TABLE I. Lung Surface Area and Alveolar Parameters in Several Species.

	Wt (kg)	FRC (cc)	Area (m^2)	Dia. alv. (calc.), μ	Dia. alv. (obs.*), μ	No. of alv. (millions)
Rat	.2	5	.18	167	60	8.0
Cat	2.	100	2.075	290	130	19.5
Dog	10.	400	10.3	230	75	290.
Man	70.	2250	70.	190	150†	500.

* From Macklin and Hartroft(6). † Recalculated for 2250 cc lung vol.

capacity of 2250 cc is associated with an alveolar volume of 1750 cc comprising about 80% of the total volume. The number of alveoli is 500 million and—from Macklin and Hartroft—their mean diameter is 150 μ. The surface film has a surface tension of 20-25 dynes/cm. The surface tension rises to 40-50 dynes/cm on maximum inspiration and falls to 15-20 dynes/cm on expiration to residual volume.

Summary. The surface tension of pulmonary edema fluid was 5-10 dynes/cm as measured in aged, compressed bubbles; it was 40-50 dynes/cm as measured by capillary tube. Nasal mucus on aging and compression exhibits a fall of surface tension from 45-50 dynes/cm to 17 dynes cm with a minimum compressibility coefficient of 0.016 cm per dyne. Calculations of relative surface tension in lungs of rats, cats and dogs assuming 50 dynes/cm for the upper limit showed a fall to 5-10 dynes/cm during deflation with minimum compressibility coefficient of 0.012 to 0.020 cm/dyne. The lung surface areas calculated for these species were proportional to body weight and extrapolated to 70 m^2 for a 70 kg man.

1. Radford, E. P., Jr., PROC. SOC. EXP. BIOL. AND MED., 1954, v87, 58.

2. Willson, H. C., *Am. J. Anat.*, 1922, v30, 267.

3. Gertz, H., *Z. f. Biol.*, 1928, v88, 172.

4. von Neergaard, K., *Z. f. d. ges. Exp. Med.*, 1929, v66, 373.

5. Pattle, R. E., *Nature*, 1955, v175, 1126.

6. Macklin, C. C., and Hartroft, W. S., *Rep. to Canad. Subcom. on Physiolog. Aspects of Chemical Warfare, Defense Research Board, Ottawa*, June, 1943.

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Surface Tension of Lung Extracts. (23156)

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Von Neergaard described the important role played by surface forces in the recoil of the lungs and made measurements of surface tension in lung extracts(1). Recently, Radford and his coworkers repeated and extended von Neergaard's experiments, again calling attention to the importance of surface tension in the static pressure-volume characteristics of the lungs(2) and pointing out the need for proper determination of the surface tension of the lung lining. In the interim Radford used the so-called static tension of serum (50 dynes/cm) in interpreting his results, assuming the surface to be thermodynamically reversible. From microscopic study of air bubbles squeezed from lung slices Pattle(3) concluded that the pulmonary alveoli are lined with mucoprotein (suggested previously on the basis of histochemical evidence by Macklin(4)) and that this material reduced the surface tension to less than 1 dyne per cm. In the last year Brown(8) repeated Radford's experiments and by assuming the lung to be composed of many identical hemispherical units computed surface tension from the pressure-volume data. The tension-area relationship so derived is similar to that of bubbles of nasal mucus, but depends upon an assumed

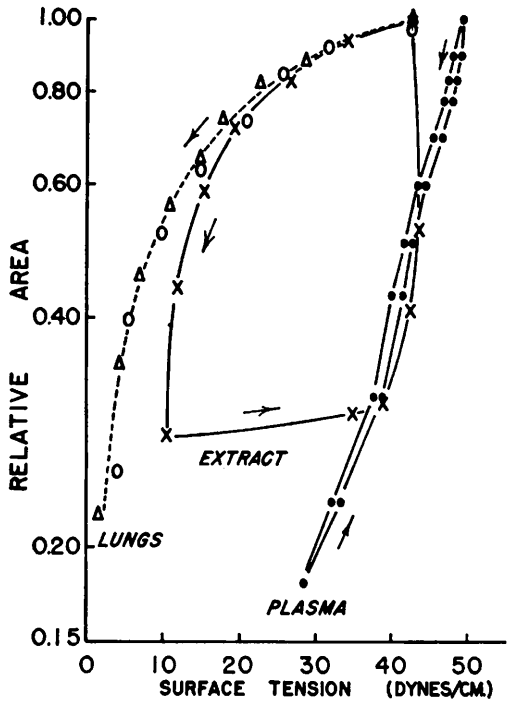

FIG. 1. Variation of surface tension with surface area. Upper curve (lungs) calculated on the basis of relative area from Brown's data. Large loop constructed from measurements on lung extract in Wilhelmy balance. Narrow loop constructed from measurements on blood plasma in Wilhelmy balance.

area-volume function ($A = KV^{2/3}$) which is not acceptable if the lung units deviate significantly from the mean radius. In addition Brown's calculations did not correct for the tendency of the units to close off above zero volume as the transpulmonary pressure is reduced. To obtain more direct evidence bearing on the above points, we have studied the tension-area behavior of lung-derived surfaces, using modifications of the Langmuir-Adam film balance and the Wilhelmy balance (5). Surfaces of the following fluids were examined: a. normal saline (0.85% NaCl) after it had been used to inflate degassed lungs via the trachea; b. mince of whole lungs in normal saline, filtered through loosely-packed cotton; c. normal saline, to which slices of lung parenchyme had been touched. These were prepared from rat, cat, and dog lungs.

Results. The results were similar in all cases. A typical tension-area plot is shown in Fig. 1. This figure demonstrates that the tension of the lung-derived surface varied from 46 to 10 dynes/cm as its area was changed, and further that the surface exhibited extreme hysteresis, although 80 minutes was used for the compression-expansion cycle. The same pattern was obtained when the cycle was repeated. Thus, the mechanical behavior of the surface was far from reversible, within the duration of most pressure-volume measurements on lungs.

The coefficient of compressibility $\left(\frac{1}{A}\frac{dA}{d\gamma}\right)$ of these surfaces ranges from 0.010 to 0.025 cm/dyne at the higher tensions, agreeing well with Brown's values. This characteristic of the surface has a stabilizing influence and might be called an "anti-atelectasis factor." At lower tension the surface compressibility rises and closure of lung units becomes probable. It is in this range that Brown's data depart from the extract data, signalling trapping of gas within the lungs(6).

We have examined Pattle's conclusion that the surface tension of his "alveolar bubbles" (about 40 μ diameter) and hence of the pulmonary alveoli was less than 1 dyne/cm. While repeating his experiments we found that lung bubbles which were "stable" in static air-saturated saline, dissolved slowly when the saline continuously perfused the microscope chamber. Determining increments of hydrostatic pressure necessary to double the instantaneous rates of solution permitted calculation of the surface tension of the bubbles. Although the method was crude, it gave values from 10 to 15 dynes/cm. Bubbles of the same diameter prepared in an air-saturated soap solution having a surface tension of 27 dynes/cm dissolved rapidly. The transfer coefficients were 9.3×10^{-5} and 1.7×10^{-3} cc/cm^2 -atm.-sec., respectively. Taking the difference of the reciprocals we estimated the specific diffusion resistance of the lung bubble surfaces at 1.0×10^{4} sec/cm; this is much higher than the specific resistance of compressed films of 18- to 20-carbon fatty acids to water diffusion found by Archer and LaMer(7). Thus the slow solution of the lung bubbles appears due mainly to the diffusion characteristics of the surface. Cal-

culation shows that if this surface existed in the lungs, it would more than account for the diffusion resistance at rest. Measurement of the relationship between surface pressure and diffusion resistance of lung-derived films is indicated.

Summary. Saline-extractable surface-active material has been found in the lungs of rat, cat, and dog. This material, probably mucoprotein, imparts large hysteresis and characteristic elasticity to the fluid surface. Its effect on lung mechanics has been studied. Its possible influence on diffusion across the alveolar barrier remains to be elucidated.

1. von Neergaard, K., *Z. f. d. ges. exp. Med.*, 1929, v66, 373.
2. Radford, E. P., Jr., PROC. SOC. EXP. BIOL. AND MED., 1954, v87, 58.
3. Pattle, R. E., *Nature*, 1955, v175, 1125.
4. Macklin, C. C., *Lancet*, 1954, v266, 1099.
5. Adam, N. K., *The Physics and Chemistry of Surfaces*, 3rd Ed. (1941, Oxford Univ. Press, London)
6. Clements, J. A., *A. J. Physiol.*, 1956, v187, 592.
7. Archer, R. J., and LaMer, V. K., *Ann. N. Y. Acad. Sci.*, 1954, v58, 807.
8. Brown, E. S., PROC. SOC. EXP. BIOL. AND MED., 1957, v95, 168.

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^{14}C Studies on Ketogenicity of Metabolites in Lactating Dairy Cows.*† (23157)

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Recent studies upon the intermediary precursors of B-hydroxybutyric acid, acetoacetic acid and acetone in the intact dairy cow have been mainly concerned with ability of the administered compound to elevate the serum and urinary ketones(1-6). Extensive investigations have been made by Kleiber *et al.* (7-10) concerning transfer of carbon-14 of intravenously injected metabolites into milk casein, lactose and fat. In these trials ^{14}C-labeled carbonate, the lower fatty acids from formate to caproate, norleucine, and glucose were injected into normal lactating dairy cows and efficiency of transfer(11) to milk products calculated. Since up to 85% of milk lactose may originate from the plasma glucose(12), incorporation of relatively large numbers of carbon-14 atoms from a metabolite into lactose should indicate glucogenicity. Entrance of carbon-14 atoms into milk fat from an injected metabolite is a measure of its role in lipogenesis and not necessarily its ketogenicity. The present study was undertaken to measure relative transfer of carbon-14 atoms of injected compounds into the urinary ketone bodies.

Materials and methods. Mature lactating dairy cows were injected intravenously with glycine-1-^{14}C, butyrate-2-^{14}C, norvaline-3-^{14}C, carbonate-^{14}C, glucose-1-^{14}C, and propionate-2-^{14}C by methods previously reported by Kleiber(11). The urine was voided at the time of administering the isotope and then collected for the first hour following the injection for preparation of the ketone bodies. Two hundred fifty ml of urine was first treated with 58 ml of a solution containing 1.5% $K_2Cr_2O_7$ in 15.6N H_2SO_4 to convert the B-hydroxybutyric and acetoacetic acid to acetone(13). Another 50 ml of 5% $K_2Cr_2O_7$ was added after boiling had commenced to insure complete oxidation(14). The carboxyl carbon of B-hydroxybutyric and acetoacetic acid was not recovered. The mixture was next doubly distilled first into cold distilled water and secondly into 150 ml of Deninges' solution(15), adding 1 g Na_2O_2 per 100 ml of distillate prior to the second distillation to insure complete oxidation of

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