Atelectasis and Pneumothorax:

Effect on Lung Function and Shunting

Frank J. Colgan, M.D., Tae B. Whang, M.D.,† Alastair J. Gillies, M.D.‡*

Lung mechanics and physiologic shunting were measured before and after experimentally-produced atelectasis and pneumothorax in dogs breathing air or oxygen. Atelectasis of the left lung was accomplished with an endobronchial blocker; pneumothorax by injecting an amount of air equal to the functional residual capacity of the dog. Increases in physiologic shunting following atelectasis and pneumothorax were less than expected from the amount of collapsed lung involved, indicating that the measurement of shunt is an insensitive index of atelectasis. Reductions in lung compliance, however, were related directly to the amount of induced atelectasis confirmed by postmortem examination. Functional residual capacity was found to be related linearly and inversely to the degree of shunting during breathing of air but not during inhalation of oxygen. Thus, maintenance of an optimal state of resting lung volume seems necessary to minimize shunting whenever the inspired gas is not oxygen.

CHANGES in lung compliance and/or physiologic shunting frequently have been assessed as indices of atelectasis.[1-5] Data correlating changes in lung compliance and shunting with the actual amount of atelectasis present are lacking, however. Changes in lung compliance also may reflect changes in functional residual capacity (FRC),[6] surface tension [7] or cycling dynamics during controlled ventilation [8] without development of atelectasis. Accordingly, spontaneously-breathing dogs were studied to determine the effect of a known amount of atelectasis produced by bronchial blockage or pneumothorax on lung compliance, FRC and physiologic shunting, and to assess the relative contributions of ventilation–perfusion defects to the observed shunts.

* Associate Professor of Anesthesiology.
† Instructor in Anesthesiology. Present address: Georgetown University Hospital, Washington, D. C.
‡ Professor and Chairman, Division of Anesthesiology.
Received from the Anesthesiology Laboratory, University of Rochester School of Medicine and Dentistry, Rochester, New York. Accepted for publication February 14, 1968. Supported in part by U. S. Public Health Service Grant HE-09609.

Methods

Twenty-six dogs were anesthetized with a 50:50 mixture of sodium pentobarbital and sodium thiopental, administered intravenously. An initial dose of 16 mg./kg. was followed by supplementary doses of pentobarbital, as required. The dogs were placed in the supine position and an esophageal balloon was passed into the stomach, withdrawn to the lower third of the esophagus, and 0.5 ml. of air was added. A large double-cuffed endotracheal tube was passed and attached to a modified T piece. Thirteen dogs breathed air and 13 breathed oxygen throughout the study. Either oxygen or air was admitted through the sidearm at 6–8 liters per minute, a flow more than sufficient to eliminate rebreathing.[9] Denitrogenation was assessed by analysis of end-tidal samples for O_2 and CO_2. Measurements of FRC and compliance were made in duplicate approximately 30 minutes after induction of anesthesia. Femoral arterial blood and expired gas samples were obtained for gas analysis between the duplicate FRC determinations. In 12 dogs a catheter for sampling mixed venous blood was inserted through the jugular vein into the pulmonary artery, using the method of Fife and Lee.[10]

ATELECTASIS

Atelectasis was produced in the following manner: following collection of control data, the trachea was extubated and a McCarthy double-lumen bronchial blocker passed through a #10 Jackson bronchoscope into the left

main-stem bronchus. The bronchoscope was removed and reinserted beside the bronchial blocker, and the blocker withdrawn slowly until the proximal end of the cuff was just visible below the carina. The cuff was inflated under direct vision following expiration, so that the blocked lung contained an amount of gas equal to its normal contribution to the total FRC. The snugness of the block was tested by gentle tugs after which the endotracheal tube was reinserted. As much gas as possible was removed from the blocked lung by gentle aspiration through the blocker tubing opening distal to the balloon. This was usually less than half the expected left lung volume. A period of at least ten minutes then was allowed, to permit complete absorption of the remaining oxygen from the blocked lung.[11, 12] All measurements made in the control period were repeated 30 minutes after institution of atelectasis, since shunting is maximal during the first hour.[11] At this point eight dogs were sacrificed immediately with intravenous pentobarbital, the endotracheal tube clamped, and the extent of atelectasis determined by postmortem examination. In the remaining dogs the endobronchial blocker was removed and the lungs were hyperinflated actively several times by sustained pressures of 40 cm. H_2O for 15–20 seconds, to re-expand them adequately. Spontaneous respiration was permitted for 30 minutes to allow the lungs to attain their normal resting volume following reinflation, after which control measurements were repeated.

Pneumothorax

Pneumothorax was produced with injection into the left chest of air in a volume equal to the control FRC, using a syringe and an 18-gauge needle. Care was exercised to avoid puncturing the lung. Following measurements made 30 minutes after pneumothorax, four dogs were sacrificed and examined to determine the extent of lung collapse. In the remaining dogs the gas was aspirated from the chest and repeat measurements were made 30 minutes later. Finally, reinflation of the lungs was accomplished in a manner similar to that following atelectasis, and after the resumption of spontaneous respiration for 30 minutes the measurements were repeated.

FRC determinations were made using the closed-circuit helium-dilution technique. Helium meter readings were corrected for changes in oxygen concentration which occurred during the determinations, by a method described elsewhere.[13] The per cent change in helium concentration was measured at 30-second intervals during helium equilibration to assess the efficiency of intrapulmonary mixing. When plotted on semilog paper, a straight line results if mixing is normal. If the lung contains poorly-ventilated components, the plot is represented best by two or more exponential equations, as suggested by Nye,[14] and observed clinically.[15, 16]

Dynamic lung compliance was computed as the change in lung volume per unit change in transpulmonary pressure measured from the beginning of inspiration to the end of inspiration. Transpulmonary pressure was represented as the difference in pressure between airway and esophageal pressure. Tidal volume was determined by integrating the flow signal from a Fleisch #1 pneumotachograph attached to the endotracheal tube. All blood gas analyses were done with a Beckman 160 Analyzer or an Instrumentation Laboratories Analyzer.

Calculations

Alveolar oxygen tension during inspiration of oxygen was calculated from the equation:

$$P_{A_{O_2}} = P_B - P_{H_2O} - P_{A_{CO_2}} \quad (1)$$

When air was inspired, the alveolar air equation was used:

$$P_{A_{O_2}} = F_{I_{O_2}}(P_B - P_{H_2O}) - P_{A_{CO_2}}\left[F_{I_{O_2}} + \frac{1 - F_{I_{O_2}}}{R}\right] \quad (2)$$

The respiratory exchange ratio (R) was determined from analyses of the inspired and expired air, the latter collected at the time of femoral arterial blood sampling. Both equations were solved assuming that $P_{A_{CO_2}} = P_{a_{CO_2}}$. Actually, there is a CO_2 gradient of less than 2 mm. Hg in right-to-left shunts of less than 20 per cent, and it can be ignored. The existence of a 5-mm. Hg gradient in the presence of a 40 per cent shunt during air inhalation

would lead to an underestimation of the shunt by less than 1 per cent.

The total physiologic shunt was calculated from the shunt equation:

$$\dot{Q}_s/\dot{Q}_t = \frac{Cc_{O_2} - Ca_{O_2}}{Cc_{O_2} - C\bar{v}_{O_2}} \quad (3)$$

where $\dot{Q}_s$ represents that portion of the total blood flow ($\dot{Q}_t$) which is shunted past nonventilated alveoli, blood coming from regions with low ventilation–perfusion ratios, as well as blood flowing through anatomical shunts. Cc_{O_2}, Ca_{O_2}, and $C\bar{v}_{O_2}$ represent the oxygen contents of pulmonary capillary, arterial and mixed venous bloods, respectively. Ca_{O_2} during oxygen breathing was calculated from the hematocrit and addition of the amount physically dissolved—a method found to give results similar to the direct Van Slyke technique.[17] When air was inspired, Ca_{O_2} was determined utilizing the nomogram of Rossing and Cain, which determines saturation of dog's blood from Pa_{O_2}, *p*H, and temperature.[18] During inhalation of oxygen when pulmonary capillary blood reaches full equilibration at the observed PA_{O_2} only anatomical shunting and shunt past nonventilated alveoli are measured. During inhalation of air, pulmonary capillary blood fails to achieve equilibration at the observed PA_{O_2}. The difference between the Cc_{O_2} predicted from full equilibration and that actually achieved (Ca_{O_2}), represents the total physiologic shunt. Therefore, Cc_{O_2} was calculated assuming full equilibration of pulmonary capillary blood at the observed PA_{O_2}. Oxygen consumption was measured spirometrically and the cardiac output determined by the Fick principle:

$$\text{C.O. (l/min.)} = \frac{\dot{V}_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}} \quad (4)$$

Since Ca_{O_2}–$C\bar{v}_{O_2}$ did not change significantly in twelve dogs following atelectasis, whether air or oxygen was inhaled, the observed mean value of 3.2 volumes per cent was used in estimating shunt in the remaining 14 dogs.

Results

Experimental data are summarized in tables 1 and 2. Lung compliance and FRC during quiet breathing in anesthetized dogs exhibited a loosely dependent relationship ($r = 0.50$). The regression equation expressing this relation was $FRC = 0.37 + 4.78\ C_L$. The mean C_L was 0.056 ± 0.02 l./cm. H_2O and mean FRC of the group was 0.635 ± 0.19 l. The coefficients of variation for C_L and FRC were 36 per cent and 30 per cent, respectively.

The relationship of helium-mixing time to respiratory minute volume and FRC was determined by analysis of 42 simultaneous measurements of these parameters during the control periods. No correlation was found between mixing time and minute volume ($r = 0.06$). A positive correlation ($r = 0.38$) was found between mixing time and FRC, which is significant at the 1 per cent level. The formula expressing the relationship was: mixing time (min.) $= 1.27 + 1.6\ FRC_L$. During the control periods and with atelectasis produced by lung blockage and pneumothorax, the mixing times required for complete helium dilution were less than three minutes. Only following pneumothorax did mixing time differ significantly ($P < 0.05$) when air or oxygen was inhaled because of the marked difference in FRC. In all situations, however, the slopes of the helium-dilution curves, when plotted semilogarithmically, were straight, indicating absence of poorly-ventilated areas of the lung.

Atelectasis

The large A-aO_2 gradient present during inhalation of oxygen in the control period suggested significant atelectasis when dogs are allowed to breathe spontaneously during anesthesia. During breathing of air or oxygen, 27 per cent or 22 per cent, respectively, of venous blood was shunted. When the left lung was made atelectatic following bronchial occlusion, tidal volume was reduced approximately 17 per cent, but a 23 per cent increase in respiratory rate also occurred and the minute volume remained virtually unchanged. The loss of approximately 40 per cent[11, 19] of the total lung tissue was reflected by a decrease in lung compliance of equal magnitude (42 per cent and 46 per cent) in both groups of dogs. The FRC was reduced by 41 per cent in the group breathing air and 23 per cent in the group breathing oxygen. Shunting

increased to 43 per cent during breathing of air and 34 per cent during breathing of oxygen following atelectasis. No significant change in cardiac output occurred following institution of atelectasis, whether oxygen or air was inhaled (table 2). In all eight dogs, examination of the lung following inhalation of oxygen and bronchial blockage revealed that the left lung was completely liver-like in both color and consistency. The right lungs appeared fully inflated without evidence of atelectasis in the dependent portions. In each dog, correct positioning of the bronchial blocker in the left main-stem bronchus and the catheter within the pulmonary artery was confirmed.

Pneumothorax

Introduction into the thorax of air equal in volume to the FRC of the dog resulted in a reduction in tidal volume and almost doubling of the respiratory rate. Minute volume increased approximately 50 per cent. A 53 per cent reduction of the FRC during breathing of air and a 67 per cent reduction during breathing of oxygen also occurred. The difference between the two groups was significant at the 1 per cent level. Larger reduction in FRC were not expected, since some oxygen is absorbed from the pneumothorax and the thoracic volume actually increases somewhat with the introduction of air. The negative intrapleural pressure resulting from the elastic retractive force of the lung was reduced, allowing the rib cage to enlarge.[21]

Pneumothorax decreased lung compliance by 52 per cent and 44 per cent of control values when air and oxygen, respectively, were inspired. For dogs breathing oxygen, the physiologic shunt following pneumothorax, which presumably represents shunting past nonventilated alveoli, was also the same as that observed following bronchial blockage. The total shunt was again higher when air was breathed, suggesting that ventilation–perfusion abnormalities of patent alveoli contribute a significant amount to the total physiologic shunt. Both lungs of four dogs sacrificed

Table 1. Respiratory and Blood Gas Changes Due to Induced Atelectasis and Pneumothorax in Dogs Breathing Either air or Oxygen (Mean values and standard deviations. Significant differences between the air versus oxygen groups: $*P < 0.05$; $**<0.01$.)

		Control	Atelectasis	Control	Pneumothorax	Aspiration	Reinflation
	Air O_2	13 dogs 13 dogs	13 dogs 13 dogs	9 dogs 9 dogs	9 dogs 9 dogs	7 dogs 7 dogs	7 dogs 7 dogs
C_L (l./cm. H_2O)	Air O_2	0.055 ± 0.021 0.057 ± 0.017	0.032 ± 0.018 0.031 ± 0.010	0.067 ± 0.022 0.057 ± 0.013	0.032 ± 0.021 0.032 ± 0.018	0.032 ± 0.021 0.033 ± 0.009	0.066 ± 0.039 0.047 ± 0.006
FRC (l.)	Air O_2	0.690 ± 0.214 0.583 ± 0.085	0.412 ± 0.141 0.454 ± 0.130	0.727 ± 0.192 0.594 ± 0.163	0.347 ± 0.194 0.192 ± 0.046	0.529 ± 0.136* 0.383 ± 0.083*	0.691 ± 0.243 0.500 ± 0.089
FRC (ml./kg.)	Air O_2	25.4 ± 4.9 21.6 ± 6.6	17.0 ± 3.7 16.6 ± 4.9	26.7 ± 2.8 21.9 ± 6.6	12.5 ± 2.2 7.2 ± 3.7**	19.7 ± 2.2 13.0 ± 3.7**	25.1 ± 5.9 17.5 ± 5.1*
V_T (ml./kg.)	Air O_2	9.3 ± 2.8 8.6 ± 3.9	7.8 ± 2.5 7.0 ± 3.0	6.6 ± 3.5 6.9 ± 2.9	5.7 ± 1.5 6.3 ± 3.6	6.3 ± 2.3 6.1 ± 3.2	6.2 ± 1.6 6.0 ± 3.0
Rate (resp./min.)	Air O_2	13 ± 4 13 ± 7	16 ± 5 16 ± 8	17 ± 7 15 ± 6	30 ± 14 22 ± 10	32 ± 16 25 ± 13	25 ± 7 25 ± 8
Minute volume (ml./kg./min)	Air O_2	121 112	125 112	112 104	171 139	202 152	155 150
Mixing time (min.)	Air O_2	2.5 ± 0.8 2.6 ± 0.9	2.1 ± 0.8 2.3 ± 1.0	2.6 ± 0.7 1.9 ± 0.2*	2.3 ± 0.6 1.2 ± 1.2*	2.1 ± 0.5 1.7 ± 0.5	2.5 ± 0.9 1.5 ± 0.6*
pH	Air O_2	7.34 ± 0.06 7.32 ± 0.06	7.32 ± 0.05 7.28 ± 0.05	7.35 ± 0.05 7.31 ± 0.05	7.31 ± 0.07 7.31 ± 0.04	7.32 ± 0.07 7.32 ± 0.06	7.34 ± 0.06 7.33 ± 0.04
P_{ACO_2} (mm. Hg)	Air O_2	43 ± 7 43 ± 7	46 ± 10 49 ± 9	49 ± 6 45 ± 6	52 ± 10 48 ± 9	49 ± 8 44 ± 8	48 ± 8 48 ± 8
P_{AO_2} (mm. Hg)	Air O_2	70 ± 7 369 ± 62	59 ± 6 138 ± 84	72 ± 7 311 ± 129	58 ± 16 153 ± 93	63 ± 9 158 ± 83	70 ± 12 317 ± 153
$A-aO_2$ (mm. Hg)	Air O_2	29 ± 9 287 ± 89	37 ± 11 519 ± 85	21 ± 8 344 ± 140	32 ± 12 499 ± 155	30 ± 13 489 ± 95	24 ± 13 335 ± 161
$\dot{Q}s/\dot{Q}t \times 100$	Air O_2	27 22	43 34	23 25	43 33	36 32	26 24

TABLE 2. Cardiac Output, Arteriovenous Oxygen Difference, and Total Physiologic Shunt before and following Atelectasis Induced by Left Bronchial Blockage in 8 Dogs and by Pneumothorax in 4 Dogs
(Means ± S.D.)

	Cardiac Output (L./min.)	$C_{aO_2} - C\bar{v}_{O_2}$	$\dot{Q}_s/\dot{Q}_t \times 100$
Control			
O_2	2.51	3.3 ± 0.6	22
Air	2.68	2.9 ± 0.5	29
Atelectasis			
O_2	2.36	3.4 ± 0.6	34
Air	2.43	3.1 ± 0.6	40

after pneumothorax were partially collapsed, with patchy atelectasis in the dependent portions. Lung volume was estimated visually to have been reduced to 50–60 per cent of normal volume by the pneumothorax.

Aspiration of pneumothorax air produced no increase in compliance in either group, and since no decrease in shunting occurred in the oxygen-breathing group, presumably there was no reduction in atelectasis. FRC did increase in both groups, however, and the increase in resting lung volume in the air-breathing group was associated with a reduction in the total shunt from 43 per cent to 36 per cent of the cardiac output. Compliance values and shunting returned to control levels only in the period following vigorous hyperinflation.

Discussion

It is well documented that if anesthetized dogs are allowed to breathe spontaneously, atelectasis is present, usually in the dependent portions of the lung.[5, 17] Hyperventilation, whether spontaneous [20] or artificially produced,[1-4] may lead to elimination or marked reduction in shunting and significant increase in compliance. Invariably, however, these changes are followed by return to prehyperinflation levels.[2, 5, 17] When air is breathed, the total shunt is considerably greater than during inhalation of oxygen, presumably because of abnormalities in ventilation relative to perfusion, since an appreciable diffusion gradient has not been demonstrated in dogs.[20, 22]

LUNG COMPLIANCE, FRC, AND ATELECTASIS

The present study shows that, following an increase in the amount of atelectasis caused by bronchial blockage or pneumothorax, a proportional decrease in lung compliance can be expected, whether air or oxygen is inspired. Factors other than atelectasis, such as changes in respirator pressure and cycling dynamics during controlled respiration, can influence compliance measurements, however.[8, 23] During spontaneous respiration, changes in frequency [24] and depth of respiration [25] as well as changes in alveolar surface tension,[7, 26] bronchial tone,[27] and position,[6, 26, 29] can alter compliance significantly. The observations of Williams *et al.*[7] suggest that during controlled respiration, reductions in lung compliance can be expected in hypoventilated alveoli on the basis of increasing surface tension alone, without atelectasis. Whether these changes occur during spontaneous respiration is not known. In our animals alveoli undoubtedly were hypoventilated during the control periods, and particularly during bronchial blockage and pneumothorax, as evidenced by the increased shunt during breathing of air. It is unlikely, however, that changes in surface tension played a significant role in reducing compliance values, since increases in FRC following aspiration of pneumothorax air, while effecting major increases in alveolar volume, left compliance unchanged. Measurement of lung compliance, then, should be considered a sensitive method for assessing changes in the amount of atelectasis, provided other factors known to influence lung compliance remain relatively unchanged.

Reduction in FRC also occurred after atelectasis. However, changes in resting intrapleural pressure or tone of musculature of the chest wall, quite apart from atelectasis, may affect the resting lung volume, also. That changes of this nature occur is evident from the responses to aspiration of pneumothorax air: following aspiration, dogs breathing oxygen experienced no reduction in shunting and atelectasis but a marked increase in FRC. In spite of this increase, lung compliance remained unchanged, reflecting the persistence of atelectasis. Only following the high sustained inflation pressures required to overcome

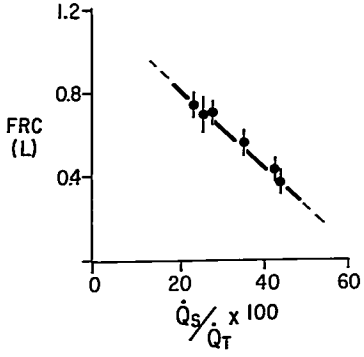

FIG. 1. Relationship of FRC to total physiologic shunt during breathing of air and following induced atelectasis and pneumothorax. Data from Table 1. FRC mean values ± S.E.

the surface tension forces involved in atelectasis did compliance values and reduction in shunting reflect the reopening of collapsed alveoli. Thus, lung compliance, unlike the FRC, consistently reflects the amount of underlying atelectasis, regardless of whether air or oxygen fills the lungs.

Resting lung volume following bronchial blockage also is influenced by the presence or absence of nitrogen in the lung distal to the block. We found, as did Dale and Rahn,[30] that no significant change occurred in the FRC of the unblocked lung if the other lung contained air before blockage. When oxygen was present in the blocked lung, however, absorption of the trapped oxygen occurred, causing mediastinal shift and a larger resting lung volume for the unblocked lung. Presumably this explains the smaller decrease in FRC following bronchial blockage during oxygen inhalation (23 per cent) than during air inhalation (41 per cent).

Atelectasis and Shunting

We were unable to explain why the shunt only increased from a control value of 27 per cent to 43 per cent during breathing of air following blockage of the left lung and from 22 per cent to 34 per cent during inhalation of oxygen unless some pulmonary blood was shunted towards the unaffected lung. Both shunting and FRC were greater when air rather than oxygen was breathed following pneumothorax. Hypoinflated alveoli containing air, although contributing significantly to the total physiologic shunt, may sustain a greater volume than O_2-filled alveoli because of the "nitrogen scaffold"[31, 32] and may account for the larger FRC's measured during air breathing throughout the study.

Changes in the amount of shunting were observed to be closely related to changes in FRC during breathing of air. When changes in shunt, determined from table 1 data, are plotted against changes in FRC, physiologic shunting increases about 5 per cent with each 100-ml. decrease in FRC (fig. 1). We observed that a reduction in shunting can be accomplished without a reduction in atelectasis by increasing the resting lung volume, as occurred following aspiration of pneumothorax air. When the lung contains air, partially-collapsed alveoli are maintained patent by slowly-absorbed nitrogen and are more readily re-expanded when pneumothorax air is aspirated. When the lung contains only oxygen, partially-collapsed alveoli are more likely to become completely atelectatic. Aspiration of pneumothorax air leads only to overexpansion of the remaining lung without reopening completely atelectatic alveoli. The $\dot{V}/\dot{Q}$ ratio of ventilated alveoli was noted to improve with increases in FRC during breathing of air, suggesting that changes in resting lung volume, quite apart from the presence or absence of atelectasis, may play a significant role in determining the overall efficiency of respiration.

How resting lung volume influences the $\dot{V}/\dot{Q}$ ratio is not altogether clear. We were unable to demonstrate a distribution defect in ventilation during atelectasis and pneumothorax. The possibility exists that the helium-mixing time may be too insensitive to ventilation defects in normal but hypoventilated lung, yet its value in the presence of lung disease is well chronicled.[15, 16, 33] Alterations in perfusion may be affected by resting lung volume, however. Rahn has shown that in anesthetized supine spontaneously-breathing dogs, even though more ventilation occurs in dependent portions of the lung, considerably

more blood per unit volume of lung tissue flows through the dependent portions, more than offsetting any increase in ventilation.[34] With some shunting of blood toward unaffected lung tissue following institution of atelectasis, the increase in the total physiologic shunt would be less than predictable from the amount of induced atelectasis. Yet a further reduction in the $\dot{V}/\dot{Q}$ ratio of nonatelectatic lung, now relatively overperfused, would occur, partially offsetting the reduction in shunt due to redistribution. Additional reduction in resting lung volume in such a situation will enhance the shunt further. An optimal lung volume must exist, below which increases in shunting can occur during air inhalation. Thus, the achievement and maintenance of this volume seems necessary to minimize shunting whenever the inspired gas is not oxygen.

Conclusions

Judging from our results, it seems unlikely that a sensitive assessment of atelectasis can be made from measurement of the physiologic shunt alone. Increases in shunting were less than expected from the loss of nearly half the functioning lung, and these changes probably reflected blood shunting towards unaffected lung tissue. Still further changes in shunting can be produced by altering the state of inflation (FRC) of nonatelectatic lung without changing the degree of atelectasis, when air is inspired. Changes in lung compliance during spontaneous respiration, however, consistently reflected the degree of atelectasis (determined by postmortem examination), regardless of changes in the FRC or the calculated shunt, whether air or oxygen was inhaled.

The data also suggest that FRC determinations may be helpful in suspected cases of atelectasis. Reductions in FRC may suggest atelectasis but, more important, may foretell significant ventilation–perfusion defects. In such a situation measurement of shunt during both inhalation of oxygen and breathing air would allow assessment of the relative contributions of atelectasis and ventilation–perfusion defects to the total shunt.

References

1. Bendixen, H. H., Hedley-Whyte, J., and Laver, M. B.: Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation, New Engl. J. Med. 269: 991, 1963.
2. Egbert, L. D., Laver, M. B., and Bendixen, H. H.: Intermittent deep breaths and compliance during anesthesia in man, Anesthesiology 24: 57, 1963.
3. Hedley-Whyte, J., Laver, M. B., and Bendixen, H. H.: Effect of changes in tidal ventilation on physiologic shunting, Am. J. Physiol. 205: 891, 1964.
4. Laver, M. B., Morgan, J., Bendixen, H. H., and Radford, E. P., Jr.: Lung volume, compliance and arterial oxygen tensions during controlled ventilation, J. Appl. Physiol. 19: 725, 1964.
5. Mead, J., and Collier, C.: Relation of volume history of lungs to respiratory mechanics in anesthetized dogs, J. Appl. Physiol. 14: 669, 1959.
6. Lim, T. P. K., and Luft, V. C.: Alterations in lung compliance and functional residual capacity with posture, J. Appl. Physiol. 14: 164, 1959.
7. Williams, J. V., Tierney, D. F., and Parker, H. R.: Surface forces in the lung, atelectasis and pulmonary pressure, J. Appl. Physiol. 21: 819, 1966.
8. Watson, W. E.: Some observations on dynamic lung compliance during intermittent positive pressure respiration, Brit. J. Anaesth. 34: 153, 1962.
9. Inkster, J. S.: The T-piece technique in anesthesia. An investigation into the inspired gas concentrations, Brit. J. Anaesth. 28: 512, 1956.
10. Fife, W. P., and Lee, B. S.: Construction and use of self-guilding, right heart and pulmonary artery catheter, J. Appl. Physiol. 20: 148, 1965.
11. Niden, A. H.: The acute effects of atelectasis on the pulmonary circulation, J. Clin. Invest. 43: 810, 1964.
12. Robertson, W. G., and Farhi, L.: Rate of lung collapse after airway occlusion on 100% O_2 at various ambient pressures, J. Appl. Physiol. 20: 228, 1965.
13. Colgan, F. J., and Whang, T. B.: A method for measuring the functional residual capacity and dynamic lung compliance during oxygen and halothane inhalation, Anesthesiology 28: 559, 1967.
14. Nye, R. E., Jr.: Closed circuit method for measuring uneven ventilation, J. Appl. Physiol. 16: 1109, 1961.
15. Briscoe, W. A.: Comparison between alveolar arterial gradient predicted from mixing studies and the observed gradient, J. Appl. Physiol. 14: 299, 1959.

16. Scherrer, M.: Das studium der intrapulmonalen gasmischung zur beurteilung der ungleichmassigen ventilation und perfusion der lungen, II. Proc. Kon. Ned. Adad. Wet. Amsterdam, Ser. c58, 84, 1955.
17. Finley, T. N., Lenfant, C., Haab, P., and Rahn, H.: Venous admixture in the pulmonary circulation of anesthetized dogs, J. Appl. Physiol. 15: 418, 1960.
18. Rossing, R. G., and Cain, S. M.: A nomogram relating P_{O_2}, *p*H, temperature, and hemoglobin saturation in the dog, J. Appl. Physiol. 21: 195, 1966.
19. Rahn, H., and Bahnson, H. T.: Effect of unilateral hypoxia on gas exchange and calculated pulmonary blood flow in each lung, J. Appl. Physiol. 6: 105, 1953.
20. Williams, M. H., Jr.: Alveolar–arterial oxygen pressure gradient in normal dogs, Amer. J. Physiol. 173: 77, 1953.
21. Simmons, D. H., and Hemingway, A.: Acute respiratory effects of pneumothorax in normal and vagotomized dogs, Amer. Rev. Tuberc. 76: 195, 1957.
22. Suskind, M.: Alveolar–arterial O_2 and CO_2 differences in the dog breathing air and low O_2 mixtures, Amer. J. Physiol. 177: 227, 1954.
23. Ayres, S. M., Kozam, R. M., and Lucas, D. S.: The effects of intermittent positive pressure breathing on intrathoracic pressure, pulmonary mechanics, and the work of breathing, Am. Rev. Resp. Dis. 87: 370, 1963.
24. Otis, A. B., McKerrow, C. B., Bartlett, R. A., Mead, J., McIlroy, M. B., Selverstone, N. J., and Radford, E. P., Jr.: Mechanical factors in distribution of pulmonary ventilation, J. Appl. Physiol. 8: 427, 1956.
25. Salazar, E., and Knowles, J. H.: An analysis of pressure–volume characteristics of the lungs, J. Appl. Physiol. 19: 97, 1964.
26. Collier, C. R., and Mead, J.: Pulmonary exchange as related to altered pulmonary mechanics in anesthetized dogs, J. Appl. Physiol. 19: 659, 1964.
27. Colgan, F. J.: Relationship of changing bronchial caliber to respiration in the dog, J. Appl. Physiol. 19: 803, 1964.
28. Kilburn, K. H., McDonald, J., and Piccinni, F. P.: Effect of ventilatory pattern and body position on lung volume in dogs, J. Appl. Physiol. 15: 801, 1960.
29. West, J. B.: Distribution of blood flow and the pressure–flow relationship of the whole lung, J. Appl. Physiol. 20: 175, 1965.
30. Dale, A. W., and Rahn, H.: Experimental pulmonary atelectasis. Changes in chest mechanics following block of one lung, J. Appl. Physiol. 9: 359, 1956.
31. Harris, T. A. B.: The Mode of Action of Anesthetics. Edinburgh, E & S Livingston Ltd., 1951, p. 529.
32. Dery, R., Pelletier, J., Jacques, A., Clavet, M., and Houde, J.: Alveolar collapse induced by denitrogenation, Can. Anaesth. Soc. J. 12: 531, 1965.
33. Hickam, J. B., Blair, E., and Frayser, R.: An open circuit helium method for measuring functional residual capacity and defective intrapulmonary gas mixing, J. Clin. Invest. 33: 1277, 1954.
34. Rahn, H., Sadoul, P., Farhi, L. E., and Shapiro, J.: The distribution of ventilation and perfusion in the various lobes of the dog lung. *In* Studies in Respiratory Physiology, Second Series. Wright Air Development Center Technical Report 55-357. Springfield, Ohio, Carpenter Litho. & Printing Co., p. 195.

Drugs

NARCOTICS The pulmonary and systemic hemodynamic effects of meperidine and hydroxyzine, individually and in combination, were investigated. The preparation consisted of intact, unanesthetized dogs in which pulmonary artery, left atrial and aortic catheters and an electromagnetic flowmeter had been implanted at operation. Meperidine produced significantly increased computed pulmonary and systemic vascular resistance. Hydroxyzine produced significantly increased systemic vascular resistance, but had little effect on the pulmonary circulation. A combination of meperidine and hydroxyzine produced considerably fewer changes than meperidine alone. Both agents individually and in combination produced hemodynamic changes which could alter the interpretation of a cardiac catheterization. (*Goldberg, S. J., and others: The Pulmonary and Systemic Hemodynamic Effects Produced by Meperidine and Hydroxyzine, J. Pharmacol. Exper. Therap. 159: 306 (Feb.) 1968.*)