rupt the respiratory cycle and impair load compensation. Cotes and colleagues find that mitral stenosis increases the exercise respiratory frequency relative to tidal volume, presumably because of an altered reflex status. Similar conclusions have been drawn by Phillipson using experimental pneumonitis in dogs. His results show, in addition, that both vagal and non-vagal reflexes play an important role. Whatever the complications posed by pulmonary disease, it seems likely that analysis of the spirogram will provide information regarding alterations in the control of breathing not derivable from measurements of respiratory minute volume.

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Occlusion Pressure As A Technique In Evaluating Respiratory Control* 

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The ventilatory response to hypoxia and hypercapnia has usually been measured to estimate respiratory chemosensitivity but its usefulness for this purpose is limited. One reason for this is that the range of ventilatory changes elicited by hypercapnia and hypoxia is extremely wide. More important, impaired lung and chest wall mechanics and severely increased airway resistance can decrease the ventilatory response to chemical changes even when the chemoreceptors are functioning normally.1,2

Animal studies suggest that measurement of the pressure generated when the inspiratory muscles are made to contract isometrically during complete airway occlusion may be a better way of assessing respiratory neuron efferent activity than is ventilation.3 Although small changes in lung volume occur during this maneuver

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because of gas decompression, these changes are negligible and can, for practical purposes, be ignored. Both occlusion pressure and electrical activity increase proportionally with hypercapnia. Good correlations are also observed within a single breath between changes in phrenic nerve activity and airway pressures produced during occlusion. Since occlusion pressures are measured under conditions of zero flow and volume changes in the lung, the pressures developed should be insensitive to changes in airway resistance or lung and chest compliance, and therefore could be used to evaluate chemosensitivity even in patients with lung disease. Furthermore, studies in anesthetized animals suggest that airway occlusion may also be used to assess the neuro-mechanical control of breathing. Inspiratory time during an occluded breath is greater than during unoccluded breaths and is about the same as it is after vagotomy. Thus, the ratio of inspiratory time of the breath taken before and during complete occlusion has been used to estimate the effects of vagally mediated pulmonary stretch receptors. Also, the ratio of the pressure measured during occlusion compared to the volume of the preceding unoccluded breath (effective compliance) has been used as a quantitative measure of the neuro-mechanical response to loading of the chest. These studies suggest that one kind of measurement, occlusion pressure, which can be determined noninvasively, might be valuable in assessing chemosensitivity, the strength of stretch reflexes, and neuromuscular compensation to lung or chest wall loading.

However, it was recognized from the onset that the pressures measured during occlusion might be affected by changes in resting lung volume, as well as by respiratory neuron output. It was known that for a given level of electrical stimulation, the pressure generated by respiratory skeletal muscle, like other striated muscles, varied with their length and hence would depend upon functional residual capacity. However, it was hoped that corrections might be developed so that occlusion pressure could be used in man even when functional residual capacity was abnormal.

**Methods of Measuring Occlusion Pressure**

Figure 1 illustrates a circuit which can be used to measure both occlusion pressure and ventilation during progressive hypercapnia. In this circuit, hypercapnia at full arterial oxygen saturation is produced by rebreathing 6 or 7 percent CO2 in O2. Ventilation is measured continuously by integration of the pneumotachygraph signal and PA CO2 with the infrared CO2 analyzer.

A large bore stopcock included in the inspiratory line is turned randomly to completely occlude inspiratory flow for single breaths and a pressure transducer is used to determine changes in airway pressure. The unidirectional breathing valve allows the stopcock on the inspiratory side to be turned during expiration so that expiration continues unaffected to functional residual capacity, but the subsequent inspiration occurs against total occlusion.

In anesthetized animals, inspiratory occlusion increases inspiratory time. Airway pressure decreases curvilinearly during the occluded inspiratory effort, as shown in Figure 2.
than lengthened by occlusion. In man, as in the vagotomized animal, this shortening may occur by stimulation of diaphragm tendon receptors during the occluded breath, intercostal spindle receptors activated by chest wall distortion, or intrathoracic vascular receptors distended by the negative pressure occurring as the inspiratory muscles contract against the blocked airway.

Whitelaw and associates suggested that cortical effects in conscious man are of major importance in reducing inspiratory time and in determining the characteristics of the pressure changes developed after the first 100-200 milliseconds of total airway closure. To the extent that these cortical effects are caused by apprehension, they can be minimized by carefully explaining the test and by a trial run. However, even when care is taken to reduce anxiety, the pressures developed in the first 100-200 milliseconds after occlusion at a constant level of chemical stimulation are still usually more reproducible than pressures developed later in the inspiratory effort. Thus, the airway pressure measured early after the start of the occluded inspiratory effort in conscious man may be a better index of isometric inspiratory force than the end-inspiratory pressure actually produced. This would be true if, in conscious man, as in the anesthetized animals, pressure would be developed in a stereotyped fashion except for interference from higher nerve centers which do not usually participate in normal breathing. This assumption remains to be proven.

In recent studies, airway pressure has usually been measured at 100 to 200 milliseconds after occlusion rather than end-inspiration, but it still remains uncertain when pressure should be measured in the course of the occluded inspiratory effort. Until this uncertainty is resolved, it may be advisable to measure pressure at several intervals during the occluded breath.

It is obviously important that the subject be unable to anticipate when the occlusion will occur if the apparatus shown in Figure 1 is used. Therefore, it is crucial that occlusions be performed randomly. Alternatively, an electrically operated shutter can be used to occlude every breath for fixed but brief intervals after the onset of inspiration.

**Comparison of Occlusion Pressure and Ventilatory Responses During Hypoxia and Hypercapnia**

In man, respiratory efferent nerve activity and occlusion pressure responses cannot be directly compared to test the validity of using occlusion pressure as a measure of chemosensitivity. However, ventilatory responses seem to adequately reflect respiratory efferent activity in normal man.

Therefore, the following studies were performed during hypercapnia and/or hypoxia produced by rebreathing techniques: (1) occlusion pressure responses and ventilatory responses in the same individuals were compared in the same rebreathing trial; (2) reproducibility of the occlusion pressure and ventilatory response in the same individuals on different days were compared; (3) variations in the ventilatory and pressure responses were compared in different individuals; and (4) ventilatory and occlusion pressure responses were measured before and after increased inspiratory or expiratory resistances were compared.

A circuit similar to that diagrammed in Figure 1 was used to produce progressive hypercapnia. To produce progressive hypoxia, 6 or 7 percent CO₂ in air was rebreathed and a portion of the expired gas was diverted through a CO₂ absorber to keep Pco₂ constant. Fine meshed screen discs were inserted in the inspiratory or expiratory lines to increase separately the resistance to inspiration or expiration.

In most experiments, a single breath was randomly occluded by manually turning a value in the inspiratory line. However, in some experiments, an electrically operated shutter was used to occlude every breath for 100 milliseconds. Preliminary experiments showed that airway occlusion by itself had no significant effect on ventilatory responses.

In 35 trials performed in seven normal volunteers during progressive hypercapnia, there was a linear correlation between P₁₀₀ and ventilation and between Pco₂ and P₁₀₀ which exceeded .80 in but one of the 35 studies. This is similar to the results we have obtained in anesthetized dogs and in awake and anesthetized goats. Correlations were not improved in this study by plotting the log of the occlusion pressure versus Pco₂ as has been previously suggested.

Considerable day-to-day variation occurred in the ventilation and P₁₀₀ responses to progressive hypercapnia repeatedly measured in seven seated subjects. However, when ventilatory and pressure responses obtained at different times were compared, they seemed to vary in the same direction so that greater ventilatory responses were associated with increased pressure responses. These results suggested that, at least in the same subject, the correlation between ventilatory and occlusion pressure response to hypercapnia is reasonably good.

To determine whether ventilatory responses in different individuals correlate with pressure responses, we compared pressure and ventilatory responses measured in 14 subjects in the same rebreathing trial. The variation in ventilatory response was as great as the variation in pressure response so that the ratio of the standard deviation to the mean was 0.7 for pressure responses and 0.6 for ventilatory responses. However, the correlation coefficient between ventilatory and pressure responses was good (r = .83). Although P₁₀₀ and ventilation increased hyperbolically during hypoxia, these responses could be linearized by plotting ventilation and P₁₀₀ against the reciprocal of Po₂ as suggested by Well et al. Again, reasonably good correlations (r = .81) were obtained between ventilatory and pressure responses in nine subjects tested.

The effect of the pattern of breathing on occlusion pressure response was examined in two subjects. These subjects maintained a constant tidal volume of 500 ml on room air and breathed at a frequency of 20, 30 and later 40 breaths per minute. P₁₀₀ was measured by an electrically activated shutter technique at each level of breathing frequency. Studies were repeated at the three breathing rates after tidal volume was increased to 1 and subsequently to 2 L. As shown in Figure 3, P₁₀₀ increases with both tidal volume and with frequency; but
Effect of Different Breathing Patterns on Relationship between Ventilation and $P_{100}$

![Figure 3](http://journal.publications.chestnet.org/pdaccess.ashx?url=/data/journals/chest/20982/)

Figure 3. Relationship between ventilation produced by different breathing patterns and $P_{100}$. Note that relationship is largely unaffected by wide differences in breathing pattern.

the relation between $P_{100}$ and ventilation was unchanged by pattern of breathing.

### The Effects of Added Resistance to Airflow on Occlusion Pressure and Ventilatory Responses

Increased expiratory resistance should increase functional residual capacity (FRC). When FRC is increased, the resting length of the inspiratory muscles is decreased which might depress occlusion pressure responses. To study the effect of small alterations in FRC, the $P_{100}$ and ventilatory responses to hypercapnia were examined in subjects in both the sitting and supine positions. In these studies summarized in Table 1, not only was ventilatory response to CO$_2$ unaffected by body position, confirming observations reported by Rigg and coauthors, but so was the $P_{100}$ response. Functional residual capacity is not usually changed by added inspiratory resistance. As expected, studies in anesthetized animals showed that added inspiratory resistance had no effect on occlusion pressure responses to chemical stimulation.

On the other hand, added inspiratory resistance did alter the occlusion pressure response to both hypoxia and hypercapnia in conscious man. In 18 volunteers tested during either hypoxia or hypercapnia, elevated inspiratory resistance was associated with an increase in $P_{100}$ at the time level of chemical stimulation in 16; and in 12, the change in $P_{100}$ for a given change in $PO_2$ or $PCO_2$ was greater with the inspiratory resistance. This effect of inspiratory resistance on occlusion pressure is shown in two subjects in Figure 4. Lung volumes measured before and after the application of the resistance were unchanged so that the increase in occlusion pressure could not be explained by a decrease in FRC.

The occlusion pressure response to CO$_2$ rebreathing is the same in normal subjects and in eucapnic patients with obstructive lung disease and increased FRC. However, in patients with chronic obstructive lung disease, preliminary studies suggest that there is little or no increase in $P_{100}$ with increased inspiratory resistance. Whether differences in FRC or changes in respiratory neuron output account for the difference in the occlusion pressure response to inspiratory flow resistive loads in normal subjects and in patients, is not clear. However, the failure to respond to increased inspiratory resistance may predispose patients with chronic obstructive lung disease to respiratory failure when lung infections occur.

To examine the effect of inspiratory resistance on occlusion pressure further, $P_{100}$ was measured by the electrically activated shutter technique in four subjects. They rebreathed CO$_2$ in a circuit in which an inspiratory resistance could be added for one or two consecutive breaths randomly during the course of the study. The increase in occlusion pressure was present by the second of two consecutive breaths with elevated resistance. Whether this pressure response persists when inspiratory resistance is increased for long periods of time remains to be determined. Studies in goats suggest that the acute increase in occlusion pressure with inspiratory resistance depends on consciousness and is largely abolished by anesthesia.

### Occlusion Pressure in the Evaluation of Neuromechanical Responses

Comparison of occlusion pressures with phrenic nerve activity and with respiratory muscle electrical activity supports the idea that the pressure developed during complete inspiratory occlusion in fact reflects respiratory motor neuron activity. In normal individuals, occlusion pressure responses also seem to be an adequate index of chemosensitivity, but the best method of measuring occlusion responses is still not certain and occlusion response appears to be as variable as ventilatory response. It also seems clear that if suitable corrections are developed for differences in functional residual capacity, oc-

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**Table 1—Effect of Body Position on Respiratory Response to Hypercapnia (Mean ± 1 Standard Error)**

<table>
<thead>
<tr>
<th></th>
<th>Sitting</th>
<th>Supine</th>
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<tbody>
<tr>
<td>$\Delta P_{100}/\Delta P_{CO2}$ cm H$_2$O/mm Hg</td>
<td>0.60 ± 0.11</td>
<td>0.63 ± 0.10</td>
</tr>
<tr>
<td>$\Delta V_T/\Delta P_{CO2}$ ml/mm Hg</td>
<td>77 ± 6</td>
<td>82 ± 5</td>
</tr>
<tr>
<td>$\Delta V/\Delta P_{CO2}$ l/min/mm Hg</td>
<td>2.98 ± 1.83</td>
<td>3.02 ± 0.64</td>
</tr>
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the effect of respiratory motor neuron responses to both loading and changes in chemical drive. The occlusion pressure technique has already been used quite effectively in evaluating neuromechanical responses in infants. It is possible that with further experiments, the occlusion pressure technique may reveal unsuspected defects in neuromechanical response which, like blunted chemosensitivity, may predispose to respiratory failure. By measuring occlusion pressure response to hypoxia and hypercapnia at different levels of increased loading, it may be that abnormalities in neuromechanical response can be distinguished from abnormalities in chemosensitivity.

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