Atelectasis:

Effect on Distribution of Ventilation and Perfusion

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The effects of ventilatory and circulatory events on oxygen uptake by the blood and their temporal relationships were studied in dogs before and after induced atelectasis. Analysis of helium washin curves revealed no significant changes in the ventilatory characteristics of the lungs following atelectasis. Oxygen washin curves, however, revealed an increase in the rate of alveolar equilibration and a marked decrease in the rate of oxygen uptake by the blood. The absence of demonstrable change in cardiac output or distribution of ventilation in the remaining lung suggests that perfusion of atelectatic lung is primarily responsible for the increase in the A-aDo₂ following induced atelectasis. (Key words: Atelectasis; Ventilation; Perfusion.)

ATELECTASIS in dogs results in a reduction in functional residual capacity and an increase in the amount of blood shunted through the lung. The purpose of the present work was to define changes in the distribution of ventilation and perfusion following induced atelectasis in the dog and to determine the effects of the changes on oxygen uptake by the blood.

Methods

Six dogs were anesthetized with 25 mg/kg thiopental sodium intravenously, placed supine, and allowed to breathe spontaneously. A swivel Y-piece incorporating nonrebreathing valves and a Rahn end-tidal sampler was attached to the endotracheal tube. The input side of the Y-piece was connected to a T-piece with attached anesthesia breathing tube, and air was admitted at the T-connection at a rate of 12 l/min. A similar breathing tube with an inline Fleisch #2 pneumotachograph was attached to the exhalation side of the Y-piece.

The left femoral artery was cannulated, and a central venous catheter advanced through the jugular vein into the right ventricle. Proper placement of the catheter tip was achieved by monitoring the pulse wave during advancement (and confirmed at postmortem examination). The dogs were then heparinized with 50 mg heparin, intravenously.

The distribution of ventilation was defined utilizing the open-circuit helium dilution method of Briscoe,¹ and continuous recordings of alveolar and arterial oxygen tensions were made during oxygen washin of the lungs to determine the effect of atelectasis on the development of A-aDo₂.

Helium washin (0.8 per cent in air) was monitored by continuously drawing the end-expired air from the Rahn end-tidal sampler through the thermal conductivity meter of a Godart pulmonet. The galvanometer signal was further amplified and recorded. Following amplification, the galvanometer signal was processed by a Sanborn logarithmic preamplifier, and the resulting signal, a logarithmic expression of the helium washin curve, was adjusted to record full-scale when 99 per cent (or two log cycles) of the total helium washin had occurred. The time required for 99 per cent of equilibration to occur is hereinafter called equilibration time. The determination of actual (100 per cent) equilibration time becomes highly subjective because of the relative insensitivity of open-circuit (He and N₂) analyzers.² The logarithmic expression of each helium washin curve was separated into two exponential components and the relative size (L/Lₜ) and ventilation (V̇ₐ/L) of each compartment determined by the method of Briscoe.¹ V̇ₐ/L relates alveolar ventilation per minute per unit lung volume to the respiratory

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TABLE 1. Effects of Induced Atelectasis on Ventilation*

	Before Atelectasis	After Atelectasis
f(/min)	21 ± 2	31 ± 6
V_D/V_T	0.40 ± 0.03	0.52 ± 0.05
Equilibration time (99 per cent)(min)	1.3 ± 0.3	1.0 ± 0.2
L_1/L_t (per cent)	88.5 ± 1.0	86.5 ± 1.4
L_2/L_t (per cent)	11.5 ± 3.2	13.8 ± 4.1
V_1/L (l/min/l)	6.7 ± 1.2	8.5 ± 0.53
V_2/L (l/min/l)	1.9 ± 0.44	1.2 ± 0.35

* Mean values ± SE (n = 6).

rate and the time required to achieve 90 per cent washin or washout of the compartment analyzed.

Oxygen washin was monitored by continuously withdrawing gas from the Rahn end-tidal sampler at a flow of 200 ml/min, using a Beckman microcatheter sample pump. The gas was drawn through a Beckman C-2 Pauling paramagnetic oxygen analyzer and recordings were made at ten-second intervals. The gas sample was further analyzed for CO_2 using an inline Beckman LB-1 CO_2 analyzer and a Texas Instruments rectilinear recorder. A stable, sustained end-expired CO_2 record assured the proper functioning of the nonrebreathing valves and the validity of the sampling during oxygen washin.

During helium or oxygen washin, the flow rate of expired air was recorded and the pneumotachographic signal integrated electronically to determine the tidal and minute volumes. Expired air was also collected in a 30-liter meteorological balloon for determination of V_T, V_{O_2}, f, R and V_D/V_T.

Arterial and right ventricular blood samples were drawn during inhalation of air and oxygen for the determination of cardiac output by the Fick principle, and analyzed for P_{O_2}, P_{CO_2}, and pH. Arterial and mixed venous blood oxygen contents were determined directly using a mixture of deoxygenated potassium ferricyanide and blood.[3] Pulmonary capillary blood equilibration of pulmonary capillary blood at the observed PA_{O_2}. Intrapulmonary shunting during inhalation of air and oxygen was determined using standard formulae.[4]

During oxygen washin, arterial blood was

withdrawn from the femoral artery and through a Beckman cuvette at a constant rate of 1 ml/min, utilizing a Braun precision infusor–withdrawal pump. Oxygen tension of the blood was measured with a Beckman 160 Physiological Gas Analyzer and the galvanometer signal recorded during oxygen washin. Oxygen tension values were corrected for differences in the temperature of the blood in the cuvette during withdrawal. Blood was allowed to equilibrate in the cuvette immediately before and after withdrawal. The lower temperature in the cuvette during withdrawal reduced the oxygen tension of the blood approximately 4 per cent.

The rate of change of the Beckman 160 galvanometer in response to an instantaneous change in blood oxygen tension from 80 torr to 680 torr was 27 torr/sec when the blood was drawn through the cuvette at the experimental rate of 1 ml/min. This rate of rise was at least three times faster than that of arterial blood during oxygen washin. The 100 per cent response times of the helium galvanometer and the C-2 oxygen analyzer to a
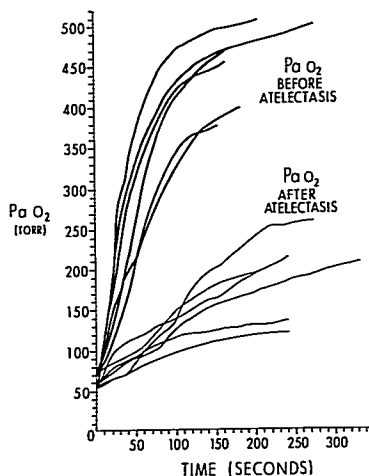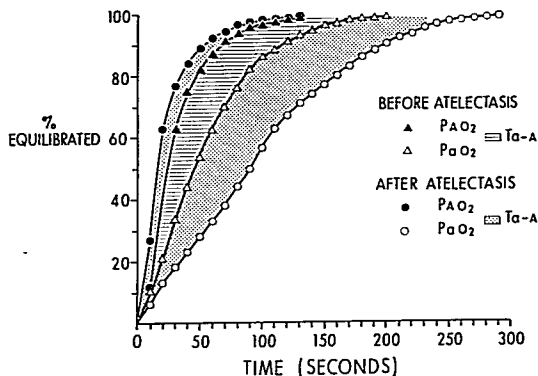

FIG. 1. Arterial oxygen tension curves during washin, before and after atelectasis.

FIG. 2. Alveolar and arterial oxygen washin curves plotted as percentages of full equilibration. Shaded areas represent the arterial–alveolar time gradient (T_{a-A}) before and after atelectasis.

"square-wave" change in helium or oxygen tension were 7 seconds and 4 seconds, respectively. These rise times are significantly shorter than those which can be achieved by progressive alveolar dilution even at excessive ventilatory rates.

Significance levels were determined by the method of paired comparisons and values of t.

EXPERIMENTAL PROTOCOL

Following 30 minutes of anesthesia and spontaneous respiration, the following measurements were made for each dog: 1) physiologic shunt during inhalation of air and oxygen; 2) end-expired helium and oxygen washin analyses, as described above; 3) continuous recording of arterial oxygen tension during oxygen washin. Following control measurements, an endobronchial blocker was inserted under bronchoscopic control, and the left lung made atelectatic. Thirty minutes later the measurements were repeated, and the animal was sacrificed with intracardiac KCl. Postmortem examination was done to determine the amount of atelectasis present.

Results

HELIUM WASHIN FOLLOWING ATELECTASIS

Exponential analysis of the helium washin curves indicated that the lungs of supine anesthetized dogs behaved as if composed of two compartments ventilating at different exchange

rates. Eighty-eight per cent of the lung volume exchanged at a mean rate of 6.7 l/min/l of lung volume, and the smaller compartment at 1.9 l/min/l. No significant change in the mean size or ventilatory exchange rate of either compartment occurred following the institution of atelectasis (table 1). The mean respiratory rate increased following atelectasis, from 21 to 31/min, and deadspace-to-tidal volume ratio (V_D/V_T) increased from 0.40 to 0.52. The time required to reach 99 per cent of equilibration was shorter following atelectasis, however, and is probably related to both the reduction in functional residual capacity and the increase in respiratory rate following atelectasis.[5]

ALVEOLAR–OXYGEN WASHIN FOLLOWING ATELECTASIS

Transient reductions in respiratory rate and tidal volume on switching from air to oxygen inhalation commonly occur in anesthetized dogs. Respiratory rates were reduced 25 to 30 per cent during oxygen washin in our dogs following atelectasis. Oxygen washin, however, was accomplished significantly faster following atelectasis ($P < 0.01$).

EQUILIBRATION OF P_{aO_2} DURING ALVEOLAR OXYGEN WASHIN

Figure 1 plots the actual P_{aO_2} changes, corrected for circulation and system lag time, be-

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fore and after atelectasis for each dog during oxygen washin. Percentage changes of the total changes in PA_{O_2} and Pa_{O_2} during oxygen washin were also determined. Mean values for the group of six dogs are plotted against time in figure 2. Analysis of the Pa_{O_2} equilibration curves before and following induced atelectasis reveal that less than 30 seconds after the start of equilibration, a significant difference ($P < 0.01$) in the rate of rise in the arterial oxygen tension is apparent. This difference reaches a peak between 80 and 90 per cent of equilibration (fig. 2). Ninety-nine per cent equilibration was achieved in 3.3 minutes in the control period and in 4.8 minutes following atelectasis.

CHANGES IN THE A-aD$_{O_2}$ DURING OXYGEN WASHIN

The A-aD_{O_2} during equilibration increased to values in excess of those ultimately achieved at full equilibration (fig. 3). The mean times for peaking of the A-aD_{O_2} were 40 seconds in the control period and 85 seconds following atelectasis.

ARTERIAL–ALVEOLAR TIME GRADIENTS DURING EQUILIBRATION

Figure 2 depicts the changes in the mean arterial–alveolar time gradient (T_{a-A}) during progressive stages of equilibration before and

after atelectasis. The T_{a-A} following atelectasis was increased approximately threefold throughout the period of equilibration. Most of this increase was due to a delay in the rate of equilibration of the arterial blood. A slight increase in the rate of equilibration of the alveolar oxygen further increased the time gradient. The T_{a-A} usually was greatest when alveolar and arterial equilibration were 90 per cent completed. Equilibration of alveolar oxygen tensions proceeded exponentially during oxygen washin; equilibration of arterial oxygen tensions was nearly exponential. T_{a-A} at 90 per cent completion of equilibration (T_{a-A} 90 per cent) was found to be significantly related to the amount of shunting ($r = 0.64$). Figure 4 relates the time gradient to the amount of shunting in each dog before and after the institution of atelectasis. The mean time gradient at 90 per cent of equilibration was 49 seconds before, and 145 seconds after, atelectasis. Thus, for every 10 per cent increase in shunting the 90 per cent time gradient increased approximately a minute. There was a still closer correlation between A-aD_{O_2} and T_{a-A} 90 per cent (fig. 5). A time gradient (T_{a-A} 90 per cent) increase of one minute was associated with a rise in A-aD_{O_2} of 120 torr.

No change in mean cardiac output occurred following atelectasis. Both the true shunt during inhalation of oxygen and the total shunt
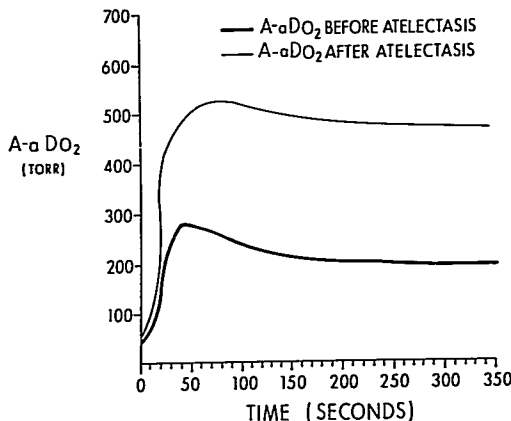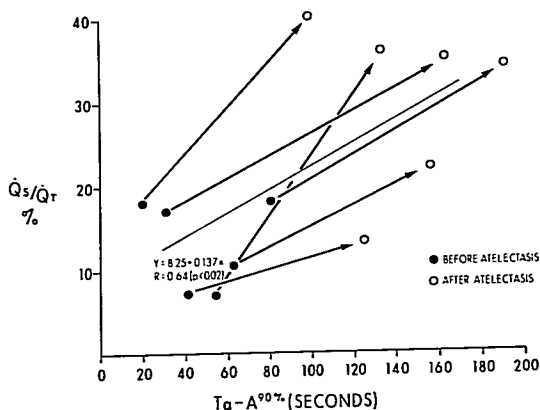

FIG. 3. A-aD_{O_2} during oxygen washin, before and after atelectasis. Mean values.

FIG. 4. Relationship of per cent true shunt ($\dot{Q}_s/\dot{Q}_t \times 100$) to the arterial-alveolar time gradient at 90 per cent of full equilibration (T_{a-A} 90 per cent).

measured during breathing of air nearly doubled, yet the ratio of true-to-total shunt remained unchanged (0.6) (table 2). At postmortem examination we estimated that 25 to 40 per cent lung collapse had been instituted by bronchial blockage in the six dogs. Mean collapse amounted to approximately 31 per cent for the group.

Discussion

The present study was undertaken to evaluate simultaneously the pulmonary and circulatory events which affect the uptake of oxygen by the blood in anesthetized dogs with and without induced atelectasis. How rapidly and to what degree the arterial blood responds to a change in inspired oxygen concentration are dependent on the distribution of inspired oxygen,[6] diffusion across the alveolar-capillary membrane,[7] cardiac output,[8] and distribution of the pulmonary blood flow.[9] Since pulmonary capillary blood can take up oxygen only to the extent of the concentration presented in alveoli, the mechanics involved in ventilatory exchange and the speed and equality of distribution of inspired air play dominant roles in alveolar-blood gas exchange. Our results indicate that atelectasis expedites alveolar washin of oxygen, presumably by reducing functional residual capacity and increasing respiratory rate. These changes, however, had little effect on the relative sizes or turnover

rates of the lung compartments. Diffusion of oxygen across the alveolar-capillary membrane probably had a minimal effect on gas exchange, since the alveolar oxygen concentration never was reduced to levels known to affect diffusion significantly.[7] The relative distribution of pulmonary blood flow to ventilated and to unventilated areas of the lung also affects the rate and degree of arterialization of the blood following a change in inspired oxygen. Both the amount of perfusion to unventilated areas of the lung and the time required to recirculate the blood (i.e., the cardiac output) affect the rate of arterialization of blood. Perfusion of unventilated areas of the lung probably accounts for most of the observed decrease in the arterialization of blood following atelectasis, since cardiac output did not change in this study. Thus, induced atelectasis results in both a reduction in the amount of ventilated lung tissue and at least partial continued perfusion of atelectatic lung. This situation contributes to a reduction in the overall V̇/Q̇ ratio of the lungs and an increase in the final alveolar-arterial oxygen tension gradient.

THE DEVELOPMENT OF THE A-aDO₂

Oxygenation of the blood is retarded in proportion to the magnitude of intrapulmonary shunting, since mixed venous blood passing through the shunt continually contaminates
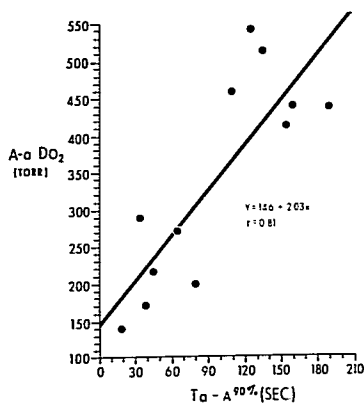
FIG. 5. Relationship of final A-aDO_2 to the arterial–alveolar time gradient at 90 per cent of full equilibration (T$_{a-A}$ 90 per cent).

the arterial blood. Thus, the magnitude and the timing of the A-aDO_2 peaking effect are influenced by the size of the intrapulmonary shunt. Were the distribution of ventilation or respiratory rate to change as well, the A-aDO_2 would be further affected during equilibration. Since no reduction in cardiac output, which would increase the circulation time and reduce the C$\bar{v}_{O_2}$, occurred, the delay in peaking presumably reflects the increase in the size of the intrapulmonary shunt. The larger the shunt, the greater the venous contamination of arterial blood during equilibration. Figure 3 demonstrates that the A-aDO_2 remained high for approximately three minutes after an in-

crease in inspired oxygen tension and after reasonable stabilization of the end-expired oxygen tension. Thus, a stable end-expired oxygen tension does not necessarily indicate that the arterial blood has achieved maximal uptake of oxygen in the presence of a large shunt for several minutes.

THE ARTERIAL–ALVEOLAR TIME GRADIENT

The difference between the rates of equilibration of alveolar gas and arterial blood following a change in inspired oxygen tension serves as a useful guide to the efficiency of ventilation relative to perfusion in gas exchange from lungs to blood. In an idealized situation in which no intrapulmonary shunting exists and ventilation and perfusion are distributed equally throughout the lung, the rates of change in alveolar and arterial tensions would be equal throughout the period of equilibration. The existence of some intrapulmonary shunting of blood, however, may partially negate an efficient ventilatory exchange by contaminating the arterial blood with mixed venous blood. The greater the shunt, the more delayed would be the attainment of a stable arterial oxygen tension following a change in inspired oxygen. This was demonstrated in the present study, in which an increase in intrapulmonary shunting was produced by inducing atelectasis, resulting in an overall increase in the arterial–alveolar time gradient (T$_{a-A}$). Since this time gradient was usually maximum at 90 per cent of full equilibration and thus more inherently accurate, this was chosen as a convenient reference point (T$_{a-A}$ 90 per cent) in the present study.

Changes in ventilation may affect T$_{a-A}$ 90

TABLE 2. Effects of Induced Atelectasis on Blood Gases, Cardiac Output and Shunting*

	Before Atelectasis		After Atelectasis	
	Breathing Air	Breathing Oxygen	Breathing Air	Breathing Oxygen
pH	7.46 ± 0.037	7.42 ± 0.037	7.37 ± 0.041	7.33 ± 0.041
Po₂ (torr)	71 ± 3.06	451 ± 18.6	58 ± 2.74	189 ± 19.4
Pco₂ (torr)	38 ± 1.03	38 ± 1.54	43 ± 2.75	50 ± 3.81
a − ⊽Do₂ (vol per cent)	2.53 ± 0.437	2.74 ± 0.514	2.79 ± 0.489	3.00 ± 0.420
Per cent shunt (Q̇s/Q̇t × 100)	22 ± 2.65	13 ± 1.99	46 ± 5.09	30 ± 3.91
Cardiac output (l/min)	2.4 ± 0.2		2.5 ± 0.3	

* Mean values ± SE (n = 6).

per cent and arterial rise time. In the presence of a fixed amount of intrapulmonary shunting, for example, it could be expected that hyperventilation, while affecting the arterial rise time, would have a minimal effect on T_{a-A} 90 per cent, since both alveolar and arterial rise times would decrease. However, T_{a-A} 90 per cent would be expected to decrease with hypoventilation (either generalized or regional), since prolonged alveolar washin would tend to minimize the effects of intrapulmonary shunting.

The effects of changes in cardiac output on T_{a-A} 90 per cent were not demonstrated in the present study; yet, under certain conditions (*i.e.*, a large intrapulmonary shunt) these changes would be expected to have a significant effect. Reduced $C\bar{v}_{O_2}$ secondary to a decreased cardiac output would increase T_{a-A} 90 per cent by further contamination of arterial blood through the shunt. Similarly, an increased cardiac output would decrease T_{a-A} 90 per cent. An increase in cardiac output then, in the presence of intrapulmonary shunt, would improve the efficiency of perfusion relative to ventilation.

References

1. Briscoe, W. A., and Cournand, A.: Uneven ventilation of normal and diseased lungs studied by an open-circuit method, J. Appl. Physiol. 14: 284, 1959.
2. Nye, R. E., Jr.: Theoretical limits to uneven ventilation, J. Appl. Physiol. 16: 1115, 1961.
3. Theye, R. A.: Blood O_2 content measurement using the O_2 electrode, ANESTHESIOLOGY 28: 773, 1967.
4. Colgan, F. J., and Mahoney, P. D.: The effects of major surgery on cardiac output and shunting, ANESTHESIOLOGY 31: 213, 1969.
5. Colgan, F. J., Whang, T. B., and Gillies, A. J.: Atelectasis and pneumothorax: Effect on lung functions and shunting, ANESTHESIOLOGY 29: 923, 1968.
6. Said, S. M., Davis, R. K., and Crosier, J. L.: Continuous recording in vivo of arterial blood P_{O_2} in dogs and man, J. Appl. Physiol. 16: 1129, 1961.
7. Staub, N. C.: Alveolar–arterial oxygen tension gradient due to diffusion, J. Appl. Physiol. 18: 673, 1963.
8. Briscoe, W. A., Cree, E. M., Filler, J., Houssay, H. E. J., and Cournand, A.: Lung volume, alveolar ventilation and perfusion interrelationships in chronic pulmonary emphysema, J. Appl. Physiol. 15: 785, 1960.
9. Finley, T. H.: The determination of uneven pulmonary blood flow from the arterial oxygen tension during nitrogen washout, J. Clin. Invest. 40(2): 1727, 1961.

Drugs

PARATHYROID POLYPEPTIDES Thyrocalcitonin, a hormone which induces hypocalcemia and hypophosphatemia, has been isolated, analyzed for aminoacid sequence, and synthesized chemically. It is secreted from the perifollicular cells found in mammalian thyroid but related embryologically to the ultimobranchial body of lower vertebrate species. Sensitive radioimmunoassays for thyrocalcitonin and parathyroid hormone have shown that secretion of each is controlled by calcium. Current findings show that the major physiologic parathyroid hormone actions are mediated by adenosine 3′,5′-monophosphate (cyclic AMP) produced as a consequence of direct, specific hormonal stimulation of the enzyme adenyl cyclase in bone and kidney. Thyrocalcitonin acts through another mechanism to inhibit bone resorption. In healthy subjects, but not in patients with pseudohypoparathyroidism, parathyroid hormones cause a marked increase in urinary excretion of cyclic AMP. This observation forms the basis for a useful diagnostic test and suggests that the metabolic abnormality of pseudohypoparathyroidism may be attributable to a genetic lack or defect of a specific adenyl cyclase in renal and skeletal tissue. (*Aurbach, G. D., and others: Polypeptide Hormones and Calcium Metabolism, Ann. Intern. Med. 70: 1243 (June) 1969.*)