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THE EFFECT OF TEMPERATURE ON GAS TRAPPING IN EXCISED LUNGS

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Abstract. In this study the effect of temperature on gas trapping in excised lungs was examined with two types of experiments in rats. In the first, changes in gas trapping following ten successive inflation–deflation cycles at the same constant ventilation rate were examined at 17, 27, 37 and 42 °C. In the second, the effects of five different ventilation rates at temperatures of 17, 27 and 37 °C were determined. The fraction of gas trapped in lungs repeatedly ventilated for ten inflation–deflation cycles at constant ventilation rates remained nearly constant with time at 17 and 27 °C but decreased with time at 37 and 42 °C. The amount of gas trapped in the lung at 27 °C fell with the logarithm of increasing ventilation rate. Lowering the temperature shifted this relationship toward lower ventilation rates while increasing the temperature caused an apparent shift toward higher ventilation rates.

Pressure–volume curves
Rat
Respiratory mechanics
Temperature effects
Trapped gas

The excised lungs of most mammals, including the rat, accumulate trapped gas during repetitive inflation–deflation cycles at a slow and constant rate (Faridy and Permutt, 1971; Frazer *et al.*, 1979). In the past we have shown that the gas trapping mechanism in the lung can be altered by procedures which affect the alveolar surfactant system. For instance, rinsing the lung with Tween 20, a nonionic detergent that presumably displaces the normal alveolar lining layer, nearly eliminates gas trapping (Frazer and Weber, 1976).

Temperature changes should also affect gas trapping because of the temperature dependence of surfactant properties. In 1971, Lempert and Macklem found that the relationship between area, A, and surface tension, γ, of lung extracts measured in

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a Wilhelmy surface tension balance changed when those extracts were cooled from room temperature to 15 °C. With a reduction in temperature, the maximum value of surface tension increased, the minimum value decreased, and the hysteresis of the γ-A relationship increased. Increasing surface temperature from 27 to 40 °C caused very different effects. The maximum value of surface tension declined, the minimum value rose, and the hysteresis of the γ-A relationship diminished. An increase in temperature, however, not only affects the surface tension properties of alveolar surfactant but has other effects as well. For example, the rate of stress adaptation of alveolar surfactant has been shown to be a function of temperature (Tierney and Johnson, 1965).

Various investigations of temperature effects on pressure-volume (PL-VL) curves have produced conflicting results, and these results have not always been consistent with what one would extrapolate from surface tension studies. Clements and Trahan (1963) warmed lungs to 47 °C. This greatly reduced lung hysteresis when volume was changed in a stepwise manner with a 2-min pressure equilibration at each temperature. These investigators concluded that the reduction in hysteresis could be explained by the increase in the minimum value of surface tension of lung extracts observed in a surface tension balance at similar temperatures. Wohl *et al.* (1968) ventilated dog lungs in volume steps followed by 2-sec stress-adaptation periods. In this case there was no difference in hysteresis between PL-VL curves recorded at room temperature and those recorded at 37 °C. The findings of Horie *et al.* (1974), who slowly ventilated lungs at constant rates at temperatures of 22, 37 and 47 °C, were consistent with those of Wohl *et al.* (1968) with the exception of a slight increase in transpulmonary pressure during part of the deflation curve. In contrast, Lempert and Macklem (1971) found that the PL-VL hysteresis area of continuously recorded curves was greater at 37 °C than at 21 °C, but quasi-static curves, for which the lung was ventilated in volume steps and allowed to equilibrate with respect to pressure at each step for 30 sec, were not significantly different at the two temperatures. Also, PL-VL curves of excised lungs recorded at room temperature and 4 °C (Nagao *et al.*, 1977) revealed that as temperature was lowered, total lung capacity fell and recoil pressure at 80% TLC increased during lung deflation resulting in a reduction in hysteresis. These results are not consistent with what one would have expected from the previous surface tension studies. The apparent inconsistencies between the effects of temperature observed in a surface tension balance and those evident in PL-VL curves led Lempert and Macklem (1971) to conclude that 'one cannot necessarily predict the pressure-volume behavior of lungs on the basis of area-tension behavior of surface films'.

It is equally difficult to predict what effect, if any, temperature would have on the gas trapping mechanism in the intact lung. Lempert and Macklem (1971) have stated that temperature does not seem to have any systematic influence on the amount of gas trapped in the lung. Recently, however, we have shown that there is a high correlation between gas trapping and lung hysteresis which suggests a mechanism common to both mechanical phenomena (Frazer and Franz, 1981).

Thus, the effect of temperature on lung hysteresis should be paralleled by a corresponding change in gas trapping. The object of this study was to use sensitive methods recently developed (Frazer and Weber, 1976, 1980) to determine if heating or cooling the lung does in fact have any consistent measurable effect on lung P_L-V_L curves and on the gas trapping mechanism.

Methods

Following intraperitoneal sodium pentobarbital injection (85 mg/kg), Long–Evans Hooded male rats weighing between 250 and 300 g were exsanguinated via the abdominal aorta. The heart, lungs and diaphragm were removed *en bloc*, degassed in a vacuum chamber, and placed in the plethysmograph shown in fig. 1. Lungs were inflated–deflated with a positive pressure generated by a syringe pump (Harvard Apparatus, model 901). Transpulmonary pressure (Setra, Model 233) and lung volume (Med. Sci., model 118) were measured and recorded on an X-Y recorder

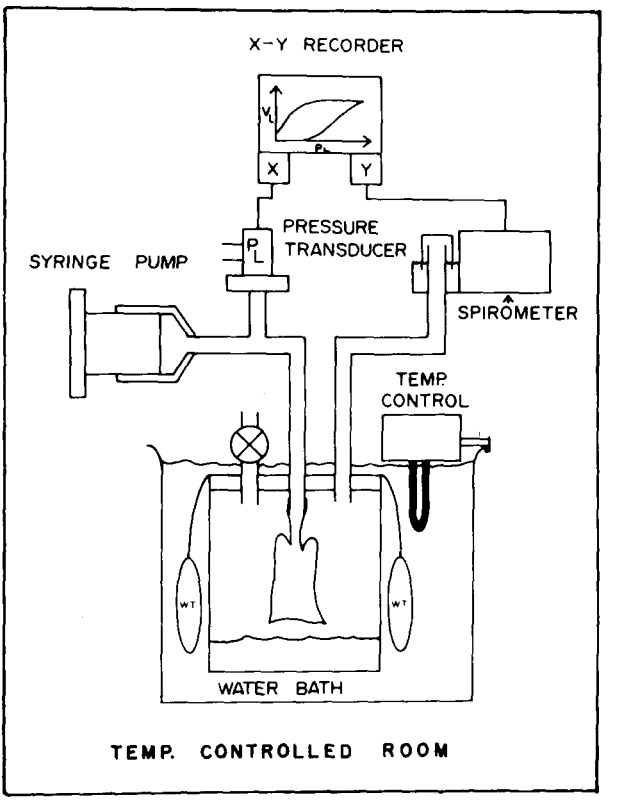

Fig. 1. Schematic diagram of the system used to record pressure-volume curves of excised rat lungs. Gas was preheated in the temperature bath before entering the lung.

(Houston, model 2000). A water bath maintained selected temperatures in an environmental chamber room with a temperature controller (Thermomix, model 1140). The lung was allowed to equilibrate in the plethysmograph until there was less than a 0.1 ml change in volume of gas surrounding the lung over a 5 min period. Air entering the lungs from the syringe pump was preheated to the temperature of the water bath as it passed through a copper heat exchanger before entering the trachea. Experiments were performed at ambient temperature (27 °C), below ambient temperature (17 °C), and above ambient temperature (37 and 42 °C).

The first series of experiments were performed to determine how the gas trapping mechanism in the lung was affected by temperature over an extended period of time. Four consecutive sets of 10-cycle PL-VL curves were recorded for each lung in four groups of six animals each. For each group the temperature was kept constant, namely at 17, 27, 37 or 42 °C. The curves were obtained between maximum and minimum transpulmonary pressures of + 30 and − 5cm H_2O and at a rate of 3.82 ml/min. Before recording a set of PL-VL curves, lungs were always degassed according to the method of Stengel *et al.* (1980). The amount of gas trapped in the lungs after each cycle, Vm, was divided by the maximum lung volume for that cycle, Vmax, in order to obtain a gas trapping index for each set of curves so that changes in gas trapping between sets could be compared. Values of the gas trapping index, Vm/Vmax, were plotted against the cycle number for the four curve sets at the different temperatures. In order to determine if the shape or position of the deflation limb of the PL-VL curves changed during repeated ventilation, the transpulmonary pressure at 85% TLC (PL85) during the tenth inflation–deflation cycle was measured for the first and fourth curve sets at 17, 27, 37 and 42 °C.

In the second series of experiments, the combined effects of temperature and ventilation rate on gas trapping in the lung were determined. As before, lungs were ventilated between + 30 and − 5 cm H_2O for five 10-cycle PL-VL curve sets at either 17, 27 or 37 °C, but the inflation–deflation rate at which each curve set was recorded was reduced from 38.2 ml/min for the first curve set to 15.8, 7.64, 3.82, and 1.91 ml/min for the second through fifth curve sets. Values of Vm/Vmax were determined for each of the five 10-cycle curve sets at each temperature and plotted as a function of ventilation rate. Difficulties arose at 37 °C as shown in the Results section.

Results

Typical 10-cycle PL-VL curve sets following repeated ventilation at a constant inflation–deflation rate are shown in fig. 2. The first and fourth curve sets at temperatures of 17, 27, 37 and 42 °C are shown in order to reveal any time dependence of the gas trapping mechanism.

The average trapped gas index, Vm/Vmax, (N = 6) was determined as a function of cycle number for each curve set at each temperature. Since there was little varia-

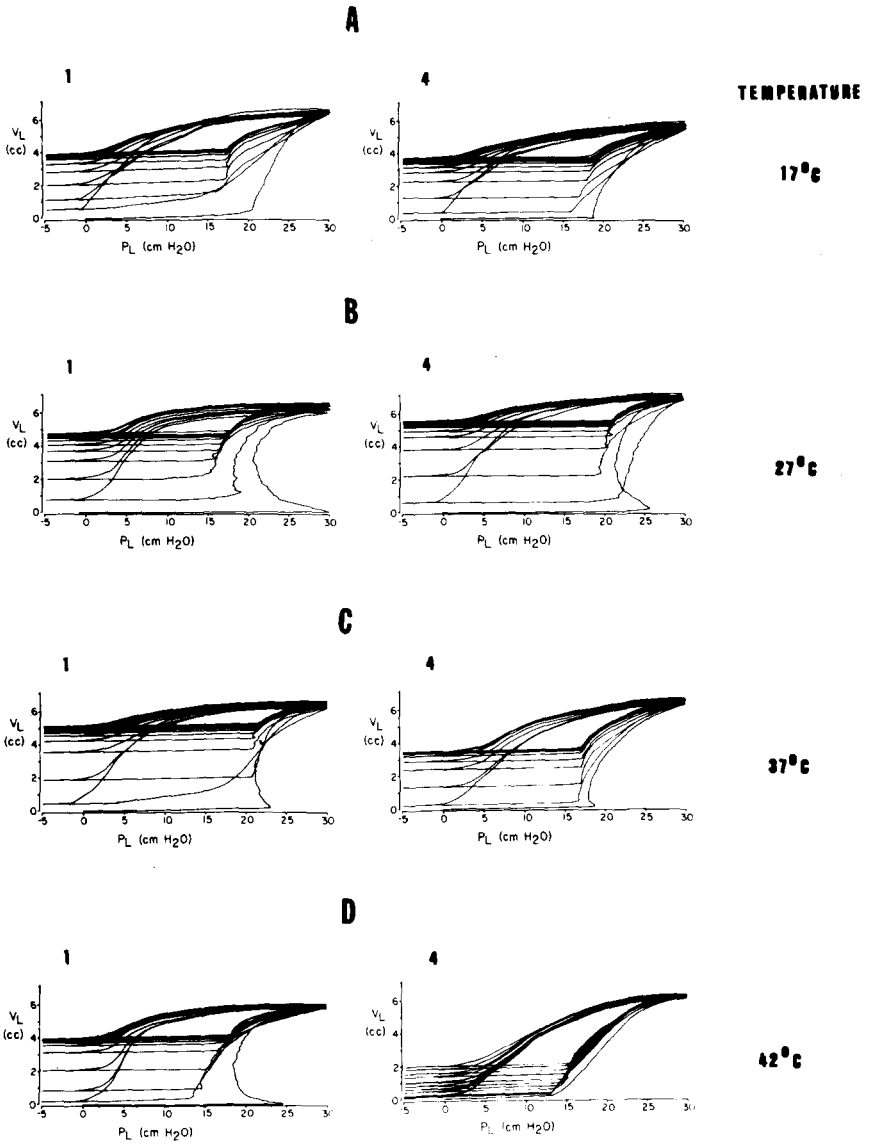

Fig. 2. The first and fourth PL-VL curve sets of lungs repeatedly ventilated at (A) 17 °C, (B) 27 °C, (C) 37 °C, and (D) 42 °C. Each curve set consisted of 10 inflation–deflation cycles and was recorded at 3.82 ml/min.

tion in the fraction of gas trapped between curve sets at either 17 or 27 °C, Vm/Vmax was plotted for only the first and fourth sets as shown in figs. 3A and 3B. The results from all four sets are plotted for 37 and 42 °C (figs. 3C and 3D) because gas trapping is a function of time at these temperatures. A paired *t*-test was performed between curve sets 1 and 4 for the first, second, third, and tenth cycles

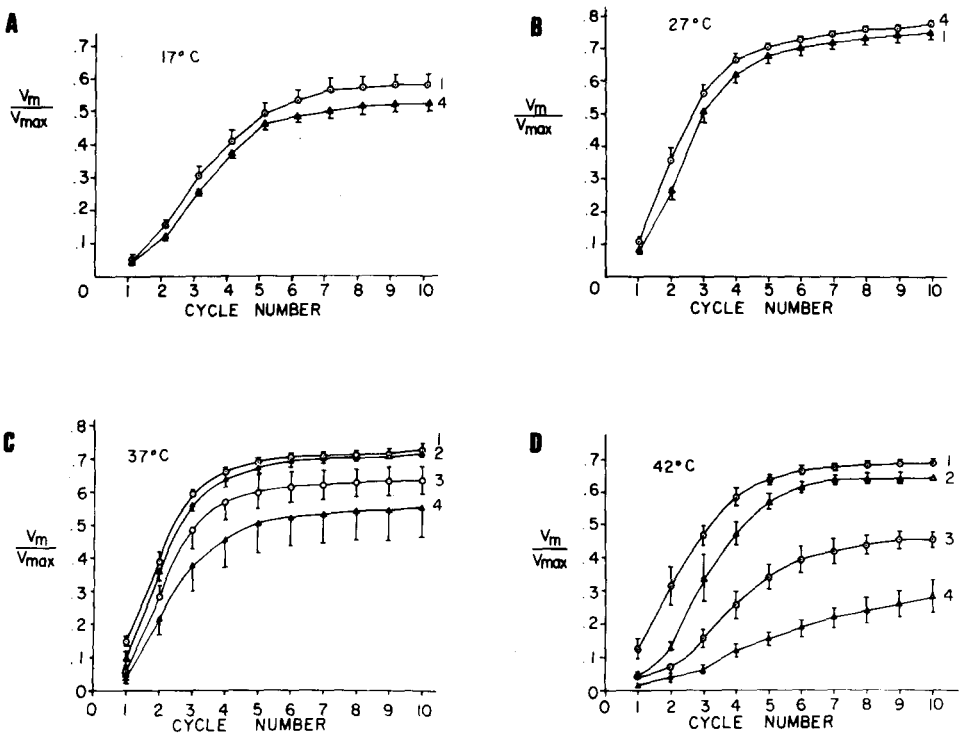

Fig. 3. Average values of Vm/Vmax (N = 6) versus cycle number for the first and fourth 10-cycle PL-VL curve sets recorded consecutively at (A) 17 °C, (B) 27 °C, and for the first, second, third, and fourth consecutive 10-cycle PL-VL curve sets recorded at (C) 37 °C, and (D) 42 °C.

at 17, 27, 37 and 42 °C. There was no significant difference ($P < 0.05$) between curve set 1 and curve set 4 for these four cycles at 17 and 27 °C. There was a significant difference, however, between curve sets 1 and 4 for these same cycles at 37 and 42 °C.

Values of PL85 were measured following ten inflation–deflation cycles for curve sets one and four at 17, 27, 37 and 42 °C. At 27 °C values of PL85 remained constant for all curve sets. As temperature was decreased from 27 to 17 °C the PL85 for curve set one increased. Upon repeated ventilation PL85 appeared to increase between the first and fourth curve sets, although the increase was not significant ($P < 0.05$). The values of PL85 for curve set one were nearly identical for 27, 37 and 42 °C. After the fourth curve set, however, there was a significant increase in the PL85 ($P < 0.01$) at both 37 and 42 °C. The largest increase occurred at 42 °C.

In a second group of experiments, 10-cycle PL-VL curves were recorded at 5 different inflation–deflation rates (fig. 4). The average Vm/Vmax index (N = 6) following the tenth cycle decreased monotonically as the ventilation rate increased. The ventilation rate at which Vm/Vmax was midway between its maximum and minimum value was approximately 6.5 ml/min at 17 °C and 18.5 ml/min at 27 °C. Since the gas trapping properties of the lung change with time at 37 °C (fig. 3),

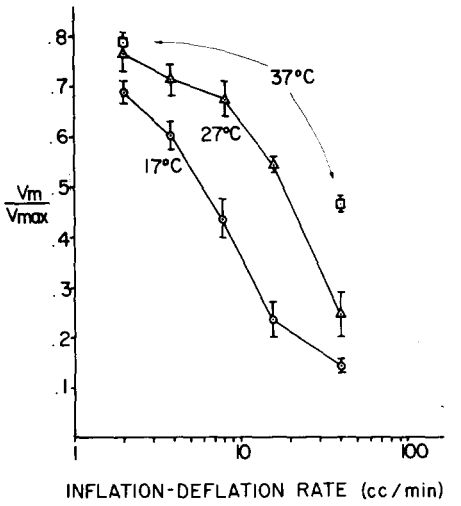

Fig. 4. Average values of Vm/Vmax (N = 6) after ten cycles versus inflation–deflation rate for 17 and 27 °C. At 37 °C only two points from two different ($N_1 = 6$; $N_2 = 6$) sets of lungs were obtained because the time dependence demonstrated in fig. 3C makes the data a function of the previous inflation history.

it was not possible to obtain time-invariant values of Vm/Vmax at that temperature for a particular lung. Two points along the curve were found, however, by ventilating one set of lungs (N = 6) at a rate of 38.2 and a second set (N = 6) at 1.91 ml/min.

Discussion

In contrast to the conclusions of Lempert and Macklem (1971), we have found that the temperature does, indeed, affect gas trapping in the lung in a systematic manner. Our first set of experiments showed that when lungs were repeatedly ventilated in the same manner at either 17 or 27 °C, there was only a relatively small change in the amount of gas trapped in the lung after ten cycles; *i.e.*, there was little time dependence. When lung temperature was held at 37 or 42 °C, however, the amount of trapped gas decreased significantly as the lungs were repeatedly ventilated. This slow decrease in gas trapping with time is probably due to the slow rearrangement of the surfactant material in the lung. The rearrangement may result from the time-dependent loss of surfactant because of inactivation, depletion, irreversible alterations of the surface film, or may represent mechanical rearrangement of the lung air–liquid interface such as the formation of micelles or multilayers (Nagao *et al.*, 1977).

According to measurements of PL85 from PL-VL curves as in fig. 2 there is both a reduction in gas trapping and an increase in the lung recoil pressure with time at 37 and 42 °C. An increased recoil pressure at temperatures of 37 °C and above

have been described previously by Gruenwald (1964) and Clements and Trahan (1963) while other investigators have found either no effect or the opposite effect (Wohl *et al.*, 1968; Lempert and Macklem, 1971; Nagao *et al.*, 1977). This study indicates that gas trapping and lung recoil both depend on the previous pressure-volume history of the lung because of the time dependence of gas trapping at temperatures of 37 °C and above.

Even though there appeared to be a trend there was no significant difference between the first and fourth curve sets at 27 and 17 °C (figs. 3A and 3B). Because of this nearly constant relationship with respect to time, it was possible to ventilate individual lungs at several different rates to determine how the inflation–deflation rate affected gas trapping at those temperatures.

The curve relating Vm/Vmax to inflation–deflation rate was shifted to the left when the lung was cooled to 17 °C from 27 °C. A shift to the right appears likely for the limited data at 37 °C. In other words, at 27 and 17 °C there appears to be a time–temperature equivalence in which the gas trapping behavior at one temperature is related to that at another temperature by a change in the rate and magnitude scales. This type of equivalence is common in many viscoelastic systems (Ward, 1971). At 37 and 42 °C, it is difficult to show such an equivalence, possibly because of a time-dependent rearrangement of the surface lining of the lung. As the temperature is raised from 37 to 42 °C, the rearrangement seems to occur more quickly.

Recently, we have proposed a model of the gas trapping mechanism in the lungs (Frazer and Khoshnood, 1979). This model assumes that gas diffuses across a liquid barrier, such as a meniscus, to enter the trapped gas space. The importance of such a diffusion process was subsequently documented by Frazer and Weber (1980) through the use of various gases and gas mixtures. According to this model the volume of gas entering the trapped gas space during lung inflation is proportional to $D\alpha\gamma$, where D is the diffusion constant for the gas, α is its Bunsen solubility coefficient, and γ is the surface tension of the meniscus surface. It is known that for a diffusion process, $D\alpha$ is a function of temperature and changes by approximately 1% per degree C. Gas would enter the trapped gas space at a slower rate, therefore, as temperature is reduced and at a faster rate when temperature is increased.

If it is assumed that gas entering the trapped gas space follows Fick's law, the fraction of gas entering the lung during inflation would be proportional to $(D\gamma\alpha) \times$ (time to inflate/Vmax). When the temperature dependence of this relationship is taken into account, the ventilation rate at which the trapped gas volume was midway between its maximum and minimum value at 27 °C, 18.5 ml/min, corresponds to a calculated value of 12.0 ml at 17 °C. Since the measured value at 17 °C was 7.5 ml/min, the temperature dependence of diffusion accounts for about 60% of the observed change in gas trapping. In other words, if the lung airways opened and closed in exactly the same way at 27 and 17 °C and the differences in gas trapping were due only to differences in diffusion alone, there would be a shift in the rate curves of fig. 4 with respect to temperature. Since a larger

shift is observed, the results indicate that the lungs do not expand in the same manner at 17 and 27 °C. It is possible that the temperature dependence of the viscoelastic properties of the lung's surface film, as previously predicted by Nagao *et al.* (1977), may also be responsible for some part of the shift in gas trapping with respect to ventilation rate.

Figure 4 shows that the curve relating the index Vm/Vmax to the logarithm of the inflation–deflation rate for 27 °C has a reverse sigmoid shape which is consistent with our previous work (Frazer and Weber, 1979). Lowering lung temperature tends to inhibit gas trapping in the lung and shifts the curve toward lower ventilation rates. There is a very large dependence of gas trapping on temperature near the mid value for trapped gas, but at very fast or very slow rates the curves have nearly the same maximum and minimum, and there is much less dependence upon temperature. If lung hysteresis responds to temperature and ventilation rate changes in a manner similar to that observed for gas trapping, it might explain why Lempert and Macklem (1971) found little dependence of hysteresis on temperature when the lung was ventilated very slowly at room temperature and at 37 °C.

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