PATTERN OF REDUCTION OF VENTILATORY AND OCCLUSION PRESSURE RESPONSE TO CARBON DIOXIDE BY PENTAZOCINE IN MAN

G. B. DRUMMOND, J. FISHER, A. ZIDULKA AND J. MILIC-EMILI

SUMMARY

Mean inspiratory flow, occlusion pressure and end-tidal P\textsubscript{CO\textsubscript{2}} were measured in six healthy, sitting subjects, during breathing air and rebreathing carbon dioxide, before and after pentazocine 0.5 mg kg\textsuperscript{-1} i.v. and again after naloxone 20 \mu g kg\textsuperscript{-1}. Pentazocine reduced the occlusion pressure and inspiratory flow responses at a given P\textsubscript{CO\textsubscript{2}} during carbon dioxide rebreathing and these effects were antagonized by naloxone. The relationship of inspiratory flow and end-tidal carbon dioxide during rebreathing was used to measure the P\textsubscript{CO\textsubscript{2}} value at which mean inspiratory flow was 1 litre s\textsuperscript{-1}. Occlusion pressure at this P\textsubscript{CO\textsubscript{2}} was reduced in all the subjects by pentazocine, suggesting that the generation of inspiratory flow required less muscle activity. This effect was antagonized by naloxone.

Drugs such as sedatives, narcotics and general anaesthetics are thought to cause respiratory depression by a central action. Externally imposed loads to breathing, such as an added resistance, may also cause respiratory depression (Lourenco et al., 1966), but in these circumstances, neuromuscular activity is augmented although the resultant ventilation is diminished. By occlusion of the airway and measurement of the decrease in airway pressure during an inspiratory effort, a more direct assessment of the activity of the respiratory muscles can be made (Whitelaw, Derenne and Milic-Emili, 1975). This is because no gas flow and no lung volume changes occur during the measurement and the composite action of the inspiratory muscles is transformed into decrease of airway pressure. If the inspiratory attempt starts at the same lung volume on each occasion, then the muscles will be at the same initial length, and the pressure decrease correlates well with the neural activation of the muscles (Eldridge, 1975).

The ratio of the rate of change of pressure during an occluded breath to the rate of change of lung volume during a normal breath is an index of the “effective impedance” of the respiratory system during active inspiration.

Derenne and others (1976) measured occlusion pressure and rate of change of lung volume (as mean inspiratory flow rate, V\textsubscript{T}/T\textsubscript{1}) during carbon dioxide rebreathing in patients anaesthetized with methoxyflurane. The average response of occlusion pressure to carbon dioxide was reduced less than the response of mean inspiratory flow rate. This was interpreted as an increase in effective impedance and attributed to the decreased passive compliance of the respiratory system during anaesthesia. They suggested that part of the ventilatory depression observed during anaesthesia was the result of the reduced compliance of the respiratory system. In animals, however, ventilatory depression or stimulation are not associated with changes in effective impedance (Goldberg and Milic-Emili, 1977; Bopp et al., 1979).

We have studied the effects of pentazocine in conscious subjects to determine if the ventilatory depression was associated with a change in effective impedance.

METHODS

Six healthy male volunteers were studied after written consent. The study was approved by the Montreal General Hospital Ethics Committee. No subject was taking medication or had taken drinks containing caffeine for 12 h before. One subject (PB) smoked 20 cigarettes daily. Each subject was studied 2–3 h after a light non-fatty breakfast. Vital capacity and forced expiratory volume in 1 s were measured with the subject

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standing. Functional residual capacity (FRC) was measured in the sitting position in a constant volume body plethysmograph (Warren Collins). The subject then left the plethysmograph and sat comfortably with the arms supported in a carefully standardized position in an adjustable chair. He wore a noseclip, and breathed through the apparatus mouthpiece.

The apparatus consisted of two one-way valves connected to taps to allow either air breathing or rebreathing from a bag in box system (fig. 1). A pneumotachograph (Fleisch no. 2) was connected so that inspiratory flow could be measured in both circumstances using a Hewlett-Packard 270 transducer. This position allowed only room air to pass through the pneumotachograph, which was not heated. Inspired volume was derived by electrical integration of the inspiratory flow signal (Hewlett-Packard 8815A). The inspiratory and expiratory flow resistances of the apparatus were 0.14 and 0.15 kPa litre⁻¹ s respectively at a flow rate of 3 litre s⁻¹. Gas was sampled at the mouthpiece with a mass spectrometer (Medspect MS8) to allow measurement of end-tidal $P_{CO_2}$ ($P_{E_{CO_2}}$) and $P_{O_2}$ to check that hyperoxia was present throughout the rebreathing manoeuvre.

A pneumatically-damped solenoid was used to move a piston to close the channel of the inspiratory valve. The piston movement could not be seen or heard by the subject.

The solenoid was activated during expiration without the knowledge of the subject, to prevent inspiratory flow during the early part of the next inspiratory effort. The expiratory valve was adjusted and checked to make sure that no return flow could occur during this inspiratory attempt. The resultant subatmospheric pressure was measured at the mouthpiece (Hewlett-Packard 267B transducer) and recorded on FM magnetic tape. The piston was withdrawn from the inspiratory port after about 300 ms of the effort and the delayed inspiration started, and in this way the rhythm of breathing was not greatly disturbed. The frequency response of the pressure measurement system was linear to 20 Hz.

The flow, pressure, volume and carbon dioxide concentration signals were processed and displayed on a chart recorder. An electrocardiogram taken from chest leads was displayed continuously on an oscilloscope and arterial pressure measured intermittently by sphygmomanometer.

After the subject had breathed from the mouthpiece until $P_{E_{CO_2}}$ was constant, 10 airway occlusions were performed at random intervals, each separated by at least 10 normal breaths. The taps of the apparatus were then turned to allow rebreathing, and random occlusions made at intervals of about 10 breaths during rebreathing. The bag volume was adjusted to about half the subject's vital capacity. The bag was filled with 50% oxygen, 7% carbon dioxide and nitrogen.

After a practice run, a control series of measurements were made. A slow i.v. infusion of sodium chloride 154 mmol litre⁻¹ was then started and pentazocine 0.5 mg kg⁻¹ given i.v. over a 5-min period, while arterial pressure was checked. Ten minutes later, the subject was moved into the body plethysmograph and FRC was measured again. He returned from the box and a further series of measurements of occlusion pressure and ventilation was made during air breathing and rebreathing. About 30 min after the pentazocine had been given, naloxone 20 μg kg⁻¹ was given i.v. over a 5-min period and all measurements were repeated for a third time 10 min later.

Measurements were taken from the rebreathing records after the increase in $P_{E_{CO_2}}$ had become linear. Measurements were made from the breath preceding the airway occlusion (fig. 2). The
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made at a suitable speed for measurement of occlusion pressure (50 mm s⁻¹). This avoided making changes in recorder speed during the experiment which could have warned the subject that an airway occlusion was imminent.

Occlusion pressure was measured 100 ms after the airway pressure had become less than −0.1 kPa (P₀.₁) rather than after the pressure became less than atmospheric (fig. 3). This method is similar to that advocated by Kryger, McCullough and Weil (1976) who measured the pressure change from 50 to 100 ms after the pressure became less than atmospheric. Occlusion pressure was also measured by the original method of Whitelaw, Derenne and Milic-Emili (1975).

The mean values of the measured and derived variables during air breathing were compared using Student’s t test for paired values. Linear regression relationships for the values obtained during rebreathing were calculated by the least squares technique. Occlusion pressure values at an inspiratory flow rate of 1 litre s⁻¹ were estimated from the linear regression relationship of mean inspiratory flow PE'CO₂ and the logarithm of occlusion pressure with PE'CO₂. These values were compared using the Wilcoxon signed rank test.

RESULTS

Details of subjects are given in table I. Subject JF had a moderately reduced FRC and RV.

No significant changes in breathing pattern were found after pentazocine or naloxone when the subjects breathed air. Mean PE'CO₂ in the control state was 5.95 kPa ± 0.62, and this

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**Table I. Details of subjects studied.** FEV₁₀ = forced expiratory volume in 1 s; VC = vital capacity; RV = residual volume; FRC = functional residual capacity; FVC = forced vital capacity

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (yr)</th>
<th>Height (m)</th>
<th>Weight (kg)</th>
<th>FEV₁₀/FVC (%)</th>
<th>VC (%)</th>
<th>RV (% predicted)</th>
<th>FRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZ</td>
<td>36</td>
<td>1.78</td>
<td>79</td>
<td>71</td>
<td>119</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>RR</td>
<td>27</td>
<td>1.79</td>
<td>85</td>
<td>80</td>
<td>115</td>
<td>97</td>
<td>96</td>
</tr>
<tr>
<td>JF</td>
<td>25</td>
<td>1.85</td>
<td>90</td>
<td>74</td>
<td>95</td>
<td>65</td>
<td>76</td>
</tr>
<tr>
<td>PB</td>
<td>30</td>
<td>1.75</td>
<td>63</td>
<td>77</td>
<td>99</td>
<td>93</td>
<td>99</td>
</tr>
<tr>
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<td>28</td>
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<td>74</td>
<td>78</td>
<td>110</td>
<td>88</td>
<td>89</td>
</tr>
<tr>
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<td>1.80</td>
<td>68</td>
<td>93</td>
<td>99</td>
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<td>94</td>
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</tbody>
</table>
increased by 0.59 kPa ($P<0.001$) after pentazocine and decreased by 0.64 kPa ($P<0.001$) after naloxone. The values after naloxone were not significantly different from control. No significant change in FRC was detected after pentazocine administration.

The results obtained from rebreathing experiments in an individual subject (AZ) are shown in figure 4. Pentazocine reduced the ventilatory response to $P_{e}CO_{2}$ and displaced the relationship towards greater $P_{e}CO_{2}$ values (panel A). Naloxone returned the relationship towards control values. Panel B shows the relationship of $V_{t}$ to $V_{T}$. There is no apparent difference between the three sets of measurements. In panel C, the relationship between $V_{t}$ and $V_{T}/T_{i}$ is linear for the control state and after drug administration. However, the values of $V_{t}$ for a given $V_{T}/T_{i}$ value are less after pentazocine administration ($P<0.05$). This change in relationship was accompanied by a reciprocal change in the duration of inspiration ($T_{i}$) relative to the

<table>
<thead>
<tr>
<th>Subject</th>
<th>Control</th>
<th>After pentazocine</th>
<th>After naloxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZ</td>
<td>0.48±0.03</td>
<td>0.41±0.06</td>
<td>0.47±0.02</td>
</tr>
<tr>
<td>RR</td>
<td>0.49±0.04</td>
<td>0.53±0.09</td>
<td>0.50±0.02</td>
</tr>
<tr>
<td>JF</td>
<td>0.44±0.03</td>
<td>0.42±0.07</td>
<td>0.44±0.03</td>
</tr>
<tr>
<td>PB</td>
<td>0.47±0.02</td>
<td>0.42±0.02</td>
<td>0.44±0.03</td>
</tr>
<tr>
<td>BH</td>
<td>0.44±0.03</td>
<td>0.45±0.03</td>
<td>0.45±0.04</td>
</tr>
<tr>
<td>RD</td>
<td>0.48±0.03</td>
<td>0.49±0.04</td>
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</table>

<table>
<thead>
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<th>Subject</th>
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<th>Pentazocine</th>
<th>Naloxone</th>
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<td>AZ</td>
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</tr>
<tr>
<td>RR</td>
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<td>0.53±0.05</td>
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<td>0.56±0.05</td>
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</tr>
<tr>
<td>PB</td>
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<td>0.51±0.09</td>
<td>0.51±0.03</td>
</tr>
<tr>
<td>BH</td>
<td>0.51±0.06</td>
<td>0.50±0.05</td>
<td>0.47±0.07</td>
</tr>
<tr>
<td>RD</td>
<td>0.59±0.04</td>
<td>0.60±0.05</td>
<td>0.62±0.05</td>
</tr>
</tbody>
</table>

FIG. 4. Results of rebreathing procedure in a representative subject. Each point represents a single measurement. ● = control measurements; △ = after pentazocine; □ = after naloxone.
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Table IV. Regression relationships of mean inspiratory flow rate (\(V_T/T_1\)) with \(P_{\text{ET}}CO\), and \(\log P_{\text{ET}}CO\), with \(P_{\text{ET}}CO\), \(C = \) control; \(P = \) after pentazocine, \(N = \) after naloxone *Predicted value is based upon extrapolation of the relationship to 7 kPa

<table>
<thead>
<tr>
<th>Subject</th>
<th>State</th>
<th>Slope ((\text{litres s}^{-1} \text{kPa}^{-1}))</th>
<th>Predicted value when (P_{\text{ET}}CO = 7) kPa ((\text{litres s}^{-1}))</th>
<th>(r)</th>
<th>Slope ((\ln \text{Pa kPa}^{-1}))</th>
<th>Predicted value when (P_{\text{ET}}CO = 7) kPa ((\ln \text{Pa}))</th>
<th>(r)</th>
</tr>
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<tbody>
<tr>
<td>AZ</td>
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<td>0.98</td>
<td>1.47</td>
<td>5.80</td>
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</tr>
<tr>
<td></td>
<td>P</td>
<td>0.79</td>
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<td>0.96</td>
<td>0.85</td>
<td>4.92</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>0.82</td>
<td>0.92</td>
<td>0.97</td>
<td>1.56</td>
<td>5.48</td>
<td>0.97</td>
</tr>
<tr>
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<td>C</td>
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<td>0.98</td>
<td>1.80</td>
<td>6.04</td>
<td>0.90</td>
</tr>
<tr>
<td></td>
<td>P</td>
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<td>0.63</td>
<td>0.95</td>
<td>1.01</td>
<td>4.43</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>N</td>
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<td>0.98</td>
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<td>0.97</td>
</tr>
<tr>
<td>JF</td>
<td>C</td>
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<td>0.80</td>
<td>0.97</td>
<td>0.66</td>
<td>6.33</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>P</td>
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<td>0.21</td>
<td>0.99</td>
<td>0.27</td>
<td>5.80</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>1.21</td>
<td>0.95</td>
<td>0.99</td>
<td>1.03</td>
<td>6.30</td>
<td>0.86</td>
</tr>
<tr>
<td>PB</td>
<td>C</td>
<td>0.60</td>
<td>0.60</td>
<td>0.98</td>
<td>1.18</td>
<td>5.27</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.65</td>
<td>0.19*</td>
<td>0.99</td>
<td>1.28</td>
<td>4.21</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>0.63</td>
<td>0.52</td>
<td>0.98</td>
<td>0.72</td>
<td>5.15</td>
<td>0.96</td>
</tr>
<tr>
<td>BH</td>
<td>C</td>
<td>0.84</td>
<td>2.09*</td>
<td>0.99</td>
<td>1.00</td>
<td>7.18</td>
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</tr>
<tr>
<td></td>
<td>P</td>
<td>0.43</td>
<td>1.42*</td>
<td>0.84</td>
<td>0.37</td>
<td>5.92</td>
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<tr>
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<td>0.72</td>
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</tr>
<tr>
<td>RD</td>
<td>C</td>
<td>0.78</td>
<td>0.52*</td>
<td>0.98</td>
<td>0.91</td>
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<tr>
<td></td>
<td>P</td>
<td>0.57</td>
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<td>5.66</td>
<td>0.90</td>
</tr>
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</table>

The relationship of \(V_T/T_1\) and \(V_T/T_1\) did not change significantly in any of the subjects with drug administration. The ratio of these values remained close to 0.5, indicating that the inspiratory waveform remained linear (table III).

The relationship between \(P_{0.1}\) and \(P_{\text{ET}}CO\), was not linear (panel D), whereas that between \(\log P_{0.1}\) and \(P_{\text{ET}}CO\), appeared to be so (panel E). In five of the six subjects, the correlation of \(\log P_{0.1}\) with \(P_{\text{ET}}CO\), was greater than that of \(P_{0.1}\) with \(P_{\text{ET}}CO\). The relationship of \(P_{0.1}\) with \(V_T/T_1\) (panel F) shows that, for a given value of \(V_T/T_1\), \(P_{0.1}\) values after pentazocine were less than the \(P_{0.1}\) values in the control state.

Table IV gives the details of the linear regression relationships of both \(V_T/T_1\) and \(\log P_{0.1}\) with \(P_{\text{ET}}CO\), for each subject in each state, and these relationships are shown in figures 5 and 6. The relationship between \(V_T/T_1\) and \(P_{\text{ET}}CO\), was displaced towards greater values of \(P_{\text{ET}}CO\), in all subjects after pentazocine and in four (RR, AZ, BH and RD), the slope was less than in the control state. (In three of these subjects, the mean value for \(T_1/T_1\) was increased after pentazocine, whereas in the other subjects it decreased.) The pattern of change in the relationship of \(\log P_{0.1}\) with \(P_{\text{ET}}CO\), caused by pentazocine and naloxone (fig. 6) resembled the changes found in the relationship of \(V_T/T_1\) with \(P_{\text{ET}}CO\), except in subject PB.

The \(P_{0.1}\) values associated with a mean inspiratory flow of 1 litre s\(^{-1}\) were less after pentazocine than in the control state \((P < 0.05)\) whereas those
Fig. 5 Individual linear regression relationships of mean inspiratory flow ($V_{T}/T_{I}$) with $P_{E}\cdot CO_{2}$,
--- = control measurements; --- = after pentazocine; --- = after naloxone.

Fig. 6. Individual linear regression relationships of log $P_{O_{2}}$, with $P_{E}\cdot CO_{2}$ (same symbols as in figure 4).
after naloxone were not significantly different from control (table V).

**DISCUSSION**

**Methods**

This study was undertaken to determine if the relationship of occlusion pressure and mean inspiratory flow was altered after ventilatory depression. A dose of pentazocine was selected that caused significant depression (Belville and Green, 1965) and a dose of naloxone that would antagonize this (Kallos and Smith, 1968). All the subjects were able to detect when pentazocine had been given. We did not believe that a blind study would have shown different effects since we studied breathing during stimulation by rebreathing carbon dioxide. Naloxone was used to show that the changes caused by pentazocine could be reversed and that the changes were not a result of the sequence of the study. Naloxone does not influence respiration in normal subjects when given alone (Evans et al., 1974; Fleetham et al., 1980).

Inspection of the recording of the pressure signal showed that the occlusion pressure wave had a variably gradual onset. The exact time at which airway pressure became less than atmospheric was difficult to define because the rate of change of pressure was small. However, the time at which the pressure became less than 0.1 kPa below atmospheric was easy to define and in this study, \( P_{o1} \) was measured as the pressure change in the subsequent 100 ms. The time taken for the airway pressure to decrease from atmospheric to \(-0.1 \) kPa varied from subject to subject. It decreased as \( P_{o1} \) increased in each subject.

Measurements of occlusion pressure by our method were less variable and had a better correlation with \( P_{E_{CO}} \) than measurements made by the original method of Whitelaw, Derenne and Milic-Emili (1975), so we used these values for analysis. In other rebreathing experiments in man (Drummond and Danylewick, unpublished data) measurements made from \(-0.1 \) kPa correlated more closely with the pressure decrease from 50 to 100 ms used by Kryger, McCullough and Weil (1976). Drummond and Scott (1980) suggested that the gradual decrease in pressure at the onset of the occlusion pressure wave in man was caused by the compliance of the upper airway.

**Results**

Neural activation of the inspiratory muscles increases progressively during inspiration. If the airway is occluded, the contraction of the muscles is isometric and the pressure generated indicates the magnitude of the neural activation, as long as the initial muscle length is the same on each occasion. The pressure produced is greater than the pleural pressure change that occurs when the muscles are allowed to shorten in a normal breath, because of the length–tension characteristics of active muscle (Mognoni et al., 1968).

If the volume inspired at the end of a normal inspiration is compared with the pressure produced after the same duration of an occluded effort, the “effective elastance” of the respiratory system can be calculated. This value is measured at zero flow and represents the sum of the passive elastic properties of the respiratory system, the intrinsic length–tension characteristics of the muscles, and possibly neural reflex components (Eldridge and Vaughn, 1977). This “effective elastance” allows prediction of the response of the respiratory system to external loads, whereas the passive elastance does not (Lynne-Davies et al., 1971).

In conscious subjects, occlusion pressure cannot be reliably measured for more than about 150 ms since the effort becomes altered by conscious influences (Whitelaw, Derenne and Milic-Emili, 1975). Consequently, occlusion pressure cannot be measured at a time equivalent to the end of a normal inspiration, and effective elastance cannot be measured. Measurement of \( P_{o1} \) is made when the inspiratory muscles would normally be generating inspiratory flow as well as volume change. Consequently the relationship of \( P_{o1} \) with mean inspiratory flow rate \((V_T/T_I)\) is an index of “effective impedance” which is a value that contains both elastic and resistive components.

The relationship of \( P_{o1} \) with \( V_T/T_I \) is not constant as ventilation is increased. We found that \( V_T/T_I \) increased linearly with increasing \( P_{E_{CO}} \) as shown by Barcroft and Margaria (1931). However we found that \( P_{o1} \) increased exponentially with increasing \( P_{E_{CO}} \) as found by others (Whitelaw, Derenne and Milic-Emili, 1975; Zackon, Despas and Anthonisen, 1976). This exponential relationship is probably because airway resistance increases exponentially as inspiratory flow increases (Cotes, 1975). Because \( V_T/T_I \) and \( P_{o1} \)
are not related to $P\mathrm{e}'_{\text{CO}_2}$ in the same way, they will not bear a constant relationship to each other and the "effective impedance" of the respiratory system will increase with increasing inspiratory flow (as does airway resistance). Consequently, we chose to compare $P_{0.1}$ values that were associated with identical mean inspiratory flow rates before and after drug administration, so that the pressure component related to flow would be similar. This pressure component could change if airway resistance were to change, but pentazocine does not influence bronchomotor tone (Aviado, 1975) and we found no change in FRC that could have altered airway resistance.

Occlusion pressure is measured early in inspiration and mean inspiratory flow is calculated from values measured at the end of inspiration. Their relationship could be changed by change in the pattern of the increasing activation of the respiratory muscles leading to a change in the pressure and volume wave forms. However, the ratio of the volume inspired in the first 0.5 s of inspiration with the rate of volume inspired over the whole of inspiration ($V_t/T_t$) was similar in all the subjects and did not change after pentazocine, showing that the pattern of increase in muscle activation did not alter.

In animals, a change in FRC has been shown to alter the occlusion pressure produced by the same amount of neural activation because the initial length and shape of the muscles has been changed (Eldridge and Vaughn, 1977). However, Burki (1977) found that the relationship of $P_{0.1}$ to $P\mathrm{e}'_{\text{CO}_2}$ in man was not influenced by moving subjects from the seated to the supine position despite a mean decrease in FRC of 0.8 litre. The method of FRC measurement used in the present study could detect an FRC change of 0.4 litre. Even if the relationship of $P_{0.1}$ to neural drive were altered by changes in this range, this would only preclude estimation of neural drive from $P_{0.1}$ values. The relationship of $P_{0.1}$ with inspiratory flow would still indicate the effective mechanics of the respiratory system.

We found that a smaller $P_{0.1}$ was associated with the same inspiratory flow rate after pentazocine, suggesting that the effective elastance of the respiratory system had decreased. The passive elastic properties were unlikely to have changed since pentazocine does not influence the elastance of the respiratory system even in larger doses (Hanato et al., 1975) and FRC is unlikely to have changed enough to alter elastance significantly.

Other workers have reported relative changes in occlusion pressure and ventilatory responses after narcotics. Kryger and others (1976) studied five normal subjects before and after a small, variable oral dose of pethidine. $P_{0.1}$ appeared to be less reduced than ventilation after pethidine during steady state hyperoxic hypercapnia and progressive isocapnic hypoxia. Kryger and others did not, however, report either the relative duration of inspiration (which would have influenced the relationship between $P_{0.1}$ and $V_t$) or the posture of the subjects. Knill and others (1976) studied supine adolescent patients after i.m. morphine or pethidine. At the same values of occlusion pressure, $V_t/T_t$ was less after drug administration. They suggested that this probably indicated an increase in effective respiratory impedance because of increased tonic activity of chest wall and abdominal muscles. This pattern of activity has been described during morphine and nitrous oxide anaesthesia (Sokoll, Hoyt and Gergis, 1972; Freund et al., 1973) but has not been seen after large doses of pentazocine (Hanato et al., 1975). The present study shows that pentazocine reduces the effective impedance of the respiratory system, contrary to the findings of Kryger and others (1976) and Knill and others (1976). In our subjects, the decrease in ventilation that occurred was less than it would have been if the effective elastance had not changed.

The most likely explanation for these findings is that, in adult upright subjects, the sedative effect of pentazocine reduces the tonic activity of chest wall muscles and hence the muscular contribution to the stiffness of the chest wall, allowing the diaphragm to drive the ribcage more easily (Goldman, 1974; Sharp et al., 1975). However, such a decrease in effective elastance means that the respiratory system is less able to compensate if loads to breathing are imposed (Margaria et al., 1973).

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VENTILATORY DEPRESSION BY PENTAZOCINE

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TYPE DE REDUCTION DE LA REPONSE DE LA PRESSION DE VENTILATION ET D'OCLUSION A L'ANHYDRIDE CARBONIQUE DUE A LA PENTAZOCINE CHEZ L'HOMME

RESUME

On a mesure chez six sujets sains en position assise le flux inspiratoire moyen, la pression d'occclusion et le Pco2 respiratoire terminal, au cours de la respiration d'air et d'une nouvelle respiration d'anhydride carbonique, avant et aprés avoir administré 0,5 mg kg-' de pentazocine i.v. et de nouveau aprés 20 μg kg-' de naloxone. La pentazocine a fait diminuer la réponse de presision d'occclusion et du flux inspiratoire a un Pco2 donne au cours d'une nouvelle respiration d'anhydride carbonique et ces effets ont été antagonises par la naloxone. Le rapport entre le flux inspiratoire et l'anhdydride carbonique respiratoire terminal au cours de la nouvelle respiration a été utilise pour mesurer le valeur du Pco2 a laquelle le flux inspiratoire moyen etait de 1 litre s-1. La pression d'occlusion a ce Pco2 a baisse chez tous les sujets sous l'effet de la pentazocine, ce qui suggere que la generation du flux inspiratoire exige moins d'activite musculaire. Cet effet fut antagonise par la naloxone.

REDUKTIONSBLIED DER ATMUNGSPRASY- UND ABSELSSUSSPRASS-REAKTION AUF KOHLENSTOFFDURCH PENTAZOCIN BEIM MENSCHEN

ZUSAMMENFASSUNG

Mittlerer inspiratorischer Druck, Abschlusspression und Endatmungs-Pco2 wurden bei sechs gesunden sitzenden Menschen während der Atmung von Luft und der Wiederer- nachung intravenös von 0,5 mg kg-' und auch nach Naloxon 20 μg kg-' gemessen. Pentazocin reduzierte die
Abschliessungsdruck- und Einatmungsfluss-Reaktionen bei einem vorgegebenen $P_{\text{CO}_2}$ Wert während der Wieder- 
enatmung von Kohlendioxyd, und die Auswirkungen wurden durch Naloxon bekämpft. Die Verbindung zwischen inspiratorischem Fluss und Endatmungs-$P_{\text{CO}_2}$ während der Wieder- 
enatmung wurde verwendet, um den $P_{\text{CO}_2}$-Wert zu messen, bei dem der mittlere inspiratorische Fluss 1 litres$^{-1}$ entsprach. Der Abschliessungsdruck bei diesem $P_{\text{CO}_2}$-Wert wurde bei allen Versuchspersonen mittels Pentazocin reduziert, was vermuten lässt, dass die Erzeugung des inspiratorischen Flusses weniger Muskelaktivität braucht. Diese Auswirkung wurde durch Naloxon bekämpft.

CONFIGURACION DE LA REDUCCION DE LA 
RESPUESTA DE LA PRESION VENTILATORIA Y 
DE OCCLUSION AL ANHIDRIDO CARBONICO POR 
LA PENTAZOCINA EN EL HOMBRE

SUMARIO
Se midieron el flujo inspiratorio medio, la presión de oclusión y el $P_{\text{CO}_2}$ respiratorio terminal en seis personas sentadas en el curso de la respiración de aire y de la nueva respiración de anhidrido carbónico, antes y después de administrarles 0,5 mg kg$^{-1}$ de pentazocina i.v. y, de nuevo, después de una de 20 μg kg$^{-1}$ de naxolona. La pentazocina redujo las respuestas de la presión de oclusión y del flujo inspiratorio en un $P_{\text{CO}_2}$ dado en el curso de una nueva respiración de anhidrido carbónico y dichos efectos se hallaron antagonizados por la naxolona. La relación entre el flujo inspiratorio y el anhidrido carbónico respiratorio terminal en el curso de la nueva respiración se usó para medir el valor del $P_{\text{CO}_2}$ en que el flujo inspiratorio medio era de 1 litres$^{-1}$. La presión de oclusión en este $P_{\text{CO}_2}$ se reducía por acción de la pentazocina en todas las personas, lo que hace pensar que la generación del flujo inspiratorio necesitaba una actividad muscular menor. La naxolona antagonizó dicho efecto.