Seven patients with status asthmaticus intubated for respiratory failure who had elevated airway pressures and persistent respiratory acidosis were successfully ventilated using a mixture of 60 percent helium and 40 percent oxygen. All patients experienced a rapid reduction in airway pressures, CO₂ retention, and resolution of acidosis while breathing a helium-oxygen mixture. There were no untoward effects. Helium-oxygen mixtures improve ventilation by reducing the Reynolds number and reducing density dependent resistance. Helium’s beneficial effects are due to its high kinematic viscosity, high binary diffusion coefficient for CO₂, and high diffusivity. Helium-oxygen mixtures should be considered for use in mechanically ventilated asthmatics with respiratory acidosis who fail conventional therapy.

| EFF | equal pressure print; Helio = mixture of 60% helium and 40% oxygen |

**Status asthmaticus** is a familiar clinical management problem confronting emergency, pulmonary and critical care physicians. It represents the penultimate event in a complex cascade of pathologic processes including diffuse airway inflammation, bronchoconstriction, and abnormal ventilation/perfusion relationships. In general, deaths due to asthma are uncommon, yet there appears to be a multifactorial mediated rise in asthma mortality over the last ten years. Classic teachings suggest that normocapnia and hypercapnia portend “impending respiratory failure” which requires endotracheal intubation and mechanical ventilation. However, this position has recently been challenged. In fact, endotracheal intubation may intensify the degree of bronchospasm. Moreover, generated airway pressures may exceed pressure limits causing ventilators to prematurely recycle, resulting in decreased alveolar ventilation. Despite disabling the alarms, there are instances of severe bronchospasm in which the ventilator is incapable of delivering sufficient tidal volume to reverse hypoventilation. In the past, halothane anesthesia has been employed to ameliorate bronchospasm, hypoxia, and hypercapnia. Halothane therapy is logistically difficult to obtain and carries inherent risks. Helium is an inert gas which has a long history of safe utilization in pulmonary medicine. Helium, because of its unique position on the periodic table, is ideally suited to ventilation in asthmatic patients.

We report seven intubated patients in whom severe status asthmaticus and respiratory acidosis was not amenable to aggressive conventional therapy but responded immediately to the inhalation of heliox.

**Materials and Methods**

Between June 1, 1987, and Dec 31, 1988, all patients 15 to 40 years old with a prior history of asthma presenting to the emergency departments of Hartford Hospital or Mount Sinai Hospital, Hartford, CT, were considered eligible for a trial of helium-oxygen therapy. Patients were initially evaluated by emergency department physicians in conjunction with medical housestaff and intubated on clinical grounds after arterial blood gas measurements were obtained. All patients were immediately treated with 125 mg methylprednisolone, 0.5 to 1.0 mg aerosolized albuterol, 300 mg aminophylline bolus followed by a 0.6 mg/kg continuous infusion and 0.3 ml subcutaneous epinephrine. Ventilator parameters were adjusted to minimize peak airway pressures. After review of the pertinent history, diagnostic and ventilator parameters, patients were entered into the heliox treatment protocol if they exhibited a pH<7.20, PaO₂>60, PaCO₃>50; a persistently elevated peak airway pressure in excess of 75 cm H₂O after 1 hour of conventional therapy; and a persistent hypercapnia and acidosis after 1 hour of conventional therapy. Excluded from the protocol were patients who exhibited a 20 percent fall in PaCO₂ on subsequent arterial blood gas measurements, or a reduction in peak airway pressures to less than 75 cm H₂O on conventional therapy; a combined respiratory acidosis and metabolic alkalosis on initial blood gas measurements; historic or physical evidence of cardiac, renal, neurologic, gastrointestinal or restrictive lung disease; and roentgenographic evidence of infection or diffuse lung injury. Patients were admitted to the medical intensive care unit, monitored by ECG and pulse oximeter, and continued receiving intravenous aminophylline, corticosteroids, and aerosolized β-agonists. All patients were paralyzed and sedated. All patients were initially managed on a Puritan Bennett 7200. All patients were switched to a Bear I ventilator prior to the substitution of helium for nitrogen because the tidal volume is not regulated by in-line flow meters.
Arterial blood gas measurements were obtained at ten-minute intervals until two consecutive values for PaCO₂ measured less than 42 mm Hg. Ventilator settings were periodically adjusted to maximize flow and minimize peak airway pressure. Pure helium at 50 psi, and pure oxygen at 50 psi were delivered to the air port and oxygen port, respectively. Adjustments were made with the internal blender to provide heliox mixtures from 80 to 60 percent helium. Gas from the patient side of the inspiratory limb was analyzed for oxygen percentage. An in-line Wright spirometer, recalibrated for the density of helium, was utilized to measure the tidal volumes and the inspiratory/expiratory ratios.

A two-way analysis of variance was performed to test for the significance of differences in the measured variables.

**RESULTS**

All seven patients experienced a statistically significant (p<0.001) reduction of PaCO₂ within 20 minutes after the introduction of helium as the carrier gas (Table 1). The mean elapsed time for the reduction in PaCO₂ was 22.2 minutes. The mean reduction in PCO₂ was 35.7 mm Hg. There were no statistically significant changes in PaO₂ (Fig 1).

Six out of the seven patients had a precipitous fall in peak airway pressure after the onset of heliox breathing. The mean duration of time until peak airway pressure nadir was 2.5 minutes. The mean reduction in airway pressure was 32.86 cm H₂O. Patient 6 had a 2-hour trial of halothane anesthesia prior to the introduction of a 60 percent helium-40 percent oxygen mixture. After 5 minutes of heliox treatment, both the peak airway pressure and the PaCO₂ were rapidly reduced.

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*PIP, peak inspiratory pressure in cm H₂O; Pco₂, partial pressure of CO₂ in mm Hg; Po₂, partial pressure of O₂ in mm Hg.

**Table 1—Arterial Blood Gases and Ventilation Parameters of Intubated Status Asthmaticus Patients Breathing a 60%-40% Heliox-Oxygen Mixture**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age</th>
<th>Sex</th>
<th>I:E Ratio</th>
<th>PIP</th>
<th>pH</th>
<th>PaCO₂</th>
<th>PaO₂</th>
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<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>F</td>
<td>1:1.8</td>
<td>100</td>
<td>6.95</td>
<td>110</td>
<td>120</td>
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<tr>
<td>2</td>
<td>21</td>
<td>F</td>
<td>1:1.1</td>
<td>95</td>
<td>7.01</td>
<td>82</td>
<td>102</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>M</td>
<td>1:1.5</td>
<td>85</td>
<td>7.10</td>
<td>75</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>39</td>
<td>M</td>
<td>1:1.2</td>
<td>80</td>
<td>6.87</td>
<td>103</td>
<td>75</td>
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<tr>
<td>5</td>
<td>28</td>
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<td>7.15</td>
<td>62</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>M</td>
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<td>90</td>
<td>7.08</td>
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<td>84</td>
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<tr>
<td>7</td>
<td>30</td>
<td>M</td>
<td>1:1.4</td>
<td>75</td>
<td>7.00</td>
<td>84</td>
<td>96</td>
</tr>
</tbody>
</table>

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**Figure 1.** The response of PaO₂, PaCO₂, and pH after changing from nitrogen-oxygen to helium-oxygen mixtures.
All patients were extubated within 24 hours of intubation without complications. The mean duration of heliox treatment was 6.3 hours (SEM ± 2.3 hours).

**Discussion**

Ramsey first isolated helium from the mineral cleavite in 1895. Forty years later, Barach7-10 introduced mixtures of helium and oxygen to the medical community advocating its use for obstructive lesions of the larynx, trachea and airways. Helium enjoyed therapeutic use until 1940 when international hostilities, pharmacologic bronchodilators and mucolytic agents relegated helium to use as an investigational agent. In addition, autopsy reports suggesting mucus plugging as a prominent feature in deaths due to status asthmaticus further distanced helium from therapeutic use.11 During the three decades after World War II, reports of helium applications have punctuated the clinical literature.12-15 Yet, helium has rarely been used for the treatment of asthma.16,17 The physical properties of helium make it uniquely suited for use as a temporizing agent in patients with severe reactive airways disease, whether or not it is accompanied by mucus plugging.

Helium is a biologically inert gas of low molecular weight whose density is one quarter the density of ambient air. Helium is virtually insoluble in human tissues at atmospheric conditions. In addition, helium is nonreactive with biologic membranes and other common respiratory gases.18 At 1 atmosphere, long-term inhalation of helium-oxygen mixtures has failed to show any deleterious effects.19 As a result of its lower density, helium has a larger binary diffusion coefficient for carbon dioxide when compared to air. The addition of helium to other gases will enhance the diffusivity of the combination.20

Mixtures of helium and oxygen are only slightly more viscous than air, although they possess a much larger kinematic viscosity due to their lower density (Table 2). Kinematic viscosity is the ratio of viscosity to density. Gases of equal kinematic viscosity will become turbulent at equal flow rates. Compared to nitrogen-oxygen mixtures, helium-oxygen mixtures should allow laminar conditions to persist at significantly higher flow rates.21,22

The Reynolds number is the ratio of kinetic and viscous forces affecting the airflow, and predicts whether the airflow in a tube will be laminar or turbulent.23 For a given set of airway dimensions, turbulent flow has a greater resistance than laminar flow. Theoretically, turbulent flow is present when the Reynolds number exceeds 2,000 units. Under high flow conditions in the human trachea and mainstem bronchi, the Reynolds number is estimated between 2,100 and 2,500 units.24 Even under low flow conditions, air movement in the trachea is turbulent owing to the larynx and the irregular surface due to the cartilaginous rings.25,26 It is probable that adherent mucus and heterogeneous bronchoconstriction in the decompensated asthmatic further contribute to elevated airways resistance.27 As a result of its reduced density, a substitution of helium for nitrogen as the carrier gas would reduce the Reynolds number fourfold, leading to a change from predominantly turbulent to laminar flow. For a given driving pressure, this substitution should be manifest as significantly less density dependent flow-resistive forces, allowing greater flow during inspiration and expiration. Similarly, this substitution should lead to a reduction in the flow resistive work performed by the patient or the ventilator.

One of the causes of ineffective ventilation in mechanically ventilated asthmatic patients results from proximal airway pressure exceeding the maximum pressure limits of the ventilator causing the apparatus to recycle. This phenomena leads to smaller tidal volumes than expected, resulting in alveolar hypoventilation. The increase in laminar flow in concert with reduction in internal airway resistance while breathing helium-oxygen mixtures enables larger tidal volumes and larger inspiratory flows for any given set of ventilatory parameters. Experimentally, our data demonstrate a statistically and clinically significant reduction in Pco2 (35.7 ± 9.5 mm Hg); reduction in proximal airway pressure (32.7 ± 12.7 cm H2O); and a elevation of pH (0.30 ± 0.06 units).

Pulmonary gas exchange during periods of breathing variable density gas is not entirely understood. Lon-

<table>
<thead>
<tr>
<th>Table 2—Physical Properties of Respiratory Gases</th>
</tr>
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<tbody>
<tr>
<td>%/%</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>Oxygen</td>
</tr>
<tr>
<td>Air</td>
</tr>
<tr>
<td>Helium</td>
</tr>
<tr>
<td>He-O2</td>
</tr>
<tr>
<td>He-O2</td>
</tr>
<tr>
<td>He-O2</td>
</tr>
</tbody>
</table>

*Air assigned arbitrary value of 1.00. Viscosity measured in micropoise.
Gas Mixtures in Intubated Patients (Gluck, Onorato, Castriotta)

Figure 2. A, upper left: Under normal quiet breathing conditions, convective and diffusive forces are balanced. The dissipation of energy at the interface of convective and diffusive forces augments gas mixing. Gas transport and alveolar gas mixing are equally dependent on convection and diffusion. B, upper right: Under conditions of bronchoconstriction, airways are narrowed accentuating penetration of the wave "front" deeper into distal bronchioles preserving facilitated diffusion at the expense of increased work of breathing. Alveolar gas mixing is primarily dependent on overall ventilation. C, lower left: With the onset of fatigue, ventilation becomes less efficient, and gas transport and alveolar gas mixing becomes dependent on diffusive forces. D, lower right: The substitution of helium for nitrogen as the carrier gas provides increased laminar flow and distal respiratory unit penetration, as well as reducing the diffusion distance for CO₂. Additionally, facilitated diffusion is enhanced.
fusion would be enhanced and the inhomogeneity of ventilation would be reduced. Moreover, helium may enhance transport through collateral ventilation.35

Under conditions of sustained inspiratory loading, increases in FRC have been noted.36 Patients who are in extremis from status asthmaticus likely have an increased FRC from inspiratory and expiratory resistive loading. It is possible that helium-oxygen breathing under these conditions would cause a reduction in FRC. Thus, respiratory muscles would have a mechanical advantage while simultaneously reducing resistive load. Since patients with respiratory failure and hypercapnia are on the steep portion of the alveolar ventilation VS CO2 asymptote, a small increase in alveolar ventilation would result in a significant reduction in Pco2.

It is also interesting to consider the effect helium has on equal pressure points. During a forced expiration, airway and pleural pressures approximate each other, generating an equal pressure point. Mouthward, a flow-limiting segment is propagated. Flow on the upstream segment, between the alveolus and the equal pressure point, is laminar and dependent on viscosity. Flow between the equal pressure point and the flow-limiting segment is turbulent, and density-dependent. Helium-oxygen mixtures move the EPP upstream, without altering the position of the FLS.37,38 A more upstream position of the EPP would result in an increase in the cross-sectional area of the lung that is density dependent. Increasing the area of density dependent lung, while simultaneously breathing a low density gas, should combine to reduce the total airway resistance and increase maximum expiratory flow. This has been demonstrated in excised human lungs.39

In bronchoconstricted airways, a wide distribution of time constants accentuates the pendelluft effect resulting in an uneven ventilation and perfusion. The substitution of helium for nitrogen should normalize time constants and produce a more uniform ventilation/perfusion ratio. Still, in patients with significant airflow obstruction, there is evidence to suggest that the pleural pressure time constants may be different from normal patients.40 Breathing helium-oxygen mixtures may normalize the difference between airway and pleural pressure time constants, thus facilitating removal of alveolar gas.

Since the reduction in peak airway pressures, the increase in tidal volume, and the reduction in inspiratory/expiratory ratios all were manifest within the first two minutes in all patients after the transfer to the helium-oxygen mixtures, it is unlikely that the previously administered medication caused this effect. In fact, one patient who had failed a trial of halothane anesthesia, promptly responded to ventilation with heliox.

In our trial, we relate our experience in seven intubated patients in whom severe status asthmaticus and respiratory acidosis were resistant to aggressive medical management, but promptly responded to the addition of helium-oxygen blends. Although the sample size is small, we have demonstrated a statistically and clinically significant reduction in Pco2 and peak airway pressures while breathing helium-oxygen mixtures. In all patients, tidal volume and inspiratory flow rates while breathing helium were able to be increased. There were no untoward effects. Helium's therapeutic benefit is related to its high kinematic viscosity, high binary diffusion coefficient, low density, and the subsequent effects of these properties on airway resistance and facilitated diffusion. On practical and on theoretical grounds, the utility of helium-oxygen mixtures to reduce barotrauma and improve ventilation represents a beneficial addition to the conventional therapeutic armamentarium.

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