34 No 11

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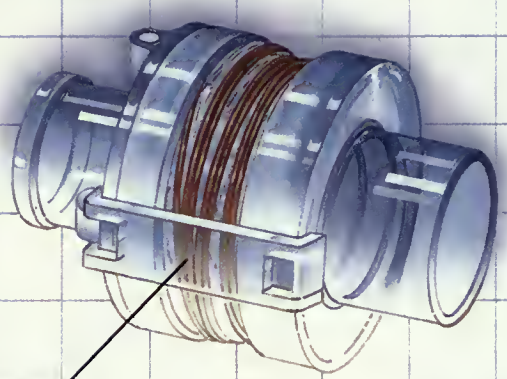

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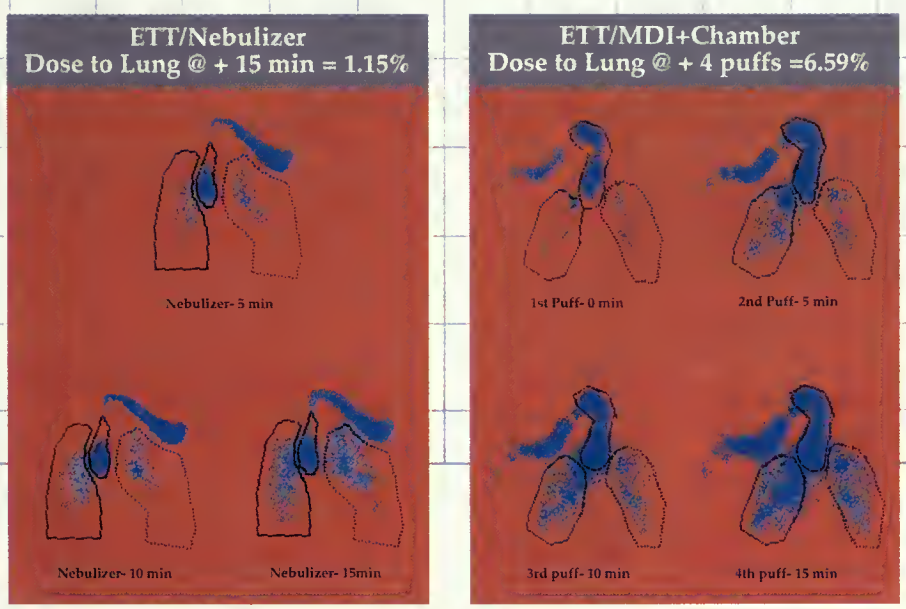

Graphic Representation of Actual Lung Deposition Data.

* Fuller HD, Dolovich MB, Posmituck G, Wong Pack W. and Newhouse MT. Pressurized Aerosol versus Jet Aerosol Delivery to Mechanically Ventilated Patients: Comparison of dose to the lungs. Am Rev Respir Dis; 141:440-444

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Reviews, Editorials, and Statements to Note

Intermediate Care Units: Graded Care Options (editorial)—J Popovich Jr. Chest 1991;99:4. (Pertains to Elpern et al paper abstracted below.)

Methotrexate: Does It Treat or Induce Asthma?(editorial)—D Fertel, A Wanner. Am Rev Respir Dis 1991;143:1. (Pertains to Jones et al paper abstracted below.)

The Noninvasive Respiratory Care Unit:Patterns of Use and Financial Implications—EH Elpern, MR Silver, RL Rosen, RC Bone. Chest 1991;99:205.

Clincial, socieconomic, and ethical dilemmas have prompted reevaluation of traditional methods of providing intensive care. Six years ago, we established a noninvasive respiratory care unit (NRCU) for selected patients in need of intensive respiratory monitoring and therapy, particularly those requiring prolonged mechanical ventilation. One impetus for the formation of the NRCU was the expectation that it might prove to be a less costly alternative to the intensive care unit for selected patients. We reviewed data from all patients admitted to the NRCU from July 1, 1987 through June 30, 1988 to identify characteristics of the patient population and to evaluate potential cost savings. During one year of operation, 136 patients were admitted to the unit, 107 of whom were mechanically ventilated. Overall, hospital costs for these patients exceeded payments by $1,519,477. Losses were greatest for mechanically ventilated patients and those for whom Medicare or Medicaid were the primary payors. Daily costs of care for mechanically ventilated patients were $1,976 lower in the NRCU than in the medical intensive care unit. We conclude that the NRCU represents a cost-effective approach to the care of substantial numbers of patients requiring specialized respiratory care.

Methotrexate-induced Asthma—G Jones, E Mierins, J Karsh. Am Rev Respir Dis 1991;143:179.

A patient with rheumatoid arthritis developed pulmonary symptoms and function test adnormalities consistent with asthma during methotrexate therapy. Assessments of airway responsiveness to methacholine during therapy revealed airway hyperreactivity that reverted to normal when the methotrexate was stopped. An extension of the methotrexate dosage interval from 7 to 10 days resulted in an abolition of the asthma, which remained in remission despite a return to a weekly cycle after a 3-month period of 10-day cycles.

Controlled Trial of a Home and Ambulatory Program for Asthmatic Children—RM Hughes, M McLeod, B Garner, RB Goldbloom. Pediatrics 1991;87:54.

Care of asthmatic children is often episodic and more therapeutic than preventive. A 2-year randomized, controlled trial involving 95 children measured the impact of a comprehensive home and ambulatory program for pediatric asthma management using objective outcome measures. Interventions for the study group during the first year included 3-month clinic visits, education, and home visits by a specially trained research nurse. Control subjects continued to receive regular care from a family physican or pediatrician. Eighty-nine subjects (93%) completed the study. Study subjects had less school absenteeism than control subjects (10.7 vs 16.0 days, $p = 0.04$) and showed significantly better small airway function after 1 year. Asthma severity improved in 13 study subjects and worsened in 5. The reverse was true for control subjects. Study subjects exhibited better metered aerosol technique than control subjects ($p = 0.0005$). Fewer days were spent in hospital by the study subjects admitted compared with control subjects (3.67 vs 11.2 days, $p = 0.02$). After 1 year, more study than control families (72.1% vs 33.1%, $p = 0.006$) reported that their asthmatic child took responsibility for the asthma management. The intervention failed to reduce exposure to secondhand smoke or to household pets. There were no significant differences in medical visits, theophylline levels, or records

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† Shapiro S, Hendler J, Ogirala R, Aldrich T, Shapiro MB: An evaluation of the accuracy of Assess and Mini-Wright peak flow meters. *Chest 99*:358-362, 1991.

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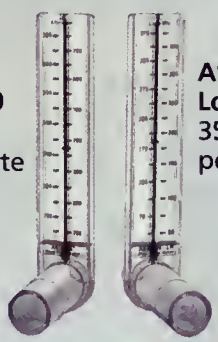

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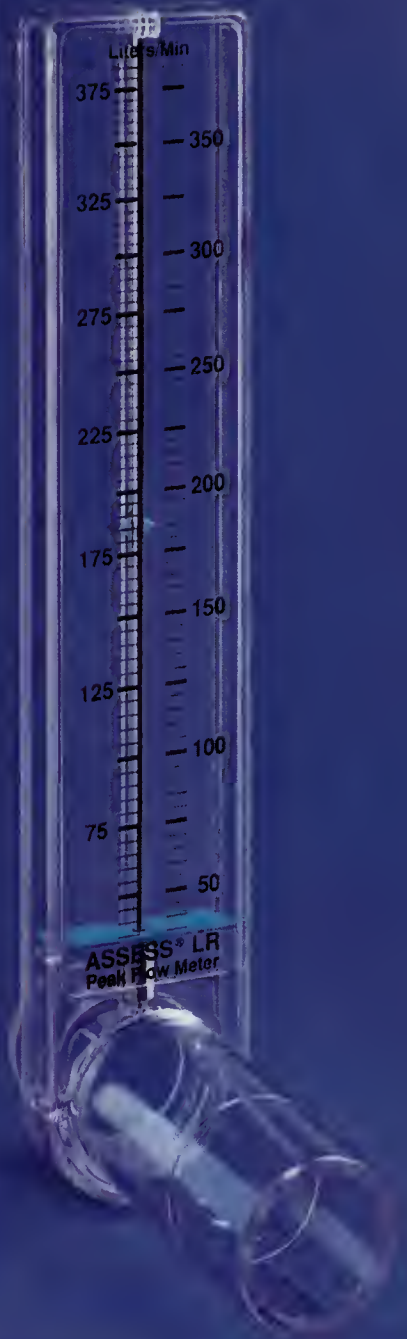

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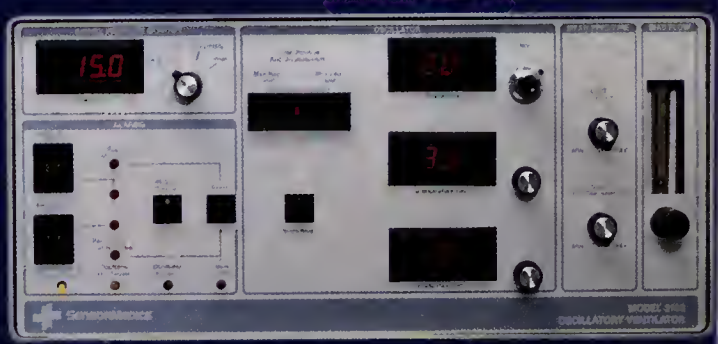

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2 High Frequency Oscillation Decreases the Incidence of Air Leak Syndrome in Infants with Severe Respiratory Distress Syndrome. HIFO Study Group, Snowbird High Frequency Conference, 1991.

3 High Frequency Oscillatory Ventilation and ECMO for Treatment of Acute Neonatal Respiratory Failure. J. Carter, D. Gerstman, R. Clark, D. Cornish, D. Null, R deLemos, Pediatrics, February 1990.

of asthma symptoms. One year after discontinuing the intervention, a marked 'washout' effect was observed. Comprehensive ambulatory programs of childhood asthma management can improve objective measures of illness severity but must be sustained.

Respiratory Arrest in Near-Fatal Asthma—NA Molfino, LJ Nannini, AN Martelli, AS Slutsky.N Engl J Med 1991;324:285.

Background and Methods. The majority of asthma-related deaths occur outside the hospital, and therefore the exact factors leading to the terminal event are difficult to ascertain. To examine the mechanisms by which patients might die during acute exacerbations of asthma, we studied 10 such patients who arrived at the hospital in respiratory arrest or in whom it developed soon (within 20 minutes) after admission. *Results.* The characteristics of the group were similar to those associated in the literature with a high risk of death from asthma, including a long history of the disease in young to middle-aged patients, previous life-threatening attacks or hospitalizations, delay in obtaining medical aid, and sudden onset of a rapidly progressive crisis. Extreme hypercapnia (mean [SD] partial pressure of arterial carbon dioxide, 97.1 [31.1] torr) and acidosis (mean [SD] pH, 7.01 [0.11] were found before mechancial ventilation was begun, and four patients had hypokalemia on admission. Despite the severe respiratory acidosis, no patient had a serious cardiac arrhythmia during the resuscitation maneuvers or during hospialization. We observed systemic hypertenison and sinus tachycardia in eight patients, atrial fibrillation in one, and sinus bradycardia in another. In both patients with arrhythmia the heart reverted to sinus rhythm immediately after manual ventilation with 100% oxygen was begun. The median duration of mechanical ventilation was 12 hours, and all patients had normocapnia on discharge from the hospital. *Conclusions.* We conclude that at least in this group of patients, the near-fatal nature of the exacerbations was the result of severe asphyxia rather than cardiac arrhythmias. These results suggest that undertreatment rather than overtreatment may contribute to an increase in mortality from asthma.

Analysis of Expiratory Pattern for Monitoring Bronchial Obstruction in School-Age Children—R Cutrera, SI Filtchev, R Merolla, G Willim, J Haluszka, R Ronchetti. Pediatr Pulmonol 1991;10:6.

This study was designed to assess the validity of the percent of volume expired at tidal peak flow (dV/V_t, ratios as an indicator of bronchial obstruction in school-age children. We analyzed 126 dV/V_t, ratios and compared them with spirometric and plethysmographic results measured in 24 healthy (14 males) and 60 asthmatic (41 females) children; 42 of them underwent measurements before and after bronchial challenge with histamine. The two groups differed in resistance, forced expiratory volume in 1 second (FEV_1), and forced expiratory flows, as percents of predicted (FEV_1 94.6 $\pm$ 2.4% in controls vs 86.7 $\pm$ 1.6% in asthmatics; $p < 0.001$). They did not differ in peak expiratory flow (PEF), forced vital capacity, functional residual capacity, measured by body plethysmography, and in dV/V_t. The dV/V_t was found to correlate with FEV_1 ($r = 0.58, p < 0.001$), PEF ($r = 0.57, p < 0.001$) and other lung function parameters. Forty-two of the asthmatic children performed a bronchoprovocation histamine test. The fall of dV/V_t after histamine was significantly correlated ($r = 0.61$, $p < 0.001$) with the variation in FEV_1 and other lung function parameters. We conclude that dV/V_t is a good indicator of bronchial obstruction, as useful in school-age children as in adults and infants, with no need for the subjects cooperation.

Reductions in Exercise Lactic Acidosis and Ventilation as a Result of Exercise Training in Patients with Obstructive Lung Disease—R Casaburi, A Patessio, F Ioli, S Zanaboni, CF Donner, K Wasserman. Am Rev Respir Dis 1991;143:9.

Though exercise training is part of most pulmonary rehabilitation programs, whether there is a physiologic basis for increased exercise tolerance is unclear. We sought to determine whether patients with chronic obstructive pulmonary disease (COPD) are capable of obtaining a physiologic training effect, as manifested by a reduction in blood lactate and ventilation ($\dot{V}_E$) at a given level of exercise. We also sought to determine whether training work rate determines the size of the training effect. Nineteen participants with COPD of predominately moderate severity in an inpatient rehabilitation program performed two cycle ergometer exercise tests at a low and a high work rate for 15 min or to tolerance and also an incremental exercise test to tolerance. Arterial blood was sampled for blood gas and lactate analyses. Identical tests were performed before and after 5-day-per-week cycle ergometer training for 8 wk either for 45 min/day at a high work rate (average, 71 W) or for a proportionally longer time at a low work rate (average, 30 W). Average FEV_1 was 56 $\pm$ 12% predicted and did not change with training. Peak exercise lactate (average, 6.5 mEq/L) was not correlated with FEV_1. For the high work rate training group, identical work rates engendered less lactate (4.5 vs 7.2 mEq/L) and less $\dot{V}_E$ (48 vs 55 L/min) after training; the low work rate training group had significantly less lactate and $\dot{V}_E$ decrease ($p < 0.01$). Further, endurance time for the high constant work

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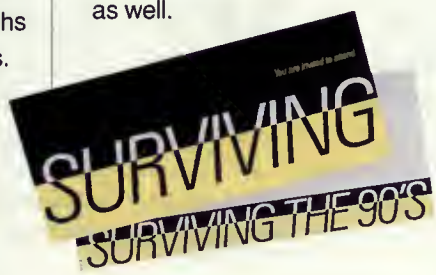

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[1] Nocturnal Oxygen Therapy Trial Group. Continuous or nocturnal oxygen in hypoxemic chronic obstructive lung disease: a clinical trial. *Ann Intern Med.* 1980; 93:391-8.

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rate increased 73% in the high work rate training group but only 9% in the low work rate training group. At identical work rates, $\dot{V}_E$ decrease averaged 2.5 L/min per mEq/L decrease in lactate ($r = 0.75$). We conclude that most COPD subjects studied increased blood lactate at low work rates. Many of these patients were able to achieve a physiologic training effect. Though total work was the same, training at a high work rate was more effective than was training at low work rates. The lower $\dot{V}_E$ requirement to perform exercise was in proportion to the lower lactate level, but the $\dot{V}_E$ decrease for a given decrease in lactate was smaller than that seen in normal subjects (7.2 L/min/mEq/L) apparently because patients with COPD fail to hyperventilate in response to lactic acidosis (P_{aCO_2} does not drop). These findings provide a physologic rationale for exercise training of patients with COPD.

Cooling Mediates the Ventilatory Depression Associated with Airflow through the Larynx—OP Mathew, JW Anderson, GP Orani, FB Sant'Ambrogio, G Sant'Ambrogio. Respiration Physiology 1990;82:359.

Although constant airflow through the upper airway has been shown to induce ventilatory depression in anesthetized newborn animals, the role of laryngeal temperature in this response has not been studied. Experiments were performed in fourteen 1- to 5-day-old anesthetized puppies breathing through a tracheostomy. Tidal volume and laryngeal temperature were recorded while a constant stream of air (15-25 mL/s) at room temperature was passed in the expiratory direction for 20 seconds through the isolated upper airway. Warm (35-37°C), humidified air at the same flow served as control. When laryngeal temperature was decreased by 7.5 ± 0.9°C, a marked change in breathing pattern was observed ($V_T = 54 \pm 5$ mL, $t_i = 187 \pm 33$ ms, $t_e = 636 \pm 179$ ms, $V_T/t_i = 45 \pm 10\%$ of control; $n = 9$). Warm air at the same flow induced no significant changes. Superior laryngeal nerve section abolished the effects of cooling on breathing pattern. In 5 puppies we compared the effect of 'fast' and 'slow' laryngeal cooling. Fast trials altered breathing pattern earlier than slow trials. We conclude that the depressant effect of airflow through the upper airway is entirely due to a decrease in laryngeal temperature and is mediated by superior laryngeal nerve afferents.

Effect of Inhaled Beclomethasone Dipropionate on Bronchial Hyperreactivity in Asthmatic Children during Maximal Allergen Exposure—AL Boner, GL Piacentini, C Bonizzato, V Dattoli, L Sette. Pediatr Pulmonol 1991;10:2.

In this double-blind study we evaluated the effect of a 2 months long treatment with inhaled beclomethasone dipropionate (300 μg/day) on methacholine responses in asthmatic children, during a period of maximal allergen exposure. Baseline values of methacholine PC_{20}-FEV_1 were 0.66 ± 0.22 mg/mL (mean ± SEM) in 10 children treated with the active drug and 0.78 ± 0.21 mg/mL in 10 children treated with placebo. After 1 month of treatment PC_{20}-FEV_1 was 1.91 ± 0.64 and 0.80 ± 0.33 mg/mL, respectively, in the groups treated with beclomethasone versus placebo. A statistically significant reduction in bronchial hyperreactivity (PC_{20}-FEV_1, 5.49 ± 1.86 mg/mL) but no systemic side effects were observed after 2 months of treatment with beclomethasone dipropionate. This is compared with a PC_{20}-FEV_1 of 1.38 ± 0.52 mg/mL in the placebo group. The results confirm the effect of inhaled corticosteroids in reducing bronchial hyperreactivity, even during a period of maximal allergen exposure.

The Diagnostic Utility of the Antibody-Coated Bacteria Test in Intubated Patients—RG Wunderink, GB Russell, E Mezger, D Adams, J Popovich. Chest 1991;99:84.

Purpose: Pilot study to determine if the presense of antibody-coated bacteria (ACB) in sputum specimens obtained from endotracheal tube suctioning would aid in the diagnosis of lower respiratory tract infection (LRTI). *Patients and Methods:* All endotracheally intubated and mechanically ventilated patients for a 2-month period were recruited for study. The diagnosis of LRTI was based on a clinical suspicion sufficient enough to start or change antibiotic therapy. Specimens were obtained by blind endotracheal tube suctioning. After processing, sputum smears were stained with fluorescein-labelled antibody to the Fc portion of IgG, IgM, and IgA. More than five fluorescein-labelled bacteria per oil immersion field were considered positive smears. *Results:* Seventy-one specimens were obtained from 36 patients. Eighteen specimens were positive in 12 patients, all of whom had LRTI. No specimen was positive in patients not diagnosed as having LRTI. The ACB test was postive in 12 of 25 patients with LRTI. Patients with LRTI but negative ACB were more likely to have received prior antibiotic therapy ($p < 0.001$). ACB was positive prior to the clinical diagnosis of LRTI in seven of nine patients (average 4.1 days, range 2-6 days) and converted to negative in three specimens obtained seven or more days after starting appropriate antibotics, while in three specimens it remained positive 3-6 days post treatment initiation. *Conclusions:* The ACB test appears to be highly specific for the presense of LRTI in intubated patients. Sensitivity of the test may

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be adversely affected by prior antibotic therapy. A positive ACB test may predict the subsequent development of LRTI. Further study is warranted.

Total Parenteral Nutrition in the Newborn Infant: Energy Substrates and Respiratory Gas Exchange—B Piedboeuf, P Chessex, J Hazan, M Pineault, JC Lavoie. J Pediatr 1991;118:97.

The hypothesis that a high-fat parenteral regimen was beneficial for respiratory gas exchanges, in comparion with a high-glucose regimen, was tested in a paired crossover design. Ten parenterally fed newborn infants with no respiratory problems received two 5-day isoenergetic and isonitrogenous regimens that differed in their nonprotein source of energy; the level of fat intake (low fat [LF] 1 g · kg^{-1}; high fat [HF] 3 g · kg^{-1} · day^{-1}) varied inversely with that of glucose. Continuous transcutaneous P_{O_2} (P_{tcO_2}) and P_{CO_2} (P_{tcCO_2}), respiratory gas exchange (indirect calorimetry), and plasma arachidonate metabolites were measured at the end of each regimen. Oxygen consumption and resting energy expenditure were not affected by modification of the source of energy. However, carbon dioxide production ($\dot{V}_{CO_2}$) was higher during LF than during HF (6.9 ± 0.2 versus 6.2 ± 0.1 mL · kg^{-1} · min^{-1}; $p < 0.01$), as was the respiratory quotient (1.08 ± 0.02 versus 0.96 0.02; $p < 0.001$). Despite the differences in $\dot{V}_{CO_2}$, the P_{tcCO_2} was not affected, suggesting adequate pulmonary compensation during LF, as documented by the higher minute ventilation (160 ± 7 vs 142 ± 5 mL · kg^{-1} · min^{-1}; $p < 0.01$). The lower P_{tcCO_2} during the HF regimen (73.8 ± 2.8 versus 68.8 ± 2.6 torr; $p < 0.015$) indicated a disturbance at the alveolocapillary level induced by the lipid emulsion. No differences were found in circulating levels of prostaglandins and thromboxanes. The substitution of glucose for lipid did not modify fat storage (2.1 ± 0.3 vs 2.1 ± 0.3 g · kg^{-1} · day^{-1}). We conclude that the supposed beneficial effect of a fat emulsion on respiratory gas exchange is questionable.

Bronchiolar Inflammation and Fibrosis Associated with Smoking: A Morphologic Cross-sectional Population Analysis—AM Adesina, V Vallyathan, EN McQuillen, SO Weaver, JE Craighead. Am Rev Respir Dis 1991;143:144.

The lungs of 42 smokers and 13 nonsmoking males of various ages who died suddenly and unexpectedly were examined grossly using Gough-Wentworth whole-lung sections and by microscopic planimetry to assess the severity and prevalence of emphysema. The bronchioles in representative histologic sections were evaluated for inflammation and epithelial metaplasia as well as for fibrosis and muscular hypertrophy. Postmortem interviews with next of kin established a history of cigarette smoking and excluded possible occupational exposures to toxic or particulate inhalants. Emphysematous changes were not prominent in members of the study group, but they tended to be more severe in smokers ($p = 0.059$) and increased in severity with age ($p < 0.001$). Inflammatory changes (so-called smoker's bronchiolitis) were evident in smokers of all ages, although they were significantly less prominent in the lungs of older smokers. On the other hand, respiratory and membranous bronchiolar wall fibrosis was increasingly evident in older smokers ($p < 0.05$). Muscular hypertrophy in the bronchiolar walls was significantly greater in smokers, but a change with age was not observed. These findings strongly suggest that bronchiolar fibrosis is associated with chronic cigarette use. These lesions occur independently of emphysema and may account for some of the subtle physiologic alterations observed in smokers.

Treatment of Tuberculosis in Patients with Advanced Human Immunodeficiency Virus Infection—PM Small, GF Schecter, PC Goodman, MA Sande, RE Chaisson, PC Hopewell. N Engl J Med 1991;324:289.

Background and Methods: Infection with the human immunodeficiency virus (HIV) increases the risk of tuberculosis chemotherapy. To examine the outcomes in patients with both diagnoses, we conducted a retrospective study of all 132 patients listed in both the acquired immunodeficiency syndrome (AIDS) and tuberculosis case registries in San Francisco from 1981 through 1988. *Results:* At the time of the diagnosis of tuberculosis, 78 patients (59%) did not yet have a diagnosis of AIDS, 18 patients (14%) were given a concomitant diagnosis of AIDS (as determined by the presence of an AIDS-defining disease other than tuberculosis), and the remaining 36 patients (27%) already had AIDS. The manifestiations of tuberculosis were entirely pulmonary in 50 patients (38%), entirely extrapulmonary in 40 patients (30%), and both pulmonary and extrapulmonary in 42 patients (32%). The treatment regimens were as follows: isoniazid and rifampin supplemented by ethambutol for the first 2 months, 52 patients; isoniazid and rifampin supplemented by pyrazinamide and ethambutol for the first 2 months, 39 patients; isoniazid and rifampin, 13 patients; isoniazid and rifampin supplemented by pyrazinamide for the first 2 months, 4 patients; and other drug regimens, 17 patients. The intended duration of treatment for patients whose regimen included pyrazinamide was 6 months, and for patients who did not receive pyrazinamide, 9 months. Seven patients received no treatment because tuberculosis was first diag-

nosed after death. Sputum samples became clear of acidfast organisms after a median of 10 weeks of therapy. Abnormalities on all chest radiographs taken after three months of treatment were stable or improved except for those of patients who had new nontuberculous infections. The only treatment failure occured in a man infected with multiple drug-resistant organisms who did not comply with therapy. Adverse drug reactions occured in 23 patients (18%). For all 125 treated patients, median survival was 16 months from the diagnosis of tuberculosis. Tuberculosis was a major contributor to death in 5 of the 7 untreated patients and 8 of the 125 treated patients. Three of 58 patients who completed therapy had a relapse (5%); compliance was poor in all 3. *Conclusions:* Tuberculosis causes substantial mortality in patients with advanced HIV infection. In patients who comply with the regimen, conventional therapy results in rapid sterilization of sputum, radiographic improvement, and low rates of relapse.

A New System for Location of Endotracheal Tube in Preterm and Term Neonates—M Blayney, S Costello, M Perlman, K Lui, J Frank. Pediatrics 1991;98:44.

A randomized controlled trial was conducted to evaluate a new noninvasive system for placement of the endotracheal tube, based on a magnetic field interference-sensing technique. Seventy-two neonates treated by the standard technique were compared with 70 treated by the new system (TRACH MATE), with radiographic localization as the standard. As judged by the author(s) on the morning after the intubation, correct initial placement was achieved in 69 (78%) of 88 intubations using the new system, compared with 71 (66%) of 107 using the standard technique (Fisher's Test, one-tailed; $p = 0.044$). Repositioning was actually done in 23 (26%) of 88 TRACH MATE intubations, compared with 42 (39%) of 107 standard intubations (Fisher's test, one-tailed; $p = 0.037$). Intubation of the right main bronchus occurred in 7 standard intubations, but in none of the TRACH MATE intubations (Fisher's test, one-tailed; $p = 0.014$). Endotracheal tube position (high, low, or appropiate) was correctly determined by TRACH MATE in 77 (90%) of 85 intubations; the position was not recorded on three occasions. No differences in the number of complications (eg, unplanned extubations, distal displacement, subglottic stenosis) were found between the two groups. It is concluded that the TRACH MATE technique is superior to the standard clinical method in initial placement of the endotracheal tube.

Effects of Initial Flow Rate and Breath Termination Criteria on Pressure Support Ventilation—NR MacIntyre, L-I Ho. Chest 1991;99:134.

To assess whether adjustments in the initial flow rate or breath termination criteria affected patient-ventilator synchrony, we studied the ventilatory pattern response to pressure support (PS) in 33 patients under two sets of circumstances: during seven different levels of delivered initial PS flow and during PS termination at 50% and at 25% of peak flow. In the study on initial PS flow, we found the following: (a) an optimal initial PS flow could be defined for a given level of PS that resulted in the patient obtaining maximal pressure and volume from the ventilator; (b) initial PS flows above and below this optimal flow were associated with faster breathing frequencies, shorter inspiratory times, smaller tidal volumes and a tendency for airway pressure to not reach the selected PS level; and (c) optimal initial PS flow was fastest in patients with the lowest compliances and the most active ventilatory drives. Changing PS termination criteria from 50 to 25% of peak flow had minimal effects on the ventilatory pattern or synchrony. We conclude that the initial PS flow to achieve the selected PS level is important in patient-ventilator synchrony but that termination criteria set between 25 and 50% of peak flow is not.

Effect of Infant Position on Breath Amplitude Measured by Transthoracic Impedance and Strain Gauges—TM Baird, MR Neuman. Pediatr Pulmonol 1991;10:52.

Continuous monitoring of respiration by transthoracic electrical impedance gives a signal that has certain not well understood irregularities. Among them is a change in the amplitude of the signal when there is no apparent change in the infant's tidal respiration. One factor that could hypothetically account for alterations of the impedance signal is a change in current path through the thorax secondary to a change in body position. To test this hypothesis we have studied the relationships between breath amplitude measured by transthoracic impedance, one strain gauge on the chest and one on the abdomen, and tidal volume by intergrated flow in four body positions. Median breath amplitude was found to vary significantly with body position according to the measuring device. The median impedance breath amplitude increased by 27% in the supine position compared with the prone position, with no associated change in tidal volume. Differences in the strain gauge signal amplitude for these positions were not statistically significant. Correlation between breath amplitude measured by impedance changes and tidal volume was minimal ($r = 0.114$). These results indicate that infant position affects impedance breath amplitude independently of changes in tidal volume.

The Effect of Varying Inspiratory Flow Waveforms on Peak and Mean Airway Pressures with a Time-Cycled Volume Ventilator: A Bench Study

Joseph L Rau Jr PhD RRT and David C Shelledy PhD RPFT RRT

We examined the effect of seven inspiratory flow waveforms on peak (PAP) and mean (MAP) airway pressures using a lung model. METHODS: The Hamilton Veolar ventilator was operated in assist-control mode with standardized settings. PAP and MAP were measured for each inspiratory flow waveform under three simulated lung conditions: (1) a baseline of low 'airway' resistance (R_{aw}) and high compliance, (2) low compliance, and (3) increased airway resistance. RESULTS: With the baseline and low-compliance conditions, the inspiratory flow waveform resulted in PAP from 21.4 to 31.4 and 49.5 to 57.1 cm H_2O [2.1-3.08 and 4.85-5.6 kPa], respectively. PAP was lowest with the full decelerating waveform and increased in this order: modified-sine, sine, partial-decelerating, square, partial-accelerating, and full-accelerating waveforms. MAP was inversely related to PAP ($r = -0.94$, $p = 0.0014$ for baseline and $r = -0.884$, $p = 0.0083$ for low compliance). With increased R_{aw}, PAP increased from 33.5 to 67.8 cm H_2O [3.29-6.65 kPa]. R_{aw} was lowest with the partial-decelerating waveform and increased in this order: square, modified-sine, partial-accelerating, sine, full-decelerating, full-accelerating waveforms. MAP was not related to PAP ($r = -0.083$, $p = 0.8602$). CONCLUSION: Under all three test-lung conditions, a form of decelerating flow produced the lowest PAP and the highest MAP; whereas, the full-accelerating waveform produced the highest PAP and the lowest MAP. Under the baseline and low-compliance conditions, as PAP increased MAP decreased. With elevated R_{aw}, PAP is a function of the peak flow value more than of the pattern of flow. Knowledge of the effects of inspiratory flow waveform on PAP and MAP may aid clinicians in selecting an appropriate flow pattern for a given condition. (Respir Care 1991;36:347-356.)

Background and Introduction

With the development of third-generation microprocessor-controlled mechanical ventilators has come a proliferation of operator-selectable inspiratory flow waveforms. The Hamilton Veolar (Hamilton Medical Inc, Reno NV) originally offered four patterns of inspiratory flow, and recently this has been expanded to seven.

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The effects of variations in inspiratory flow pattern and resulting pressure waveforms have been examined in studies measuring a variety of outcomes. Cournand and associates[1] studied three types of inspiratory pressure waveforms in 1947, and reported that as mask pressures increased, cardiac output fell. Between 1963 and 1969, Bergman[2-4] reported similar work on healthy anesthestized human subjects and in a dog model. He concluded that increases in mean airway pressure (MAP) improve oxygenation and that the actual shape of the pressure waveform is not the important variable.

Other studies have examined inspiratory flow patterns rather than the pressure waveforms, with inconsistencies in the results reported. Some investigators found no difference in cardiopulmonary variables such as dead-space-to-tidal-volume

Abbreviations Used in This Paper

C.O.	—	Cardiac output
I:E	—	Ratio of inspiratory-to-expiratory time
$P_{(A-a)O_2}$	—	Alveolar-to-arterial oxygen gradient
P_{aCO_2}	—	Arterial carbon dioxide tension
P_{aO_2}	—	Arterial oxygen tension
PAP	—	Peak airway pressure
Q_s/Q_t	—	Venous admixture
R_{aw}	—	Airway resistance
V_d/V_t	—	Dead-space-to-tidal-volume ratio

A Guide to the Use of SI Units in This Paper

The SI unit for pressure is kPa.
(cm H_2O)(0.098 06) = kPa.

The SI unit for compliance is L/kPa.
(L/cm H_2O)(10.20) = L/kPa.

The SI unit for resistance is kPa·s·L^{-1}.
(cm H_2O·s·L^{-1})(0.098 06) = kPa·s·L^{-1}.

ratio (V_d/V_t), alveolar-to-arterial oxygen gradient [$P_{(A-a)O_2}$], arterial oxygen (P_{aO_2}) levels, or venous admixture (Q_s/Q_t), using different inspiratory flow waveforms.[3,5-8] Two of these studies,[7,8] one of which was reported in abstract form only,[7] utilized the four inspiratory waveforms on the earlier version of the Hamilton Veolar. Other studies have reported improvement in P_{aO_2}, $P_{(A-a)O_2}$, and compliance, with a decelerating-flow pattern.[9-14] Several studies found no changes in cardiac output (C.O.) with different inspiratory flow patterns.[6,11,12] However, Baker and others reported that inspiratory flow patterns that raise MAP depress C.O. in dogs with autonomic blockade.[10] Results are also inconsistent regarding the effect of different inspiratory flow patterns on P_{aCO_2}. Several studies found that varying inspiratory flow patterns makes no difference in P_{aCO_2}.[7,11,12] Others have reported that different flow patterns produce significant changes in P_{aCO_2}.[10,13,14] Banner and co-workers[15] found that a decelerating-flow pattern improves CO_2 elimination and decreases end-tidal CO_2, in a lung model.

Lyager and others[16] have reported poor distribution of inspired gas in a lung model when the effects of accelerating flow were compared to the effects of constant flow. A theoretical study by computer simulation also predicted a more even pulmonary gas distribution with a decelerating-flow pattern.[17] In contrast however, Johansson and Löfstrom[18] found that a decelerating pattern improved gas distribution in large airways but an accelerating pattern gave the greatest benefit on the "total effects of gas exchange." Their study with a Servo 900 ventilator measured breathing mechanics and gas exchange. Johansson and Löfstrom also reported an increase in V_d/V_t with the decelerating as compared to the accelerating pattern. However, Baker and associates[10] reported a decrease in V_d/V_t with the decelerating-flow pattern produced by an experimental waveform generator in a dog model.

Some of the conflicting results may be due to the variability in study conditions. The ventilators used have ranged from the Bennett PR-2 and Engstrom 300 to the Servo 900 series and the more recent Hamilton Veolar. The condition of the pulmonary system may also affect the ability to detect differences in the effects of inspiratory flow waveforms. A study by Modell and Cheney[12] (using animal models of pulmonary disease) found that the inspiratory flow pattern is significant in improving gas exchange when severe ventilation-perfusion imbalance is present, but produces no change in normal dogs. In that study, the descending patterns gave a 10% increase in P_{aO_2} in the lung-injured dogs.

The effect of flow pattern on peak airway pressures (PAP) and MAP is particularly interesting because these measures are readily available to clinicians with current ventilators. Gas distribution in the lung and gas exchange and oxygenation may improve with increases in MAP.[19,20] This was, in fact, suggested by Bergman's early work in 1963.[2] At the same time, the hazards of high PAP or MAP in promoting barotrauma or depressing cardiac output must be minimized.[1,10,21-25] There is surprising agreement (despite the differences in machines and subjects studied) that decelerating patterns can reduce peak pressure, whereas accelerating patterns increase such pressure.[7,8,11,16,17] Investigators also agree that the opposite is true of MAP: Decelerating-flow patterns tend to increase and accelerating patterns tend to decrease mean pressure.[5,7,8,10,13,14,16] Results are mixed for the effect of square or sine patterns on MAP and may reflect differences in the subjects' pulmonary status.[5,7,10,13,14]

Our search of the literature did not reveal reports of the effect of modifications of the accelerating, decelerating, and sine patterns on peak and mean pressures or the effect of systematic changes in compliance and airway resistance on pressures generated by various inspiratory flow patterns.

The array of inspiratory flow waveforms now available suggests the following research questions. (1) Which inspiratory flow waveform produces the lowest and which the highest peak inspiratory pressure under different lung conditions? (2) Which inspiratory flow waveform produces the lowest and which the highest mean inspiratory pressures under different lung conditions? (3) Is there a relationship between peak and mean inspiratory pressures with different flow waveforms under different lung conditions? A lung model allowed us to seek answers to these questions without the presence of the confounding factors of mixed or unknown impedance changes seen in patients. The purpose of our study was to examine the effect in a lung model of seven inspiratory flow waveforms on peak and mean inspiratory pressures with changes in compliance and resistance, using a time-cycled, microprocessor-controlled volume ventilator.

Methods and Materials

The Hamilton Veolar is a third-generation, time-cycled, volume-preset, microprocessor-controlled ventilator. In the assist-control mode, the controls determining ventilation are the rate, V_T, and the ratio of inspiratory-to-expiratory time (I:E). The rate and I:E determine the inspiratory time. Flowrate is determined by the V_T and inspiratory-time settings. Flowrate can be further modified by the choice of inspiratory flow pattern. In a square, or constant, flow pattern, the flowrate equals the volume/unit inspiratory time. The full-decelerating wave doubles the square-wave flowrate at the given rate, volume, and I:E settings. Table 1 describes the influence of all seven flow patterns on peak flow, with the Hamilton Veolar.[26]

We obtained the ventilator from the manufacturer for this study, and operated it in the assist-control mode. Control settings for each of the seven inspiratory flow patterns were frequency 12/min; V_T 1.0 L; I:E 1:4 (20%); and pause 0. The pressure limit was set at maximum to avoid pressure cycling.

Table 1. The Determination of Peak Flow of the Hamilton Veolar during a Machine Breath. Inspiratory Time Is Held Constant at All Patterns. Peak Flows at 1-L Tidal Volume and 1-Second Inspiratory Time

Pattern	Peak Flow	Peak Value
Square	Flowrate is constant and equals V_T/t_i	60 L/min
Accelerating	Flowrate goes from 0 to 2 × square-wave value at given settings.	120 L/min
Decelerating	Flowrate begins at 2 × square-wave value and goes to 0.	120 L/min
Sine	Flowrate goes from 0 to 157% of square-wave value at mid-inspiration, then returns to 0.	94 L/min
50% Decelerating	Flowrate begins at 133% of square-wave value and declines to 66% at end-inspiration.	80 L/min
Modified Sine	Flowrate goes from zero to approximately 133% of the square-wave value by the first third of inspiration and then declines to zero.	80 L/min
50% Accelerating	Flowrate begins at 66% of the square-wave value and increases to 133% at end-inspiration.	80 L/min

These settings resulted in an inspiratory time of 1 second and a flowrate of 60 L/min with the square-wave pattern. The lung analog was passively ventilated with no simulation of active inspiration. No positive end-expiratory pressure (PEEP) was used, and all measurements were made with the humidifier bypassed to protect the test lung. A low-compliance breathing circuit from the manufacturer connected the ventilator to the lung analog.

Measurements of peak and mean pressure at the airway connection were obtained from the VT-1 Adult Ventilator Tester (Bio-Tek Instruments Inc, Winooski VT). This device consists of a 2.2-L lung analog connected to a microprocessor. Inspiratory pressures are measured using a pressure transducer connected to the inlet side of the simulated airway

on the lung analog, and represent pressure at the airway rather than alveolar pressures. Instrument accuracy was verified using a 1-L syringe, a known flowrate, and a water manometer. Kacmarek and co-workers[27] have reported a correlation coefficient of 1.0 for pressure readings in their evaluation of accuracy for the VT-1. Precision for pressure measurements is rated at ±2% by the manufacturer. All pressure measurements were corrected to their BTPS equivalents. Tracings of both inspiratory flow and pressure waveforms were obtained from an X-Y recorder (Model 750A, Cardiopulmonary Instrument Corp, Houston TX) using the analog output of the VT-1. The analog waveform outputs of the VT-1 are not compensated for temperature, humidity, or atmospheric pressure, and are suitable only for inspection of waveform shape rather than detailed quantitative measurement or calculation.

Pressures with each inspiratory flow pattern were measured using three different test-lung conditions. A baseline lung state was obtained using an airway resistance setting of 2.7 cm $H_2O \cdot s \cdot L^{-1}$ [0.265 $kPa \cdot s \cdot L^{-1}$] and a compliance factor of 0.05 L/cm H_2O [0.51 L/kPa]. The decreased-compliance condition lowered the compliance factor to 0.02 L/cm H_2O [0.204 L/kPa] with the same airway resistance setting. The increased-resistance condition used an airway resistance of 20.8 cm $H_2O \cdot s \cdot L^{-1}$ [2.04 $kPa \cdot s \cdot L^{-1}$], with the compliance returned to the baseline of 0.05 L/cm H_2O [0.51 L/kPa]. Thus, effects of changing compliance and airway resistance were examined separately.

PAP and MAP were measured three times for each flow pattern, and the mean reported as an estimate of the true value. Descriptive statistics consisting of histograms and scattergrams were used to report measurements of peak and mean airway pressures with the three lung conditions. Pearson correlation coefficients and their probabilities as determined by Student's *t* test were calculated for the relation of peak and mean pressures, for each of the three lung conditions. Because a single ventilator was used, there was no intermachine variability, and inferential statistical tests of differences in peak or mean pressures were not possible.

Results

Tracings of each of the inspiratory flow patterns across all three lung conditions can be seen in Figure 1, and verify the shape of the flow curves as described in the ventilator operator's manual.[26] Visual inspection of the inspiratory waveforms showed that the flow patterns were not modified by changes in resistance or compliance.

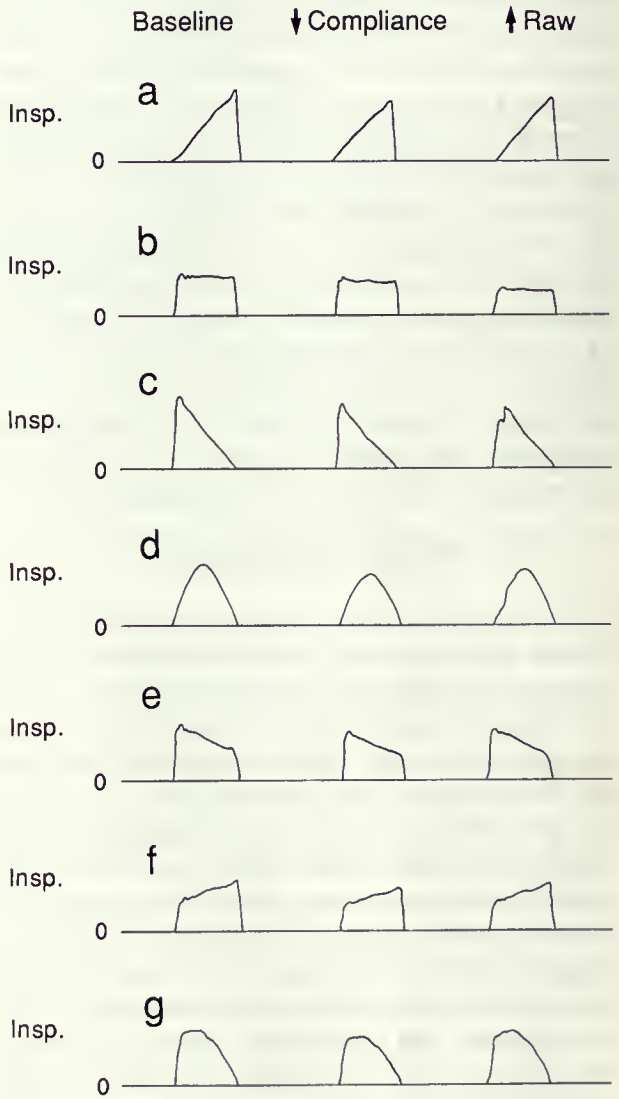

Fig. 1. Tracings of the seven inspiratory waveforms available with the Hamilton Veolar: (a) full accelerating, (b) square, (c) full decelerating, (d) sine, (e) partial decelerating (50%), (f) partial accelerating (50%), and (g) modified sine. (Adapted, with permission, from Reference 26.)

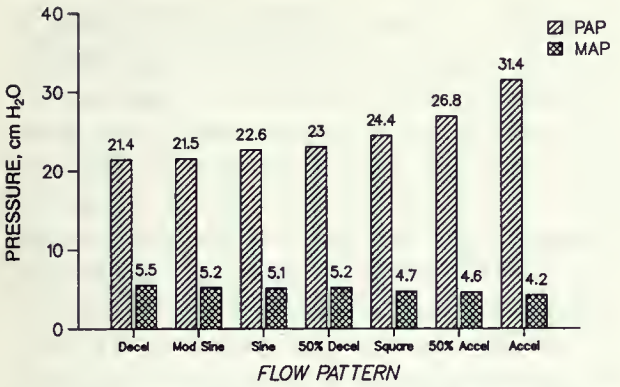

Fig. 2. Histograms of peak (PAP) and mean (MAP) airway pressures with each inspiratory flow pattern, arranged in order of minimum-to-maximum peak pressure, for the baseline condition. 50% Decel = partial decelerating; 50% Accel = partial accelerating.

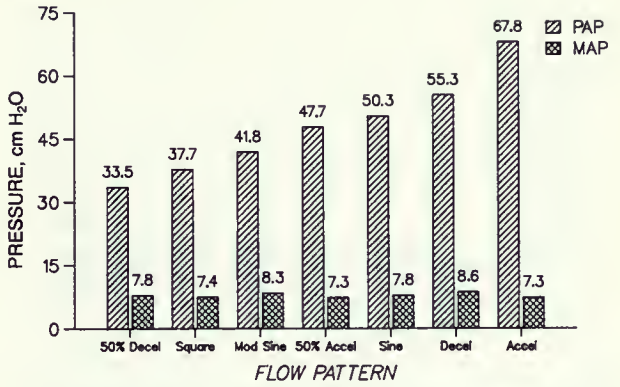

Fig. 4. Histograms of peak (PAP) and mean (MAP) airway pressures with each inspiratory flow pattern, arranged in order of minimum-to-maximum peak pressure, for the high-resistance condition. 50% Decel = partial decelerating; 50% Accel = partial accelerating.

Figures 2-4 display minimum-to-maximum peak inspiratory airway pressures for the seven flow patterns and the corresponding MAP. The order of the flow patterns producing the smallest-to-largest peak pressure was the same for both the baseline and the low-compliance condition (Figs. 2 & 3), but varied for the high-resistance condition (Fig. 4). In all three conditions, some form of decelerating-flow pattern gave the lowest PAP. For the baseline condition and the low-compliance condition, the lowest PAP were also associated with the highest MAP. It should be noted that with high airway resistance, while the partial-decelerating pattern (50%) produced the lowest peak pressure, the full-decelerating pattern gave the second highest peak pressure and the highest MAP. In all three conditions, the full-accelerating pattern resulted in the highest PAP and the lowest MAP. Though not as effective as a decelerating flow pattern, the sine and modified-sine flow patterns also tended to minimize peak pressure under all three conditions.

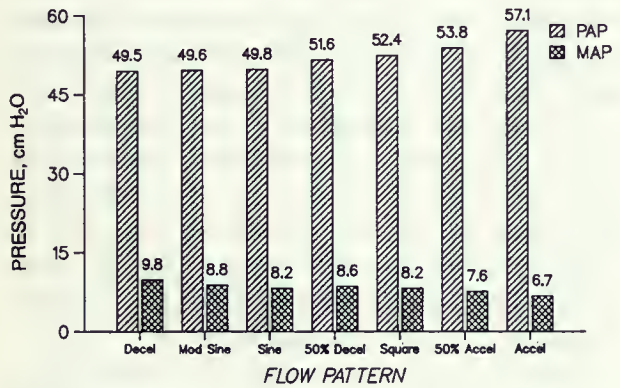

Fig. 3. Histograms of peak (PAP) and mean (MAP) airway pressures with each inspiratory flow pattern, arranged in order of minimum-to-maximum peak pressure, for the low-compliance condition. 50% Decel = partial decelerating; 50% Accel = partial accelerating.

Scattergrams of PAP and MAP with the seven flow patterns and the Pearson correlation coefficients are given in Figure 5 for the three lung conditions used. A strong and significant inverse correlation was seen between peak and mean pressures for the baseline ($p = 0.0014$) and low-compliance conditions ($p = 0.0083$), and no relationship was seen between the two pressures with high airway resistance ($p = 0.8602$).

Because of the inverse correlation between peak and mean airway pressures, and because the decelerating and accelerating patterns represent the extremes of the spectrum of peak and mean pressures, pressure curves for the full-decelerating and full-accelerating patterns with the baseline lung condition are superimposed for comparison in Figure 6. The difference between decelerating and accelerating flow patterns with respect to peak and mean pressures can be clearly seen. With the accelerating pattern, pressure rises throughout inspiration to peak at the end of the breath. In

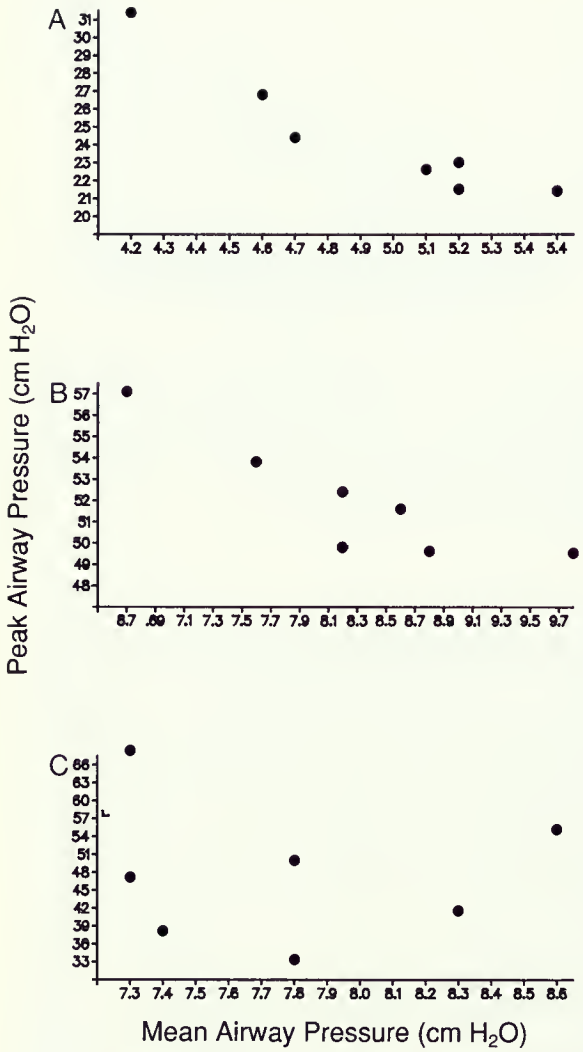

Fig. 5. Scattergrams of peak vs mean airway pressures, with Pearson correlation coefficients for the seven flow patterns. A. at baseline, r = −0.944, p = 0.001; B. with low compliance, r = −0.884, p = 0.0083; C. high resistance, r = −0.083, p = 0.8602.

contrast, the decelerating pattern produces a rapid initial rise in pressure that then increases only slightly during the breath to give a lower peak pressure and a greater mean pressure.

Discussion

The pattern of PAP and MAP found in this study is consistent with results predicted from lung mechanics. In a simplified model, total impedance of the respiratory system is comprised of airway resistance and lung compliance.[28,29] When a machine breath is delivered to the lung, pressure is generated to overcome both airway resistance and the forces that oppose volume change. For a given airway resistance, as flow increases the observed pressure increases (pressure = flow × resistance). Resistance and, therefore, pressure, can increase even more as flowrate increases and laminar flow becomes turbulent. Consequently, the highest pressure observed due to resistance occurs when the inspiratory flow is at its highest. For a given lung compliance, pressure is a function of the volume delivered (compliance = volume/pressure, and, therefore, pressure = volume/compliance). As volume delivered increases, so does the observed pressure increase. In addition, combined chest-wall and lung compliance is lowest as the lung expands, further increasing the observed pressure. Consequently, the highest pressure due to the effect of forces that oppose volume change occurs at the end of a breath as all of the volume is delivered. These principles of pressure (as a function of resistance and compliance for a given flowrate and volume) are confirmed by the pressures observed with the flow patterns studied.

As seen in Figure 6, a decelerating-flow pattern causes a high initial pressure as the first and highest flow meets resistance in the airway. Then as the flowrate declines, pressure due to airway resistance lessens, but pressure due to volume changes (compliance forces) begins to increase as the lung fills. The result is a more constant pressure throughout inspiration with lower peak pressures and higher mean pressures. The pressure and flow waveforms with a decelerating-flow pattern for a volume-cycled breath resemble those for pressure-supported and pressure-controlled breaths. Pressure maintained by flow meeting airway resistance is replaced by pressure due to volume change with decreasing compliance as flow declines in pressure-supported or pressure-controlled breaths.

With an accelerating flow pattern the beginning flow is low, resulting in a very low initial pressure. Further, because the volume in the lung is small at the beginning of inspiration, the initial pressures due to compliance forces are low. However, at the end of the breath when the flowrate is at its maximum, pressures due to airway resistance and

lung compliance combine to give a high peak pressure. As illustrated in Figure 6, the mean pressure tends to be reduced.

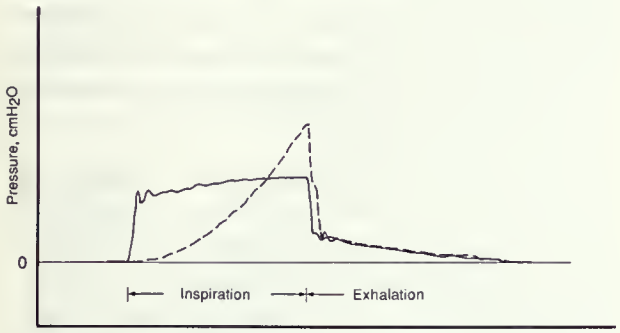

Fig. 6. Pressure waveforms superimposed for a full-decelerating (—) and full-accelerating (– –) inspiratory flow pattern. See text for discussion.

Finally, with very high airway resistance, high pressures due to resistance can occur throughout the inspiratory cycle, and the highest pressures tend to coincide with the point of maximum flow. In this case, mean pressures tend to be uncorrelated with peak pressures. Further, the greater the peak flow, the higher the peak pressure. As both the full-accelerating and full-decelerating flow patterns produce very high peak flows, the peak pressures associated with these flow patterns are high under the condition of increased airway resistance.

Inspiratory flow patterns between the two extremes of full-accelerating and full-decelerating exemplify the same principles of lung mechanics. In both the baseline and low-compliance conditions (ie, with normal airway resistance), peak pressure increases and mean pressure decreases as the highest point of flow moves from the beginning to the end of the inspiratory cycle. The bar graphs in Figures 2 and 3 confirm this progression as the patterns range from full- to partial-decelerating (modified-sine, sine, and 50%-decelerating) through a square pattern to the accelerating pattern.

Similarly, with high airway resistance, where peak pressure is partially a function of the peak flow value, the bar graph in Figure 4 shows that peak pressures increase as the peak flow value increases. The sine, full-decelerating, and full-accelerating patterns give the highest peak pressures. The 50%-decelerating pattern has a higher peak flow than the square wave but a lower peak pressure, which seems to contradict this predicted result. However, the square pattern maintains a higher flow than the 50%-decelerating pattern at the end of the inspiratory cycle when the pressure due to compliance and volume is also highest. This has an additive effect on peak pressure. For the same reason, the 50%-accelerating pattern gives a higher peak pressure than the 50%-decelerating form. The peak flow with the 50%-accelerating pattern occurs at the end of inspiration when the pressure due to compliance and resistance coincide.

Our findings agree with the predictions of the theoretical study by Jansson and Jonson,[17] as might be expected. Their computer model indicated that the lowest mean pressure and highest peak pressure occurs with an accelerating flow. More importantly, there is general agreement between our results and those of other studies showing the extremes of low and high peak pressures with a full-decelerating and full-accelerating flow pattern, for normal airway resistance.[8,15,18] In particular, our results agree with those of Smith and Venus,[8] who also used the four flow patterns available on an earlier version of the Hamilton Veolar in a pig model. Although they used a methacholine challenge, which would be expected to increase airway resistance, the order of waveforms giving the lowest to highest peak pressures matched our order for the two normal-resistance conditions (baseline, low-compliance). Al-Saady's result,[11] showing lower peak pressures with a decelerating compared to a square-flow waveform, also agreed with our baseline and low-compliance conditions. Branson's results[7] using a Hamilton Veolar with 10 trauma patients showed that an accelerating pattern produced significantly higher peak pressures compared to the other flow patterns (sine, square, decelerating). No significant differences in peak pressures among the sine, square, or decelerating patterns were seen. Our study also found that the accelerating flow pattern produced the highest PAP with increased airway resistance. The other three patterns produced lower and more homogeneous peak pressures.

Our results also agree with several studies reporting mean airway pressures.[7,10,13,14] The highest mean pressures are seen with the decelerating and

the lowest with the accelerating patterns. However, our results disagree with the three studies of Baker and colleagues[10,13,14] regarding the effect of the sine- and square-wave patterns on mean pressures. In two of the studies by Baker et al[10,13] results show that a square-wave flow pattern gives higher mean pressures than does a sine-wave pattern. However, differences in mean pressure for these two flow patterns were extremely small in both of Baker's studies as well as in our own. In fact, for the low-compliance condition, we found the mean pressure to be the same for the sine- and square-wave patterns. Adams' study with a dog model found the order of flow patterns giving highest-to-lowest mean pressures to be sine, decelerating, accelerating, and square.[5] Our results did not agree with this order because we found the sequence of highest-to-lowest mean pressures achieved with a decelerating, sine, square, and accelerating pattern, across all three lung conditions. Mean pressures reported by Adams varied only from 2.7 to 3.2 cm H_2O [0.26-0.31 kPa], and, perhaps, measurement error obscured the differences. Adams' study used an experimental waveform generator that may have added a source of variability.

The Hamilton Veolar utilizes a time-cycling mechanism in the assist-control mode when delivering a preset volume breath. Because of this, as flow patterns change from a constant or square-wave to a variable, nonconstant pattern, peak flows vary in order to deliver the preset volume within the time limit dictated by the rate and I:E controls (Table 1). Both PAP and MAP also vary. It is possible for the operator to change the I:E control and, in turn, the inspiratory time in order to keep the peak flow value relatively constant as the flow pattern is changed. Had this been done, the observed pressures might have varied with changes in the inspiratory time. We did not manipulate I:E in our study, but instead held the I:E and inspiratory time constant.

It should also be noted that when the inspiratory flow pattern of a volume-cycled ventilator is changed, the peak flow remains constant and inspiratory time and I:E vary. Generally, with a volume-cycled machine, inspiratory time lengthens when the flow pattern is changed from a constant to a nonconstant flow pattern. For this reason, it is important to apply our findings only to the study conditions of a constant I:E and inspiratory time. The observed pressures also vary with actively inspiring patients. Because we used a passively ventilated lung model, generalization of our results to spontaneously breathing patients may be limited and possibly inappropriate.

The overall clinical effect on gas exchange of changing inspiratory flow patterns is a function of other variables in addition to PAP and MAP. This may be why previous studies report sometimes-conflicting results. As peak airway pressures change, the volume delivered to the lungs also changes due to the compressible volume lost in the system and patient tubing. Although not reported in this study, preliminary measures using a low-compliance patient circuit showed that delivery of volume to the lung is very efficient. At a peak inspiratory pressure of 100 cm H_2O [9.806 kPa], 87% of the tidal volume was delivered to the test lung. Compressible volume loss at a given pressure varies with length, temperature, and type of tubing. Our test conditions bypassed the humidifier, and the patient circuit was at ambient temperature. Alveolar pressure is not represented by the airway pressures we measured, especially as airway resistance increases. A high MAP should not depress cardiac output if that pressure is not transmitted into the thorax. Barotrauma is also a function of volume and overdistention in the lung, and this may not be indicated by a high airway pressure if high resistance is present. With these qualifications in mind, the agreement between our results for peak and mean pressures with other studies suggests that airway pressures can be predicted for a given flow pattern, compliance, and resistance in patient situations. When using a time-cycled, volume-preset ventilator, a clinician may be able to use these results, together with knowledge of the patient's pulmonary and cardiovascular status, to optimize ventilatory support. Future in-vivo studies would be useful to correlate airway pressures and effects on the lung, as compliance and resistance change, to further guide selection of inspiratory flow patterns during mechanical ventilation.

Conclusion

We conclude that under all these lung conditions a decelerating flow produces the lowest peak inspiratory pressure; whereas, the accelerating-flow pattern produces the highest peak inspiratory pressure.

Under all lung conditions, the lowest MAP is produced by an accelerating-flow pattern. Under all test-lung conditions, the highest mean inspiratory pressures are produced by using a form of decelerating flow.

Under the baseline and low-compliance condition, an inverse relationship exists between peak and mean pressures. As peak pressure increases, mean pressure decreases. There is no such relationship with increased resistance. We believe that a form of decelerating inspiratory flow can be useful in minimizing PAP. A sine- and modified sine-wave flow can also minimize PAP under some conditions. Accelerating-flow waveforms may be of value in reducing mean airway pressure; however, corresponding peak pressure may be high.

ACKNOWLEDGMENTS

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Urticaria following Inhaled Albuterol Administration by a Hand-Held Nebulizer

Russell W Harland MD, Burnestean G Miller CRTT, and Basil Varkey MD

Introduction

Albuterol, a widely used selective beta$_2$-agonist, is equal or superior to other beta$_2$-agonists in its efficacy in treating bronchospasm, while displaying only a few significant adverse effects.[1-6] The most frequently described side effects are muscle tremor, mild palpitation, and tachycardia. Less frequently encountered side effects include elevations in serum glucose[4,6] and insulin levels,[6] reduction in serum potassium levels,[4,6] alterations in fat metabolism,[4] nausea,[3,5] and headache.[4,5] We report a case of an adverse reaction to inhaled albuterol, which, to our knowledge, has not been previously described.

Case Summary

A 62-year-old white man with a history of coronary artery disease and chronic obstructive pulmonary disease was transferred to our institution for direct myocardial revascularization. At the time, he was taking only an oral nitrate and a multivitamin tablet. Physical examination was unremarkable except for mild wheezing diffusely over all lung fields. Following his physician's order for bronchodilator treatment, albuterol 0.083% (Proventil, Schering Corp, Kenilworth NJ), 3 mL, was given by hand-held nebulizer. Pretreatment and posttreatment heart rates were not different. Approximately 20 minutes after the administration of albuterol, the patient developed an intensely pruritic urticarial eruption that involved the trunk, neck and chest (Fig. 1), and arms. There were no accompanying findings of angioedema, respiratory distress, or hemodynamic compromise. Diphenhydramine hydrochloride, 50 mg intravenously, was administered with striking improvement in 30 minutes and resolution of the urticarial rash in 2 hours.

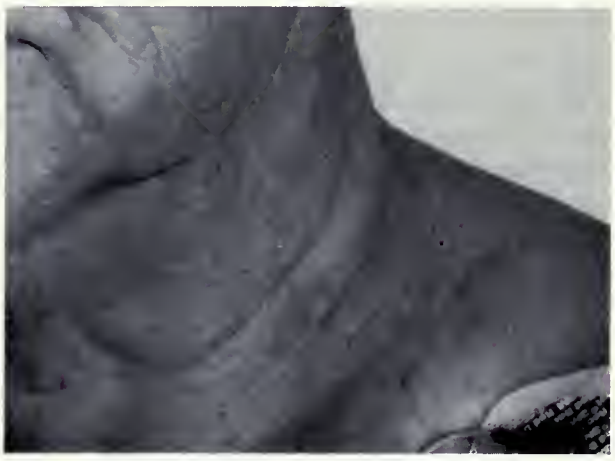

Fig. 1. View of neck and chest showing urticaria (commonly referred to as "hives").

Upon further questioning, the patient related the history of a similar reaction after using albuterol via metered-dose inhaler one week previously. He also noted that he had used metaproterenol via metered-dose inhaler in the past without any adverse reaction. The patient was subsequently maintained on a regimen of metaproterenol and experienced no further reactions of the type evoked by albuterol.

Discussion

Urticaria is not recognized in the literature as an adverse effect of albuterol. In reviewing the pertinent literature, we found the closest description to the adverse reaction that occurred in our patient in a case reported by Shurman and Passero.[7] They

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described a hypersensitivity reaction to albuterol in a 42-year-old woman manifested by chest heaviness, facial flushing and edema, and hoarseness. Urticaria, however, was not part of this reaction.

Urticaria caused by drugs is usually of immunologic origin. Drugs trigger cutaneous mast cells to secrete histamine and other chemical inflammatory mediator substances when they combine with corresponding IgE antibodies on the mast cell surface.[8,9] The most common medications causing urticaria via this Type I hypersensitivity mechanism are penicillin and the sulfonamides.[8] Drug additives such as tartrazine dye and sulfite preservatives have also been shown to cause urticaria.[10] Other drugs, notably opiates and some muscle relaxants, can cause urticaria via a non-immunologic mechanism of direct action on the mast cells, with degranulation and subsequent histamine release.[8] Aspirin can exacerbate chronic urticaria by its blocking action on the cyclooxygenase pathway of arachidonic acid metabolism, resulting in the enhanced formation of leukotrienes and other chemical mediators.[8,10]

A true hypersensitivity Type I reaction is the most likely explanation in our case, because the urticarial rash developed shortly after the administration of the drug and responded to antihistamine. Ironically, the pharmacologic effect of albuterol is, via beta-$_2$ receptor stimulation, to stimulate adenyl cyclase, which increases levels of cyclic-AMP and inhibits the release of mediators of immediate hypersensitivity from mast cells.

It is difficult to implicate preservatives and propellants in the drug preparation as the causative agents of the urticarial reaction, as the patient reportedly developed "hives" after using albuterol in a metered-dose inhaler. The metered-dose inhaler and solution for nebulization forms of the drug share no common compounds other than albuterol itself. Also, as in the case reported by Shurman and Passero,[7] our patient experienced no adverse reactions after being started on a metaproterenol metered-dose inhaler, a preparation that shares common propellants with albuterol metered-dose inhalers.

In summary, we have reported an adverse reaction to nebulized albuterol that has not been previously described. The urticarial reaction appears to have been mediated by the products of mast cell degranulation, probably through an immunologic mechanism. Respiratory therapists, physicians, and nurses must remain alert to this unexpected and uncommon adverse reaction to albuterol.

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What's New in Respiratory Care?

David J Pierson MD

Respiratory care is a rapidly changing, dynamic, 'cutting-edge' profession, whose practitioners must work hard to stay abreast of everything that's new. As in previous years, visitors to the exhibit area at last December's AARC Annual Meeting in New Orleans were confronted by row upon dazzling row of newness—new ventilators, monitors, and accessories, plus new applications of existing ventilators, monitors, and accessories. Presented at the RESPIRATORY CARE Open Forum and in the lecture halls was a continuous stream of experience and advocacy for new devices, new techniques, and new therapies. Invention, innovation, and experimentation are the principal reasons why many of the profession's members were attracted to this field. New developments make respiratory care exciting.

But how much is really new? And of that which *is* actually new, how much produces genuine improvement over what we had before? Which of the many 'new' developments presented to the clinician in any given year should be accepted, adopted, purchased, or put into routine clinical use? And of those, which ones will justify all the initial enthusiasm? These are not just rhetorical questions. They represent one of the most important challenges faced by every manager, educator, practitioner, and student in the profession. This is because each new device, technique, or approach presents not only a possible improvement but also the potential for complicating patient management or even causing harm.

Any development has three possible fates. Time can prove it to be a genuine breakthrough—an effective therapy where none existed before, an important new diagnostic or monitoring capability, or a different, better way of approaching a clinical problem. It can turn out to be a minor improvement of the 'fine-tuning' variety—not revolutionary but simpler, less expensive, or otherwise better in some way than what was already available. Both of these possibilities are desirable. However, a new development can also turn out to be a mistake, about which the initial enthusiasm proved to be a false alarm. It may not work as well, or be more dangerous, or cost more (in dollars, discomfort, complexity, or inconvenience) when compared with established therapies or devices.

The problem, of course, is that every new development is initially promoted as a breakthrough. Most will eventually end up in one of the other two categories, but this is never apparent in the first blush of enthusiasm that comes with something new. Only after considerable clinical experience—and occasionally some unfortunate outcomes—does the profession assign a given device or technique to the second or third category.

During the 1980s, respiratory care changed dramatically. Much of this change was foisted on the profession by outside forces—a constricting health care economy, prospective payment, AIDS—but clinical practice underwent considerable change as well. Among the many new developments that changed the profession during the last decade, these 12 (listed in no particular order) would have to be included:

- Nasal CPAP
- Pulse oximetry
- Pressure support
- Surfactant for IRDS
- High-flow oxygen blenders
- Transtracheal oxygen therapy
- High-frequency jet ventilation
- Microprocessor ICU ventilators
- Mixed-venous oxygen monitoring
- Aerosolized ribavirin and pentamidine

- Pressure-controlled inverse-ratio ventilation
- Metabolic carts for nutritional and respiratory monitoring

Although introduction of some of these antedated the 1980s, they all became widely used and changed the practice of respiratory care during the last decade. But were they all really breakthroughs? For how many is there proof of improved patient outcome, or fewer complications, or shorter ICU stay, or improved clinician efficiency? Few would argue that surfactant treatment for respiratory distress of prematurity represents a genuine breakthrough. But what about the others? How much proof is there that high-frequency jet ventilation and pressure-controlled inverse-ratio ventilation have improved survival, reduced complications, made patient care less complicated, or saved money in the management of ARDS? Of the 'hot' new developments in respiratory care during the 1960s and 1970s, relatively few have passed unscathed through the gauntlet of clinical investigation and practical experience: In another 10 years, how much of what was new in the 1980s will still be considered valid and useful?

My purpose here is not to denigrate these or other new developments, but to emphasize the importance of critical, objective assessment whenever a departure from accepted therapy is introduced or proposed. Everyone attracted to respiratory care is also attracted to the new and different. New developments will continue to appear, and when they do they will stimulate intense interest and the urge to try them out. While this is both understandable and healthy, the clinician must remember the three possible outcomes from any new development—breakthrough, minor improvement, or false alarm—and maintain enough objectivity to tell the difference as clinical experience accumulates.

Each of the five articles that follow this introductory editorial addresses some aspect of the challenge, "What's new in respiratory care?" The articles are the work of acknowledged leaders in the field, and were developed from presentations at the sixth annual symposium, "New Horizons in Respiratory Care," held during the 1990 AARC Annual Meeting.

First, in a thorough, insightful analysis, Richard Branson discusses the question, "Enhanced capabilities of current ICU ventilators: Do they really benefit patients?" He considers four categories of enhancement that could benefit patients: range of operation, improvements in functional design, new modes, and new monitoring capabilities. After summarizing the enhancements and other new features of present-day microprocessor ventilators and their clinical operation, he concludes that some patients have indeed benefited. Examples include increased pressure, PEEP, and minute ventilation capabilities for the small subset of most critically ill patients; reduction in the imposed inspiratory work of breathing, at least in some ventilators and with some modes; the availability of pressure support to reduce patient work and increase comfort, at least in some applications; and greater accessibility and ease of operation, again in some of the ventilators discussed.

Branson also points out that most of the new ventilatory modes of the 1980s remain unproven in terms of patient benefit (and in some cases present an increased potential for harm). He concludes that although many of the new ventilators' monitoring capabilities are intuitively attractive, in few cases can tangible benefit be shown: It remains uncertain whether the increased monetary cost of these new capabilities can be justified.

In the second paper, Dean Hess attempts to answer the question, "How should bronchodilators be administered to patients on ventilators?" In a comprehensive, practical analysis, he focuses on the current controversy over whether the metered-dose inhaler (MDI) or the traditional small-volume nebulizer is more effective, easier to use, and more cost-effective. After reviewing the available literature on these two delivery techniques, he points out numerous remaining gaps, and lists areas in which reliable information is badly needed. His article includes a cost analysis of MDI vs nebulizer that demonstrates a 50% cost savings if the former is used.

Finally, Hess provides illustrations and data on all the currently available adapters and devices for use with bronchodilator delivery via MDI in intubated patients. Although much additional work is needed, the conclusion would appear to be that

in this particular area of "what's new," the new method (MDI) offers real improvement, at least in terms of convenience and cost.

Following these two articles focused primarily on new devices are three that deal with clinical approaches to common problems in intensive respiratory care. First, Martin Tobin addresses the frequent but largely uninvestigated circumstance of 'fighting the ventilator': A patient who previously seemed comfortable is now agitated, triggering several alarms, and 'bucking' the ventilator. In a systematic fashion Tobin considers the most likely causes, including problems with artificial airways, pneumothorax, bronchospasm, the buildup of airway secretions, dynamic hyperinflation, and changes in respiratory drive.

The author also discusses problems related primarily to the ventilator itself—the implications of mode and other settings as well as the normal operation of its components—and to patient-ventilator asynchrony. He provides practical advice to the clinician for approaching these problems quickly and systematically in order to provide safe care while discovering the most likely cause for the patient's distress.

In the fourth paper, Philip Boysen revisits an old subject in the light of current knowledge: "Weaning from mechanical ventilation: Does technique make a difference?" In the course of reviewing his own experience with weaning during the last two decades, he describes the diverging concepts that have emerged during this time—that the respiratory muscles should be exercised during acute respiratory failure, and that they should be rested—and the persisting lack of convincing clinical evidence that either one is distinctly superior.

Boysen emphasizes the principle that the specific weaning technique employed is not as important as appropriate patient evaluation and accurate identification of complicating chronic or acute medical conditions. Based on the literature and his own extensive experience, he offers the reader a framework for rationally approaching ventilator weaning irrespective of which technique is used.

Finally, this series of symposium papers concludes by examining an area of patient care that is not so much new as neglected: "Withholding and withdrawal of life support from the critically ill: How does it work in clinical practice?" John Luce, an acknowledged authority in this field, provides a frank discussion of the process of withholding or withdrawing life support as it is most commonly encountered in intensive respiratory care.

Luce first discusses what is meant by life support (or perhaps more correctly organ support), and its implications in such different clinical settings as the patient with an acute deterioration complicating a debilitating chronic illness, the patient in a persistent vegetative state, and the individual who is brain dead but whose cardiorespiratory and other organ systems continue to function. He then briefly reviews the main ethical principles pertaining to patient care: autonomy, disclosure, beneficence, and nonmalfeasance. This is followed by a summary of several important recent legal cases bearing on the subject.

The bulk of the article, however, is devoted to "what's new," an evolving understanding of how clinicians actually carry out the withholding and withdrawal of life support in critically ill patients, including the administration of sedatives and analgesics, based on a recently completed study carried out at the University of California, San Francisco. Analysis of how clinicians currently manage the withholding or withdrawal of life-sustaining therapy from patients whom they expect to die as a result (and who constituted 7% of all admissions to the ICUs in the two hospitals studied) places this stressful but important aspect of respiratory care into current perspective, and can aid clinicians in both the appropriateness and the comfort with which they deal with it.

These five articles will be useful references for clinicians involved with all aspects of intensive respiratory care. They place what's new into the context of established principles and therapeutic modalities. By stressing fundamental concepts and clinical needs, these resources should assist the reader in assessing not only these new developments but also the many others that will surely follow during the 1990s and beyond.

Enhanced Capabilities of Current ICU Ventilators: Do They Really Benefit Patients?

Richard D Branson RRT

Introduction

Modern-day mechanical ventilators are a testament to recent advances in electronic and microprocessor technology. The current generation of ventilators (Table 1) is more sophisticated, has a wider range of capabilities, is more flexible, and is easier to upgrade and repair than were their predecessors. And while few, if any, would argue that these statements are true, it is unclear whether these enhancements actually benefit the patient. Webster defines enhance as: to make greater, as in cost, value, attractiveness, to heighten, improve, augment, etc.[1]

I will attempt to ascertain through review of the available literature and use of common sense and clinical intuition whether this new technology is of value and improves patient care or whether it simply makes ventilators more attractive and more expensive. Ventilator enhancements will be discussed in four categories: range of operation, functional design improvements, new modes, and new monitoring capabilities.

Range of Operation

The maximum capabilities and range of operation of current ventilators far exceed those of their predecessors of only 10 years ago (Table 2). Both the 7200a and Bear 5 provide a greater range of tidal volume (V_T) and set respiratory frequency (f), and have greater maximum limits for set inspiratory flowrate, f, peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and peak flow for spontaneous breathing than the MA-1 or Bear 1. The importance of these changes will be considered individually.

During mechanical ventilation, V_T is normally set at 10-15 mL/kg of patient body weight.[2] In cases of obesity, this should be referenced to ideal body weight, not actual weight. With a maximum V_T capability of 2500 mL, the 7200a, in theory, should be able to ventilate a patient weighing slightly more than 150 kg (330 lb) ideal body weight. This capability is only slightly greater than that of the MA-1, and for the most part can be expected to meet the needs of nearly all patients.

Table 1. Microprocessor-Controlled Ventilators Available in 1991

Bear 5	Bear Medical Systems Inc, Riverside CA
IC-5	Bio-Med Devices Inc, Madison CT
6400ST and 8400ST	Bird Products Corp, Palm Springs CA
Erica	Gambro-Hospital, Engstrom Div, Williamsburg VA
Veolar and Amadeus	Hamilton Medical, Reno NV
Adult Star	Infrasonics Inc, San Diego CA
Breeze	Newport Medical Instruments, Newport CA
Advent	Ohmeda, Columbia MD
IRISA	PPG Biomedical, Lenexa KS
7200a	Puritan-Bennett Corp, Carlsbad CA
2200	Sechrist Industries, Anaheim CA
900C*	Siemens Life Support Systems, Schaumburg IL

*Although the 900C is a third-generation ventilator on par with the other ventilators in this list, it is not truly microprocessor controlled.

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A version of this paper was presented by Mr Branson in the Schering Symposium New Horizons in Respiratory Care "What's New in Respiratory Care?" during the 1990 Annual Meeting of the AARC in New Orleans, Louisiana.

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Abbreviations Used in This Paper

AMV	— Assisted mechanical ventilation
APRV	— Airway-pressure-release ventilation
ARDS	— Adult respiratory distress syndrome
CPAP	— Continuous positive airway pressure
f	— Respiratory frequency
1:E	— Ratio of inspiratory time to expiratory time
IMV	— Intermittent mandatory ventilation
MIP	— Maximal inspiratory pressure
MMV	— Mandatory minute volume
$\bar{P}_{aw}$	— Mean airway pressure
PCIRV	— Pressure-control inverse-ratio ventilation
PCV	— Pressure-control ventilation
PEEP	— Positive end-expiratory pressure
PIP	— Peak inspiratory pressure
PSV	— Pressure-support ventilation
$\dot{V}_I$	— Inspiratory flowrate
$\dot{V}_E$	— Minute volume
V_T	— Tidal volume
WOB_i	— Imposed work of breathing

Another more common situation where high set V_T may be required is during ventilatory support of the patient with massive air leak.[3] Increasing the set V_T can enhance elimination of carbon dioxide (CO_2) when significant volumes are being lost through chest tubes or around incompetent artificial airways. Another use for a high set V_T is to compensate for compressible volume lost in the ventilator circuit and humidifier. Compressible volume is normally considered to be 3-4 mL/cm H_2O [0.3-0.4 mL/kPa] of PIP.[4] A patient with abnormally low compliance, requiring a delivered V_T of 1300 mL with a PIP of 80 cm H_2O [7.8 kPa], would require a set V_T of 1620 mL (compressible volume = 4 mL × 80 cm H_2O = 320 mL, 1300 + 320 = 1620 mL). The ability of current ventilators to provide a slightly greater V_T is probably of little or no benefit to the patient.

Table 2. Comparative Ranges of Operation for Two Current Ventilators and Their Non-Microprocessor Predecessors*

	Ventilators			
	Puritan-Bennett		Bear Medical	
Variables	MA-1	7200	Bear 1	Bear 5
V_T (mL)	100-2200	100-2500	100-2000	50-2000
$\dot{V}_I$ (L/min)	5-100	10-120	10-120	5-150
f (breath/min)	6-60	0.5-70	0.5-60	0.5-150
PIP (cm H_2O)	80	120	100	150
PEEP (cm H_2O)	15	35	30	50
Peak spontaneous $\dot{V}_I$ (L/min)	100	180	100	150

* All data obtained from manufacturers' literature.

Early investigations suggested that a low inspiratory flowrate (V_T) during mechanical ventilation would allow more uniform distribution of inspired gases and improved elimination of CO_2 compared to that obtained with a high inspiratory flowrate.[5-7] However, more recent evidence has shown that increased inspiratory flow helps to improve gas exchange in COPD,[8,9] reduce the incidence and severity of auto-PEEP,[10,11] and reduce the work of breathing during assisted mechanical ventilation (AMV).[12] Although no data exist to demonstrate the need for inspiratory flows ≥ 120 L/min, a small percentage of patients may benefit from the higher inspiratory flows that current ventilators are capable of providing.

The range of f is expanded, allowing for the ventilation of a greater variety of patients. With the capability of providing f up to 150 breaths/min, the Bear 5 can be used to ventilate pediatric and adult patients successfully. Frequencies < 1 breath/min may be used during intermittent mandatory ventilation (IMV), but I doubt the usefulness of this technique. Although extension of the range of frequencies benefits the respiratory care practitioner, who can now use the same ventilator for both pediatric and adult patients, it probably does not benefit the patient in any measurable way.

Current ventilators provide higher (50% increased) levels of PIP than their predecessors. Because volume-cycled ventilators dump excess volume to the atmosphere when the peak pressure limit is reached, this capability of current-generation ventilators to generate higher PIP enables better V_T delivery to patients with low lung compliance. Few data are available to demonstrate the need for PIP ≥ 80 cm H_2O [7.8 kPa]. However, our most recent experience demonstrates that approximately 21% (37 of 170) of patients with adult respiratory distress syndrome (ARDS) require a PIP ≥ 80 cm H_2O [7.8 kPa] (Table 3). Based on these data, I conclude that the higher PIP capability of current ventilators may benefit the patient.

Table 3. Ventilatory Requirements of 170 Patients with ARDS at the University of Cincinnati (1986-1988)

Ventilator Requirements	Patient number (% of total)
PIP > 80 cm H_2O	37 (21%)
PEEP > 20 cm H_2O	12 (7%)
Set f > 20 cm breaths/min	0
Set V_T > 100 L/min	0
Set $\dot{V}_I$ > 100 L/min	28 (16%)
Set $\dot{V}_E$ > 20 L/min	19 (11%)

Although the era of 'super-PEEP' seems to have come and gone, current ventilators are capable of delivering up to 50 cm H_2O [4.9 kPa] of PEEP.[13] Our experience demonstrates that a few patients require PEEP ≥ 20 cm H_2O [2.0 kPa] (Table 3), and 32 cm H_2O [3.1 kPa] was the maximum level we applied. The controversies over the use of PEEP are many and beyond the scope of this paper. Suffice it to say, a small group of patients with severe ARDS may benefit from the availability of PEEP ≥ 20 cm H_2O [2.0 kPa].

Pierson et al[13] provide the only scientific evidence of improved capabilities of current ventilators. They studied the maximum minute volume ($\dot{V}_E$) available from the MA-1, Veolar, Bear 5, 900C, and 7200a under changing conditions of lung compliance and PEEP, and found the MA-1 to be inferior in its $\dot{V}_E$ capabilities under all study conditions (Fig. 1). Additionally, this report demonstrated that even with current ventilators, actual $\dot{V}_E$ was less than set $\dot{V}_E$ as compliance was reduced and PEEP increased (Fig. 2). They attributed the limitation in maximum $\dot{V}_E$ to available f in the 7200a and Veolar, and to

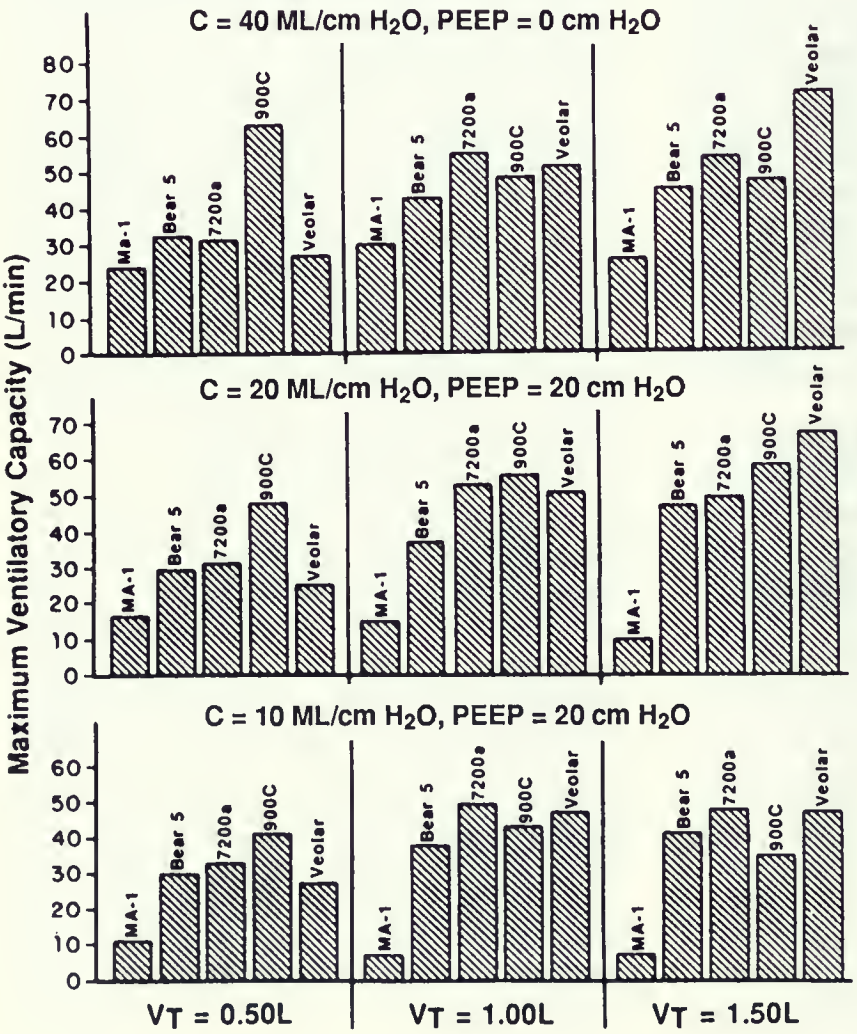

Fig. 1. For each of the three test-lung-compliance (C) and positive-end-expiratory-pressure (PEEP) conditions tested, the maximum ventilatory capability (largest minute ventilation achieved before the ratio of inspiratory time to expiratory time exceeded 1.0), shown on the vertical axis, is given for each of the three test tidal volumes (V_T), shown on the horizontal axis. (Reprinted, with permission, from Reference 14.)

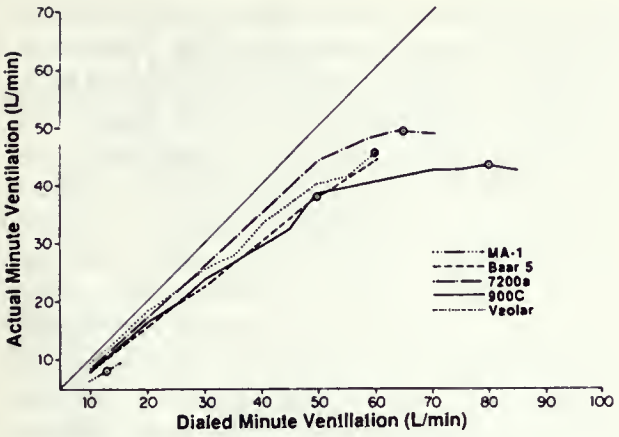

Fig. 2. Actual (measured) minute ventilation (vertical axis) compared to that dialed on each ventilator when tidal volume (V_T) = 1.00 L, test-lung compliance (C) = 10 mL/cm H_2O, and positive end-expiratory pressure (PEEP) = 20 cm H_2O. Maximum ventilatory capability, the minute ventilation above which the ratio of inspiratory time to expiratory time became greater than 1.0, is indicated for each ventilator by a circle. (Reprinted, with permission, from Reference 14 .)

decay of the inspiratory flow pattern in the 900C and Bear 5. The authors did not demonstrate the need for these high levels of $\dot{V}_E$, but other work from their institution[15] has demonstrated that in 164 mechanically ventilated patients, 5 patients required $\dot{V}_E \geq$ 20 L/min. Based on these findings, it appears that the higher $\dot{V}_E$ available from current ventilators is justified and probably benefits the most critically ill patients.

Maximum capabilities and operational range of the current-generation ventilators appear to be geared toward that small group of critically ill patients with the most severe lung disease. Within that context, these new capabilities appear to benefit patient care and are for the most part justifiable.

Functional Design Improvements

Microprocessor control of today's ventilators is the single most important functional ventilator-design improvement that has occurred. Microprocessor control allows greater flexibility and versatility with respect to available modes of ventilation and control of inspiratory flow pattern, reduces the number of moving components, enhances monitoring capabilities and data management, and allows upgrading or addition of new features with only a change in software. With the role of the microprocessor in mind, the following represents the major improvements in actual function of the new ventilators.

Response to Patient Effort—Reducing the Imposed Work of Breathing

Few topics in respiratory care have received as much attention in recent years as has the work of breathing during mechanical ventilation.[16] The work of breathing done by the mechanically ventilated patient includes the work required to overcome the elastic and resistive forces of the lung, and the imposed work of breathing (WOB_i) required to overcome the resistance of the artificial airway,[17,18] and to trigger a breath during assisted mechanical ventilation (AMV) or pressure-support ventilation (PSV), or to initiate demand flow during IMV (Fig. 3).

Numerous investigators have shown that demand-flow systems incorporated into ventilators, create a greater WOB_i than do continuous-flow systems.[19-29] There are two components of a spontaneous breath that can be adversely affected by ventilator WOB_i (Fig. 3). The first is work required to trigger

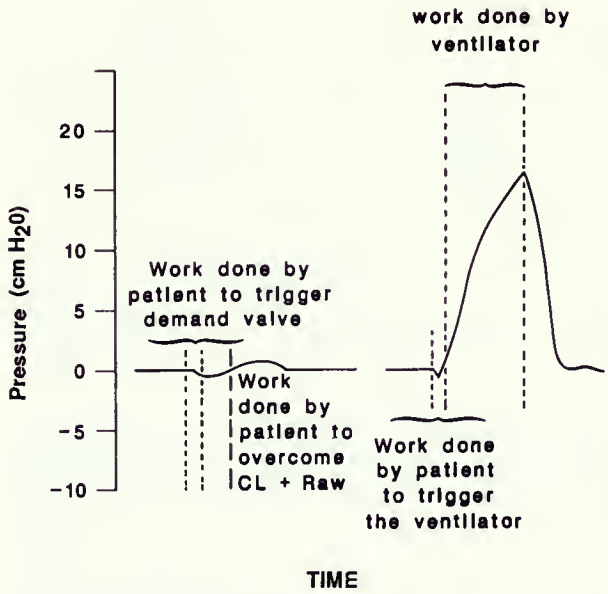

Fig. 3. A spontaneous (left) and assisted (right) breath during mechanical ventilation. In both, imposed work of breathing (WOB_i) can occur during triggering of the breath. In the spontaneous breath, once the breath is initiated, the patient continues to perform work to overcome elastic and resistive forces; R_{aw} while in the assisted breath, the ventilator provides the work.

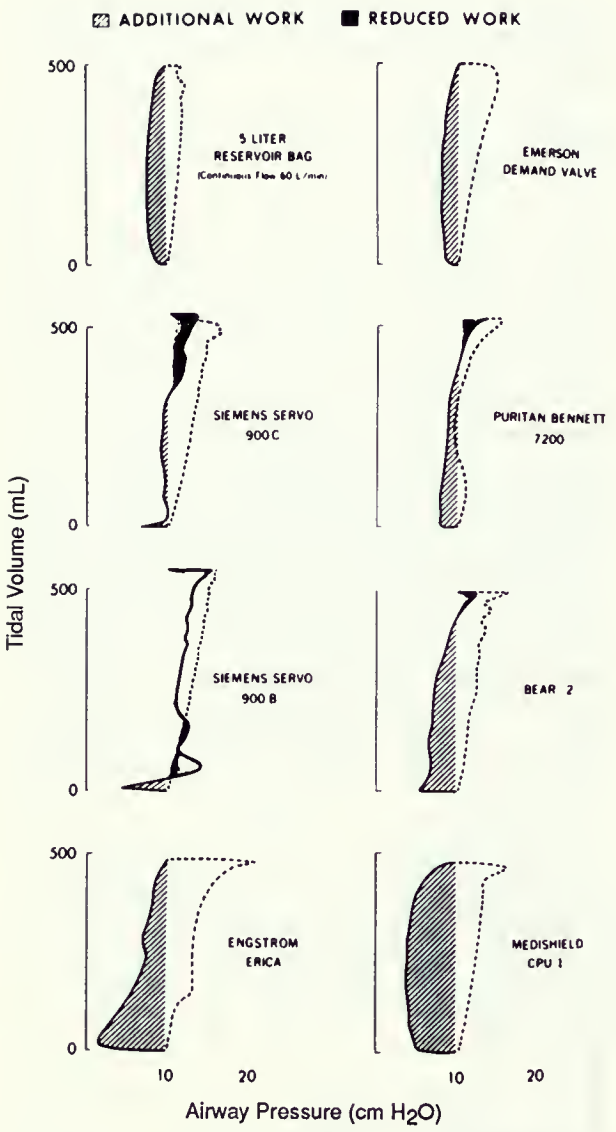

Fig. 4. Pressure-volume curves for CPAP delivery systems at 10-cm H_2O PEEP and inspiratory flow of 40 L/min. (Reprinted, with permission, from Reference 28.)

the ventilator on. Appropriately set sensitivity and the pressure monitoring capabilities of the ventilator determine the work done during this part of the breath. Once the demand valve is open, the patient must overcome elastic and resistive forces of the lung and ventilator circuit. Within this part of the breath, further WOB_i may be caused by a poorly responsive system (ie, either there is a time delay between the sensing of patient effort and the delivery of flow or the available flow is insufficient).

Katz et al[28] were among the first to compare the current generation of ventilators to their predecessors from a work of breathing perspective (Fig. 4). This report demonstrated that some new-generation ventilators (900C, 7200a) reduced WOB_i compared to older ventilators (900B, Bear 2), but that others (Ohmeda CPU-1, Erica) actually increased WOB_i. As can be seen in Figure 4, Katz et al show WOB_i as additional work, but also show reduced work. Reduced work occurs when ventilator flow exceeds patient demand and a slight positive pressure develops. Essentially, this reduced work is caused by a low level of pressure support provided by current ventilators to help overcome WOB_i, even though the pressure-support control is inactive. Further scrutiny of Figure 4 reveals the two components of the breath discussed previously. The pressure-volume curve for the 900B shows a marked negative pressure spike prior to initiation of flow followed by 'overshooting' pressure shortly thereafter, with pressure support. The clinical importance of this finding is unclear. My thought is that this initial work, when the patient is inspiring and the demand system has failed to open, may be the most significant WOB_i. However, because conditions prior to triggering on the demand valve are isovolumetric, no external work has actually been done (work is force times distance and no distance has been achieved); but effort has been expended.

More recently, Cox et al[30] investigated these two components of a spontaneous breath during ventilation with six ventilators. They measured sensitivity (maximum pressure drop prior to initiation of flow) and time delay (calculated as onset of inspiratory effort minus onset of ventilator gas flow) at 0, 5, and 10 cm H_2O [0, 0.5, and 0.98 kPa] pressure support. Results from this study are shown in Figures 5 and 6. Figure 5 depicts maximum pressure drop and clearly demonstrates the superiority of the new-generation ventilators compared to the 900B.

The negative pressure spike seen in Figure 4 is reaffirmed here in graphic representation (maximum negative pressure for the 900B is –6 cm H_2O [–0.6 kPa]). Figure 6 shows that time delay is also reduced for the newer ventilators. This paper also introduces flow triggering. Flow sensing, available on the Puritan-Bennett 7200a, senses inspiration as a reduction in flow, measured by inspiratory and expiratory flow transducers. Upon sensing inspiration, gas flow is augmented up to 180 L/min. Airway

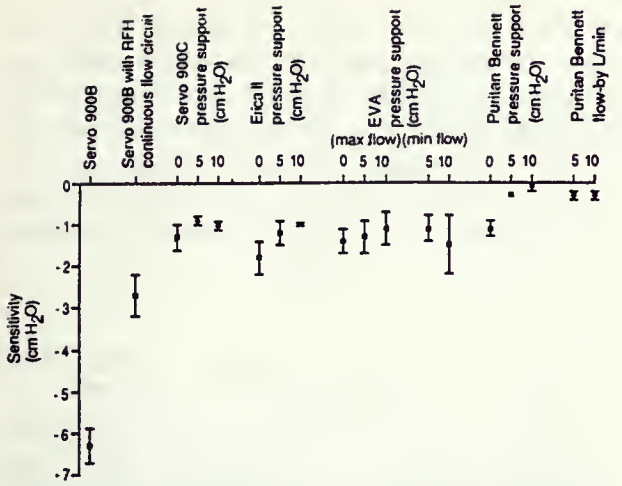

Fig. 5. Maximum pressure drop during spontaneous breathing with 6 ventilators at 0, 5, and 10 cm H_2O pressure support. This demonstrates WOB_i required to trigger the demand valve. (Reprinted, with permission, from Reference 30.)

pressure is continuously monitored and used to servo-control flow via the microprocessor. Flow triggering appears to eliminate the initial WOB_i seen during triggering of demand-valve systems, and subsequent work[31] has confirmed the superiority of flow triggering over pressure triggering. It should be remembered, however, that flow triggering cannot help overcome the work of breathing required to inflate the lungs.

Two new studies have also demonstrated the superiority of current ventilators in reducing

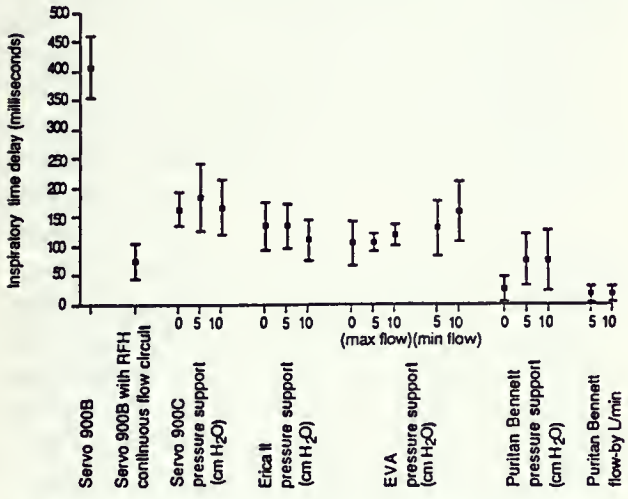

Fig. 6. Time delay during spontaneous breathing with 6 ventilators at 0, 5, and 10 cm H_2O pressure support. (Reprinted, with permission, from Reference 30.)

WOB_i.[32,33] This superiority is in part due to the improved placement of pressure-monitoring transducers and the speed with which signals are processed by the microprocessor. Proximal pressure-sensing lines are preferred because they eliminate artifact caused by the ventilator circuit and humidifier. However, they are exposed to secretions and water, which may impair their accuracy. Pressure sensing on the expired side is a suitable alternative, which protects the sensor and appears to maintain a reasonable response time. Sensing pressure on the inspired side, proximal to the humidifier and circuit, is least efficient. Figure 7 shows the sites of pressure monitoring for old and new ventilators.

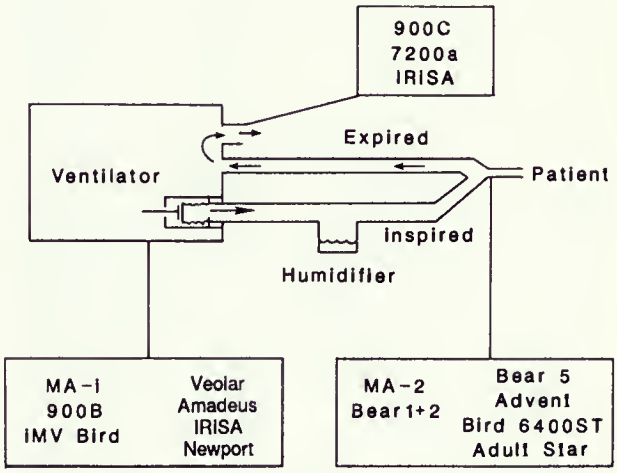

Fig. 7. Pressure monitoring sites of old and new ventilators. The IRISA ventilator uses measurements of pressure from the inspired and expired side in an effort to calculate proximal airway pressure.

Certainly, the current ventilators reduce WOB_i and as such benefit the patient who must perform the work. Other benefits may include improved patient-ventilator synchrony and reduced weaning time.

Control of Inspiratory Flow Pattern

For the most part, the current-generation ventilators use a sophisticated flow-control valve to control the volume, flow, and shape of gas delivery. Because of the combination of servo-control by the microprocessor and the continuous measuring of drop in pressure across this valve, these ventilators

are capable of delivering a variety of inspiratory flow patterns. A few ventilators produce four flow patterns (sine, square, accelerating, and decelerating) while others provide only one. Often a modified flow pattern is used and described as a 'ramp.' The interest in varying flow pattern during ventilatory support is not new. Extensive studies on this subject were performed in Europe and reported in the literature nearly 20 years ago.[34-36] These studies had conflicting results, and the availability of equipment that could produce these flow patterns in the clinical setting was limited. A host of more recent investigations have also produced conflicting results:[37-42] Some have shown advantages of each flow pattern under certain conditions, and some have shown no differences between flow patterns. The fact that each study used a different lung model, animal model, or group of patients may explain the lack of uniform results. Additionally, as flow pattern was changed, either flowrate or inspiratory time was also changed. This caused changes in PIP and, by virtue of compressible volume, may have varied delivered tidal volume as the flow pattern was changed. The confounding variables seem endless. In my experience, changing flow pattern does seem to offer some advantages by lowering PIP and/or increasng mean airway pressure ($\bar{P}_{aw}$), and by meeting patient demand for inspiratory flow (using a ramp or decelerating flow pattern), but the benefit to the patient remains unproven.

Exhalation Valve Design

The mushroom-type exhalation valves of the 1960s have given way to larger, electronically controlled valves that incorporate a large diaphragm. These new valves are more precisely controlled to produce a more consistent level of circuit pressure regardless of flowrate.[43] Marini et al[44] were the first to demonstrate the imprecise control of circuit pressure, in particular PEEP, that mushroom- and scissors-type exhalation valves were capable of providing. They found that, at the beginning of expiration, airway pressure initially rose 15-20 cm H_2O above set PEEP. These findings have subsequently been confirmed by others.[43,45] Banner has recently suggested that exhalation-valve design can also affect the inspiratory work of breathing.[46] Flow-resistor PEEP valves are associated with wider airway pressure swings. Exhalation valves of today's ventilators perform more accurately and, through improved performance, may reduce work of breathing and the potential for auto-PEEP and pulmonary barotrauma. Although clinical data are lacking, improved exhalation-valve design may benefit the patient by reducing work of breathing during mechanical ventilation.

Monitoring Devices

New ventilators are equipped with more-sophisticated and better-placed flow-volume and pressure sensors. Early ventilators monitored airway pressure with an aneroid manometer, which may have been placed inside the ventilator or connected to the proximal airway by several feet of small-diameter tubing. If pressure was measured inside the ventilator prior to the humidifier and circuit, airway pressure reflected the resistance of these components resulting in overestimation of end-expiratory pressure and underestimation of PIP.

The response times and accuracy of today's pressure transducers are improved tenfold over aneroid gauges. Additionally, the microprocessor allows airway-pressure measurements to be used to calculate mean airway pressure and in some cases auto-PEEP.[47]

Flow-volume monitoring devices have also been improved with the newest generation of ventilators. All early ventilators if they measured exhaled volume did so distal to the expiratory valve (Fig. 8). A typical device used was the Puritan-Bennett monitoring spirometer, which had an accuracy of ±100 mL.[47] Because these spirometers did not correct for compressible volume of the circuit, they did not reflect actual delivered V_T. Ideally, flow-volume should be monitored at the endotracheal tube, as is done by the Veolar and Amadeus ventilators. More frequently, however, volume continues to be measured distal to the exhalation valve (Fig. 8). Microprocessor control (eg, Bear 5, 7200a, and Advent ventilators) can allow correction of measured volume for circuit compressible volume. No published data are available on the accuracy of flow-volume sensors of the new-generation ventilators; however, I believe it is reasonable to assume that because of their construction, they are considerably more accurate and reliable than their predecessors. Their benefit to the patient is unknown.

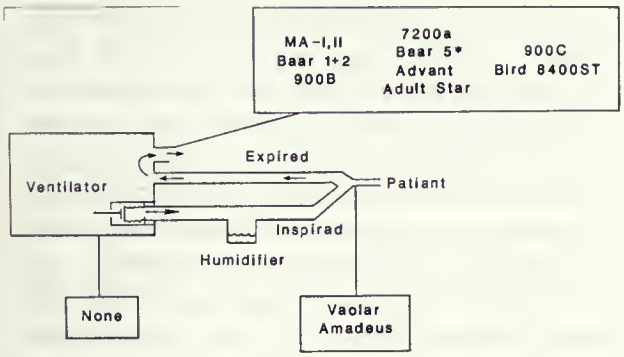

Fig. 8. Placement of flow-volume transducers in old and new ventilators. Although the Bear 5, 7200a, and Advent measure flow and volume on the expired side, microprocessor compensation for compressible volume is available.

Repair and Maintenance

Because of their modular construction, few moving parts, and software design, current ventilators should prove to be easier to repair and service than were their predecessors. Built-in self-diagnostics are also extremely helpful in troubleshooting and maintaining proper care of equipment. In many cases, a problem can be solved simply by changing a circuit-board. This is a far cry from the early ventilators filled with yards of tubing and numerous electronic and pneumatic components. However, few of these new ventilators have been around long enough to allow us to make statements as to whether they can actually be repaired more easily or more quickly than their predecessors. The cost of maintenance is also unknown compared to previous ventilators. No statement concerning patient benefit can be made at this time.

Ease of Use

One of the theoretical advantages of microprocessor technology is improved ease of use. 'User friendliness' of current ventilators is actually quite variable. The Bear 5 probably represents the standard for easy operator-ventilator interaction via the simple control panel and CRT display of variables.

The recently introduced Adult Star takes this one step further by having only one knob and a CRT with 3 separate screens. This system operates like a personal computer equipped with a mouse. The single control knob is turned until the desired variable is illuminated and then the Enter key is pressed. Movement of the control knob allows a change in that variable, after which the Enter key can be depressed and the desired manipulation made. Other ventilators have dual- or multiple-function controls and are somewhat more difficult to use. This can be a problem especially when the same control manipulates a different function in different modes.

The '++' key of the 7200a is used to access most optional functions by scrolling through a message window. Because of this feature and the number of key strokes required to activate a single function, the 7200a has been criticized as being the most 'user-unfriendly' ventilator of the current generation.[48] The trend in new ventilators is toward more straightforward controls and ease of use. The resulting benefit to the patient is unknown.

New Modes

New modes of ventilation are introduced as methods to avoid or prevent complications of old modes or to improve the efficiency of previous modes (ie, to expedite weaning). Prior to evaluating a new mode we should ask ourselves the following questions: (1) Does it reduce the incidence of common complications associated with old modes? (2) Does it improve gas exchange in situations in which old modes have failed? (3) Does it facilitate weaning? and (4) Does it fill a gap in current technology? With the current generation of ventilators, several new and some not-so-new modes have been introduced including: pressure-support ventilation (PSV), pressure-control ventilation (PCV) and pressure-control inverse-ratio ventilation (PCIRV), airway pressure-release ventilation (APRV), and mandatory minute volume (MMV). I will discuss each mode individually.

Pressure-Support Ventilation (PSV)

PSV is a patient-triggered, pressure-limited, flow-cycled mode of ventilatory support that allows patient control of respiratory frequency, inspiratory time, and inspiratory flowrate.[49] There is, however, considerable variation among ventilators operating in the PSV mode.[16]

A PSV breath can be divided into four parts: (1) inspiratory trigger; (2) rise time to set pressure; (3) time at set pressure (plateau); and (4) expiratory trigger. Most ventilators initiate inspiratory flow

when a pressure drop is sensed. Once triggered, flow increases until the set pressure is reached. In all but one ventilator, this rise time to set pressure is preset. The IRISA allows the time required to reach pressure to be adjusted up to 2.5 seconds by altering available inspiratory flowrate.[50] In the other ventilators, time to reach set pressure is a function of patient demand and available inspiratory flow. Inspiration is flow-cycled according to a percentage of initial inspiratory flow. The Veolar, 900C, Bear 5, Bird 6400ST, and Bird 8400ST terminate inspiration when patient demand for flow falls below 25% of initial peak flowrate. Other ventilators utilize a low terminal flow as an expiratory trigger (7200a = 5 L/min, Adult Star = 4 L/min). Because inspiration is flow-cycled, the patient maintains control over the volume, duration, and flow of each breath. Thus, PSV allows the patient more control, which explains why patient-ventilator synchrony appears to be improved. The literature suggests that PSV can reduce ventilatory work load, prevent diaphragmatic fatigue, compensate for additional work of breathing caused by poorly functioning demand valves and undersized endotracheal tubes, improve patient-ventilator synchrony, and facilitate weaning.[49-55]

Since its introduction by MacIntyre in 1986,[49] PSV's popularity has reached a level equivalent to that of IMV in the 1970s. Although no data are available to prove that PSV reduces weaning time, PSV does appear to fill the gap between AMV and spontaneous breathing. Additionally, compared to AMV and IMV, PSV appears to improve patient-ventilator synchrony in some patients. Thus, PSV does seem to benefit the patient.[56]

Pressure-Control Ventilation (PCV)

PCV is a patient- or time-triggered, pressure-limited, time-cycled mode of ventilatory support. Actually, PCV is not new, although its appearance in the new generation of adult ventilators is. PCV is characterized by a rapid rise to peak pressure, afforded by a decelerating inspiratory-flow pattern. In its new configuration, PCV might be more correctly considered a breath-delivery technique, rather than a new mode. A pressure-controlled breath can be delivered in IMV or AMV instead of volume oriented breaths, or in conjunction with PSV. The potential advantage of PCV is that because flowrate is geared to reach PIP as quickly as possible, flow will exceed patient demand and consequently improve patient-ventilator synchrony and decrease work of breathing. Another potential advantage of PCV is that distribution of gas within the lung can be improved by using the decelerating flow pattern and square-wave airway-pressure pattern.[57] The most obvious disadvantage is that, because the pressure remains constant, V_T will vary as compliance and resistance of the airways change. Therefore, use of PCV should be monitored carefully by setting low-and high-alarm limits for V_T and $\dot{V}_E$, if available. There is no evidence as of yet to show the benefit of using PCV over volume oriented modes of ventilation.

Pressure-Control Inverse-Ratio Ventilation (PCIRV)

PCIRV is a time-triggered, pressure-limited, time-cycled mode of ventilation characterized by a decelerating inspiratory-flow pattern, square-wave airway-pressure pattern, and inspiratory-to-expiratory ratio (I:E) of ≥ 1:1.

Theoretically, prolonged inspiratory times during PCIRV recruit collapsed alveoli and allow alveolar units with slow time constants to fill.[58] This should improve both oxygenation and ventilation. However, short expiratory times invariably lead to the development of auto-PEEP. Several authors have suggested that the early reported success of PCIRV[59-62] is due solely to unrecognized auto-PEEP.[63,64] While this may be partially true, attributing improvements in gas exchange to auto-PEEP in a system in which inspiration is up to 4 times longer than expiration is like ignoring the effects of PEEP during conventional ventilation with an I:E of 1:4. However, as Kacmarek and Hess noted,[64] the available reports on PCIRV are poorly done, which prevents useful gleaning of the literature at this time. Disadvantages of PCIRV include unrecognized auto-PEEP and consequent high $\bar{P}_{aw}$ and potential pulmonary barotrauma and hemodynamic embarrassment. Any benefits to the patient created by the availability of PCIRV have yet to be determined.

Airway Pressure-Release Ventilation (APRV)

APRV is a time-triggered, time-cycled, pressure-limited mode of ventilatory support that allows

spontaneous breathing throughout the respiratory cycle.

APRV was introduced by Stock and Downs,[65,66] and is available only on the IRISA ventilator. The rationale for use of APRV is similar to that of PCIRV. APRV can be thought of as 'intermittent' or 'bi-level' CPAP, in that, regardless of the pressure applied by the ventilator, spontaneous breathing is allowed. In fact, with the exception of spontaneous breaths, the pressure waveforms created by APRV appear identical to those seen during PCIRV. The difference then becomes a matter of perspective: whether you believe you start at a higher pressure and release to a lower pressure (APRV); or whether you believe you start at a lower pressure and go up (PCIRV). Results of a multi-institutional trial of APRV[67] demonstrated that in a group of 50 patients, APRV maintained similar arterial blood gas status, hemodynamic status, and minute ventilation—at a substantially lower PIP (mean decrease of 28 ± 12 cm H_2O [2.7 ± 1.2 kPa]), but higher P_{aw}—as did PCIRV. Like the other pressure-oriented modes of ventilation, APRV adds to our expanding armamentarium of ventilatory methods; however, at present no proven patient benefits can be attributed to APRV.

Mandatory Minute Volume (MMV)

MMV guarantees a clinician-set minimum level of minute ventilation by monitoring expired volume and automatically increasing or decreasing ventilator output as variations in spontaneous $\dot{V}_E$ approach set $\dot{V}_E$.

Mandatory minute volume was introduced in 1977 by Hewlett et al.[68] At the time, MMV was available via a mechanically operated modification to existing ventilatory equipment. Microprocessor technology, however, has allowed MMV to be added to existing equipment with only a software update. Quan and colleagues[69] recently reviewed the history, application, and indications of MMV in this journal. They concluded that MMV is a unique method of ventilatory support that may be useful in ventilating patients with fluctuations in ventilatory drive and during weaning. The literature supporting the use of MMV is sparse,[70-80] and for the most part consists of case reports and descriptions of ventilator operation, some of which appeared in non-refereed journals. East et al[74] has described the most cogent application of MMV, as a backup to PSV. The idea of using MMV in the recovery room to automatically wean patients seems attractive; however, using an expensive microprocessor-controlled ventilator for a patient with normal lungs who requires less than 4 hours of support to recover from an anesthetic hardly seems practical. To date, none of the proposed advantages of MMV have been demonstrated to benefit the patient.

Mechanical ventilation is clearly as much art as it is science, and perhaps the most important determinant of the success of any ventilatory mode is clinician experience and vigilance. One man's practiced success can easily be another man's inexperienced folly. Manufacturers need to provide new-generation ventilators with appropriate algorithms to apply these modes, but successful use requires an astute, careful clinician.

New Monitoring Capabilities

Microprocessors have also extended monitoring capabilities. I will discuss respiratory-mechanics monitoring, graphic presentation of monitored variables, trending, data management, and array of alarms that the new-generation ventilators are capable of providing.

Monitoring Respiratory Mechanics

Most of the new-generation ventilators are capable of deriving several indices of respiratory function based on measurements of airway pressure, volume, and flow. Most commonly, these include static compliance, dynamic compliance, and airway resistance. Additionally, depending upon the ventilator and its software, maximal inspiratory pressure (MIP), inspiratory work of breathing, auto-PEEP, vital capacity, inspiratory time/total cycle time (t_i/t_{tot}), pressure during the first 100 ms of inspiration against an occluded airway ($P_{0.1}$), and peak spontaneous inspiratory flow may be measured and/or calculated.

The technical aspects of measuring respiratory mechanics during mechanical ventilation have recently been reviewed by Marini,[81] and are too numerous to list here. However, I would like to mention a few things about the most frequently measured variables: compliance and resistance. The true measurement of static and dynamic lung com-

pliance requires that a nonassisted, constant-flow breath be delivered and an inspiratory pause be maintained until pressure equalizes throughout the patient-ventilator system.[82] Few ventilators impose these rigid criteria on their measurements of static compliance. Additionally, depending upon the measurement sites for flow, volume, and pressure, the value may represent the compliance of the humidifier, ventilator circuit, or patient. As such, changes in water volume in the humidifier, and distensibility of the circuit (as occurs with heating and cooling), may cause changes in measured compliance when the patient's condition is unchanged. The 'garbage-in, garbage-out' theory reigns supreme. If you measure tidal volume on the expired limb of the ventilator (without correcting for compressible volume), measure pressure inside the ventilator, and then take these two inaccurate values and divide one by the other, the result will also be inaccurate.

Korst et al[83] have presented data in abstract form that suggest that the current-generation ventilators can accurately measure compliance and resistance in a lung model. However, these data are very limited, and no validation in the intensive-care unit has been done.

Because during inspiration the airways are mechanically dilated by positive pressure, inspiratory resistance is a fairly insensitive measurement of response to bronchodilator therapy. Expiratory resistance is a more appropriate measurement and is offered by several manufacturers.[84]

The inability of the 7200a to accurately measure MIP in mechanically ventilated patients has been demonstrated.[85] This inability is due to the fact that only one breath is considered for the measurement when 8-10 breathing efforts are required.[86]

Several new monitoring packages measure the work of breathing, but none of these has been validated to date. In fact, lack of validation is a good way to describe the majority of ventilator-monitored parameters. Aside from the questionable accuracy of the monitored parameters, there are also few data to show that the accurate measurement of these parameters is beneficial to the patient!

Graphic Presentation of Data

Through the use of built-in CRTs (Bear 5), viewing screens (IRISA, 7200a), or personal computers interfaced to the ventilator via an RS-232 connector (Veolar), the new-generation ventilators can provide graphic representation of airway pressure, volume, and flow. This has long been done by researchers, but only with the introduction of the Bear 5 did this technology come into the hands of the everyday clinician.

Because this technology is so new, few data are available regarding its usefulness. MacIntyre[87] has suggested that graphic representation of data may allow clinicians to optimize mechanical ventilation and troubleshoot ventilator operation in a more efficient and sophisticated manner than ever before.

A description of the potential uses and interpretation of 'graphics' is beyond the scope of this manuscript. However, I believe that we, the 'television generation,' may benefit from these visual displays of information compared to numerical values. For example, most clinicians may be unfamiliar with the calculation and meanings of work-of-breathing measurements, particularly when these values are expressed in J/L or $kg \cdot m \cdot min^{-1}$. Using a graphic representation of work (a pressure-volume curve), clinicians can be taught that the area below the pressure axis represents increased work of breathing. Diminution of this area, by adjusting sensitivity or increasing inspiratory flowrate, can easily be seen on the display without the need for actual calculation of work. My own experience,[50] using the Leonardo system from Hamilton Medical, is that graphic representation of pressure-volume and flow increases the clinical staff's interest and understanding of many ventilatory techniques. Reluctantly, however, I must conclude that, although I consider graphic representation of data to be one of the most promising enhancements of the new ventilators, no evidence suggests that it is beneficial to the patient.

Trending and Data Management

Like personal computers, the microprocessors in ventilators are capable of storing and manipulating data. These data can be used to plot trends of ventilator and/or patient variables. These trends (eg, the response of lung compliance to changes in end-expiratory pressure) can be viewed over a period of hours or days. This information can be helpful to clinicians responsible for managing the mechan-

ically ventilated patient with worsening hypoxemia. Trending the f, V_T, and $\dot{V}_E$ during CPAP trials over a period of days—as a way to evaluate patient progress—may also be useful. Data management possibilities include automatic ventilator checks and the creation of a paperless chart. East[88] recently reviewed these possibilities, and provided both encouraging and discouraging news. These possibilities are still untested, and any benefit to patient care undetermined.

Alarms

An alarm is defined as a mechanism that warns of potentially dangerous events. During mechanical ventilation, dangerous events may result from ventilator malfunction, disruption of the patient-ventilator interface, or deterioration in patient condition.[89] Early mechanical ventilators had no alarms at all. The MA-1 came with an alarm package that included a high-pressure limit, a ratio alarm (activated when inspiratory time exceeded expiratory time), a low-oxygen-inlet pressure alarm, and a low-exhaled-volume alarm. Its third-generation offspring, the 7200a, has alarms for 12 different conditions: high pressure limit, low exhaled tidal volume, low pressure oxygen inlet, low inspiratory pressure, low exhaled minute volume, low pressure air inlet, low CPAP/PEEP, high respiratory rate, low battery, apnea, inappropriate I:E, and exhalation valve leak. Additionally, if a failure of the ventilator occurs, alarms for back-up ventilator, safety-valve open, and ventilator-inoperative are activated.[90]

Microprocessor technology seems to improve alarm function by automatically setting alarms based on measured parameters. For example, if set V_T is 1,000 mL, the ventilator may automatically set the low-exhaled-tidal-volume alarm at –25% of that setting. If exhaled V_T falls below 750 mL, the alarm will be activated. These alarm limits can be modified to be more or less stringent according to the clinical situation and clinician preference.

The number of alarms in intensive care units today is in itself alarming. New-generation ventilators seem to add to this problem, and for this reason may actually prove to be detrimental. Problems with alarms are multifactorial, not the least of which are human error and legal issues. I believe we, as clinicians, should provide guidelines to the manufacturers, in which the number of necessary alarms and the most important conditions warranting alarms are specified. Certainly standardization is needed.

In the future, we may have 'smart' alarm systems that, on the basis of a predetermined hierarchy of importance, sound only the most important violated alarms. This might help to relieve the stress felt by many caregivers in the ICU.

Cost

No discussion of ventilators is complete without mention of cost. The current-generation ventilators range in price from just under $10,000 to almost $30,000, depending upon the number of options or add-ons. I'm not sure whether these prices are justified; but, as a result of inflation, insurance costs, and research and development expenditures, they may well be. I would like to think, however, that as this generation of ventilators matures and updates are completed by changing circuit boards or EPROMS (erasable programmable read-only memory), the prices will either remain constant or go down. Reducing health-care expenditures is everybody's business, including manufacturers.

Summary

The current-generation mechanical ventilators are certainly enhanced in performance, style, and cost. Many of these enhancements appear to benefit both the patient (eg, reduced work of breathing, wider range of operation) and the hospital (eg, reduced maintenance costs). Although vast areas for refinements remain, my plea is that efforts be made to learn about and take advantage of the current technology, before embarking upon new technology. As we have learned, you have to have the right tool for the right job. Unfortunately, it's not the right tool, if you don't know how to use it.

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How Should Bronchodilators Be Administered to Patients on Ventilators?

Dean Hess MEd RRT

Introduction

Therapeutic aerosols are commonly used in ambulatory patients with lung disease, and the most common of these are the $beta_2$-agonist bronchodilator aerosols. However, other aerosolized medications are used as well, including anticholinergics, cromolyn sodium, steroids, pentamidine, and ribavirin. The use of aerosols to treat lung disease produces an ideal therapeutic ratio,[1,2] meaning that they produce optimal therapy with minimal side effects. It has even been suggested that aerosolized medications may have made theophylline obsolete.[3]

Aerosolized medications are also commonly administered to mechanically ventilated patients, but the delivery of these medications to this patient population has not received much attention in the literature. This paper reviews the literature related to aerosol therapy in mechanically ventilated patients, makes some recommendations for the appropriate use of this therapy, and identifies areas where further work is needed relative to this subject.

Factors Affecting Aerosol Penetration and Deposition

If aerosols are to produce a therapeutic effect, they must be deposited at an appropriate site in the respiratory tract. Bronchodilators must be deposited in airways. Ideally anticholinergics should be deposited in larger airways, and $beta_2$-agonists should be deposited in smaller airways.[4,5] Medications such as pentamidine and ribavirin should be deposited in the lung parenchyma. Aerosol penetration and deposition in nonintubated, spontaneously breathing patients have been thoroughly reviewed in the literature.[6-8] From a physical standpoint, factors that affect aerosol penetration and deposition include inertial impaction, sedimentation, and diffusion. From a clinical standpoint, factors that affect aerosol penetration and deposition are particle size, ventilatory pattern, and lung function.

Aerosols with larger than 5-μm mass median aerodynamic diameter (MMAD) generally do not penetrate the upper respiratory tract (Fig. 1).[9] Aerosols with an MMAD of 1-2 μm tend to have maximum deposition in alveoli, whereas aerosols with an MMAD of 2-5 μm tend to be deposited in airways. Aerosols with an MMAD < 1 μm tend to be very stable and are exhaled.

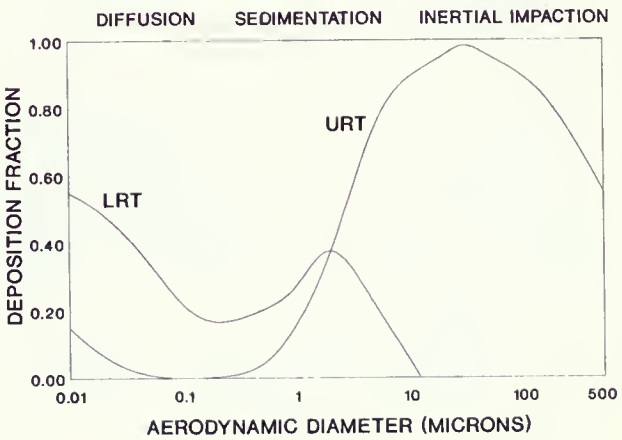

Fig. 1. Particle size and deposition in the upper respiratory tract (URT) and the lower respiratory tract (LRT). (Adapted, with permission, from Reference 9.)

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Abbreviations Used in This Paper

AIDS	— Acquired immunodeficiency syndrome
MMAD	— Mass median aerodynamic diameter
BPD	— Bronchopulmonary dysplasia
ET	— Endotracheal
IPPB	— Intermittent positive-pressure breathing
LRT	— Lower respiratory tract
MDI	— Metered-dose inhaler
SPAG	— Small-particle aerosol generator
SVN	— Small-volume nebulizer
URT	— Upper respiratory tract

In spontaneously breathing patients, the pattern of inhalation affects the amount of aerosol deposited in the lower respiratory tract. Aerosol particles are more likely to be deposited in the lower respiratory tract if inspiratory flow is decreased.[10,11] Although some investigators have found that an increase in tidal volume may improve aerosol deposition in the lung periphery,[10] this has not been confirmed by others.[11] End-inspiratory breath-holding also appears to improve aerosol deposition in the lungs.[12,13] However, the importance of a slow inspiratory flow and breath-holding time has been questioned.[14,15] Inhalation of aerosol through the mouth, rather than the nose, may also improve aerosol delivery to the lower respiratory tract,[16] although this has been questioned.[17]

Aerosol penetration and deposition are decreased in the presence of airway obstruction.[10,18] Aerosol deposition in the lower respiratory tract is decreased with COPD, and has been shown to decrease with a decrease in FEV_1. It is ironic that aerosol deposition is decreased in these patients who might benefit most from this therapy. For this reason, bronchodilators may need to be administered more frequently or in higher dosages to patients with acute reversible airflow obstruction.

Aerosol Generators: Small-Volume Nebulizer vs Metered-Dose Inhaler

Therapeutic aerosols can be delivered by small-volume nebulizer (SVN), metered-dose inhaler (MDI), ultrasonic nebulizer, dry-powder inhaler, or intermittent positive-pressure breathing (IPPB).[19] However, IPPB, ultrasonic nebulizers, and dry-powder inhalers are infrequently used for therapeutic aerosol delivery. Although the SVN (jet nebulizer) is commonly used, the MDI has become an increasingly popular means of delivering therapeutic aerosols.

When an SVN is used, a small volume of medication and a larger volume of diluent (usually normal saline or water) are placed into the nebulizer. The performance of an SVN is affected by the gas flow used to power it, the medication-diluent volume, and the construction of the nebulizer.[20-24] Some medication-diluent remains in the nebulizer at the completion of nebulization, which is called the dead volume. The percentage of dead volume increases with low flows and low diluent volumes (Fig. 2). There is variability in dead volume among commercially available SVNs, and considerable variability within nebulizers of a specific manufacturer has been reported.[25,26] To minimize dead volume, Clay et al[20] recommended using a medication-diluent volume of 4 mL and a flow of 6-8 L/min. Kradjan and Lakshminarayan[21] recommended using medication-diluent volumes of 2-2.5 mL; however, they used a flow of only 6 L/min and medication-diluent volumes only in the range of 1-3 mL. From data obtained in our laboratory,[22] my colleagues and I recommend using a medication-diluent volume of 4 mL and a flow of 8 L/min to power an SVN. Aerosol particle size is also affected by the flow used to power the SVN; smaller particles are produced at higher flows.[27]

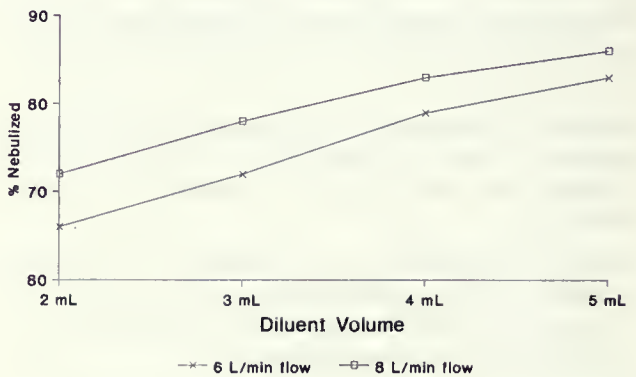


Fig. 2. Effect of flow and diluent volume on nebulizer dead volume (data from Reference 22).

It is commonly known by respiratory care practitioners that the nebulizer solutions cool and concentrate during nebulization.[28] The drop in solution temperature is the result of evaporative heat loss. Phipps and Gonda[29] have shown that the solute concentration contained in the aerosol produced by an SVN increases significantly with a fall in SVN temperature, and that this is associated with a concomitant decrease in aerosol particle size. This is probably because the cold aerosol particles produced from the SVN solution evaporate a substantial amount of water as they warm to room temperature. This effect is accentuated when a gas with a low relative humidity (eg, cylinder oxygen) is used to power the nebulizer, rather than a gas with a higher relative humidity (eg, from an air compressor). Phipps and Gonda[29] recommended that the gas that powers the SVN be saturated with water vapor, and that the nebulizer solution be maintained at room temperature. Unfortunately, it may not be technically feasible to comply with these recommendations; because this was a bench study, the clinical implications are unclear.

Whether nebulizer performance affects physiologic response has been questioned.[30,31] However, Johnson et al[24] found that nebulizer function can influence both aerosol deposition in the lungs and physiologic response. They compared a Turret nebulizer operated at a flow of 12 L/min (MMAD 3.3 μm) to an Inspiron nebulizer operated at a flow of 6 L/min (MMAD 7.7 μm). For albuterol (salbutamol) nebulization, they found that bronchodilation was significantly greater with the Turret at each dosage level used (mean [SD] 9.1 [1.1%] vs 2.7 [0.2] %) (Fig. 3). They also found better deposition with the Turret (Fig. 4). When nebulizers are used, it is important for the respiratory care practitioner to appreciate that the performance of the SVN can affect patient responsiveness to the inhaled medication.

It is frequently unappreciated that only a small fraction of the aerosol from an SVN or MDI is retained in the lower respiratory tract. Newman[32] and Spiro[33] have shown that only about 10% of the aerosol from a MDI is deposited in the lower respiratory tract. Similarly, Lewis and Fleming[34] have shown that approximately 10% of the aerosol from an SVN is deposited in the lower respiratory

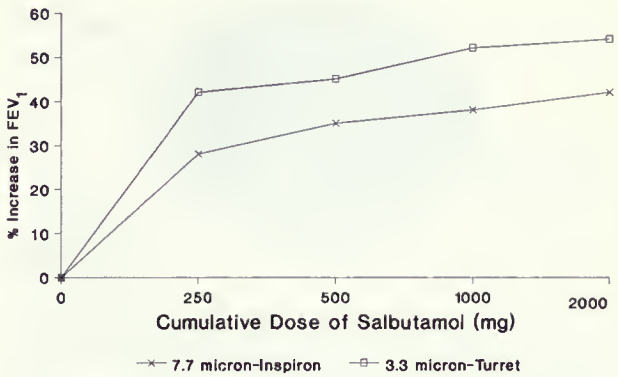


Fig. 3. Effect of nebulizer performance on physiologic response of FEV_1. (Adapted, with permission, from Reference 24.)

tract (Fig. 5). With the MDI, a large fraction of the aerosol is deposited in the upper airway (unless an auxiliary device is used, in which case a large fraction is deposited in the auxiliary device). With the SVN, a large fraction of the aerosol is retained in the nebulizer (dead volume).

An interesting paradox appears when the results of bronchodilator administration by SVN and MDI are compared.[35] Although the dose used with an SVN is approximately ten times the dose used with an MDI, the deposition and physiologic response from each is similar (at least in ambulatory patients). For example, a 0.3-mL dose of metaproterenol (5% solution) is equivalent to 15 mg, whereas 2 puffs

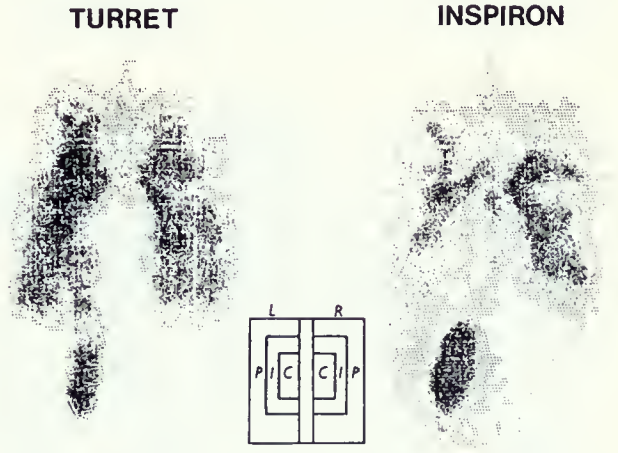


Fig. 4. Effect of nebulizer performance on pulmonary deposition of aerosol. (Reprinted, with permission, from Reference 24.)

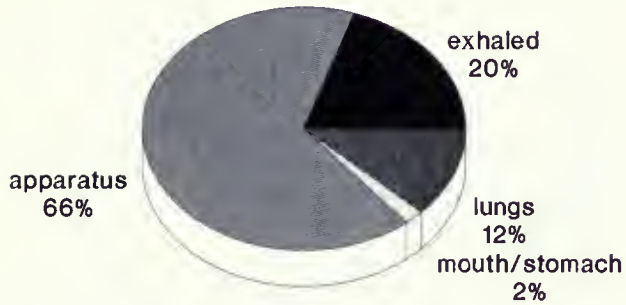


Fig. 5-A. Deposition from small volume nebulizer. (Adapted, with permission, from data in Reference 34.)

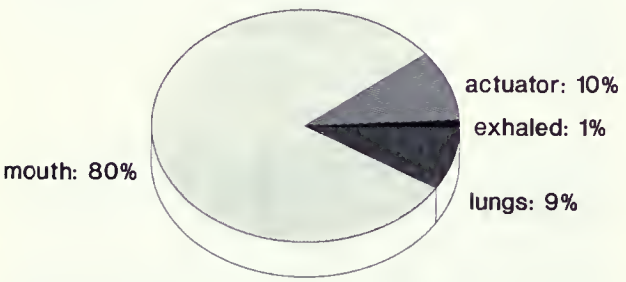


Fig. 5-B. Deposition from metered-dose inhaler. (Adapted, with permission, from data in Reference 32.)

of metaproterenol (0.65 mg each) is equivalent to 1.3 mg. The dose from the SVN may need to be greater to compensate for the volume of drug retained in the nebulizer and the amount of drug lost during the patient's expiratory phase.

In the 1980s, there was considerable resurgence of interest in using MDI in place of SVN. This occurred for two principal reasons: (1) substantial pressure to contain health-care costs evolved, and use of the MDI is less expensive than use of the SVN,[36,37] and (2) MDI auxiliary devices (spacers) became available, which allowed MDIs to be used effectively by patients with poor hand-breath coordination.[38-45] A plethora of studies have reported equivalence between SVN and MDI in acutely ill adult patients, stable adult patients, adult patients with asthma, adult patients with COPD, and pediatric patients.[46-64]

Aerosol Delivery during Mechanical Ventilation: Use of SVN

Aerosolized bronchodilators are commonly administered to intubated adult patients, often by SVN. There has also been increasing use of aerosolized bronchodilators in mechanically ventilated infants and children. Aerosol bronchodilator administration was described nearly 30 years ago in the anesthesia literature,[65,66] and since then emergency-medicine, anesthesia, and critical-care applications have been described.[67,68]

MacIntyre et al[69] studied aerosol delivery by SVN in seven mechanically ventilated adult patients and found that a mean (SD) of only 2.9 (0.7) % of a radioactive aerosol was deposited in the lungs (Fig. 6). In three healthy, nonintubated subjects using an SVN, 11.9 (2.2) % of the radioactive aerosol was deposited in the lungs. In another group of 15 mechanically ventilated adult patients reported in the same study, it was observed that aerosolized metaproterenol had no significant effect on lung mechanics.

In a group of 10 postoperative intubated mechanically ventilated patients, none of whom had

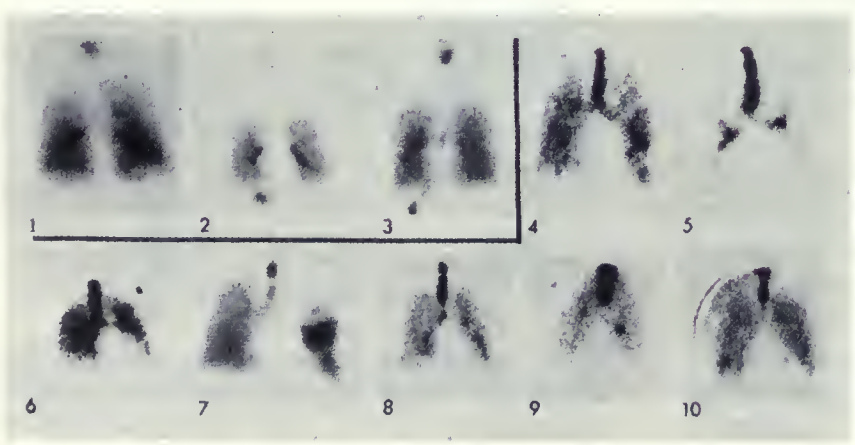


Fig. 6. Aerosol deposition by SVN in nonintubated subjects (1-3) and intubated subjects (4-10). Note radioactivity in mouth and stomach of nonintubated subjects and ET tube of intubated subjects. (Reprinted, with permission, from Reference 69.)

Fig. 7. Position of nebulizer at Y-piece.

Fig. 8. Position of nebulizer at manifold.

COPD, Zandstra et al[70] found that nebulization of a mucolytic agent caused a significant increase in inspiratory resistance. This effect was blocked by the addition of a bronchodilator to the aerosol. Interestingly, no significant change in airway resistance was noted when these patients received bronchodilator alone or a saline control.

Using a bench model, Ahrens et al[71] showed that the endotracheal (ET) tube is a formidable barrier to the penetration of aerosols from an SVN into the lower respiratory tract. They used a FanJet nebulizer and showed that the amount of aerosol deposition in a lung model decreased as ET-tube size decreased and as inspiratory flow increased. It was also found that the amount of aerosol delivered into the lung model was increased when a nebulizer that produced smaller particles (MMAD 0.54 μm) was used in place of the FanJet nebulizer, which produced particles of 3.95-μm MMAD.

When an SVN is used in a ventilator circuit, it can be placed at the ventilator Y-piece (Fig. 7) or at the circuit manifold approximately midway between the ventilator and the Y-piece (Fig. 8). Furthermore, the nebulizer can be powered continuously from an auxiliary gas flow or from the nebulizer drive line of the ventilator. Hughes and Saez[72] used a bench model to evaluate the effect of nebulizer mode and position on the amount of medication available to a mechanically ventilated patient. This study evaluated the amount of aerosol delivered to the ET tube (not the amount of aerosol that passed through the ET tube). Using a radioactive aerosol, they found that significantly more medication was delivered to the ET tube if the nebulizer was placed at the manifold, and was operated during inspiration only (Fig. 9). It is interesting to note that the least amount of aerosol was delivered to the ET tube with the nebulizer placed at the Y-piece and operated continuously—the technique that appears to be most commonly used in clinical practice. Continuous nebulization and placement of the nebulizer at the manifold of the ventilator circuit presumably allows the inspiratory tubing to fill with aerosol during the expiratory phase of the ventilator. A system for mechanical ventilation that delivers aerosol into the inspiratory circuit only during the expiratory phase

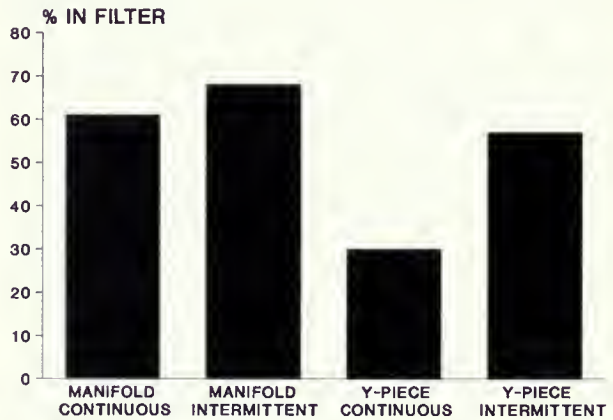


Fig. 9. Effect of nebulizer position (in ventilator circuit) and continuous versus intermittent nebulization on amount of aerosol delivered to the ET tube. (Reprinted, with permission, from Reference 72.)

has been described,[73] but is not commonly used in the United States.

Using a lung model with an ET tube and MA-1 ventilator, Fraser et al[74] determined that 4.8% of the SVN dose was deposited in the lower respiratory tract when the SVN was powered during inspiration only. They also found that alterations of respiratory rate, tidal volume, ET-tube size, and movement of the SVN to a position 15 cm from the ET tube did not affect deposition.

Aerosolized pentamidine has been shown to be effective in the treatment of pneumocystosis in patients with acquired immunodeficiency syndrome (AIDS).[75] Girard et al[76] compared plasma pentamidine concentrations after pentamidine aerosolization in spontaneously breathing and mechanically ventilated patients. Interestingly, they found much higher plasma pentamidine levels in the patients who were mechanically ventilated.

Several studies have also evaluated the use of SVN in infants. Brudno et al[77] administered aerosolized terbutaline to 8 ventilator-dependent infants with bronchopulmonary dysplasia (BPD), and found a significant reduction in inspiratory and expiratory resistance and a significant increase in tidal volume. Wilkie and Bryan[78] administered aerosolized salbutamol and ipratropium bromide to 17 ventilator-dependent infants with BPD (age range 19-103 days), and found a significant reduction in resistance and a significant improvement in compliance. Although intermittent nebulization during mechanical ventilation has been shown to be superior to continuous nebulization during manual ventilation for pediatric patients,[79] the aerosol treatments were administered during hand-ventilation in both of these studies.[77,78]

A lung model was used by Cameron et al[80] to evaluate nebulizer function in neonatal ventilator circuits. Five nebulizers were used to deliver an aerosol to a lung model using a time-cycled, pressure-limited ventilator. The lung model consisted of a 3.5-mm-ID ET tube, a filter onto which aerosol particles impacted, and a rubber test lung. The ventilator settings were pressures 20/2 cm H_2O, I:E 1:1, and respiratory rate 30/min. Nebulizers were powered at 6-8 L/min, and a 4-mL medication-diluent volume was used. Very small amounts of aerosol were deposited onto the filter (simulating lung deposition). The best performing nebulizer only deposited 1.52% of the aerosol onto the filter. The authors attributed this poor performance to the continuous flow through the ventilator circuit, which they presumed carried much of the aerosol out through the expiratory port of the ventilator. It is of interest that the poorest nebulizer performance in this study was that of the small-particle aerosol generator (SPAG), which is used to administer ribavirin. Although the technical aspects of ribavirin administration during mechanical ventilation have been described,[81,82] the amount of ribavirin actually deposited in the lung has not been reported.

Flavin et al[83] used a rabbit model with an infant ventilator to simulate aerosol delivery to intubated mechanically ventilated infants. The rabbits were intubated with 3.0-mm-ID ET tubes, and ventilated with a Bourns LS-104 ventilator. A radioactive aerosol was used, so that the amount of aerosol deposited in the lung could be quantified. Three nebulizers were used, and one nebulizer was used at two flows. Although there were differences between the nebulizers used, the amount of aerosol deposited in the lung was extremely low (mean [SD] 1.96 [1.19] % at best)—lower than the deposition reported by MacIntyre et al[69] in mechanically ventilated adult patients.

From the previous discussion, it seems obvious that the delivery of aerosolized medications to intubated mechanically ventilated patients is not very efficient. Furthermore, the delivery of aerosolized medications to intubated mechanically ventilated infants is worse than delivery in adults. In spite of this, a physiologic response to use of aerosolized bronchodilators has been reported in mechanically ventilated infants and adults. The amount of aerosol delivered to the ET tube can be increased by using appropriate diluent volumes and nebulizer flows and by proper placement of the nebulizer in the ventilator circuit. However, in my opinion, the major barrier to efficient delivery of aerosolized medications to intubated patients is the ET tube.

There are several potential problems related to the use of SVN with mechanical ventilators. Contaminated medication nebulizers can be a source of bacterial aerosols in mechanical ventilator

circuits. Craven et al[84] have recommended that in-line SVNs be cleaned or disinfected after each treatment—an expensive and time-consuming task. The continuous flow from an SVN will increase the tidal volume (and associated pressure) delivered when volume ventilators are used (Fig. 10). Although this may be inconsequential in many adult patients, it may be important when low tidal volumes and/or high ventilation pressures are used. The continuous flow from an SVN also introduces a bias flow, which makes it more difficult for the patient to generate the negative pressure required during assisted modes of ventilation (pressure support, assist-control); this may lead to underventilation in some patients during SVN treatments.[85] The continuous flow of aerosol from the SVN can also damage the expiratory flow transducer of the Servo 900C ventilator; therefore, it is common practice to place filters in the expiratory limb to protect the flow transducer during aerosol administration (personal experience).

Aerosol Delivery during Mechanical Ventilation: Use of MDI

The use of MDI with intubated patients is not new, and has been reported in the anesthesia literature since the mid-1960s.[86-95] Most of these reports were short descriptions of various techniques used to adapt the MDI to the ET tube and anesthesia circuitry. In 1966, Fresoli et al[88] described their experience with administering isoproterenol by MDI to 8 patients, 7 of whom experienced relief of bronchospasm. As many as 5 puffs of isoproterenol were used in the patients who had a favorable response, and 8 puffs were used in the patient who did not respond. The MDI was placed between the Y-piece of the anesthesia circuit and the ET tube, the MDI was actuated during inhalation, and an inspiratory hold of several seconds was used.

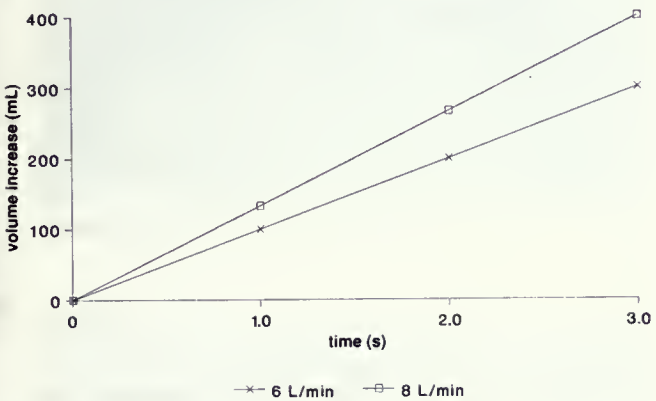


Fig. 10. Effect of nebulizer flow on tidal volume delivery when using an SVN in a ventilator circuit.

In 1975, Gold[89] reported his experience with the use of isoproterenol by MDI in 12 cases of bronchospasm during anesthesia. The MDI was placed between the anesthesia circuit and the ET tube, 2 puffs from the MDI were used, and the MDI was actuated during inhalation. Clinical improvement occurred in 11 patients. Overall, peak airway pressure decreased from mean (SD) 43 (2) torr to 31 (2) torr, P_{aCO_2} decreased from 60 (6) torr to 47 (4) torr, P_{aO_2} increased by 39 (13.4) %, and no adverse cardiac side effects were observed.

Similar results were reported by Sprague,[90] who observed improvement in 14 of 16 patients. Sprague placed the MDI between the anesthesia circuit and the ET tube, the MDI was actuated during inhalation, and a 3-second end-inspiratory breath-hold was used. Two puffs of isoetharine were used, and repeated as necessary at 5-minute intervals; 4 patients received 2 puffs, 9 patients received 4 puffs, and 3 patients received 6 puffs. Sprague reported decreases in wheezing and ventilating pressures, and no significant cardiac side effects.

Several adapters are commercially available to adapt the MDI to a ventilator circuit (Fig. 11 and Table 1). The Boehringer Laboratories' Bronchodilator T-piece (Boehringer Laboratories, Norristown PA) attaches directly to the ET tube (Fig. 12), as does the Intec 178710 (Marquest Medical, Englewood CO) (Fig. 13). Instrumentation Industries (Bethel Park PA) adapters are available in several configurations: The RTC-21 (Fig. 14) is used to deliver MDI medication through a bronchoscope adapter or directly down the ET tube; the RTC-23 is placed on the inspiratory limb of the ventilatory circuit; the RTC-22 (Fig. 15) is placed between the ventilator Y-piece and the ET tube; and the RTC-15 (Fig. 16) is also placed between the ventilator Y-piece and the ET tube. The RTC-22, RTC-23, and RTC-15 adapters differ only in their dimensions, and each delivers medication mainstream into the

Fig. 11. In-line MDI aerosol adapters. Back: AeroVent. Front (left-right): Instrumentation Industries RTC-21, Hudson/RCI, Instrumentation Industries RTC-22, Boehringer Laboratories, and Intec.

gas stream. Instrumentation Industries also makes the KMO 046-052 series of adapters, in which the MDI adapter is part of the ventilator Y-piece. Hudson/RCI (Temecula CA) makes an MDI adapter (Fig. 17) that can be placed either at the Y-piece of the ventilator or upstream in the ventilator circuit. When the Boehringer, Intec, Instrumentation Industries, and Hudson/RCI adapters are used, the MDI should be actuated at the beginning of inspiratory flow to the patient. The Monaghan

Table 1. Comparison of Costs of Commercially Available MDI Adapters for Intubated Mechanically Ventilated Patients

	Disposable/ Reusable	Cost*
Monaghan		
AeroVent	Disposable	$ 3.95
AeroChamber	Reusable	$ 7.00
Boehringer Labs	Reusable	$71.50
Hudson/RCI	Disposable	$ 1.10
Instrumentation Industries		
RTC 15-D, 21-D, 22-D, 23-D	Disposable	$ 1.50
RTC 21	Reusable	$ 4.50
RTC 22, 23	Reusable	$ 6.75
KMO 046-052	Disposable	$ 1.20
Intec	Disposable	$ 1.72

*Fall, 1990, cost. These are list prices, and may vary due to volume of purchase and other purchase considerations.

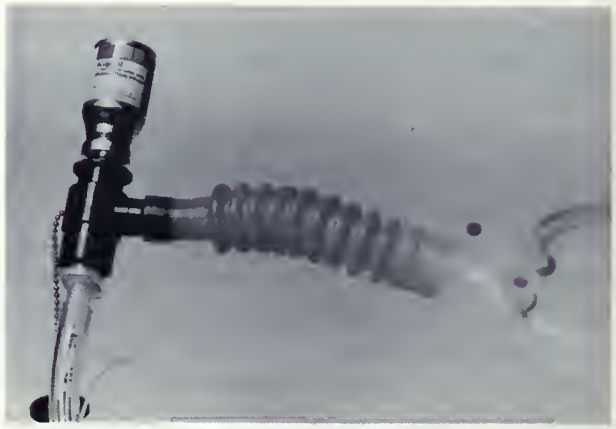


Fig. 12. Boehringer Laboratories MDI adapter.

Fig. 13. Intec MDI adapter.

Fig. 14. Instrumentation Industries RTC-21 MDI adapter.

AeroVent adapter (Monaghan Medical, Plattsburgh NY) fits on the inspiratory limb of the ventilator circuit (Fig. 18A). Between treatments, the AeroVent is collapsed in the ventilator circuit (Fig. 18B). The AeroVent is an aerosol holding chamber;

Fig. 15. Instrumentation Industries RTC-22 MDI adapter.

Fig. 16. Instrumentation Industries RTC-15 MDI adapter.

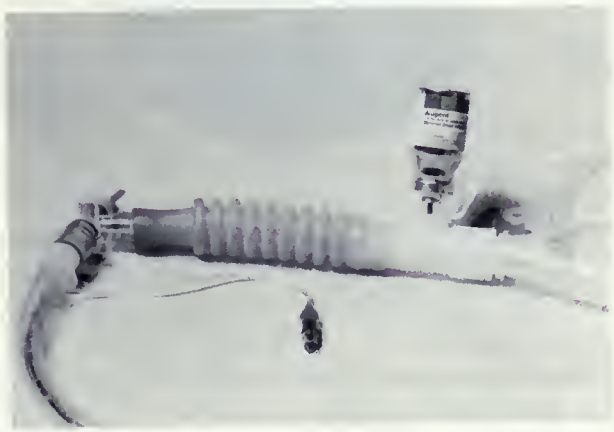
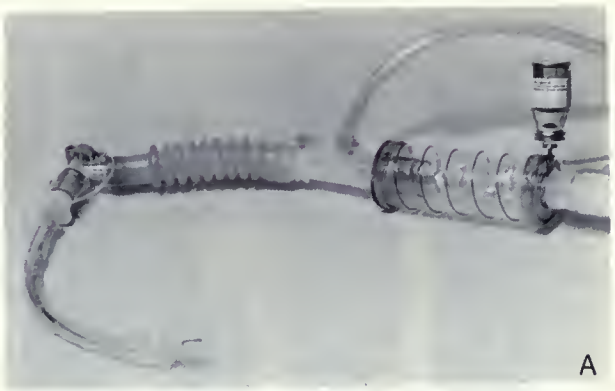


Fig. 17. Hudson/RCI MDI adapter.

when it is used, the MDI is actuated at the end of exhalation (just prior to the onset of inhalation).

In a bench study, Bishop et al[96] compared the volume of particles delivered to the distal end of the ET tube when several different MDI adapters



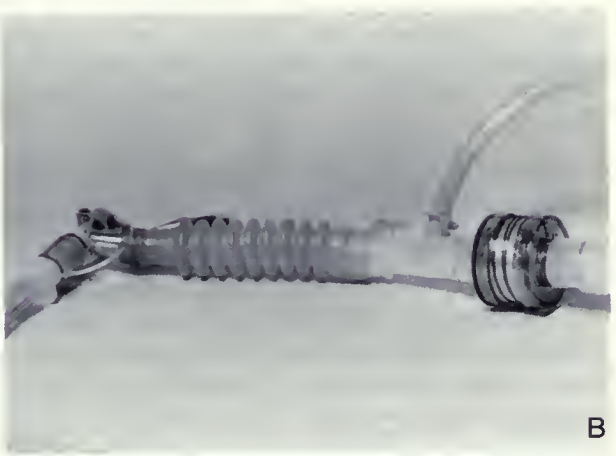


Fig. 18. A: Monaghan AeroVent open in ventilator circuit, as used to deliver aerosolized medication. B: Monaghan AeroVent closed in ventilator circuit.

were used. They found that each of the adapters evaluated delivered less aerosol through the ET tube than that delivered from a standard actuator (ie, the one supplied by the manufacturer for use with ambulatory patients). They also found differences between the types of actuators (Fig. 19) and recommended that the number of puffs be increased when an MDI is used with intubated patients (50% increase with the AeroVent, 350% with the Instrumentation Industries MDI adapter, and 800% with the Intec adapter). Although this information is useful in the determination of an appropriate MDI dose in intubated patients, it should be recognized that these data have not been subjected to clinical evaluation (eg, on patients).

Several bench studies have evaluated the delivery of aerosols by MDI through ET tubes. Crogan and Bishop[97] evaluated the delivery efficiency of MDI-generated metaproterenol through an ET tube. They

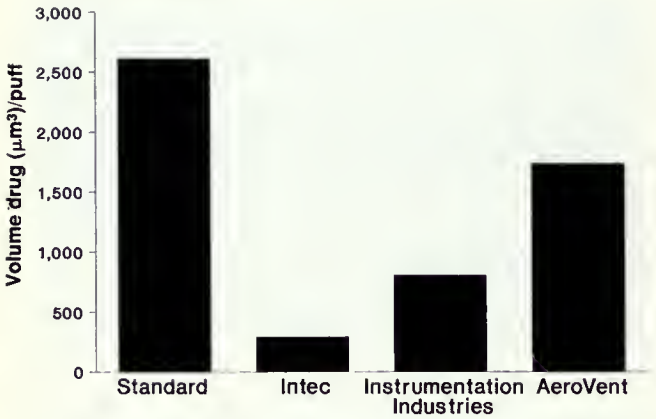


Fig. 19. Comparison of aerosol delivery from various MDI adapters, ie, volume of drug per puff that reached the distal end of the ET tube (drawn from data in Reference 96).

found that the amount of aerosol delivered varied from mean (SD) 3.0 (1.9) % for a 6-mm-ID ET tube to 6.5 (4.4) % for a 9-mm-ID ET tube (Fig. 20). Significantly more aerosol traversed the ET tube when the MDI was activated into a continuous flow of gas (analogous to actuation of the MDI near the beginning of the inspiratory phase of the ventilator), rather than actuation of the MDI before gas flow was initiated (analogous to actuation before the initiation of the inspiratory phase of the ventilator). In this study, an Intec MDI adapter was placed between the ventilator Y-piece and a swivel adapter attached to the ET tube.

In work done in our laboratory,[98] my colleagues and I found most of the aerosol from an MDI

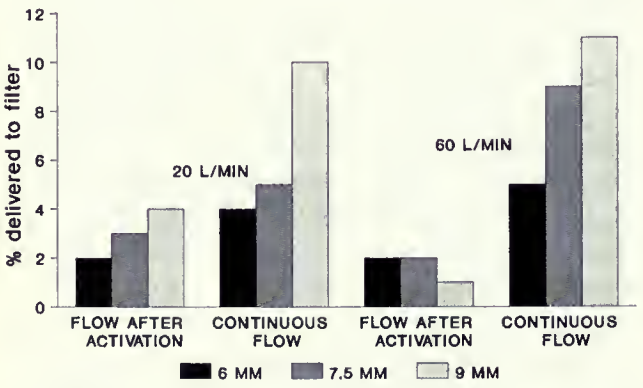


Fig. 20. Effect of flow, ET-tube size, and activation before or after gas flow on MDI-aerosol delivery through the ET tube. (Adapted, with permission, from Reference 97.)

impacted on the ET tube, and only a mean (SD) of 3.3 (2.1) % traversed the ET tube (Fig. 21). Visual inspection of the ET tube showed considerable deposition of drug on the proximal end of the tube (Fig. 22). We used an Instrumentation Industries adapter that was attached directly to the ET tube and a metaproterenol MDI. Flow and tidal volume had no effect on the amount of aerosol that traversed the ET tube. ET-tube size had no effect, but tubes of only two sizes (7-mm-ID and 9-mm-ID) were used. It is interesting to note that the amount of aerosol that we found to traverse the ET tube with an MDI is similar to that reported by MacIntyre et al[69] when an SVN was used. With nonintubated patients, only about 10% of the MDI aerosol is deposited in the lungs, with the majority impacting in the oropharynx. Thus, one might conclude that MDI-aerosol deposition in intubated patients is no worse than SVN-aerosol deposition in intubated patients, and the amount of drug delivered to the lungs of intubated patients may approach that of nonintubated patients if the dose (number of actuations) is increased.

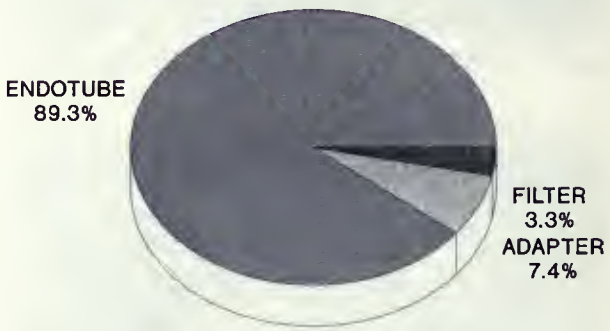


Fig. 21. Relative deposition of aerosol in MDI adapter, ET tube, and filter placed at the end of the ET tube (drawn from data in Reference 98).

In the patient who is not intubated, aerosol from the MDI that impacts on the oropharynx is swallowed, may be systemically absorbed, and may produce bronchodilation and side effects. It is interesting to speculate about the fate of the aerosol that impacts on the ET tube in intubated patients. Although much of it may be coughed or suctioned out of the tube, some of it may eventually enter the respiratory tract. This may be cause for concern about side effects, although the current-generation

Fig. 22. Illustration of aerosol impaction on proximal end of ET tube.

beta-agonists are very safe even at high dosages. Most importantly, some of the MDI aerosol that impacts on the ET tube may eventually enter the lungs and produce bronchodilation.

Fernandez et al[99] compared the use of salbutamol by MDI, ipratropium bromide by MDI, and aminophylline by I.V. in mechanically ventilated patients with COPD. They used a self-inflating resuscitator bag and delivered the drug during a slow, deep breath (5-6 seconds, 1.5 L), followed by a 10-second breath-hold. To accomplish this maneuver, they sedated and paralyzed the patients during the treatment, making it impractical for routine therapy with an MDI. They found that these three drugs were equally effective in producing bronchodilation (Fig. 23), and concluded that ipratropium bromide and salbutamol administered by MDI were as effective as aminophylline administered intravenously.

In work done in our ICU,[100] my co-workers and I compared the use of SVN to MDI in 16 intubated

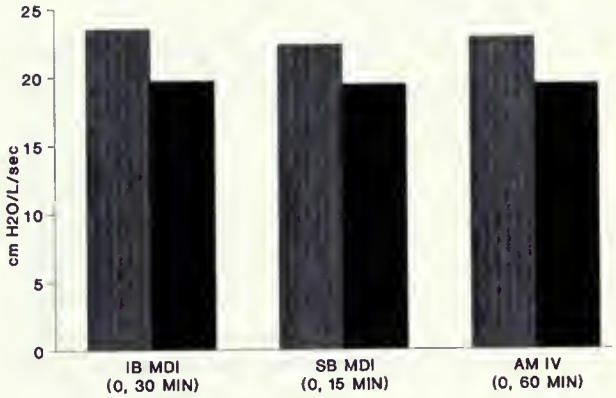


Fig. 23. Response (changes in expiratory resistance) to ipratroprium MDI, salbutamol MDI, and aminophylline I.V. in intubated mechanically ventilated patients (drawn from data in Reference 99.)

mechanically ventilated adult patients. We evaluated breath sounds, peak pressure, pause pressure, inspiratory resistance, expiratory resistance, and compliance before and after each treatment, as well as after a control evaluation in which no aerosol was administered. With the exception of expiratory resistance, the changes in measured variables were similar for MDI, SVN, and control. The mean decrease in expiratory resistance was 18% with MDI and 12% with SVN (Fig. 24). Breath sounds improved in 7 patients with MDI, 7 patients with SVN, and 2 patients with control. We used 4 puffs of MDI and an Instrumentation Industries MDI adapter placed between the Y-piece of the ventilator circuit and the ET tube. We used ventilator settings

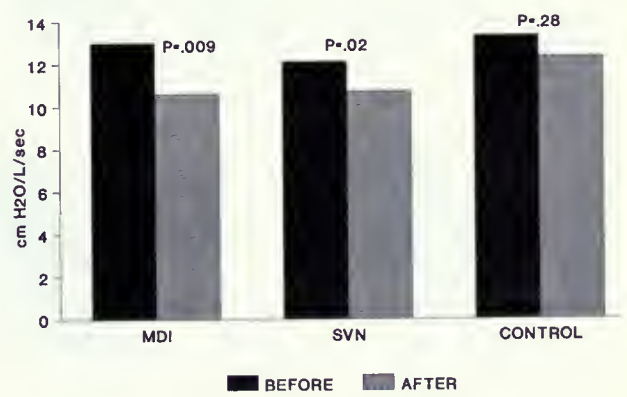


Fig. 24. Changes in expiratory resistance with MDI bronchodilator, SVN bronchodilator, and control (data from Reference 100).

of 12-15 mL/kg tidal volume, 25% inspiratory time, and 5% pause time.

Fuller et al[101] compared the delivery of labeled fenoterol by MDI and by SVN in mechanically ventilated patients and found significantly greater deposition by MDI (5.76% of the dose deposited in the lung) than by SVN (1.22% of the dose deposited in the lung). The nebulizer was powered during inspiration only, and placed 70 cm from the ET tube. For MDI delivery, the AeroVent adapter was used; inspiratory pause was not used, and no other ventilator-setting changes were made. The aerosol deposition that occurred with four puffs of MDI at 5-minute intervals is shown in Figure 25. In another study by Fuller et al,[102] it was found that there was no significant effect of ET tube vs tracheostomy tube in the percentage of MDI aerosol deposited in the lungs.

Taylor and Lerman[103] evaluated the delivery of MDI aerosols through pediatric ET tubes of 3.0-6.0 mm ID, using a bench model similar to that used by Crogan and Bishop.[97] Using an Intec MDI adapter, Taylor and Lerman actuated the MDI into a continuous gas flow of 60 L/min; and 2.5 ± 7.0% of the dose was deposited on a filter at the distal end of the 3.0-mm-ID ET tube, and 12.3 ± 8.4% of the dose was deposited on a filter at the distal end of the 6.0-mm-ID ET tube. There was no significant difference in the percentage of the dose deposited on the filter between the 4.0-mm, 5.0-mm, and 6.0-mm-ID tubes. In the same study, Taylor and Lerman evaluated the actuation of the MDI into a 19-gauge catheter placed through the ET tube so that its tip was positioned at the distal end of the ET tube. Using this configuration, 96.7 (4.3) % of the dose was delivered to the filter. Although the results of this bench study are intriguing, it is premature to recommend this method, particularly before appropriate clinical studies are conducted.

Gay et al[104] used a single-blind, randomized crossover design to compare the response to MDI albuterol (3 puffs) vs SVN albuterol (2.5 mg, 0.5 mL of a 0.5% solution in 3 mL of saline) in 20 adult intubated mechanically ventilated patients. The nebulizer was placed at the Y-piece of the ventilator. Each puff from the MDI was administered during a slow manual inflation, and the lungs were held at hyperinflation for several seconds. The MDI puffs were administered at 1-minute intervals. The brands of SVN and MDI adapter used were not reported. Passive expiratory flow was measured before and 30 minutes after each treatment. All of the patients had an increase in expiratory flow in response to at least one of the administration

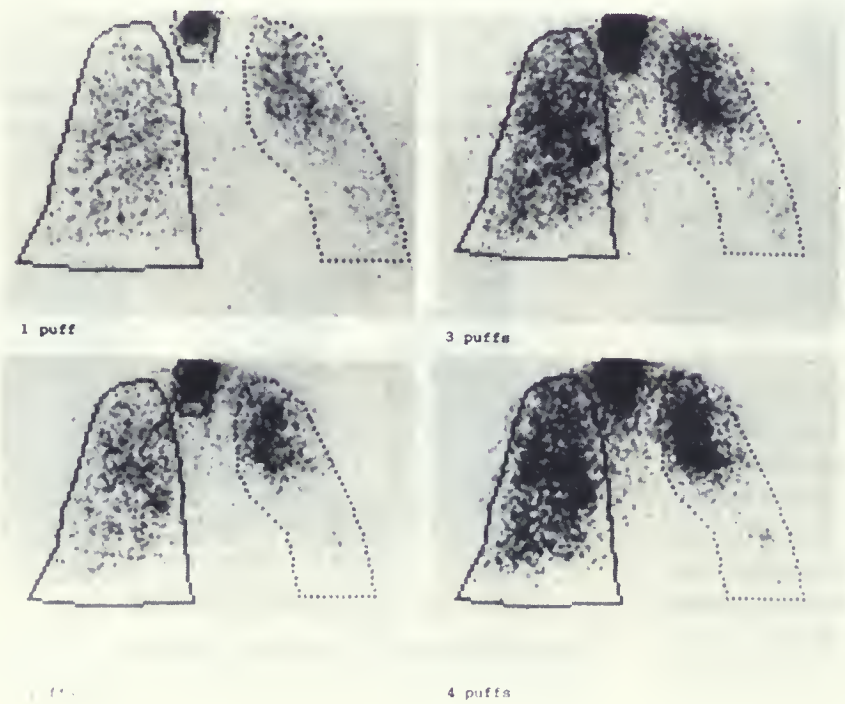


Fig. 25. Dose of bronchodilator deposited in the lungs of an intubated mechanically ventilated patient by four puffs from an MDI at 5-minute intervals. (Reprinted, with permission, from Reference 101.)

methods; 3 patients responded only to SVN, and 1 patient responded only to MDI. The mean time required to administer MDI was 5.8 min, vs 15.5 min with SVN. The data from this study persuasively suggest that MDI can be substituted for SVN in intubated mechanically ventilated patients. Unfortunately, the interrupter technique used in this study is original with the authors, making the importance of the results difficult to interpret, and also making it difficult for others to replicate the results.

From the above data, it can be concluded that a measurable amount of aerosol is delivered through the ET tube when an MDI is used, and the response of an intubated patient to bronchodilator delivered by MDI is similar to the response to bronchodilator delivered by SVN. I believe that MDI can be safely and effectively substituted for SVN in adult intubated mechanically ventilated patients. At my institution (York Hospital, York PA) all bronchodilators for intubated mechanically ventilated adult patients are administered by MDI. From the available deposition data, I think that it is reasonable to use a dose greater than the standard dose used in ambulatory patients; we usually use a dose of 4 puffs, with a 1-minute interval between each puff. In patients with refractory bronchospasm, I also think that it is reasonable to use higher dosages of bronchodilator by MDI, and we have done so on occasion in our ICU. Although I think it is reasonable to substitute MDI for SVN in mechanically ventilated adult patients, I do not think that there is enough information available to make this recommendation for infants and children.

Use of MDI during mechanical ventilation avoids the problems associated with SVN described above. Further, it takes about half as much time to deliver MDI compared to SVN. This decreases the cost of therapy (Table 2), and frees the respiratory care practitioner to perform other duties.

I believe that the available evidence supports the use of MDI in place of SVN in intubated adult patients. However, as I pointed out in an editorial in this journal,[105] several questions about this therapy remain unanswered:

- What are the best ventilator settings to use when delivering MDI therapy to intubated patients? Is there an ideal flow and tidal volume? In ambulatory patients, the MDI aerosol is delivered with the patient taking a slow, deep breath, followed by a breath-hold (for as long as 10 seconds). In mechanically ventilated patients, is this desirable or even possible?
- What is the appropriate number of puffs from the MDI for intubated patients? How is the appropriate dose determined? Should there be a standard dose, or is the dose patient-dependent? Are

Table 2. Cost Comparison of SVN to MDI at York Hospital, York, Pennsylvania (A 588-Bed Community Teaching Hospital, Referral Center, and Regional Trauma Center)

Cost of MDI therapy:	
Cost of 4 puffs MDI (cost of albuterol MDI = $5.57)	$ 0.12
Cost of 10 min of therapist's time to deliver 4 puffs (hourly cost of therapist = $13.50)	$ 2.25
Cost of MDI adapter per treatment (Instrumentation Industries disposable, $1.50, used for 10 treatments)	$ 0.15
TOTAL COST PER TREATMENT FOR MDI	$ 2.52
Cost of SVN therapy:	
Cost of 0.5 mL albuterol solution (cost of 20 mL 0.5% solution = $6.03)	$ 0.15
Cost of diluent	$ 0.07
Cost of 20 min of therapist's time to administer treatment (hourly cost of therapist = $13.50)	$ 4.50
Cost of SVN ($1.00, used for 10 treatments)	$ 0.10
TOTAL COST PER TREATMENT FOR SVN	$ 4.82
COST SAVINGS PER TREATMENT OF MDI OVER SVN	$ 2.30
Number of ventilated patients/year	800
Average ventilator days/patient	7
Percent ventilated patients receiving aerosolized bronchodilators	40%
Usual number of treatments/day/patient	5
Estimated total number of treatments/year	11,200
ESTIMATED ANNUAL COST SAVINGS BY USING MDI	$25,760

high doses of inhaled bronchodilators safe and effective in mechanically ventilated patients?[106]

- Where in the ventilator circuit should the MDI be placed?
- Are there differences between the penetration of available bronchodilators (eg, metaproterenol, albuterol) through an ET tube when delivered by MDI? In other words, do some aerosols adhere to the ET tube more than others?
- Is the amount of MDI-generated aerosol that penetrates the ET tube affected by the temperature and humidity of the carrier gas?
- Is there a role for MDI in mechanically ventilated pediatric patients?
- What is the appropriate amount of time to wait between actuations of the MDI? In ambulatory patients, it has been suggested that sequential inhalations might be superior to bolus administration.[107,108]
- Is there any clinical benefit to delivery of bronchodilators through a catheter passed through the ET tube (as described by Taylor and Lerman)?[103]

Final Comments

Inhaled beta-agonists are commonly used in intubated mechanically ventilated patients, even though such patients often have no history of lung disease. It has been my impression that many intubated patients receive aerosolized bronchodilators who would not receive the drugs if they were not intubated. Many patients benefit from this therapy, but many also do not. In a small group of patients, Gay et al[109] found that 10 of 13 mechanically ventilated patients showed a decrease in airway resistance in response to inhaled metaproterenol. Of these 10, 2 had no pulmonary history, and only 3 used bronchodilator medications prior to their acute illness. In ARDS patients, Wright and Bernard[110] found that airflow resistance was uniformly elevated, and averaged six times normal. Auler et al[111] have also noted an increased airway resistance in patients with ARDS. My impression is that aerosol bronchodilator therapy has been overused in mechanically ventilated patients, and certainly all intubated patients do not require it; however, this therapy may be useful in a surprising percentage of patients.

It is difficult to evaluate the response of intubated patients to aerosolized bronchodilators. Procedures to measure airway resistance have been described in the literature, but they are not easily used in everyday clinical practice.[112-121] Although spirometry is commonly used to evaluate bronchodilator response in ambulatory patients, this technique is not feasible in mechanically ventilated patients. Furthermore, the ET tube is a major site of resistance in intubated patients;[122] thus, the fixed resistance of the ET tube may mask changes in airway resistance in the lungs. Gay et al[109] have suggested that it may be useful to monitor changes in peak airway pressure and auto-PEEP in the evaluating of bronchodilator response in intubated patients. A number of current-generation mechanical ventilators provide measurements and calculations of lung mechanics that may be useful in evaluating bronchodilator response. However, it must be recognized that the measurement of lung mechanics provided by some of these ventilators has not been independently validated. It must also be recognized that the measurement of lung mechanics from the proximal airway assumes that the lungs are being passively inflated and deflated, which is not the case with spontaneous breathing modes such as SIMV and pressure-support, and may not always be the case with assisted ventilation (if the flow is set too low).

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What Should the Clinician Do When a Patient "Fights the Ventilator"?

Martin J Tobin MD

Introduction

The term "fighting the ventilator" is often used to describe the development of sudden respiratory distress in a ventilator-supported patient who had been stable for several hours before this event. The rhythm of the patient's spontaneous respiratory efforts is no longer in synchrony with that of the machine, and the patient appears to be 'bucking' the ventilator. This is a common and difficult emergency in the intensive care unit (ICU) setting, and it has several possible causes (Table 1). This article reviews the many causes of this problem and their management.

Table 1. Causes of Sudden Respiratory Distress in a Patient Receiving Mechanical Ventilation

Patient-Related Causes	Ventilator-Related Causes
Artifical airway problem	System leak
Pneumothorax	Circuit malfunction
Bronchospasm	Inadequate F_{IO_2}
Secretions	Inadequate ventilatory support
Pulmonary edema	Improper trigger sensitivity
Dynamic hyperinflation	Improper inspiratory flow setting
Abnormal respiratory drive	Patient-ventilator asynchrony
Alteration in body posture	
Drug-induced problems	
Abdominal distention	
Anxiety	
Patient-ventilator asynchrony	

Recognition of the Problem

Detection of change in a patient's symptoms can be very difficult because speech is usually prohibited by the presence of a tracheal tube. Sudden respiratory embarrassment usually results in the development of dyspnea, with or without chest pain, which in turn is usually manifested as anxiety or agitation in the ventilator-supported patient.[1] By asking directed questions or requesting a patient to provide a written description of his or her complaint, the attendant can derive a considerable amount of information regarding the nature of this and other symptoms. The major physical signs of respiratory distress are depicted in Figure 1.[2] These include tachypnea, diaphoresis, nasal flaring, recruitment of the accessory muscles (scalenes and sternomastoids), recession of the suprasternal/supraclavicular/intercostal spaces, rib cage-abdominal asynchrony and paradox, abnormal auscultatory findings, tachycardia, arrhythmias, and hypotension.[3,4] In addition, if mechanical ventilation is being delivered in an assisted (triggered) mode, the patient may be making obvious respiratory efforts without being able to trigger the ventilator.

In addition to symptoms and signs of respiratory distress, the practitioner may have access to a number of cardiorespiratory variables that are being monitored (Table 2).[5] Indeed, it is the goal of most monitoring devices to provide a warning about the likely development of a life-threatening disaster,

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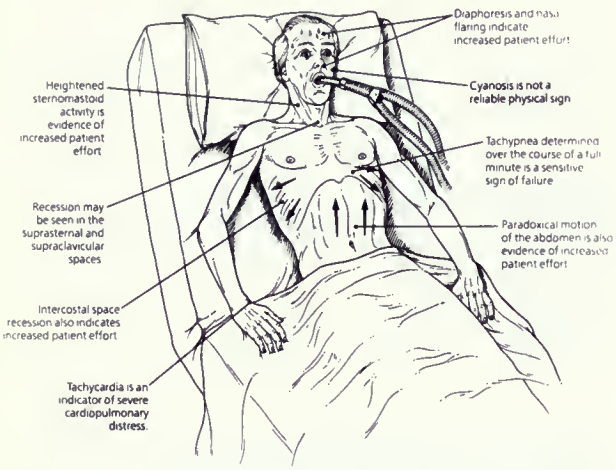

Fig. 1. Physical signs of severe respiratory distress. (Reproduced, with permission, from Reference 2.)

and, thus, provide an opportunity for the institution of life-saving measures. Arterial blood gases (ABGs) are a routine and indispensable part of intensive care, but are not without drawbacks.[5] There may be a considerable time lag between drawing an arterial sample and obtaining the results. Also, deterioration in ABGs may occur late in the evolution of acute respiratory failure. Pulse oximeters are far more accurate for detecting worsening oxygenation than is assessment of cyanosis. However, in patients with a high baseline arterial oxygen tension (P_{aO_2}), considerable deterioration in gas exchange may occur before a fall in the pulse oximetry readout is noted (due to the shape of the oxygen dissociation curve).[5] Another problem with pulse oximetry is its questionable accuracy in darkly pigmented patients.[6] Capnography or end-tidal carbon dioxide (P_{tcCO_2}) monitoring can be useful in detecting esophageal intubation (absent tracing) or sudden pulmonary embolism or air embolism (sudden fall in P_{tcCO_2}), but is usually inaccurate in providing a reflection of arterial CO_2 tension (P_{aCO_2}) in patients with underlying lung disease.[5] A sudden increase in respiratory rate is an extremely sensitive sign of respiratory embarrassment,[5-8] but further assessment is necessary to determine the precise cause of the disturbance. Detection of a fall in tidal volume is a valuable indicator of respiratory center depression or increased respiratory load,[5,8] but it is important to note that clinical estimation of tidal volume is notoriously unreliable.[9]

Asynchronous or paradoxic motion of the rib cage and abdomen indicates an increased respiratory load.[4,10] Thoracic compliance is easy to measure during mechanical ventilation, and it provides important information in the ventilator-supported patient who develops sudden distress.[5] The presence of auto-PEEP (positive end-expiratory pressure) should be checked[11] (Fig. 2). The contour of the airway pressure tracing provides important information regarding patient comfort and the appropriateness of the ventilator settings (Fig. 3). Electrocardiography, arterial pressure, and pulmonary artery pressure monitoring provide useful information regarding cardiovascular performance.

Table 2. Variables Used To Monitor the Respiratory and Cardiac Systems

Arterial blood gas values
Pulse oximetry values
End-tidal CO_2 values
Respiratory rate, tidal volume
Rib cage-abdominal motion
Thoracic compliance
Auto-PEEP level
Airway pressure tracing
Electrocardiogram
Arterial pressure
Pulmonary artery pressure

Fig. 2. Estimation of auto-PEEP by the occlusion technique. The expiratory port of the ventilator circuit is occluded at end-expiration (arrow), causing equilibration of pressure in the lungs and ventilation circuit. The pressure registered on the ventilator manometer provides an estimate of the level of auto-PEEP. (Reproduced, with permission, from Reference 12.)

General Principles of Management

The cardinal principle of management is to ensure the delivery of adequate ventilation to the patient.[1] This takes precedence over everything else, although at the same time one should begin to try

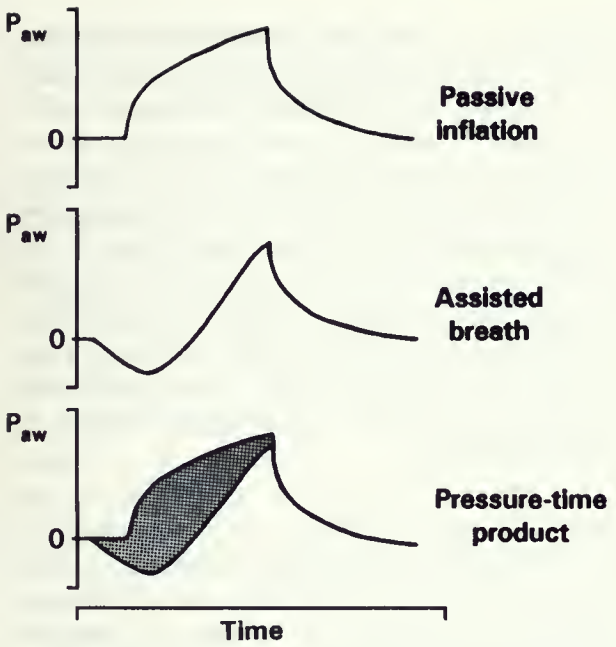

Fig. 3. Airway pressure (P_{aw}) tracings during controlled mechanical ventilation in a completely relaxed patient (top) and during an assisted breath (middle). The shaded area in the bottom tracing is the pressure-time product of the inspiratory muscles calculated as the difference in area subtended by the P_{aw}-time curve in the presence (middle) and absence (top) of inspiratory muscle activity. (Reproduced from Reference 12, with permission.)

to determine the underlying cause. The general principles of management are listed in Table 3. Once the patient has been disconnected from the ventilator, manual ventilation should be initiated with a self-inflating bag containing 100% oxygen. This is helpful both from a therapeutic and diagnostic standpoint. If the distress resolves, it indicates that the problem is due to the ventilator. If the distress continues, it indicates the presence of a patient-based problem. A rapid physical examination should be performed, and the physiologic indices being monitored should be assessed in an attempt to determine the cause of the respiratory distress. The patency of the patient's airway should be assessed, and passage of a suction catheter will help in determining the presence of a blocked airway or large quantities of secretions. If death appears imminent, one needs to consider and treat the most likely causes such as tension pneumothorax or airway obstruction, before undertaking further diagnostic studies. Once the patient has been stabilized, more detailed assessment and management can be undertaken.

Table 3. Steps To Be Taken in the Management of Sudden Distress in a Ventilator-Supported Patient

1. Remove the patient from the ventilator.
2. Initiate manual ventilation using a self-inflating bag containing 100% oxygen.
3. Perform a rapid physical examination and assess monitored indices.
4. Check patency of the airway and pass a suction catheter.
5. If death appears imminent, consider and treat most likely causes:
   —pneumothorax
   —airway obstruction.
6. Once the patient is stabilized, perform more detailed assessment and management.

Specific Causes of Sudden Respiratory Distress

Conditions that can cause sudden respiratory distress in a ventilator-supported patient are listed in Table 1. As mentioned earlier, the persistence or resolution of distress upon disconnecting the patient from the ventilator and the institution of manual ventilation with a self-inflating bag containing 100% oxygen is helpful in determining whether the underlying problem is patient- or ventilator-based.

Artificial Airway Problems

Problems with artificial airways are a particularly important source of trouble, and several factors may be responsible.

Migration of Tube into Main-Stem Bronchus. Main-stem bronchus intubation is estimated to occur in about 10% of ventilated patients.[13,14] This is usually due to inadequate external fixation of the endotracheal tube and/or excessive neck movement.[1,15] In a study of adult patients with ventilatory failure, Conrardy et al[15] found that neck flexion caused an endotracheal tube to move an average of 1.9 cm (range 0-3.1 cm) towards the carina (Fig. 4). The distance moved was similar with the cuff inflated or deflated and with oral or nasal tubes. Main-stem intubations apparently occur more often in women than in men, possibly because of the shorter anatomic distance between the lips and the

carina in women.[14] Main-stem intubation occurs more often on the right side probably because the right main-stem bronchus forms a less acute angle with the trachea than does the left main-stem bronchus. The lack of ventilation to the contralateral lung results in atelectasis, which, in turn, leads to shunting of blood and hypoxemia. Although breath sounds are typically reduced over the atelectatic lung, this is a very unreliable sign; in a recent prospective study, breath sounds were equal over both lung fields in 60% of patients with main-stem bronchial intubations.[14] The delivery of a high volume to the intubated lung may produce a pneumothorax.[1]

If main-stem bronchial intubation is suspected, the endotracheal tube should be pulled back a few centimeters, the chest should be re-auscultated, and the position of the tube confirmed by x-ray. The problem can be prevented by securing the tip of the tube at least 3-4 cm from the carina and obtaining an x-ray at the time of intubation.[15] The presence of centimeter markings on an endotracheal tube to reference the tube position is also helpful, although not completely reliable.[14] In general, an endotracheal tube should be secured at the 23-cm reference mark in men and at the 21-cm mark in women.[14]

Migration of Tube above Vocal Cords. Migration of an endotracheal tube above the vocal cords can result in sudden distress accompanied by a decrease in tidal volume and in the ability to phonate, and the escape of air through the nose and mouth. As in the case of endobronchial intubation, this is usually due to inadequate tube fixation and/or excessive neck movement. In the study by Conrardy et al,[15] neck extension caused an endotracheal tube to move an average of 1.9 cm away from the carina, but movement was as much as 5.2 cm in some patients. Migration of the tube above the cords can be prevented by securing the tube with the tip 3-4 cm from the cords and carina (ie, midway between) and by obtaining an x-ray following intubation to verify tube position.

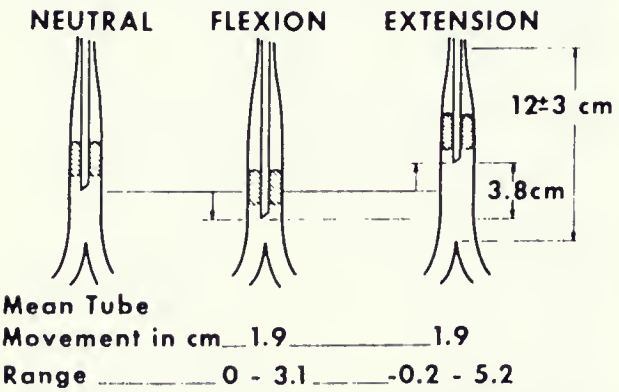

Fig. 4. The mean and range of endotracheal tube movement with flexion and extension of the neck from a neutral position. The mean distance between the position on flexion and extension (3.8 cm) is about one third of the length of the normal adult trachea (12 cm). (Reproduced, with permission, from Reference 15.)

Cuff Herniation. Occlusion of a tracheal tube may result from herniation of the cuff over the end of the tube. This most commonly occurs following changes in the posture of the head and neck or changes in position of the tube. It may result in a decrease in tidal volume, an increase in airway pressure, an increased resistance during manual ventilation, difficulty in passing a suction catheter, and the presence of an abnormal musical sound during inspiration.[1] Relief is immediately achieved by deflating the cuff. If the source of airway obstruction is unclear and the patient is stable, the diagnosis can be confirmed by bronchoscopy.

Cuff Rupture. Manifestations of cuff rupture include a decrease in delivered tidal volume; an inability to maintain the set level of PEEP; aspiration of saliva, vomitus, or food; and the failure to withdraw the same volume of air that was used to inflate the cuff. Management consists of replacing the tube.

Endotracheal Tube Kinking. This is a relatively uncommon complication, and is associated with changes in the position of the head and neck, and the use of soft rubber nasotracheal tubes. Slight manipulation of the head, neck, or tube will commonly correct the problem.

Tracheoesophageal Fistula. This rare complication is primarily due to ischemia of the tracheal wall secondary to pressure of the tube or an overinflated cuff.[16] Patients with this complication typically have had both a tracheal tube and a nas-

ogastric tube in place for a long time.[1] The inability to deliver a preset tidal volume despite a functional cuff is a characteristic finding in this setting.

Innominate Artery Rupture. Rupture of the innominate artery may occur at some point during the first 3 weeks after a tracheotomy.[17] It has an extremely high mortality, 93% in a recent series.[18] Factors that are important in causing this complication include: (1) placing the tracheotomy incision too low (below the third tracheal ring), with the result that the inferior concave surface of the cannula erodes into the artery; (2) use of an excessively long tracheal tube, with the result that the tip erodes the tracheal wall and the vessel deep to it; (3) pressure erosion by an inflated cuff; and (4) infection of the tracheal wall.[17] The clinical presentation may be quite dramatic, with blood gushing from the tracheal tube, or it may be heralded by a "sentinel bleed." If this sign is recognized, the cuff should be overinflated in an attempt to achieve tamponade. Manual compression of the artery should be attempted: A finger should be inserted into the stoma, passed as far as possible towards the carina, and then pulled forward in an attempt to compress the artery against the posterior surface of the sternum.[1,17] If this is successful, a blood transfusion should be administered while the patient is being transported to the operating room for definitive surgery.

Pneumothorax

Development of a pneumothorax is a key complication to consider in a ventilator-supported patient who develops sudden respiratory distress, especially since 60-90% of pneumothoraces in ventilator-supported patients are reported to be under tension.[19] A full discussion of this topic is beyond the scope of this article, and the reader is referred elsewhere.[20,21] In brief, excessive alveolar distending volume causing rupture of an alveolus appears to be the initiating factor.[21] Gas tracks along the bronchovascular sheath, producing features of interstitial emphysema, and, rarely, it may enter the pulmonary circulation to produce systemic air embolism.[20] More commonly, it enters the mediastinum, the peritoneal cavity, or the subcutaneous tissue.[20] If the pleura is ruptured, a pneumothorax results.[20] While peak airway pressure is not directly responsible, it can be easily measured, and it appears to be a useful indicator of the risk of a pneumothorax. In a recent study, no patient whose peak airway pressure was less than 60 cm H_2O developed barotrauma, whereas it occurred in 43% of those with pressures greater than 70 cm H_2O.[22] Particularly vulnerable patient subgroups are those with adult respiratory distress syndrome (ARDS), chronic obstructive pulmonary disease (COPD), or necrotizing pneumonia.

Clinical manifestations include respiratory distress, hyperresonance, decreased breath sounds, tracheal deviation to the contralateral side, a decrease in thoracic compliance (both static and 'dynamic') (Table 4), and cardiovascular collapse.

If a pneumothorax is suspected and death is imminent, a 14- to 16-gauge needle attached to a liquid-filled syringe should be inserted into the second intercostal space. If the patient is stable, however, a chest x-ray should first be performed to verify the diagnosis before inserting a chest tube.

Table 4. Patterns of Alteration in Thoracic Pressure-Volume Relationships

	Case 1		Case 2	
	1 hr ago	Now	1 hr ago	Now
Tidal volume, mL	600	600	600	600
Plateau pressure, cm H_2O	10	10	10	30
Peak pressure, cm H_2O	20	40	20	40
Static compliance (mL/cm H_2O)	60	60	60	20
"Dynamic compliance" (mL/cm H_2O)	30	15	30	15

Interpretation: In Case 1, because plateau pressure is unchanged, suspect an airway problem. In Case 2, because plateau pressure is increased and there is no increase in the gradient between peak and plateau pressures, suspect a pneumothorax, main-stem intubation, or atelectasis.

Bronchospasm

Bronchospasm is a common cause of sudden respiratory distress. It results in dyspnea, wheezes, and evidence of increased work of breathing (such as heightened activity of the accessory muscles, rib cage-abdominal discoordination, recession of the

suprasternal/supraclavicular/intercostal spaces, and pulsus paradoxus. Peak airway pressure will be increased resulting in a decrease in so-called dynamic compliance,[5] while static compliance shows little or no change (Table 4). Management consists of the administration of inhaled bronchodilator agents, which may need to be supplemented by parenteral corticosteroids and/or theophylline.[23]

Secretions

Secretions may cause problems by being too dry or by being too copious in amount. Because a tracheal tube bypasses the upper airway, which normally heats and humidifies inspired gas, secretions may become excessively dry and encrusted, and result in significant blockage of the tracheal tube over a relatively short period of time. This problem should be suspected if difficulty is experienced during passage of a suction catheter. The problem can be avoided by ensuring that gas being delivered is 100% humidified at body temperature. Excessive secretions can lead to mucus plugging and atelectasis. To avoid this problem, careful bronchial toilet and frequent suctioning are necessary in patients with copious secretions. If atelectasis occurs and fails to resolve with conservative measures, bronchoscopy should be undertaken.

Pulmonary Edema

Pulmonary edema is an important cause of sudden distress, and the reader is referred elsewhere for reviews of this common condition.[23,24] Cardiac and non-cardiac causes need to be considered, and if the distinction is difficult to make, passage of a pulmonary artery catheter may be necessary.

Acute Pulmonary Embolism

Acute pulmonary embolism is an uncommon but important cause of respiratory distress. Typical clinical manifestations include dyspnea, tachypnea, chest pain, fever, hemoptysis, pleural rub, and features of deep vein thrombosis.[23,25] The presence of a normal thoracic compliance (60-100 mL/cm H_2O) in a hypoxemic patient with sudden respiratory distress is an important diagnostic clue. However, clinical manifestations are neither sensitive nor specific, and > 50% of suspected cases do not have the diagnosis confirmed on angiography. Diagnostic tests include ventilation-perfusion scan, angiography, and impedance plethysmography (to detect venous thrombosis). Therapy usually consists of heparin followed by warfarin. Occasionally, thrombolytic therapy or venous interruption procedures may be undertaken, and rarely, an acute embolectomy is performed.[23]

Dynamic Hyperinflation

In normal subjects, the lung volume at end-expiration generally approximates the relaxation volume of the respiratory system (ie, the lung volume determined by the static balance between the opposing elastic recoil of the lung and chest wall).[26] In some critically ill patients, however, the end-expiratory volume may no longer be determined by an equilibrium between static forces, and, instead, end-expiratory lung volume may exceed predicted functional residual capacity (FRC).[27] Such hyperinflation may arise in patients with airflow limitation as a result of dynamic airway collapse (air trapping). Hyperinflation can also arise in patients without airflow limitation if there is inadequate time available during expiration for the pressure in the alveoli to come to equilibrium with the effective downstream pressure. This condition most commonly occurs when respiratory frequency and/or tidal volume are relatively high for the resistance or compliance (ie, time constant) properties of the respiratory system.[28]

The static recoil pressure of the respiratory system is normally zero at end-expiration, whereas a positive value is observed in patients with dynamic hyperinflation.[11,27] This positive recoil pressure has been termed auto-PEEP or intrinsic-PEEP.[11,29] In patients receiving mechanical ventilation, it has been termed occult PEEP, because, unlike externally applied PEEP, it is not registered on the ventilator pressure manometer because the latter is open to atmosphere. If, however, the expiratory port of the ventilator circuit is occluded immediately before the onset of the next breath, the pressure in the lungs and ventilator circuit will equilibrate and the level of auto-PEEP will be displayed on the ventilator manometer (Fig. 2).[11]

The presence of auto-PEEP has several important implications for patients receiving mechanical ventilation. It predisposes to barotrauma and hemodynamic embarrassment,[11] it increases the work of breathing,[30] and decreases the efficiency of force generation by the respiratory muscles.[30] The presence of auto-PEEP poses a significant inspiratory threshold load if a patient is breathing spontaneously because a negative pressure equal in magnitude to the opposing elastic recoil pressure (ie, level of auto-PEEP) will need to be generated to initiate inspiratory airflow. Likewise, if a patient with auto-PEEP is triggering a mechanical ventilator, he or she will need to generate a negative pressure equal in magnitude to the level of auto-PEEP in addition to the set minimum circuit-pressure drop before a ventilator-assisted breath is initiated. This is one of the factors that may account for the not infrequent observation of a patient who is unable to trigger a ventilator despite obvious respiratory effort.[31]

Therapeutic measures to decrease the amount of auto-PEEP include implementing bronchodilator therapy, employing a large-bore endotracheal tube, decreasing the minute ventilation by controlling fever or pain, and minimizing the ratio of inspiratory time to expiratory time by increasing inspiratory flowrate or using nondistensible tubing in the ventilator circuit.[32] External PEEP has been recently advocated as a means of decreasing work of breathing in patients with auto-PEEP.[28,29,33-35] In the patient with auto-PEEP who has difficulty in triggering the ventilator, the addition of external PEEP can be helpful because to trigger the ventilator, alveolar pressure needs to be decreased only below the level of alveolar pressure rather than below zero. This may seem paradoxical: External PEEP, which is commonly used to induce hyperinflation in patients with microatelectasis, is being used to decrease the work of breathing induced by hyperinflation consequent to auto-PEEP. We recently used the analogy of waterfall to explain this paradox.[28] The height of the waterfall represents the critical closing pressure of airways in patients with auto-PEEP and COPD (Fig. 5). Thus, elevating downstream pressure, such as with external PEEP, has no influence on either expiratory airflow or the pressure upstream (auto-PEEP) from the site of critical closure (upper panel, Fig. 5). This situation exists up until downstream pressure is elevated to a value equal to the critical closing pressure (middle panel, Fig. 5). However, once downstream pressure is elevated above the critical closing pressure (height of the waterfall), the pressure upstream increases immediately and hyperinflation is exacerbated (lower panel).

Abnormalities in Respiratory Drive

Increases or decreases in respiratory center output may lead to sudden deterioration in respiratory status.

Inadequate Respiratory Output. An inadequate respiratory neuromuscular output results in hypoventilation with consequent hypercapnia and/or hypoxemia. Respiratory drive may be decreased as a result of heavy sedation, acute neurologic disorders, or neuromuscular blocking agents.[23] Although drive per se may not be decreased, it may

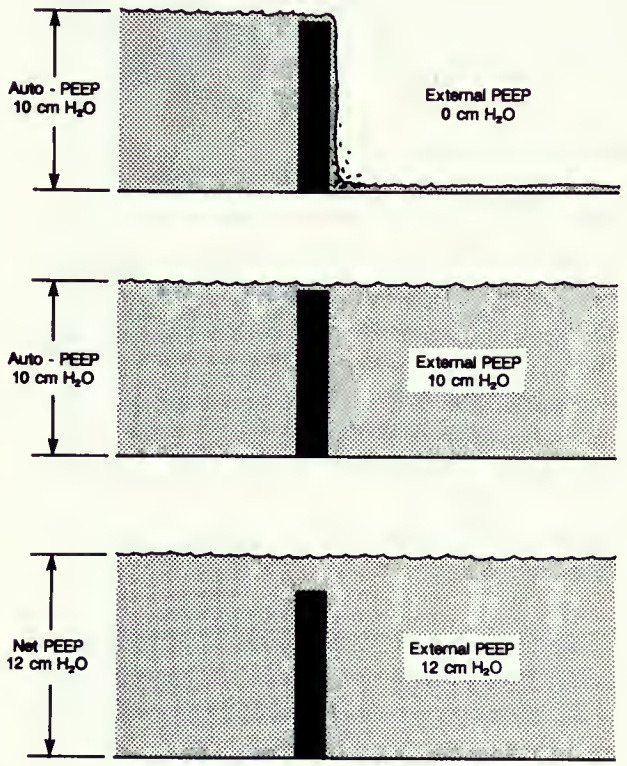

Fig. 5. The analogy of a waterfall over a dam (indicated by the solid block) is used to explain the effect of external PEEP ("upstream pressure") during expiration. (Reproduced, with permission, from Reference 28.)

be inadequate to maintain a satisfactory level of minute ventilation if there is a sudden increase in ventilatory demands or in mechanical load. Development of respiratory muscle fatigue may also affect respiratory drive, but the nature of the alteration in respiratory center response to fatigue is poorly understood.[36]

Elevated Respiratory Output. An increased respiratory drive may result from pain, anxiety, hypoxic stimulation, hypercapnic stimulation, peripheral sensory-receptor stimulation, medications, increased ventilatory demands, or improper ventilatory settings. Severe respiratory alkalosis can cause arrhythmias, hypotension, cerebral vasoconstriction, and seizures.[37]

Alteration in Body Posture

An alteration in body posture can cause significant hypoxemia, a fall in P_{aCO_2} of as much as 30%,[38] especially in patients with unilateral lung disease. This is secondary to the effect of gravity on blood flow, as blood is shunted through the diseased dependent lung.

Drug-Induced Distress

Agitation or seizures may result from use of theophylline. Aminoglycoside antibiotics can provoke or aggravate neuromuscular blockade, and produce respiratory embarrassment. Hypoxemia may result from worsening of ventilation-perfusion relationships secondary to bronchodilators or vasodilators (nitroglycerine, nitroprusside). Administration of intravenous lipid compounds can also produce hypoxemia.[38]

Abdominal Distention

Abdominal distention may produce elevation of the diaphragm, basilar atelectasis, and deterioration in ventilation-perfusion relationships. Abdominal distention may result from gastric distention, ascites, peritoneal dialysis, or bowel perforation. Gastric distention may result from: (1) elevation of mouth pressure above lower esophageal sphincter pressure during the delivery of manual ventilation; (2) elevation of tracheal pressure above cuff and lower esophageal sphincter pressure, during mechanical ventilation (with mouth closed); or (3) a prolonged or difficult attempt at intubation.[21,39,40] Massive distention (ie, meteorism) can produce gastric rupture.[21] Insertion of a small-bore nasogastric tube helps in preventing or alleviating this complication.

Ventilator-Related Problems

If manual ventilation with an anesthesia bag containing 100% oxygen relieves the respiratory distress, this suggests that the problem is ventilator related (Table 1).

Leak in the System. Malfunction of the ventilator may result from connection of tubing to the wrong outlet, uncoupling of connections, a poor fit of connections, defective material, or obstruction of the circuit due to kinks, intraluminal fluid, or a malfunctioning valve. If a leak is suspected, the ventilator should be replaced while each component of the defective ventilator is checked against the schematic circuit diagram.

Inadequate F_{IO_2}. If delivered tidal volume is adequate and distress is relieved by manual ventilation, a fault in the F_{IO_2} setting should be suspected. This can be verified by obtaining an independent direct measurement of F_{IO_2}.

Inadequate Ventilator Support. The optimal amount of ventilator support in a patient requiring prolonged mechanical ventilation is unknown. Too much support may produce disuse atrophy and weakness of the respiratory muscles (Fig. 6),[42] whereas insufficient support predisposes to respiratory muscle fatigue and may produce or aggravate respiratory distress.[43] It has been suggested that patients with respiratory disease may suffer from chronic fatigue of the respiratory muscles,[44] which could be reversed by rest therapy. However, recent studies of respiratory muscle rest using negative-pressure ventilation have yielded no improvement in respiratory performance,[45] suggesting that chronic fatigue of the respiratory muscles does not exist. On the other hand, if partial ventilator sup-

port is being provided in an insufficient amount, it may lead to the development of acute respiratory muscle fatigue and distress.

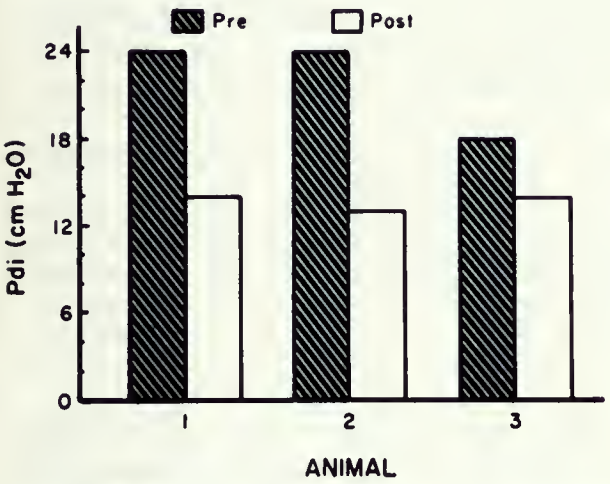

Fig. 6. Respiratory muscle strength, as reflected by the maximal transdiaphragmatic pressure ($P_{di\ max}$) response to bilateral phrenic nerve stimulation at 100 Hz, in 3 baboons before and after 11 days of controlled mechanical ventilation. Strength decreased by an average of 46% over the period of mechanical ventilation. (Reproduced, with permission, from Reference 41.)

Two major forms of partial ventilator support exist: intermittent mandatory ventilation (IMV) and pressure-support ventilation (PSV).[46] During IMV, the patient is able to breathe spontaneously between a preset number of mechanically delivered breaths. A demand valve is commonly used to facilitate spontaneous breathing, and several investigators have shown that such a system leads to a two-fold or greater increase in work of breathing.[46] During the breaths being delivered by the ventilator, it is thought that the respiratory muscles are being rested. However, a dyspneic patient may not be able to respond to such intermittent unloading, and studies have shown that a patient's work of breathing during a machine breath is about 80% of the value during an unassisted breath.[47] Indeed, critically ill patients who are receiving no more than 60% of total ventilatory support by IMV display a breathing pattern and swings in transdiaphragmatic pressure that are in the fatigue range.[47]

Pressure-support ventilation is triggered by the patient (or by a time lapse backup in some systems) and continues until the patient's inspiratory flow decreases to a system-specific minimal level (usually 5 L/min or 25% of peak inspiratory flow), at which time exhalation ensues. Some physicians believe that patients find PSV to be more comfortable than they do conventional ventilatory modes because they can control the depth, length, and flow profile of each breath.[48] Problems with PSV include the fact that every breath has to be triggered by the patient (unless the ventilator is equipped with a backup mode), and thus it is unreliable if the patient has an unstable respiratory drive. Delivered tidal volume will decrease if patient effort decreases or lung mechanics deteriorate. Other problems with PSV are beginning to unfold. In the presence of a cuff leak, the flowrate of the leak may exceed the inspiratory flowrate that normally terminates PSV. Consequently, PSV will be maintained throughout the respiratory cycle, which is similar to applying a high level of CPAP.[49] A problem may also arise in patients who are receiving in-line continuous nebulizers, in that the flowrate of the nebulizer may exceed the patient's mean inspiratory flow, and, thus, the negative pressure necessary to trigger PSV cannot be generated.[50] In this situation, the low-minute-ventilation alarm may also fail because the ventilator monitoring system falsely interprets the nebulizer flow as coming from the patient.

Improper Trigger Sensitivity Setting. During assist-control ventilation, IMV or PSV, delivery of an assisted mechanical breath is triggered by the patient's inspiratory effort. Fine-tuning the sensitivity of the trigger setting is imperative because the ventilator may autocycle if it is too sensitive and very large negative pressures may be required if it is not sensitive enough. For example, decreasing the trigger sensitivity from –2- to –5-cm H_2O has been shown to increase the active component of respiratory work by 34%.[51] Manufacturers measure the ventilator response time as the time from attainment of the required triggering pressure drop until the commencement of ventilator gas flow. In reality, it would be more meaningful if it were related to the onset of respiratory muscle contraction. Factors that may produce a significant lag time between the onset of respiratory muscle contraction and the commencement of ventilator gas flow in-

clude paradoxic motion of the rib cage and abdomen, the presence of auto-PEEP, tubing compliance and dead space, transducer variability, and the presence of a high bias flow within the circuit.[31]

Improper Inspiratory Flow Setting. If the flow setting of the ventilator is inadequate to meet the flow demands of the patient, he or she will pull both against his or her own pulmonary resistance and compliance and against the resistance of the ventilator circuit, leading to a marked increase in respiratory work.[51,52] The likelihood of high levels of active respiratory work is increased in patients with heightened respiratory drive and high minute ventilation.[51]

Patient-Ventilator Asynchrony

Fighting the ventilator may be due to any of the patient-related and ventilator-related causes listed in Table 1 and described previously. In addition, it may reflect asynchrony of the patient's spontaneous ventilatory pattern and that of the ventilator. If the latter is suspected, the practitioner should vary (one setting at a time) the trigger sensitivity, inspiratory flow, delivered tidal volume, the mode of mechanical ventilation, and should even consider the use of external PEEP (to minimize the effect of auto-PEEP). After each modification, the patient should be questioned as to whether the level of comfort has increased. At the bedside, inspection of a pressure-time curve allows the physician to assess the amount of active work being performed by a patient during assisted breathing (Fig. 3).

If the muscles are inactive, the pressure-time curves have a smooth rise, remain positive throughout the breath, and are highly reproducible from breath to breath.[52] If the muscles are contracting actively, such as with an improper trigger sensitivity or inspiratory flow setting, the curves will vary from breath to breath, their contour will be scooped, and negative values may persist throughout a large portion of the breath. Thus, efforts should be made to achieve a more relaxed airway pressure pattern.

Once medical and mechanical problems have been excluded and the patient continues to show distress despite modifications in the ventilator settings, a sedative agent with or without a neuromuscular blocking agent can be administered (Table 5). These should only be given as a last resort because of the dangers associated with neuromuscular blockade: masking of the patient's complaints and physical findings, and the absence of spontaneous ventilation (if accidental disconnection of the ventilator circuit should occur).

Table 5. Pharmacologic Agents Used To Produce Sedation and Neuromuscular Blockade

Diazepam:	2-5 mg I.V. every 5 min to a max of 20-30 mg
Morphine:	2-5 mg I.V. every 5 min to a max of 20-30 mg
Succinylcholine:	0.6-1.0 mg/kg (2-10 min duration)
Pancuronium:	0.06-0.1 mg/kg (1-2 hr duration)

In summary, sudden distress in a ventilator-supported patient is a true medical emergency. The first rule is to ensure adequate ventilation. The patient should be disconnected from the ventilator and manually ventilated with 100% oxygen. While this is being performed, a systematic effort should be made to try to determine the cause of the distress and correct it.

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Weaning from Mechanical Ventilation: Does Technique Make a Difference?

Philip G Boysen MD

Introduction

When I was asked to review the topic of weaning from mechanical ventilation for this symposium, the request was for a perspective on and a balanced coverage of the subject. In addition, it was suggested that because I had "lived through it all," my analysis and expression of opinions would be appropriate. To achieve balance, my first thought was to review the figures and slides I had used over the years. However, it became obvious that this was the wrong approach because the presentations frequently had revolved around a technique being proposed as *the way* to wean patients from mechanical ventilation. My next step was more reflective. When I reviewed my personal files on the subject, I discovered a number of articles that have been instrumental in formulating my approach to patient care. I took this file in its native state, and neither added articles to 'beef it up,' nor accounted for others that may have been loaned and never returned. I reasoned that an important article would have been missed, prompting its return to the folder by retrieving or recopying.

Background

Figure 1 is a numerical and chronological summary of the weaning papers in my reprint file. Two elements are striking. A notable increase in activity occurred in the late 1970s following the publication of the weaning technique using intermittent mandatory ventilation (IMV). Interestingly, IMV was proposed more as a useful ventilatory technique than as a pure weaning mechanism. Regardless of how it was perceived, clinicians rapidly divided into two vocal and disparate camps. Either you were for IMV and against volume-assist (or so-called assist-control) or you adhered to the opposite philosophy and technique.

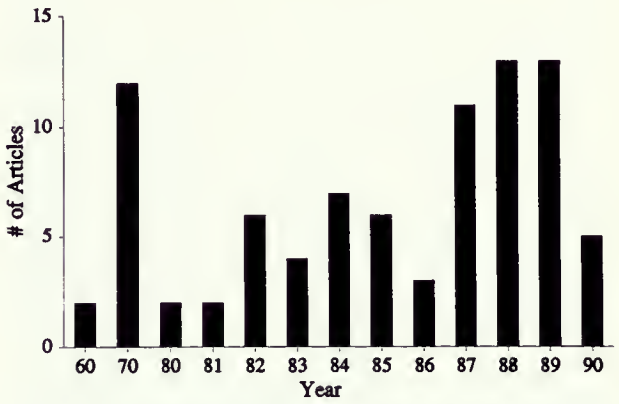

Fig. 1. The frequency distribution of articles on weaning from mechanical ventilation collected in the author's personal file.

In retrospect, it is apparent that the development of IMV was an important milestone because it refocused our attention on the spontaneously breathing patient and forced us to re-examine the characteristics of the modes of ventilation available to us. The technique was carefully defined as a means of allowing "unrestricted yet unassisted" breathing in addition to a designated number of mechanical breaths of a specific tidal volume.[1] It became apparent that few ventilators were available that would not impose a ventilatory work load on the patient because of inspiratory flow resistance[2]—

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a problem that should have been obvious and anticipated. (The volume-assist mode had actually been developed as a compromise. Rather than completely controlling a patient's ventilation, it allowed patient-machine interaction.) Fortunately, the impetus to examine the patient-ventilator interaction and to assess patient work effort extended from IMV to assist-control, and we were able to learn more about this technique and dispel ongoing myths.[3]

Therefore, the early 1980s were a time of examining techniques and options open to us as we designed therapeutic regimens and learned how the patient interacted with life-support equipment. In 1987 in the proceedings of the RESPIRATORY CARE Journal Conference, I reviewed weaning in the context of respiratory muscle work.[4] Since that time, some unanswered questions have been studied—in particular, the assessment of breathing patterns and how to identify patients who will fail to wean.[5-9] Thus, we have come full circle, and recent interest clearly focuses on the patient, his underlying and superimposed disease states, and the means we have of maintaining support.

Early therapeutic considerations were for patients who experienced neuromuscular respiratory failure, especially as a consequence of contracting poliomyelitis during the early 1950s. The inability of those patients to activate the thoracic pump and effect bulk flow of gas to and from the lungs was overcome by negative-pressure ventilation. Not only was ventilation with iron lungs physiologic in approach, but also consistent with prevailing practice. Through most of the 1950s, ether was the volatile gas most frequently employed during anesthetic management. Unlike today's volatile agents that cause cardiorespiratory depression, ether was an anesthetic agent that stimulated central drive to respiration and supported cardiovascular function. For this reason, it was safely administered through an ether mask (open-drop method) during spontaneous breathing with a native airway (ie, without intubation). Concomitant with development of newer anesthetic agents and the ability to intubate the trachea and support ventilation with positive-pressure breathing came the development and use of neuromuscular blockers to improve relaxation during surgery. Airway control via the endotracheal tube and positive-pressure ventilation became commonplace in intensive care units because these measures had been instituted at the time of surgery. Postoperative positive pressure ventilation has been provided for many reasons, not the least of which is the anticipation that volatile anesthetics, narcotics, preoperative sedative medication, or residual neuromuscular blockade may necessitate mechanical ventilatory support because of depression of central drive or alteration of neuromuscular physiology (ie, an iatrogenic neuromuscular respiratory failure).[10] For this reason, appreciation of the early development of criteria for weaning is still pertinent to today's practice.

An understanding of neuromuscular respiratory failure can be developed from an anatomic viewpoint. Beginning with intracerebral and brainstem function, one can trace transmission of impulses down the spinal cord to anterior horn cells, peripheral nerves, the neuromuscular junction, and the respiratory muscles. Interference with physiologic function at any of these anatomic sites may result in neuromuscular respiratory failure.

Early Tests of Weanability

Early investigators relied on tests of weanability that required activation of the respiratory muscles (including muscles of the upper airway).[5-9] Their assessment included observations of the patient's ability to sustain head lift in the supine position, to generate appropriate negative pressure against an occluded airway, and to demonstrate an adequate vital capacity and the absence of need for excessive minute ventilation ($\dot{V}_E$). Although the range of values that might constitute limitation varied among investigators, the reliability of the tests has always been substantiated—particularly, the progression toward respiratory failure and the return of function were well-defined.

Weaning by Criteria

The practice patterns for weaning a patient by criteria developed in two directions.[11] For the patient with an acute episode of respiratory failure and no underlying lung disease, mechanical ventilation was abruptly discontinued, with return to a native airway as soon as feasible. Complicating factors (such as age, underlying lung disease, or prolonged mechan-

ical ventilation) prompted a more cautious approach. In general, this has been referred to as gradual T-tube weaning—periods of spontaneous breathing alternating with periods of mechanical ventilation.[12]

Although well-established in clinical practice, such weaning protocols have been empirical and with varying endpoints. The techniques have recently been reviewed.[13] More sophisticated analyses of respiratory rates and breathing patterns indicate that tachypnea, dyspnea, dysfunctional breathing patterns (eg, abdominal paradox) indicate a failed weaning attempt. Arterial oxygen desaturation and carbon dioxide retention may or may not accompany the trial, but presumably would inevitably occur if the patient were allowed to continue spontaneous breathing. Evidence suggests that for some patients, inspiratory muscle resistive training may enhance the weaning process.[14] Ventilation-perfusion mismatch may worsen during the trial, but the resultant hypoxemia may be minimized by concomitant increases in cardiac output.[15] Other patients may fail to wean because of left-ventricular dysfunction and decreased cardiac output.[16]

Recent Methods of Predicting Weanability

Airway Occlusion Pressure

Recent attempts to define respiratory drive during the weaning process have involved measurement of airway occlusion pressure, the airway pressure generated against an occluded airway at 0.1 second into inspiration ($P_{0.1}$). In normal subjects, $P_{0.1}$ is usually less than 2 cm H_2O. Herrera and co-workers[17] reported that a $P_{0.1} > 4.2$ cm H_2O is associated with weaning failure 89% of the time. Sassoon et al[18] reported weaning failure in every case in which the $P_{0.1}$ exceeded 6 cm H_2O. Conversely, Montgomery and colleagues[19] found no significant differences in the $P_{0.1}$ among those who weaned and those who did not. Furthermore, the stimulation of increased carbon dioxide in rebreathed gas did not significantly alter the $P_{0.1}$ between the two groups, but the ratio between the CO_2-stimulated $P_{0.1}$ and the baseline $P_{0.1}$ did appear to discriminate between the two groups (Fig. 2).

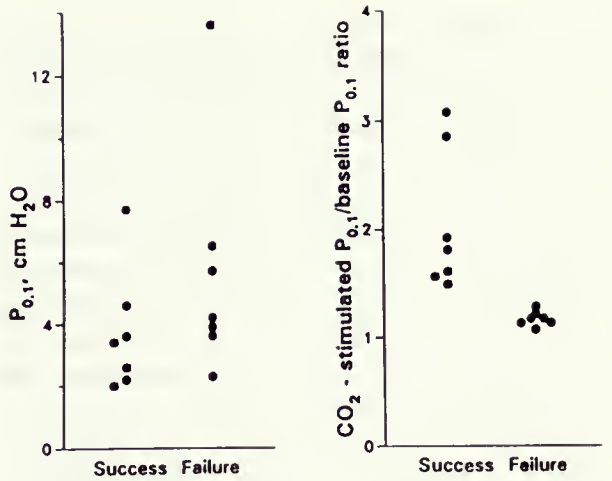

Fig. 2. The airway occlusion pressure ($P_{0.1}$) in patients being weaned from mechanical ventilation showing overlap between success and failure (left) and improved discrimination following remeasurement after CO_2 stimulation. (Reprinted, with permission, from Reference 18).

Further investigation is essential to define the applicability of this test.

It is particularly important to consider the effect of medication on the central respiratory drive of patients who may be already compromised. As an example, the combination of subanesthetic doses of volatile anesthetic agents and small doses of narcotics may depress ventilation to the point of alteration of response to CO_2 and lead to an elevated resting arterial carbon dioxide tension. Weaning trials should be undertaken only when such drugs are required infrequently or have been eliminated altogether.

Diaphragm and Paradoxical Breathing

In 1984, Cohen et al[20] reported the results of weaning trials in patients with chronic obstructive lung disease. They sought to characterize diaphragmatic function and fatigue by measuring the power output and frequency of the diaphragm using surface electrodes. The high-to-low frequency output (H-L) is reduced as fatigue is manifested. In the patients studied, this sophisticated measurement correlated with the clinical signs of altered respiratory rate, minute ventilation, and hypercarbia in combination with respiratory acidosis. This study elegantly confirmed some of the previous data and

practice patterns frequently relied on by clinicians. The patient failing the weaning trial is thus characterized as being tachypneic, with an increase in $\dot{V}_E$ and respiratory rate but usually with a reduced tidal volume (Fig. 3). Rapid, shallow breathing is associated with an elevated inspiratory flow and minute ventilation but a reduced alveolar ventilation as bulk gas flow moves in and out of anatomic dead space (Fig. 4). This explains the increased dead space-to-tidal-volume ratio (V_D/V_T) reported by early investigators.[21] It further emphasizes the importance of assessing resting $\dot{V}_E$ as suggested by Sahn and Lakshminarayan.[22] A $\dot{V}_E$ in excess of 10 L/min in association with a dysfunctional breathing pattern is a negative prognostic sign.[23]

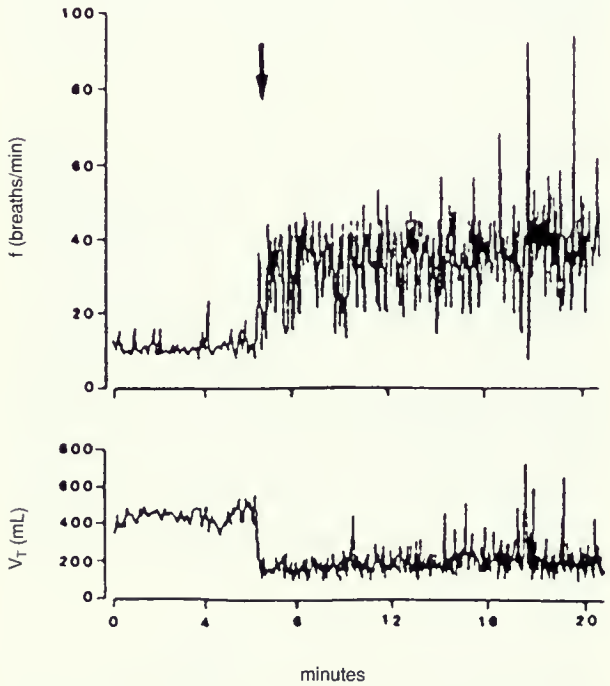

Fig. 3. Spontaneous breathing over time after discontinuation of mechanical ventilation in a patient who failed his weaning trial. The arrow indicates the point of resuming spontaneous breathing. (Reprinted, with permission, from Reference 7.)

Paradoxical breathing in addition to alterations in rate, tidal volume, and $\dot{V}_E$ frequently has been noted, with bedside evaluation signaling changes that precede alterations in pH and P_{aCO_2}. This confirms the necessity of careful bedside monitoring

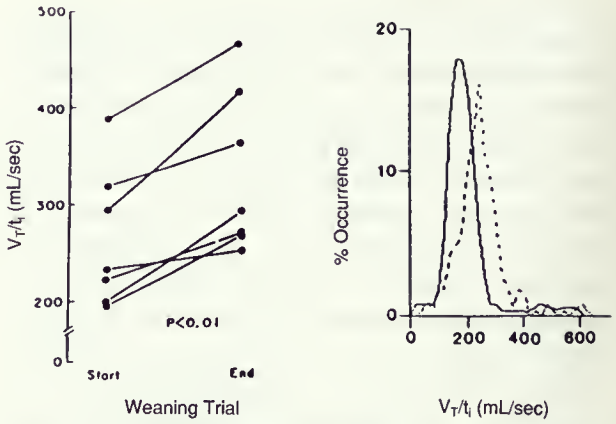

Fig. 4. A. Individual mean values of mean inspiratory flowrates V_T/t_i at the beginning and end of weaning trials in 7 patients with unsuccesfull weaning outcomes. B. The change in the frequency histogram of V_T/t_i from the beginning (——) to the end (------) of the weaning trial of a single patient who failed to wean. The percentage occurrence of breaths with a higher V_T/t_i is obviously greater at the end of the weaning trial. (Reprinted, with permission, from Reference 7.)

during any weaning trial. It also implicates the atrophy and dysfunction of the respiratory muscles that have been confirmed in animal models.[24,25]

Although paradoxical breathing may be obvious at the bedside, more subtle changes may also be occurring. Inductance plethysmography can be used to delineate the contribution of rib-cage motion and diaphragmatic excursion to the generated tidal volume and minute ventilation at a specific respiratory rate.[5-8] Normal subjects and patients successfully negotiating a weaning trial have a respiratory rate-to-tidal-volume ratio ($f:V_T$, in breaths/min/L) less than 100. Most unsuccessful trials are associated with ratios exceeding this level (Fig. 5). Similarly, when the rib cage-to-tidal-volume ratio ($RC:V_T$, expressed in %) is assessed, successfully weaned patients maintain synchronous breathing with good excursion of the rib cage. Patients with a ratio less than zero show paradoxic motion of the rib cage; a ratio in excess of 100% indicates abdominal paradox (Fig. 6).

Thus, not all patients will manifest frank paradoxical breathing during bedside assessment, but abnormalities do persist. Paradoxical breathing has been a reliable sign of respiratory muscle fatigue under the appropriate clinical circumstances. In the postoperative patient, it is often seen with partial

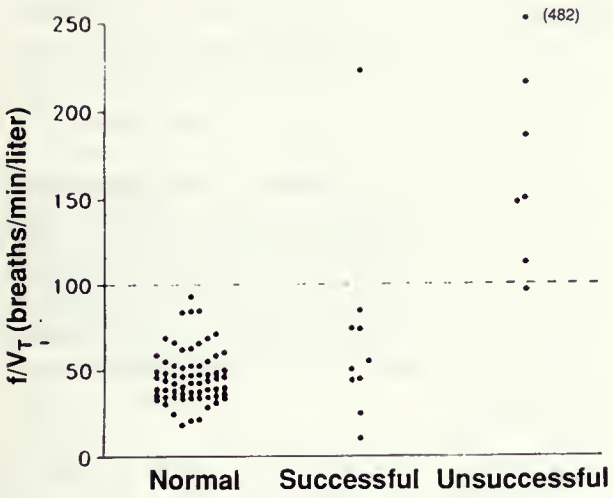

Fig. 5. The ratio of respiratory frequency to tidal volumes (f/V_T) in 65 normal subjects and 10 successful and 7 unsuccessful patients being weaned from mechanical ventilation. Failed attempts show increased f/V_T. (Reprinted, with permission, from Reference 9.)

or complete upper-airway obstruction.[26] It can be associated with retained volatile anesthetic, which seems to selectively reduce rib-cage activity altering chest-wall configuration and function.[27] Lastly, residual neuromuscular blockade may result in paradoxical breathing, even with full return of peripheral neuromuscular-twitch activity.[10]

Work of Breathing

Work of breathing is usually altered during abnormal breathing patterns. Meaningful work-of-breathing determinations are often difficult to obtain because of the ventilator circuitry employed and because we usually assume that inspiratory work is the major component of the total work of breathing.[28] Peters and co-workers[29] suggested that a work of breathing ≥ 0.10 kg · m · L^{-1} or 1.0 kg · m · min^{-1} separated ventilator-dependent patients from those able to sustain spontaneous ventilation; whereas Proctor and Woolson[30] found that 1.34 kg · m · min^{-1} separated the two groups, but there were false positives and false negatives that made clinical decision making difficult. Fiastro and associates[31] found that all of their ventilator-dependent patients had work values > 1.6 kg · m · min^{-1}. This may not be true if pressure is added to the exhalation valve, changing its configuration from that of a threshold resistor to that of a flow resistor. In such a case, exhalation is no longer passive and work of breathing is increased.[32,33] Hyperinflation during mechanical ventilation may also occur and is not limited to patients with chronic obstructive lung disease.[34] With hyperinflation, additional work is imposed on the respiratory muscles, and the lung-thorax unit is held in a position that impairs diaphragmatic function and movement of the thoracic cage, and may even impair blood supply to the respiratory muscles. This dynamic hyperinflation has been well documented as a cause of respiratory muscle dysfunction and, thus, should be considered a factor impeding the weaning process.

To minimize respiratory muscle work or to more nearly approximate normal pressure-volume relationships during the respiratory cycle, pressure support (PS) ventilation has been proposed as a

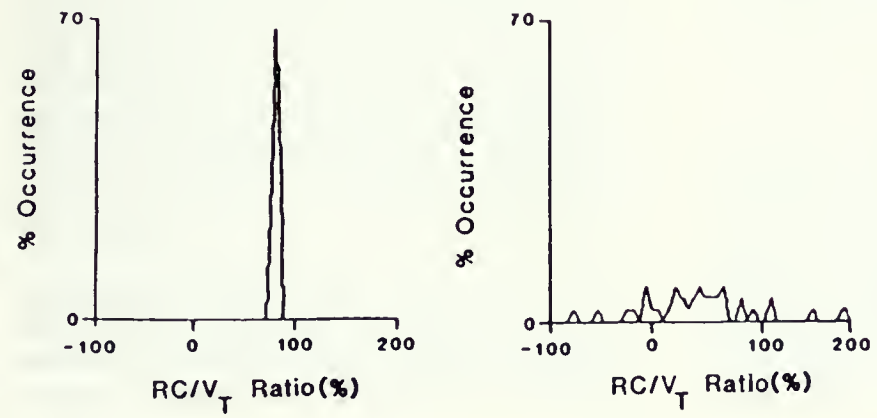

Fig. 6. Frequency histogram distribution of the cage contribution to tidal volume (RC/V_T) during successful (left) and unsuccessful (right) weaning attempts. A ratio of less than zero indicates rib-cage paradox, in excess of 100% abdominal paradox. (Reprinted, with permission, from Reference 9.)

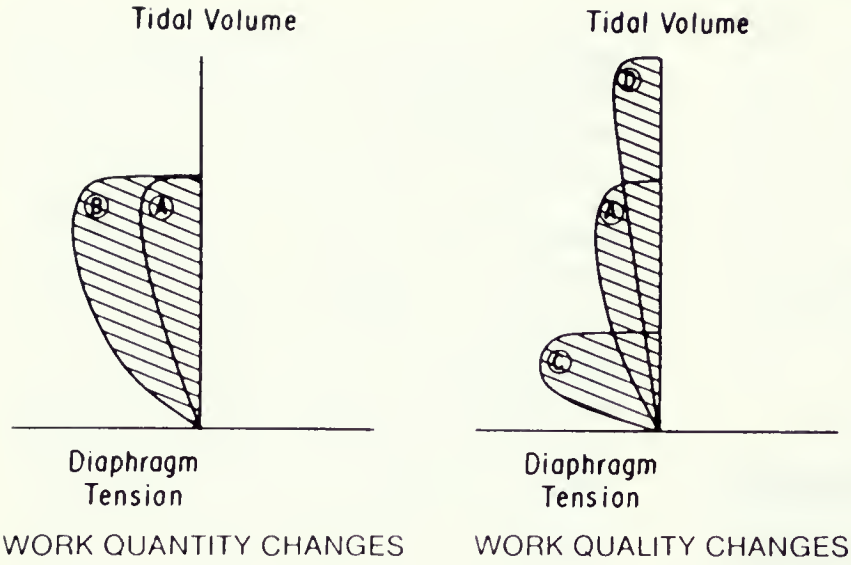

Fig. 7. Diagram of the application of pressure-support ventilation with increasing pressure limits to improve the quantity and quality of work performed by respiratory muscles to facilitate weaning. (Adapted, with permission, from Reference 35.)

technique to hasten or smooth the weaning process. Consistent with this technique are the concepts of pressure work and volume work (Fig. 7)[35]. The former implies large pressure changes (both airway and intrapleural) to achieve minimal volume changes in the lung. A high amount of energy is expended, which may overwhelm the patient's ability to maintain ventilation. The more normal lung, with normal lung-thorax compliance and airway resistance, can achieve the necessary volume changes without an inordinate energy expenditure.[36] Here again the ventilator circuits and values may impose an additional load—particularly inspiratory flow-resistor work—on the patient's own respiratory system. The pressure support system overcomes internal or external impedance loads by allowing the patient to trigger the ventilator and then augmenting inspiratory flow to rapidly achieve a set pressure limit, the goal being to approximate the normal pressure-volume relationships of a spontaneously breathing patient.

Pressure Support in Weaning

Like the IMV technique, the PS system has found favor as a ventilatory technique, but has yet to prove itself as a weaning technique. Also, as in volume-assist a number of variables can be manipulated. Both pressure-assist and volume-assist systems depend on the patient to activate or trigger the system. Volume-assisted breaths deliver the chosen tidal volume at the pressure necessary to achieve the goal. Pressure-assisted breaths deliver the designated pressure with rapid gas inflow. The flow wave rapidly peaks then decelerates as the pressure limit is held constant; during volume assist, the inspiratory flow can often be preselected. It is not surprising that the PS technique has been so widely accepted. In essence, the patient can control his own respiratory rate, tidal volume, and inspiratory flow depending on his interaction with the ventilator. Safety of the technique is increased by our ability to measure the breath-by-breath volume of exhaled gas. Like volume assist, there must be a backup system to switch to controlled ventilation should the patient become apneic.

Unfortunately, some PS systems are combined with the IMV technique—or more precisely synchronized IMV, a volume-assisted breath that must be triggered within a certain time window. Volume-assisted and pressure-assisted breaths are thus intermingled. Because IMV implies spontaneous breathing (unassisted and unrestricted!) it has been erroneously assumed by some that a patient breathing on PS is actually breathing spontaneously. Nothing could be further from the truth. A patient on a SIMV rate of 2/min combined with PS and a pressure limit of 30 cm H_2O is receiving positive-pressure ventilation, and is far from being weaned. The concept, however, is still physiologically sound. One increases the pressure limit with PS to achieve adequate tidal volumes, which should be accom-

panied by a slower respiratory rate. As support is withdrawn (ie, the pressure limit is lowered), no major increase in respiratory rate should be observed if lung mechanics are in fact improving.

Thus, pressure support may offer distinct advantages as a ventilatory technique, but its role in weaning has yet to be proven. The decelerating flow wave with its prolonged inspiratory time may achieve a better distribution of inspired gas with improvement in gas exchange (both oxygen tension and carbon dioxide) with no alteration in ventilation rate or tidal volume. We have been particularly impressed with the results using a pressure-control format, in situations in which the clinical goal was complete rest of the respiratory muscles. Low levels of pressure support (5-7 cm H_2O) are useful in overcoming endotracheal-tube and ventilator-circuit resistance, and may facilitate weaning by preventing respiratory muscle fatigue.

Lung Mechanics in Weaning

On-line measurement of lung mechanics has also been a useful adjunct to the weaning process, particularly if the presentation of information allows trends to be detected. In a series of ventilated surgical patients who were recovering from anesthesia and neuromuscular blockade, we observed that lung-thorax changes corresponded to changes in $S_{\bar{v}O_2}$ at a time when arterial blood gas analysis and noninvasive oxygen saturation monitoring did not suggest abnormal lung function. This suggests a loss of lung volume or an increase in extravascular lung water, but with minimal alveolar fluid accumulation that would alter gas exchange. It is for this reason that indices of gas exchange have infrequently correlated well with the demonstrated ability to wean, even though important trend information is provided. The alveolar-to-arterial oxygen tension gradient, the P_{aO_2}:F_{IO_2}, and calculation of physiologic shunt provide important information concerning lung function, but may be nearly normal at a time when important abnormalities still exist.

Underlying Problems in Failure To Wean

Finally, in assessing my own ongoing experience with ventilator patients, I decided to do a prospective analysis in preparation for this symposium. Interestingly, we often have a tendency to say one thing, then do another. As I began a week as the attending physician on our Surgical Intensive Care Unit service, the service had its usual complement of 22 patients. During rounds on the first morning, 5 of the 22 patients were identified as difficult to wean, and a sixth was added from the 10 admissions to our service over the next 24 hours. Of the 6 difficult-to-wean patients, 3 had moderate-to-severe underlying COPD, and the surgical episode precipitated respiratory failure that in truth, may have occurred with a viral infection or any of a number of other factors. These patients are described in Table 1. Note that three patients had undergone tracheostomy and that hemodynamic problems and fluid balance were as big a concern as respiratory status.[37] Of the second group of 3 patients (Table 2), two had moderate COPD but again systemic disease, fluid balance, and metabolic abnormalities impeded the weaning process. Both IMV and pressure-support weaning techniques failed in these patients. This experience supports my premise that under current practice conditions, the weaning technique is not as important as patient evaluation and the identification of chronic underlying disease or a superimposed acute process that is interfering with patient recovery.

A Two-Fold Approach

I suggest then a two-fold approach. The first, which seems quite obvious, is to evaluate the patient (Table 3) and the factors that can be dealt with to promote improved patient status and to facilitate weaning.[38] A most important aspect of this evaluation includes pain relief. Intermittent narcotic dosing may be a two-edged sword because the pain relief may be associated with suppression of ventilatory drive. Newer techniques such as patient-controlled analgesia, patient-controlled anxiolysis, and epidural analgesia allow pain relief without severely altering central drive to ventilator. Patient JM in our series failed PS weaning in part due to a rapid respiratory rate because of abdominal pain. Epidural analgesia in combination with 48 hours of pressure-control ventilation allowed us to completely discontinue all sedative-narcotic medications.

Table 1. Details Related to the Condition of Three Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease Who Failed To Wean following Surgical Procedures (Hemodynamic Status and Fluid Imbalance Impeded Weaning)

	WS	JM	CM
Age	68	76	67
Surgery	AAA*	Cysto/perf	AAA
COPD?	Severe	Severe	Severe
Hypoxic?	No	No	No
Hypercarbic?	No	No	No
Bronchospasm?	Yes	Yes	Minimal
Hemodynamic status	Stable	Stable	Hypotension
Metabolic alkalosis?	Yes	No	No
Type of airway	Tracheostomy	Tracheostomy	Tracheostomy
Weaning technique?	Y-Tube	T-Tube	T-Tube
Intake > output	10-15L	Even	20L
Weight	98-95 Kg	80 Kg	90-79 Kg

*AAA = Aortic aneurysm resection; Cysto/perf = cystoscopy/perforation.

Table 2. Details Related to Three Patients, Two of Whom Had Moderate COPD, Who Failed To Wean following Surgical Procedures (Systemic Disease, Fluid Imbalance, and Metabolic Abnormalities Impeded Weaning)

	EF	JM	CM
Age	71	34	74
Surgery	FND*	GI Bleed	FEM/FEM
COPD?	Yes	No	Yes
Hypoxic?	Yes	Yes	Yes
Hypercarbic?	No	Yes	No
Bronchospasm?	Yes	No	No
Hemodynamic status?	SVT	ECF	SVT
Metabolic alkalosis?	No	Yes	No
Type of airway	Tracheostomy	ETT	ETT
Weaning technique	IMV	IMV/PS	IMV/PS
Intake & output	Even	Ascites	15-20L
Weight	45 Kg	42 Kg	75 Kg

*FND = functional neck dissection; FEM/FEM = femoral-to-femoral artery bypass; SVT = superventricular tachycardia; ECF = extracellular fluid.

Table 3. Facets of Patient's Condition To Be Evaluated before a Weaning Trial

Acid-base status favorable?
Fluid-electrolyte balance satisfactory?
Nutritional status satisfactory?
Is the patient rested?
Peripheral muscles—Able to stand?
Bronchospasm present?
Nature and volume of secretions?

This leads to the second leg of the evaluation process, which is to evaluate the technique (Table 4). In this age of multidisciplinary care, it is essential that all personnel agree on the plan and communicate with and support the patient. The psychologic aspect of weaning, though rarely mentioned, is foremost in the minds of patients who have experienced the ordeal of respiratory failure, airway manipulation, and mechanical ventilation. Their experience should guide us in establishing a careful, compassionate,

Table 4. Management Considerations To Be Evaluated before Weaning a Patient

Review the medications
—depressants
—stimulants
—antibiotics
Agree on the weaning plan
Provide psychological support
Assure pain relief

rational, and scientific approach to a serious problem that must be an unimaginable, traumatic experience for those experiencing it.

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Withholding and Withdrawing Life Support from the Critically Ill: How Does It Work in Clinical Practice?

John M Luce MD

The Complexity of Withholding and Withdrawing Life Support

The withholding and withdrawal of life support are processes by which various medical interventions either are not given to or are taken away from patients, with the expectation that they will die as a result.[1,2] These processes are carried out in many medical settings but especially in the intensive care unit (ICU), where an array of therapies capable of sustaining life are employed, which may be withheld or withdrawn when they are not likely to be of benefit or are no longer found to be beneficial. An example of withholding life support is not providing mechanical ventilation to a patient with chronic obstructive pulmonary disease (COPD) in acute respiratory failure (ARF), who if not placed on a ventilator will probably die but if placed on a ventilator will probably be unweanable. An example of withdrawing life support is removing mechanical ventilation from a COPD patient, with the provision that he will neither be ventilated again if ARF recurs nor receive cardiopulmonary resuscitation (CPR) in the event of cardiopulmonary arrest. This second patient is different from a patient with COPD who is being weaned from mechanical ventilation and will be ventilated again or resuscitated if he deteriorates during the weaning process.

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Strictly speaking, all patients who die while receiving close medical attention in an ICU or elsewhere do so as a direct result of the withholding or withdrawal of life support. This is either because a decision has been made—in advance of decompensation—not to resuscitate the patient, or because vigorous resuscitation will not be provided indefinitely. For example, the third patient described earlier would receive CPR if he were to suffer an unexpected cardiopulmonary arrest during weaning, but CPR would be discontinued if a viable cardiac rhythm could not be restored in a reasonable amount of time. The withdrawal of life support from this third patient is comparable to the withholding of CPR from the second patient, except for the fact that with the second patient deliberate planning has taken place before cardiopulmonary arrest. It is this more deliberate form of withholding and withdrawal that will be focused on in this article.

It should be noted that the only patients who die in the ICU during the withholding or withdrawal of life support, who are not expected to die, are those who are dead already due to complete and irreversible loss of function of the cerebral hemisphere and brain stem. These patients frequently receive mechanical ventilation and other forms of life support either because the diagnosis of brain death has not been confirmed by apnea testing (after which the ventilator will be removed), or because vital organs (excluding the central nervous system) are being preserved prior to transplantation. Indeed, if transplantation is accomplished, the withholding or withdrawal of mechanical ventilation and other therapies usually takes place in the operating room, where the patient's organs are harvested. Because in brain-dead patients interventions such as mechanical ventilation are removed after death, instead of before death, they are better thought of as organ support than as life support.

What Form of Life Is Supported?

The mention of brain death raises the question of what form of life is being supported. One form is *biological life*, which requires not only functional organs but also a functional organism. Brain-dead patients are considered biologically dead because they have lost the integrative functions of the brain stem, without which individual organs cannot survive for a prolonged period. These patients are distinguished from biologically active patients in a persistent vegetative state who maintain brain-stem and hence integrative function but have lost the sentient functions of the cerebral hemisphere. Without *sentient life*, patients in a persistent vegetative state are incapable of self-awareness or social interaction; however, they may successfully tolerate weaning from mechanical ventilation and be capable of breathing on their own.

A third form of life is *worthwhile life*, a life that is considered worth living by the patient, by other persons, or by society. This form of life does not lend itself to medical diagnosis, and it is open to many interpretations. For example, some might consider life worthwhile only if it contains less pain than pleasure, whereas others might see pain as a necessary part of living or even take pleasure in it. Similarly, one patient with COPD and ARF who cannot ventilate and oxygenate adequately without the ventilator may prefer to have mechanical ventilation withdrawn because he considers life no longer worth living, but another patient in the same condition might prefer to remain on the ventilator in the ICU or elsewhere because he still wants to live. In our society, which values freedom of choice and has adequate critical care resources at present, a patient is allowed to refuse treatment or to accept or request it based upon his perception of whether life is worthwhile.

Judicial Decisions

The American judicial system has wrestled with the ethical dilemmas associated with the withholding and withdrawal of life support from patients who are not brain dead. In the process, the courts have underscored the importance of privacy and the right to refuse treatment, affirmed the concept that human life is more than a biologic process, defined how therapies may or may not benefit patients, argued against a distinction between the withholding and withdrawal of support, and established guidelines for how support may be withheld or withdrawn.[3]

Perhaps the best known judicial decision regarding the withholding and withdrawal of life support occurred in the case of Karen Ann Quinlan (1976), in which the father of a girl who was in a persistent vegetative state petitioned the court to be appointed guardian with the power to remove her from mechanical ventilation. The lower court denied the petition, but the New Jersey Supreme Court reversed the decision. In doing so, the court reasoned that patients generally would accept or refuse medical treatment on the basis of its ability to support sentient life rather than mere biological existence. Having concluded that Ms Quinlan, if she had been capable of making decisions herself, would have forgone therapy that could only prolong biological life but not sentient life, the court decided that her right to privacy would be abrogated if it prevented the exercise of this right on her behalf. The court therefore granted the father's petition, allowing him to exercise "substituted judgment" for his daughter, and stated that life support could be withdrawn if physicians and a hospital ethics committee agreed that such support did not alter Ms Quinlan's underlying condition.

The case of *Barber v. Superior Court* (1983) confirmed the utility of substituted judgment and also answered the question of physician liability in withholding or withdrawing life support. This case involved two California physicians who performed surgical closure of an ileostomy on a Mr Herbert, who subsequently suffered cardiopulmonary arrest. Five days later they determined that his coma was irreversible; with the consent of his family, the physicians withdrew not only mechanical ventilation but also intravenous fluids and nutrition. Although the family found no fault with this at the time, the physicians were accused of murder by a district attorney. After the case was heard by several courts, the California Court of Appeals ruled that because the physicians had considered it medically futile to continue life support because sentient life could not be restored, the physicians had not failed to perform their duty. The court did

not distinguish between removing mechanical ventilation or removing fluids and nutrition because all were interventions that could either help or hurt the patient. The court thereby discarded the traditional dichotomy between ordinary and extraordinary forms of treatment in favor of a distinction between measures that benefit and burden. Finally, the court held that, without evidence of malevolence, family members are the proper surrogates for an incompetent patient, and that prior judicial approval is not necessary if families and physicians decide to withhold or withdraw support.

The most recent case to wrestle with the issue of withholding and withdrawing life support is that of *Cruzan v. Missouri,* which was heard by the U.S. Supreme Court in 1990. This case involved Nancy Cruzan, a young woman in a persistent vegetative state who required tube feeding rather than mechanical ventilation. Believing that she would not want to live in such a state, her parents asked to have tube feeding discontinued and were authorized to do so by a trial judge in Missouri. However, the Missouri Supreme Court reversed this decision, arguing that no one could exercise Ms Cruzan's right to refuse treatment on her behalf. The court also said that because the state had an interest in preserving life regardless of its quality, support could be terminated only if it could be shown by "clear and convincing evidence" that Ms Cruzan had rejected such treatment. The U.S. Supreme Court, while acknowledging that patients had a constitutional right to refuse life-saving hydration and nutrition, also concluded that the Constitution did not prohibit Missouri or other states from requiring evidence of a patient's wishes regarding life support. The reasons for this decision, given by Chief Justice Rehnquist for the 5-justice majority, were that states have a legitimate interest in "the protection and preservation of human life," that "the choice between life and death is a deeply personal decision," and that abuses can occur in the case of incompetent patients who do not have "loved ones available to serve as surrogate decision makers."[4]

The minority dissent to the Cruzan decision (which was written by Justice Brennan for three of the four dissenting justices) was based on the position that the right of patients to refuse treatment was greater than the state's interest in supporting life. Even if the preservation of life was a legitimate state interest, Justice Brennan argued, the Missouri decision probably would lead to more deaths by discouraging health professionals from initiating medical interventions because of fear that later the interventions could not be withdrawn. By requiring strong evidence of a patient's wishes, Missouri was accused of depriving Ms Cruzan of the best judgment of those who loved her and of forcing her loved ones to suffer due to the protraction of her persistent vegetative state. Finally, Justice Brennan argued that Missouri was out of touch with reality in expecting patients to write elaborate documents about all the ways in which they might die and in which their lives could or could not be supported. By ignoring the insights of family and friends, the Missouri statute "transforms [incompetent] human beings into passive subjects of medical technology."[4]

Although the Cruzan decision states that the Missouri law, requiring clear and convincing evidence of a formally competent patient's wishes, is constitutional and may be used in Missouri, it does not require that other states follow Missouri's lead, nor does it prevent Missouri from changing its statute. The decision also does not alter the laws, ethical principles, or clinical practices permitting the withholding or withdrawal of life support that have evolved in the United States since the Quinlan case 14 years earlier. Additionally, in the Cruzan decision the Supreme Court affirmed the right of competent patients to refuse life-sustaining treatment and did not treat the withholding or withdrawal of hydration and nutrition differently than the withholding and withdrawal of other medical interventions. And, finally, the Supreme Court highlighted the desirability of all persons' filling out advance directives, including living wills and durable powers of attorney for health care, to facilitate medical decision making if and when they become critically ill.[5]

Studies of the Withholding and Withdrawal of Life Support

If Missouri's position in the Cruzan case was out of touch with reality, as Justice Brennan argued,

it may have been due to the fact that relatively little information regarding the reality of withholding or withdrawing life support is available in the medical or lay literature. Most writings on the subject have dealt with issues such as CPR and do-not-resuscitate (DNR) orders. Regarding CPR, it has been noted that most institutions adopted universal CPR policies when this technology was first introduced in 1960. However, recent studies have shown that many patients do not want CPR and that it is rarely effective in hospitalized patients[6] or those over 70 years of age.[7] This has led the American Heart Association[8] and other groups to state that CPR is not required in terminally, irreversibly ill patients. At the same time, New York and other states have drafted statutes stipulating that patient preferences regarding CPR be solicited on or shortly after hospital admission. Although seeking input from patients and families seems appropriate in most situations, some investigators[9] have argued that patient autonomy is irrelevant when CPR has no potential medical benefit, and that this information should not even be offered to the terminally, irreversibly ill.

Despite emerging policies in New York and elsewhere, most studies[10-13] have demonstrated that DNR orders are written relatively late in a patient's admission, even when the patient is hospitalized in an ICU. Justification for the orders frequently is lacking, as are treatment goals after the order is written. The brief interval between writing an order and death or ICU discharge suggests that the DNR order often represents a decision point for placing broader limits on therapy. Indeed, although many hospital policies consider DNR status compatible with aggressive medical management, in actual practice the writing of a DNR order usually leads to less aggressive care.

Withholding and Withdrawing Life Support at the University of California, San Francisco

How and why life support is withheld or withdrawn. The fact that the writing of a DNR order often results in less-aggressive care was borne out in a study[1] of the withholding and withdrawal of life support from critically ill patients conducted in two hospitals affiliated with the University of California, San Francisco. This study took place in the medical-surgical ICUs of Moffitt-Long Hospital and San Francisco General Hospital. Moffitt-Long Hospital is a 560-bed tertiary care facility with an 18-bed medical-surgical ICU, a 5-bed neurosurgical ICU, and an 8-bed coronary care unit. San Francisco General Hospital is a 430-bed facility containing a Level-1 trauma center that has a 14-bed medical-surgical ICU, a 6-bed medical (formerly respiratory) ICU, and an 8-bed coronary care unit.

The medical-surgical ICUs at the two hospitals are the setting for a multidisciplinary training program in critical care medicine that involves attending faculty, fellows, and residents from the departments of anesthesia, medicine, and surgery. These intensive-care teams are consulted about all admissions to the ICU, and they assist the primary services (such as surgery, medicine, and pediatrics) with patient care. The medical-surgical ICUs did not provide care for all the critically ill patients treated at either hospital during the study period; in fact, they provided care for a disproportionate number of surgical patients. Nevertheless, because the study investigators were part of the medical-surgical intensive-care teams, and because the two units functioned in a similar fashion, only patients admitted to these two ICUs were included in the study.

All patients over 1 year of age who were admitted to either of the two medical-surgical ICUs from July 1987 through June 1988, and from whom life support was subsequently withheld or withdrawn, were identified by the attending critical-care physicians for inclusion in the study. Patients who were included were expected to die after the withholding or withdrawal of life support, either in the ICUs or shortly after transfer to other areas of the hospital. The latter patients were transferred with the provision that they would not be resuscitated or readmitted to the ICUs if their conditions deteriorated. Also included were organ donors who were brain dead, and from whom cardiopulmonary support was withdrawn in the operating room rather than the ICU, because the process leading to organ donation is similar to the process leading to the withholding or withdrawal of support in other patients.

A three-part, detailed, standardized questionnaire was used to collect information about the patients, their families, and the physicians and nurses who cared for them. This questionnaire had a closed format, and most questions required choosing from a limited number of responses. The first part of the questionnaire was completed by the critical-care fellows, who reviewed the patients' medical records to determine age, sex, diagnoses on admission and discharge, outcome, length of stay in the ICU, DNR status, any previously expressed wish to limit care, and the sequence in which life support was withheld or withdrawn. The fellows also interviewed the attending physicians and chief residents (on the primary services) to determine why life support had been withheld or withdrawn. The second and third parts of the questionnaire were completed by a research nurse and the family counselors from the ICUs. It focused on the intensive-care nurses' and families' understanding of and involvement in the withdrawal process.

A total of 1,719 patients were admitted to the medical-surgical ICUs during the 1-year study period; 968 patients were admitted to Moffitt-Long Hospital and 751 to San Francisco General Hospital. Life support was withheld or withdrawn from 115 (7%) of the 1,719 patients—36 (4%) of those admitted to the ICU at Moffitt-Long Hospital and 79 (11%) of those at San Francisco General Hospital. Of these 115 patients, support was withheld from 22 (19%) and withdrawn from 93 (81%).

Of the 1,719 patients admitted to the two ICUs, 198 (12%) died there—127 (13%) of those admitted to the ICU at Moffitt-Long Hospital and 71 (9%) of those at San Francisco General Hospital. Eighty-nine (45%) of the 198 patients who died in the ICUs died after support was withheld or withdrawn. The remaining 26 of the 115 patients from whom support was withheld or withdrawn were transferred from the ICUs with the expectation that they would die. Only one of these was discharged from the hospital; the remainder died on the ward within 2 weeks of discharge from the ICU.

The median stay in the ICU for all patients was 2 days (3 days at Moffitt-Long Hospital and 2 days at San Francisco General Hospital). The median stay of the patients who died in the ICUs as a result of the withholding or withdrawal of life support was 8 days at Moffitt-Long Hospital and 4 at San Francisco General Hospital. These stays were considerably longer than those of patients who survived after treatment in the ICU and patients who died there but did not have life support withheld or withdrawn.

Intracranial lesions were present in 66 patients from whom support was withheld or withdrawn; this included 6 (17%) of the patients from whom support was withheld or withdrawn at Moffitt-Long Hospital and 60 (76%) of the patients from whom support was withheld or withdrawn at San Francisco General Hospital. The corresponding median stays in the ICUs were 4 and 3 days, respectively. Eighteen patients were considered brain dead, 17 of whom were at San Francisco General Hospital. Head trauma accounted for 10 (56%) of the cases of brain death; intracerebral and arachnoid hemorrhage and anoxic injury were responsible for 5 (28%) and 3 (17%) of the cases of brain death, respectively. Five patients were organ donors. Seventeen patients from whom support was withheld or withdrawn were admitted postoperatively. Twelve of the 17 had had emergency surgery. The median stay in the ICU was 9 days at Moffitt-Long Hospital and 14 days at San Francisco General Hospital.

Respiratory failure was present in 30 patients from whom support was withheld or withdrawn (excluding those with postoperative multiple-organ failure) during their admission to the ICU. The median duration of intensive care was 7 days at both hospitals. Four patients had severe underlying lung disease and were admitted because of a decline in pulmonary function. Six patients, three at each hospital, had the acquired immunodeficiency syndrome (AIDS); five of the six had *Pneumocystis carinii* pneumonia, and one had diffuse pulmonary lymphoma. The remainder of the patients had severe acute lung injury due to sepsis, aspiration, or multiple trauma.

Fourteen patients from whom support was withheld or withdrawn were admitted with known underlying cancers. All but two of these patients were admitted to the ICU at Moffitt-Long Hospital. Eleven of the 14 patients had solid tumors. Eight of the 14 had respiratory failure, three were postoperative, one had a brain tumor, one was bleeding from an upper gastrointestinal hemorrhage,

and one had intra-abdominal sepsis. The median stay in the ICU was 3 days. Only three patients had hematologic cancers, two of whom had previously undergone bone marrow transplantation. Their numbers were too small to permit definitive conclusions, but the patients with hematologic cancers tended to stay in the intensive care unit longer (9, 21, and 27 days) than the patients with solid tumors.

The issue of withholding or withdrawing life support usually first came up during the work rounds of the primary and intensive-care teams. The primary attending physicians and the attending physicians in the ICU then began to discuss the issue with the patients (if they were sufficiently competent to make medical decisions) or their families (if family members were available).

Five (4%) of the 115 patients, from whom support was withheld or withdrawn, were competent in the judgment of their physicians. Three of these patients had severe underlying lung disease and either elected not to be intubated during an exacerbation (one patient) or declined reintubation after repeatedly unsuccessful attempts to wean them from mechanical ventilation (two patients). The other two patients had AIDS with respiratory failure; one declined to receive ventilatory support for pneumocystis pneumonia, and the other had previously expressed a desire to limit the duration of mechanical ventilation.

The great majority of the patients—110 (96%) of the 115 from whom support was withheld or withdrawn—were not competent to make the decisions themselves. Family members were involved in the decisions to withhold or withdraw support from 102 (93%) of these 110 patients. For the remaining eight patients (7%), all at San Francisco General Hospital, no family members could be found. Seven of these eight patients were admitted after severe traumatic injuries, three of which were neurologic. The decisions to withhold or withdraw support from these eight incompetent patients, who had no accessible family members, were the result of the deliberations of the primary attending physician and the attending physician in the intensive care unit, after consultation with other physicians about the prognosis.

Once a consensus was reached among the attending physicians and the patients or family members, DNR orders were written for 107 (93%) of the 115 patients before support was withheld or withdrawn. These orders were always written by the primary attending physicians. Orders were not written for the five patients who were organ donors or for three patients whose attending physicians were present at the bedside during the process of withdrawing life support. Of the 107 for whom DNR orders were written, 105 (98%) died or were discharged from the unit within 48 hours of the DNR order.

Thirteen patients had previously expressed a wish to limit terminal care through a living will or in discussions with family members or friends. None had signed a durable power of attorney for health care, which is sanctioned by California law. The median length of stay in the ICU for these patients was 7 days, which was not different from the group as a whole. However, four patients with solid tumors who had expressed such a wish had a median stay of 2 days.

The presence of brain death was cited by the primary attending physician as the sole reason for withholding or withdrawing support from the 18 patients who were brain dead. A poor prognosis was given as the reason for withholding or withdrawing support from the other 97 patients. Additional reasons given for withholding or withdrawing support from specific patients were the futility of continued intervention in 29 (30%), extreme suffering in 8 (8%), and a request by the patient or a family member in 6 (6%). There were no family members who requested withholding or withdrawing life support while the patient was competent to make decisions; in the past, such requests at the two institutions have not been honored and would be viewed today as violating the patient's autonomy. Although the allocation of resources was discussed frequently among the physicians caring for the patients, concern about resources was never cited as a reason for withholding or withdrawing support, nor was the lack of availability of ICU beds cited (although the units were frequently full).

The primary and intensive-care teams initially agreed to withhold or withdraw support from all

but three patients. In two of these cases, the intensive-care team decided that support should be withdrawn before the primary team reached this conclusion. Care was continued until both teams were in agreement.

Family members were available for 106 (92%) of the 115 patients, and all those available were involved in the process of deciding whether life support should be withheld or withdrawn. As noted earlier, relatives of 102 of the incompetent patients and 4 of the competent patients were available. Ninety-six (91%) of the 106 families either agreed with the course of withholding or withdrawing support suggested by the physicians or had asked beforehand that support be withheld or withdrawn; 10 (9%) of the families disagreed at first with the suggested course, but 8 of these 10 accepted the recommendations within 2-3 days; and 2 families continued to insist on intensive care against the advice of physicians, and in these cases care was administered until the time of the patients' deaths.

Twenty-six (60%) of the 43 families who were interviewed with regard to their attitudes toward the process of withholding and withdrawal said they believed that the patients or their families should make such decisions jointly with the physicians; 12 (28%) thought that the physicians should make these decisions on their own; and 4 (9%) thought these decisions should be the exclusive responsibility of patients or their families.

Support was withheld from 22 patients and withdrawn from 93; as noted earlier, 5 patients were organ donors. At both institutions mechanical ventilation was the intervention most commonly withdrawn, and vasopressors the intervention most frequently withheld. The initial step in withdrawing mechanical ventilatory support usually consisted of discontinuing supplemental oxygen and positive end-expiratory pressure (PEEP). If these actions did not result in death, patients were then placed on a T-piece. Sedatives and analgesic agents were administered during the process of withholding or withdrawing support to 68 (70%) of the 97 patients who were not brain dead. Antibiotics, blood transfusions, intravenous fluids, and dialysis were withheld from 8 patients and withdrawn from 13. In the patients from whom these interventions were withdrawn, mechanical ventilation or vasopressors were withdrawn either simultaneously or within a few hours.

The applicability of the findings of this study are uncertain because no one has extensively studied the withholding and withdrawal process in ICUs before. Nevertheless, the 7% incidence of withholding or withdrawing life support in the study was comparable to the 0.4%-13.5% range of frequency of DNR orders in medical-surgical ICUs[13] and the 14% incidence of such orders in a medical ICU,[12] assuming that support was withheld or withdrawn after DNR orders were written, as was the case in this study.

The most important finding of the study was that brain death and poor prognosis were the major reasons for withholding or withdrawing life support. Other findings were that patients were most often unable to participate in decision making, but that family members were willing to take an active part; advance directives were rarely available and did not significantly shorten time in the ICU; DNR orders were almost always written and were crucial turning points in patient care; and allocation of resources was never cited as a reason for withholding or withdrawing life support, even though it was an issue discussed frequently in the two ICUs.

Administration of sedatives and analgesics during the withholding and withdrawal of life support. An unpublished follow-up study of how and why sedatives and analgesics are administered during the withholding and withdrawal of life support was conducted in the medical-surgical ICUs of San Francisco General Hospital and Moffitt-Long Hospital from November 1988 through October 1989. All 22 patients from whom life support was withheld or withdrawn, and who were not brain dead, in the San Francisco General Hospital ICU over a 1-year period were included in the study. For comparison purposes, an equal number of similar patients was selected at random from the 79 patients from whom life support was withheld or withdrawn over the same period in the medical-surgical ICU at Moffitt-Long Hospital.

During the year of the following study, 657 patients were admitted to the San Francisco General Hospital medical-surgical ICU, and 1,075 patients were admitted to the Moffitt-Long Hospital medical-

surgical ICU. Of these 1,732 patients, 199 (11%) died in the ICUs and 101 (6%) of 1,732 had their support withheld or withdrawn.

In the first study on how and why life support was withheld or withdrawn in the same two medical-surgical ICUs, organ donors who were brain dead, as well as patients who did not die in the ICUs but were expected to die shortly after transfer to other areas of the hospitals, were included. In the follow-up study, brain-dead patients were excluded because they were not likely to receive sedatives and analgesics. Also excluded were patients who were expected to die in other areas of the hospitals because the ICU teams would no longer be responsible for ordering sedatives and analgesics for them. Therefore, the only patients included in the second study were those who were not brain dead and were expected to die in the ICUs after life support was withheld or withdrawn. This explains why the number of patients included in the second study was less than that in the first investigation (44 vs 115).

Sedatives and analgesic drugs were administered to 18 (82%) of the 22 patients from whom life support was withheld or withdrawn in the medical-surgical ICU at San Francisco General Hospital, and to 15 (68%) of the 22 patients in the medical-surgical ICU at Moffitt-Long Hospital. Thus, 33 (75%) of the 44 patients from whom life support was withheld or withdrawn received sedatives, analgesics, or both. Seventeen (39%) of these 44 patients had medical diagnoses, and 27 (61%) of the 44 had surgical diagnoses. Thirty-seven (84%) of the 44 patients were not hemodynamically stable, and 42 (97%) of the 44 were mechanically ventilated at the time of withholding or withdrawal. The median time in the ICU prior to withholding or withdrawal of life support was 5.1 days (mean 8.9 days, range 1 to 67 days). The median time until death following the initiation of withholding or withdrawal of life support was 3.5 hours (mean 11 hours, range 5 minutes to 5.5 days) in the patients who received drugs vs 1.3 hours (mean 5.3 hours, range 6 minutes to 1 day) in patients who did not receive them.

Decisions to withhold or withdraw therapy were made by patients or, more frequently, by family members or other surrogates on the recommendations of their primary physicians and ICU physicians. These recommendations were based on assessment of patient prognosis as described in the previous study. All the ICU physicians interviewed in the second study considered themselves part of the decision-making process, as did 36 (82%) of the 44 nurses interviewed. Although the physicians ordered all sedatives and analgesics, nurses felt that they contributed to the selection of drugs in 33 (75%) of 44 instances.

Physicians ordered sedatives and analgesics to relieve pain in 29 (88%) of the 33 patients who received these drugs, to decrease agitation in 28 (85%), to prevent air hunger in 22 (67%), to comfort family members in 17 (52%), and to hasten death in 12 (36%). No other reasons were given on the questionnaire. Eleven (25%) of the 44 patients in the study did not receive drugs because they were deeply comatose and considered by physicians to be incapable of experiencing pain, anxiety, or air hunger.

All the physicians said they were satisfied with the type, dose, route, and frequency of drug administered. Physicians stated that 43 (98%) of the 44 of patients appeared to be comfortable at the time life support was withheld or withdrawn.

Nurses administered sedatives and analgesics to relieve pain in 28 (85%) of the 33 patients who received drugs, to decrease agitation in 17 (52%), to prevent air hunger in 25 (76%), to comfort family members in 27 (82%), and to hasten death in 13 (39%). No other reasons were given on the questionnaire.

Thirty-three (75%) of 44 patients received medication at the time life support was withheld or withdrawn. The mean dose of benzodiazepines (expressed as diazepam equivalents) increased from 2.2 mg/h to 9.8 mg/h, whereas the mean dose of opiates (expressed as morphine equivalents) increased from a baseline of 3.3 mg/h to 11.2 mg/h. Not all patients who received medication at the time life support was withheld or withdrawn received both benzodiazepines and opiates: 24 patients received benzodiazepines, 31 patients were given opiates.

Although the amounts of drugs given on an hourly basis were not formally recorded, the investigators did not notice any major increases in drug dosage

from one hour to the next. Furthermore, although it was not recorded whether drugs were given by intravenous infusion or in boluses, the impression was that drugs most often were given as infusions, titrated incrementally upward, rather than as boluses. The investigators did not observe the administration of any individual boluses that would have been considered potentially lethal in themselves.

Like the physicians, all the nurses said they were satisfied with the type, dose, route, and frequency of drug administered during withholding or withdrawal. Many nurses wrote on the margins of the data collection form that the reason they were satisfied was because when they considered an order inadequate for the patient they would discuss this with the physician and the order would be changed appropriately. The nurses indicated that 43 (98%) of the 44 patients appeared to be comfortable at the time life support was withheld or withdrawn. The one patient considered to be uncomfortable by both physicians and nurses was a surgical patient whose agonal breathing was interpreted as a manifestation of respiratory distress.

Three (1%) of the 33 patients who received sedatives or analgesics at the time life support was withheld or withdrawn had low respiratory-system compliance and were also given muscle relaxants to facilitate mechanical ventilation. In none of these patients was extubation or removal from mechanical ventilation the primary mode of withholding or withdrawal. Two of the patients had vasopressors withdrawn and one had oxygen removed. The time until death for this subset of patients ranged from 1.7 to 5.3 hours, with a mean of 3.5 hours. In no case was potassium chloride or any other potentially lethal agent given to a patient to hasten death.

A comparison cannot be made between the behavior and attitudes observed in the two hospitals in the study with those of other institutions, because no one has studied and reported how and why sedatives and analgesics are given during the withholding or withdrawal of life support. Nevertheless, the supportive care described is consistent with recent recommendations from many investigators,[14-16] and the investigators of this study believe that similar care is widely administered elsewhere. The recommendations for supportive care are based on the ethical principle of double effect, which holds that hemodynamic and ventilatory depression are permissible during the withholding and withdrawal of life support if the relief of pain, agitation, and air hunger is provided.[17] However, these recommendations do not generally sanction the giving of drugs to hasten death, an intent acknowledged by a considerably large number of physicians and nurses in the study.

The study used a closed data collection format in which hastening death was one of a limited number of answers to the question of why physicians ordered and nurses administered sedatives and analgesics during withholding and withdrawal. This format may have prompted physicians and nurses to choose an answer that they would not otherwise have provided if they had been responding to an open questionnaire. It is also possible respondents were not assured that confidentiality could be maintained, and if they had been assured of this that more of them may have indicated their intent to hasten death.

Concern over this issue led the investigators to discuss the hastening of death with physicians and nurses in the two ICUs, following completion of the study. From these discussions it was clear that many physicians and nurses considered hastening death due to hemodynamic or respiratory depression a possible, if not likely, result of giving sedatives and analgesics. Respiratory depression probably was not of consequence because the patients generally remained on the ventilator until death or until late in the withholding and withdrawal process, and the patients who received drugs actually died later in the withholding and withdrawal process than did those who did not receive drugs. Nevertheless, the physicians and nurses thought that even if it were of consequence, such depression was ethically acceptable if pain and air hunger were alleviated. Several also said that once the decision to withhold or withdraw life support was made, there was no reason to delay the process.

Summary and Conclusions

Withholding and withdrawing life support from the critically ill commonly occurs in clinical practice. Sedatives and analgesics are frequently given during this process to patients who are not

Abbreviations Used in this Paper

AIDS	—	Acquired immunodeficiency syndrome
ARF	—	Acute respiratory failure
COPD	—	Chronic obstructive pulmonary disease
CPR	—	Cardiopulmonary resuscitation
DNR	—	Do not resuscitate
ICU	—	Intensive care unit

so deeply comatose that they cannot benefit from them. The withholding and withdrawal of life support is compatible with several judicial decisions, including the recent Cruzan decision of the U.S. Supreme Court. Recent studies are providing insights into how, why, and under what circumstances the withholding and withdrawal of life support take place, and how drugs are administered during these processes. Additional studies are needed to further elucidate these processes and to contribute to the shaping of realistic and humane standards of terminal care.

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1895 Advice on Hygiene and Chronic Bronchitis

HYGIENE

In the following pages we shall introduce to the reader's attention several important hygienic subjects, although there are many more that ought to receive special notice. Such as we do mention, demand universal attention, because a disregard of the conditions which we shall enumerate, is fraught with great danger. Our lives are lengthened or shortened by the observance or neglect of the rules of common sense, and these do not require any great personal sacrifice, or the practice of absurd precautions.

PURE AIR FOR RESPIRATION

Ordinary atmospheric air contains nearly 2,100 parts of oxygen and 7,900 of nitrogen, and about three parts of carbonic acid, in 10,000 parts; expired air contains about 470 parts of carbonic acid, and only between 1,500 and 1,600 parts of oxygen, while the quantity of nitrogen undergoes little or no alteration. Thus, air which has been breathed has lost about five percent of oxygen and has gained nearly five percent of carbonic acid. In addition the expired air contains a greater or less quantity of highly decomposable animal matter, and, however dry the atmospheric air may be, the expired air is always saturated with watery vapor, and, no matter what the temperature of the external air may be, that of the exhaled is always nearly as warm as the blood. An adult man on an average breathes about sixteen times in a minute and at every inspiration takes in about thirty cubic inches of air, and at every expiration exhales about the same amount. Hence, it follows that about 16 $^{2}/_{3}$ cubic feet of air are passed through the lungs of an adult man every hour, and deprived of oxygen and charged with carbonic acid to the amount of nearly five percent. The more nearly the composition of the external air approaches that of the expired air, the slower will be the diffusion of carbonic acid outwards and of oxygen inwards, and the more charged with carbonic acid and deficient in oxygen will the blood in the lungs become. Asphyxia takes place whenever the proportion of carbonic acid in the external air reaches ten percent, providing the oxygen is diminished in like proportion, and it does not matter whether this condition of the external air is produced by shutting out fresh air from a room or by increasing the number of persons who are consuming the same air; or by permitting the air to be deprived of oxygen by combustion by a fire. A deficiency of oxygen and an accumulation of carbonic acid in the atmosphere, produce injurious effects, however, long before the asphyxiating point is attained. Headache, drowsiness, and uneasiness occur when less than one percent of the oxygen of the atmosphere is replaced by other matters, and the constant breathing of such an atmosphere lowers vitality and predisposes to disease.

Therefore, every human being should be

This material is from The People's Medical Advisor, by RV Pierce MD, which was published in 1895 by the World Dispensary Printing Office and Bindery in Buffalo, New York. Dr Pierce was President of the World Dispensary Medical Association and consulting physician and surgeon at the Invalid's Hotel and Surgical Institute, also in Buffalo. Dr Pierce guaranteed in the book's preface that all his suggestions had received the "sanction and endorsement of medical gentlemen of rare professional attainments and mature experience." The section on chronic bronchitis was followed by several pages of testimonials from sufferers of asthma, consumption, bronchitis, and lung abscess.

These excerpts from Dr Pierce's book were made available to RESPIRATORY CARE by Crystal L Dunlevy EdD RRT, Assistant Professor and Director of Clinical Education, Respiratory Therapy Division, School of Allied Medical Professions, The Ohio State University, Columbus, Ohio.

supplied, by proper ventilation, with a sufficient supply of fresh air. Every adult individual ought to have at least 800 cubic feet of air-space to himself, and this space ought to communicate freely with the external atmosphere by means of direct or indirect channels. Hence, a sleeping-room for one adult person should not be less than nine by ten feet in breadth and length and nine feet in heighth. What occurred in the Black Hole at Calcutta is an excellent illustration of the effect of vitiated air. One hundred and forty-six Englishmen were confined in a room eighteen feet square, with two small windows on one side to admit air. Three hours after their imprisonment, only twenty-three were alive.

VENTILATION OF SCHOOL ROOMS. The depression and faintness from which many students suffer, after being confined in a poorly ventilated school room, is clearly traceable to vitiated air, while the evil is often ascribed to excessive mental exertion. The effect of ventilation upon the health of students is a subject of universal interest to parents and educators, and at present is receiving the marked attention of school authorities. Dr F Windsor, of Winchester, Mass, made a few pertinent remarks upon this subject in the annual report of the State Board of Health, of Massachusetts, 1874. One of the institutions, which was spoken of in the report of 1873, as a model, in the warming and ventilation of which much care had been bestowed, was visited in December, 1873. He reports as follows: "I visited several of the rooms, and found the air in all, offensive to the smell, the odor being such as one would imagine old boots, dirty clothes, and perspiration would make if boiled down together;" again, in the new model school-house the hot air enters at two registers in the floor on one side, and makes (or is supposed to make) its exit by a ventilator at the floor, on the other side of the room. The master said "the air was supposed to have some degree of intelligence, and to know that the ventilator was its proper exit." Thorough ventilation has been neglected by many school officials on account of the increased expense it causes. In our climate, during seven months at least, pure atmospheric air must be paid for. The construction of vertical ducts, the extra amount of fuel, and the attendant expenditures are the objections which, in the opinion of many persons, outweigh the health and happiness of the future generation. It is necessary for the proper ventilation of our school rooms that an adequate supply of fresh air should be admitted, which should be warmed before being admitted to the room, and which should be discharged as contaminated, after its expiration. The proper ventilation of the school room consists in the warming and introduction of fresh air from without, and the discharge of the expired and unwholesome air from within. This may be accomplished by means of doors, windows, chimneys, and finally by ventilators placed, one near the level of the floor, and the other near the ceiling of the room. The ventilators ought to be arranged on the opposite sides of the room, in order to insure a current, and an abundant supply of air. When trustees and patrons realize that pure air is absolutely essential to health, and that their children are being slowly poisoned by the foul air of school rooms, then they will construct our halls of leaming with a due regard for the laws of hygiene, and students will not droop under their tasks on account of the absence of Nature's most bountiful gift, pure air.

VENTILATION OF FACTORIES AND WORKSHOPS. This is a subject which demands the immediate attention of manufacturers and employers. The odors of oil, coal gas, and animal products, render the air foul and stagnant, and often give rise to violent diseases among the operatives. From two to four hundred persons are often confined in workshops six hundred feet long, with no means of ventilation except windows on one side only. The air is breathed and rebreathed, until the operatives complain of languor and headache, which they attribute to overwork. The real cause of the headache is the inhalation of foul air at every expansion of the lungs. If the proprietors would provide efficient means for ventilating their workshops, the cost of construction would be repaid with compound interest, in the better health of their operatives and the consequent increase of labor. Our manufacturers must leam and practice the great principle of political economy, namely, that the interests of the laborer and employer are mutual.

VENTILATION OF OUR DWELLINGS. Not less important is the ventilation of our dwellings; each apartment should be provided with some channel for the escape of the noxious vapors constantly accumulating. Most of the tenements occupied by the poor of our cities are literally dens of

poison. Their children inhale disease with their earliest breath. What wonder that our streets are filled with squalid, wan-visaged children! Charity, indeed, visits these miserable homes, bringing garments and food to their half-famished inmates; but she has been slow to learn that fresh air is just as essential to life as food or clothing. Care should be taken by the public authorities of every city, that its tenement houses do not degenerate into foul hovels, like those of the poor English laborer, so graphically portrayed by Dickens. But ill-ventilated rooms are not found exclusively in the abodes of the poor. True, in the homes of luxury, the effect of vitiated air is modified by food, etc. Men of wealth give far more attention to the architecture and adornment of their houses, to costly decorations and expensive furniture, than to proper ventilation. Farmers, too, are careless in the construction of their cottages. Their dwellings are often built, for convenience, in too close proximity to the barn. Because they do not construct a suitable sewer or drain, the filth and refuse food is thrown out of the back door, where it accumulates and undergoes putrefaction; the vitiated air penetrates the interior of the house, and, there being no means of ventilation, it remains to be breathed by the occupants. The result is, that for the sake of saving a few dollars, which ought to be expended in the construction of necessary flues and sewers, the farmer often sees the child he prizes far more than his broad acres gradually decline, or suddenly fall a victim to fevers or malignant disease. Parents, make your homes healthy, let in the pure, fresh air and bright sunlight, so that your conscience may never upbraid you with being neglectful of the health and lives of your little ones.

CHRONIC BRONCHITIS

This is a subacute or chronic form of inflammation of the bronchial tubes, of a very persistent character and variable intensity. There are few diseases which manifest a greater variety of modifications than this.

SYMPTOMS. The symptoms of this disease vary greatly with its violence and progress. Cough is always present, and is very often the first symptom to attract the patient's attention. It is usually increased by every slight cold, and with each fresh accession becomes more and more severe, and is arrested with greater difficulty. The cough is always persistent, sometimes short and hacking, at other times deep, prolonged, and harsh. Sometimes it is spasmodic and irritating and particularly so when it is associated with affections of the larynx, or with asthma, involving irritation of the branches or the filaments of the pneumogastric nerve.

When the chronic follows the acute form of the disease, or follows inflammation of the lungs, the expectoration may be profuse from the first, and of a yellowish color and tenacious character. When the disease arises from other causes, the expectoration is generally slight at first, and the cough dry or hacking. This may continue some time before much expectoration occurs. The expectorated matter is at first whitish, opaque, and tenacious, mixed sometimes with a frothy mucus, requiring considerable coughing to loosen it and throw it off. As the disease progresses, it becomes thicker, more sticky, of a yellowish or greenish color, mixed with pus, and sometimes streaked with blood. In the latter stages, it becomes profuse and fetid, and severe hemorrhage may occur. Sometimes the cough and expectoration disappear when the weather becomes warm, to appear again with the return of winter, which has gained for it the appellation of winter cough. The sufferers feel as if something was bound tightly round the chest, rendering inhalation difficult. Soreness throughout the chest is often a persistent symptom, especially when the cough is dry and hard. Behind the breastbone there is experienced a sense of uneasiness, in some cases amounting to pain, more or less severe.

As the disease progresses, the loss of strength is more and more marked, the patient can no longer follow his usual employment, his spirits are depressed, and he gradually sinks, or tubercular matter is deposited in the lungs, and consumption is developed.

TREATMENT. Thorough attention to hygiene, with the avoidance of the causes concerned in the production and perpetuation of the disease, is necessary. The patient must be protected from the vicissitudes of the weather by plenty of clothing; flannel should be worn next to the skin, with a pad of flannel or buckskin over the chest, and the feet should be kept warm and dry. Exercise in the open air is essential. When the weather is so cold as to excite coughing, something should be worn over the mouth, as

a thin cloth, handkerchief, muffler, or anything which will modify the temperature of the atmosphere before it comes into contact with the mucous lining of the lungs. Good ventilation of sleeping-rooms is all-important; not that the air should be cold, but that it should be as pure as possible.

The diet must be nutritious, carbonaceous, and of sufficient quantity. Beef, milk, rich cream, plenty of good butter, eggs, fish, wheat bread from unbolted flour, supply the appropriate alimentary substances for perfect nutrition and the maintenance of animal heat.

To overcome the modified form of inflammation in the bronchial tubes, all sources of irritation should be avoided, as the inhalation of dust, or excessively cold air. It is in the cure of severe and obstinate cases of this disease that Dr Pierce's Golden Medical Discovery has achieved unparalleled success, and won the highest praise from those who have used it. Its value will generally be enhanced in treating this complaint by adding one-half a teaspoonful of the fluid extract of Veratrum Viride to each bottle. This can be added by any respectable druggist. Especially should it be thus modified if the pulse be accelerated so as to beat ninety or a hundred times in a minute. The "Golden Medical Discovery" should be taken in teaspoonful doses, repeated every two hours. When the cough is dry and hard, with no expectoration, it arises from irritation of some of the branches of the pneumogastric nerve, which this remedy will relieve. It may, however, be aided by inhaling the hot vapor of vinegar and water, or vapor from a decoction of hops, to which vinegar has been added.

The use of Dr Pierce's Golden Medical Discovery should be persisted in, taking it in frequent doses, every two or three hours, and keeping up its use until the disease yields and is perfectly stamped out. Do not expect a formidable disease of perhaps weeks' or months' duration to be speedily cured. Chronic diseases are generally slow in their inception and development and can only be cured by gradual stages. Perseverance in treatment is required. Many invalids do not possess the strength of purpose—the will power—to continue the use of the "Golden Medical Discovery" long enough to receive its full benefits. It is worse than useless for such to commence its use, for without persistency it cannot be expected to cure such obstinate maladies as chronic bronchitis.

Blood Gas Corner #29—

A Case of Oxygen-Induced Hypoventilation

Jonathon W Gietzen BS RRCP

A 73-year-old Caucasian woman came to the emergency room complaining of shortness of breath and lower back pain. She was alert, oriented, dyspneic, and stated that she was "worn out and needed her sleep." She was admitted to the hospital with a primary diagnosis of low back pain, due to degenerative changes in her lumbar vertebrae, and a secondary diagnosis of exacerbation of chronic obstructive pulmonary disease.

The patient had a smoking history of > 70 pack years, and was on nasal oxygen at home (1.5 L/min) 20-24 hours/day. Her weight was 100 lb (45.4 kg), height 61 inches (155 cm), heart rate (HR) 92/min, and respiratory rate (RR) 20/min. Breath sounds were decreased but equal bilaterally, and an occasional slight end-expiratory wheeze could be heard on forced expiration. The chest radiograph revealed marked emphysematous changes.

Intravenous morphine sulfate was administered to reduce her back pain. The respiratory therapist on duty was requested to place the patient on nasal oxygen at 2 L/min, institute continuous pulse oximetry, and draw an arterial blood gas (ABG) sample in 30 minutes. The results of arterial blood analysis were: pH 7.26, P_{aCO_2} 87 torr [12 kPa], HCO_3^- 37 mEq/L [37 mmol/L], P_{aO_2} 187 torr [24.9 kPa], S_{aO_2} 94%, and COHb 5%. At the time the ABG sample was drawn, oxygen saturation determined by pulse oximeter (S_{pO_2}) was 99%, and RR was 20/min. Bedside pulmonary function testing revealed: FVC 1.2 L (48% of predicted), FEV_1 0.82 L (42% of predicted), FEV_1/FVC 68%, V_T 0.25 L, and $\dot{V}_E$ 5.0 L.

Upon reviewing the results, the attending physician requested that the patient's nasal oxygen flow be reduced to 0.5 L/min and that an ABG sample be obtained in 30 minutes. The results of the second arterial blood analysis were: pH 7.44, P_{aCO_2} 50 torr [6.67 kPa], HCO_3^- 34 mEq/L [34 mmol/L], P_{aO_2} 33 torr (4.39 kPa), S_{aO_2} 65%. At the time the second ABG sample was obtained, S_{pO_2} was 70%, RR 35/min, and $\dot{V}_E$ 9.0 L.

Study Questions

1. Why do you think this patient exhibited such a dramatic change in ABG status with such a minor change in nasal oxygen flow?
2. What type of oxygen administration device should be used with this patient?
3. How should the appropriate oxygen flow or F_{IO_2} be determined for this patient?

Answers and Discussion on Next Page

Mr Gietzen is Director of Clinical Education and Adjunct Professor NDSU, St Luke's Hospitals—MeritCare School of Respiratory Therapy, Fargo, North Dakota.

Answers

1. Change in ABG Status. It is obvious that this chronically hypercapnic patient is dependent upon the hypoxic drive to breathe. The results of the first ABG sample, with the patient breathing 2 L/min of nasal oxygen, reveal oxygen-induced hypoventilation. The results of the second ABG sample reveal that as the nasal oxygen flow was decreased to 0.5 L/min, the patient's hypoxic drive was no longer obtunded and consequently ventilation improved.

2. Appropriate Oxygen Administration Device. Whenever a change in ventilation pattern is anticipated (eg, during sleep, sedation, or acute exacerbation of lung disease) in the hypercapnic, hypoxic-drive-dependent patient, the use of a high-flow oxygen device is most appropriate. A high-flow oxygen device (eg, air-entrainment mask) provides flow in excess of the patient's inspiratory flow and thus ensures a fixed F_{IO_2}.

When reporting the results of the second ABG sample to the physician, the respiratory therapist recommended that the patient be treated with a high-flow oxygen device. The physician agreed and the patient was placed on a 28% air-entrainment mask. Arterial blood analysis performed 30 minutes later revealed: pH 7.38, P_{aCO_2} 63 torr [8.39 kPa], HCO_3^- 36 mEq/L [36 mmol/L], P_{aO_2} 46 torr [6.13 kPa], S_{aO_2} 78%; and RR at this time was 26/min.

3. Appropriate F_{IO_2}. When a high-flow oxygen system is used, it is possible to accurately predict the F_{IO_2} needed to achieve a desired arterial oxygen tension. In a case such as this, in which arterial blood analysis at a known F_{IO_2} has already been performed, the appropriate F_{IO_2} can be predicted using a derivation of the alveolar air equation (see box).[1,2]

The therapist used this equation to calculate that approximately 30% oxygen would be required to achieve a P_{aO_2} of 55 torr [7.33 kPa], and made the recommendation to increase the F_{IO_2} to 0.30. The physician agreed and requested that an ABG sample be obtained 30 minutes after the F_{IO_2} change. The results of arterial analysis were pH 7.37, P_{aCO_2} 62 torr [8.26 kPa], HCO_3^- 36 mmol/L, P_{aO_2} 58 torr [7.73 kPa], S_{aO_2} 89%; and RR at this time was 22/min.

$$nF_{IO_2} = \frac{[dP_{aO_2}/(kP_{aO_2} \div kP_{AO_2})] + kP_{aCO_2}}{\text{barometric pressure - 47}},$$

where n is needed, d desired, and k known.

Discussion

Patients with chronic hypercapnia ($P_{aCO_2} \geq 50$ torr [6.7 kPa]) are likely to develop a blunted hypercapnic drive and exhibit an attenuated ventilatory response to increasing levels of P_{aCO_2}.[3] These patients will then rely on their hypoxic drive mechanism (peripheral chemoreceptors located in the carotid bodies) to maintain adequate minute ventilation. Activation of the hypoxic drive usually occurs when the P_{aO_2} drops below approximately 60 torr [8.0 kPa].[4] In patients with chronic hypoxemia, the hypoxic drive 'switch' may be shifted even lower.[3-5] Inappropriate dosage of oxygen to a hypoxic-drive-dependent patient may cause the hypoxic drive to become satisfied, thus eliminating the patient's 'backup' drive to breathe.[6]

It is therefore crucial that the respiratory therapist pay close attention to what level of oxygenation appears to obtund, or satisfy, the patient's respiratory drive, and then ensure that an F_{IO_2} is provided that will maintain oxygenation just below this respiratory-drive threshold and keep the patient breathing adequately.[7] To determine the level of oxygenation and corresponding F_{IO_2} at which the patient succumbs to a satisfied hypoxic drive, proper monitoring of patient status (eg, RR, HR, S_{pO_2}, cerebration) must be performed while F_{IO_2} is gradually increased from 0.21 (room air). When the hypoxic-drive threshold appears to be reached, arterial blood gas analysis must be performed. To determine the hypoxic-drive threshold and to provide appropriate oxygen therapy thereafter, it is necessary that an oxygen-delivery device be used that provides a constant, known F_{IO_2}.

Two types of oxygen-delivery devices are available: low-flow devices and high-flow devices. A low-flow oxygen-delivery device is one that does not provide the entire inspiratory gas needs of the patient; and, as a result, cannot provide a known, fixed F_{IO_2}. As the patient's ventilatory pattern changes, the F_{IO_2} will change. As a result, when using a low-flow oxygen device, titrating the oxygen flow to achieve appropriate oxygenation at one moment during a time of crisis will not guarantee that that level of oxygenation will be maintained indefinitely. Although calculations are available that the practitioner can use to quickly estimate F_{IO_2} when low-flow oxygen devices are being used,[6,8-10] these calculations are useful and practical only when a relatively stable ventilatory pattern is present. If an attempt is made to use a low-flow oxygen device when a patient is in a labile

period, the respiratory therapist will be unable to accurately adjust the oxygen flow to compensate for rapid changes in breathing pattern and may either overoxygenate or underoxygenate the patient. Generally speaking, low-flow oxygen devices can be used safely in patients who have a reliable respiratory drive, a V_T of 300-700 mL, and a RR < 25/min.[6,8] Notable reasons to use low-flow oxygen devices include the relative comfort and cost savings compared to high-flow oxygen devices.[8,11]

A high-flow oxygen device, by definition, meets all of the inspiratory gas needs of the patient, and therefore is capable of providing a steady F_{IO_2}, regardless of patient breathing drive, respiratory rate, or tidal volume.[6-9] Therefore, a high-flow oxygen device is the appropriate oxygen-delivery device to use when attempting to determine the hypoxic-drive threshold, and when desiring to provide safe oxygen therapy to the hypoxic-drive dependent patient with a labile ventilatory pattern.

Conclusions

A patient suspected of being hypoxic-drive dependent should be treated with a high-flow oxygen-delivery system during any labile periods of his or her disease process. The patient's ABG status should be monitored closely and an F_{IO_2} provided that maintains oxygenation just below the level at which the hypoxic drive is obtunded.

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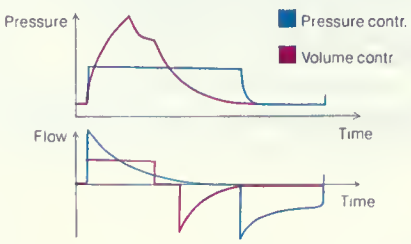

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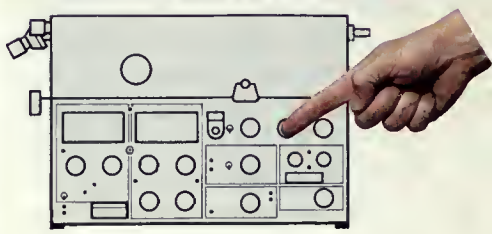

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Can the Pressure Tracings Be Trusted?

Alexander B Adams MPH RRT and John J Marini MD

During the course of inserting a pulmonary artery (PA) catheter a normal sequence of pressure tracings was observed. Immediately following catheter insertion, a chest radiograph was obtained (Fig. 1).

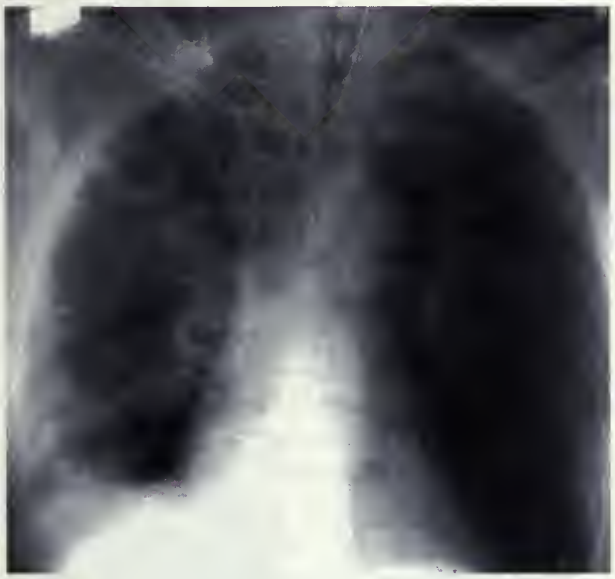

Fig. 1. Chest radiograph obtained immediately after insertion of a pulmonary artery catheter.

Questions

Radiographic Findings: What does the chest radiograph reveal about PA-catheter placement?

Pressure Tracings: Why can't pressure tracings be trusted to confirm proper placement of a PA catheter?

Mr Adams is a Research Technician, Pulmonary Research, St Paul Ramsey Medical Center; and Dr Marini is Director of Medical Intensive Care, St Paul Ramsey Medical Center, and Professor of Medicine, University of Minnesota—St Paul, Minnesota.

Answers

Radiographic Findings: The chest radiograph (Fig. 2) reveals that the coronary sinus (CS) was inadvertently entered during attempted catheterization of the PA.

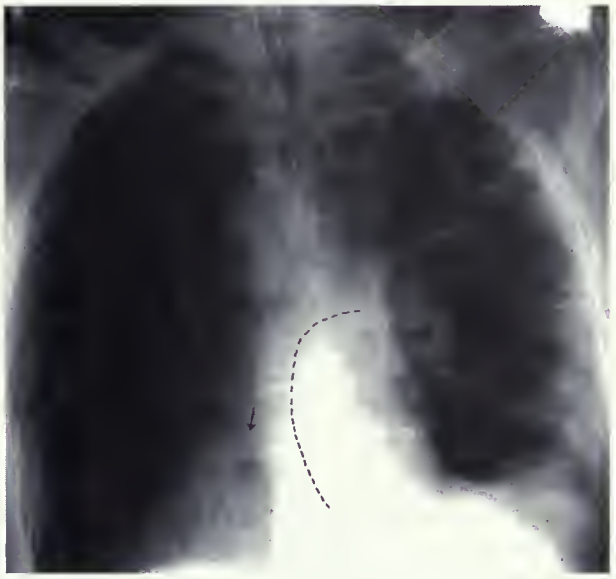

Fig. 2. Chest radiograph obtained immediately after insertion of a pulmonary artery catheter (identical to radiograph shown in Figure 1). The catheter was inserted using the right internal jugular approach. The catheter entered the right ventricle through the tricuspid valve. Instead of entering the pulmonary artery, the catheter doubled back on itself and reentered the right atrium where its tip then lodged in the coronary sinus (arrow). The dotted line shows the typical path that a properly placed left pulmonary artery catheter would have taken.

Pressure Tracings: CS pressures measured during cardiac catheterization have been reported to mimic PA, arterial, right-ventricular, and right-atrial

pressures.[1] CS-pressure tracings most often resemble those of the right atrium.[1] Apart from the diagnostic and therapeutic errors that could result from misinterpreting CS-pressure tracings as PA pressures, CS catheterization could, at least theoretically, irritate or perforate the CS.

Discussion

Other than an aberrant sequence of pressure tracings that may be recognized during catheter insertion, there are at least two other nonradiographic clues that may alert the clinician to the possibility of CS catheterization. First, difficulty is usually experienced in advancing the catheter from the right atrium to the pulmonary artery. Second, CS blood is depleted of oxygen because it perfuses the metabolically active myocardium. Oxygen saturation of CS blood is typically 40-50%, which is much lower than the 65-80% oxygen saturation typical of mixed-venous blood drawn from the PA. If the low saturation of CS blood is mistaken for low mixed-venous saturation, the clinician may assume that there is a low cardiac output and intervene inappropriately.[2] Prompt recognition of CS catheterization is critical; complications reported during cardiac catheterization include phlebitis, perforation, myocardial ischemia, and infarction.[3,4]

PA catheters frequently migrate only a short distance (a few centimeters) from the targeted, gravity-dependent portion of the PA. A catheter may migrate distally to oppose an arterial wall, which may partially or completely occlude the catheter opening to cause pressure damping. Such damped readings may also be elevated, influenced by the high pressure generated by the continuous-flow system. Initially well-placed catheters can also migrate to non-dependent regions of the lung (Zone 2) where, upon balloon inflation, alveolar pressures may be recorded and striking respiratory variations may be observed.[5] Such problems are not as likely to occur in diffuse lung injury.[6]

Inappropriate catheter insertions or long-distance migrations are less frequent, but the potential consequences are more serious. Catheters have been inserted into the pleura, peritoneum, renal vein, aorta, and vertebral artery.[7] Coils, kinks, loops, and knots have formed in PA catheters during insertion or as a result of migration.[8-10] In one reported case of catheter knotting the papillary muscles were literally tied up.[11] Venotomy and surgical intervention have sometimes been required to undo or extract knots.[12,13]

Inadvertent CS catheterization during PA-catheter insertion was first identified by Kozlowski in 1986.[14] Baciewicz[2] subsequently reported PA-catheter migration to the CS during coronary bypass surgery. In the latter case, migration to the CS was not suspected on the basis of abnormal pressure tracings, but rather by the abnormally low oxygen saturation of the PA-catheter blood sample.

To the best of our knowledge, the case we report is the third reported occurrence of CS catheterization. In our case, the catheter was withdrawn from the CS and advanced to the PA without incident. There were no adverse clinical consequences of the malplacement.

This case report underscores the importance of obtaining a chest radiograph immediately following PA-catheter insertion, not only to rule out induced pneumothorax but to confirm proper placement of the catheter. To enable careful examination of catheter position, the chest radiograph should be centered properly and have good penetration. An infrahilar, left-directed catheter tip that fails to cross the midline is characteristic of CS catheterization. Considerable care must be exercised during PA-catheter insertion; the radiographic image pattern and catheter length required to wedge in the CS may closely mimic those appropriate for left PA catheterization. If the left PA appears to be catheterized, careful radiographic identification of the left PA and the course of the catheter are essential for confirmation. Subsequent chest radiographs should also be examined carefully for catheter position because delayed catheter migration, although unusual, can occur. Before a clinician can responsibly interpret PA-catheter pressures, correct placement of the catheter must be confirmed.

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Clinical Applications of Ventilatory Support, edited by Robert R Kirby, Michael J Banner, and John B Downs. Hardcover, 527 pages, 244 illustrations. New York: Churchill Livingstone, 1990. $69.95.

Clinical Applications of Ventilatory Support is actually the second edition of **Mechanical Ventilation** with a change of editorship, a couple of new chapters, and revision of previously published chapters. The editors are known for their expertise in the field of ventilatory support, and Drs Kirby and Downs have been credited with the development of IMV and APRV. As such, they are well qualified to tackle such a project, although their bias toward the subject is evident to this reviewer throughout most of the text.

Chapter 1, by E Trier Mörch, covering the history of mechanical ventilation, has been "updated" (that is, if updating history is possible), and remains one of the excellent parts of this text. Dr Mörch's personal experience with history, anecdotes, and good-natured writing make this chapter a joy to read. The chapters on ventilator-performance evaluation and neonatal and pediatric ventilatory support are updated from the previous edition and are both excellent.

Drs Neil MacIntyre and Christine Stock co-authored the chapter on weaning, and together provide a balanced look at weaning the patient from ventilatory support, appropriately representing all the 'camps' and their own viewpoints. This, too, is an excellent chapter.

I believe that the chapter on ventilatory support during anesthesia, an all too often overlooked topic, is the best new chapter. The unique challenges of mechanical ventilation in the operating room of monitoring and of the limitations of current anesthesia ventilators are discussed.

The new chapter on concepts of microprocessor-controlled ventilation systems provides an introduction to computers and how they allow the new generation of ventilators to perform their intended functions. This chapter is informative but slow reading.

The last chapter written by an engineer from ECRI concerns equipment safety, and covers the ECRI experience over the last 18 years with resuscitation, anesthesia, and respiratory care equipment. Although the material is interesting, it is, for the most part, review. The chapter's references are all from ECRI alerts or other ECRI publications, which serves to point up what I believe to be tunnel vision shown throughout the chapter. Perhaps this prompted the editors to add the short note explaining the reasons the chapter was included. Although I appreciate the many contributions made by ECRI over the years, this chapter was too self-glorifying for my taste. It also adds little to the understanding of mechanical ventilation.

On the whole, **Clinical Applications of Ventilatory Support** is an excellent text that should be useful to physicians, respiratory care practitioners, nurses, and others interested in mechanical ventilation. I recommend it to anyone concerned with the care of mechanically ventilated patients and mechanical ventilators.

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Resuscitation Handbook, Peter JF Baskett. Soft-cover, 160 illustrations, 128 pages. Philadelphia: JB Lippincott. $19.95.

Resuscitation Handbook is a manual that details the resuscitation of the patient following cardiorespiratory arrest or major trauma. In effect, it is a condensed version of the Advanced Cardiac Life Support (ACLS) and Advanced Trauma Life Support (ATLS) manuals produced by the American Heart Association and the American College of Surgeons. The author, Peter Baskett, is an anesthesiologist from the United Kingdom. Dr Baskett has long been involved in the field of emergency and disaster medicine and is widely known for his expertise in these areas. The text is divided into five sections: Introduction, Cardiac Life Support, Trauma Life Support, Pain Relief, and Training Requirements.

The Introduction provides a brief description of the causes of cardiorespiratory arrest, who should or shouldn't be resuscitated, definitions of death (eg, brain death and cortical death), and practical information related to infection hazards during resuscitation.

Section 2 details the ABCs of resuscitation, techniques of CPR, and ACLS treatment of arrhythmias. The illustrations of airway-control techniques and anatomy in this section are excellent. Each technique is described in narrative, and important details and complications are highlighted in colored boxes offset from the text—one of the major assets of the text.

Illustrations of equipment in this section are adequate but without great detail. For instance, a self-inflating bag (shown in gray) is recognizable but

lacks detail that would provide real understanding of its components of operation. Of course, this is not an equipment text and description of the equipment's use is done very nicely.

In Section 3, trauma life support is addressed based upon ATLS courses and emphasizes diagnosis of life-threatening injuries such as tension pneumothorax and shock and their treatment. The same lucid, concise writing is present in this section and the many illustrations are excellent.

Pain relief is covered in five pages that describe the appropriate use and complications of opiates, nitrous oxide-oxygen mixtures, and local and general anesthetics. This is a topic not always associated with resuscitation but I believe it is quite fitting here.

Training requirements are listed in Section 5, and consist of a 2-page chart describing who should learn to do what. For instance, it describes which airway techniques should be taught to the lay public and which to medical students.

The content of this text is excellent, and the numerous illustrations are instructive. As I mentioned earlier, much of this information is provided in ACLS and ATLS manuals, but those pale in comparison to Dr Baskett's smooth writing style and insight. Because Dr Baskett is from the United Kingdom, he does not mention respiratory care practitioners—he isn't used to having them around. However, I would still recommend this text for anyone interested in the techniques of resuscitation. It is easy to read, well—illustrated, and pertinent for every member of the health care team.

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Letters

Well-Being of Caregivers vs Patient Needs: A Review of the Ribavirin Evidence

Health-care professionals should base treatment decisions on scientific information and not on subjective decisions that could restrict optimal patient care. We believe that fears over the safety of caregivers who administer aerosolized medications such as ribavirin (Virazole) may have resulted in restrictions in patient care. An editorial in this journal entitled "Ribavirin and Pentamidine Aerosols: Caregivers Beware!"[1] recently described these fears. In order to balance the critical needs of patients with the well-being of caregivers, a thorough review of scientific information is warranted.

It is prudent for caregivers to minimize their unnecessary exposure to any medication or chemical substance. However, restriction or elimination of ribavirin use solely to avoid caregiver exposure is not scientifically justified based on the safety and tolerance record of ribavirin use in humans. Prior to 1985 in the United States, an estimated 2,000 to 4,000 infants each year died from severe RSV infections.[2] The results of several clinical studies that investigated the efficacy of aerosolized ribavirin in the treatment of severe RSV infections support the conclusion that ribavirin is effective.[3-8]

Smith et al reported a dramatic decrease in days of mechanical ventilation, supplemental oxygen, and days of hospitalization in intubated infants receiving ribavirin compared to water placebo.[9] Additionally, two patients in the placebo group worsened. One of these patients died.

Since 1972, ribavirin has developed an extensive safety record. About five million patients worldwide have been treated with the dosage forms of this drug with no long-term or irreversible adverse reactions reported.[10,11]

The possibility of environmental exposure to aerosolized ribavirin and the description of teratogenic potential in animal species has raised concerns among health-care workers. Specifically, a single oral dose of 2.5 mg/kg produced teratogenicity in hamsters,[12] as did a single oral dose of 10 mg/kg in the rat.[13,14] Doses as low as 1 mg/kg administered orally resulted in embryo death in rabbits.[15] However, no teratogenic effects were noted in a small number of baboons receiving 120 mg/kg administered orally in 4-day pulses during critical periods of gestation.[15]

In one multicenter study, the potential exposure to ribavirin aerosol in the environment was assessed in nurses caring for infants and children with severe lower-respiratory-tract infections due to RSV.[16] For several weeks prior to participation in the study, these nurses had been working in areas in which ribavirin aerosol was being administered. Fifteen nurses worked directly with infants receiving ribavirin aerosol for 20 to 35 hours over the 3-day observation period.[16] No toxic or adverse effects of ribavirin aerosol were observed in any of the 15 nurses administering ribavirin aerosol nor in 4 other nurses (controls) who were working in the area where the drug was being administered. Ribavirin was not detected in erythrocytes, plasma, or urine collected after the exposure period.

Harrison et al[17] similarly measured plasma, erythrocyte, and urine levels of ribavirin in 10 nurses and 2 respiratory therapists. One red blood sample was found to have a ribavirin level of 0.44 μg. Concurrent serum and urine samples in this subject were negative. None of the other subjects had any drug detected in any of the plasma, erythrocyte, or urine samples.

What is the degree of exposure to caregivers who administer aerosolized medications in models of experimental exposure? Montgomery et al[18] have reported in abstract their study that determined that the amount of second-hand exposure of caregivers to aerosolized pentamidine is 1×10^{-6} of that received by patients. A similar unpublished study seems to suggest similar findings with ribavirin (personal communication, V Knight MD).

In efforts to minimize escape of aerosolized ribavirin, the manufacturer has developed and offers On/Off switches for the small particle aerosol generators (SPAG) that allow the practitioner to shut off the aerosol flow before administering direct patient care. There are also specially designed aerosol delivery hoods that greatly reduce the ambient levels of aerosol particles.

Several independent investigators have reported success with other ideas designed to reduce caregiver exposure to aerosolized ribavirin. One such idea is the use of containment and scavenging systems. Charney et al[19] reported no detectable levels of drug in breathing-zone and area sampling when they used a double containment system in which medication is delivered to the patient in an inner compartment and is scavenged by two

vacuum pumps with tubing positioned in the outer compartment. Other institutions are developing comparable systems.

Torres et al[20] achieved similar significant reductions of released ribavirin in a double containment system that was scavenged with wall suction. Using SPAG-2 units that were not equipped with On/Off switches, Stevens[21] obtained and reported in an abstract significant reductions in a single compartment system that was scavenged with wall suction.

Exposure may also be reduced by modifying the drug dosing schedule. Englund et al[22] recently reported on the treatment of infants hospitalized with severe lower-respiratory-tract RSV infections by administering high-dose, short-duration therapy: 6 grams of ribavirin diluted in 100 mL of sterile water and delivered over 2 hours 3 times a day. Caregivers were able to attend to the patients without concern for exposure during the 6 hours between doses. Additional studies of the efficacy of this dosing schedule are required prior to recommendation of its routine use.

The Canadian Pediatric Society published the following statement regarding ribavirin administration:[23]

> Consequently, the risk to pregnant staff involved in the care of infants being treated with ribavirin appears to be negligible. Extraordinary methods to protect staff, such as wearing special masks or respirators, goggles, gowns, etc are not warranted.

The Hazard Evaluation and Technical Assistance Branch of the United States National Institute for Occupational Safety and Health has stated:[24]

> At this time no information exists which describes an occupational exposure/effect relationship in humans, nor are there any existing recommended standards that suggest a safe level of exposure. However, given the teratogenic effects observed in many of the animal models tested, prudent public health and occupational health practice dictates that caution be exercised when using this drug and that appropriate steps be taken to reduce worker exposure.

Our current thoughts, which are also reflected in the manufacturer's current policy on ribavirin administration and safety, are: When used as directed, aerosolized ribavirin poses no significant risk to males and nonpregnant females. The following recommendations will provide a means to administer aerosolized ribavirin safely and effectively while significantly reducing potential risks for all health-care workers (including pregnant females).

- Hospitals should establish appropriate procedures and training for personnel.
- Health-care workers should shut off the aerosol delivery flow before administering direct patient care. Patients requiring oxygen may need a supplemental delivery source.
- Staff should ensure adequate room ventilation (at least 6 room-air changes/hour).
- Supervisors should not assign pregnant health-care workers to administer care to patients receiving aerosolized ribavirin treatment. Likewise, visiting pregnant mothers should not be in the room while this therapy is administered to patients.

In those cases in which individuals feel additional measures are desirable, the following steps might be considered:

- Utilize the new aerosol delivery hood available from ICN or alternative containment systems as cited above.
- The 3M Corporation #9970 personal-use mask provides high levels of protection when properly fitted.

For the sake of those infant patients who could benefit from ribavirin therapy, a balance between the critical needs of patients and the well-being of caregivers must be established.

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Dr Kacmarek responds:

In response to my recent editorial,[1] Dr Krilov et al[2] emphasize that we must "balance the critical needs of patients with the well-being of caregivers." I agree completely with their statement and would add that we must also take all steps necessary to prevent caregiver exposure to potentially dangerous drugs.

It is always difficult to argue against the treatment of small children, and I will not do so, but I must point out that I believe that the literature that Dr Krilov and his coauthors have referenced supporting the efficacy of ribavirin[3-8] is weak at best. All of the published studies are of small groups, with most using clinical scores of severity of illness or practitioner evaluation of specific indices (eg, cough, presence of rales) as indications of drug effect. Some of the studies use what I believe to be relatively weak statistical analysis to establish significance. The one study cited that does appear to indicate efficacy in mechanically ventilated patients has been published only in abstract form.[9]

Dr Krilov and his associates have correctly summarized the data on the teratogenicity of ribavirin and correctly imply that the risks are remote at best. However, the ICN literature states that ribavirin is "contraindicated in women and girls who are or may become pregnant during exposure to the drug."[10] In addition, in my experience many practitioners complain of upper and lower airway irritation and eye irritation when they are exposed to the drug. As a result, it would be irresponsible for us not to err on the side of ultra conservatism, particularly when systems[11] are

available to ensure that mean time-weighted aerosol-exposure levels to ribavirin are kept below maximum allowable levels.[12,13] One may argue that cost of protecting caregivers is high. I argue that it is low compared to the actual cost of the drug itself, particularly when actual cost is compared to the established efficacy of the drug. Again, I am not arguing against the use of ribavirin but arguing for a rational use of this drug, with all possible precautions taken to minimize or eliminate the exposure of practitioners to the drug.

In my institution, we are administering ribavirin but only to those patients at greatest risk—specifically, patients with positive RSV cultures who also either (1) have bronchopulmonary dysplasia, (2) have cardiac disease, (3) are immunosuppressed, or (4) are otherwise healthy but present critically ill. This season (1990-91) we have administered ribavirin to 3 mechanically ventilated patients and 3 patients in double hoods. All were treated in negative-pressure HEPA-filtered isolation rooms that received 6 air-volume exchanges per hour. Each SPAG unit was equipped with an On/Off switch. With mechanically ventilated patients, we placed 2 filters in the expiratory line and ensured that patients were intubated with endotracheal tubes of proper size to eliminate oral leaks. In addition, the SPAG unit was turned off for one minute before the infant was disconnected from the ventilator.

In spontaneously breathing patients, we either used the setup by Charney et al[11] or the ICN hood inside a large cuboidal tent equipped with two ICN scavengers. Our system, as does the Charney et al system, maintains mean time-weighted average-exposure levels below that recommended by the California Department of Health[12] and the Massachusetts Department of Labor and Industries.[13] Prior to removing a child from one of these enclosures, we turn the SPAG unit off, turn on a secondary oxygen source, and wait 5 minutes before opening the tent. If a child has to be removed because of an emergency, caregivers are instructed to remove the child completely from the tent, with minimal opening of the enclosure, shut off the SPAG unit, and wait 5 minutes before placing the child back into the enclosure. During both of these procedures, the scavenger units run continuously. In addition, we wear barrier protection (mask, gloves, and gown) whenever the drug is administered. All practitioners are instructed to limit their time in the room.

Finally, as I stated in my editorial "to many, these guidelines may seem to be an unnecessary overreaction. However, I believe that too few data are available to justify a less conservative approach when the well-being of caregivers and future offspring is at stake."

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Caveats Related to Use of the Novametrix C/D Adaptor during Neonatal HFOV

Having read "Bench Evaluation of the Novametrix Neonatal C/D Endo-

tracheal Tube Adaptor for Use during High-Frequency Ventilation,"[1] we believe some caveats to the use of other oscillatory/flow interuptor devices are in order.

Proximal high-frequency oscillatory ventilation (HFOV) amplitude bears little resemblance to that measured distally and is directly dependent on the time constants of the delivery circuit (which involves ETT diameter and length[2,3] and any resistance added by the adaptor). As the authors point out, the adaptor increased airway resistance, particularly with the 2.5-mm-ID tube. In HFOV systems, virtually all of the system inertance resides within the ETT.[4] Pressure drops due to resistors may best be determined by recording distal pressure.[2,5] We have found in our clinical experience with HFV that the single variable that appears to have the most influence on ventilation is the amplitude (therefore, tidal volume) delivered at the distal endotracheal tube. This observation has been confirmed by several authors;[3,6,7] thus, measurement of distal pressure would have been the ideal test for changes in resistive load and its effect on ventilation. A more complete evaluation of the adaptor might include these measurements as compared to the standard ETT connector.

Because we are familiar with the SensorMedics 3100 HF ventilator and high frequency devices from other vendors, we conclude that the SensorMedics 3100 has a greater capacity to compensate for the loss of distal amplitude caused by increased airway resistance by increasing the power setting. Users of other devices may not have this ability, and should evaluate the adaptor in this context.

Given the complexity and confusion surrounding the mechanisms of gas exchange during HFV,[6] we're uncertain of the validity of the use of a single-compartment lung model to ascertain that pulmonary ventilation is not affected by the use of this device. Unfortunately, the appropriateness of some in-vitro models of an RDS lung is problematic; however, the authors could have followed a previously described model,[3] including adiabatic stability to standardize their work with that of others.

Finally, it has been our experience that the proximal temperature probe on the circuit supplied by Infrasonics occludes the narrow opening of the C/D adaptor.

We agree that the authors' call for further clinical testing is warranted.

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The authors respond:

We thank Mr Wagner and Mr MacDonald for their thoughtful comments on our paper, and are delighted to respond.

We agree that distal airway pressure would have been an indicator of the effect of resistive load on ventilation; however, our goal was to determine whether the inclusion of the Novametrix Neonatal C/D endotracheal tube adapter (CD) would affect the ability of the SensorMedics 3100 (SM) to eliminate CO_2 through the mechanical circuit, which included the endotracheal tube (ETT) and connector. It is true that the SM can compensate for loss of distal amplitude because of the design of the driver and circuit; however, we maintained a constant proximal amplitude throughout the evaluation. If there was a difference in distal amplitude, it did not affect the rate of CO_2 elimination through the ETT, its connector, and the circuit.

We did not conclude that pulmonary ventilation was unaffected by the use of this device. Our conclusion pertains entirely to the performance of SM and its circuit. We speculate that CD may be a useful adjunct to ventilation by SM in neonates, but are unable to validate that claim from the data we report. Further studies are needed to substantiate this application.

Finally, it is true that some difficulties may arise when CD is used with other high-frequency ventilator-circuit configurations. We make no claims about the performance of these; however, we have described a

simple method for evaluating the effect of circuit modifications on ventilator performance that may be applied to a variety of high-frequency systems now in clinical use.

Again, thank you for your comments and interest in our work.

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A Home Oxygen Supplier's Perspective on Oxygen-Conservers

As a respiratory care practitioner who operates a home care/home oxygen service, I am responding to Dr Shigeoka's special article, "Oxygen-Conservers, Home Oxygen Prescriptions, and the Role of the Respiratory Care Practitioner"[1] (Mar 1991 issue). The article is a quite accurate, short summation of some of the problems and concerns regarding the controversy of using oxygen-conserving devices and their impact on cost and patient care.

We have evaluated a number of oxygen-conserving devices over the past couple of years—SCOOP transtracheal catheters, reservoir nasal cannulas and pendant reservoirs, and demand valves. None of them is ideal, and patient acceptance of the first two has been only average, at best. The demand oxygen valve, as Dr Shigeoka noted, leaves much to be desired in dependability and the anticipated long-term cost of maintaining it without reimbursement.

Two primary concerns that were not addressed by Dr Shigeoka are (1) the impact of decreased reimbursement on the oxygen supplier, and (2) the interface between the supplier and the physician if, as Dr Shigeoka wrote, the physician is the most appropriate person to select the equipment. This has particular impact if the physician wishes to select the flowrate and modality (eg, liquid oxygen at 5 L/min) but refuses to approve any type of conserving device. I don't know of a dealer that could accept such a referral based on current Medicare and Medicaid reimbursement policy.

This issue is certainly at the root of the controversy regarding the recent proposal by the American Association for Respiratory Care in reference to hospital practitioners' making such decisions.[2] Such decisions must include all the players, and a very important player in home oxygen therapy is the oxygen supplier. The oxygen supplier must have the prerogative to refuse or decline the referral based on economic considerations. I do not accept the proposition that the physician is always more objective and altruistic than oxygen suppliers; we all—both physicians and suppliers—provide our share of uncompensated care. But to accept a patient, or a series of patients, as referrals, knowing at the initiation of therapy that the reimbursement would not cover the cost, would soon preclude such suppliers from continuing in business.

On the second issue, there are occasional patients who do not tolerate oxygen-conserving devices, specifically demand valves. I would certainly concede that those patients may be candidates for transtracheal catheters or reservoir cannulas. However, we also may face the problem of patient acceptance of those devices. We have had three patients in the last two years who desaturated significantly when provided with demand valves because of their inability to trigger the valves. I am aware that demand valves can be calibrated closely for individual patients; however, my contention is that these valves are not a panacea and should not be used indiscriminately or across the board for every patient referral for purely economic reasons.

I congratulate Dr Shigeoka for an excellent overview of some of the problems we face in home oxygen therapy. I believe we agree that oxygen-conserver technology must still be applied very carefully, with close attention to cost, appropriate therapy for the individual patient, and communication and input from all the players in the home-care arena—the physician, the patient, and the oxygen supplier. The respiratory care practitioner may be involved on both sides of this issue and can indeed, as mentioned by Dr Shigeoka, be very informative and helpful in selecting the most appropriate oxygen-delivery system.

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Dr Shigeoka responds:

I thank Mr Good for his comments. Concerning his first point: Another benefit of allowing vendors a chance to work with the patient and family before discharge is that this provides time to discuss any problems in the

discharge plan. Most physicians appreciate learning when a prescription is unreasonable, either logistically or financially. Of course, the explanation should be lucid and presented diplomatically, along with an alternative that should be in the best interest of the patient.

Concerning Mr Good's second point: Therapy must always be tailored to the needs of the patient. Oxygen-conserving devices may be appropriate for most but not all patients. The advantages and disadvantages must be carefully considered.

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Salt Lake City, Utah

Calendar of Events

Not-for-profit organizations are offered a free advertisement of up to eight lines to appear, on a space available basis, in Calendar of Events in RESPIRATORY CARE. Ads for other meetings are priced at $5.50 per line and require an insertion order. Deadline is the 20th of month two months preceding the month you wish the ad to run. Submit copy and insertion orders to: Calendar of Events, RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229.

AARC & AFFILIATES

May 7-10 in Brandon, Florida. The FSRC Sunshine Seminar is hosted by the Hillsborough County Respiratory Care Managers' Group at Saddlebrook Golf and Tennis Resort. Topics will range from the implications of CLIA '88 and *Pneumocystis carinii* pneumonia to directions for the future of the profession, with specialty workshops in management, critical care, neonates, and peds. Contact Arlen Black at (813) 238-8631.

May 10 in Industry Hills, California. CSRC, Chapter IV, & Kaiser Permanente present Pediatric Pulmonary Care at Sheraton Hotel and Resort. The meeting features CV/HFV in PICU and cardiac surgery topic and a poster session. CSRC Scholarship Golf Tournament, top 25 rated courses in the U.S., May 11. Contact Dennis Vinson (213) 667-5176.

May 16-17 in Wichita, Kansas. The KRSC presents its 14th Annual Education Seminar at the Airport Hilton. Topics range from future directions of the profession to PFT, asthma, and critical care issues. Scheduling allows for golf, exhibits and a great time for everyone. Contact Don Richards MS RRT, VA Medical Center,(316) 685-2221.

May 28-31 in Jekyll Island, Georgia. The Georgia/South Carolina Region VI presents its 15th Annual Conference and Assembly at the Holiday Inn, Jekyll Island. Contact Mike Payne RRT, 730 South Pleasantburg Dr, Suite 525, Greenville SC 29607. (803) 879-0130.

May 29-31 in Brainerd, Minnesota. The MSRC invites all practitioners to its spring educational meeting. An excellent educational program is featured in the enjoyable setting of Madden's Resort in Northern Minnesota. Contact Gary Johnson, North Country Regional Hospital, 1100 West 38th St, Bemidji MN 56601. (218) 751-5430 (7 AM—9:30 PM CST).

June 12-14 in Vail, Colorado. The CSRC State Convention's theme "Bringing It All Together" focuses on the crossover between hospital and home care. A golf tournament is featured for the morning of the 12th, followed by a barbecue picnic in the evening. Contact Jim Bowman, Vencor Hosn, 1920 High St, Denver CO 80218, (303) 320-5871.

June 12-14 in St Charles, Illinois. The ISRC presents its annual convention, "It's a Jungle Out There," to be held at Pheasant Run. Contact Trudy Watson RRT, Black Hawk College, 6600 34th Avenue, Moline IL 61265. (309) 796-1311, ext. 3303 or Vince Madama RRT, Rock Valley College, 3301 N Mulford Drive, Rockford IL 61103. (815) 654-4413 or (815) 654-4410.

June 27-29 in Monterey, California. The CSRC holds its 23rd annual meeting at the Doubletree Inn and Monterey Convention Center. Conference topics include "Liquid Perfluorchemical Ventilation," "DNAse Aerosol Therapy in Cystic Fibrosis," "Adult Exosurf" and Professor's Rounds, a 4-hour presentation featuring Neil MacIntyre MD, David Pierson MD, John Marini MD, and Robert Kacmarek PHD RRT. Contact John Bigler, Executive Director, CSRC, 24307 Magic Mountain Parkway #288, Valencia Ca 91355. To register call (800)-543-CSRC (2772).

July 10-12 in Houston, Texas. The TSRC meeting features AARC President Patrick Dunne, Kevin Shrake, Diane Lewis, Connie Podesta, and Ulf Borg. For information contact TSRC Executive Office, PO Box 515239, Dallas TX 75251. (214) 239-8772 or fax (214) 239-6418.

July 12-14 in Vail, Colorado. The AARC presents the Summer Forum. See the April issue of AARC Times for more information or call the AARC Convention Department at (214) 243-2272.

OTHER MEETINGS

May 12-15 in Anaheim, California. The American Lung Association and the American Thoracic Society host an International Conference in Anaheim. Contact Maureen J O'Donnell, Associate Director, Professional Development, American Lung Association, 1740 Broadway, New York NY 10019-4374.

May 17-18 in Las Vegas, Nevada. The American Lung Association of Nevada sponsors the 6th Annual Southern Nevada Respiratory Health Conference at the Sahara Hotel. Contact American

Lung Association of Nevada, PO Box 44137, Las Vegas NV 89116. (702) 454-2500.

June 7-9 in Hilton Head Island, South Carolina. "Sleep Disorders and Other Related Problems in Infants and Children" is held at the Westin Resort, with guest faculty Richard Ferber MD. Contact Darlene Baugus, CME Coordinator, Education Department, Scottish Rite Children's Medical Center, 1001 Johnson Ferry Rd, Atlanta GA 30363. (404) 250-2138.

June 16-23 on Caribbean Cruise. Embark on a "Cruise for Pulmonary Patients & Friends" aboard the S.S. Seabreeze. The seven-night cruise travels from Miami to the Eastern Caribbean (San Juan, St Barts, St Thomas) with professional medical supervision. Enjoy the wonderful world of therapeutic relaxation. Contact Dave Robbins (LIFE Unlimited) in Miami at 1-800-345-0269.

June 25-27 in Caln Township, Pennsylvania. Sky FlightCare hosts a flight physiology and aeromedicine course. "The Basics and Beyond: Aeromedical Concepts" offers the principles of flight physiology and aeromedicine to RNs, PAs, EMT-Ps, and RCPs. Contact Jeffrey Hamilton, President, ATS Inc, 368 Denbigh Village Centre, Suite 153, Newport News VA 23602. (804) 874-4030.

Notices

Notices of competitions, scholarships, fellowships, examination dates, new education programs, and the like will be listed here free of charge. Items for the Notices section must reach the Journal 60 days before the desired month of publication (January 1 for the March issue, February 1 for the April issue, etc). Include all pertinent information and mail notice to RESPIRATORY CARE Notices Dept, 11030 Ables Lane, Dallas TX 75229.

AARC SUMMER FORUM—July 12-14, 1991

Come and "climb the highest mountain" with your fellow therapists at the AARC Summer Forum in Vail, Colorado, at the Westin Hotel. Contact the AARC Conventions Dept. at (214) 243-2272.

AARC ANNUAL CONVENTION SITES & DATES

1991—Atlanta, Georgia, December 7-10
1992—San Antonio, Texas, December 12-15
1993—Nashville, Tennessee, December 11-14
1994—Las Vegas, Nevada, December 12-15
1995—Orlando, Florida, December 2-5

THE NATIONAL BOARD FOR RESPIRATORY CARE

1991 Examination and Fee Schedule

CRTT Examination

EXAMINATION DATE:	JULY 20, 1991
Applications Accepted Beginning:	March 1, 1991
Application Deadline:	May 1, 1991
EXAMINATION DATE:	NOVEMBER 9, 1991
Applications Accepted Beginning:	July 1, 1991
Application Deadline:	September 1, 1991

CPFT Examination

EXAMINATION DATE:	JUNE 1, 1991
Applications Accepted Beginning:	December 1, 1990
Application Deadline:	April 1, 1991

RRT Examination

EXAMINATION DATE:	JUNE 1, 1991
Applications Accepted Beginning:	December 1, 1990
Application Deadline:	February 1, 1991
EXAMINATION DATE:	DECEMBER 7, 1991
Applications Accepted Beginning:	June 1, 1991
Application Deadline:	August 1, 1991

RPFT Examination

EXAMINATION DATE:	DECEMBER 7, 1991
Applications Accepted Beginning:	July 1, 1991
Application Deadline:	September 1, 1991

Fee Schedule

Entry Level CRTT—new applicant:	$ 75.00
Entry Level CRTT—reapplicant:	$ 50.00
RRT Written and Clinical Simulation—new applicant:	$175.00
Written Registry Only new applicant:	$ 75.00
Written Registry Only reapplicant:	$ 50.00
Clinical Simulation Only new and reapplicant:	$100.00
Entry Level CPFT—new applicant:	$100.00
Entry Level CPFT—reapplicant:	$ 80.00
Advanced RPFT—new applicant:	$150.00
Advanced RPFT—reapplicant:	$130.00
CRTT Recredentialing:	$ 25.00
RRT Recredentialing:	
Written Registry Examination	$ 25.00
Clinical Simulation Examination	$ 65.00
CPFT Recredentialing:	$ 25.00
RPFT Recredentialing:	$ 90.00
Membership Renewal CRTT/RRT/CPFT/RPFT	$ 12.00

8310 Nieman Road • Lenexa, Kansas 66215 • (913) 599-4200

1991 Call for Abstracts

The American Association for Respiratory Care and its science journal, RESPIRATORY CARE, invite submission of brief abstracts related to any aspect of cardiorespiratory care. The abstracts will be reviewed, and selected authors will be invited to present papers at the Open Forum during the AARC Annual Meeting in Atlanta, Georgia, December 7-10, 1991. Accepted abstracts will be published in the November 1991 issue of RESPIRATORY CARE. Membership in the AARC is not necessary for participation.

Specifications

An abstract may report (1) an **original study**, (2) the **evaluation of a method or device**, or (3) a **case or case series**. Topics may be aspects of adult acute care, continuing care/rehabilitation, perinatology/pediatrics, cardiopulmonary technology, health occupations education, or management of personnel and health-care delivery. The abstract may have been presented previously at a local or regional—but not national—meeting and should not have been published previously in a national journal.

The abstract will be the only evidence by which the reviewers will decide whether the author should be invited to present a paper at the Open Forum. Therefore, *the abstract must provide all important data, findings, and conclusions.* Give specific information. Do not write such general statements as "Results will be presented" or "Significance will be discussed."

Essential Content Elements

An **original study** abstract ***must*** include (1) Introduction: statement of research problem, question, or hypothesis; (2) Method: description of research design and conduct in sufficient detail to permit judgment of validity; (3) Results: statement of research findings with quantitative data and statistical analysis; (4) Conclusions: interpretation of the meaning of the results.

A **method/device evaluation** abstract ***must*** include (1) Introduction: identification of the method or device and its intended function; (2) Method: description of the evaluation in sufficient detail to permit judgment of its objectivity and validity; (3) Results: findings of the evaluation; (4) Experience: summary of the author's practical experience ***or*** a notation of lack of experience; (5) Conclusions: interpretation of the evaluation and experience. Cost comparisons should be included where possible and appropriate.

A **case report** abstract ***must*** report a case that is uncommon or of exceptional teaching/learning value and must include: (1) case summary and (2) significance of case. Content should reflect results of literature review. The author(s) should have been actively involved in the case and a case-managing physician must be a co-author or must approve the report.

Abstract Format and Typing Instructions

An optical scanner will be used to process abstracts. First line of abstract should be the title. Title should explain content. Type or electronically print the abstract ***double-spaced*** on ***plain white bond paper***, on ***one page*** only (copier bond is excellent). Do not underline or boldface and insert only one letter space between sentences. Provide a 1-inch margin top and bottom, a ½-inch left margin, and an approximate ½-inch ragged-right margin. Text may be submitted on diskette but must be accompanied by a hard copy.

No identification of authors or institutions is to appear on the abstract sheet or in the abstract itself. Make the abstract all one paragraph. Data may be submitted in table form ***provided the table width is limited to 60 letter spaces*** (ie, letters or numbers plus necessary blank spaces = 60). ***No*** figures or illustrations are to be attached to the abstract.

Type all information required to complete the author information form on the other side of this page. A photocopy of good quality may be used.

Standard abbreviations may be employed without explanation. A new or infrequently used abbreviation should be preceded by the spelled-out term the first time it is used. Any recurring phrase or expression may be abbreviated if it is first explained.

Check the abstract for (1) errors in spelling, grammar, facts and figures; (2) clarity of language; (3) conformance to these specifications. An abstract not prepared as requested may not be reviewed.

Questions about abstract preparation may be telephoned to the editorial staff of RESPIRATORY CARE at (214) 243-2272.

Deadlines

The mandatory Final Deadline is June 5 (postmark). Authors will be notified of acceptance or rejection ***by letter only***—to be mailed by August 15.

Authors may choose to submit abstracts early. Abstracts received by March 20 will be reviewed and the authors notified by April 26. Rejected abstracts will be accompanied by a written critique that should in many cases enable authors to revise their abstracts and resubmit them by the final deadline (June 5).

Mailing Instructions

Mail (Do not fax!) 1 copy of the abstract, 1 author information sheet, and a stamped, self-addressed postcard (for notice of receipt) to:

RESPIRATORY CARE
11030 Ables Lane
Dallas TX 75229

1991 OPEN FORUM
AUTHOR INFORMATION SHEET

Please type:

Abstract title

Principal author | Institution

Corresponding author

Mail station, building, or room

Institution

Street address

City, State, Zip

Telephone

Presenter

Mail station, building, or room

Institution

Street address

City, State, Zip

Telephone

Co-author | Institution

Co-author | Institution

Co-author | Institution

Mail, with abstract and stamped self-addressed postcard, to RESPIRATORY CARE Open Forum
11030 Ables Lane, Dallas TX 75229

RESPIRATORY CARE

Instructions for Authors and Typists

These Instructions are meant to guide authors and typists, including veterans in those roles, in the production of quality manuscripts. Perfection is not expected, but the well-prepared manuscript has the best chance for prompt review and early publication.

General Requirements

Submissions should (1) be related to respiratory care, (2) be planned for one of the publication categories below, and (3) be prepared as indicated in these Instructions. A letter accompanying the manuscript must specify the intended publication category, be signed by all the authors, and, when there are two or more authors, state that "We, the undersigned, have all participated in the work reported, read the accompanying manuscript, and approved its submission for publication."

Publication Categories

Research Article (Study): A report of an original investigation.
Evaluation of a Device/Method/Technique: A description and evaluation of an old or new device, method, technique, or modification.
Case Report: A report of a clinical case that is uncommon or of exceptional teaching value. The author(s) must have been associated with the case. A case-managing physician must be one of the authors or, if not an author, must supply a letter approving the manuscript.
Case Series: Like a Case Report but including a number of cases.
Review Article: A comprehensive, critical review of the literature and state of the art of a pertinent topic that has been the subject of 40 or more published research papers.
Overview: A critical review of a pertinent topic about which not enough research has been published to merit a Review Article.
Update: A report of subsequent developments in a topic that has been critically reviewed (not necessarily in this journal).
Point of View: A paper expressing the author's personal opinions on a pertinent topic.
Special Article: If a paper does not fit one of the foregoing categories but is pertinent, the editors may consider it as a Special Article.
Editorial: A paper that draws attention to a pertinent concern.
Letter: A signed communication about material published in this journal or on topics of interest or value to readers.
Blood Gas Corner: A brief, instructive case report (real or fictional) involving invasively or noninvasively obtained respiratory care blood data, followed by questions for readers—with answers and discussion.
PFT Corner: Like Blood Gas Corner but involving pulmonary function testing.
Test Your Radiologic Skill: Like Blood Gas Corner and PFT Corner but involving pulmonary-medicine radiography and including one or two 4 × 5 or 5 × 7 inch prints of radiographs. The case must be real.
Review of Book, Film, Tape, or Software: Anyone interested in writing a review can discuss it with an editor.

Editorial Consultation and Author's & Typist's Kit

To discuss a writing project, write to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229 or call 214/243-2272.

Authors are urged to obtain the RESPIRATORY CARE Author's & Typist's Kit. The Kit provides *authors* with specific guidance about writing a research paper, writing a case report, converting to and from SI units, and in-house manuscript review. *Typists* can use the Kit's Model Manuscript, a list of journal name abbreviations, and a copy of these Instructions. The Kit is free from the Journal office.

Preparing the Manuscript

General Concerns—*Typist*

- Double-space ALL lines, including those in references, figure legends, and tables. Do not justify right margins.
- Number pages in upper right corner and leave margins of 1½" or more on all four sides of the page.
- For research articles, follow format of Model Manuscript, Respir Care 1984;29:182 (Feb 1984).
- Meticulously follow instructions for typing references.

General Concerns—*Author:*

- Structure manuscript as specified hereafter.
- Provide all requested information on title page as specified hereafter.
- Proofread manuscript for completeness, clarity, grammar, spelling; be sure all references, figures, and tables are cited in the text.
- Consider having paper reviewed in-house before submission.
- Have all co-authors proofread and approve manuscript and sign submission letter.

Manuscript Structure

Most kinds of papers have standard parts in a standard order. However, papers can vary individually, and not every paper will have all the parts listed here.

Research Article: Title page, abstract page, continuous text (Introduction, Materials & Methods, Results, Discussion), Product Sources page, Acknowledgments page, references, tables, figure legends. Please consult "Writing a Research Paper," Respir Care 1985;30:1057 (Dec 1985) and Model Manuscript, Respir Care 1984;29:182 (Feb 1984).
Evaluation of Device/Method/Technique: Title page, abstract page, continuous text (Introduction, Description of Device/Method/Technique, Methods of Evaluation, Results of Evaluation, Discussion), Product Sources page, Acknowledgments page, references, tables, figure legends.
Case Report or Case Series: Title page, abstract page, continuous text (Introduction, Case Summary, Discussion), Acknowledgments page, references, tables, figure legends. Also see "How To Write a Better Case Report," Respir Care 1982;27:29 (Jan 1982).
Review Article: Title page, Table of Contents page, continuous text (Introduction, History, Review of Literature, State of the Art, Discussion, Summary), references. May include figures & tables. No abstract. Table of Contents optional. Other formats may be appropriate.
Overview, Update, Point of View, or Special Article: Title page, text (introduction, message), references, tables, figure legends. No abstract.
Letter: Title page (provide a title), text, writer's name & affiliation, references. Tables & figures may be included. Double-space everything. Write "For Publication" on title page.

Structure: Important Details

Title Page: List title of paper, all authors' full names, degrees, credential letters, professional positions, and affiliations. List correspondence address, telephone number, and reprint address if desired. Name sources of grants or other support. Identify any author's consulting or commercial relationships that pertain to the paper's topic.

Abstract Page: Number this Page 1. List paper's title but omit authors' names. Abstract should be 200 words or less and must be informative, briefly specifying main points of paper, such as methods, results, and conclusions drawn.

Statistical Analysis: In research articles, identify statistical tests and chosen level of significance in the Methods section. In Results section, report actual P values.

Figures (illustrations): All photographs, diagrams, & graphs must be numbered as Figure 1, Figure 2, etc, according to the order in which each is first mentioned in the text. Photographs must be glossy prints 5 × 7 to 8 × 10 inches and should be black & white unless color is essential. Letters and numerals must be neat and large enough to remain legible if figure is reduced in size for publication. Final figures must be of professional quality, but 'rough' sketches may accompany the submitted manuscript, with final figures to be prepared after review. Identify each figure on back with a stick-on label showing figure number and arrow indicating top; omit author's name. Cover label with clear tape so ink will not smudge other prints. Supply three sets of unmounted figures. If figure has been published before, include copyright-holder's written permission to use it.

Figure Legends: List figure legends on a separate page, not on figures. If a figure has been published before, list the source in the legend.

Tables: Type each table on a separate page. Avoid more than 8 columns across. Continue a deep table on following pages. Give each table a number and descriptive title, placed above the table. Double-space ALL lines in tables, including column headings and footnotes.

Drugs: Brand names may be given, but always also show generic names.

Units of Measurement: In addition to conventional units of measure, show SI values and units in brackets after conventional expressions: ie, "PEEP, 10 cm H_2O [0.981 kPa]." For conversion to SI, see RESPIRATORY CARE 1988;33:861-873 (Oct 1988).

Commercial Products: If three or fewer commercial products are named in the text, list the manufacturer's name and location in parentheses the first time each is mentioned. If four or more products are named, do not list manufacturers in the text; instead, name the products and manufacturers in a Products Sources list at the end of the text. Provide model numbers when available.

Abbreviations: Use an abbreviation only if the term occurs several times in the paper. Write out the full term the first time it appears, followed by the abbreviation in parentheses. Thereafter, employ the abbreviation alone. Never use an abbreviation without defining it. Do not create new abbreviations unless absolutely necessary.

References:

- Use references to support statements of fact, indicate sources of information, or guide readers to further pertinent literature.
- Cite only published works—or works accepted for publication. When listing an accepted but still unpublished work, designate the accepting journal's name, followed by "(in press)."
- In the text, cite references by superscript numerals (half space above text), not in parentheses. The first reference cited in the text is number 1, the next is number 2, etc.
- In the reference list, place the cited works in numerical order.
- For the reference list, obtain author names, article and book titles, dates, volume and page numbers from the *original* cited articles and books, not from secondary sources such as other articles' reference lists, which often are inaccurate.
- Type references in medical-journal style. Examples appear at the end of these Instructions. Abbreviate journal names as in *Index Medicus*. A list of many journal-name abbreviations was published in Respir Care 1988;33:1050 (Nov 1988).
- DOUBLE-SPACE the lines of references.
- List ALL authors' names. Do not use "et al" to substitute for names.
- Identify abstracts, editorials, and letters as such. See examples.

Personal Communications, Unpublished Papers, and Unpublished Observations: List unpublished items in parentheses in the text, not in the reference list.

Examples of How To Type References

Notes: Although the examples here are printed with single-spaced lines, please double-space references in manuscripts. Also, note that words in article and book titles are not capitalized—except proper names.

Standard Journal Article:

1. Shepherd KE, Johnson DC. Bronchodilator testing: An analysis of paradoxical responses. Respir Care 1988;33:667-671.

Corporate Author Journal Article:

2. American Association for Respiratory Care. Criteria for establishing units for chronic ventilator-dependent patients in hospitals. Respir Care 1988;33:1044-1046.

Article in Journal Supplement:

(Journals differ in their methods of numbering and identifying supplements. Supply sufficient information to allow retrieval.)

3. Reynolds HY. Idiopathic interstitial pulmonary fibrosis. Chest 1986;89(3, suppl):139s-143s.

Abstract in Journal:

(Abstracts are not strong references; when possible, full papers should be cited. When cited, abstracts should be identified as such.)

4. Lippard DL, Myers TF, Kahn SE. Accuracy of pulse oximetry in severely hypoxic infants (abstract). Respir Care 1988;33:886.

Editorial in Journal:

5. Rochester DF. Does respiratory muscle rest relieve fatigue or incipent fatigue? (editorial). Am Rev Respir Dis 1988;138:516-517.

Letter in Journal:

6. Smith DE, Herd D, Gazzard BG. Reversible bronchoconstriction with nebulised pentamidine (letter). Lancet 1988;2:905.

Personal Author Book:

7. Nunn JF. Applied respiratory physiology. New York: Appleton-Century-Crofts, 1969.

Note: To specify pages cited in a book, place a colon after the year and then list the page(s). Examples: 1969:85 (one page), 1963:85-95 (series of contiguous pages), 1963:85,95 (separated pages).

Corporate Author Book:

8. American Medical Association Department of Drugs. AMA drug evaluations, 3rd ed. Littleton CO: Publishing Sciences Group, 1977.

Book with Editor, Compiler, or Chairman as 'Author':

9. Guenter CA, Welch MH, eds. Pulmonary medicine. Philadelphia: JB Lippincott, 1977.

Chapter in Book:

10. Pierce AK. Acute respiratory failure. In: Guenter CA, Welch MH, eds. Pulmonary medicine. Philadelphia: JB Lippincott, 1977:171-223.

Submitting the Manuscript

After preparing the manuscript according to these Instructions, perform a final proofreading and check for accuracy and completeness. Then mail three copies of the manuscript and three sets of figures to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229 (or Federal Express to RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229). Manuscript copy on IBM-compatible or Macintosh disks in addition to the requisite three hard copies will facilitate processing (Macintosh preferred). Enclose a letter as specified under **General Requirements** at the beginning of these Instructions. Do not submit material that has been published or is being considered elsewhere.

Author's Checklist

1. Is paper for a listed publication category?
2. Does cover letter meet specifications?
3. Is title page complete?
4. Are all pages double-spaced and numbered?
5. Are all references, figures, and tables cited in the text?
6. Are references typed in requested style?
7. Have SI values been provided?
8. Has all arithmetic been checked?
9. Has manuscript been proofread by all authors?

News releases about new products and services will be considered for publication in this section. There is no charge for these listings. Send descriptive release and glossy black and white photographs to RESPIRATORY CARE Journal, New Products and Services Dept, 11030 Ables Lane, Dallas TX 75229.

New Products & Services

MEDICALLY SUPERVISED CRUISES. LIFE Unlimited provides medically supervised 8-day/7-night cruises for patients with chronic health ailments from the Port of Miami to the Eastern and Western Caribbean. The Eastern Cruise includes stops at San Juan, St Barts, and St Thomas. Two Eastern Cruises are scheduled for 1991, with departure dates of June 16th and November 3rd. The Western Cruise includes stops at Grand Cayman, Montego Bay, and Cozumel. Two Western Cruises are scheduled for 1991, with departure dates of August 11th and September 22nd. According to LIFE Unlimited, all transportation, transfers, baggage handling in Miami, and all meals and entertainment on-board ship are included in the Cruise Package; and private escorted tours are arranged at each port of call. Arrangements can be made for all required medical equipment, airline reservations, and pre- or post-cruise hotel accommodations for those who wish to extend their vacations. Group discounts are available if reservations are made at least 90 days prior to departure dates. LIFE Unlimited, Dept RC, 17101 SW 200 St, Box Z28, Miami FL 33187. 1-800-345-9269.

OXYGEN CANNULA SUPPORT. The Dale Oxygen Cannula Support is designed to relieve cannula-induced pain and discomfort to the ears and to help prevent accidental cannula dislodgment during patient activity. The Cannula Support attaches to the cannula and is either placed on the patient's head or applied to the back of the neck. According to the manufacturer, the Cannula Support is easy to apply: Velcro-brand fasteners attach quickly and easily and adjust to all head sizes; and the soft, hypoallergenic material of the support band is comfortable to wear and allows Velcro attachment at any point on its surface. Dale Medical Products Inc, Dept RC, 7 Cross St, PO Box 1556, Plainville MA 02762. 1-800-343-3980.

PULSE OXIMETER. According to the manufacturer, the compact, lightweight Lifecare Oximeter 100 is ideal for portable applications; the Oximeter 100 operates up to 16 hours on its own internal battery, and can store up to 9 hours of Spo_2 and pulse data. Spo_2 and pulse rate are continually displayed, specific alarm conditions and alarm set-points are always visible, and pulse signal strength is constantly monitored by a full-range pulse bargraph. Pulse waveform and oxygen trending can be viewed by connecting the Oximeter 100 to a Smart printer or compatible computer terminal. Lifecare, Dept RC, 655 Aspen Ridge Drive, Lafayette CO 80026. (303) 666-9234.

POCKET COMPUTER. The LOGI-Cal Pocket Computer is programmed for critical care. Pulmonary, hemodynamic, and renal programs are available. Included among the variables that can be calculated with the pulmonary program are $P_{(A-a)O_2}$, C_{dyn}, C_{st}, MVV_{pred}, P_{aO_2pred}, Q_{sp}/Q_t, REE, and V_d/V_t. According to the manufacturer, the LOGI-Cal is compact and fits conveniently into a lab-coat pocket; is powered by four AAA alkaline batteries; and features automatic power-down to save battery life, constant memory to retain data, and the special ability to prompt for the appropriate entry and retain the response for all equations requiring that entry. Clinical Logic Systems, Dept RC, 114 Glenn St, Decatur GA 30030. (404) 378-4862.

ASTM PUBLICATIONS CATALOG. The 1991 Publications Catalog of the American Society for Testing and Materials (ASTM) describes 68 volumes of the **Annual Book of ASTM Standards** and several hundred related technical publications. ASTM standards and related publications are used worldwide to specify materials, assure quality, integrate production processes, promote trade, and enhance safety. The catalog is available free. ASTM Customer Service, Dept RC, 1916 Race St, Philadelphia PA 19103. (215) 229-5585.

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Information Requests or Change of Address

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City/State/Zip _____

New Address

Street _____

City/State/Zip _____

Check the boxes below for information from the AARC

- ☐ Change of Address
- ☐ AARC Membership Info
- ☐ AARC Catalog
- ☐ AARC Position Statement

RESPIRATORY CARE

May Information Service — Expires August 31, 1991

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I. Type of Instn/Practice
1. ☐ Hosp. 500 or more beds
2. ☐ Hosp. 300 to 500 beds
3. ☐ Hosp. 200 to 300 beds
4. ☐ Hosp. 100 to 200 beds
5. ☐ Hosp. 100 or less beds
6. ☐ Clinic/Group Practice
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B. ☐ Cardiopulmonary
C. ☐ Anesthesia Service
D. ☐ Emergency Dept.

III. Specialty
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2. ☐ Perinatal Pediatrics
3. ☐ Critical Care
4. ☐ Clinical Research
5. ☐ Pulmonary Func Lab
6. ☐ Home Care/Rehab
7. ☐ Education
8. ☐ Management

IV. Position
A. ☐ Dept. Head
B. ☐ Chief Therapist
C. ☐ Supervisor
D. ☐ Staff Technician
E. ☐ Staff Therapist
F. ☐ Educator
G. ☐ Medical Director
H. ☐ Anesthesiologist
I. ☐ Other MD
J. ☐ Nurse

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J. ☐ Nurse

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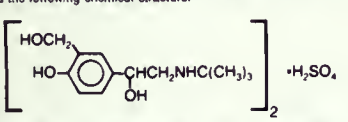
IT'S THE EASY SOLUTION

Proventil®
(albuterol sulfate)
Solution for Inhalation
Unit Dose 0.083%*
0.5%* 20 mL bottle
*Potency expressed as albuterol

DESCRIPTION PROVENTIL, brand of albuterol sulfate, Solution for Inhalation, is a relatively selective beta$_2$-adrenergic bronchodilator (see **CLINICAL PHARMACOLOGY** section below). Albuterol sulfate has the chemical name α^1-[(*tert*-Butylamino) methyl]-4-hydroxy-*m*-xylene-α,α'-diol sulfate (2:1) (salt), and the following chemical structure:



Albuterol sulfate has a molecular weight of 576.7 and the empirical formula $(C_{13}H_{21}NO_3)_2{\cdot}H_2SO_4$. Albuterol sulfate is a white crystalline powder, soluble in water and slightly soluble in ethanol.

The international generic name for albuterol base is salbutamol.

PROVENTIL Solution for Inhalation is available in two concentrations. The 0.5% solution is in concentrated form. Dilute 0.5 mL of the solution to 3 mL with normal saline solution prior to administration. The 0.083% solution requires no dilution prior to administration.

Each mL of PROVENTIL Solution for Inhalation (0.5%) contains 5 mg of albuterol (as 6.0 mg of albuterol sulfate) in an aqueous solution containing benzalkonium chloride; sulfuric acid is used to adjust the pH between 3 and 5. PROVENTIL Solution for Inhalation (0.5%) contains no sulfiting agents. It is supplied in 20 mL bottles.

Each mL of PROVENTIL Solution for Inhalation (0.083%) contains 0.83 mg of albuterol (as 1.0 mg of albuterol sulfate) in an isotonic aqueous solution containing sodium chloride and benzalkonium chloride; sulfuric acid is used to adjust the pH between 3 and 5. PROVENTIL Solution for Inhalation (0.083%) contains no sulfiting agents. It is supplied in 3 mL bottles for unit-dose dispensing.

PROVENTIL Solution for Inhalation is a clear, colorless to light yellow solution.

CLINICAL PHARMACOLOGY The prime action of beta-adrenergic drugs is to stimulate adenyl cyclase, the enzyme which catalyzes the formation of cyclic-3',5'-adenosine monophosphate (cyclic AMP) from adenosine triphosphate (ATP). The cyclic AMP thus formed mediates the cellular responses. *In vitro* studies and *in vivo* pharmacologic studies have demonstrated that albuterol has a preferential effect on beta$_2$-adrenergic receptors compared with isoproterenol. While it is recognized that beta$_2$-adrenergic receptors are the predominant receptors in bronchial smooth muscle, recent data indicate that 10 to 50% of the beta receptors in the human heart may be beta$_2$ receptors. The precise function of these receptors, however, is not yet established. Albuterol has been shown in most controlled clinical trials to have more effect on the respiratory tract, in the form of bronchial smooth muscle relaxation, than isoproterenol at comparable doses while producing fewer cardiovascular effects. Controlled clinical studies and other clinical experience have shown that inhaled albuterol, like other beta-adrenergic agonist drugs, can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or ECG changes.

Albuterol is longer acting than isoproterenol in most patients by any route of administration because it is not a substrate for the cellular uptake processes for catecholamines nor for catechol-*O*-methyl transferase.

Studies in asthmatic patients have shown that less than 20% of a single albuterol dose was absorbed following either IPPB or nebulizer administration; the remaining amount was recovered from the nebulizer and apparatus and expired air. Most of the absorbed dose was recovered in the urine 24 hours after drug administration. Following a 3.0 mg dose of nebulized albuterol, the maximum albuterol plasma level at 0.5 hour was 2.1 ng/mL (range 1.4 to 3.2 ng/mL). There was a significant dose-related response in FEV_1 and peak flow rate (PFR). It has been demonstrated that following oral administration of 4 mg albuterol, the elimination half-life was 5 to 6 hours.

Animal studies show that albuterol does not pass the blood-brain barrier. Recent studies in laboratory animals (minipigs, rodents, and dogs) recorded the occurrence of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis) when beta-agonists and methylxanthines were administered concurrently. The significance of these findings when applied to humans is currently unknown.

In controlled clinical trials, most patients exhibited an onset of improvement in pulmonary function within 5 minutes as determined by FEV_1. FEV_1 measurements also showed that the maximum average improvement in pulmonary function usually occurred at approximately 1 hour following inhalation of 2.5 mg of albuterol by compressor-nebulizer, and remained close to peak for 2 hours. Clinically significant improvement in pulmonary function (defined as maintenance of a 15% or more increase in FEV_1 over baseline values) continued for 3 to 4 hours in most patients and in some patients continued up to 6 hours.

In repetitive dose studies, continued effectiveness was demonstrated throughout the 3-month period of treatment in some patients.

INDICATIONS AND USAGE PROVENTIL Solution for Inhalation is indicated for the relief of bronchospasm in patients with reversible obstructive airway disease and acute attacks of bronchospasm.

CONTRAINDICATIONS PROVENTIL Solution for Inhalation is contraindicated in patients with a history of hypersensitivity to any of its components.

WARNINGS As with other inhaled beta-adrenergic agonists, PROVENTIL Solution for Inhalation can produce paradoxical bronchospasm, which can be life threatening. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs and with the home use of sympathomimetic nebulizers. It is, therefore, essential that the physician instruct the patient in the need for further evaluation if his/her asthma becomes worse. In individual patients, any beta$_2$-adrenergic agonist, including albuterol solution for Inhalation, may have a clinically significant cardiac effect.

Immediate hypersensitivity reactions may occur after administration of albuterol as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema.

PRECAUTIONS General: Albuterol, as with all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias and hypertension, in patients with convulsive disorders, hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines.

Large doses of intravenous albuterol have been reported to aggravate preexisting diabetes mellitus and ketoacidosis. Additionally, beta-agonists, including albuterol, when given intravenously may cause a decrease in serum potassium, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation. The relevance of these observations to the use of PROVENTIL Solution for Inhalation is unknown.

Information For Patients: The action of PROVENTIL Solution for Inhalation may last up to 6 hours and therefore it should not be used more frequently than recommended. Do not increase the dose or frequency of medication without medical consultation. If symptoms get worse, medical consultation should be sought promptly. While taking PROVENTIL Solution for Inhalation, other antiasthma medicines should not be used unless prescribed.

Drug Interactions: Other sympathomimetic aerosol bronchodilators or epinephrine should not be used concomitantly with albuterol.

Albuterol should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of albuterol on the vascular system may be potentiated.

Beta-receptor blocking agents and albuterol inhibit the effect of each other.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Albuterol sulfate, like other agents in its class, caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium in a 2-year study in the rat, at oral doses corresponding to 10, 50, and 250 times the maximum human nebulizer dose. In another study, this effect was blocked by the coadministration of propranolol. The relevance of these findings to humans is not known. An 18-month study in mice and a lifetime study in hamsters revealed no evidence of tumorigenicity. Studies with albuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Teratogenic Effects–Pregnancy Category C: Albuterol has been shown to be teratogenic in mice when given subcutaneously in doses corresponding to the human nebulization dose. There are no adequate and well-controlled studies in pregnant women. Albuterol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. A reproduction study in CD-1 mice with albuterol (0.025, 0.25, and 2.5 mg/kg subcutaneously, corresponding to 0.1, 1, and 12.5 times the maximum human nebulization dose, respectively) showed cleft palate formation in 5 of 111 (4.5%) of fetuses at 0.25 mg/kg and in 10 of 108 (9.3%) of fetuses at 2.5 mg/kg. None were observed at 0.025 mg/kg. Cleft palate also occurred in 22 of 72 (30.5%) of fetuses treated with 2.5 mg/kg isoproterenol (positive control). A reproduction study in Stride Dutch rabbits revealed cranioschisis in 7 of 19 (37%) of fetuses at 50 mg/kg, corresponding to 250 times the maximum human nebulization dose.

Labor and Delivery: Oral albuterol has been shown to delay preterm labor in some reports. There are presently no well-controlled studies which demonstrate that it will stop preterm labor or prevent labor at term. Therefore, cautious use of PROVENTIL Solution for Inhalation is required in pregnant patients when given for relief of bronchospasm so as to avoid interference with uterine contractibility.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because of the potential for tumorigenicity shown for albuterol in some animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of albuterol solution for inhalation in children below the age of 12 years have not been established.

ADVERSE REACTIONS The results of clinical trials with PROVENTIL Solution for Inhalation in 135 patients showed the following side effects which were considered probably or possibly drug related:

Central Nervous System: tremors (20%), dizziness (7%), nervousness (4%), headache (3%), insomnia (1%).
Gastrointestinal: nausea (4%), dyspepsia (1%).
Ear, Nose and Throat: pharyngitis (<1%), nasal congestion (1%).
Cardiovascular: tachycardia (1%), hypertension (1%).
Respiratory: bronchospasm (8%), cough (4%), bronchitis (4%), wheezing (1%).

No clinically relevant laboratory abnormalities related to PROVENTIL Solution for Inhalation administration were determined in these studies.

In comparing the adverse reactions reported for patients treated with PROVENTIL Solution for Inhalation with those of patients treated with isoproterenol during clinical trials of 3 months, the following moderate to severe reactions, as judged by the investigators, were reported. This table does not include mild reactions.

Percent Incidence of Moderate To Severe Adverse Reactions

Reaction	Albuterol N = 65	Isoproterenol N = 65
Central Nervous System		
Tremors	10.7%	13.8%
Headache	3.1%	1.5%
Insomnia	3.1%	1.5%
Cardiovascular		
Hypertension	3.1%	3.1%
Arrhythmias	0%	3.0%
**Palpitation	0%	22.0%
Respiratory		
*Bronchospasm	15.4%	18%
Cough	3.1%	5%
Bronchitis	1.5%	5%
Wheeze	1.5%	1.5%
Sputum Increase	1.5%	1.5%
Dyspnea	1.5%	1.5%
Gastrointestinal		
Nausea	3.1%	0
Dyspepsia	1.5%	0
Systemic		
Malaise	1.5%	0

*In most cases of bronchospasm, this term was generally used to describe exacerbations in the underlying pulmonary disease.

**The finding of no arrhythmias and no palpitations after albuterol administration in this clinical study should not be interpreted as indicating that these adverse effects cannot occur after the administration of inhaled albuterol.

Rare cases of urticaria, angioedema, rash, bronchospasm, and oropharyngeal edema have been reported after the use of inhaled albuterol.

OVERDOSAGE Manifestations of overdosage may include anginal pain, hypertension, hypokalemia, and exaggeration of the pharmacological effects listed in **ADVERSE REACTIONS.**

The oral LD_{50} in rats and mice was greater than 2,000 mg/kg. The inhalational LD_{50} could not be determined.

There is insufficient evidence to determine if dialysis is beneficial for overdosage of PROVENTIL Solution for Inhalation.

DOSAGE AND ADMINISTRATION The usual dosage for adults and children 12 years and older is 2.5 mg of albuterol administered 3 to 4 times daily by nebulization. More frequent administration or higher doses is not recommended. To administer 2.5 mg of albuterol, either dilute 0.5 mL of the 0.5% solution for inhalation to a total volume of 3 mL with normal saline solution, or administer the contents of one unit-dose bottle (3 mL of 0.083% nebulizer solution) by nebulization. The flow rate is regulated to suit the particular nebulizer so that the PROVENTIL Solution for Inhalation will be delivered over approximately 5 to 15 minutes.

The use of PROVENTIL Solution for Inhalation can be continued as medically indicated to control recurring bouts of bronchospasm. During treatment, most patients gain optimum benefit from regular use of the nebulizer solution.

If a previously effective dosage regimen fails to provide the usual relief, medical advice should be sought immediately, as this is often a sign of seriously worsening asthma which would require reassessment of therapy.

HOW SUPPLIED PROVENTIL Solution for Inhalation, 0.5%, is a clear, colorless to light yellow solution, and is supplied in bottles of 20 mL (NDC-0085-0208-02) with accompanying calibrated dropper; boxes of one. **Store between 2° and 25°C (36° and 77°F).**

PROVENTIL Solution for Inhalation, 0.083%, is a clear, colorless to light yellow solution, and is supplied in unit-dose bottles of 3 mL each, boxes of 25 (NDC-0085-0209-01.) **Store between 2° and 25°C (36° and 77°F).**

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THE *ONLY* APPROVED ALBUTEROL SULFATE UNIT DOSE

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