Mechanics of Respiration in Unanesthetized Guinea Pigs

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ABSTRACT

AMDUR, M. O. AND J. MEAD. Mechanics of respiration in unanesthetized guinea pigs. Am. J. Physiol. 192(2): 364-368. 1958.—A technique has been described by which tidal volume, intrapleural pressure and rate of flow of gas in and out of the respiratory system can be measured simultaneously in unanesthetized guinea pigs for periods of several hours. These data permit the calculation of the pulmonary flow-resistance and compliance for an experimental animal with normal reflex behavior. The values obtained on 200 normal and 20 tracheotomized animals for tidal volume, respiratory rate, minute volume, resistance and compliance are given.

A MEANS of studying the mechanical properties of the lungs of unanesthetized guinea pigs was devised for use as a toxicological tool to examine responses to respiratory irritants. The toxicological aspects of this work have been described elsewhere (1, 2). This paper presents a detailed description of the techniques used along with values found for normal guinea pigs.

METHODS

Measurement of Intrapleural Pressure.

Intrapleural pressure was measured by inserting a fluid-filled tube directly into the chest cavity with the animal under light ether anesthesia. The intrapleural catheter was a 9-inch length of polyethylene tubing 0.03 inches i.d. Three holes were cut in the mid-portion (1 cm) of the tube to allow for pressure transmission.

For insertion, one end of the catheter was fed over a piece of stiff wire and the other end was plugged to prevent air from being drawn into the intrapleural space. The wire was grasped with pliers and pushed through the skin at the level of the sixth intercostal space near the posterior mid-line. Once under the skin the wire was passed through the chest wall into the chest cavity, moved along under the chest wall for about a centimeter, and brought out again through the chest wall and skin on the right side. The catheter was then pulled through by means of the wire and placed so that the three holes were centered in the chest cavity. Two rubber buttons made from vial caps were fed over the catheter and pushed up against the skin to hold the tube in position.

A guinea pig with the intrapleural catheter in position is shown in figure 1. The whole procedure took only a few minutes since no surgical technique was required. The animals recovered rapidly from the ether anesthesia and showed no signs of discomfort from the presence of the catheter.

In about 40% of the animals the catheter punctured the lung, but the damage was always local on the lower right lobe. When data from animals with and without lung puncture were compared, there was no significant difference between the two groups.

The ends of the catheter were connected through adapters to three-way stopcocks. This permitted the tube to be flushed through regularly with saline containing a little heparin, the pressure being kept sufficiently below atmospheric pressure to prevent fluid retention in the intrapleural space. For pressure recording a Sanborn electromanometer, a direct-current amplifier, and a direct-writing recorder were used. The system was calibrated with a water manometer. The zero base line for the intrapleural pressure tracings was the pressure...
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obtained with the level of fluid in the reservoir bottle of the manometer at the level of mid-thorax of the guinea pig.

**Ventilatory Measurements.** Tidal volume as measured by recording the pressure changes produced in a body plethysmograph connected to a 5-liter reservoir bottle. It was necessary to have a chamber in which the animal would sit comfortably enough to remain quiet and at the same time have an air-tight seal around the neck. Figure 2 shows the body plethysmograph used in these studies. The sloping front of the cylinder permitted the animal to sit with the front feet extended, the only position in which an unanesthetized guinea pig will sit quietly. The animal was placed in the cylinder and the removable segment was taped in place. The animal’s neck and the joints of the cylinder were coated with Aquaresin and inner and outer latex collars, also shown in figure 2, were placed around the neck and over the joints of the cylinder forming an air-tight seal. Figure 3 shows an animal in the plethysmograph.

As the animal breathed, the pressure in the plethysmograph and reservoir bottle varied directly with the volume. A 2-cm volume change, which corresponds to a normal tidal volume for a guinea pig, caused a pressure change of approximately 4 mm of water. The pressure changes of the system were transmitted to a sensitive pressure transducer, strain-gauge amplifier, and direct-writing recorder. For calibration, a cylinder of the same volume as the plethysmograph containing about 200 ml of water to approximate the volume of the guinea pig was connected to the reservoir bottle by the same stopper and tubing used for the plethysmograph. A syringe was connected to this system and the pen deflection produced by moving known volumes of air in and out (at frequencies similar to those found in the guinea pigs) was measured.

Rates of flow of air in and out of the respiratory system were obtained by electrical differentiation of the volume signal with respect to time. A tracing of the flow pattern was obtained by feeding the flow-rate signal

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2 Aquaresin was obtained from Glyco Products Co., Inc., Empire State Building, New York, N. Y. This material is nonirritating, does not affect rubber and washes off readily with water.

3 The latex collars were made by dipping Lucite molds first in coagulant solution and then in latex. The latex was cured for 20 min. in hot running water and 20 min. in an oven at 80°C. The coagulant no. 3 and Latex r-N-57 were obtained from General Latex and Chemical Corp., 66 Main St., Cambridge, Mass.

4 Under these conditions the gas compression was approximately adiabatic.
FIG. 4. Sample of respiratory tracings from guinea pig.

into a direct-current amplifier and the direct-writing recorder.

A cathode-ray oscilloscope was used for monitoring the system during an experiment. Intrapleural pressure appeared on the X-axis and either volume or flow-rate as desired on the Y-axis. Observations of these patterns on the oscilloscope face permitted an estimate of the current condition of the animals. Any technical difficulties in the pressure or volume recording could thus be detected and corrected. The final calculations were made, however, from the recorded tracings. A sample of the type of tracing obtained is shown in figure 4.

Method of Analysis. By relating the volume and the flow rate to intrapleural pressure at specific points during the respiratory cycle information on the mechanical properties of the lungs may be obtained. The intrapleural pressure has an elastic component which relates to elastic recoil of the lungs and a flow-resistive component which relates to resistance to flow of gas in the lungs and airway and to 'viscous' resistance of the lung tissue. The elastic and flow-resistive components can be evaluated separately.

At the beginning and end of inspiration, no air is being moved into or out of the respiratory system, hence at these moments the flow-resistive component drops out and any pressure change must relate to elastic forces alone. The relationship between the elastic pressure change and the accompanying volume change (the tidal volume) is used as a measure of the elastic distensibility of the lungs. This method of measuring compliance is shown schematically in figure 5A.

At points of equal volume during the respiratory cycle the elastic forces must be approximately equal, and the pressure change between two such points must relate chiefly to resistance to flow in the lungs and airway. This is shown schematically in figure 5B. This pressure change is related to the associated flow change to give a measure of the flow-resistance of the lungs and airway. This


FIG. 6. Relationship of pulmonary flow resistance to pulmonary compliance in 60 guinea pigs.
method gives a value which represents the average inspiratory and expiratory resistance near peak inspiratory and expiratory flows. It does not express the change of resistance with flow rate that is to be expected, but since the resistance tracings monitored on the oscilloscope were nearly rectilinear, the results must closely approximate the average resistance during the respiratory cycle. This method was chosen because it greatly facilitates the multiple serial determinations necessary for toxicological studies.

**PROCEDURE**

Observations could be made on the animals for periods of several hours. In some of the early toxicological studies, control periods were extended up to 5 hours. During this time no major changes in respiration were observed. In other instances, animals which had had a control period of air alone, followed by a 3-hour exposure to low concentrations of a respiratory irritant were studied for periods of 3-4 hours after the exposure ended. Values obtained at the end of the recovery period correspond closely to those obtained during the control period 6-8 hours earlier. These results indicate that when the preparation is successful it can be utilized for long periods. As might be expected, the preparation is not always trouble-free. As experience is gained with the method, however, it becomes possible to recognize and correct the various difficulties encountered. A gradual damping of the intrapleural pressure tracing can be caused by plugging of the intrapleural catheter. It has been found that plugging of the catheter is less likely to occur if it is flushed through immediately after insertion. Two syringes are connected to it and saline containing a little heparin is pulled through to remove any blood and air before the animal is placed in the plethysmograph. As a rule the tube may be kept free by flushing once every 15 minutes, but some animals require more frequent flushing. If the tube becomes seriously plugged, it can sometimes be cleared by connecting the ends directly to the needles of two syringes filled with heparin-saline and manipulating the syringes to force the obstruction out of the tube.

A sudden decrease in amplitude or the complete disappearance of the intrapleural pressure fluctuation results if the tube is pulled out of position. In general the rubber buttons will hold the tube in position throughout the day, but some animals tend to move about so as to twist the right foot over the tube. When the foot is disentangled from the tube, the pres-

<table>
<thead>
<tr>
<th>No. of animals</th>
<th>Body wt., gm</th>
<th>Tidal vol., ml</th>
<th>Respiration/ min.</th>
<th>Resistance, cm H₂O/ml/sec</th>
<th>Compliance, ml/cm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human adult</td>
<td>70</td>
<td>18.5</td>
<td>1.3</td>
<td>0.18</td>
<td>0.130</td>
</tr>
<tr>
<td>Human infant</td>
<td>3.04</td>
<td>18.0</td>
<td>0.055</td>
<td>0.005</td>
<td>0.001</td>
</tr>
<tr>
<td>Guinea pig</td>
<td>0.209</td>
<td>7.9</td>
<td>0.00106</td>
<td>0.00022</td>
<td>0.137</td>
</tr>
</tbody>
</table>

**Table 2. Resistance and Compliance—200 Guinea Pigs**

<table>
<thead>
<tr>
<th>Resistance, cm H₂O/ml/sec</th>
<th>Compliance, ml/cm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean and Standard Deviation</td>
<td>Range</td>
</tr>
<tr>
<td>0.73±0.31</td>
<td>0.26±0.10</td>
</tr>
<tr>
<td>0.20±0.05</td>
<td>0.10±0.04</td>
</tr>
</tbody>
</table>

**Table 3**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Normal</th>
<th>Tracheotomy</th>
<th>Diff.</th>
<th>Level of Signif.</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of animals</td>
<td>20</td>
<td>20</td>
<td>-20</td>
<td>None</td>
</tr>
<tr>
<td>Body wt., gm</td>
<td>209±30</td>
<td>192±20</td>
<td>-17</td>
<td>0.001</td>
</tr>
<tr>
<td>Tidal vol., ml</td>
<td>1.7±0.1</td>
<td>1.3±0.3</td>
<td>-0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Respiration/ min.</td>
<td>81±13</td>
<td>104±28</td>
<td>+23</td>
<td>0.001</td>
</tr>
<tr>
<td>Minute vol., ml</td>
<td>137±23</td>
<td>125±26</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>Resistance, cm H₂O/ml/sec</td>
<td>0.09±0.18</td>
<td>0.38±0.16</td>
<td>-0.31</td>
<td>0.001</td>
</tr>
<tr>
<td>Compliance, ml/cm H₂O</td>
<td>0.22±0.05</td>
<td>0.24±0.04</td>
<td>+0.02</td>
<td>None</td>
</tr>
</tbody>
</table>
sure recording usually returns to normal. In such cases the tube can be taped to the animal’s back out of its reach.

RESULTS AND DISCUSSION

The mean, standard deviation and range of the ventilatory data obtained on 200 animals are shown in table 1. Using a method similar in principle to ours, Guyton (3) reported data on the tidal volume, respiratory rate and minute volume of various species of laboratory animals. The mean and range of his observations on 61 guinea pigs are given for comparison. The guinea pigs he used were larger than ours, hence the agreement is not as good as would appear from looking at the values alone. Values obtained in the two groups of observations are, however, of the same order of magnitude. Within our own data there was no correlation found between body weight and tidal volume, respiratory rate, or minute volume. The range of body weights is probably too small to expect such a correlation in a series of this size.

The average values for resistance and compliance along with the range and standard deviation are given in table 2. The individual values for resistance and compliance are plotted in figure 6. There is a tendency for the animals having a higher resistance to have a lower compliance. The correlation coefficient was -0.578 which indicates a correlation significant at the 1% level. If by chance the amplitude of the intrapleural pressure change as recorded for a given animal was below the true value, the compliance would appear higher and the resistance would appear lower than the true value. This might explain the values on the extreme left of the graph, however all 27 animals showing a resistance of 0.72 or above showed a compliance of 0.24 or lower. This probably represents a true inter-relationship between resistance and compliance in our animals. Such an inverse relationship presumably reflects differences in lung size between animals.

The compliance values for the guinea pig lung are approximately one-thousandth of the values obtained for the compliance of the human lung. In table 3 the data from human adults, human infants and guinea pigs are compared on the basis of lung weight. The lung weight/body weight ratio for human adults was obtained from Flury and Zernick (4) and that for human infants from Cook et al. (5). Webster and Liljegren (6) determined the organ/body weight ratios for guinea pigs of various body weights. They report a lung weight of 7.9 gm/kg for guinea pigs weighing 150 gm and a lung weight of 7.4 gm/kg for guinea pigs weighing 250 gm. The lung weight/body weight ratios determined on six animals gave a value of 7.9 ± 1.5 gm/kg which is in agreement with the data reported in the literature. Expressed in terms of compliance per kilogram lung weight, the figure for the human adult is 0.139, that of the human infant is 0.091, and that of the guinea pig is 0.133. Thus the lungs of the two species show similar elastic behavior when the weight difference is taken into account.

In the course of toxicological investigations, 20 animals were used in which a cannula was inserted into the trachea. The data from these animals are compared with the data of the normal animals in table 4. The resistance of the tracheotomized animals has been reduced, while the lung compliance remains unchanged. The comparison of the normal and tracheotomized animals suggests that in the guinea pig the upper airway accounts for about 45% of the total resistance to air flow. The tidal volume was decreased and the frequency increased in the tracheotomized animals, while the minute volume remained unchanged.

REFERENCES