Pulmonary Surfactant and Atelectasis

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SHIRLEY BERK

Surface activity of atelectatic lung extracts was studied with a surface film balance. All 16 atelectatic specimens demonstrated decreased surface activity regardless of etiology. Of those 12 not associated with pneumonia, contiguous lung tissue was normally surface active. Only atelectatic portions, no matter how tiny, were inactive.

To clarify factors involved with the 4 atelectatic specimens associated with pneumonia, 23 specimens of pneumonia were studied. All produced inactive extracts. Eleven of 19 contiguous sections studied were also abnormal. Into this group fell the 4 atelectatic areas. The opposite lungs, uninvolved with pneumonia, were normal.

These findings suggest that a decrease in pulmonary surfactant may occur secondary to atelectasis due to noninfectious factors. A surfactant antagonist may be produced during pulmonary infection, and diffuse out into neighboring lung tissue, causing the atelectasis occasionally seen with pneumonia. This concept implies that other substances introduced into the alveoli may also result in atelectasis.

IN recent years the principles of surface physics have been applied to the study of pulmonary physiology. The importance of interfacial forces has been recognized,[1] and a rather powerful substance, pulmonary surfactant, has been described as a major influence upon these forces.[2,3,4] The effect of this surfactant is such that it theoretically promotes stability of the alveolar structure. A deficiency of this material has been blamed for the atelectasis seen in several clinical conditions.[5-8]

The studies herein reported evaluate surface phenomena in extracts of lungs with atelectasis associated with bronchial obstruction, compression of lung tissue, and infection and inflammation, in an attempt to elucidate the specific relationships of surfactant to atelectasis in man.

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Materials and Methods

The surface characteristics of extracts of 21 normal nonatelectatic lungs were examined as control specimens for this study, and to support previous documentation of normal standards of surface activity in human lungs.[7] We studied the lungs of 16 adult patients found at autopsy to have atelectasis of varying degrees. Two of these 16 had obstructive atelectasis; 3 resulted from compression by pleural effusion, tumor, or elevated diaphragms; 4 were associated with pneumonia; and 7 had no obvious cause of the atelectasis.

The gross criteria for atelectasis included evidence of depression, a bluish grey color, decreased or absent crepitus and a tendency for the specimen to sink below a water surface. Microscopically there was evidence of alveolar collapse. These changes were present in all specimens in varying degrees.

Lung specimens contiguous to the atelectatic areas were studied in all cases. These specimens all appeared normal except for those 4 containing pneumonia. Nineteen additional lungs containing pneumonia without atelectasis were studied. They either showed classic lobar pneumonia or had the nodular appearance of bronchopneumonia. Some had purulent exudate in the bronchi, but others had no clear-cut excessive bronchial secretions. In 14 of the 19 with pneumonia alone, we also examined contiguous, normal-appearing portions of the same lungs for surface activity, and in 10, specimens of the contralateral lungs which also appeared normal.

The average age in all groups of subjects was comparable. The control lungs were from patients ranging from 43 to 91 years with an average of 63. Those with atelectasis ranged from 38 to 95, averaging 59. There were several particularly young patients with pneumonia, the youngest being 17. However,

even the average of this group was 60 years. Associated diseases were present equally in all three groups of patients, including those with normal lungs. Congestive heart failure, pulmonary emboli, myocardial infarction, and some form of cancer were distributed among the 3 groups. Two of the patients with pneumonia were uremic, but so were 4 of the controls. Serious liver disease was present in one patient with pneumonia, and one with atelectasis. One of those with pneumonia had asthma. One of the patients with atelectasis also had bronchiectasis, but not related to the etiology of atelectasis. Emphysema of significance was found among those with pneumonia and the control cases. The other pathologic entities would not be expected to influence the results either on a local or general metabolic basis. Most of the patients in all groups had received many medications, and there was no consistent influence of any of these.

All determinations were performed on a modified Langmuir-Wilhelmy surface film balance. The surfactant was extracted from 3 g. of lung tissue in each case. The lung was minced into small pieces approximately 3 by 3 mm. and stirred in 50 ml. of 0.85 per cent saline for 15 minutes. This was then filtered through 2 thicknesses of gauze into a polytetrafluoroethylene (Teflon) trough.

The trough is 14 cm. × 6 cm. × 0.9 cm., and forms part of the modified Langmuir-Wilhelmy apparatus as used by Clements. As the extract lies in the trough, the surfactant presumably forms a monomolecular layer at the air-liquid interface. A frosted platinum rider, 2.5 cm. in length, on which surface forces may act, is lowered into the surface. The surface of the extract is compressed to 20 per cent of its original area, and then expanded to its original dimensions by means of a motor-driven Teflon barrier lying across the trough. The area to be compressed is completely lined with Teflon tape to insure against loss of surfactant. The compression-expansion cycle lasts 15 minutes. The force of surface tension is measured by a transducer on an X-Y recorder.

Results

Normal lung extracts produced a typical tension-area curve indicative of definite surface activity (fig. 1). On compression of the surface there was a rapid drop in surface tension, with a steep slope to the curve. On expansion the tension rapidly rose to its original level, resulting in a wide hysteresis loop. The minimal surface tension reached on compression of the surface to 20 per cent of its original area was a consistently reproducible figure in the control extracts. All 21 of these reached minimal surface tensions below 10 dynes/cm., with an average of 5.7 dynes/cm. (table 1).

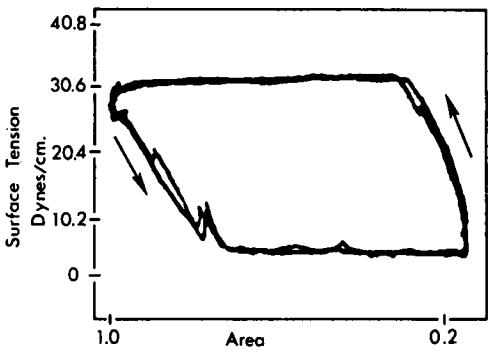

FIG. 1. Changes in surface tension as extract of normal lung tissue is compressed to 20 per cent of original surface area, and re-expanded. Very low minimal surface tension (4 dynes/cm.) is reached rapidly on compression, while values rise again to previous levels on expansion.

Inactive extracts were markedly different from normal lung (fig. 2), and had the following characteristics: a gradual slope to the curve, a much higher minimal surface tension, and a narrow hysteresis loop. The 16 atelectatic specimens were relatively inactive, none reaching levels as low as 10 dynes/cm. (table 2). The average of these was 18.5 dynes/cm. These abnormalities did not depend on the degree of atelectasis. In some lungs, lobar or multilobar atelectasis was present, and in some, segments or even smaller areas were involved. The normal appearing sections of all 12 atelectatic lungs without pneumonia demonstrated perfectly normal surface activity. Many of these were taken from areas contiguous to atelectatic portions.

The extracts of the 23 lobes involved with pneumonia demonstrated decreased surface activity when compared with the control specimens. The mean minimal surface tension was 19.7 dynes/cm. (table 3). Among the 19 specimens contiguous to the area of pneumonia, including the 4 previously mentioned atelec-

TABLE 1. Minimum Surface Tension (Dynes/cm.) on Compression of Normal Lung Extracts

Subject	
D. J.	6.8
M. R.	6.4
D. K.	4.5
W. G.	2.8
F. K.	6.8
J. B.	5.6
J. F.	6.8
H. S.	5.6
A. H.	4.5
A. A.	4.5
F. M.	5.6
E. T.	6.8
H. B.	6.8
E. H.	3.4
C. W.	6.8
M. V.	8.0
A. S.	5.7
E. S.	5.7
R. M.	4.6
A. H.	4.6
A. F.	7.3

tatic specimens, 11 demonstrated a decrease in surface activity, and only 8 were normal. The average minimal surface tension in this group was 12.4 dynes/cm. The 10 cases showing no pneumonia in the opposite lung were quite comparable to the normal controls, with a mean minimal surface tension of 6.7 dynes/cm. (table 3).

All of the above findings are summarized in figure 3.

TABLE 2. Minimum Surface Tension (Dynes/cm.) on Compression of Surface Film in Atelectatic Human Lungs

Subject	Atelectatic Portion	Non-Atelectatic Portion
E. S.	22.0	4.2
F. K.	18.1	5.4
Y. G.	14.2	5.4
B. B.	22.7	7.9
S. S.	13.6	7.9
E. S.	21.5	4.5
L. B.	13.6	4.5
G. M.	18.1	9.1
E. G.	23.8	6.8
L. M.	22.7	4.6
M. R.	20.4	4.6
A. R.	18.1	9.1
S. C.	19.3	
S. C.	25.0	
C. S.	19.3	
R. S.	10.2	

Discussion

Atelectasis has long been etiologically associated with three basic phenomena: (1) obstruction of bronchi with distal absorption of air, (2) hypoventilation, and (3) external compression of all or part of a lung. To these have recently been added (4) "contraction atelectasis," resulting from reflexes activating smooth muscle in the walls of respiratory bronchioles and alveoli,[9,10] and (5) "surfactant-deficiency atelectasis," due to loss of or degradation of the surface tension lowering alveolar lining layer.[3]

The present studies represent an attempt to clarify the role of surfactant in atelectasis in the adult human being. Surface activity is diminished or absent in atelectatic segments of lungs with atelectasis not associated with pneumonia. Areas contiguous to the atelectasis are normal, implying that there is no basic surfactant deficiency which predisposes these patients to the development of atelectasis. Studies in dogs have shown that surfactant abnormalities may be produced in lungs as a result of atelectasis due to bronchial occlusion.[7,11] The findings in autopsy specimens suggest that a similar relationship exists in adult human beings. The resultant abnormality in surfactant may serve to reinforce the atelectasis which has been produced, because the surface tension is allowed to rise despite a continued decrease in size of the alveoli.

Benfield and his associates[12] have supported the concept of abnormal lung mechanics secondary to atelectasis by demonstrating de-

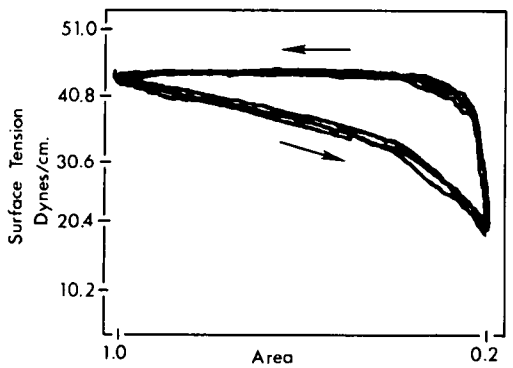

FIG. 2. Tension-area curve of inactive lung extract. Surface tension falls only to 18 dynes/cm. upon compression.

creased compliance in chronically atelectatic dog lungs.

The infected lobes of lungs containing pneumonia demonstrated decreased surface activity, as did contiguous atelectatic but uninfected portions of the same lungs. Of interest was the finding that many contiguous uninfected specimens not containing atelectasis also showed a decrease in surface activity, while the contralateral lungs were normal. The abnormality among the nonatelectatic lung sections was not anticipated on the basis of roentgenologic examination during life or at post-mortem examination. On the basis of these findings, we think there may be a substance present in pneumonic lungs which is responsible for altering the surface phenomena normally found as a result of the activity of the pulmonary surfactant. This substance consistently diminishes surface activity in the infected portion of the lungs, and frequently produces similar abnormalities in areas contiguous to those actively involved with the infectious process. These alterations often result in some degree of atelectasis associated with the pneumonia, and may be responsible for the massive atelectatic collapse of the lung occasionally reported as occurring with pneumonia.

The implications of the influence of the pulmonary surfactant in anesthesiology are apparent. Numerous substances added to lung extracts have been reported to diminish surface activity.[13,14,15] Perhaps inspired substances which contact the alveoli may do the same. Yoshida[16] has shown that irrigation of the tracheo-bronchial tree with petroleum ether will alter the pressure-volume characteristics of the lung. Cannot diethyl ether and other anesthetic agents have the same effect?

Clements and Wilson[17] have studied the influence of various anesthetic agents on lipo-

TABLE 3. Minimum Surface Tension (Dynes/cm.) of Lung Extracts in Subjects with Pneumonia

Subject	Pneumonia	Contiguous Area	Other Lung
H. S.	17.0		5.7
A. H.	25.0		3.4
P. E.	15.9		5.7
S. C.	23.8	19.3	5.7
W. T.	22.7	11.3	
M. P.	23.8	13.6	
A. P.	17.0	15.9	8.0
S. C.	23.8	25.0	
		25.9	
C. S.	17.0	19.3	5.7
S. L.	23.8	5.7	5.1
W. L.	21.5	4.6	5.7
D. D.	25.0	5.1	
H. V.	15.9		
P. B.	9.1	9.1	
H. N.	23.8	4.6	6.2
N. M.	14.8	3.4	
N. K.	14.8		
W. F.	13.6	20.4	
R. S.	21.5	10.2	
J. T.	19.3	22.0	
C. R.	22.7	4.6	
J. S.	22.7	4.6	3.4
T. B.	19.3	14.8	

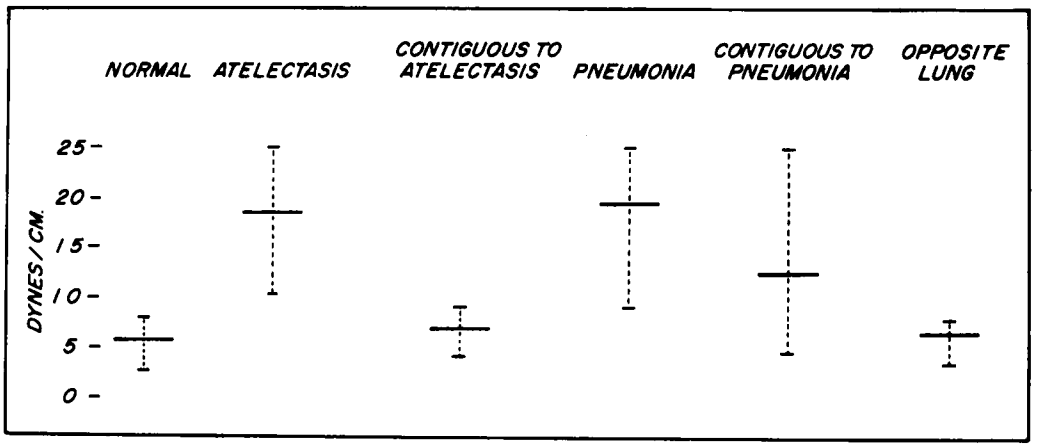

FIG. 3. Average minimal surface tension of normal and pathologic lung extracts with range of values obtained.

protein film-covered distilled water. A fall in surface tension occurred with all agents, those producing a greater change presumably having a greater affinity for the surface. There appeared to be a relationship between this surface affinity and the anesthetic potency of the agents. The authors concluded that this affinity for the surface film may be related to the mechanism of action of anesthetic agents since this film has similar composition to cellular membranes. Not only may this be the mechanism of alveolar absorption, but it could be the means of altering excitability of cells by the effect upon their membrane.

Although Clements and Wilson did not imply that these changes in surface tension might predispose to atelectasis, we are not certain of the influence of these agents upon the variation of surface tension with surface area. Even a drop in surface tension may result in alveolar instability if there can be no further fall upon compression of the surface.[18] It may be possible, then, that some anesthetic agents could be the cause of postoperative atelectasis.

Mead and Collier[19] have pointed out that compliance falls in anesthetized dogs, and suggested that surface forces may be responsible by resulting in collapse of lung units. Forced inflation resulted in an increase in compliance attributed to an increase in the number of distended alveoli. They implied that intermittent deeep inflation might be an important maneuver in preventing this reduction in compliance during anesthesia, thus keeping the lungs more uniformly ventilated.

On the other hand, rather prolonged positive pressure can have an adverse effect upon surfactant.[20] Convincing studies by Klaus and his associates[21,22] have shown that the mitochondria of alveolar epithelial cells are the site of surfactant production, and disruption of these cells by forcible positive pressure may cause enough damage to interfere with output of surfactant.

Since atelectasis can in itself secondarily destroy or antagonize the surfactant,[7] any patient with a previous history of prolonged atelectasis from whatever cause is suspect for possible recurrence. Surfactant destruction may be associated with other pulmonary functional abnormalities,[23,24] another factor to be considered in patients with a past history of atelectasis.

A recent history of pneumonia is another warning of a possible surfactant deficient patient. Not only might this incapacitate the lobe involved with pneumonia, but other parts of the lung as well.

The development of the concept of surface tension phenomena has been a major advance in our understanding of pulmonary physiology. Theoretically the absence of the pulmonary surfactant results in atelectasis. We have not yet found adult human lungs with a basic deficiency of surfactant to explain a predisposition to the development of atelectasis. Pulmonary infection appears to destroy or antagonize the surfactant, and may produce some degree of atelectasis. It is not clear whether this is a direct effect of the microorganism involved, or a reaction of the human host in an attempt to confine the infectious process.

This investigation has demonstrated that degradation of surfactant due to bacterial invasion may be a cause of alveolar collapse in the adult human. Conversely, obstructive and compression atelectasis may secondarily result in a loss of surfactant in the affected alveoli. Thus, atelectasis may be both cause and effect of abnormalities in the pulmonary surfactant.

The pulmonary surfactant certainly appears to be a real substance with powerful influences upon structure and function of the lung. Absence of the surfactant may be disastrous, and even a relative deficiency may seriously interfere with effective ventilation. The patient's adequacy of surface film is of major importance to the anesthesiologist from the standpoint of pulmonary function. Anesthetic agents may destroy surfactant, as may other factors in the surgical procedure. Postoperative atelectasis may result from such inadequacy. These phenomena require further investigation to improve our understanding of the pathophysiology of the lung in anesthesia and surgery.

Summary

Surface tension phenomena of 16 atelectatic lungs were evaluated with a surface film balance, and all were found to have decreased surface activity. A study of areas contiguous to the atelectatic portions, and of infected

lungs, suggests that atelectasis associated with pneumonia results from destruction of pulmonary surfactant by some unknown substance in the course of infection. Atelectasis produced by obstruction or compression may itself cause inactivation of surfactant, and then result in persistent collapse which is resistant to therapy.

These findings imply that atelectasis may be produced when surfactant is destroyed by some substances which may come in contact with the alveolar surface. A theoretic rationale is suggested for suspecting the presence of pulmonary function abnormalities and the dedevelopment of postoperative atelectasis in patients with antecedent respiratory illnesses or a past history of prolonged episodes of atelectasis.

The principles of surface tension phenomena have widespread application in medicine. They promise to improve our understanding of pulmonary physiology in relation to anesthesia and surgery, in preoperative evaluation, anesthetic management, and postoperative care.

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