JOURNAL OF APPLIED PHYSIOLOGY
Vol. 40, No. 6, June 1976. *Printed in U.S.A.*

# Trapped air in ventilated excised rat lungs

DAVID G. FRAZER AND KENNETH C. WEBER
*Department of Physiology and Biophysics, West Virginia University Medical Center, Morgantown 26506; and Appalachian Laboratory for Occupational Respiratory Diseases, National Institute for Occupational Safety and Health, Center for Disease Control, U.S. Public Health Service, Morgantown, West Virginia 26505*

FRAZER, DAVID G., AND KENNETH C. WEBER. *Trapped air in ventilated excised rat lungs.* J. Appl. Physiol. 40(6): 915–922. 1976. – Degassed excised rat lungs were ventilated in a water-filled plethysmograph with the carina as the zero pressure reference. Pressure-volume curves were recorded from a minimum transpulmonary pressure ($P_{min}$) of −5 $cmH_2O$ to a maximum pressure ($P_{max}$) of 30 $cmH_2O$. An index of the minimum volume for the lung ($V_m$) divided by the maximum lung volume for the same cycle ($V_{max}$) was used as an index of the amount of air trapped within the lung. As the flow rate was decreased from 38.2 to 1.9 ml/min, there were significant increases in the amount of air trapped in the lung. As the maximum pressure was decreased to 25 and 20 $cmH_2O$, or the minimum pressure was increased to 6 and 11 $cmH_2O$, the amount of trapped air in the lung significantly decreased. The rate of lung inflation had a much greater influence on the amount of trapped air than either the deflation rate or stress relaxation. The results are consistent with the theory that bubbles are formed during inflation and are the main cause of air trapped in the excised lung.

lung pressure-volume curves; ventilation rates in excised lungs; bubble formation in lungs

INVESTIGATORS STUDYING EXCISED LUNGS have recently shown evidence (4, 5, 9) that perfused and unperfused excised lungs continually accumulate trapped air as they are being ventilated. This is illustrated by the fact that pressure-volume (PL-VL) curves do not form closed paths at zero or even negative transpulmonary pressures. Following continued ventilation at slow or intermittent rates, bubbles exuded from the airways (4, 5, 15, 16). It has been proposed that these bubbles are responsible for trapping air in the lung by obstructing the airways (16).

One purpose of this study was to examine how specified variables affected the amount of trapped air in the lung as 10 consecutive inflation-deflation curves were recorded. These variables were *1)* the maximum and minimum pressure achieved during a cycle and *2)* the inflation-deflation rate of the cycle. Another purpose of the study was to determine whether the air becomes trapped in the lung during inflation or deflation.

## METHODS

Long-Evans hooded male rats weighing between 250 and 300 g were anesthetized with sodium pentobarbital (50 mg/kg) given intraperitoneally. Following a tracheotomy, the animals were ventilated for 10–15 min with 100% $O_2$ using a Harvard Apparatus (model 665) positive-pressure respirator. While the lungs were being ventilated, an open bilateral pneumothorax was achieved by opening the abdominal cavity and sectioning the diaphragm. At the end of the first deflation following oxygen washout, the trachea was clamped and oxygen remaining in the lungs was removed by the blood (2). When the lungs appeared atelectatic, they were quickly removed by cutting the rib cage on both sides of the midline and removing the heart and lungs simultaneously.

Approximately 15 min elapsed between removing the lungs and beginning an experiment as the lungs were weighed and placed upside down in chamber C(A) shown in Fig. 1, and the chamber was filled with saline. Figure 1 also shows that the trachea was always open to ambient pressure and that the carina was chosen as the zero transpulmonary pressure reference. As the liquid (normal saline) was removed from the chamber with a syringe pump (Harvard model 9014), the pressure surrounding the lungs decreased and the lungs inflated. Deflation was achieved by pumping the saline back into the chamber. Volume was measured with a linear motion potentiometer attached to the plunger of the syringe; pressure was detected with a capacitance type transducer (Serta model 2334). Transpulmonary pressure (PL) and volume (VL) were plotted on an *X-Y* recorder.

Initially, control pressure-volume curves were recorded for each set of lungs. A control curve was defined as 10 inflation-deflation cycles recorded between a minimum transpulmonary pressure ($P_{min}$) of −5 $cmH_2O$ and a maximum transpulmonary pressure ($P_{max}$) of 30 $cmH_2O$ at an inflation-deflation rate of 3.82 ml/min.

To measure the amount of trapped air in the lung during a given number of inflation-deflation cycles, a variable was defined as $V_m/V_{max}$. The minimum volume of the lung ($V_m$) following a particular cycle was measured at −5 $cmH_2O$; $V_{max}$ was the maximum lung volume during that same cycle. The ratio $V_m$ divided by $V_{max}$ then equaled the normalized minimum volume of the lung and represented the accumulated amount of trapped air within the lung after a particular cycle.

A liquid-filled plethysmograph was found to be more advantageous than an air-filled plethysmograph of equal dimensions because the former has greater sensitivity and temperature stability. This was an important

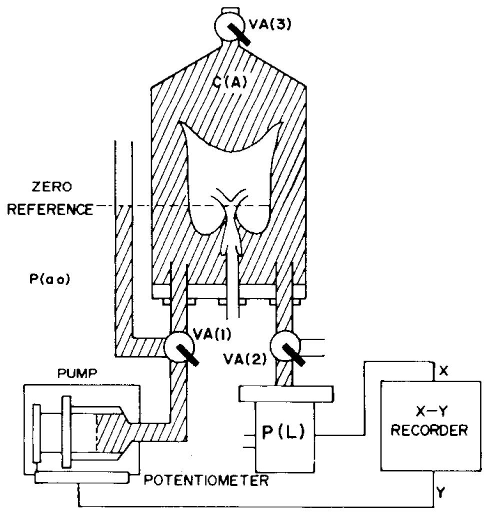

FIG. 1. Schematic diagram of the experimental apparatus for recording rat lung pressure-volume curves. Zero pressure reference was adjusted to correspond to the level of the carina. VA stands for valves or stopcocks.

consideration since some experiments required that the lungs remain in the plethysmograph for time periods of up to 2 h. A third asset of the liquid-filled plethysmograph was that even minute leaks could be easily detected as bubbles rising from the lung surface.

There were two disadvantages associated with the liquid-filled plethysmograph; namely, the lung could easily gain or lose water from its liquid environment and a pressure gradient existed between the base and apex of the lung. It has been shown that immersion of lungs in either hypotonic or hypertonic saline can alter their pressure-volume curves while immersion in normal saline does not affect the curves (4). To determine whether excised rat lungs lost or gained weight (water) as they were ventilated in the liquid-filled plethysmograph, the dry/wet weight ratios of 10 lungs were measured upon completion of control curves. These ratios were compared with the dry/wet weight ratios of 10 lungs measured immediately after they had been excised.

There was a range of transpulmonary pressures along the lung pleura from apex to base because the lung was immersed in a liquid. Since the distance from apex to base never exceeded 5 cm, the transpulmonary pressure difference between the lower and upper extremities of the lung was always less than 5 $cmH_2O$. To find if the liquid gradient influenced the amount of trapped air in the lungs, five lungs were ventilated in an air-filled plethysmograph in the same manner as controls had been ventilated in the liquid-filled plethysmograph.

Linearity and hysteresis of the measuring system were experimentally determined. The tracheal cannula at the base of the plethysmograph was clamped and an air-filled tube was inserted through the top of chamber C(A) until it was within 2 cm of the base. The top of the tube was open to the atmosphere through a cannula having the same dimensions as the tracheal cannula. As water was withdrawn from or infused into chamber C(A) by the syringe pump, the level of water moved vertically in the tube. In this configuration inflation and deflation curves for the tube should have been identical. Equipment linearity was determined by analyzing the difference between the recorded curve and the known straight line curve for the tube. Hysteresis was determined from the differences between the inflation and deflation curves (6).

Long-term stability of the system was necessary since lungs sometimes remained in the plethysmograph for extended time periods. System stability was established by ventilating a finger cot for 20 inflation-deflation cycles at 3.82 ml/min and −5 to +30 $cmH_2O$ transmural pressures and determining how repeatable the finger cot's pressure-volume characteristics were with time. To discover how lung properties changed with time, four successive sets of control PL-VL curves were recorded for three individual lungs. These lungs were completely degassed in a vacuum chamber between each set of curves and $V_m/V_{max}$ was calculated for each cycle.

Following a control curve for each lung, the lung was normally degassed in a vacuum jar to assure the same volume history (3, 14) and one of five experiments was completed. Atelectasis produced by $O_2$ washout appeared visually to be more complete than when using the vacuum chamber; therefore, during the initial cycle in each experiment $V_{max}$ was examined to ensure that the lungs had been degassed and reinflated properly. If differences in $V_{max}$ were not less than 0.5 ml, the vacuum degassing procedure was repeated. The five types of experiments that were performed in this investigation following the control curves were *1)* finding how limiting the maximum pressure per cycle affects the manner in which the normalized volume of the lung increases; *2)* determining the effects of increasing the minimum pressure per cycle on the accumulation of trapped air in the lungs; *3)* finding how the flow rate used to ventilate the lungs alters the manner in which the volume of trapped air increases; *4)* examining whether either inflation or deflation rate is the most important factor to consider when predicting or controlling the amount of trapped air in the lung; and *5)* determining if the viscoelastic interaction between lung inflation and deflation or ventilatory sequence whose rates of inflation and deflation are varied from cycle to cycle affects the accumulation of trapped air in the lungs.

## RESULTS

A typical PL-VL control curve recorded for 10 consecutive inflation-deflation cycles is given in Fig. 2. When the normalized minimum volume was plotted for 30

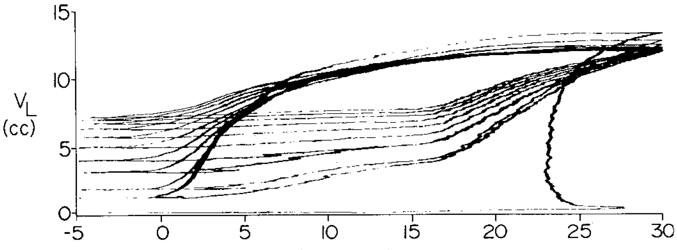

FIG. 2. A typical control pressure-volume curve recorded during 10 consecutive inflation-deflation cycles. Curve illustrates how trapped air accumulates in the lung following successive cycles. Inflation-deflation rate was 3.82 ml/min.

control lungs, the results in Fig. 3 were obtained. The mean value and standard error of the mean for each measurement are indicated. Air accumulated most rapidly in the lung during the initial cycles approaching approximately 60% of maximum lung volume after ten cycles.

The dry/wet weight ratios of 10 rat lungs measured immediately after they had been removed from the rats were 0.199 ± 0.005 SEM. When these lungs were compared with other lungs that had been in the liquid-filled plethysmograph whose average dry/wet weight ratio was 0.202 ± 0.006 SEM (*N* = 30) there was no significant difference.

Air was trapped in the lung whether the lung was ventilated in a liquid or air-filled plethysmograph (Fig. 4*A*). Actually slightly more air was trapped with each cycle in the air-filled plethysmograph. Trapped air accumulated in the lungs (Fig. 4*B*) when four successive control curves were recorded for the same lung. Although the standard error is small when recording curves under similar conditions for the same lung, it was noted that the lungs appeared to trap slightly more air per cycle in succeeding experiments.

System linearity and hysteresis were examined by comparing the theoretical straight line pressure-volume curve of a water-filled glass tube with a recorded pressure-volume curve of the tube. Results in Fig. 5*A* show that the total error due to the hysteresis and nonlinearities of the system never exceeded 0.5 $cmH_2O$ at the maximum inflation-deflation rate used in this study, 38.2 ml/min. In general, a synthetic rubber balloon can exhibit both plastic (nonrecoverable) and elastic (recoverable) deformation when it is inflated and deflated over a large pressure range (8). When using the finger cot to determine the stability of a ventilation system, care had to be taken so that the finger cot was not overstretched and that it behaved as a perfectly elastic body. When the finger cot was ventilated under purely elastic conditions in place of the lungs at a rate of 3.82 ml/min, there was no difference between its 1st and 20th P-V curves (Fig. 5*B*) indicating that the measuring system remained stable over a period of at least 2 h.

To determine the effects of limiting the maximum pressure achieved per cycle, $P_{max}$, on the normalized minimum volume, the inflation-deflation rate was kept at 3.82 ml/min. Following an initial cycle to 30 $cmH_2O$ to ensure that the lung had opened completely, $P_{max}$ was reduced to either 25 or 20 $cmH_2O$ for 9 consecutive cycles. Under these conditions the total amount of air trapped during the initial cycle was large compared to following cycles. To ensure that the air trapped during the first cycle did not bias the results; therefore, the volume of the lungs following the initial cycle was considered to be zero when calculating the normalized volume for cycles 2–10 in Fig. 6. As $P_{max}$ decreased, $V_m/V_{max}$ also decreased dropping to approximately one-third of the control value as $P_{max}$ decreased from 30 to 20 $cmH_2O$.

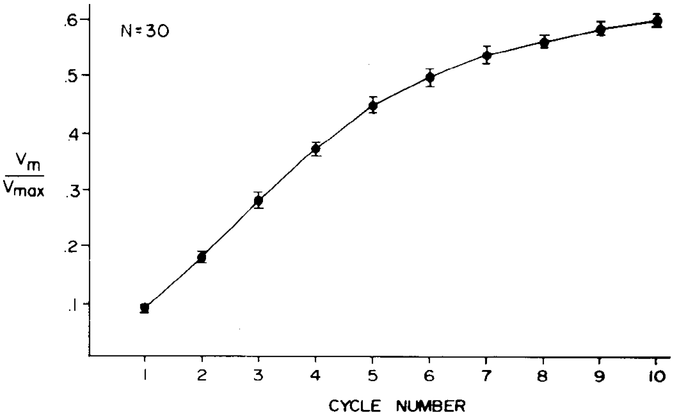

FIG. 3. Normalized minimum volume ($V_m/V_{max}$) for control lungs measured at a transpulmonary pressure of −5 $cmH_2O$. Standard error for individual measurements is given.

Effects of increasing the minimum pressure per cycle, $P_{min}$, were examined next. Following an initial control cycle, $P_{min}$ was increased from −5 $cmH_2O$ to either +1, +6, or +11 $cmH_2O$ for 9 cycles, then returned to −5 $cmH_2O$ on the 10th cycle. Since the normalized minimum volume, by definition, could only be measured at −5 $cmH_2O$, it was determined only for the 1st and 10th cycles (Fig. 7). When the minimum pressure was held at +1 $cmH_2O$, the normalized amount of trapped air contained in the lungs after 10 inflation-deflation cycles was the same as for controls. As the minimum pressure was increased to +6 or +11 $cmH_2O$, however, the

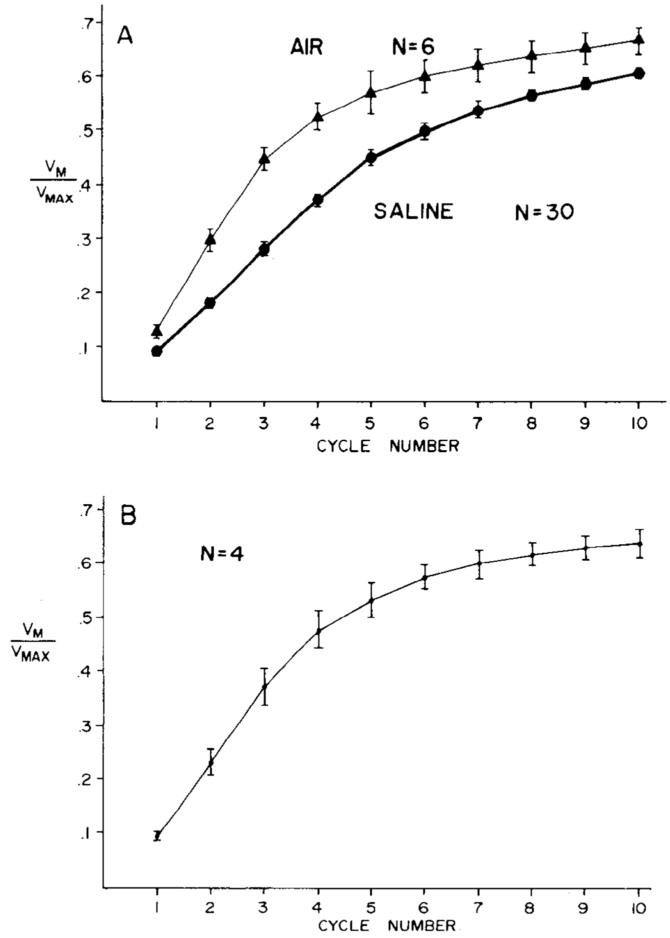

FIG. 4. *A*: normalized minimum volume for lungs ventilated in an air or liquid-filled plethysmograph. Inflation-deflation rates in both cases was 3.82 ml/min. When the same lung was ventilated under control conditions for four consecutive experiments it typically exhibited the consistent increase in normalized minimum volume as shown in *B*.

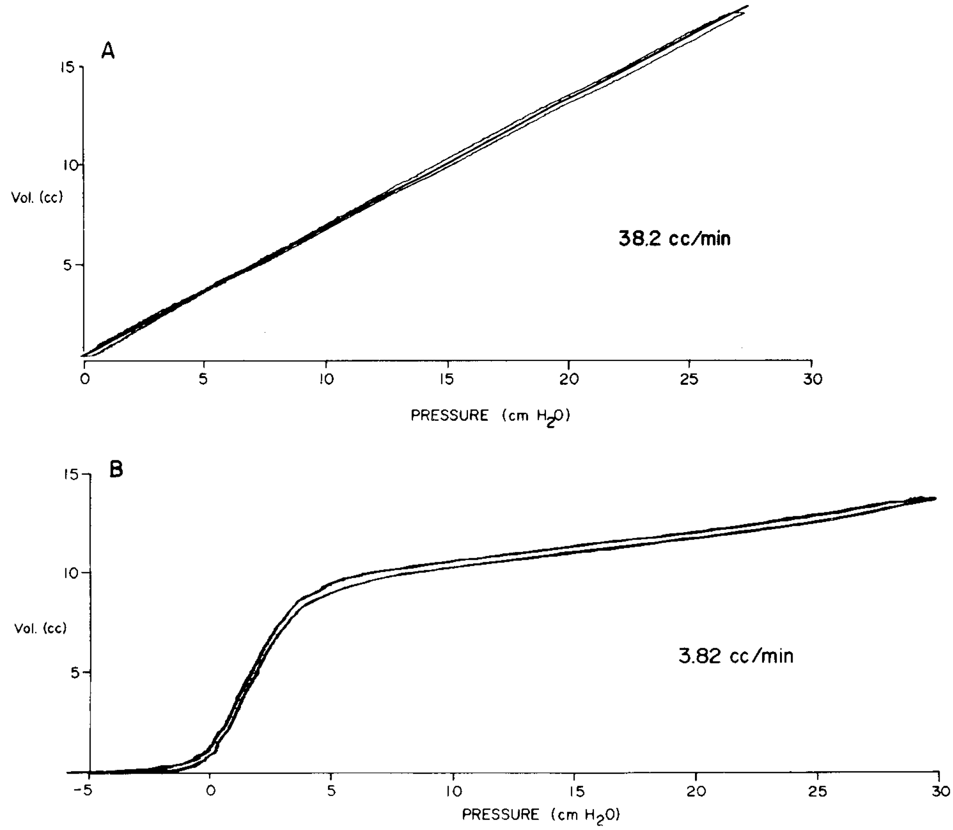

FIG. 5. *A:* linearity and hysteresis of the system which are determined by using a glass tube in place of the lungs. As the water is raised and lowered in a vertical tube it has a straight line PL-VL curve and any recorded curve deviating from that line represents errors in the measuring system (6). *B:* stability of the system as 20 continuous inflation-deflation cycles were recorded for a finger cot at a flow rate of 3.82 ml/min.

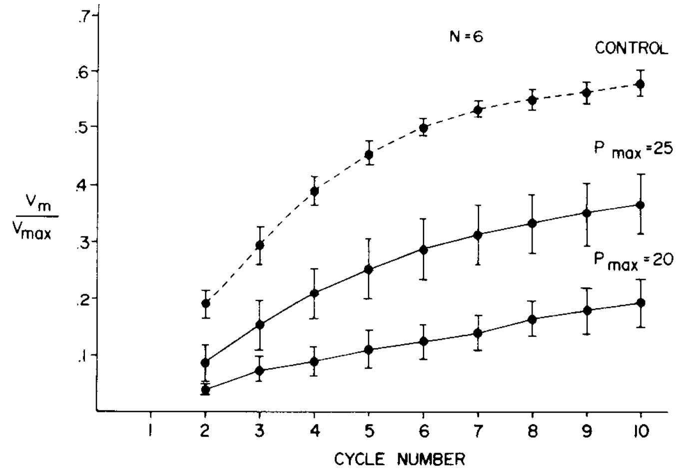

FIG. 6. Normalized minimum volume for controls ($P_{max}$ = 30 cm $H_2O$), and for the cases where $P_{max}$ was reduced to 25 or 20 $cmH_2O$. During initial cycle in each experiment the lung was inflated until transpulmonary pressure reached 30 $cmH_2O$. For purposes of comparison, lung volume following the initial cycle was used as the zero volume reference for all three curves.

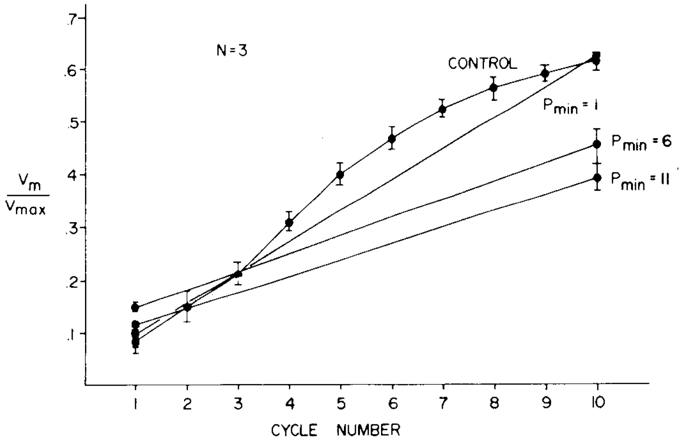

FIG. 7. Changes in the normalized minimum volume as the minimum pressure was increased from −5 $cmH_2O$ (control) to +1, +6, or +11 $cmH_2O$.

amount of trapped air in the lungs was significantly less than controls ($P < 0.05$) and represented a decrease in trapped air of approximately one-third.

Pressure-volume curves showing the results of ventilating the lungs at different rates are given in Fig. 8. The curve in Fig. 8*A* was recorded at a flow rate of 38.2 ml/min, in *B* the rate was 7.4 ml/min, and in *C* the rate was 1.91 ml/min. Both the maximum volume of the lung during a cycle and the amount of air trapped per cycle increased as the flow rate decreased. When the normalized minimum volume was plotted for the three rates shown in Fig. 8 plus two others, 15.7 and 3.82 ml/min, the results in Fig. 9*A* were obtained. The normalized minimum volume was significantly different ($P < 0.05$) for all curves after 10 inflation-deflation cycles. Plotting $V_m/V_{max}$ versus flow rate for individual cycles resulted in the curves shown in Fig. 9*B*. As the inflation-deflation rate decreased, the normalized minimum volume for a given cycle increased. Using these curves it is possible to predict by interpolation the amount of air trapped in the lungs after individual cycles as the lung is ventilated at rates other than those used in this experiment.

As shown in Figs. 8 and 9, the mechanism responsible for the trapped air within the lungs is flow rate sensi-

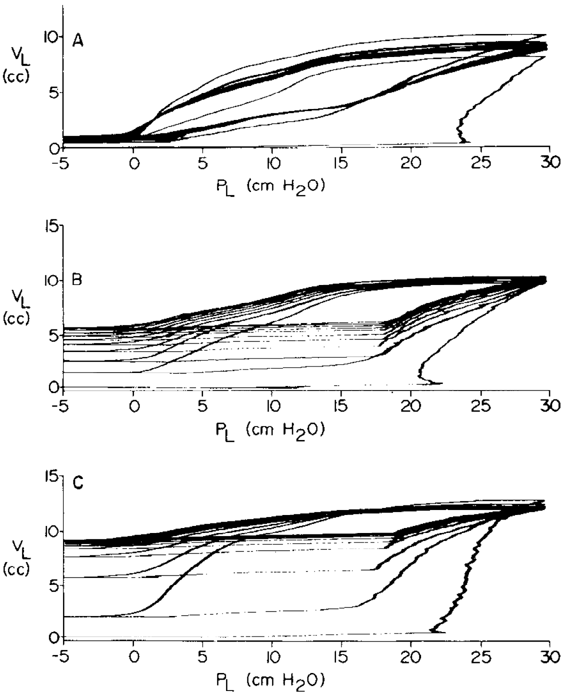

FIG. 8. Pressure-volume curves recorded for the same lung while ventilated at inflation-deflation rates of 38.2 ml/min *(A)*, 7.64 ml/min *(B)*, and 1.91 ml/min *(C)*.

tive. To further investigate this phenomenon three lungs underwent two different series of ventilation cycles after their control $P_L$-$V_L$ characteristic had been recorded. After the control series, the lung was degassed in the vacuum jar before it was inflated to $P_{max}$ at the fastest rate, 38.2 ml/min, and deflated to $P_{min}$ at the slowest rate, 1.91 ml/min, for 10 continuous cycles (Fig. 10*A*). During the 2nd series the inflation and deflation rates were interchanged and the lung was inflated at 1.91 ml/min and deflated at 38.2 ml/min for 10 cycles again starting from the atelectatic state; the results differed as shown in Fig. 10*B*. Plotting $V_m/V_{max}$ for each of the sequences plus their own controls resulted in the curves given in Fig. 11. These curves together with Fig. 9*A* show that as the lungs were inflated rapidly and deflated slowly or rapidly, there was much less air trapped than when the lungs were inflated slowly and deflated slowly or rapidly.

Figure 8, *A* and *C*, shows that $V_{max}$ was greater when the lungs had been inflated at 1.91 ml/min than when they were inflated at 38.2 ml/min. In the following experiment lungs were inflated at various rates to the same $V_{max}$ to confirm that inflation rate and not a larger $V_{max}$ was the reason for increased trapped air at slow rates. Also, the lung surface possesses a large time-dependent quality at $V_{max}$ which results in a dynamic interaction between inflation and deflation (7, 10). To show that this interaction was not directly involved in trapping air within the lung and to separate the inflation and deflation portions of the $P_L$-$V_L$ cycle, a stress adaptation period was observed at $V_{max}$ in some cycles. To determine if the order in which the experiments were performed was important, two different sequences for each lung were followed. A control curve was initially recorded to assure that the lung opened properly and

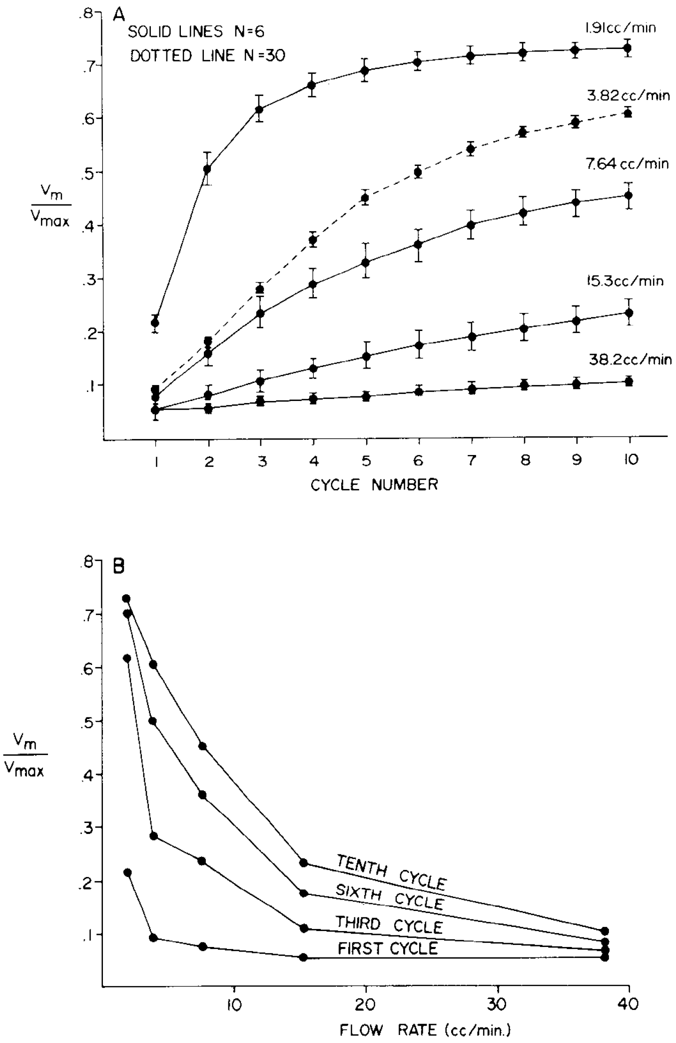

FIG. 9. *A*: normalized minimum volume of a lung following each cycle for different inflation-deflation rates. *B*: normalized minimum volume of the lung following 1st, 3rd, 6th, and 10th cycles illustrating how flow rate influences the accumulation of trapped air in the lung.

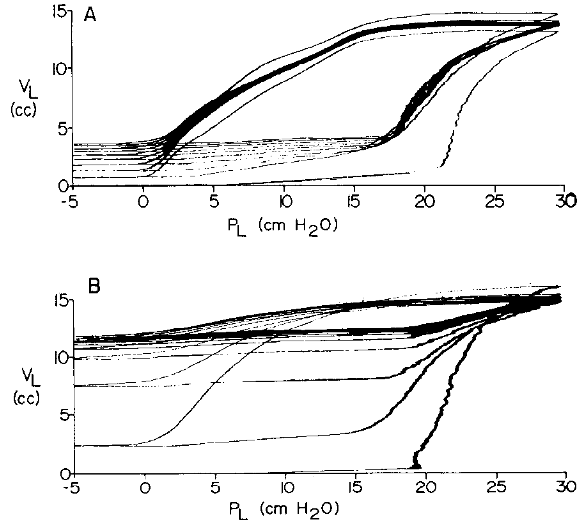

FIG. 10. Alterations of lung's pressure-volume characteristics resulting from inflating the lung at one speed and then at another speed. In *A*, lungs were inflated at 38.2 ml/min and deflated at 1.91 ml/min. In *B*, inflation occurred at 1.91 ml/min and deflation took place at 38.2 ml/min.

had no leaks, then the lungs were degassed in a vacuum chamber. In the first experimental sequence (Fig. 12*A*) the lung was initially inflated and deflated at 3.82 ml/min between a $P_{min}$ of −5 $cmH_2O$ and $P_{max}$ of 30 $cmH_2O$. The lung was inflated and deflated at 38.2 ml/min for the second cycle, and the maximum lung volume ($V_{max^*}$) corresponding to $P_{max}$ equal to 30 $cmH_2O$ for that cycle was noted. The third cycle was performed at the same rates as the second cycle but VL was limited to $V_{max^*}$ and held at that volume for a 10-min stress adaptation period between inflation and deflation. During the fourth cycle the lung was again inflated to $V_{max^*}$ at a rate of 38.2 ml/min and held there for a second 10-min adaptation period before it was deflated at a rate of 1.91 ml/min. On the fifth inflation the rate was kept at 1.91 ml/min until $V_{max^*}$ was reached (this was always below 30 $cmH_2O$), and the lung volume was again maintained constant for another 10 min before deflating at the rate of 38.2 ml/min. The last cycle was performed at an inflation and deflation rate of 1.91 ml/min and had no relaxation period.

After the above inflation-deflation sequence was concluded, each lung was again degassed and the second sequence was begun (Fig. 12*B*). The initial two cycles were performed in the same manner as those of the preceding sequence. The maximum volume during the second cycle was also noted ($V_{max^{**}}$). Then the lung was inflated again until $V_{max^{**}}$ was reached but at a rate of 1.91 ml/min. It was held at that volume for a 10-min adaptation period before deflation occurred at 38.2 ml/min. The lung was then inflated a fourth time at 38.2 ml/min ($V_{max^{**}}$), held for 10 min, and deflated at 1.91 ml/min. During the fifth cycle the lung was inflated at 38.2 ml/min and held at $V_{max^{**}}$ for 10 min before it was deflated at the same rate. The sixth and last cycle was the same as it had been for the previous sequence and had an inflation-deflation rate of 1.91 ml/min.

The results of this experiment for both sequences are given in Fig. 13. The solid line represents the average measured values for three lungs of $V_m/V_{max}$ following each cycle while the two values represented by the open (inflation rate) and crosshatch (deflation rate) areas are estimated values. The estimated values were based on the following assumptions: *1)* the amount of air trapped per cycle is either a function of inflation rate or deflation rate; *2)* the amount of air trapped in any given cycle depended on $V_m/V_{max}$ following the previous cycle; *3)*

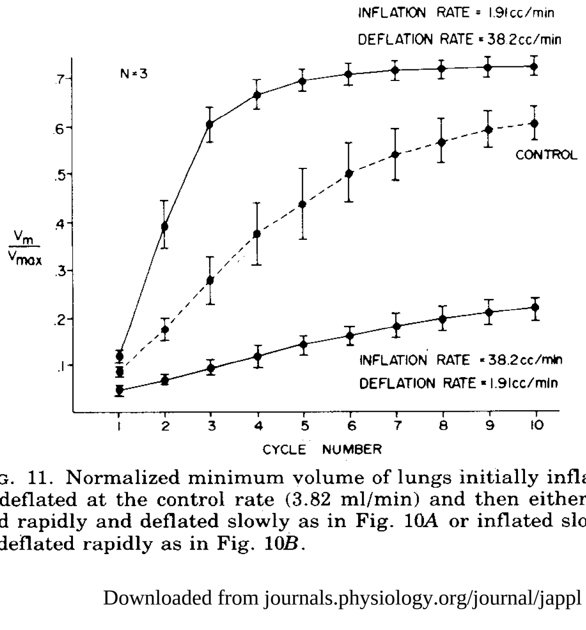

FIG. 11. Normalized minimum volume of lungs initially inflated and deflated at the control rate (3.82 ml/min) and then either inflated rapidly and deflated slowly as in Fig. 10*A* or inflated slowly and deflated rapidly as in Fig. 10*B*.

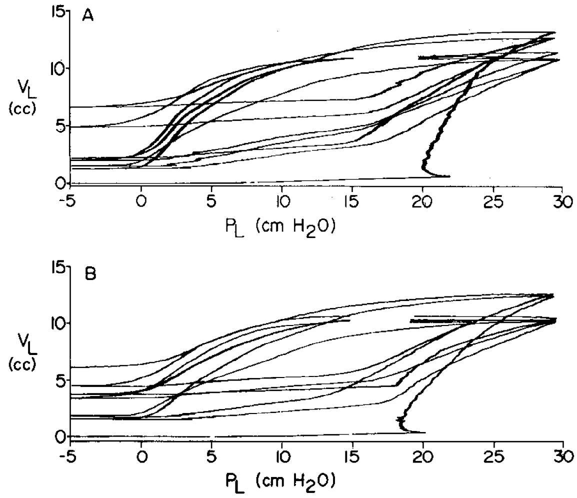

FIG. 12. Both PL-VL diagrams were recorded for the same lung as it was ventilated during two different inflation-deflation sequences. A 10-min stress-adaptation period was observed during the 3rd, 4th, and 5th cycles to separate possible viscoelastic interactions between inflation and deflation. $V_{max}$ was kept constant for cycles 2–5. Pressure-volume sequence in *A* was as follows

| Cycle | Infl Rate, ml/min | Defl Rate, ml/min |
|---|---|---|
| 1 | 3.82 | 3.82 |
| 2 | 38.20 | 38.20 |
| 3 | 38.20 | 38.20 |
| 4 | 38.20 | 1.91 |
| 5 | 1.91 | 38.20 |
| 6 | 1.91 | 1.91 |

*B:* pressure-volume sequence composed of following cycles

| Cycle | Infl Rate, ml/min | Defl Rate, ml/min |
|---|---|---|
| 1 | 3.82 | 3.82 |
| 2 | 38.20 | 38.20 |
| 3 | 1.91 | 38.20 |
| 4 | 38.20 | 1.91 |
| 5 | 38.20 | 38.20 |
| 6 | 1.91 | 1.91 |

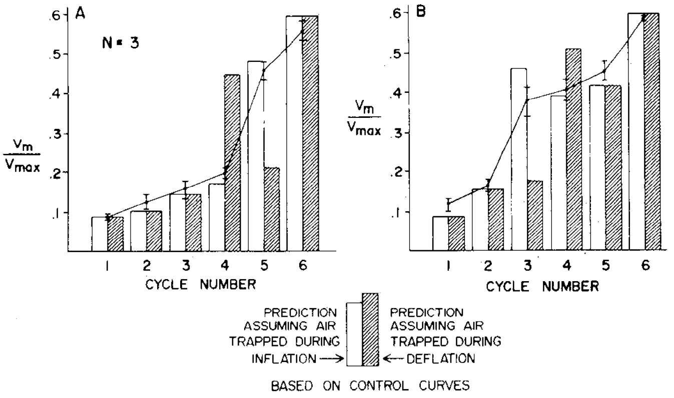

FIG. 13. Normalized minimum volume for lungs ventilated as shown in Fig. 12*A* are shown in *A* and for Fig. 12*B*. Using Fig. 9*A* and the minimum volume prior to a cycle, a predicted increase in the normalized minimum volume could be made by either assuming that all the air was trapped during inflation or deflation. These predictions are represented by the rectangles shown for each cycle.

Fig. 9*A* can be represented by a continuous line through the given points including zero; *4)* the 38.2 ml/min curve can be linearly extrapolated to a large number of cycles. Consider as an example how the amount of air trapped in a lung was predicted during the third cycle of the second sequence. During that cycle the lung was inflated at 1.91 ml/min and deflated at 38.2 ml/min. Prior to the third cycle the actual value of $V_m/V_{max}$ was 0.133. When it was assumed that all the air trapped was a function of the chosen deflation rate, the 38.2 ml/min curve in Fig. 9*A* was linearly extrapolated to predict that $V_m/V_{max}$ should increase from 0.133 to 1.39 during the third cycle. On the other hand, when it was assumed that the air trapped was a function of inflation rate, the 1.91 ml/min rate curve showed that $V_m/V_{max}$ should increase from 0.133 to 0.395 during the third cycle. The actual measured increase in $V_m/V_{max}$ for that lung during the third cycle was from 0.133 to 0.347.

The combined predicted values indicate that the manner in which most air is trapped in the lungs is controlled by the inflation rate and is only minimally influenced by the maximum volume per cycle, a stress adaptation period at $V_{max}$, or the deflation rate. It also appears that the accumulation of trapped air is purely an additive process since the amount of trapped air cannot be reduced by having a cycle with a rapid inflation rate follow a cycle with a slow inflation rate.

## DISCUSSION

The liquid-filled plethysmograph used in this study has been shown to be linear and to give reproducible results over at least a 2-h period. The temperature stability of this plethysmograph is much greater than that of an air-filled plethysmograph. For example, if it is assumed that the heart and lungs at a temperature of 39°C are placed in saline at 25°C and all the heat that leaves the tissue enters the saline, the calculated maximum error in the volume measurement for the saline-filled plethysmograph is less than 0.05 ml. This value is more than 100 times less than the calculated volume correction for an air-filled plethysmograph of equal dimensions.

The manner in which normalized minimum volume increased during 10 continuous inflation-deflation cycles under control conditions was very reproducible as the small standard error in Fig. 3 indicates. Approximately 75% of the $P_L$-$V_L$ curves recorded under control conditions showed that $V_{max}$ during the initial cycle was greater than in succeeding cycles (Fig. 2). This unexplained observation does not appear to be associated with the recording system but with the lung itself as it is ventilated in a liquid-filled plethysmograph. This conclusion is based on the facts that the system has a high degree of thermal stability and that the same observation of $V_{max}$ being greatest during the initial cycle can be made during repeated experiments with the same lung. Since $V_{max}$ varied slightly during repeated cycles, the ratio $V_m/V_{max}$ was calculated for each cycle using the $V_m$ and $V_{max}$ for that cycle.

There was no significant difference between the dry/wet weight ratios of freshly excised lungs and lungs removed from the saline-filled plethysmograph following an experiment. Possible effects of hydration or dehydration on lungs ventilated in the liquid-filled plethysmograph should, therefore, be minimal (4). Comparison of lungs ventilated under the defined control conditions in both an air and a liquid-filled plethysmograph indicate that the pressure gradient in the liquid-filled plethysmograph should not appreciably affect the air trapping mechanism.

The maximum pressure per cycle, the minimum per cycle, and the inflation-deflation rate all affect the amount of air trapped in the lung during a ventilatory cycle. It was shown as early as 1952 that increased expansion of the lung contributes to increased amounts of air trapped in the lung (13). Our study confirmed that when the quantity of trapped air per cycle is normalized with respect to maximum lung volume and the maximum pressure achieved per cycle is increased, there is a significant increase in the normalized amount of trapped air after ten cycles.

When the transpulmonary pressure, measured at the carina, was kept at 6.0 $cmH_2O$, it was never less than 0.0 $cmH_2O$ in any region of the lung, and airway closure would not be expected to occur (1, 11, 12, 17). It was found experimentally that the normalized amount of trapped air in the lung following ten successive ventilation cycles was nearly 60% greater when the airways were allowed to close, i.e., when the transpulmonary pressure was 0.0 $cmH_2O$ or less. This evidence indicates that the closing or subsequent opening of airways makes a significant contribution to the amount of air trapped in the excised lung.

It was also found that following 10 continuous inflation-deflation cycles the amount of air trapped in the lungs was inversely related to the rate at which the lungs were ventilated. Since it has been shown that the amount of air trapped during an inflation-deflation cycle was a function of ventilation rate, the mechanism responsible for trapping the air must also be rate sensitive. Consequently, this property of the mechanism was used to determine whether air was trapped during the inflation or the deflation phase of the cycle. When the lungs were inflated rapidly (38.2 ml/min) and deflated 20 times slower (1.91 ml/min) for 10 continuous $P_L$-$V_L$ cycles, little air remained in the lungs compared to when the lungs were inflated slowly and deflated slowly. This result indicated that when the lungs were inflated slowly and deflated either rapidly or slowly, a relatively larger quantity of trapped air remained in the lungs. Thus, inflation rate and not deflation rate appears to be the most important factor in determining the amount of air trapped in the lungs following a particular cycle.

Two special inflation-deflation sequences were performed to determine how $V_{max}$ and the viscoelastic interaction between inflation and deflation affected the amount of air trapped in the lungs per cycle. Assuming that most air was trapped during either inflation or deflation, two predicted values of $V_m/V_{max}$ were made based on the standard rate curves of Fig. 9*A* and were then compared with the experimental results of the first and second sequences. In both cases it was found that inflation rate was much more important than deflation rate in determining the amount of air trapped in the lung.

Another property of the air trapping mechanism is that it is reversible. Air that has been trapped can be removed from the lung in vivo with the oxygen washout procedure or in vitro by degassing the lung in a vacuum chamber. When the lung is completely degassed between each series of ventilation cycles, the second, third, and fourth series of 10 $P_L$-$V_L$ curves for the same lung are similar to the control curves.

It has been known for some time that bubbles having surface-active properties are generated in excised lungs as the lungs are ventilated. Our findings are consistent with that observation if it is assumed not only that the bubbles participate in trapping air within the lungs but also that the bubbles are formed during lung inflation. Considering Macklem's analysis of a meniscus across an airway (12), it seems feasible that a bubble could easily be formed in an airway or alveolar opening in the same manner as a bubble formed with a bubble pipe. At slower inflation rates larger and more numerous bubbles are formed while at faster inflation rates the meniscus has a greater tendency to rupture resulting in fewer and smaller bubbles being formed.

If bubbles are generated in the lungs during inflation, air could become trapped in one of at least three ways. First, the bubbles could be generated upon inflation and partially occlude the airways resulting in their premature "closing" during lung deflation. This would be compatible with Faridy and Permutt's theory (5). Second, it is possible that as the bubbles are generated during lung inflation, air is trapped behind the bubbles and this air remains trapped during all subsequent cycles. The third possibility is that the bubbles formed during lung inflation contain virtually all the trapped air in the lungs. The second and third possibilities do not depend on airway closure to trap air and suggest both that the air is confined within stable compartments within the lungs and that this air is not free to leave the lungs even when airway closure does not occur. The data in this paper are not sufficient to support any of these possibilities individually.

In summary, based on the experimental evidence of this investigation, the most logical explanation of the air trapping mechanism in the excised lung is that the air becomes trapped as a result of the generation of bubbles during lung inflation.

The authors thank Fritzi Rothlisberger, George Utt, Nancy Nehrig, and Michael Moore for their excellent technical assistance.

This study was supported in part by National Aeronautics and Space Administration Grant NGR 47-001-048. It was presented in part at the Spring FASEB Meetings in Atlantic City, N. J., April 7–12, 1974, and the Biophysics Meeting in Minneapolis, Minnesota, June 2–7, 1974.

Part of this work was performed while D. G. F. was the recipient of a National Institute for Occupational Safety and Health Postdoctoral Fellowship.

Brand names are used for information only and do not constitute endorsement by the National Institute for Occupational Safety and Health.

Received for publication 16 June 1975.

## REFERENCES

1. Cavagna, G. A., E. J. Stemmler, and A. DuBois. Alveolar resistance to atelectasis. *J. Appl. Physiol.* 22: 441–452, 1967.
2. Dale, W. A., and H. Rahn. Rate of gas absorption during atelectasis. *Amer. J. Physiol.* 170: 606–615, 1952.
3. Edmunds, L. H., and G. L. Huber. Pulmonary artery occlusion. I. Volume-pressure relationships and alveolar bubble stability. *J. Appl. Physiol.* 22: 990–1001, 1967.
4. Faridy, E. E. Effect of hydration and dehydration on elastic behavior of excised dogs' lungs. *J. Appl. Physiol.* 34: 597–605, 1973.
5. Faridy, E. E., and S. Permutt. Surface forces and airway obstruction. *J. Appl. Physiol.* 30: 319–321, 1971.
6. Frazer, D. G., R. A. Rhoades, and W. S. Adams. Error analysis of a recording system for measuring pulmonary pressure-volume curves. *J. Appl. Physiol.* 29: 534–537, 1970.
7. Hildebrandt, J. *Properties of Mammalian Lung* (doctoral dissertation). Seattle, Wash.: University of Washington, 1966.
8. Hildebrandt, J. Comparison of mathematical models for cat lung and viscoelastic balloon derived by Laplace transformation methods from pressure-volume data. *Bulletin of Mathematical Biophysics*. 31: 651–667, 1969.
9. Hughes, J. M. B., and D. Y. Rosenzweig. Factors affecting trapped gas volume in perfused dog lungs. *J. Appl. Physiol.* 29: 332–339, 1970.
10. Horie, T., and J. Hildebrandt. Dynamic compliance, limit cycles, and static equilibria of excised cat lung. *J. Appl. Physiol.* 31: 423–430, 1971.
11. Kleinman, L. I., D. A. Poulos, and A. A. Siebens. Minimal air in dogs. *J. Appl. Physiol.* 19: 204–206, 1964.
12. Macklem, P. T. Airway obstruction and collateral ventilation. *Physiol. Rev.* 51: 368–436, 1971.
13. McIlroy, M. B. The physical properties of normal lungs removed after death. *Thorax.* 7: 285–290, 1952.
14. Mead, J., and C. Collier. Relation of volume history of lungs to respiratory mechanics in anesthetized dogs. *J. Appl. Physiol.* 14: 669–678, 1959.
15. Pattle, R. E. Properties, function, and origin of the alveolar lining layer. *Proc. Roy. Soc. London* 240: 148–149, 1958.
16. Radford, E. P., Jr. Static mechanical properties of mammalian lungs. *Handbook of Physiology. Respiration.* Washington, D. C.: Am. Physiol. Soc., 1964, sect. 3, vol. i, chapt. 15, p. 429–449.
17. Stemmler, E. J., and A. B. DuBois. Pulmonary tissue and surface elastic forces at low lung volumes in rabbits. *J. Appl. Physiol.* 25: 473–478, 1968.