

CHAPTER 5

MECHANICAL WORK OF BREATHING IN THE SHEEP

INTRODUCTION

Measurement of $W_{m(r)}$ and its dynamic and elastic components, requires that the subject be artificially ventilated. A highly reproducible airflow-time relationship can be imposed on the subject with appropriately designed respirator pumps. A high level of reproducibility is necessary because the airflow-time relationship affects the respiratory work performed, independent of any changes in the respiratory resistances. However, a highly reproducible airflow-time relationship can only be guaranteed during the inspiratory phase of artificial ventilation because the expiratory phase will be at least partially driven by the elastic recoil of the inflated respiratory system. Changes in E_r will therefore alter the expiratory airflow-time relationship and the expiratory dynamic work. Dynamic work measurements should therefore be restricted to the inspiratory phase.

The use of pharmacological agents to induce respiratory muscle paralysis has been recommended for mechanical respiratory work measurements in artificially ventilated subjects (Sharp *et al.*, 1964a), but ethical considerations restrict such use of these agents in human subjects. Physiological effects other than paralysis of the respiratory musculature must also be considered when using such agents. Furthermore, as it is unethical to paralyse conscious animals (National Health and Medical Research Council, 1985), physiological responses due to anaesthesia must be taken into account.

The findings of the previous chapter confirm that conscious, non-paralysed sheep can be artificially ventilated, and that spontaneous ventilation is largely suppressed under appropriate conditions. Anaesthesia would be expected to augment this suppression. The use of muscular relaxants may therefore not be necessary in the anaesthetized and pump-ventilated sheep. A study was therefore conducted to develop and test a method for measuring $W_{dyn(i)}$, $W_{m(r)}$ and W_{el} in the anaesthetized, non-paralysed and pump-ventilated sheep.

DEVELOPMENT AND TESTING OF A METHOD FOR MEASURING THE
MECHANICAL WORK OF BREATHING

Procedure 1

Five mature Merino ewes (N7-N11) were anaesthetized with $28\text{mg}\cdot\text{kg}^{-1}$ pentobarbitone sodium delivered via a jugular vein catheter. The trachea was intubated with a cuffed endotracheal tube (I.D. 9mm) and the sheep placed in the prone position. Two lung inflations, each sufficient to raise the air-line pressure to $40\text{ cm H}_2\text{O}$ above atmospheric pressure, were then delivered to reverse any anaesthesia-related falls in C_1 (Mead and Collier, 1959). Approximately 2 minutes later, the animal was artificially ventilated by a Palmer respiratory pump with an inhalatory volume (V_i) of 375 ml (BTPS), an inhalatory to exhalatory time ratio of 1:1, and a pump frequency of $35.5\text{ strokes}\cdot\text{min}^{-1}$. Spontaneous ventilation was present in all cases immediately prior to periods of pump ventilation and the pedal and corneal reflexes absent. "Top-up" doses of pentobarbitone were required to achieve this in two cases (300 and 600 mg for sheep N10 and N11 respectively).

The Palmer pump actively inflated the lungs with an essentially sinusoidal airflow-time relationship, while exhalation resulted from the elastic recoil of the inflated respiratory system. Airflow was measured by means of a screen pneumotachograph inserted into the air-line between the endotracheal tube and the pump, and connected to a Gould differential pressure transducer. The pneumotachograph was found to give a linear response over the airflow range encountered in this study. Inhalatory volume was measured by integrating the airflow signal with a Grass polygraph integrator (Model 7P10CD), while air-line pressure was sensed with a Pitot tube inserted into the air-line just distal to the endotracheal tube. The Pitot tube faced into the inhalatory airflow and was connected to a Bell Et Howell pressure transducer. Recordings were made on a Grass polygraph.

The inhalatory volume traces from four consecutive pump-generated breaths were each examined at 12 instants. Simultaneous measurements were made from the air-line pressure traces (refer to Figure 5.1). Dynamic inhalatory P-V plots were generated from this data (refer to Figure 5.2) by computer (Minitab, Pennsylvania State University, 1981). Total respiratory system compliance was calculated by dividing V_i by the difference

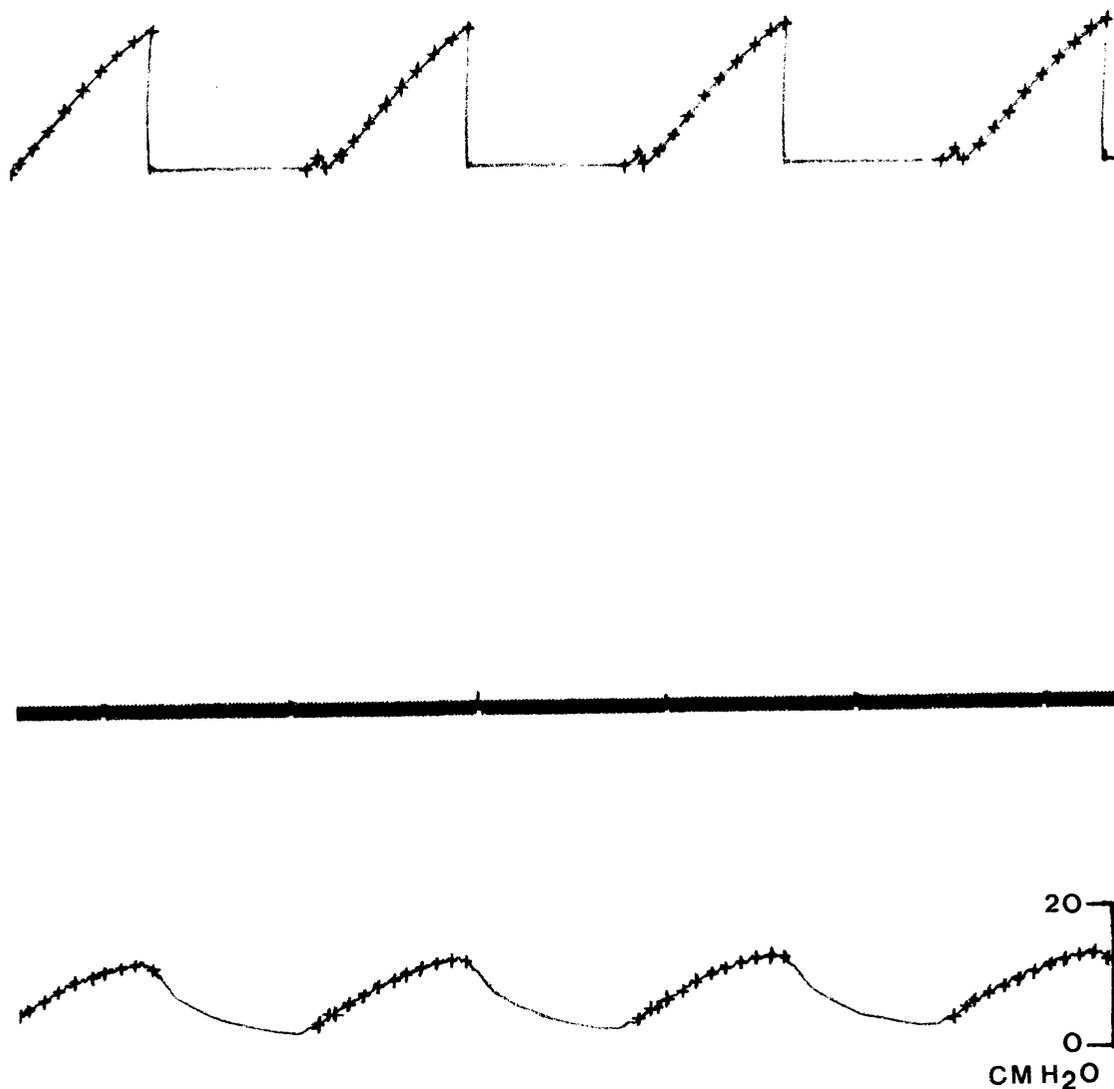


Fig. 5.1 Inhalatory volume (top), time (1 second divisions), and air-line pressure records from a prone, anaesthetized and pump-ventilated sheep as outlined in Procedure 1. Exhalatory volume was not recorded. Twelve simultaneous measurements of volume and pressure were made during each of 4 consecutive inhalations. Such measurements were used to generate a dynamic inhalatory P-V plot for each inhalation.

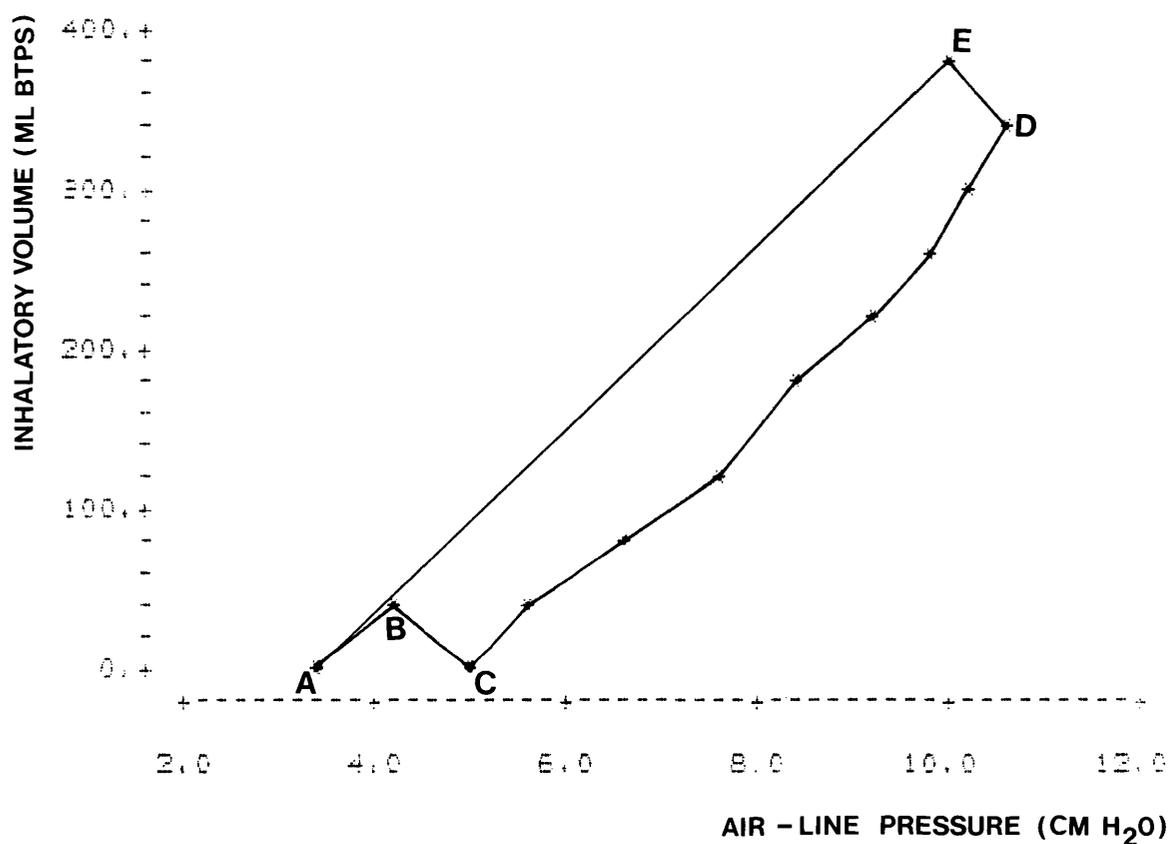


Fig. 5.2 Dynamic inhalatory P-V plot generated by computer from inhalatory volume and air-line pressure data of the 2nd inhalation in Fig. 5.1. Slope of line AE = C_r and area ABCDEA represents total dynamic work of inhalation.

between the air-line pressure at the commencement and end of inhalation. The elastic work of breathing was calculated from C_r and V_i . The total dynamic work performed per inhalation (including that performed on the endotracheal tube) was determined from area ABCDEA of the inhalatory P-V plots (refer to Figure 5.2) which was measured with a Graphics Tablet (Apple Computer Inc., California). The dynamic work performed on the sheep's respiratory system during inhalation ($W_{\text{dyn}(i)}$) was then determined. Such measurements do not include the dynamic work required to overcome air-flow resistance of the upper airways. The total mechanical work of breathing was calculated by adding W_{el} and $W_{\text{dyn}(i)}$. The precise nature of these calculations are given in Appendix 2. Compliance is expressed in $\text{ml}\cdot\text{cmH}_2\text{O}^{-1}$ and work in g cm and g cm per L of ventilation.

The air-line pressure traces were highly reproducible (refer to Figure 5.1). The Repeated Measures Analysis Test (one within factor) (Winer, 1971) was applied to the C_r , W_{el} , $W_{\text{dyn}(i)}$ and $W_{\text{m}(r)}$ data (refer to Table 5.1). No significant differences were found between the means of measurements made from each of the four consecutive inhalations.

A number of changes were observed in the inhalatory airflow-time (\dot{V}_i - T_i) and V_i - T_i relationships when sheep were pump-ventilated. These changes, which were evident from the polygraph traces (refer to Figure 5.3), consisted of:-

marked oscillations superimposed on the essentially sinusoidal \dot{V}_i - T_i relationship, especially during the early stages of T_i ,

a slight reduction in \dot{V}_i ,

the V_i trace returned to the baseline approximately 0.1 second after the commencement of inhalation, and then rose again with a reduced amplitude and in a manner which was at first essentially parallel to that seen when the pump was not connected to the sheep. The slope of the V_i trace then gradually became somewhat lower than that observed without the sheep.

Examination of the measurement system revealed similar changes when the inhalatory air-line pressure was increased to overcome a raised flow resistance in the endotracheal tube. Spirometric measurement of the stroke volume revealed that the reduction in the amplitude of the V_i trace was an artifact.

Table 5.1 Respiratory mechanics measurements made from 4 consecutive inhalations using Procedure 1

A

Sheep	C_r (ml BTPS.cmH ₂ O ⁻¹)			
	Inhalation 1	Inhalation 2	Inhalation 3	Inhalation 4
N 7	71.5	73.9	71.5	71.5
N 8	58.3	59.1	55.4	57.5
N 9	67.2	65.2	85.3	87.0
N10	43.8	46.0	46.0	46.6
N11	28.4	29.3	30.8	31.9
Mean	53.8	54.7	57.8	58.9
SE	7.9	7.8	9.5	9.6

Greenhouse-Geisser P = 0.3651

B

Sheep	W_{e1} (g cm)			
	Inhalation 1	Inhalation 2	Inhalation 3	Inhalation 4
N 7	982	951	982	982
N 8	1204	1189	1269	1221
N 9	1045	1077	823	807
N10	1605	1527	1526	1506
N11	2476	2397	2279	2201
Mean	1462	1428	1376	1343
SE	276	260	256	244

Greenhouse-Geisser P = 0.1968

C

Sheep	$W_{dyn(i)}$ (g cm)			
	Inhalation 1	Inhalation 2	Inhalation 3	Inhalation 4
N 7	168	267	151	195
N 8	337	301	199	203
N 9	262	260	120	121
N10	295	163	303	348
N11	528	476	578	369
Mean	318	293	270	247
SE	59	51	83	48

Greenhouse-Geisser P = 0.5034

D

Sheep	$W_{m(r)}$ (g cm)			
	Inhalation 1	Inhalation 2	Inhalation 3	Inhalation 4
N 7	1150	1218	1133	1177
N 8	1541	1490	1468	1424
N 9	1307	1337	943	928
N10	1900	1690	1829	1854
N11	3004	2873	2857	2570
Mean	1780	1722	1646	1591
SE	331	298	338	289

Greenhouse-Geisser P = 0.1720

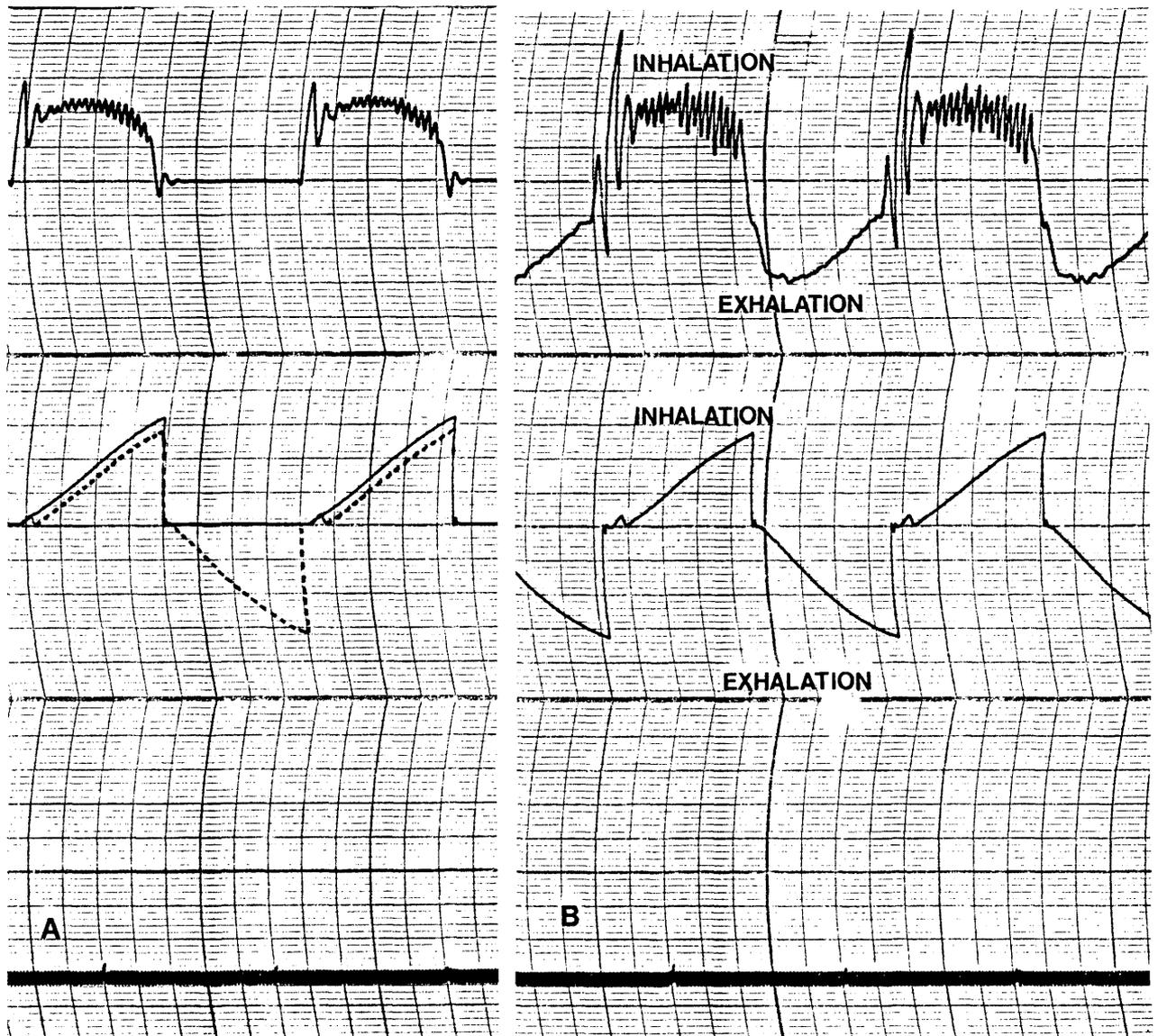


Fig. 5.3 Airflow-time (top) and volume-time relationships from Palmer respiratory pump before (A) and during (B) pump ventilation of an anaesthetized sheep using the equipment design of Procedure 1. The volume-time B trace is superimposed over its A counterpart to aid comparison. Expiratory airflow and volume are driven by the recoil of the inflated respiratory system and therefore do not occur during A. Stroke volume was 375 ml BTPS and pump frequency was $35.5 \cdot \text{min}^{-1}$ in both A and B. The bottom trace represents time (1 second divisions).

The simplest explanation which accounts for these changes was that vibration effects from the pump, which are normally present, were enhanced when the resistive load on the pump was raised. The resultant augmented oscillations in the \dot{V}_i trace caused the V_i - T_i relationship to be altered. The latter appears to have resulted primarily from the polygraph integrator's characteristic of immediately returning the volume channel pen to the baseline when airflow ceases. This accounts for the small initial peak in the V_i trace and the ensuing return to the baseline (\dot{V}_i equals zero at this instant as a result of the large initial oscillations). The V_i trace is then reduced by an amount approximately equal to that of the small initial peak. The small and gradual reduction in the slope of the V_i trace which follows can be explained by the small fall in \dot{V}_i , effects which may have resulted from gas compression.

Procedure 2

The above-mentioned changes in the V_i - T_i relationship of the polygraph records would obviously alter the shape of the inhalatory P-V plots and thereby lead to errors in the measurement of $W_{dyn(i)}$. The measurement system was therefore altered to reduce the vibration effects from the pump. A cylindrical tube (I.D. 5 cm, length 45 cm) was connected to the inhalatory air-line between the pump and the pneumotachograph (refer to Figure 5.4). This markedly reduced the vibration effects and artifacts. Replacing the Gould pressure transducer and polygraph integrator with a Greer spirometer further improved the traces (refer to Figure 5.5).

Because of the laborious nature of generating the P-V plots as outlined above, an alternative method was devised which allowed such plots to be automatically and separately recorded on a Bryan-Southern X-Y recorder (Type 2600 A3X-YY). The paper drive of this recorder was triggered by a cam operated microswitch which was connected to the driven wheel of the Palmer pump in such a manner that the paper progressed forward during each expiratory period. This allowed each inhalatory P-V plot to be separately recorded as shown in Figure 5.6, and has the advantage of recording the dynamic P-V relationship over the entire inhalation, whereas the previous method (Procedure 1) allowed this to be known at only 12 instants per inhalation. The improved measurement system is illustrated in Figure 5.4.

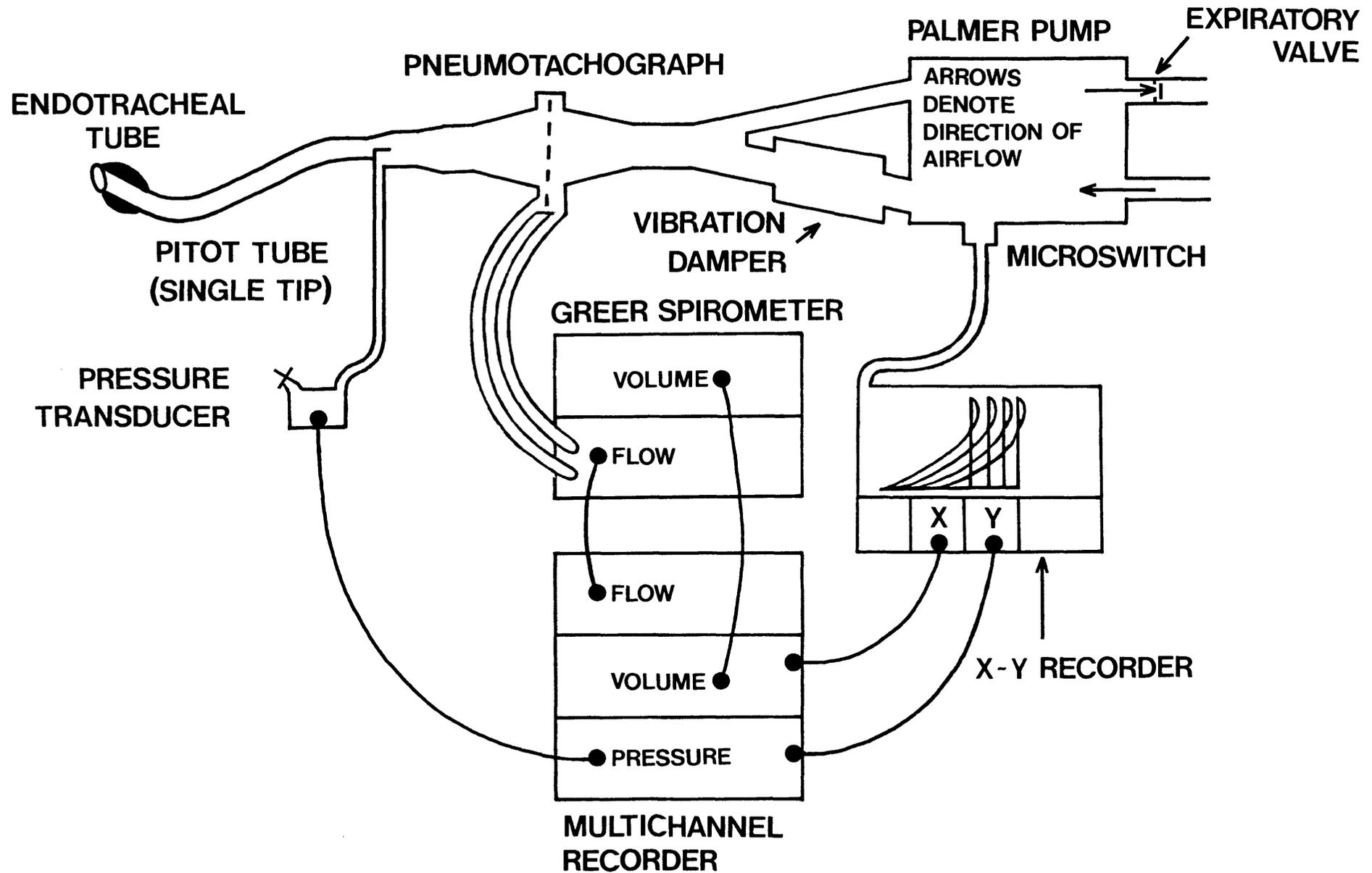


FIG. 5.4 Schematic illustration of experimental setup used to measure mechanical work of breathing.

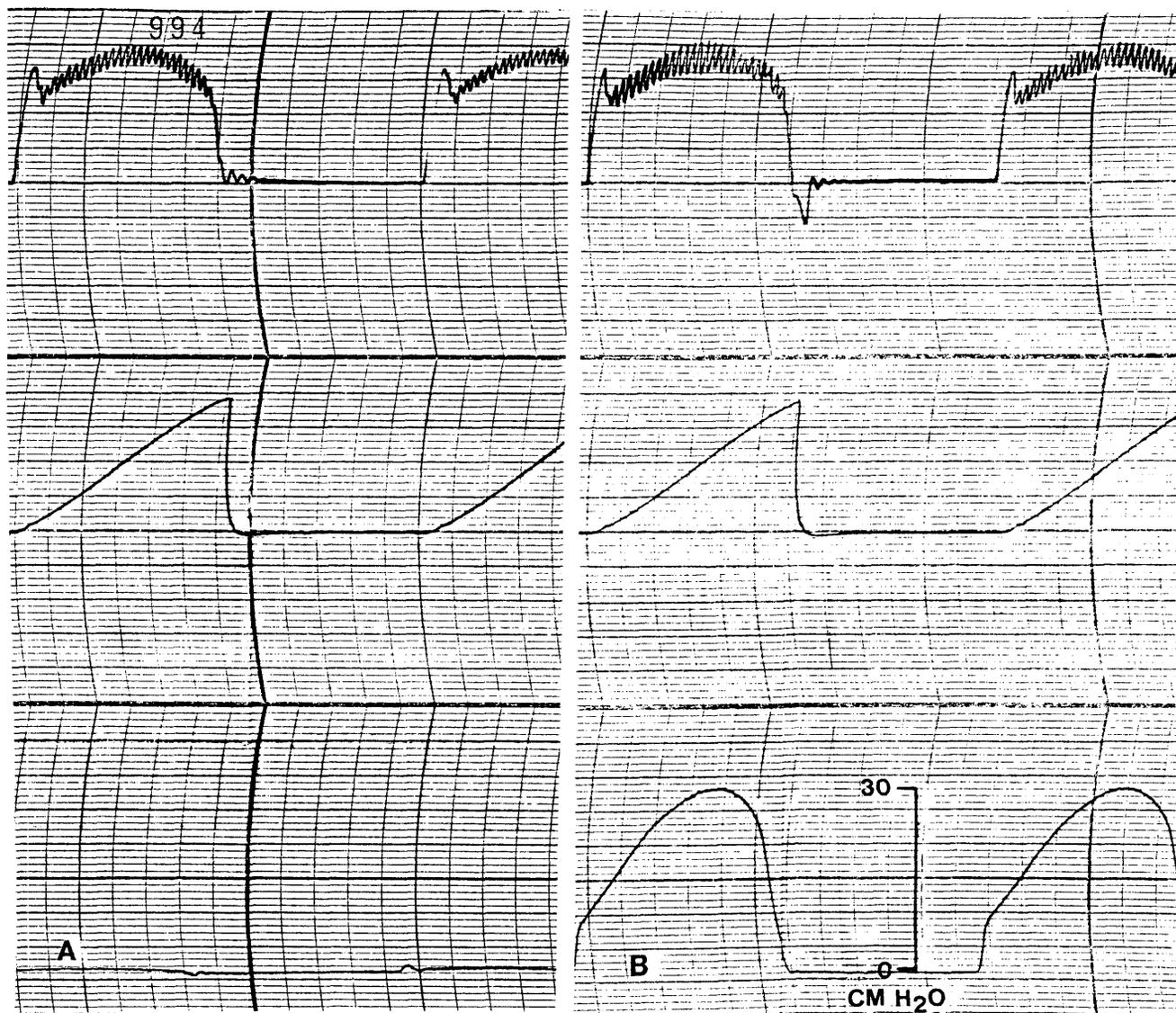


Fig. 5.5 Airflow (top), inhaled volume (middle), and air-line pressure records from Palmer respiratory pump using equipment design of Procedure 2. A with endotracheal tube attached to pump. B with endotracheal tube attached and partially occluded. Stroke volume and pump frequency are the same in A and B. Air-line pressure pen was 4 mm in front of airflow and volume pens.

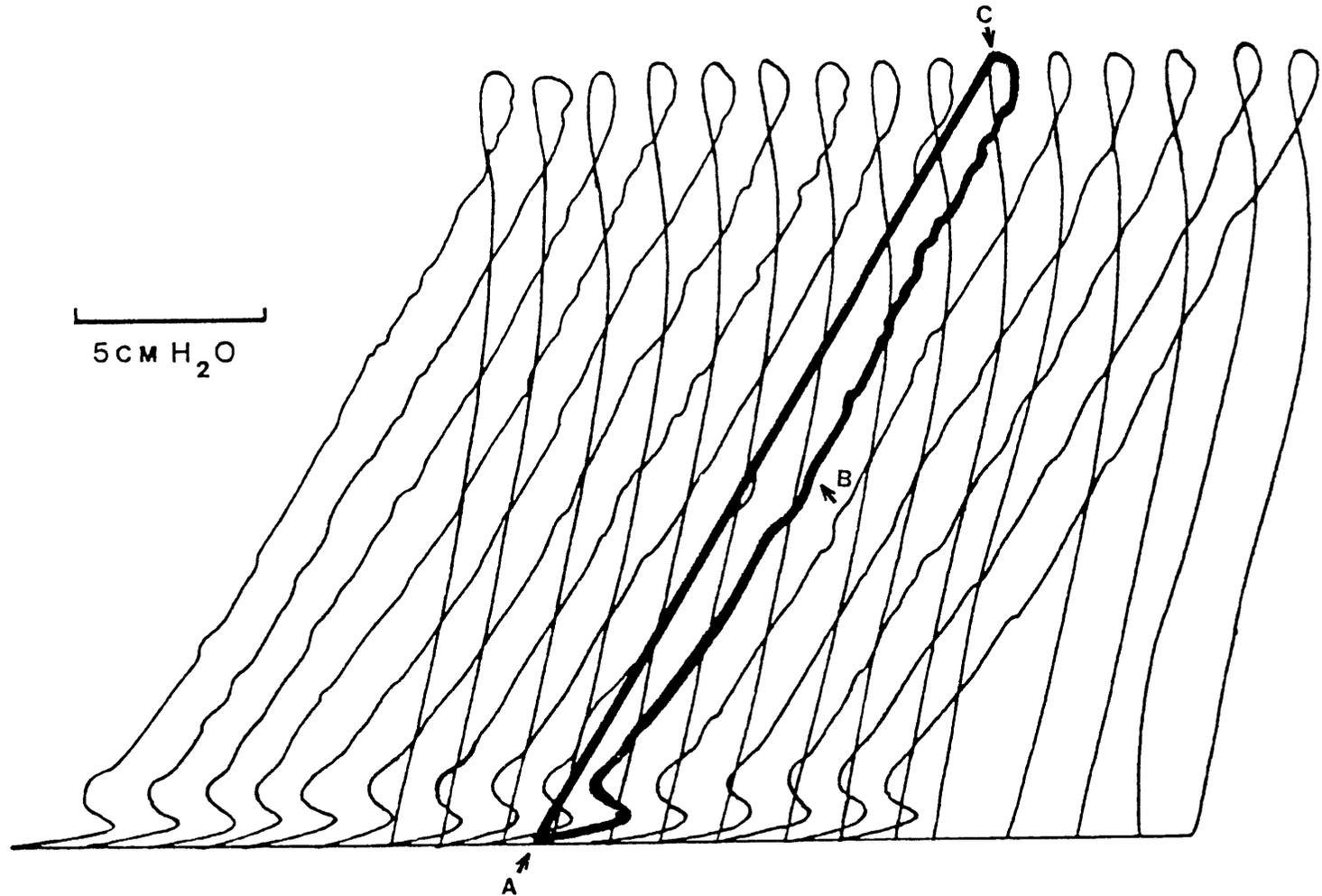


Fig. 5.6 A series of inspiratory pressure-volume curves redrawn from original records, with inspiratory volume (Y axis) set at 400 ml (BTPS), and change in airline pressure on the X axis. The paper moved to the left during each expiratory period to allow a series of curves to be separately plotted. In the labelled curve ABC, point A represents the commencement of inspiration and point C the end of inspiration. The slope of the manually inserted line AC equals C_T , and the area enclosed within this line and the curve ABC represents the dynamic work of inspiration.

Planimetric measurement of P-V plots derived from the X-Y recorder was a tedious procedure with the Graphics Tablet. An electronic planimeter (Paton Industries Pty. Ltd., Stepney, South Australia) which operates on a photoelectric principle was examined and found to be a suitable alternative. Repeated planimetric measurements of 5 inhalatory dynamic P-V plots with both instruments gave similar mean values. No significant differences were found between the means of the five series of consecutive measurements from either instrument (refer to Table 5.2).

Five mature Merino crossbreed wethers (N12-N16) were pump-ventilated to test the equipment modifications. The animals were prepared in a manner similar to that described in Procedure 1, except that the pentobarbitone sodium dose was 30 mg.kg^{-1} and pump ventilation was performed with a stroke volume of 400 ml (BTPS) at a frequency of $24.5 \text{ strokes.min}^{-1}$. "Top-up" doses of pentobarbitone were not required.

Three representative P-V plots were selected from the data of each sheep. The points representing the beginning and end of inhalation were determined by visual inspection. A line was then drawn on each plot to connect the two respective points (refer to Figure 5.6). The C_r was measured from the slope of these lines. The area of the P-V plots representing the inhalatory dynamic work was cut out manually from the recorder paper and measured with the Paton planimeter. Elastic, dynamic, and total mechanical work were calculated as described in Procedure 1.

The air-line pressure records were usually highly reproducible (refer to Figure 5.7). Measurements of respiratory mechanics were only made from highly reproducible records.

The Repeated Measures Analysis Test (one within factor) was applied to the C_r , W_{el} , $W_{dyn(i)}$, and W_{tr} data (refer to Table 5.3). No significant differences were found between the means of measurements made from each of the three series of inhalations.

PHYSIOLOGICAL CONSIDERATIONS

Many aspects of the two procedures described above can alter the mechanics of breathing. The following discussion describes the changes in respiratory mechanics which could result from these interferences, and attempts to determine to what extent they influenced the respiratory mechanics data of the present study.

Table 5.2 Consecutive measurements of dynamic P-V plot areas made with 2 types of planimeters

A		Paton Electronic Planimeter				
		Area measurements (square centimetres)				
P-V plot		1	2	3	4	5
1		8.99	9.16	8.85	8.92	8.79
2		6.91	6.95	6.84	6.98	7.12
3		9.76	9.90	10.18	9.87	10.22
4		8.99	9.26	8.98	9.04	8.98
5		11.93	11.93	11.95	11.30	11.38
Mean		9.32	9.44	9.36	9.22	9.30
SE		0.81	0.80	0.84	0.70	0.72

Greenhouse-Geisser P = 0.4756

B		Apple Graphics Planimeter				
		Area measurements (square centimetres)				
P-V plot		1	2	3	4	5
1		9.22	9.61	8.98	9.43	9.11
2		7.32	7.20	6.84	7.24	7.09
3		9.94	9.63	9.85	9.88	10.14
4		8.82	9.06	9.55	8.94	9.21
5		11.45	11.64	11.28	11.77	11.52
Mean		9.35	9.43	9.30	9.45	9.41
SE		0.68	0.71	0.72	0.73	0.72

Greenhouse-Geisser P = 0.6924

P-V plots in Table A are the same as those in Table B

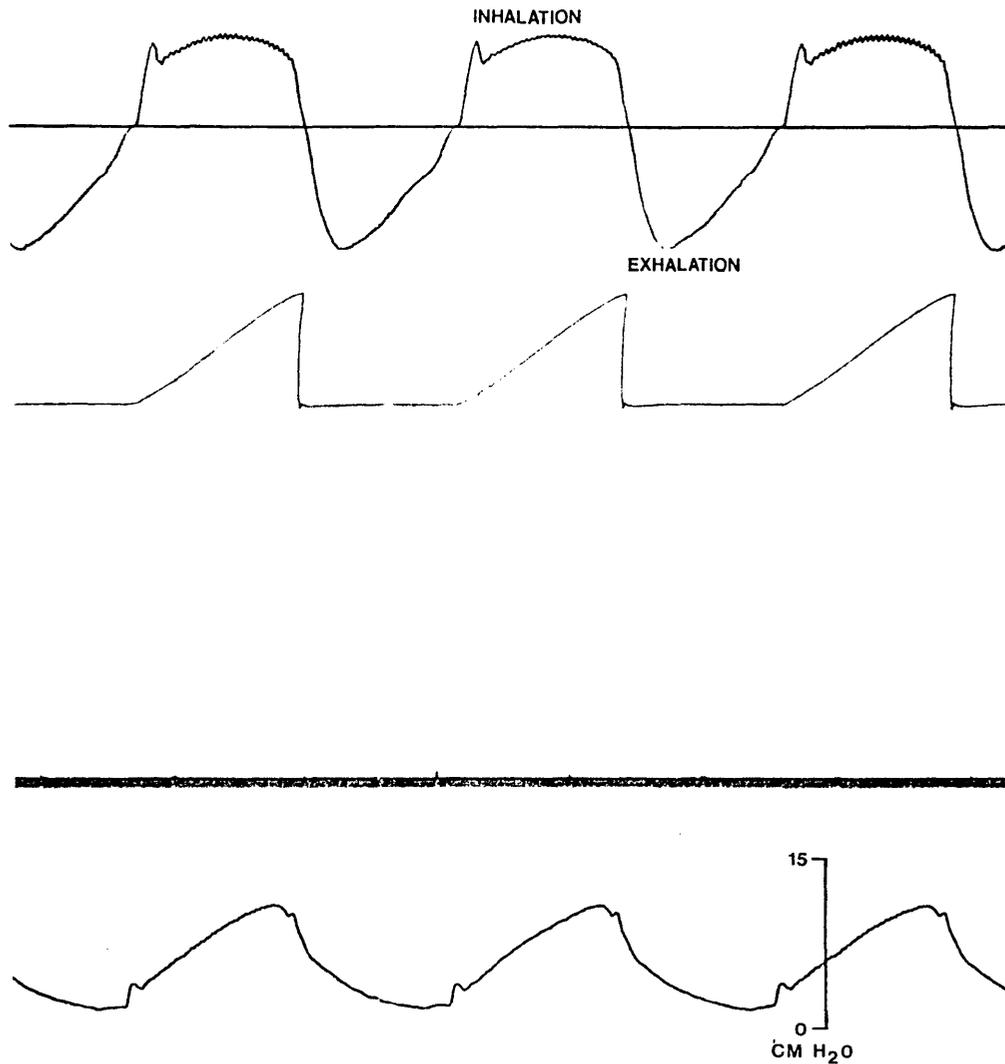


Fig. 5.7 Airflow (top), inhaled volume, time (1 second intervals), and air-line pressure records from an anaesthetized and pump-ventilated sheep using Procedure 2. Exhalatory volume was not recorded.

Table 5.3 Respiratory mechanics measurements made from 3 series of inhalations using Procedure 2

A

Sheep	Cr (ml BTPS.cmH ₂ O ⁻¹)		
	Inhalation 1	Inhalation 2	Inhalation 3
N12	50.4	50.5	50.2
N13	61.8	61.1	60.9
N14	61.1	60.1	61.1
N15	50.9	51.2	51.0
N16	59.9	58.6	56.3
Mean	56.8	56.3	55.9
SE	2.5	2.3	2.3

Greenhouse-Geisser P = 0.2897

B

Sheep	W _{e1} (g cm)		
	Inhalation 1	Inhalation 2	Inhalation 3
N12	1586	1582	1593
N13	1293	1308	1312
N14	1309	1330	1309
N15	1570	1559	1567
N16	1334	1365	1419
Mean	1418	1429	1440
SE	66	59	61

Greenhouse-Geisser P = 0.2907

C

Sheep	W _{dyn(i)} (g cm)		
	Inhalation 1	Inhalation 2	Inhalation 3
N12	263	273	264
N13	304	303	264
N14	367	358	351
N15	268	202	240
N16	254	217	358
Mean	291	271	295
SE	21	29	25

Greenhouse-Geisser P = 0.5240

D

Sheep	W _{m(r)} (g cm)		
	Inhalation 1	Inhalation 2	Inhalation 3
N12	1849	1855	1857
N13	1597	1611	1576
N14	1676	1688	1660
N15	1838	1761	1807
N16	1588	1582	1777
Mean	1710	1699	1735
SE	57	50	51

Greenhouse-Geisser P = 0.5323

Positive Pressure Ventilation

It has been suggested that positive-pressure ventilation may alter the mechanical behaviour of the lungs as a result of changes in the pulmonary blood volume (Butler and Smith, 1957; Foster, Heaf and Semple, 1957; Howell and Peckett, 1957). However, acute pulmonary vascular distension does not markedly alter lung mechanics in the dog (Borst *et al.*, 1957; Cook *et al.*, 1959), or cat (Frank, Radford and Whittenberger, 1955), although marked falls in C_1 have been observed in humans (Bondurant, Hickam and Isley, 1957).

It has been suggested that artificial ventilation with positive-airway pressure alters the pattern of regional lung ventilation, with resultant falls in C_1 (Howell and Peckett, 1957). This is supported by the marked reductions in C_1 during intermittent positive-pressure ventilation in conscious parietic human subjects reported by Opie, Spalding and Stott (1959). However, positive-pressure ventilation in human subjects is not associated with significant changes in the distribution of ventilation (Bergman, 1963; Hulands *et al.*, 1970; Hedenstierna and McCarthy, 1975), and C_1 is not altered by artificial ventilation in anaesthetized dogs and humans (Mead and Collier, 1959; Westbrook *et al.*, 1973). Furthermore, conscious sheep pump-ventilated under conditions similar to those of the present study displayed inhalatory transpulmonary pressure contours not markedly different from those observed during spontaneous ventilation at similar tidal volumes (Reinhart *et al.*, 1979).

Howell and Peckett (1957) suggested that the pattern of thoracic displacement is altered during positive-pressure ventilation, and that this may cause reductions in C_w . Positive-pressure ventilation changes the pattern of diaphragmatic displacement in human subjects (Froese and Bryan, 1974), but this would not be expected to significantly affect the static P-V relationship of the thoracic structures, as the relaxed diaphragm is highly compliant at normal and raised lung volumes (Agostoni and Rahn, 1960; Milic-Emili *et al.*, 1964).

The findings of these studies suggest that the C_r data of the present study were not significantly affected by possible changes in the pattern of lung and thoracic displacement associated with positive-pressure ventilation. However, such an effect cannot be totally discounted.

The end-expiratory air-line pressure was invariably higher than atmospheric pressure (approximately 4 cm H₂O for Procedure 1, and 2 cm H₂O for Procedure 2) during pump-driven ventilation, indicating that the sheep's EELV was elevated by some 100-200 ml (taking C_r to equal 50 ml.cm H₂O⁻¹). Although R₁ decreases with increasing lung volume (Macklem and Mead, 1967; Vincent *et al.*, 1970), it is unlikely that the small calculated increase in EELV caused significant reductions in flow resistance. Nor would it significantly affect C_r, as the static P-V relationship of the total respiratory system is generally linear from the relaxation volume to high lung volumes (Agostoni, Thimm and Fenn, 1959).

Reflex bronchoconstriction occurs in cats following distension of the airways, or irritation of the large airway mucosa or larynx (Widdicombe, 1954; Nadel and Widdicombe, 1962; Nadel, Colebatch and Olsen, 1964). A similar effect may have occurred in the present study as a result of the positive-pressure ventilation and tracheal intubation. If present, such reflex bronchoconstriction may have diminished with maintained stimulation and been antagonised by reflex bronchodilation resulting from epipharyngeal irritation (Tomori and Widdicombe, 1969).

Anaesthesia

Anaesthesia is associated with a reduction in the minute volume of ventilation which may result in hypoxia and hypercapnia (Leveringhaus and Larson, 1965), conditions associated with increases in R₁ and the dynamic component of W₁ (Widdicombe, 1963; Peters and Hedgepeth, 1966). Such an effect cannot be entirely discounted as oxygen and carbon dioxide tensions were not measured in the present study. However, the minute volumes of ventilation per unit body weight employed during pump-driven ventilation (refer to Table 5.4) were approximately 2-3 times that reported for conscious, spontaneously breathing, and eupnoeic sheep (Hemingway and Hemingway, 1966), and would therefore act to reduce any hypoxia or hypercapnia present. To avoid increases in flow resistance and the dynamic component of W₁ associated with hypocapnia (Newhouse *et al.*, 1964; Sterling, 1968), all respiratory mechanics measurements were made from data collected within the first one and a half minutes of pump-driven ventilation.

Table 5.4 Minute volumes of pump-ventilated sheep

Sheep	Body-weight kg	Minute volume ml(BTPS).minute ⁻¹ .Kg ⁻¹
N 7	37.3	357
N 8	32.6	408
N 9	41.1	324
N10	29.3	454
N11	36.9	361
N12	35.2	278
N13	39.5	248
N14	51.4	191
N15	45.3	216
N16	44.1	222
Mean	39.3	306

Note: Sheep N7 to N11 were ventilated at 13.31 L(BTPS).minute⁻¹, and the remainder at 9.80 L(BTPS).minute⁻¹.

Periodic deep inflations are required to prevent variations in alveolar surface tension, and the resultant atelectasis and fall in C_1 (Egbert, Laver and Bendixen, 1963; King, 1974). Spontaneous and progressive falls in C_1 and C_r occur during anaesthesia, which can be attributed to an anaesthesia-related absence in periodic deep lung inflations, and can largely be reversed by passive lung hyperinflations (Mead and Collier, 1959; Colebatch and Halmagyi, 1961; Egbert, Laver and Bendixen, 1963). The passive hyperinflations delivered to the sheep in the present study would therefore have minimized any such falls in C_r .

Anaesthesia is often associated with a reduced EELV, but the nature of this change is not fully understood, although reductions in chest wall recoil and tonic inspiratory muscle activity have been implicated (Westbrook *et al.*, 1973; Hewlett *et al.*, 1974; Southern, Rehder and Hyatt, 1980). The reduced EELV accounts for the increase in R_{aw} frequently associated with anaesthesia (Nunn, 1977), but would be antagonized by the raised EELV during pump-driven ventilation. Anaesthesia-related decreases in the FRC resulting from reductions in C_1 would be reversed by the lung hyperinflations delivered before periods of pump-driven ventilation.

Pentobarbitone and other barbiturates have repeatedly been shown to inhibit parasympathetic-mediated bronchoconstriction in the dog (Bernstine, Berker and Cullen, 1957; Jackson and Richards, 1977; Holtzmann *et al.*, 1982). Such an effect could induce bronchodilation by inhibiting any resting parasympathetic contribution to the bronchomotor tone. The atropine-elicited fall in the resting R_1 of conscious sheep (Ahmed *et al.*, 1980) indicate that a significant parasympathetic contribution to the resting bronchomotor tone exists in this species. Studies on the effects of pentobarbitone on the resting R_1 in dogs have given conflicting results (Jackson and Richards, 1977; Holtzmann *et al.*, 1982). Pentobarbitone does not affect R_1 , E_1 , E_w , or E_r in cats (Siafakas *et al.*, 1983). A comparison of the reported respiratory mechanics data presented in Table 5.5 suggests that R_1 is reduced in the thiopentone anaesthetized sheep, but this may be the result of a reduced EELV.

Tracheal mucus velocity is depressed during pentobarbitone anaesthesia in the sheep (Landa, Hirsch and Lebeaux, 1975), an effect which could increase R_{aw} as a result of mucus accumulation within the airways. However,

Table 5.5 Published values for R_1 and C_1 in the sheep

R_1 cm H ₂ O.sec.L ⁻¹	C_1 ml.cm H ₂ O ⁻¹	Reference
1.5-1.8	98-115	†Colebatch and Halmagyi, 1961
-	106	†Halmagyi and Colebatch, 1961
1.24	-	†Colebatch and Halmagyi, 1963
3.0	120	Wanner and Reinhart, 1978
1.4-1.8	120	Reinhart <i>et al.</i> , 1979
2.8	150	Wanner <i>et al.</i> , 1979
1.7	110	Abraham <i>et al.</i> , 1980
1.15	73	Hutchison <i>et al.</i> , 1983

† Sheep anaesthetized with thiopentone sodium; other studies relate to conscious sheep

Measurements of R_1 do not include flow resistance from the upper airways and were usually made at airflows up to 1 L.sec⁻¹.

in the present study pentobarbitone would act to decrease the build up of mucus immediately caudal to the intubated region of the trachea, and thereby reduce the associated increase in the tracheal component of R_{aw} . Increases in R_{aw} associated with mucus accumulation would counteract any decreases due to the action of pentobarbitone on bronchomotor tone.

Respiratory Muscle Activity

Neuromuscular blocking agents were not used in the present study. The possibility therefore exists that the respiratory mechanics data were affected by respiratory muscle activity. Such activity can be of a phasic or tonic nature.

The level of anaesthesia in the sheep immediately prior to pump-driven ventilation was Stage 3/Plane 2-3, as judged by the absence of corneal and interdigital reflexes and the presence of adequate spontaneous ventilation (Westhues and Fritsch, 1965a). The suppression of phasic respiratory muscle activity in the conscious sheep during pump-driven ventilation (Reinhart *et al.*, 1979; Chapter 3 of this thesis) would be enhanced by anaesthesia-related decreases in the respiratory minute volume (Severinghaus and Larson, 1965). Anaesthesia increases the duration of the vagal-mediated apnoea resulting from maintained lung inflation (Sant'Ambrogio and Widdicombe, 1965; Bouverot, Crance and Dejours, 1970; Phillipson *et al.*, 1971). This would decrease any phasic respiratory muscle activity present during pump-driven ventilation, as discussed in Chapter 3. Such arguments are consistent with the observation that the air-line pressure-time patterns from the present study were markedly more reproducible than those obtained from conscious sheep (refer to Chapter 3).

Although the air-line pressure traces were normally highly reproducible, irregularities were observed in records from 4 of the 10 sheep examined (N7, 13, 14, and 16). Such irregularities denote marked phasic activity, which was inspiratory in nature as the amplitude of the positive-air-line pressure swing during a pump cycle was reduced. Respiratory muscle activity can be in phase with the actions of the respirator pump in anaesthetized and pump-ventilated subjects (Adrian,

1933; Comroe, Nisell and Nims, 1954), but it would be unlikely that both the pattern and degree of such activity were reproducible for any length of time. The high reproducibility normally observed in the air-line pressure traces therefore indicates that significant phasic activity was absent in these instances. As the measurements of respiratory mechanics were derived only from reproducible traces, it would be unlikely that they were significantly affected by phasic activity.

Phasic respiratory muscle activity influences measurements of R_w (Otis, Fenn and Rahn, 1950) and C_w (Sharp *et al.*, 1964a). The breath-by-breath fluctuations observed in $W_{dyn(i)}$ and C_r (refer to Tables 5.1 and 5.3) could therefore be indicative of such activity. However, repeated planimetric measurements of the same dynamic P-V plots (refer to Table 5.2) appear to display a similar level of fluctuation as is found in the breath-by-breath comparisons of $W_{dyn(i)}$. This suggests that instrumental and/or other technical considerations, rather than respiratory muscle activity, accounted for these effects.

The reproducibility of the air-line pressure traces argues against the possibility that the respiratory mechanics data of the present study were significantly affected by breath-to-breath variations in tonic respiratory muscle activity. However, the presence of a consistent degree of tonic activity cannot be determined in this manner.

Many electromyographic studies have failed to demonstrate tonic respiratory muscle activity in conscious, normal and eupnoeic human subjects (Campbell, 1958; Green and Howell, 1959; Naimark and Cherniack, 1960). However, the presence of tonic inspiratory muscle activity has been demonstrated in eupnoeic human subjects (Muller *et al.*, 1979; Lopes *et al.*, 1981). The cephalid displacement of the end-expiratory diaphragmatic position following muscular paralysis (Froese and Bryan, 1974), and the reduced EELV and decreased outward pull of the chest wall during submaximal neuromuscular blockade (De Troyer and Bastenier-Geens, 1979) support this finding.

Anaesthesia is associated with a cephalid displacement of the end-expiratory diaphragmatic position (Froese and Bryan, 1974) and a reduction in tonic diaphragmatic activity (Muller *et al.*, 1979). Paralysis

does not significantly alter the EELV in the anaesthetized rat (Lai and Hildebrant, 1978), dog (Avery and Sackner, 1972; Southern, Rehder and Hyatt, 1980), or human (Howell and Peckett, 1957; Westbrook *et al.*, 1973), implying that tonic respiratory muscle activity is absent during anaesthesia. The study by Froese and Bryan (1974) indicates that the diaphragm behaves passively in the anaesthetized and positive-pressure ventilated subject. Paralysis did not alter the static P-V relationship of the total respiratory system of anaesthetized and pump-ventilated humans (Howell and Peckett, 1957). In view of these findings, it is unlikely that tonic respiratory muscle activity significantly affected the respiratory mechanics data of the anaesthetized and pump-ventilated sheep of the present study.

The findings of the present study support the report by Comroe, Nisell and Nims (1954) that muscular relaxants are not necessary to measure the mechanical properties of the total respiratory system in suitably anaesthetized and pump-ventilated subjects.

Paralysis

Paralytatics have been employed to abolish respiratory muscle activity during determinations of the mechanical work of breathing (Dean and Visscher, 1941). However, these pharmacological agents elicit many physiological responses other than muscular paralysis (Westhues and Fritsch, 1965b; Gray, 1971; Clarke, 1972). The effects on lung mechanics are not fully understood but responses such as histamine release and vagal blockade have been reported and can alter the bronchomotor tone and R_{aw} . However, the present study supports the view that such agents are not necessary to measure mechanical respiratory work, so that these "side effects" can be avoided.

THE MECHANICAL WORK OF BREATHING IN THE SHEEP

Average values for C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ measurements made in the present study are presented in Table 5.6. The author is unaware of any published data on these parameters in the sheep. A range of published R_1 and C_1 data for this species are presented in Table 5.5.

Published values for C_1 are similar to the $106 \text{ ml.cm H}_2\text{O}^{-1}$ reported for the goat (Avery and Cook, 1961), a species closely related to the sheep. Measurements of C_r in the goat by these workers equalled

Table 5.6 Compliance and mechanical work of breathing in the sheep

Sheep	C_r	W_{el}		$W_{dyn(i)}$		$W_{m(r)}$	
	ml.cmH ₂ O ⁻¹	g cm	g cm.L ⁻¹	g cm	g cm.L ⁻¹	g cm	g cm.L ⁻¹
N 7	72.1	974	2597	195	520	1170	3120
N 8	57.6	1221	3256	260	693	1481	3949
N 9	76.2	938	2501	191	509	1129	3011
N10	45.6	1541	4109	277	739	1818	4848
N11	30.1	2338	6235	488	1301	2826	7536
Mean (n=5)	56.3	1402	3740	282	752	1685	4493
N12	50.4	1587	3968	267	668	1854	4635
N13	61.3	1304	3260	290	725	1595	3988
N14	60.8	1316	3290	359	898	1675	4188
N15	51.0	1565	3913	237	593	1802	4505
N16	58.3	1373	3433	276	690	1649	4123
Mean (n=5)	56.4	1429	3573	286	715	1715	4288
Mean (n=10)	56.3						

Note: Data presented here are based on that provided in Tables 5.1 and 5.3. Means of mechanical work data from all 10 sheep are not given as such data are dependent on the ventilatory conditions (i.e. f_r and V_i) which differed in the 2 groups of animals.

50.0 ml.cm H₂O⁻¹, a value which agrees well with the C_r data from the present study.

The \dot{V}_i -T_i relationship was essentially sinusoidal in the present study. The mechanical respiratory work formulas developed by Otis, Fenn and Rahn (1950) were also based on such a relationship. Transpulmonary pressure is linearly related to \dot{V} in the intubated and anaesthetized sheep at airflows of 0.5 and 1 L.sec⁻¹ (Colebatch and Halmagyi, 1961) so that the nonviscous component of R₁ is negligible under these conditions. The work formula for W_{dyn(i)} (Otis, Fenn and Rahn, 1950) may therefore be expressed in terms of R₁, f_r and V_i, where

$$W_{\text{dyn}(i)}(\text{g cm}) = \frac{998.7}{4} R_1(\text{cm H}_2\text{O}\cdot\text{sec}\cdot\text{L}^{-1})\Pi^2 f_r(\text{breaths}\cdot\text{sec}^{-1})V_i^2(\text{L}^2).$$

Calculations based on this expression will underestimate W_{dyn(i)}, but a major error would not be expected as R_w does not comprise the major component of R_r (Opie, Spalding and Stott, 1959; Petit, Milic-Emili and Delhez, 1960; Ferris, Mead and Opie, 1964; Mead and Agostoni, 1964). A value of 1.5 cm H₂O.sec.L⁻¹ may be considered representative of the published R₁ data of the anaesthetized sheep presented in Table 5.5, and yields W_{dyn(i)} values of 307 and 243 g cm for Procedures 1 and 2 respectively. These calculations support the W_{dyn(i)} measurements of the present study.

The elastic, inhalatory dynamic, and total, mechanical work of breathing have been measured in a number of mammalian species (Dean and Visscher, 1941; Otis, Fenn and Rahn, 1950; Agostoni, Thimm and Fenn, 1959) (refer to Table 1.2). Interspecies comparisons of this data are severely limited by the dependence of respiratory work (expressed in g cm or g cm.L⁻¹) on f_r and V_i (Otis, Fenn and Rahn, 1950), which have differed in each species examined. However, the data from the present study fall within the range reported for other mammalian species, when expressed in g cm.L⁻¹ (refer to Table 5.6).

CONCLUSION

A procedure has been developed which allows the measurement of C_r, W_{el}, W_{dyn(i)}, and W_{m(r)} in the anaesthetized and artificially ventilated sheep. Although measurements from individual animals may show considerable breath-by-breath fluctuations, averaged values do not differ significantly.

It is not possible to state precisely the extent to which the respiratory mechanics were altered by physiological responses to the experimental conditions of this study. However, each source of variation has been explored in some detail and did not appear to markedly affect the data. The compliance and mechanical work measurements made were found to be consistent with the limited relevant data available in the literature. Furthermore, the findings of this study support the idea that muscular paralysis is not necessary to ensure mechanical respiratory work measurements are not significantly influenced by respiratory muscle activity in the anaesthetized and artificially ventilated sheep.

Mean values for C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ equalled 56.3 ml BTPS. $\text{cm H}_2\text{O}^{-1}$, 3740 g cm.L^{-1} , 752 g cm.L^{-1} , and 4493 g cm.L^{-1} respectively in 5 mature Merino ewes artificially ventilated with a stroke volume of 375 ml (BTPS), a pump frequency of 35.5 min^{-1} , and a T_i-T_e ratio of 1:1. Similar measurements in 5 mature Merino crossbreed wethers artificially ventilated with a stroke volume of 400 ml (BTPS), a pump frequency of 24.5 min^{-1} , and a T_i-T_e ratio of 1:1, gave respective values of 56.4 ml (BTPS). $\text{cm H}_2\text{O}^{-1}$, 3573 g cm.L^{-1} , 715 g cm.L^{-1} , and 4288 g cm.L^{-1} .

CHAPTER 6

THE EFFECTS OF A PROGRAMME OF ENDURANCE TRAINING
ON THE MECHANICAL WORK OF BREATHING

INTRODUCTION

The effects of endurance training on the mechanical properties of the respiratory system have attracted little attention. However, endurance training is frequently associated with changes in respiratory parameters such as the MBC. Although such changes have generally been attributed to improvements in the strength and endurance of the respiratory musculature, they could reflect decreases in the respiratory resistances. Furthermore, the $\dot{V}_{O_{2r}}$ comprises some 10-15% of the total \dot{V}_{O_2} during strenuous exercise (Shephard, 1966; Levison and Cherniack, 1968), so that decreases in the respiratory resistances could represent a means by which endurance training improves exercise endurance.

The mechanical work of breathing represents the ideal parameter for examining the dependency of $\dot{V}_{O_{2r}}$ on the mechanical properties of the respiratory system, because it equals the mechanical component of W_r and is directly related to the respiratory resistances. The total dynamic work of breathing (inspiratory plus expiratory) equals $W_{m(r)}$ at the high levels of ventilation which occur during strenuous exercise and the MBC (Otis, Fenn and Rahn, 1950). Margaria *et al.* (1960) used this relationship to estimate the $W_{m(r)}$ of human subjects during exercise. However, as the dynamic work measurements were restricted to the lungs, these workers assumed that R_w makes an insignificant contribution to R_r . They further assume that intraoesophageal pressure is a reliable index of intrapleural pressure during the raised minute ventilations associated with exercise. The validity of both these assumptions is questionable.

The $W_{m(r)}$ and total dynamic work of breathing can only be measured during conditions of artificial ventilation when respiratory muscle activity is absent (Otis, Fenn and Rahn, 1950; Sharp *et al.*, 1964a). These conditions cannot be achieved during strenuous exercise or high minute ventilations. Furthermore, it is not ethical to paralyse the respiratory musculature in humans for experimental purposes. The mechanical respiratory work measurements can therefore only be made on experimental

animals during physical inactivity and lower levels of ventilation, and the data extrapolated to the relevant conditions. The following reports a study which examined the effects of an eight week programme of endurance training on $W_{m(r)}$, $W_{dyn(i)}$ and W_{el} in sheep during conditions of physical inactivity and moderately elevated levels of artificial ventilation.

METHODS

Exercise Training Programme

Five mature Merino crossbreed wethers (Sheep N12-N16) were trained to walk on a treadmill several months before commencement of the exercise programme. The animals were housed in small pens from the initial period of exposure to the treadmill until the completion of the study, and would therefore have performed little physical activity over the period immediately prior to the exercise programme. The programme consisted of ten minutes treadmill walking.day⁻¹, five days.week⁻¹, for a period of eight weeks. The treadmill gradient was 9° elevation at the commencement of the programme, and was increased to 13° after three weeks of training. Treadmill speed was kept at 3.7 km.hr⁻¹ throughout the programme.

Heart Rate Response to Standardized Work

The effects of training on the heart rate response to standardized workloads on the treadmill were examined by comparing heart rates at set workloads over the course of the training programme. Heart rates were measured before, and two weeks after, commencement of training, and upon completion of the programme. Heart rates were monitored while the sheep exercised on the treadmill for five minutes at 3.7 km.hr⁻¹. The gradients (9° and 14.5°) were originally intended to equal those used during the training sessions. However, the higher training gradient had to be reduced to 13° because several of the sheep were unable to continue exercising at 14.5° for 10 minutes.

Heart rate was monitored by electrocardiography and was usually measured during the fifth minute of each workload. Measurements were occasionally made during the fourth minute where an animal was approaching exhaustion. Where electromyographic interference was too severe to determine heart rate during exercise, measurements were made during the first fifteen seconds after cessation of exercise. The validity of this

method was examined by comparing heart rate measurements obtained by both methods from 18 exercise tests. Statistical analysis of the 18 pairs of data with the two-tailed Student's t test (paired observations) revealed no significant difference ($P = 0.665$).

Mechanical Work of Breathing

Measurements of C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ were made as described in Procedure 2 of the previous chapter. Measurements were made from 3 inhalations and averaged. They were made several days prior to commencement, and several days after completion, of the training programme.

Statistical Analysis

The 2-tailed Student's t test (paired observations) was used to analyse all results for significant differences (Steel and Torrie, 1960), with each sheep acting as its own control. The level of probability used to indicate significant difference was $P < 0.05$.

RESULTS

Table 6.1 shows heart rate and body-weight (with fleece) data, before (BT), during (DT), and after (AT) the training programme.

Heart rates fell progressively and significantly throughout the course of the training programme. Body-weight increased progressively and significantly over the eight week period.

Table 6.2 presents the C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ data, before (BT), and after (AT) training. No significant change was observed in $W_{dyn(i)}$, although considerable individual variation occurred in the two sets of measurements. The C_r was reduced by 9.8% after training. As a result, W_{el} increased by 10.7%, and $W_{m(r)}$ increased by 9.0%.

A post-mortem examination was performed on each sheep after the AT measurements to identify any relevant pathology. Several small cysts were found in the lungs of sheep N12, 13, and 15, but were considered unlikely to affect the respiratory parameters examined. No other abnormalities were found.

Table 6.1 Heart rates (beats.min⁻¹) during graded workloads, and body-weights (kg) before, during, and after training

Sheep	Workload								
	9 ⁰			14.5 ⁰			Body-weight		
	BT	DT	AT	BT	DT	AT	BT	DT	AT
N12	195	188	155	-	213	182	35.0	37.1	39.2
N13	190	183	181	-	228	213	38.7	40.0	40.3
N14	210	159	146	-	210	196	51.3	51.8	55.2
N15	258	192	150	276	228	185	44.7	45.5	49.8
N16	252	208	192	-	255	245	45.0	47.2	49.7
Mean	221	186	165	-	227	204	42.9	44.3	46.8
±SE	14	8	9	-	8	12	2.8	2.6	3.1
P value	0.0431	0.0421			0.0223		0.0153	0.0200	
		0.0256						0.0031	

Only sheep N15 was capable of exercising at the 14.5⁰ workload during the BT series of exercise tests.

Table 6.2 C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ before and after training

Sheep	C_r (ml·cm H ₂ O ⁻¹)		W_{el} (g cm)		$W_{dyn(i)}$ (g cm)		$W_{m(r)}$ (g cm)	
	BT	AT	BT	AT	BT	AT	BT	AT
N12	50.4	49.3	1587	1620	267	304	1854	1923
N13	61.3	54.0	1304	1479	290	225	1595	1703
N14	60.8	50.5	1316	1581	359	354	1675	1936
N15	51.0	44.1	1565	1813	237	200	1802	2013
N16	58.3	56.4	1373	1416	276	352	1649	1768
Mean	56.4	50.9	1429	1582	286	287	1715	1869
±SE	2.4	2.1	61	68	20	32	49	57
P value	0.0342		0.0362		0.9644		0.0124	

DISCUSSION

The $W_{m(r)}$ can only be measured during artificial ventilation when respiratory muscle activity is absent (Otis, Fenn and Rahn, 1950; Sharp *et al.*, 1964a). However, ethical considerations prevent the subject manipulation necessary to achieve this in humans, so that animal subjects must be employed.

Due consideration of interspecies variation must be taken when using experimental animals as human models in physiological research. Mammals display marked differences in thoraco-pulmonary morphology (McLaughlin, Tyler and Canada, 1961; Krahl, 1964) which results in considerable variation in the respiratory resistances. The sheep has a thoraco-pulmonary morphology which differs considerably in a number of respects to that of the human (Anderson, 1971). However, of the mammals commonly used in physiological research, the sheep has R_1 and C_1 values which most closely equal that found in humans (refer to Table 1.1). The author is unaware of reported measurements on other respiratory resistances in the sheep. However, the C_w and C_r of a closely related species, the goat, are similar to that of humans (Avery and Cook, 1961; Nunn, 1977). With regard to training exercises, the sheep although quadrupedal, utilizes a form of locomotion which, comparatively speaking, is similar to that of humans (i.e. walking-running as opposed to hopping, arboreal locomotion etc.).

From a practical viewpoint, the sheep is a suitable subject because of its easy availability, docile nature and low sentimental value. Furthermore, this species has well established handling and maintenance procedures, and is of a convenient size for the necessary procedures and measurements. Difficulties associated with implementing endurance exercises other than those based on treadmill activities are also avoided because the sheep can be trained to exercise at high workloads on the treadmill.

The sheep was selected as the species most suited for the present purposes on the basis of the above mentioned criteria. Studies which employ experimental animals as human models are inherently limited by interspecies variation, but the selection criteria of the present study were primarily aimed at minimizing these differences.

Effects of Treadmill Training Regime on Heart Rate Response to Exercise and Endurance

The level of activity performed on a treadmill is dependent on the speed and gradient of the treadmill, and on the subject's body weight. In the present study, sheep were exercised at the same treadmill gradients during each of the three series of exercise tests, and speed was kept constant at 3.7 km.hr^{-1} . Body-weight increased progressively and significantly over the training period. The workload used during the exercise tests would therefore also have increased somewhat over the training period. One can therefore exclude reduced workloads as the cause of the observed reductions in heart rate. The repeated exposure of the sheep to the treadmill may have reduced the level of anxiety present during the latter series of exercise tests. However, the effect of anxiety on heart rate during exercise becomes less pronounced as the workload increases (Astrand and Rodahl, 1977), yet significant reductions in heart rate were observed at the high workloads used in the present study.

The training programme employed in the present study was intended to improve the sheep's endurance to sustained physical exertion. Such regimes must be above a minimum intensity, duration, and frequency to elicit training-related adaptations (Astrand and Rodahl, 1977; American College of Sports Medicine, 1978). Endurance training reduces the heart rate elicited by set submaximal workloads (Winder *et al.*, 1978). The heart rate data of the present study demonstrate that the endurance training programme was of sufficient intensity, duration, and frequency, to elicit this effect. The sheep's endurance to sustained physical exertion was also improved, as evidenced by the training-related increase in the maximum workload which could be sustained for five minutes (refer to Table 6.1).

Effects of Endurance Training on the Dynamic Resistances and Dynamic Work of Breathing

Comparison of the BT and AT values of $W_{\text{dyn}(i)}$ from individual sheep revealed considerable variation. The spontaneous and marked changes in R_{aw} and specific airway conductance observed in normal human subjects over periods of two hours or less (Butler *et al.*, 1960; Sterling, 1968) may account for this.

Newman, Smalley and Thomson (1961) used the MEP/FEV₁ ratio as an index of R_r and reported that elite adolescent swimmers had higher values than control subjects. However, this ratio may not give a reliable measure of R_r. The MEP of the swimmers were significantly higher than that of the controls, and as the FEV₁ is a partially effort-independent dynamic lung volume, a given increase in MEP would be accompanied by the smaller reported rise in FEV₁. This would account for the reported increase in R_r as estimated in this study.

Shapiro and co-workers (1964) reported that R₁ during maximal inspiratory and expiratory manoeuvres was somewhat elevated in athletes, although not significantly. However, members of the athletic group may have possessed a superior respiratory musculature. This would have raised the transpulmonary pressure gradients during such manoeuvres and thereby raised the R₁ (Mead and Whittenberger, 1953).

Milic-Emili, Petit and Deroanne (1962) did not observe any significant difference between the dynamic W₁ (per litre of ventilation) of trained and sedentary human subjects during exercise.

The findings discussed above support the lack of effect of endurance training on W_{dyn(i)} in the sheep of the present study. However, the published findings relate to conditions of high minute ventilations and high airflows and include data obtained during both inspiration and expiration, whereas that from the present study relate to inspirations at moderately elevated levels of airflow and minute ventilation. The W_{dyn(i)} data may therefore not be comparable with that which occurs during exercise or maximal respiratory manoeuvres, because they are less affected by the nonviscous dynamic resistances and are not influenced by effort-independent airflow maxima which occur only during expiration. Chronic exposure to underwater diving constitutes a form of endurance training and does not alter R₁ during resting levels of ventilation (Fisher *et al.*, 1970), but a more recent study suggests that airflow obstruction may occur (Crosbie, Reed and Clarke, 1979). The dynamic W₁ data reported by Milic-Emili, Petit and Deroanne (1962) were obtained during exercise, whereas the W_{dyn(i)} data of the present study were obtained during physical inactivity, but exercise does not alter R₁ at fixed airflows (Stubbing *et al.*, 1980).

The author is unaware of any studies which have examined the effects of endurance training on R_w . Several studies have investigated the relationship between endurance training and the R_l and dynamic W_l . The results of these investigations, and the $W_{dyn(i)}$ data of the present study, support the idea that endurance training does not alter the R_r and total dynamic work of breathing during resting levels of ventilation, dynamic lung volume manoeuvres, and strenuous exercise.

Effects of Endurance Training on the Elastic Resistances and Elastic Work of Breathing

Significant differences were found between the BT and AT values of C_r and W_{el} . The AT measurements were 9.8% lower for C_r and 10.7% higher for W_{el} , than BT measurements. All five sheep displayed these trends. Leith and Bradley (1976) observed no change in the static P-V relationship of the total respiratory system of human subjects exposed to a five week programme of ventilatory muscle endurance training. Chronic exposure to underwater diving does not appear to alter C_l (Fisher *et al.*, 1970). The markedly different types of training used, must however be considered when comparing their results with those from the present study. As the C_l and C_w of the sheep were not measured, it was not possible to determine whether the reduction in C_r after training resulted from the lungs, thoracic structures, or both.

The C_r is relatively constant over a considerable lung volume range above the relaxation volume, and falls progressively outside this range (Agostoni, Thimm and Fenn, 1959; Drorbaugh, 1960; Agostoni and Mead, 1964). Training-related increases in the EELV therefore cannot explain the observed fall in C_r , and as the end-expiratory air-line pressure was always positive during periods of artificial ventilation, the EELV did not fall below the relaxation volume.

Girth increases suggestive of hypertrophy of the thoracic musculature have been reported following strength-training of these muscles (Willmore, 1974). Exercise training also appears to raise the rate of bone deposition (Eisenberg and Gordan, 1961), so that increases in the thoracic bone mass may result. Such training-related adaptations would mass load the thorax and consequently reduce C_w and C_r (Sharp *et al.*, 1964b; Peters, 1969).

The latter author has commented on the reduced C_r in subjects with large, heavily boned and muscled chests. However, the large degree of mass loading required to significantly reduce C_r (Sharp *et al.*, 1964b), and the lesser degree of muscular hypertrophy elicited by endurance training as opposed to strength training (Saltin and Gollnick, 1983) argue against such an explanation for the observed fall in C_r in the present study.

Increasing the lung volume stretches the expiratory musculature (Rahn *et al.*, 1946; Agostoni and Rahn, 1960), and possibly other thoracic or abdominal muscles. The mechanical properties of the connective tissue components of skeletal muscle make a major contribution to the passive length-tension behaviour of the muscle (Eisenberg, 1983). Endurance training appears to stimulate the synthesis of connective tissue components of skeletal muscle in mice (Suominen and Heikkinen, 1975a; Suominen, Kiuskinen and Heikkinen, 1980) and humans (Suominen and Heikkinen, 1975b; Suominen, Heikkinen and Parkatti, 1977). A similar adaptation in the expiratory musculature may therefore decrease C_r . Leith and Bradley (1976) observed no change in the elastic behaviour of the respiratory systems of human subjects exposed to a programme of ventilatory muscle endurance training. However, their training regime appeared primarily to stress the inspiratory musculature.

Physical training is known to affect the physical and chemical properties of a number of connective tissues other than that found in skeletal muscle (Booth and Gould, 1975). Such changes are presumably adaptations to the increased tensions and compressions placed on these structures during physical activity. Training-related increases in the elasticity of such tissues found within the thoracic structures, could therefore conceivably explain the observed fall in C_r . The costal cartilages of the sternocostal joints are of interest in this regard, as they make a major contribution to the elasticity of the thoracic cage (Davies, 1967) and, in the present study, would have been subjected to similar stresses as a result of the jarring nature of the treadmill exercise. However, such an explanation for the post-training fall in C_r must be considered as speculative because of the lack of directly relevant data in the literature.

The elastic work of breathing is proportional to the product of E_r and V_T^2 (Otis, Fenn and Rahn, 1950), so that any training-related changes in W_{el} would parallel that in E_r (the inverse of C_r).

The literature indicates that endurance training does not alter the elastic resistances and elastic work of breathing (per litre of ventilation), except when the exercise demands a high contribution from the thoracic musculature which may be associated with increases in E_w . This is consistent with the significant post-training decrease in C_r , and increase in W_{e1} , observed in the treadmill trained sheep of the present study.

Caution must be exercised when extrapolating the results of the present study, and that by Fisher *et al.* (1970) and Leith and Bradley (1976), to the situation existing during strenuous exercise. Aerobic exercise is associated with a significant increase in E_1 (Stubbing *et al.*, 1980) and the E_r will also increase because of the raised end-inspiratory lung volume and distorted chest wall configuration (Grimby, Bunn and Mead, 1968; Goldman, Grimby and Mead, 1976). The relatively small changes in C_r (9.8% decrease) and W_{e1} (10.7% increase) observed in the present study may therefore be enhanced during strenuous exercise.

Endurance Training and the Static and Dynamic Lung Volumes

Static lung volumes

Endurance training in adults is occasionally associated with changes in the TLC, RV, VC, and FRC (Bachman and Horvath, 1968; Reuschlein *et al.*, 1968; Saltin *et al.*, 1968; Leith and Bradley, 1976; Robinson and Kjeldgaard, 1982). However, adult endurance athletes frequently possess higher vital capacities than sedentary subjects (Milic-Emili, Petit and Deroanne, 1962; Shapiro *et al.*, 1964; Raven, 1977). The raised VC appears to be the result of increases in the TLC (Milic-Emili, Petit and Deroanne, 1962; Raven, 1977). Reported differences between the lung volumes of endurance athletes and sedentary subjects in cross-sectional studies, may be the result of a selective bias which favours subjects with a superior natural endowment to participate in athletic programmes, instead of reflecting a training-related difference. However, breath-hold diving is associated with increases in the TLC and VC which are believed to result from increases in the inspiratory muscle strength (Carey, Schaefer and Alvis, 1956; Song *et al.*, 1963). A similar effect may occur with some forms of endurance training such as oarsmanship (Cotes, 1979). These findings support the idea that the elastic properties of the respiratory system are little affected by endurance training.

Dynamic lung volumes

Cross-sectional studies have irregularly reported that adult endurance athletes possess a higher FEV₁ than sedentary subjects (Newman, Smalley and Thomson, 1962; Grimby and Saltin, 1966; Raven, 1977; Mahler, Moritz and Loke, 1982). However, longitudinal studies reveal no endurance training-related changes in the FEV₁ (Reuschlein *et al.*, 1968; Saltin *et al.*, 1968; Keens *et al.*, 1977; Robinson and Kjeldgaard, 1982). This discrepancy may be the result of athletes possessing a superior natural endowment.

Endurance training by swimming may be associated with increases in the FEV₁ which result from increases in the respiratory muscle strength. The findings by Newman, Smalley and Thomson (1961) are consistent with this argument, but the longitudinal study by Robinson and Kjeldgaard (1982) revealed that distance running training was associated with increases in the MEP but the FEV₁ was not affected. Leith and Bradley (1976) observed increases in the MEP following a programme of ventilatory muscle strength training, but failed to detect any significant changes in the MEFV curve. Shapiro and co-workers (1964) found no difference between the MEF_{25%}, MEF_{50%} and MEF_{75%}, of superbly trained endurance athletes and sedentary subjects. Keens *et al.* (1977) observed no significant change in the MMEF_{25-75%} after a 4 week programme of ventilatory muscle endurance training. These findings support the idea that R_{aw} is not altered by endurance training during large expirations at high airflows, but due appreciation of the limited value of these parameters as indices of R_{aw} must be made.

Endurance training is frequently associated with increases in the MBC and MVV_s (Milic-Emili, Petit and Deroanne, 1962; Shapiro *et al.*, 1964; Grimby and Saltin, 1966; Reuschlein *et al.*, 1968; Leith and Bradley, 1976; Keens *et al.*, 1977; Robinson and Kjeldgaard, 1982).

Swim training is associated with increases in MEP (Newman, Smalley and Thomson, 1961) and ventilatory muscle endurance training is accompanied with increases in the MBC_{15sec}, MEP and MIP (Leith and Bradley, 1976). Increases in MEP, MBC_{12sec}, and MVV_{15min} have been reported following a 20 week programme of endurance running (Robinson and Kjeldgaard, 1982). However, ventilatory muscle strength training is associated with increases in the MEP and MIP, but does not alter the MBC (Leith and Bradley, 1976). Furthermore, training-related increases in the MBC are

difficult to interpret solely in terms of a superior respiratory musculature because effort-independent airflow maxima are observed during the expiratory phase of the MBC manoeuvre (Hyatt, 1965). Shapiro *et al.* (1964) suggested that trained individuals may be able to breathe at higher lung volumes during these manoeuvres and thereby encounter lower flow resistances.

The endurance of the respiratory musculature can, like other skeletal muscles, be increased by endurance training, as evidenced by training-related increases in the MVV_s (Leith and Bradley, 1976; Keens *et al.*, 1977; Bradley and Leith, 1978). Ventilatory muscle endurance training increases the maximum sustainable level of $\dot{V}_{O_{2r}}$ (Bradley and Leith, 1978), so that the aerobic capacity of these muscles is raised. Increases in the proportion of slow-to fast-twitch muscle fibres in guinea-pig diaphragms have been reported following endurance training (Leiberman, Maxwell and Faulkner, 1972). Such training is also associated with biochemical changes which are suggestive of increased glycolytic and aerobic capacities of the rat diaphragm (Ianuzzo *et al.*, 1982). Chronic elevation of the respiratory workload by tracheal banding is associated with similar changes in the aerobic capacity of the rat respiratory musculature, and with increases in the proportion of slow-to fast-twitch fibres of these muscles (Keens *et al.*, 1978). Such changes are similar to those observed in other skeletal muscles and are consistent with improvements in the endurance of the respiratory musculature (Keens *et al.*, 1978; Keens, 1979).

The MBC and MVV_s represent the maximum short-term and long-term performances of the respiratory system as a pump, and are therefore dependent on many factors which include the respiratory resistances. However, the results of the present study, and the literature, do not support the idea that endurance training-related increases in the MBC and MVV_s are the result of decreases in the respiratory resistances.

Effects of Endurance Training on the Work of Breathing

In the present study, endurance training was associated with a significant increase in the $W_{m(r)}$ (per litre of ventilation) of sheep, during physical inactivity and moderately elevated levels of ventilation. The increase in $W_{m(r)}$ was due to a significant rise in W_{e1} , while no change was observed in $W_{dyn(i)}$. As previously discussed, the training-related increase in W_{e1} may become more pronounced during strenuous

exercise and the associated high levels of ventilation. However, $W_{m(r)}$ equals the sum of the inspiratory and expiratory total dynamic work of breathing during these conditions (Otis, Fenn and Rahn, 1950). The results of the present study therefore suggest that endurance training does not alter $W_{m(r)}$ (per litre of ventilation) during strenuous exercise. This supports the findings of Milic-Elimi, Petit and Deroanne (1962) who reported that the dynamic work expended on the lungs (per litre of ventilation) was the same in athletes and sedentary subjects, and is consistent with the literature concerned with the relationship between endurance training and the dynamic respiratory resistances and dynamic lung volumes.

The present study supports the idea that endurance training does not alter the W_r and $\dot{V}_{O_{2r}}$ (per litre of ventilation) during strenuous exercise. Bradley and Leith (1978) examined the effects of ventilatory muscle endurance training on the $\dot{V}_{O_{2r}}$ during MVV_s manoeuvres and considered their results to be consistent with a lack of change in the $\dot{V}_{O_{2r}}$ (per litre of ventilation). The markedly different types of training used, must however be taken into account when comparing their findings with that from the present study.

The Role of Endurance Training-Related Changes in $V_{O_{2r}}$ in Improving Exercise Endurance

Treadmill endurance training increased the exercise endurance of the sheep in the present study, as evidenced by the reduced heart rate response to exercise and the increase in the maximum workload which could be sustained for five minutes. Exercise endurance is limited by the maximum aerobic capacity, accumulation of lactic acid in the blood and the mechanical efficiency of exercise (Fox, 1979), and the depletion of muscle glycogen stores (Holloszy *et al.*, 1971). Endurance training improves the endurance to exercise by a number of complex adaptations which include increasing the $\dot{V}_{O_{2max}}$ (Kasch *et al.*, 1973; Hickson *et al.*, 1982) reducing the blood lactic acid levels and the utilization of muscle glycogen during a given workload (Holloszy *et al.*, 1971; Karlsson *et al.*, 1972), increasing the muscle glycogen concentration (Gollnick *et al.*, 1973), and increasing the mechanical efficiency of exercise (Robinson and Harmon, 1941; Karlsson *et al.*, 1972; Rasmussen *et al.*, 1975; Le Rossignol, 1982).

Increases of 3-8% are frequently observed in the latter after a period of endurance training, and may reflect the development of a superior technique whereby the degree of unnecessary and wasteful muscular activity is reduced. Training-related reductions in the minute ventilations elicited by standardized workloads (Andrew *et al.*, 1966; Rasmussen *et al.*, 1975) would decrease the $V_{O_{2r}}$, and may therefore also contribute.

The $V_{O_{2r}}$ equals 10-15% of the V_{O_2} during submaximal exercise (Levison and Cherniack, 1968) and 10% during exercise at 80% of the maximum aerobic work capacity (Shephard, 1966). The endurance to maximal aerobic exercise is markedly affected by variations in the body's oxygen supply which are of a similar magnitude to these $V_{O_{2r}}$ values (Ekblom, Goldberg and Gullbring, 1972; Ekblom *et al.*, 1975). A training-related decrease in $V_{O_{2r}}$ could therefore significantly increase the efficiency of exercise and the exercise endurance. However, the results of the present study, and the literature, are consistent with the idea that endurance training does not alter the $V_{O_{2r}}$ (per litre of ventilation). The $V_{O_{2r}}$ (per litre of ventilation) is also dependent on the RE, but the author is unaware of any studies which have examined the effects of endurance training on the RE.

CONCLUSION

This study reports an investigation on the effects of an eight week programme of treadmill endurance training on the C_r , W_{el} , $W_{dyn(i)}$, and $W_{m(r)}$ of anaesthetized sheep measured during artificial ventilation with a fixed \dot{V}_i-T_i relationship, a stroke volume of 0.4 L (BTPS), and a pump frequency of 24.5 breaths.min⁻¹.

The training programme significantly improved the sheep's exercise endurance, did not alter the $W_{dyn(i)}$ (per litre of ventilation), but C_r was significantly reduced which resulted in significant increases in W_{el} and $W_{m(r)}$ (per litre of ventilation).

These data were extrapolated to the situations found during dynamic lung volume manoeuvres and strenuous exercise in humans. Such extrapolation indicates that endurance training -

• does not alter the dynamic respiratory resistances, but that some forms of endurance training, such as that employed in the present study, may appreciably increase the elastic resistances. Decreases in the

respiratory resistances therefore do not appear to contribute to training-related increases in the dynamic lung volumes,

. does not alter $W_{m(r)}$ (per litre of ventilation) so that training-related decreases in the $\dot{V}_{O_{2r}}$ (per litre of ventilation) do not contribute to increases in the mechanical efficiency of exercise and exercise endurance.

Despite the considerable limitations imposed by such extrapolations, these findings support the limited data available in the literature.

APPENDIX 1GLOSSARY OF RESPIRATORY MECHANICS SYMBOLS

This Appendix provides a glossary of respiratory mechanics symbols which are frequently encountered in this thesis. The symbols are based on the nomenclature by Mead and Milic-Emili (1964).

C_l	compliance of the lungs
C_r	compliance of the total respiratory system (lungs and thoracic structures)
C_w	compliance of the thoracic structures
E_l	elastance of the lungs
E_r	elastance of the total respiratory system
E_w	elastance of the thoracic structures
f_r	frequency of respiration
$P_{end(e)}$	end-expiratory (air-line) pressure; end-expiratory pressure in the airway and alveoli
R_{aw}	airway resistance; dynamic resistance to gas flow in the airways
R_l	pulmonary flow resistance; R_{aw} plus dynamic resistance of the lung tissues
R_{lt}	dynamic resistance of the lung tissues
R_r	dynamic resistance of total respiratory system (lungs and thoracic structures)
R_{rt}	Dynamic resistance of the total respiratory system tissues: $R_r - R_{aw}$
R_w	dynamic resistance of the thoracic structures
T_e	exhalatory time
T_i	inhalatory time
V	volume (relating to inhalatory or exhalatory gas, or gas in lungs)
\dot{V}	airflow; rate of change in V
V_i	inhalatory volume
V_T	tidal air volume
$\dot{V}_{O_{2r}}$	oxygen cost of respiration
$W_{dyn(i)}$	dynamic component of total mechanical work of inhalation

W_{el}	elastic component of total mechanical work of breathing
W_l	mechanical work performed on the lungs and ventilated gases
$W_m(r)$	total mechanical work of breathing
$\dot{W}_m(r)$	rate of total mechanical work of breathing
W_r	total energy cost of breathing
\dot{W}_r	rate of total energy cost of breathing

Note: respiratory work may be expressed as that expended per breath, inhalation, or exhalation (g cm), or per unit volume of ventilated gas (g cm.L⁻¹).

APPENDIX 2CALCULATIONS FOR MEASURING THE TOTAL MECHANICAL
WORK OF BREATHING, AND ITS ELASTIC AND DYNAMIC COMPONENTS

When determining the mechanical work performed on the respiratory system from dynamic P-V plots, volume changes must relate to that occurring in the lungs and are therefore expressed under BTPS conditions. Body temperature in the sheep is normally about 39°C (Andersonn, 1982) and the partial pressure of water vapour in saturated air is 52 mm Hg at this temperature (Hodgman, West and Selby, 1957).

Gas compression would be expected to cause small decreases in V_i when sheep were pump-ventilated. This would reduce the mechanical respiratory work performed per pump stroke. The error resulting from this effect was less than 2% as the barometric pressure varied little from 680 mmHg (921 cmH₂O) and the end-inhalatory airline pressure did not exceed 18 cmH₂O. Corrections for gas compression effects were not made because of the small nature of the error and the complex nature of the corrections (Jaeger and Otis, 1964).

Measurement of W_{el}

The elastic work of inhalation is equal to W_{el} when exhalation is passive.

$$\text{Therefore, } W_{el} \text{ (L.cmH}_2\text{O)} = \frac{V_i^2 \text{ (L}^2\text{)}}{2 C_r \text{ (L.cmH}_2\text{O}^{-1}\text{)}}$$

where 1 L.cmH₂O = 999 g cm (Marks, 1951).

$$\text{Therefore, } W_{el} \text{ (g cm)} = \frac{999 V_i^2 \text{ (L}^2\text{)}}{2 C_r \text{ (L.cmH}_2\text{O}^{-1}\text{)}}$$

Measurement of $W_{dyn(i)}$

Areas of the dynamic P-V plots representing the total dynamic work of inhalation were measured and expressed in cm². A 1 cm deflection on the Y axis of such plots represents α litres of lung volume change, and a 1 cm deflection on the X axis represents β cmH₂O of driving pressure.

Therefore, 1 cm^2 of area represents $999 \cdot \alpha\beta \text{ g cm}$ of mechanical work. Thus, the total dynamic work of inhalation (g cm) equals the product of the representative area (cm^2) and $999 \cdot \alpha\beta$. Such dynamic work measurements include that performed in overcoming the airflow resistance of the endotracheal tube.

Measurement of this latter work component was made by generating dynamic P-V plots for the endotracheal tube only, and converting the respective areas to dynamic work in the same manner as described for total dynamic work of inhalation. Volumes were however, expressed under ambient conditions as the air was not expanded by the warming and humidifying effects that occur in the airways.

$W_{\text{dyn}(i)}$ was then calculated as the difference between the total dynamic work of inhalation and the inhalatory dynamic work performed on the endotracheal tube. Such measurements of $W_{\text{dyn}(i)}$ do not include the dynamic work required to overcome airflow resistance in the upper airways.

Measurement of $W_{\text{m}(r)}$

$W_{\text{m}(r)}$ equals the sum of the elastic and dynamic work performed during inhalation when exhalation is entirely passive, and was therefore calculated by adding W_{el} to $W_{\text{dyn}(i)}$.

Comment

During inhalation, the single-tip-type Pitot tube used to sense air-line pressure measured a pressure head equal to the sum of the static head (air-line pressure), and the kinetic head resulting from the impact of the air on the orifice of the tube. The latter factor comprised a very small component of the air-line pressure which was essentially removed from the calculations of $W_{\text{dyn}(i)}$ when the inhalatory dynamic work performed on the endotracheal tube was subtracted from the total inhalatory dynamic work. The kinetic pressure head did not affect C_r because the relevant pressure measurements were made at moments of zero airflow.

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