COMPARISON OF ACTIVE AND PASSIVE MANOEUVRES ON THE PATTERN OF AIRWAY CLOSURE IN MAN

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SUMMARY

The effect of active and passive manoeuvres on closing volume was studied in conscious subjects. There were no significant differences in closing volume in nine of 10 non-smokers. There was a significantly greater closing volume with the passive manoeuvre (airway pressure + 3 kPa to −2 kPa) in seven of nine smokers and one non-smoker with evidence of mild obstructive airway disease. The sensitivity of the closing volume to airway pressure could not be reproduced in three non-smokers exposed to a histamine aerosol. In two of three smokers the effect of airway pressure on closing volume was abolished by salbutamol. The results suggest that subjects with irritable airways may show an increase in closing volume with a change in airway pressure.

During expiration there is progressive narrowing of the airways, particularly in the dependent parts of the lung, and at low lung volume some of these airways may close. The lung volume at which this occurs may be recognized by a sudden change in the slope of the alveolar plateau of expired tracer gas concentration when the pattern of regional lung emptying alters suddenly (Dolfuss, Milic-Emili and Bates, 1967). The change in slope marks the onset of phase IV of the alveolar plateau and this is termed the closing volume. It has been suggested that airway closure at low lung volume may be implicated in the gas exchange abnormality accompanying anaesthesia (Fairley, 1972; Hedenstierna, McCarthy and Bergstrom, 1976). Following induction of anaesthesia most patients exhibit a reduction in functional residual capacity (Hewlett et al., 1974) and may breathe within the closing volume. This results in a redistribution of ventilation away from the well-perfused dependant lung units towards less well-perfused units in the upper part of the lung and consequent impairment of gas exchange (Jones, 1975). This hypothesis assumes that the closing volume remains constant after induction of anaesthesia. However, a fundamental problem in comparing the closing volume in awake and anaesthetized subjects is the different technique required in the two circumstances. In conscious subjects the manoeuvre consists of a series of maximum inspirations and expirations, the airway pressure remaining close to zero throughout. During anaesthesia the manoeuvre has to be performed either by varying airway pressure (Lemen et al., 1975) or by a combination of increased airway pressure and external thoracic compression (Hedenstierna, McCarthy and Bergstrom, 1976). It is likely that these manoeuvres alter pleural pressure gradients (Agostoni and Miserocchi, 1970; Grassino and Anthonisen, 1975) and there may be changes in the pattern of airway closure with the two techniques. In this study we have examined the effect of active and passive respiratory manoeuvres on the magnitude of closing volume, using conscious subjects to avoid possible changes in closing volume induced by anaesthesia.

METHODS

Principal of the SF₆ bolus method for measurement of closing volume

The method has been described by Newberg and Jones (1974). There are two main techniques used for measuring closing volume: the resident gas method and the bolus method. The first relies on there being a larger residual volume of the resident gas (nitrogen) at the apex of the lung than at the base. Following a vital capacity (VC) breath of oxygen there is a greater nitrogen concentration at the apex which, when basal airways begin to close, causes a sudden increase in expired nitrogen concentrations because the lung apex empties preferentially. This method is ineffective if gas trapping in the lung base increases the residual volume in that region so that after a VC breath of oxygen there is no difference in nitrogen concentration from apex to base (Benson, Newberg and Jones, 1975). In these circumstances a bolus of tracer gas
inhaled at residual volume (RV) is distributed preferentially to the lung apex, its distribution being determined only by the phenomenon that the technique is intended to measure (basal airway closure). The bolus method usually requires a more complex gas analyser than the resident gas method. The sulphur-hexafluoride (SF₆) bolus method overcomes this problem by combining the technical simplicity of the nitrogen meter detector with the advantages of the bolus technique. The method relies on the non-linear amplifying effect of SF₆ on the nitrogen meter signal. A bolus of SF₆ inhaled at RV flows preferentially to the apex of the lung and on subsequent expiration this mixture of residual nitrogen and SF₆ is sampled when basal airways close. The SF₆ interacts with the nitrogen in the discharge tube of the analyser enhancing the intensity of the nitrogen discharge and producing a trace which resembles closely that produced by the conventional bolus method using mass spectrometry.

Procedure

Closing volume was measured in 19 hospital personnel, 10 of whom were non-smokers. Only one subject gave a history of previous respiratory disease. The subjects were allowed to practise the manoeuvres until the operator was satisfied that they could control both inspiratory and expiratory flow rates (Jones and Clarke, 1969) and achieve repeatable closing volume results.

Each subject sat in a comfortable position with the head and arms supported and he was instructed to breathe through a rubber mouthpiece attached to a three-way tap (fig. 1) with the nitrogen meter (Med. Science Inc.) sampling gas continuously from a needle-valve close to the lips. Expired volume was obtained by electronic integration of expired flow measured with a heated Fleisch II pneumotachograph and a differential pressure transducer (Validyne Inc.) with a range of ±0.25 kPa. The expired nitrogen and volume signals were recorded on a mechanical X-Y recorder (Bryans 2000). The breathing circuit was arranged so that the subject could breathe oxygen from a demand valve (Snarke II, S.C.U.B.A. regulator, Nemrod, Barcelona) arranged so that gas could be inspired actively, or, by operating the bypass button, oxygen could be released to inflate the lungs passively to an airway pressure of

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**Fig. 1.** Arrangement of the circuit for the passive manoeuvre. The subject, breathing through the mouthpiece adjacent to the nitrogen meter, may be connected to atmosphere or to the demand valve/vacuum line by turning the tap. Inflation of the lungs is achieved from the manual over-ride on the demand valve and deflation via the needle valve to vacuum. This part of the circuit can be removed at the dashed line for active expiratory manoeuvres.
ACTIVE AND PASSIVE CLOSING VOLUME

3 kPa. With the subject breathing air, the tap could be turned to connect the mouthpiece to the demand valve enabling the subject either to take a series of active breaths or to be ventilated passively. In each instance there were three components of the closing volume manoeuvre: (1) Expiration from functional residual capacity (FRC) to residual volume (RV) when a 50-ml bolus of SF$_6$ was injected into the mouthpiece; (2) inspiration of oxygen from RV to total lung capacity (TLC) and (3) slow expiration from TLC to RV. Each of the steps could be completed either actively or passively by varying the airway pressure from atmospheric to +3 kPa and —2 kPa. For passive expiration a tap was turned at TLC so that the subject was connected to a vacuum source via a needle valve adjusted to give a flow rate of 0.3 litre s$^{-1}$. The subjects were trained so that, as soon as the tap was turned at TLC, they relaxed to allow passive expiration until the airways closed at an airway pressure of about —1.5 kPa. Each subject performed at least five satisfactory manoeuvres in each active and passive series.

Using two subjects, a study was made of the effect of alternating active and passive steps within a single closing volume manoeuvre. In this way a comparison was made of closing volume data obtained with an entirely active (A), passive (P) or combination of manoeuvres (A) and (P). Thus a series of breaths was used for the three steps as follows: 1A, 2A, 3A; 1A, 2A, 3P; 1A, 2P, 3P; 1P, 2A, 3P; and 1P, 2P, 3P. As a result of this study the sequence used for the 19 subjects was 1A, 2A, 3A for the active manoeuvre and 1A, 2A, 3P for the passive manoeuvre.

Three subjects were studied before and after breathing histamine aerosols to elucidate some of the mechanisms underlying the dependence of closing volume on airway pressure in some subjects. Histamine was administered using the regimen of Benson, Newberg and Jones (1975). Each subject took five tidal breaths of 1% histamine aerosol generated by an ultrasonic nebulizer (DeVilbiss model 35A). Six subjects (three smokers and three non-smokers) breathed aerosols of salbutamol, following which measurements were made of closing volume with active or passive manoeuvres.

Subdivisions of lung volume were measured in each subject using closed-circuit helium dilution with a Respirameter (P. K. Morgan Ltd.) Further measurements of residual volume and thus closing capacity were made using duplicate closing volume manoeuvres with SF$_6$ excluded because of the effect of this gas on the nitrogen meter. Using a standard dilution equation, the residual volume was calculated from the inspired volume and nitrogen concentration (zero) and mixed expired nitrogen concentration was obtained by integrating the expired nitrogen-volume curve. This technique has been employed extensively to measure mixed expired nitrogen concentration and FRC during nitrogen clearance studies (Cumming and Jones, 1966) and to measure closing volume in epidemiological studies of airway closure (Buist and Ross, 1973).

### RESULTS

The results of a preliminary study in two subjects of the effects of different sequential patterns of active and passive manoeuvres is shown in table I. The

<table>
<thead>
<tr>
<th>Manoeuvre</th>
<th>Subject</th>
<th>CV</th>
<th>CC</th>
<th>VC%</th>
<th>CV%</th>
<th>CV%</th>
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<tr>
<td>1A, 2A, 3A</td>
<td>S1</td>
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<tr>
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<td>1.38</td>
<td>3.08</td>
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<tr>
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* Corrected for thoracic gas compression. Probability of significant change from control: $P < 0.001$. Three types of closing volume manoeuvre (each of which may be active or passive) are indicated in the first column. The main effect of changing from active to passive manoeuvres was to increase vital capacity by passive inflation of the lungs and chest wall during part two of the manoeuvre. This increase in volume was more than could be accounted for by compression of thoracic gas at 3 kPa. Differences appeared in closing volume only if this result was expressed as a fraction of the new vital capacity. No change in absolute closing volume or closing capacity was noted as a result of passive inflation in the pilot study.

There was no difference in vital capacity using active inflation followed by passive deflation.
Details of the 19 subjects in the study are shown in table II. The mean age of the non-smokers was slightly less (32.8 yr) than that of the smokers (34.7 yr). One non-smoker, subject G, showed evidence of obstructive airway disease (FEV₁/VC % 60% predicted), but he had no respiratory symptoms of note. CV/VC % following active and passive manoeuvres is shown in figure 2. There was no statistically significant difference between closing volume or vital capacity obtained using the two manoeuvres in all non-smokers except subject G. This subject, who had obstructive airway disease, showed an increase in closing volume from 15.5% VC (active) to 24.3% VC (passive) (P < 0.02). All but two of the smokers (N and R) showed a significant increase in closing volume with passive deflation, but no change in vital capacity. In no subject did the closing volume exceed the expiratory reserve volume (ERV) with the active manoeuvre. The mean ERV/VC % in the group of non-smokers except subject G was greater than in the smokers (33.8%). Figure 3 shows the lack of interaction between the ratio ERV/VA and the effect of active or passive manoeuvre on the dependence of closing volume on airway pressure during lung deflation.

In an attempt to increase the sensitivity of bronchi to changing airway pressure, three normal subjects breathed a histamine aerosol. Closing volumes were measured before and after breathing histamine using active and passive manoeuvres. These subjects showed
an increase in closing volume with histamine using the active manoeuvre \((P<0.01)\), but no significant further increase in closing volume with the passive manoeuvre.

Six subjects (three non-smokers and three smokers) breathed a salbutamol aerosol. There was no change in closing volume in the non-smokers either before or after the aerosol or with the passive manoeuvre. In two of the three smokers there was no significant change in CV with the passive manoeuvre; the third subject showed an increase in CV with the passive manoeuvre similar to that obtained before salbutamol.

Elastic recoil curves measured in two of the smokers using the passive manoeuvre showed no significant differences to explain the increase in closing volume with the passive manoeuvre.

DISCUSSION

The “passive” manoeuvre used in this study was passive only during part three of the closing volume manoeuvre, that is during expiration from total lung capacity to residual volume. Active and passive manoeuvres in steps one and two of the closing volume test may have produced some differences in regional distribution of the contrast gas, but radioactive gas techniques would have been required to demonstrate such differences. No effect could be demonstrated on closing volume in the two subjects in a pilot study. Passive inspiration to an airway pressure of 3 kPa produced a consistently larger vital capacity, but there was no change in closing volume. Closing volume expressed as a fraction of the vital capacity achieved in this manner was smaller than closing volumes expressed as a fraction of the vital capacity following active inspiratory manoeuvres. This increase in TLC with increasing airway pressure has been reported previously by Rahn and colleagues (1946). The mechanism is unclear, but it may be a result, in part, of displacement of blood from the chest. No significant change in closing volume could be demonstrated with active expiration when the preceding inspiration was either active or passive. This suggested that, if there had been a change in regional distribution of tracer gas, it was of insufficient magnitude to influence the sequential emptying pattern. Previous studies (Clarke, Jones and Glaister, 1969) have shown that considerable changes in body position are required to alter the distribution of inspired gas sufficiently to change the appearance of the expired tracer gas plateau. In order to measure minor changes in the pattern of lung emptying we increased the sensitivity of the closing volume technique by employing a bolus modification of the resident gas method (Newberg and Jones, 1974). Until recently, it was believed that, provided flow rate was controlled (Jones and Clarke, 1969), the magnitude of closing volume was the same with either bolus or resident gas methods. However, it has been shown recently (Benson, Newberg and Jones, 1975) that the closing volume obtained with the resident gas method is less than that with the bolus method, especially in the presence of mild airway obstruction. This is because that method is sensitive to regional changes in gas trapping, whereas the bolus method is not. The advantage of the sulphurhexafluoride bolus technique used here is that it avoids errors in measurement of closing volume in subjects with increased gas trapping in the dependant lung.

Most of the published work on “closing volume” is concerned with data obtained by an active manoeuvre, although recently there have been reports of studies using passive manoeuvres in anaesthetized animals (Lemen, et al., 1975); and humans (Hedenstierna, McCarthy and Bergstrom, 1976). In this study we found no significant differences between the magnitude of the closing volume obtained with an active or a passive manoeuvre in non-smokers with normal lungs. However, we found a significantly larger closing volume with the passive manoeuvre in one non-smoker with evidence of obstructive airway disease and in all but two subjects with a history of cigarette smoking. This was a fortuitous result, as there was no reason to believe before the study that either chronic smoking or mild airway obstruction should influence the
pattern of airway closure during active or passive manoeuvres. It is now believed generally that gravity plays a major role in determining the pattern of lung filling and emptying (Kaneko et al., 1966; Clarke, Jones and Glaister, 1969; Jones, Clarke and Glaister, 1969; Glaister et al., 1973), and it was proposed that a constant vertical gradient of pleural pressure accounted for these regional differences in ventilation (Milic-Emili, 1976). If this were so, then active or passive closing volume manoeuvres would be unlikely to alter the regional filling or emptying pattern of the lung. However, this hypothesis has been challenged following the observation that the pleural pressure gradient is not constant in man (Rehder et al., 1975) and the vertical gradient is altered considerably by changing thoracic shape artificially (Grassino and Anthonisen, 1975), by changing airway pressure (Agostoni and Miserocchi, 1970) and by changing volume (West and Matthews, 1972).

The study was planned to demonstrate a difference in closing volume using active and passive manoeuvres. We were thus surprised to find no differences in non-smoking subjects with normal lungs, and thought that the lack of effect of airway pressure may have resulted from the point of airway closure coinciding with functional residual capacity (functional residual capacity = closing capacity = 0), so that airway pressure was zero at the start of airway closure regardless of the manoeuvre employed. However, in our subjects there was a wide scatter of ERV - CV and it was evident that in some non-smoking subjects, when CV with passive and active manoeuvres were identical, airway pressure was as much as 1.0 kPa below atmospheric at the commencement of airway closure. The explanation for this may be provided from the observations of Agostoni and Miserocchi (1970), who found that the vertical gradient of pleural pressure was abolished with an airway pressure of 2.5 kPa. As airway pressure is reduced to zero, the pleural pressure gradient increases so that it reaches a maximum at zero pressure. When airway pressure was reduced from zero to -0.5 kPa there was a reduction in pleural pressure gradient which, with further reduction in pressure below -0.5 kPa, remained constant. If this pattern is applicable to man, it suggests that the small changes in pleural pressure gradient between airway pressures of zero and -0.5 kPa are insufficient to alter the point at which airway closure beings. The finding of an increased closing volume in cigarette smokers with the passive manoeuvre suggests two possibilities. One is that these subjects may have sustained sufficient parenchymal damage to make their pleural pressure gradients more susceptible to the effects of changing airway pressure. The trivial differences in pulmonary function and closing volume between the normal and smoking group makes this hypothesis difficult to support. The alternative explanation is that cigarette smokers have irritable airways, so that any alteration in transpulmonary pressure during the passive manoeuvre is sufficient to promote further bronchoconstriction mediated via vagal pathways, and thus increase closing volume (Lemen et al., 1973). An attempt was made to simulate this effect in three non-smoking subjects. After a series of active and passive manoeuvres three subjects breathed a histamine aerosol which induced cough, slight wheezing and an increase in closing volume similar to that reported previously (Benson, Newberg and Jones, 1975). Further active and passive manoeuvres were made, but these manoeuvres produced no significant difference in closing volume. The major problem with this investigation is that it is difficult to regulate the effect of histamine on the airways, which in this study may be of an “all or none” character, and further bronchoconstriction mediated via reflex pathways is not possible. An alternative experiment was carried out in three non-smokers and three smokers who repeated the closing volume manoeuvres before and after breathing a salbutamol aerosol. This abolished the increase in closing volume with the passive manoeuvre in two of the three smokers, suggesting that airway tone is an important variable in some of these subjects.

The effect of airway pressure on closing volume in smokers is not explained fully and requires verification. If a reflex bronchial hyperactivity is involved, it implies that there may be significant increases in closing volume in some subjects, particularly during the induction and recovery stages of anaesthesia. With steady-state halothane anaesthesia the bronchoconstrictive effects are likely to be minimized or abolished (Hickey et al., 1969; Jones, Graf and Lemen, 1978) because of the inhibitor effects of this anaesthetic agent on neurogenic bronchoconstriction.

ACKNOWLEDGEMENTS

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REFERENCES

ACTIVE AND PASSIVE CLOSING VOLUME


COMPARAISON DES MANOEUVRES ACTIVES ET PASSIVES SUR LE MODE DE FERMETURE DES PASSAGES D'AIR CHEZ L'HOMME

RESUME
On a étudié sur des sujets conscients l'effet des manoeuvres actives et passives sur le volume de fermeture. On n'a constaté aucune différence importante dans le volume de fermeture de neuf non fumeurs sur dix. Il y a eu un volume de fermeture beaucoup plus grand lorsqu'on a utilisé des manoeuvres passives (pression des passages d'air + 3 kPa à – 2 kPa) sur sept des neuf fumeurs et on a mis en évidence sur un non fumeur une maladie créant une légère obstruction des passages d'air. On n'a pas pu reproduire sur trois non fumeurs exposés à un aérosol d'histamine, la sensibilité du volume de fermeture aux pressions des passages d'air. Dans le cas de deux fumeurs sur trois, l'effet de la pression des passages d'air sur le volume de fermeture a été annihilé par le salbutamol. Les résultats obtenus laissent penser que les sujets qui ont des passages d'air irritables peuvent accuser une augmentation du volume de fermeture lorsqu'il y a des variations dans la pression des passages d'air.

VERGLEICH ZWISCHEN AKTIVEN UND PASSIVEN MASSNAHMEN AM BEISPIEL DES MENSCHLICHEN LUFTWEGVERSCHLUSSES

ZUSAMMENFASSUNG
COMPARACION ENTRE MANIOBRAS ACTIVAS Y PASIVAS EN EL ORDEN DE CIERRE DE LAS VIAS RESPIRATORIAS EN EL HOMBRE

SUMARIO

Se estudió en sujetos concientes el efecto ejercido por maniobras activas y pasivas sobre el volumen de cierre. No se presentaron diferencias significativas en el volumen de cierre en nueve de diez sujetos no fumadores. Se produjo un volumen de cierre significativamente superior con la maniobra pasiva (presión de vía respiratoria +3 kPa a −2 kPa) en siete de nueve fumadores y un no fumador con evidencia de una leve enfermedad obstructiva en las vías respiratorias. La sensitividad del volumen de cierre a la presión de las vías respiratorias no pudo ser reproducida en tres no fumadores expuestos a un aerosol de histamina. En dos de tres fumadores el efecto ejercido por la presión de las vías respiratorias sobre el volumen de cierre fue abolida por salbutamol. Los resultados sugieren que aquellos sujetos con vías respiratorias irritables podrán indicar un aumento en el volumen de cierre con cambio en la presión de las vías respiratorias.