MECHANICS OF BREATHING, GAS DISTRIBUTION AND FUNCTIONAL RESIDUAL CAPACITY AT DIFFERENT FREQUENCIES OF RESPIRATION DURING SPONTANEOUS AND ARTIFICIAL VENTILATION

GÖRAN HEDENSTIerna AND GRAHAM McCArthy

SUMMARY

Nine healthy volunteers were investigated, both while awake and breathing spontaneously, and while anaesthetized with IPPV, in all cases at rates of both 12 and 24 b.p.m. Gas flow and volume were measured with a pneumotachograph. The transpulmonary pressure (the pressure difference between the trachea or the buccal cavity and the oesophagus) was also recorded. The distribution of gas was analysed by means of nitrogen washout curves, which also permitted the determination of functional residual capacity (FRC). Lung compliance during IPPV was approximately half that during spontaneous breathing. During IPPV the compliance was dependent on the frequency of ventilation, being lower with the greater frequency. Pulmonary resistance was approximately twice as great with artificial ventilation, but no significant relationship to frequency was demonstrated. Gas distribution was within normal limits and in this respect there was no difference between low and high rates of spontaneous breathing. With IPPV at the higher rate, gas distribution was significantly less even, but still within normal limits. Differences in FRC under the different conditions during the experiments were not significant, but the values obtained were lower with artificial ventilation. Neither the reduction in dynamic lung compliance induced by anaesthesia and artificial ventilation, nor its dependence on the frequency of such ventilation, can be explained with certainty by changes in gas distribution.

It has been shown that increasing the frequency of artificial ventilation reduces the dynamic lung compliance (Hedenstierna and Lofstrom, 1972) and, in patients with chronic respiratory disease undergoing ventilator treatment, the inspiratory lung resistance (Hedenstierna, 1972a). It has also been shown (Otis et al., 1956) that changes in the mechanics of breathing may occur with changes in frequency, should different time-constants in the lung parenchyma with consequent uneven gas distribution be present. The present study was performed to determine if there is a relationship between changes in the mechanics of breathing and in gas distribution on changing the frequency of breathing, and on changing from spontaneous to artificial ventilation.

PATIENTS AND METHODS

Nine patients who were healthy apart from the condition requiring surgery, were examined both before and during anaesthesia (table I). There were two women and seven men, aged between 28 and 69 years. The nature and scope of the investigation had been explained to them and their agreement had been obtained. There were no complications.

The measurements were performed with the patient in the supine position, the measurements during spontaneous breathing being performed the day before those under anaesthesia. Anaesthesia was induced with i.v. thiopentone followed by pancuronium 0.1 mg/kg body weight. After ventilation with oxygen, the larynx was sprayed with lignocaine 2% and a cuffed Portex endotracheal tube was inserted. The patient was then connected to the ventilator (Engström model 150 or 200) which delivered a mixture of air and oxygen (9:1), the oxygen having passed through a calibrated vaporizer set to deliver halothane 5%. Thus anaesthesia was maintained with an oxygen/air mixture containing 0.5% halothane. This was found to give stable anaesthesia.

When the subject was awake and breathing spontaneously, the mechanics of breathing were meas-
LUNG MECHANICS AND GAS DISTRIBUTION

TABLE I. Patients in the study.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>FRC</th>
<th>Diagnosis</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>Smoking habits (cigs/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35</td>
<td>f</td>
<td>2.53</td>
<td>Varicose veins</td>
<td>163</td>
<td>56</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>m</td>
<td>3.69</td>
<td>Cholecystitis</td>
<td>166</td>
<td>67</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>m</td>
<td>3.70</td>
<td>Lipoma (scapular region)</td>
<td>180</td>
<td>74</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>m</td>
<td>3.44</td>
<td>Inguinal hernia</td>
<td>176</td>
<td>72</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>m</td>
<td>3.86</td>
<td>Varicose veins</td>
<td>186</td>
<td>94</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>28</td>
<td>f</td>
<td>2.90</td>
<td>Varicose veins</td>
<td>166</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>42</td>
<td>m</td>
<td>3.86</td>
<td>Varicose veins</td>
<td>180</td>
<td>75</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>69</td>
<td>m</td>
<td>3.87</td>
<td>Inguinal hernia</td>
<td>172</td>
<td>74</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>35</td>
<td>m</td>
<td>3.75</td>
<td>Phimosis</td>
<td>173</td>
<td>63</td>
<td>0</td>
</tr>
</tbody>
</table>

ured using an oesophageal balloon, 10 cm long and 2.5 cm diameter, fastened to a polyethylene catheter (PE200). The balloon was introduced through the nose so that its point was 40 cm from the nostril. The patient was asked to strain so as to empty the balloon, which was then filled with 0.2 ml of air (Milic-Emili et al., 1964). Changes in pressure were measured by means of an inductive pressure transducer (EMT490 with amplifier EMT460, Elema-Schönander) connected to a storage oscilloscope (564B with amplifier 2A63, Tektronix). Ventilation was measured with a spirometer coupled to the oscilloscope to register pressure-volume curves, while gas-flow was recorded by means of an ink-jet writer (Mingograf 42, Elema-Schönander). Recordings were made at 12 and 24 b.p.m., determined by a metronome. Lung compliance was determined from the ratio between the volume and pressure recorded from the oscilloscope. The maximum resistance to inspiration was calculated from this recording and a recording of gas-flow.

Measurements of the mechanics of breathing under artificial ventilation were made using a tracheal catheter and the oesophageal balloon described above (fig. 1). A pneumotachograph was used to measure the rate of gas-flow during breathing. The respiratory minute volume was obtained by integrating the gas-flow signal. This equipment is described in more detail in earlier publications (Hedenstierna, 1972b; Hedenstierna and Löfström, 1972). Lung compliance during artificial ventilation was calculated as the ratio of the tidal volume to the difference between the intratracheal and intraoesophageal pressures. In each case, the end-inspiratory and end-expiratory gas-flows were zero. The maximum resistance to inspiration was calculated as the difference between intratracheal and intraoesophageal pressures at maximal gas-flow, minus the pressure which at that instant was necessary to overcome the elasticity of the lungs and thoracic wall; the pressure so obtained was divided by the maximal inspiratory gas-flow.

The functional residual capacity (FRC) was measured by means of a nitrogen washout technique (Nitralyzer 505, Med. Science). Immediately after the commencement of the administration of pure oxygen, expired gas was collected in a Douglas bag and analysed for nitrogen. Nitrogen washout was terminated when the end-expired nitrogen concentration was less than 2%. Intrapulmonary gas distribution was assessed quantitatively from the curve obtained by plotting on semi-logarithmic...
paper the end-expiratory nitrogen concentration for each breath while the patient breathed oxygen. Thus an index of gas distribution could be obtained and a fractional analysis performed according to Fowler, Cornish and Kety (1952). Two inspiratory tubes of the same volume were coupled to the ventilator, one being flushed with pure oxygen before the experiment. Thus the transition from a nitrogen-containing inspirate to pure oxygen took place without oxygen being diluted in the dead-space of the ventilator (fig. 1). Measurements of FRC and gas distribution were performed in duplicate at intervals of 15 min.

The data analysis consisted of the calculation of mean, SD and SEM. The calculation of the degree of significance of the difference between means was performed using Student's t test.

**RESULTS**

*Dynamic lung compliance* (fig. 2). Lung compliance measured during spontaneous breathing was not dependent on frequency. Compliance measured under anaesthesia and IPPV was about half the value during spontaneous breathing, and it was dependent on frequency, being lower with a higher rate of ventilation.

*Inspiratory pulmonary resistance* (fig. 3). The inspiratory pulmonary resistance measured during both spontaneous and artificial ventilation was not dependent on frequency. The values obtained under anaesthesia and IPPV were almost twice those obtained during spontaneous breathing.

![Graph showing dynamic lung compliance](image)

**Functional residual capacity** (fig. 4). FRC was, on average, 0.4 litre lower under anaesthesia, and tended to be less at the higher rate of ventilation. However, this latter difference was not significant.

*Gas distribution* (fig. 5, table II). Intrapulmonary gas distribution was within normal limits (cf. Fowler, Cornish and Kety, 1952; Bouhuys, 1963) during spontaneous breathing and during anaesthesia and IPPV. It was, however, less even with the higher frequency of IPPV. Table II shows the
results of fractional analysis performed on nitrogen washout curves. It is apparent that in the majority of cases a completely uniform gas distribution occurred with the patient breathing spontaneously: no division into different lung compartments could be made. However, in two patients breathing at a rate of 12 b.p.m. and in three breathing at a rate of 24 b.p.m., the ventilated lung volume could be divided into two fractions: a smaller fraction consisting of between $\frac{1}{2}$ and $\frac{1}{3}$ of the lung volume received over 50% of the ventilating volume. Under anaesthesia and IPPV a similar division into

| Table II. Fractional analysis of nitrogen washout curves. One or two lung fractions could be distinguished graphically ($V_A$ or $V_A^2$, expressed as a percentage of lung volume). Two fractions indicate the existence of a fast and a slow space, whose percentage share of the total lung ventilation is expressed by $V_A^1$ and $V_A^2$. |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                | $V_A^1$ | $V_A^2$ | $V_A^1$ | $V_A^2$ | $V_A^1/V_A^2$ | $V_A^2/V_A^1$ |
| **Conscious**                  |         |         |         |         |                 |                 |
| $f:12$                         | 100 n:7 | 32 n:2  | 100 n:7 | 66 n:2  | 1               | 2.1             |
| $f:24$                         | 100 n:6 | 25 n:3  | 100 n:6 | 55 n:3  | 1.9             | 6.5             |
| **Anaesthetized**              |         |         |         |         |                 |                 |
| $f:12$                         | 100 n:2 | 26 n:7  | 100 n:2 | 50 n:7  | 1               | 7               |
| $f:24$                         | 100 n:1 | 26 n:8  | 100 n:1 | 54 n:8  | 0.7             | 1.9             |

**DISCUSSION**

The aim of this study was to investigate the possibility of changes in the mechanics of breathing with
changes in frequency being explained by changes in intrapulmonary gas distribution. The possibility of such a relationship has been suggested previously by Otis and his co-workers (1956). Different time-constants in the lung-parenchyma cause uneven gas distribution. The total resistance to insufflation in an area of lung with a certain time-constant may be assessed approximately according to the impedance formula:

\[ Z = \sqrt{R^2 + \frac{1}{2\pi fC^2}} \]

where:
- \( Z \) = impedance
- \( f \) = frequency
- \( R \) = resistance
- \( C \) = compliance
- \( \frac{1}{2\pi fC} \) = reactance

Thus it is apparent that reactance, corresponding approximately to dynamic compliance, and thus even impedance, are dependent on frequency. It can be shown that the degree of inflation of different areas of lung with different impedances will vary with frequency. Thus an increase in frequency will result in a greater reduction in impedance in a low-impedance unit than in a high. So it may be expected that gas distribution will be more uneven with a higher frequency. Otis and his co-workers (1956) were able to demonstrate a reduced dynamic compliance with an increase in frequency of breathing in patients with obstructive lung disease. Indeed, the measurement of dynamic lung compliance with different rates of breathing has become an accepted test for small airway disease (Woolcock, Vincent and Macklem, 1969).

That gas distribution during artificial ventilation might be dependent on frequency, even in subjects whose lungs are free from disease, was suggested by the fact that dynamic lung compliance is reduced and inspiratory lung resistance increased by such ventilation. Thus, in this study of normal patients, in which each subject acted as his own control, we found that dynamic lung compliance was approximately halved during IPPV, the reduction being even greater with the higher frequency of ventilation. This supports earlier findings (Howell and Peckett, 1957; Hedenstierna and Löfström, 1972). A smaller reduction in static lung compliance has been demonstrated previously in response to artificial ventilation (Ferris et al., 1952; Nims, Conner and Comroe, 1955; Butler and Smith, 1957; Howell and Peckett, 1957; Safar and Aguto-Escarraga, 1959).

We also found that inspiratory pulmonary resistance was almost doubled by the induction of anaesthesia and IPPV (Clements et al., 1959; Westgate, Gordon and Van Bergen, 1962; Norlander et al., 1968; Hedstrand, 1970). This increase was not significantly altered by changing the frequency of ventilation (Hedenstierna and Löfström, 1972).

The only significant change in the evenness of distribution occurred during artificial ventilation at the higher rate. Even in this case, intrapulmonary gas distribution was within normal limits for spontaneous breathing (Fowler, Cornish and Kety, 1952; Bouhuys, 1963). Thus, there is no evidence of abnormal uneven gas distribution occurring during artificial ventilation in patients with healthy lungs (Bergman, 1963; Rehder et al., 1971). Moreover, it is very doubtful if the uneven gas distribution measured under anaesthesia with a higher rate of ventilation can explain the changes in the mechanics of breathing under such circumstances.

In this study, even gas distribution is taken to mean that gas is distributed according to the dimensions of the alveolae, so that washout times will be identical for each alveolus. The method employed does not permit an assessment of either the spatial distribution of inspired gas, or its distribution relative to that of pulmonary blood (Nunn, 1969).

In this study gas distribution was measured from end-tidal nitrogen. For this to be valid, emptying of all the alveolae must occur simultaneously. The fact that the nitrogen content of the expirate does not reach a plateau, but continues to increase, shows that this is not the case. Nevertheless comparative studies between the theoretically correct mean-tidal nitrogen concentration and the actual end-tidal nitrogen concentrations have failed to show any significant differences (Bouhuys, Jönsson and Lundin, 1958; Lichtneckert, 1967). Thus it is unlikely that the index of distribution measured in this study should be wrong on that account.

Meloche and others (1969) have shown that halothane reduces lung resistance when administered to isolated lungs during perfusion. However, this effect occurred in the presence of hypocapnia, and with considerably larger doses than we used. The effect on lung compliance was very small. Therefore we assume that any effect of the agent on our results is negligible.

Since no appreciable differences in the time-constants in the lung parenchyma are apparent, the frequency-dependence of lung compliance must be explained otherwise. Westbrook and his colleagues' suggestion (1973) that the reduction in FRC during anaesthesia and IPPV alters lung mechanics, (demonstrated previously (Laws, 1968; Don et al.,...
1970) and supported here, is plausible. Whether it brings about frequency-dependence requires further study.

ACKNOWLEDGEMENTS

We would like to acknowledge the generous advice and technical assistance of Mr Mats Bergström. This study was supported by grants from the “Swedish National Association against Heart and Chest Diseases” and from the Karolinska Institute.

REFERENCES


MECANIQUE DE LA RESPIRATION, DE LA REPARTITION DU GAZ ET DE LA CAPACITE FONCTIONNELLE RESIDUELLE AUX DIFFERENTES FREQUENCES DE RESPIRATION SOUS VENTILATION ARTIFICIELLE ET SOUS VENTILATION SPONTANEE

RESUME

Neuf volontaires en bonne santé ont été soumis à des examens alors qu'ils étaient éveillés et respiraient spontanément, ou sous anesthésie avec ventilation sous pression positive intermittente, dans les cas aux taux de 12 et de 24 respirations par minute. Le débit et le volume du gaz ont été mesurés à l'aide d'un pneumotachographe. La pression transpulmonaire (c'est-à-dire la différence de pression entre la trachée ou la cavité buccale et l'esophage) a aussi été enregistrée. La répartition du gaz a été analysée au moyen des courbes d'azote de dégazage qui ont aussi permis de déterminer la capacité fonctionnelle résiduelle. Les poumons ont fonctionné sous ventilation sous pression positive intermittente à environ 50% du taux applicable pour la ventilation spontanée. Pendant la ventilation sous pression positive intermittente, le fonctionnement a été dépendant de la fréquence de la ventilation, celui-ci étant à son point le plus bas lorsque la fréquence était la plus élevée. La résistance pulmonaire a été d'environ deux fois plus importante avec la ventilation artificielle, mais on n'a pas pu démontrer de relation significative par rapport à la fréquence. La répartition de gaz s'est effectuée dans les limites normales et dans ce domaine il n'y a eu aucune différence entre le rythme de ventilation spontanée le plus bas ou le rythme le plus élevé. Avec la ventilation sous pression positive intermittente au taux le plus élevé, la répartition de gaz a été nettement moins équilibrée, mais n'en est pas moins restée dans les limites...