Quantitative and Qualitative Changes in Morphology of Alveolar Sacs with Positive-Pressure Respiration (36767)

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Previous studies of pulmonary microanatomy have been made primarily on fixed tissues (1–4). These, however, do not permit continuous observation of the same structures during respiration. Hence, dynamic changes in morphology which could affect physiologic processes may not be detected. This investigation was designed to observe fine structures of the lung continuously *in vivo* and to document findings quantitatively by incident light photomicrography.

Materials and Methods. Sprague-Dawley rats weighing 300 to 400 g were premedicated intramuscularly with atropine sulfate (0.005 mg/100 g body wt) and anesthetized intraperitoneally with sodium thiamylal (5.5 mg/100 g body wt). A thoracotomy was performed to exteriorize the lung for study with an inverted metallurgical microscope and camera. Illumination was from a xenon lamp. Respiration was supported endotracheally with a positive pressure respirator delivering a tidal volume of 5 ml at 40 cpm and 15 cm H_2O peak pressure. The diaphragmatic surface of the lung was apposed to the top of a cover slip fixed within a frame supporting the animal above the objective. An optical bench moved the microscope, camera and lamp in unison and three dimensions relative to the lung surface. The same alveolar sacs were studied at 300× and photographed at peak inspiration and end expiration. Prints of 500× were made and images measured with a micrometer. Only sacs brought into sharp focus at maximum diameter were used.

Results. Typical subpleural structures in the inspiratory and expiratory phases are shown in Figs. 1 and 2, respectively. The external form of alveolar sacs was spheroid, but internal structure varied. Some sacs were wholly subdivided by one or more septa into smaller irregularly shaped compartments. These were considered to be alveoli. Other sacs were partitioned asymmetrically by low septa, ridges or folds which formed the limits of shallow depressions. Whether these, too, should be considered alveoli is debatable. No partitions were evident in some sacs. These resembled smooth, hollow hemispheres.

Both external and internal morphology of sacs changed with ventilation as may be seen by comparing equivalent landmarks in Figs. 1 and 2. The mean diameter of sacs diminished with expiration. Simultaneously, the shapes of partitions (whenever present) were altered at random and the mean dimensions of enclosed compartments decreased. These changes are exemplified by the sac near the center of the field. The sac in the right lower quadrant shows some interesting transformations. Prominent folds appear in the wall at end expiration where only small ridges were previously barely perceptible. Similar alterations occurred commonly in many sacs. The photomicrographs also show that morphologic changes were not limited to sacs but also extended to the microvasculature and parenchyma.

The mean diameter of 100 alveolar sacs in 5 animals varied from 66.6 ± 10.7 μ at peak inspiration, to 59.3 ± 4.5 μ at end expiration; a difference of 11%. If the sac were a perfectly hollow sphere, this would represent a cyclical change in air volume of 29.4% and in surface area of 35.3%. Sac diameters were readily determined but those of alveoli were difficult to obtain, because the boundaries of labile septa could not always be identified in

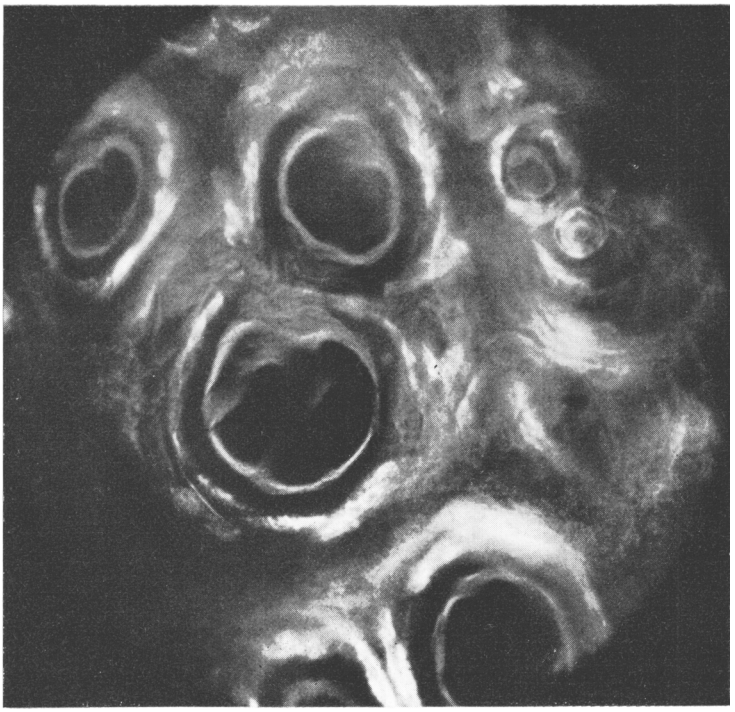

FIG. 1. Alveolar sacs in rat lung; inspiratory phase; incident light photomicrography, 500×.

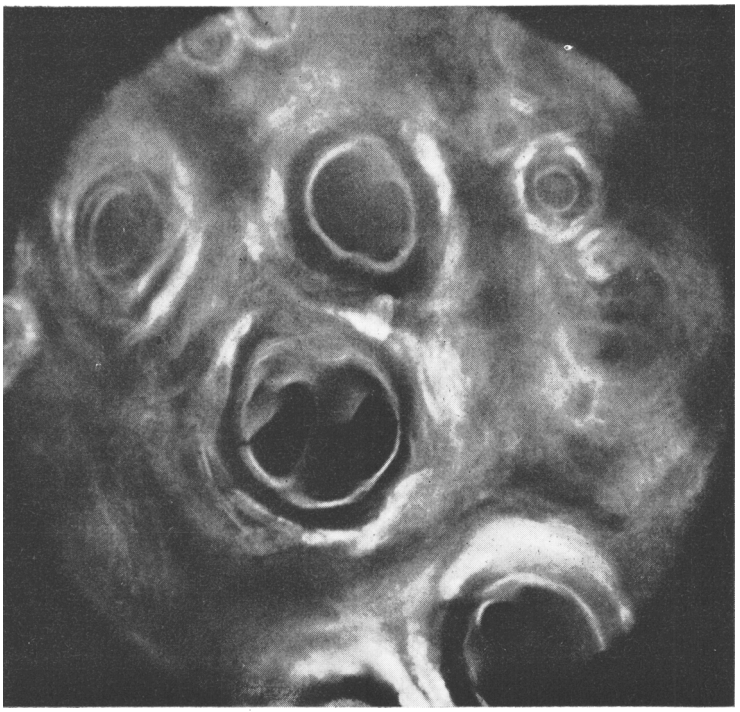

FIG. 2. Alveolar sacs in rat lung; expiratory phase. Same field shown in Fig. 1. Incident light photomicrograph, 500×. Note the differences in size and internal structure of these alveolar sacs compared with those shown in the previous inspiratory phase.

successive ventilatory phases. The mean diameter of 10 clearly defined alveoli was 27.8 μ at peak inspiration and 25.7 μ at end expiration; a change of 7.2%.

Discussion. Since the classic work of Malpighi (5), studies of lung structure *in vivo* have focused primarily on the microcirculation (6–10). Changes in morphology of alveoli with respiration have been reported, but relevant quantitative data appear to be lacking (11–14). However, data on fixed tissues are available. Tenney and Remmers (2) found mean alveolar diameters of 70.2 $\pm$ 6.6 μ in rat lungs inflated and fixed at 20 cm H_2O pressure. Macklin and Hartroft (3) using rat lungs fixed apparently in full expiration obtained corresponding values of 59.1 $\pm$ 13.1 μ. These data are at variance with the *in vivo* measurements of structures we defined as alveoli but agree closely with our findings for alveolar sacs. The discrepancy may be due to differences in terminology or possibly to histologic artefacts produced by fixation of lung tissue. Wagner (10) made quantitative measurements on alveoli in live dogs, but there is no indication that the data were related to respiration.

In the current study, direct observation and photographic evidence revealed that partition contours and internal topography of the sac wall varied with ventilatory excursions. This lability suggests that compartments formed by shallow septa, folds or ridges are not morphologic entitites in the histologic sense. Their formation may be related to physical characteristics of the sac wall and to the changing balance of forces across the sac membranes. Elastic elements, smooth muscle, and, conceivably, surfactant could contribute to the observed phenomena.

The function of sac partitions in pulmonary physiology is speculative. Olkon and Joannides (11) suggested that shallow alveolar partitions might set mechanical limits to structural deformation, trap inspired air and thus allow sufficient time for gas exchange. However, other functions are possible. The various types of partitions described in the present work may prevent streamline air flow and alter boundary layer phenomena within the sac, thereby facilitating admixture of gases and diffusion exchange. The increased surface area provided by partitions could aid such exchange. Additionally, fluid movement on both sides of the alveolar epithelium and in the capillaries may be enhanced by the folding and unfolding of the sac wall.

The cyclical alterations in wall topography and sac dimensions measured at the equatorial plane, suggest a true change in volume rather than a nonvolumetric change in morphology. This concept is of particular interest because it implies participation of the sac in the mechanics of gas exchange. Consequently, ebb and flow of gases at the microscopic level would not be a passive but rather a dynamic phenomenon related to pressure, tissue compliance, ventilatory rate and volume. In certain pulmonary diseases or pathophysiologic states where elastic properties are compromised or alveolar membranes damaged, blood–gas exchange may be significantly altered.

Summary. Effects of positive-pressure respiration on alveolar sac diameters were determined in exposed lungs of living rats using incident light photomicrography. The same sacs were photographed at peak inspiration and at end expiration. Measurements were made on enlarged prints. The mean diameter of 100 sacs at peak inspiration was 66.6 $\pm$ 10.7 and 59.3 $\pm$ 4.5 μ at end expiration. Internal structure and external form of sacs varied with ventilation. On the basis of visual studies and photographic evidence it is postulated that these morphologic changes may be associated with gas and fluid exchange.

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