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Albuquerque, New Mexico

THE DESIGN OF A CANINE INHALATION EXPOSURE APPARATUS INCORPORATING A WHOLE BODY PLETHYSMOGRAPH

by

B. B. BOECKER,
F. L. AQUILAR,
AND T. T. MERCER

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B. B. Boecker, F. L. Aguilar and T. T. Mercer

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ABSTRACT

A whole body plethysmograph has been incorporated in an apparatus for exposing dogs individually to radioactive aerosols. This makes it possible to monitor the dog's respiratory pattern during the exposure without the use of any respiratory masks or valves. After three different transducer systems were evaluated for use with the plethysmograph, the flow rate transducer was chosen for several reasons including the fact that this system produces inspiratory and expiratory flow rate data as well as tidal volume and respiratory rate information. The aerosol is continuously produced and drawn past the dog's nose during the exposure period and provision has been made for quantification of the aerosol in terms of concentration and particle size distribution for each experiment. External contamination of the dog is minimal since only the nostril area is uncovered within the aerosol exposure chamber. Pertinent design and calibration features are discussed.

ACKNOWLEDGEMENTS

The authors wish to express their appreciation to Dr. U. C. Luft for his initial guidance and helpful suggestions concerning the techniques used and to R. M. Goodrich for assistance with the electronic instrumentation requirements.

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THE DESIGN OF A CANINE INHALATION EXPOSURE APPARATUS INCORPORATING A WHOLE BODY PLETHYSMOGRAPH.*

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INTRODUCTION

The influence of various aerosol and physiological parameters on the initial deposition of inhaled material is being examined at the Lovelace Foundation as part of a long-term study of the biological effects of inhaling fission products. Dividing the amount of radioactivity found in the experimental animal at the termination of exposure by the total amount of radioactivity inhaled during exposure yields the fraction deposited. The former value can be determined by whole body counting or immediate sacrifice followed by an analysis of the radioactivity in all of the tissues and organs of the animal. The total amount of radioactivity inhaled during exposure can be obtained from an accurate knowledge of the concentration of radioactivity in the air within the exposure chamber and the total amount of air inspired. It is this last area that has been neglected most in previous inhalation experiments. To determine deposition percentages, many authors in the past have relied on handbook values for tidal and minute volumes and have not monitored the variations in breathing patterns among the animals used in any one experiment. The possibilities for error allowed by this approach are apparent. To obtain meaningful deposition data, it is imperative that accurate measurements be made of the individual respiratory patterns throughout the exposures. This paper describes the design of an inhalation exposure

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*This paper will appear in part in Health Physics 10, No. 12, 1964.

apparatus for dogs which includes provisions for obtaining these and other useful data.

Several methods have been considered for collecting the pertinent respiratory data and these fall into three general categories. The first consists of measurements made at the nostrils or within the upper respiratory tract. Ross and Kao (1) have used a small thermistor within a tracheal cannula to obtain respiratory measurements and Arentsen and Kaiser (2) employed a thermocouple inserted in one nostril to record respiration. Both of these reports have emphasized that the methods are accurate only for respiratory frequency and not for tidal volume. A method was reported by Cummings, Blevins and Craig, (3) utilizing a device containing thin metal vanes supporting strain gauge wire, which was attached in front of the nose. Bending of the vanes with air movement produced an electrical signal, but this was also found to be non-linear with respect to tidal flow. The most successful method in this general category was reported by Morrow and Casarett (4) who described an inhalation apparatus for exposing dogs to radioactive aerosols. A mask, fitted to the dog's head, was attached to a rapid-acting respiratory valve such that the expired air passed through an electrostatic precipitator for removing any remaining aerosol and then through a pneumotachograph to obtain respiratory information. In addition to yielding accurate results, the system made it possible to analyze expired air separately from inspired air.

The second category includes methods for obtaining respiratory data by measuring the volume changes of the chest with a device which encircles the thorax. Stewart, Grossman and Kadetz (5) employed a sensing element constructed from two Baldwin strain gauges, and Stoner and Holaday (7) used mercury strain gauge tubes to measure thoracic movement. Nordenström (6) made a small battery from a rubber tube filled with dilute sulfuric acid having a copper electrode at one end and a zinc electrode at the other. Volume changes of the thorax varied the length of the rubber tube which in turn altered the internal resistance and output voltage of the battery. All of these methods are subject to the same problems: the values obtained depend upon the positioning of the device and the amount of thoracic versus abdominal breathing of the subject.

The third general category of methods used for measuring respiratory patterns involves whole body plethysmography. The subject is sealed in an air-tight chamber in such a manner that only the airway is in communication with the exterior of the chamber. Variations in body volume corresponding to the volumes of air respired by the subject can be determined by measuring the pressure changes within the sealed unit or by allowing air to be moved in and out of the chamber through a metering device. The design of a typical pressure-system plethysmograph for adult human subjects has been described by Comroe, Botelho and DuBois (8). In addition to measuring various respired volumes, this system has also been used for determining thoracic gas volume, airway resistance, and abdominal gas volume. Similar pressure systems have also been used by Amdur and Mead (9) for measuring tidal volumes in guinea pigs and by Adolph and Hoy (10) and Gottelieb and Jagodzinski (11) for rats. A similar system is also being used at the Lovelace Foundation for mice, rats and guinea pigs (12). Plethysmographic methods which measure the volume of air displaced during breathing have been employed with human adults by Mead (13) and with babies by Shaw and Hopkins (14), Murphy and Thorpe (15), Cross (16), Cook, et al. (17), and others.

From the literature concerning the use of whole body plethysmographs, it appeared that a suitable adaptation could yield accurate values for respiratory patterns of dogs during inhalation exposures without requiring that the animal be encumbered by respiratory masks, any valving arrangements or devices attached around the thorax. For simplicity and since it was desirable to enclose the dog in a dry box during the exposure period to confine radioactive aerosols, means of converting a dry box to a plethysmograph were explored.

Three different measuring systems were examined for use with the plethysmographic chamber; they are depicted schematically in Figure 1. Although all three systems are shown connected to the plethysmograph,

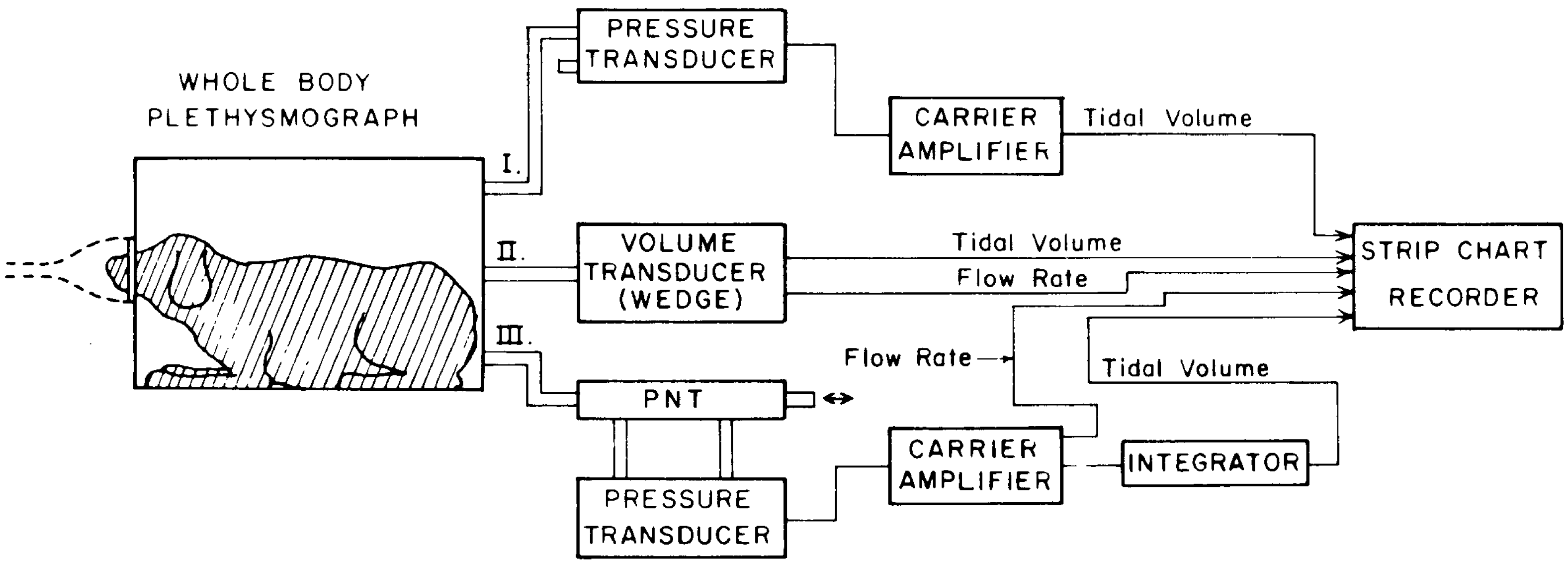


Fig. 1 Schematic Representation of Transducer Systems Which Could be Used With a Whole Body Plethysmograph to Obtain Respiratory Data.

only one was used at a time. In System I, tidal-volume information was obtained from measurements of the pressure variations occurring within the sealed chamber corresponding to alterations in the animal's body volume throughout each respiratory cycle. In the other two methods the volume of air moving in and out of the plethysmograph was monitored. A model 170 WEDGE Spirometer (Med-Science Electronics, St. Louis, Mo.) was used as the transducer in System II. Although the WEDGE is basically a volume transducer, it has two outputs, one proportional to the volume of air and the other proportional to the rate of flow of air in and out of the transducer. Thus, three sets of data were obtained; viz., tidal volumes and inspiratory and expiratory flow rates. Similar remarks apply to System III in which the air moving in and out of the plethysmograph was passed through a pneumotachograph (PNT), across which a pressure drop developed that was linearly related to flow rate. Thus, flow rate was measured directly, but tidal volume was obtained by electrically integrating the flow signal. Results gotten with all three systems are given in the following sections as well as a description of the final form of exposure apparatus developed.

METHODS AND MATERIALS

Three experimental plethysmographs were used. Two were constructed from 3/8- and 1/2-inch Plexiglas (Rohm and Haas, Philadelphia, Pa.) and had volumes of 140 and 220 liters, respectively, and the third was a 96-liter steel chamber. A Harvard Model No. 607 Respiration Pump (Harvard Apparatus Company, Dover, Mass.) with the valves removed was employed to simulate a breathing animal. When tidal volume (V_T) appears in reference to the respiration pump in this report, it refers to the stroke volume of the pump. The latter was used outside of the chamber for pumping tidal volumes in and out of the chamber as shown in Figure 2; it was also mounted inside the plethysmograph with the output of the piston chamber connected to the outside atmosphere. When the pump was employed in this second manner, the other end of the

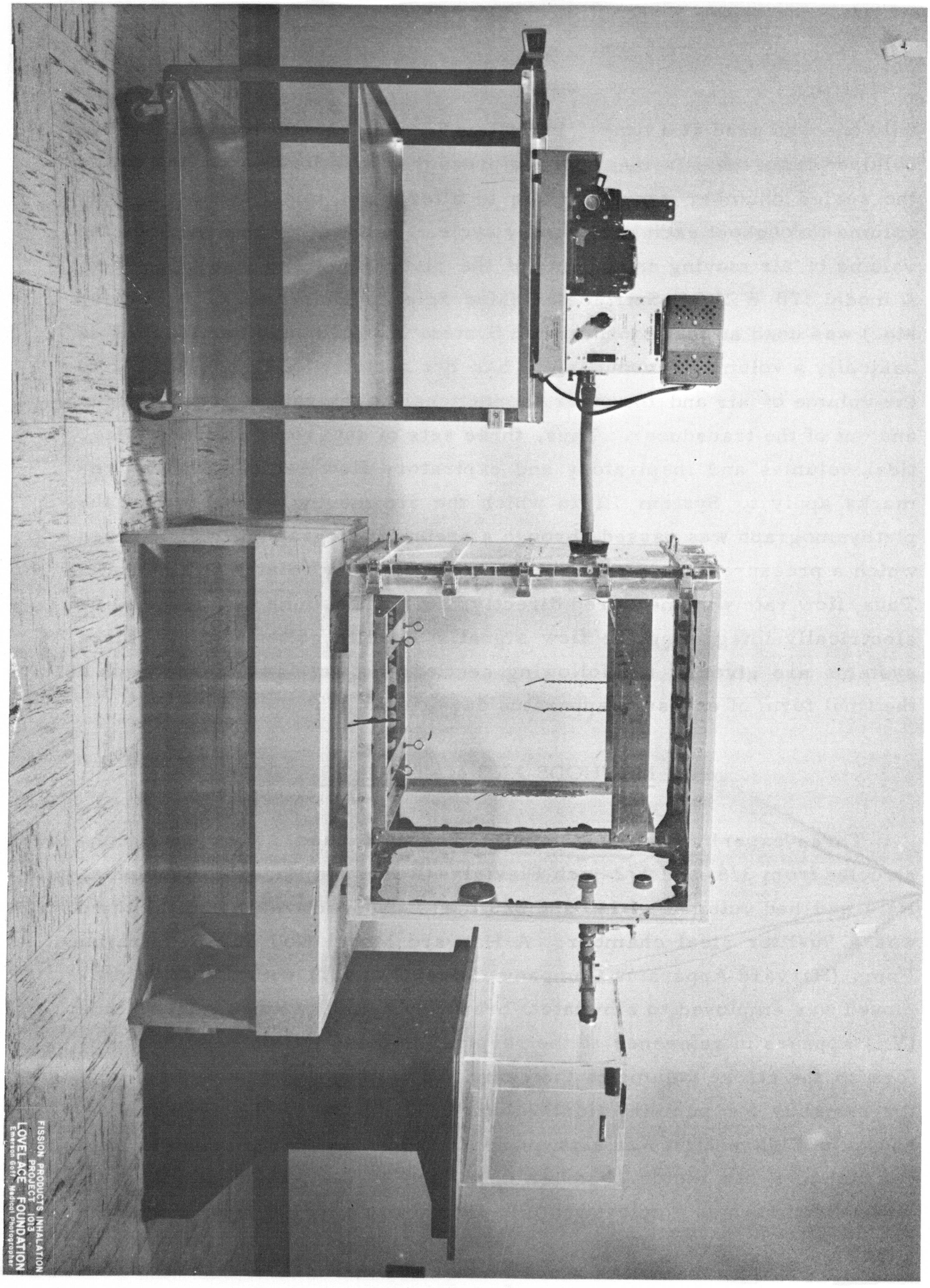
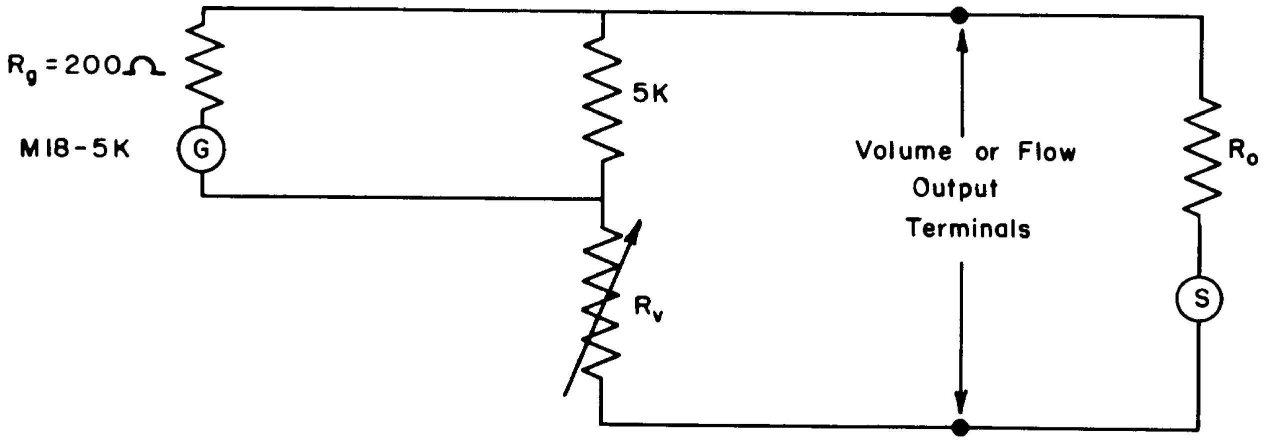


Fig. 2 Simulation of a Breathing Dog in a Whole Body Plethysmograph by Use of a Respiratory Pump.

piston chamber was open to the air in the plethysmograph, and the reciprocating movement of the piston within the chamber caused the effective volume of the pump to vary during each cycle in a manner similar to that of an animal in the same position. Since both of these techniques produced equally satisfactory results, the pump was normally used on the outside of the plethysmograph for convenience of operation. The pump allowed calibration operations to be carried out for frequencies between 4 and 58 cycles/minute using tidal volumes ranging from 80 to 750 ml. All volumes in this report are given at ambient temperature and atmospheric pressure (ATP) without a correction for relative humidity.

The pressure changes occurring within the plethysmograph chamber in System I were measured with a strain gauge transducer, Statham No. PM97, ±0.05 psid (Statham Transducers, Inc., Hato Rey, Puerto Rico). Output signals from the transducer were amplified with a Honeywell No. 130-2C carrier amplifier and recorder with a Honeywell No. 906C Visicorder oscillograph(Honeywell Industrial Products Group, Denver, Colo.). A pressure calibration was obtained by comparing the transducer output with readings taken on an inclined draft gauge measuring the same static pressures. As used in this system, the transducer measured changes in the chamber pressure with respect to a static reference system. Because of the sensitivity of this transducer, normal pressure changes in the laboratory environment made substantial changes on the static or reference side of the transducer. This effect was minimized by using a 96-liter sealed container as a reference atmosphere. This technique was useful as long as the pressure within the reference chamber did not drift significantly during the period of measurement.

Because of the low current output and high output impedance of the WEDGE Spirometer used with System II, a very sensitive galvanometer was required in the Visicorder to obtain a usable trace. The Honeywell No. M18-5K galvanometer with a current sensitivity of 0.41 μa/inch was found satisfactory. Figure 3 gives details of the resistance network used to match this galvanometer to the WEDGE output. The amplitude of the Visicorder trace was controlled by varying the value of R_V over a range



R_g = Galvanometer Coil Resistance
R_o = WEDGE Output Impedance
= 75K for Volume Signal
= 16K for Flow Signal
R_v = Variable Resistance for Impedance Matching and Amplitude Control

Fig. 3 Impedance Matching Network Between Visicorder Oscillograph and the WEDGE Spirometer.

of 47K to 150K.

The flow rate transducer in System III was a Vol-O-Flo No. 10-R-100 pneumotachograph (National Instrument Laboratories, Inc., Washington, D. C.). This pneumotachograph has a stated upper limit of 100 liters/ minute (lpm) and a total resistance to air flow of approximately 0.01 inch H_2O/lpm. The pressure drop across the pneumotachograph was measured with a Statham No. PM197, ±0.01 psid. Calibration was accomplished by drawing air through the pneumotachograph while it was connected in series with a 50 lpm rotameter (Brooks Instrument Co., Inc., Hatfield, Penn.) in order to obtain corresponding measurements of flow rate and pressure drop across the pneumotachograph. The response of the pneumotachograph was found to be linear up to a flow of 35 lpm, the highest value tested. Very similar calibration values were obtained when the flow rate through the pneumotachograph was reversed, indicating that the pneumotachograph had no significant directional characteristics.

RESULTS AND DISCUSSION

A. System I.

The basic simplicity of System I has been shown in Figure 1. As the animal's body volume increases and decreases due to respiratory motions, the corresponding pressure changes (ΔP) occurring within the plethysmograph are detected with a sensitive pressure transducer, amplified and recorded. In this manner, values for tidal volume and respiratory frequency can be obtained directly. By electronic differentiation of the volume signal, one should also be able to obtain flow rate information.

In addition to its simplicity, this system has the advantage of being equally useful for any size animal since the magnitude of ΔP associated with a respiratory cycle can be adjusted by varying the chamber air volume for animals with widely differing tidal volumes. The chamber air volume must be made small enough to cause useful pressure changes to occur without being so small that the overpressure produced in the plethysmograph is sufficiently large to affect the animal physiologically and perhaps alter the respiratory pattern.

Temperature changes within the chamber due to the addition of a warm animal body must also be considered since these can produce a considerable drift in the baseline pressure within the plethysmograph.

Data on the specific characteristics of this system are given below. Most of these data were obtained with the 96-liter steel chamber because the air volume in this chamber could be altered by adding known amounts of water to the chamber. Studies of the frequency and tidal volume response were limited to the ranges available with the respiration pump described above.

1. Frequency Response

Results are presented in Figure 4 for the values of ΔP measured within a chamber volume, V_c, of 96 liters when several different tidal volumes were each pumped in and out of the chamber at frequencies of 4 to 58 cycles/minute. There was a slight increase in ΔP with increased frequency representing a total increase of approximately 3-4 per cent over the frequency range studied. Most of the change in ΔP occurred between f = 4 and f = 23 cycles/minute and appeared to be independent of the stroke volume used. A possible reason for this increase in ΔP with increased frequency is discussed in section 3.

2. Volume Response

The data for $V_c = 96$ liters are replotted in Figure 5 to illustrate the linearity of response between tidal volume and the measured value of ΔP. The range of values given at each combination of tidal volume and V_c corresponds to the increase in ΔP with frequency shown in Figure 4. Similar data are also given for V_c = 80, 60 and 40 liters. The straight lines drawn through the data are considered to be the best fits to the values of ΔP obtained at f = 23 cycles/minute. For each of the values of

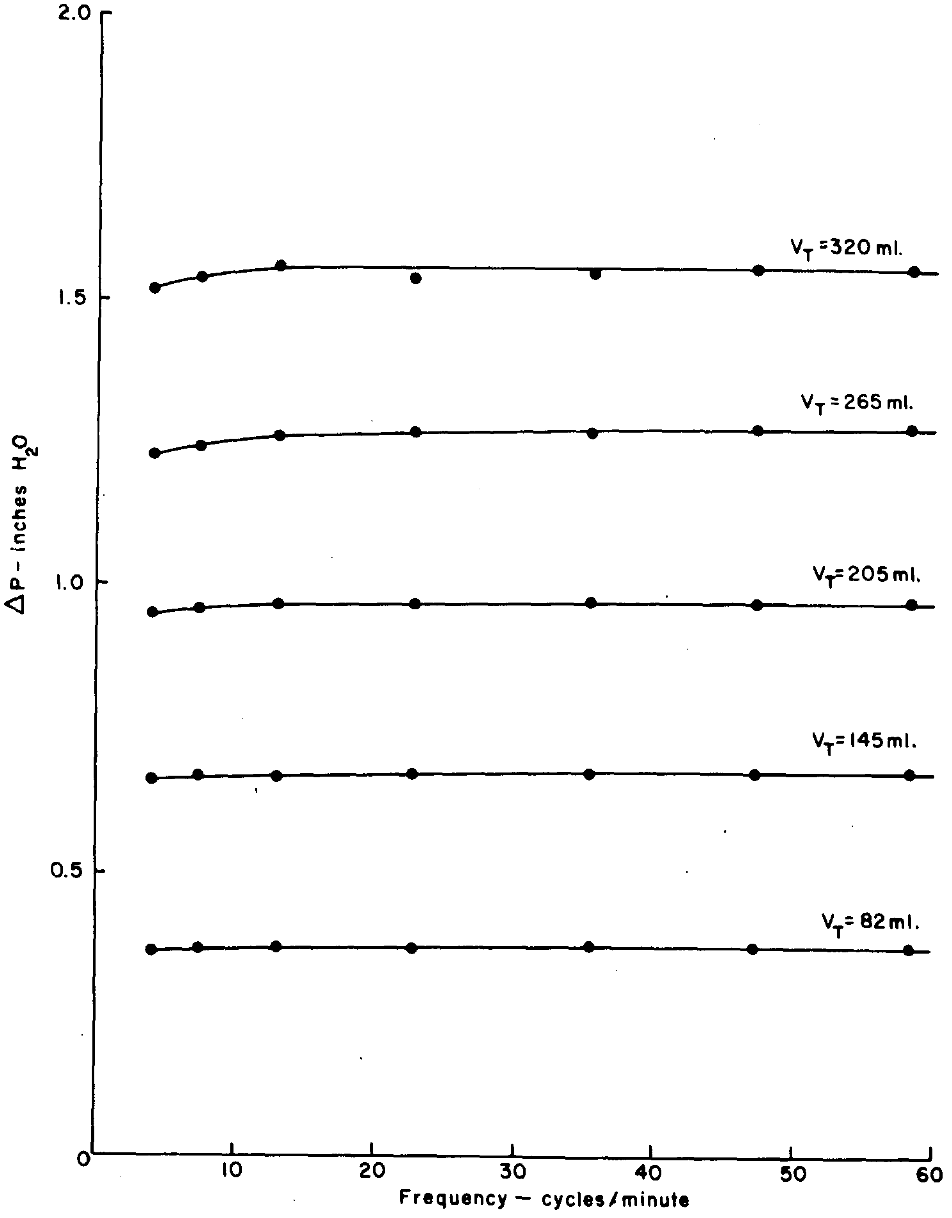


Fig. 4 Frequency Response of System I for Five Different Tidal Volumes.

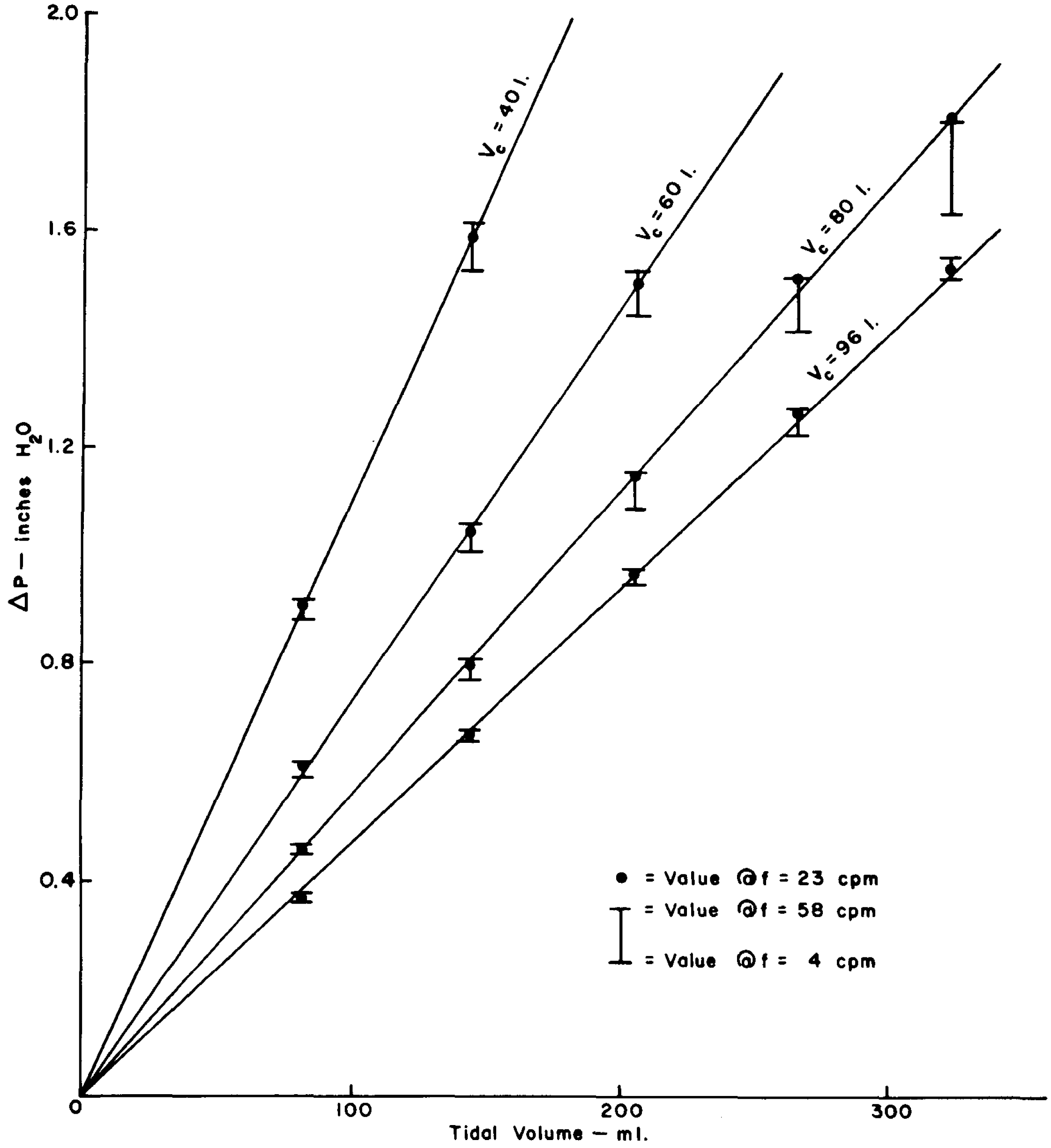


Fig. 5 Tidal Volume Response of System I for Four Different Chamber Volumes and Frequencies of 4 to 58 Cycles/Minute.

V_c used, it can be seen that there was a linear relationship between tidal volume and ΔP.

3. Calculated Value of ΔP

As an aid in the initial design of the plethysmograph, it was helpful to calculate the value of ΔP expected in the system since the information was needed to determine the proper value of V_c and the range of the pressure transducer. If the gas in the plethysmograph undergoes an isothermal compression, the expression $P_1 V_1 = P_o V_c$ is valid and from this one can derive a value for ΔP:

$$\Delta P = - \frac{P_o \Delta V}{V_c + \Delta V} \tag{1}$$

Where ΔP = Measured pressure change = $P_o - P_1$

P_o = Initial chamber pressure

V_c = Initial chamber air volume

P_1 = Final chamber pressure

V_1 = Final chamber air volume

$\Delta V = V_c - V_1$ = Change in chamber air volume at ATP $\cong$ Animal's tidal volume at BTPS

However, if the gas in the chamber undergoes an adiabatic compression, no heat enters or leaves the system and the temperature of the gas also changes. In this case, $P_1 V_1^{\gamma} = P_o V_c^{\gamma}$ where γ is the ratio of the molar heat capacity at constant pressure, C_P, to the molar heat capacity at constant volume, C_v, and has the approximate value of 1.4 for air. From this, one obtains:

$$\Delta P = \frac{-\gamma P_o \Delta V}{V_c + \gamma \Delta V} \tag{2}$$

Since both ΔV and $\gamma \Delta V$ are insignificant with respect to V_c, they can be ignored and the ratio of the adiabatic ΔP to the isothermal ΔP is γ. Therefore, if the compression is adiabatic, the measured ΔP is 1.4 times greater than if it is isothermal. In both cases, ΔP is inversely proportional to V_c so by plotting the values of ΔP vs. $\frac{1}{V_c}$, one should obtain a linear relationship. Figure 6 shows the actual values of ΔP taken from Figure 5 for a 100 ml. tidal volume and frequency of 23 cycles/minute compared with the theoretical values one would expect from adiabatic and isothermal compressions. The nearness of the experimental points to the calculated adiabatic line indicates that the conditions of expansion and compression under these experimental conditions are nearly adiabatic and that calculations using the above adiabatic equation should give better predictions of the ΔP to be expected. The increase in ΔP with increased frequency that was mentioned previously is probably due to the compressions becoming more nearly adiabatic with increasing frequency.

4. Effect of Animal Size

The calibration of the plethysmograph varies with the size of the animal used but the magnitude of this variation is dependent on the volume of the animal in relation to the volume of the empty chamber. As discussed above, ΔP is inversely proportional to V_c, the net chamber air volume (empty chamber volume minus animal volume). Usually, the animal volume is small in proportion to the chamber volume and growth of the animal changes the initial calibration very little. As an example, in the 220-liter plethysmograph used in some of these experiments, a 50 per cent increase in a dog's body volume (from 10 to 15 liters) would only alter the value of V_c from 210 to 205 liters, a change of 2.4 per cent. Variations of this order of magnitude are similar to those that could occur due to daily fluctuations in barometric pressure.

5. Effect of Tubing Length

Since it is not always convenient or desirable to connect the pressure transducer directly to the plethysmograph, a piece of tubing is usually inserted between the two. If the tubing is long enough, it is possible that some attenuation and phase lag of an oscillatory pressure variation can occur. Iberall has treated this problem theoretically (18)

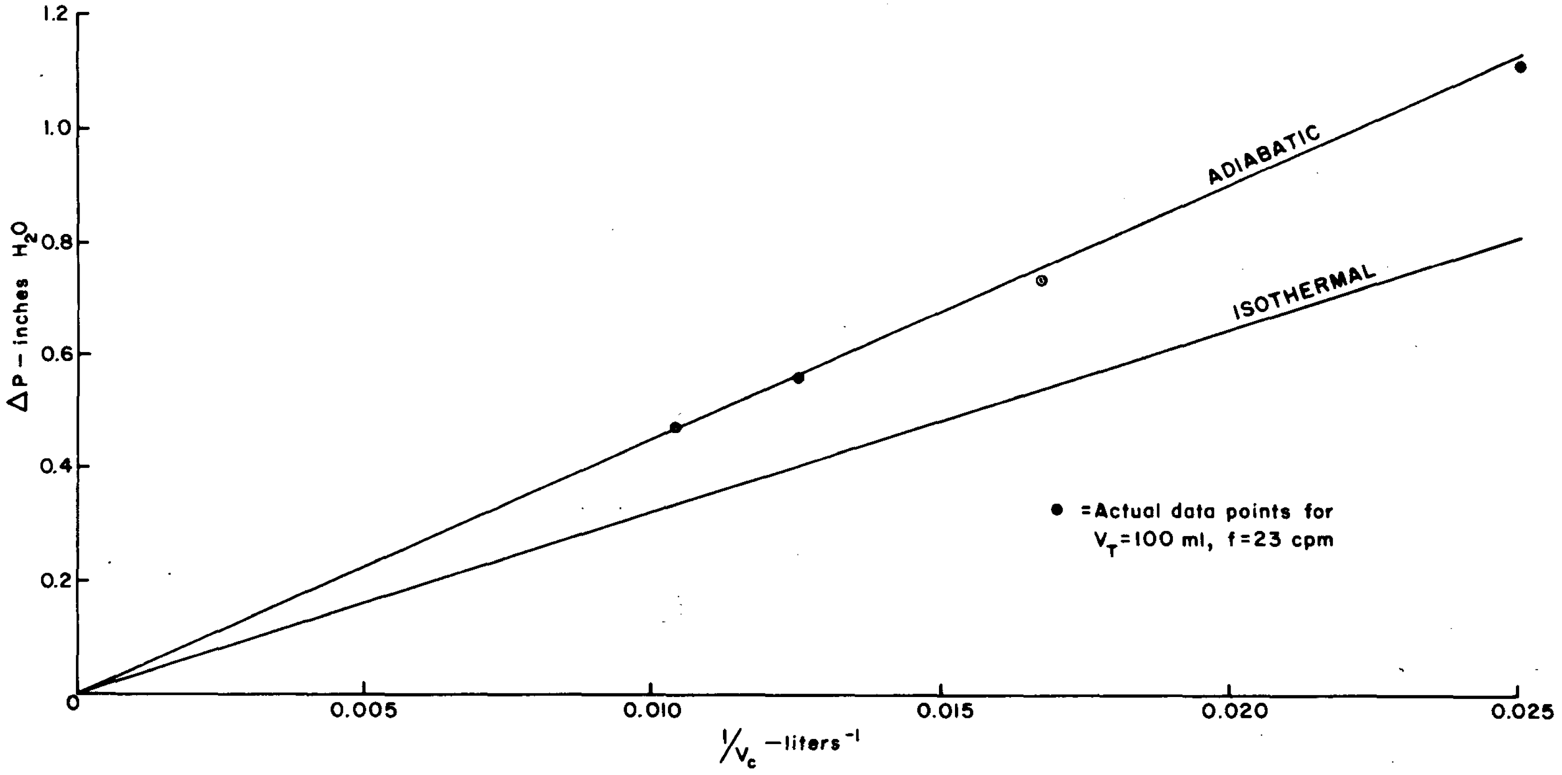


Fig. 6 Comparison of Values of ΔP Obtained in System I With Those Predicted by Considering the Compressions to be Adiabatic and Isothermal Respectively.

and in his paper, he gives methods by which these effects can be calculated for any system. Following his method, the length of 3/16-inch I. D. tubing that would transmit air pressure at a frequency of 180 cycles/minute with $<$ 5 per cent change in fundamental amplitude or $<$ 30° phase shift was determined for the Statham PM 97 transducer with internal volume ≈ 1 in.^{3}. This calculation yielded a theoretical length of ≈ 11 feet. To test these results experimentally, the length of 3/16-inch I. D. polyethylene tubing between the plethysmograph and transducer was varied from 1.5 inches to 14.7 feet and the recorded amplitude was measured at 3 frequencies for each length used. The data are given in Table 1 and, in agreement with the theoretical calculation made above, show that tubing in this range of lengths produces a negligible effect on the recorded amplitude.

6. Effect of Air Leaks in Plethysmograph

Before determining the effect of various sized air leaks on System I, a series of amplitude measurements at known frequencies was taken first utilizing the leak free 96-liter steel chamber. Following this, orifices that were 0.12 inch long and of known diameters were added to the system to produce quantitative air leaks. Observed values of ΔP for these runs are presented in Figure 7. The values of ΔP obtained with leak paths whose diameters were 0.017, 0.019 and 0.026 inch respectively were indistinguishable from those obtained with no leak path. However, when the diameter of the leak path was increased to 0.042 inch, there was a progressive decrease in the observed value of ΔP with decreasing frequency beginning at about 25 cycles/minute. A further increase in the diameter of the leak path to 0.105 inch caused the loss in observed amplitude to begin at higher frequencies and to be more severe at the lower frequencies. Similar results were obtained with tidal volumes of 82 and 265 ml.

The absence of amplitude loss with orifice diameters up to 0.026 inch over the frequency range studied indicates that the plethysmograph does not have to be absolutely leak-free in order to obtain

TABLE 1

EFFECT OF TUBING LENGTH BETWEEN PLETHYSMOGRAPH AND PRESSURE TRANSDUCER ON RECORDED AMPLITUDE.

	Recorded Amplitude (mm.)		
Tubing Length	f = 8 cycles/minute	f = 23 cycles/minute	f = 58 cycles/minute
1.5 inches	63.2	64.0	64.5
10	63.6	64.2	64.0
24	63.8	63.7	64.0
73	62.9	62.6	63.3
176 (14.7 ft.)	62.1	62.0	63.2

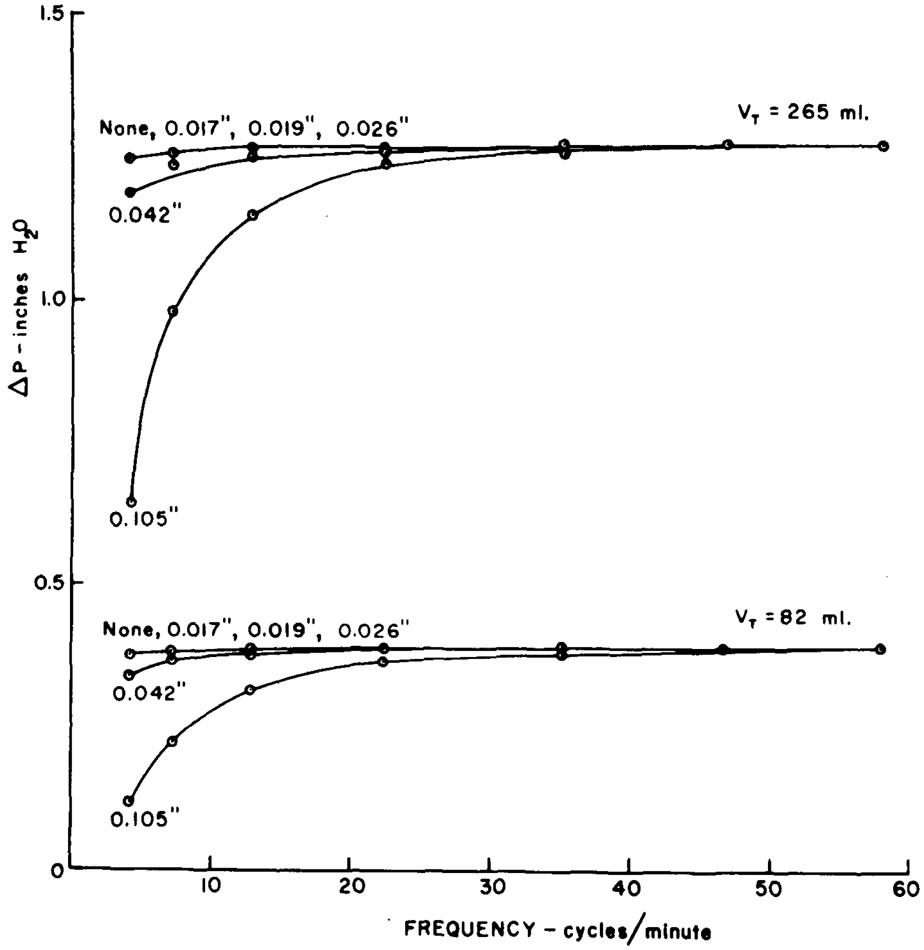


Fig. 7 The Effect of Various Diameter Leak Paths on the Measured Values of ΔP in System I for Two Different Tidal Volumes and Frequencies of 4 to 58 Cycles/Minute.

accurate, frequency independent results. This result was used to minimize the temperature effect discussed in the next section.

7. Temperature Effects

When dogs were maintained in the 220-liter plethysmograph for one hour, corresponding total increases in chamber air temperature of 1.4 - 2.2° C. were noted. These temperature changes were reflected as a shift in the pressure trace corresponding to an increase in base line pressure. Typical traces of a dog's tidal volume signal versus time in the plethysmograph are given in Figure 8. The traces read from right to left and were started when the dog was placed in the plethysmograph. The distance between two successive vertical lines represents one minute of elapsed time.

The top trace was obtained when the dog was placed in a plethysmograph that did not have an auxiliary leak path attached. There was an increase in base line pressure of approximately 0.6 inch H_2O during the first five minutes after which equilibration occurred. This change in pressure is lower than would be expected from the observed temperature changes, indicating that the plethysmograph was not absolutely leak-free and that a portion of the pressure change was lost through whatever leaks were present.

This temperature effect becomes a problem when a very sensitive pressure transducer is used since the transducer is subjected to both the increase in base line pressure due to the temperature effect and the periodic pressure changes from the animal's body volume changes. Two approaches could be used to minimize this problem. One would be to vent the chamber occasionally during the initial equilibration period. The other approach would be to attach a small vent to the chamber that would always be open and capable of bleeding off excess base line pressure without affecting the dynamic trace produced by the animal's respirations.

This second approach was examined and found to be satisfactory. After the upper trace in Figure 8 was obtained, the dog was removed

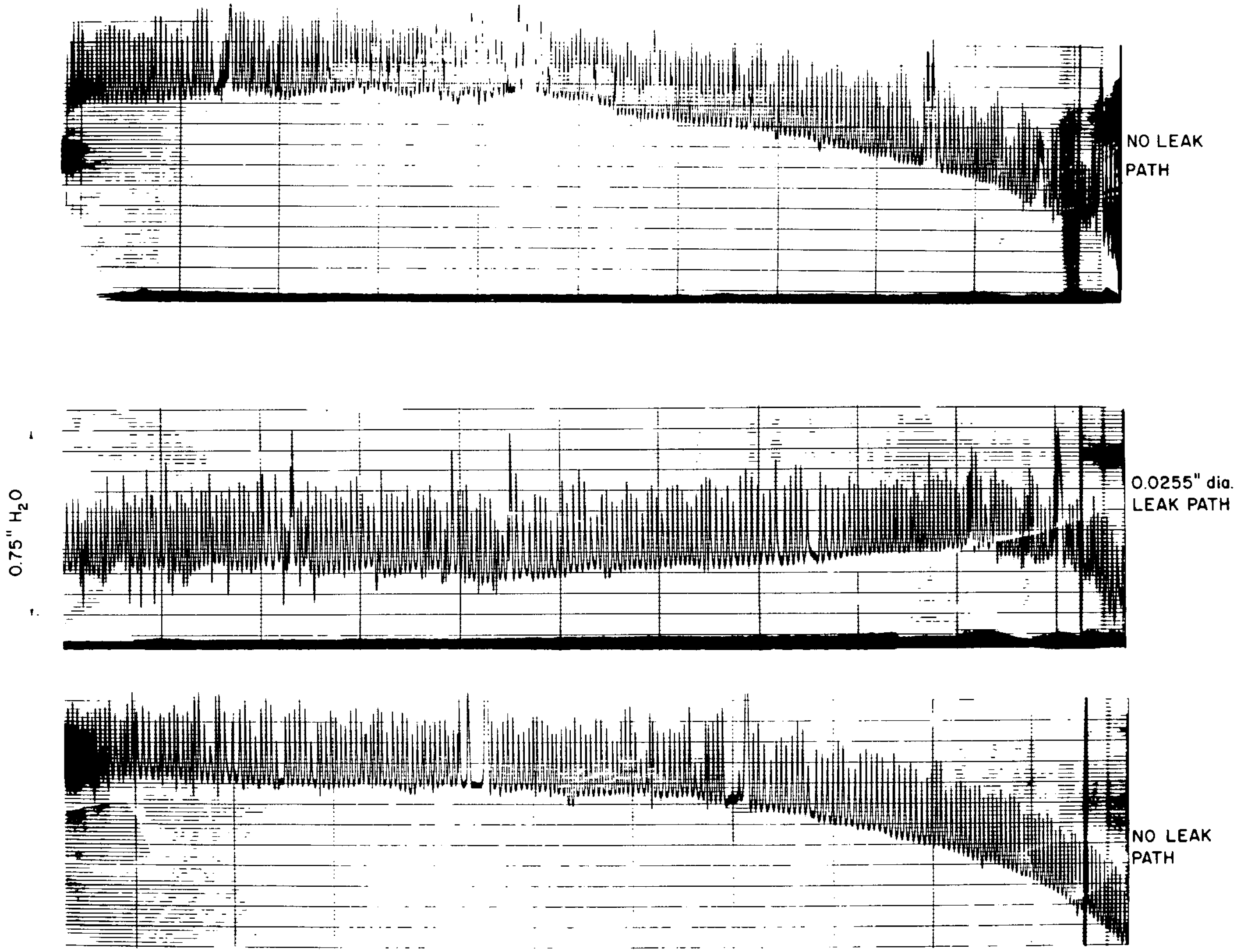


Fig. 8 Visicorder Traces Obtained With System I for a Dog in the Plethysmograph. Traces Read From Right to Left. The Distance Between Two Successive Vertical Lines Equals One Minute.

from the chamber for 5 minutes to allow the chamber air to return to room temperature. The dog was again placed in the chamber but this time a 0.026-inch dia. leak path was attached to the chamber. The base line pressure increased initially by ≈ 0.25 inch H_2O and then decreased to an equilibrium value that was only ≈ 0.16 inch H_2O higher than the initial pressure. The dog was again removed and the chamber allowed to cool off for 5 minutes prior to taking the bottom trace in Figure 8. The conditions under which this trace was obtained were the same as those used for the top trace and it can be seen that the results were also the same.

These results demonstrate that the addition of a leak path to the plethysmograph chamber is one satisfactory method of reducing the effect of air temperature changes. A 0.026-inch dia. hole proved to be large enough for this purpose without being so large that there was a significant loss in signal amplitude at low frequencies (see Figure 7).

B. System II

The WEDGE Spirometer was chosen for use as the volume transducer in System II because its capacity could easily accommodate dog tidal volumes and because signal outputs representing both flow rate and volume were available. The WEDGE is a waterless spirometer consisting of 2 flat plates, one fixed and one movable, which are hinged together on one edge and connected by an air-tight, flexible plastic bellows. Air volume changes within the spirometer cause the hinged plate to move and this, in turn, moves two transducer cores generating flow rate and volume signals.

Preliminary tests were made by pumping known volumes of air in and out of the WEDGE at known frequencies through 2-inch I.D. rubber tubing with the respiratory pump. Typical results are shown in the top half of Figure 9. A flattening of the volume signal at both maximum and minimum volume is apparent. The flow curve shows a definite zero flow pause at these same points, indicating that the bellows stopped moving before the points of maximum and minimum deflection occurred.

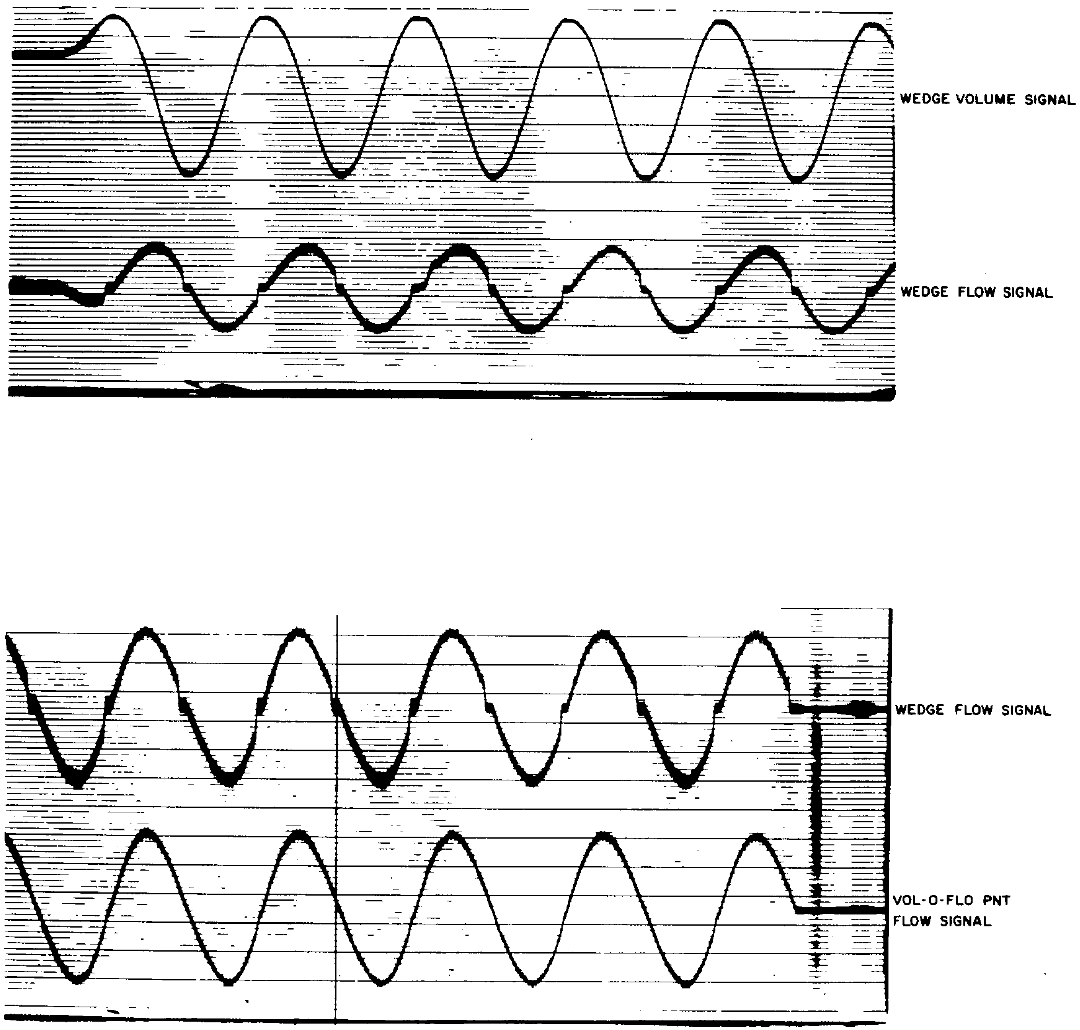


Fig. 9 Comparison of WEDGE Signals to the Flow Signal Obtained Simultaneously With a Pneumotachograph Connected in Series With the WEDGE.

To make certain that this distortion was produced by the WEDGE and not by the respiratory pump, the Vol-O-Flo Pneumotachograph was connected between the pump and the WEDGE so that the air volume moved in and out of the WEDGE would also pass through the pneumotachograph. Simultaneous flow signals obtained from these two devices are shown in the lower half of Figure 9. The zero flow pause does not appear in the pneumotachograph trace but it does in the WEDGE trace indicating that there was some restriction to movement of the WEDGE itself.

Attempts were made to rectify this situation by cleaning the transducer cores, replacing the bellows and by sending the entire device back to the factory for replacement of the flow transducer. Very little improvement was noted after any of these procedures. The flow signal continued to be distorted near zero flow and the volume signal flattened at the peaks and valleys. The loss of amplitude in the volume signal was more important at small tidal volumes as shown in Figure 10. Because of the distortion and non-linearity of response of this device, it was dropped from further consideration for use with the exposure apparatus.

C. System III

1. Theory

Figure 11 is a schematic representation of System III with a pneumotachograph connected to a plethysmograph to obtain respiratory data. The values P_1, V_1 represent the plethysmograph chamber and P_2, V_2 represent a fixed volume such as the room volume on the other end of a pneumotachograph whose resistance to air flow (inches H_2O/lpm) is denoted by R. When the effective air volume within the plethysmograph is reduced by an amount q through the inward movement of a piston or the expansion of a dog's body during the inspiration of an amount q, a portion of the displaced air, q_2, passes through the pneumotachograph into the compensatory chamber and produces a pressure drop, ΔP, across the pneumotachograph in the process. If one assumes that this occurs under isothermal conditions, the following expression is

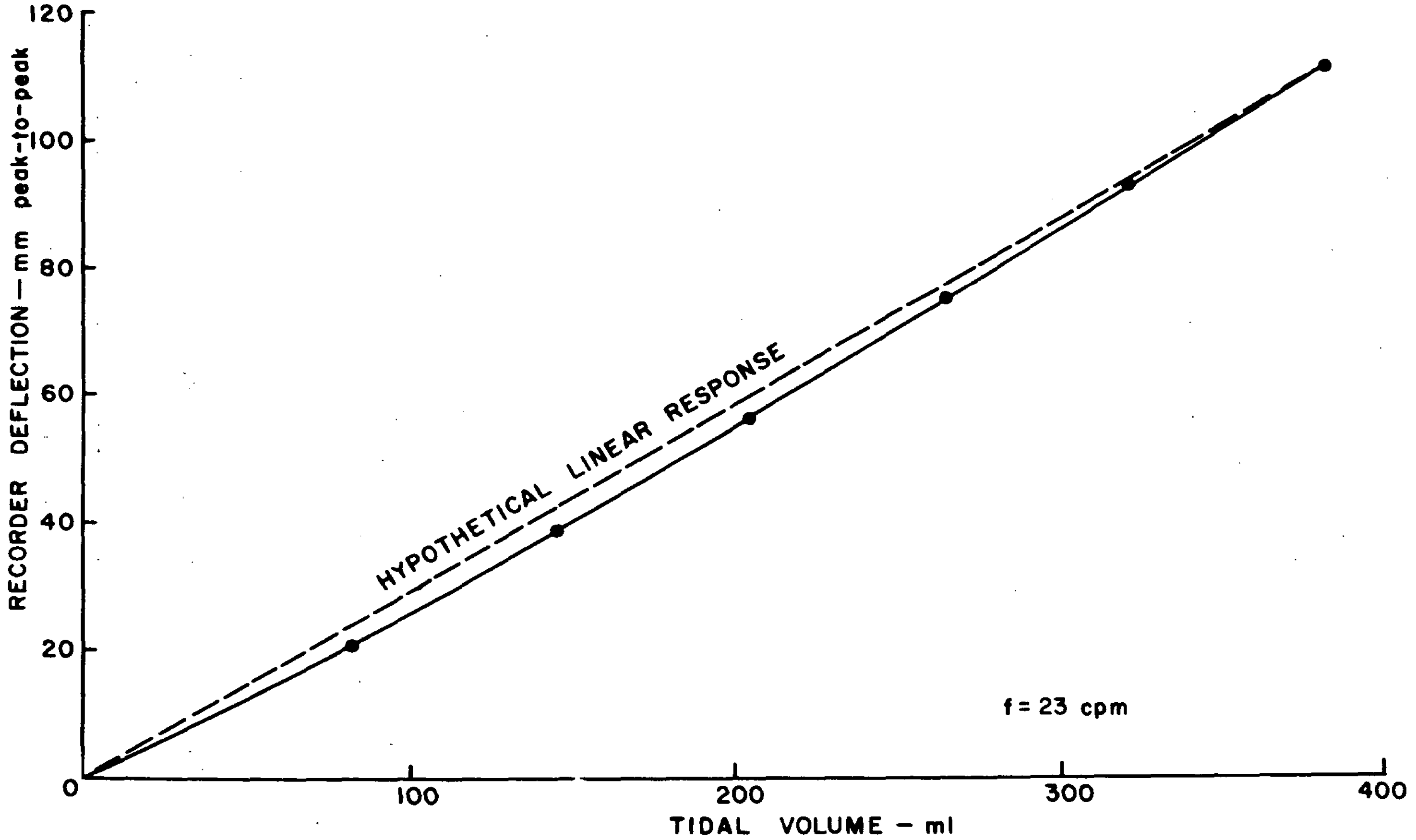
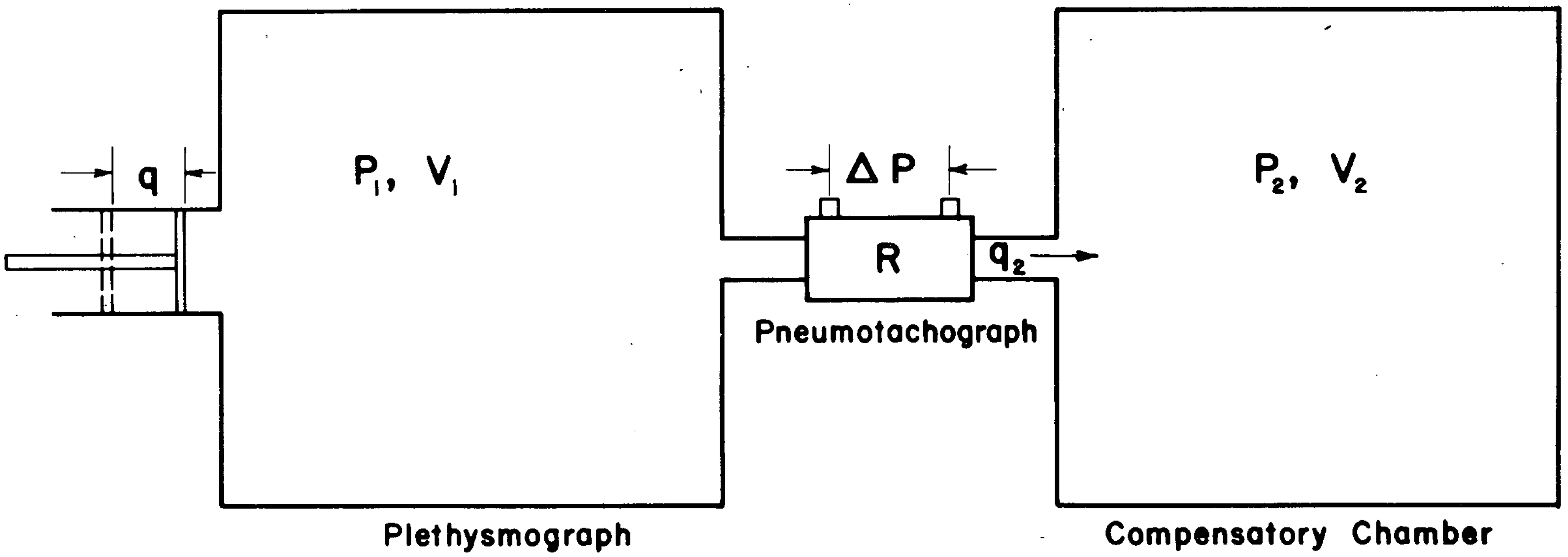


Fig. 10 Tidal Volume Response of the WEDGE Spirometer.



$$\Delta P_{max} = R \cdot \frac{q_m \omega}{2} \cdot \frac{V_2}{(V_1 + V_2)} \cdot \sin \omega t_m$$

Fig. 11 Schematic Representation of the Flethysmograph Chamber With the Pneumotachograph and Compensatory Chamber Attached.

obtained for ΔP:

$$\Delta P = P_1 - P_2 = P_o \left[\frac{q}{V_1} - q_2 \left(\frac{V_1 + V_2}{V_1 V_2}\right)\right]$$

where P_o = initial pressure

q = volume of air introduced into plethysmograph during time t.

q_2 = volume of air introduced into compensatory chamber during time t.

$q - q_2$ = volume of air remaining in plethysmograph during time t.

For an input flow rate that varies sinusoidally,

$$q = \frac{q_m}{2} (1 - \cos \omega t)$$

q_m = total input volume

$\omega = 2\pi f$

f = frequency

By definition, $\Delta P = R \frac{dq_2}{dt}$

From these relationships we obtain

$$\frac{dq_2}{dt} + a\, q_2 = b\,(1 - \cos \omega t) \qquad (3)$$

where $a = \frac{P_o(V_1 + V_2)}{R\, V_1\, V_2}$ and $b = \frac{P_o\, q_m}{2\, R\, V_1}$

The maximum flow rate $\left(\frac{dq_2}{dt}\right)_m$ occurs when $\frac{d^2 q_2}{dt^2} = 0$

$$\left(\frac{dq_2}{dt}\right)_m = \frac{q_m V_2 \omega}{2\,(V_1 + V_2)} \sin \omega\, t_m$$

where t_m = time at which $\left(\frac{dq_2}{dt}\right)_m$ occurs.

From this, the maximum pressure drop, ΔP_m is

$$\Delta P_m = R \; \frac{q_m \omega}{2} \; \frac{V_2}{(V_1 + V_2)} \; \sin \omega \, t_m \qquad (4)$$

It can be seen that there are four determinants of ΔP_m:

(a) R = resistance of the pneumotachograph

(b) $\frac{q_m \omega}{2} = F_m$ = maximum flow rate

(c) $\frac{V_2}{V_1 + V_2}$ = amplitude constant based on volumes V_1 and V_2

(d) $\sin \omega \, t_m$ = frequency factor

Determinants (a) and (b) are always present regardless of whether the pneumotachograph is connected directly to the subject or to a plethysmograph containing the subject's body. Determinant (c) is only important when the size of V_1 is significant in relation to the size of V_2. To determine when the frequency factor (d) is important, further information is required.

By solving (3), a value for q_2 is obtained:

$$q_2 = \frac{b}{a} \left(1 - \frac{\omega^2}{a^2 + \omega^2} \; e^{-at}\right) - \frac{b\omega}{a^2 + \omega^2} \sin \omega t - \frac{ab}{a^2 + \omega^2} \cos \omega t \qquad (5)$$

The constants $\underline{a}$ and $\underline{b}$ have the same values as those used in equation 3. Since t_m is the time at which ΔP_m occurs, the value of $\sin \omega \, t_m$ is defined by setting $\frac{d^2 q_2}{dt^2} = 0$.

$$\sin \omega \, t_m = \frac{a}{\omega} \left(e^{-at_m} - \cos \omega \, t_m \right)$$

For the present application ($f \leqq 60$ cycles/minute), the values of at_m can be made large enough so that

$$a^{-at_m} \approx 0 \text{ and } \sin \omega t_m = \frac{a}{\sqrt{a^2 + \omega^2}} \qquad (6)$$

The effect of frequency on the measured value of ΔP_m can be reduced or practically eliminated by making the value of $a >> \omega$ in which case the above expression for $\sin \omega t_m$ approaches 1.

Since $a = \frac{P_o (V_1 + V_2)}{R V_1 V_2}$, its value can be increased by decreasing the values of R, V_1 or V_2.

It should be noted that the value of ΔP_m is not affected by P_o except as P_o influences the frequency factor by being a part of the constant a. Since the normal operating condition is such that the frequency factor is eliminated, the value of ΔP_m for a given flow rate is not affected by daily variations in barometric pressure. This is in direct contrast to System I where the value of ΔP for a given tidal volume is directly proportional to P_o and can vary slightly from day-to-day.

The relationships derived above apply to changes occurring under isothermal conditions but experience has shown that the conditions in actual practice are more nearly adiabatic. Had adiabatic conditions been assumed, the relationships would be the same, but the values of the constants a and b would be increased by the factor $\gamma = 1.4$.

The developmental work reported here involved the simulation of a breathing dog through the use of a respiratory pump with an approximately sinusoidal flow output. From the preceding theory, it follows that for a given tidal volume, the peak flow rate (and ΔP_m) from the pump should be linearly related to the frequency of pumping when the value of a is made sufficiently large. The following sections describe the results obtained when the value of a was increased by independent adjustments in the magnitudes of V_1, R and V_2.

2. Effect of V_1

The first series of experiments was conducted with one end of the pneumotachograph connected to the plethysmograph V_1, and the other end open to the room volume ($V_2 \approx \infty$). Values of the pressure drop, ΔP, across the pneumotachograph corresponding to the peak unidirectional flow rate from the plethysmograph were measured for a constant pump tidal volume moved at frequencies of 4 to 58 cycles per minute for values of V_1 from 220 to 0.035 liters. The serious non-linearity obtained initially with this system when $V_1 = 220$ liters is shown in Figure 12. The results obtained became progressively more linear as the value of a was increased by reducing V_1 in successive steps while the values of V_2 and R were held constant. Linearity was not achieved until $V_1 \approx 0$. Since V_1 must have some finite value to be of use as a plethysmograph, it is apparent that although an adjustment in V_1 can improve the linearity of response somewhat, it is not an adequate answer to the problem.

3. Effect of R

A second approach to increasing the value of a was to decrease the resistance R to air flow from the plethysmograph. One manner in which this could be accomplished would be to construct a special pneumotachograph having a very low resistance to air flow. However, it was felt that this could be accomplished with the pneumotachograph on hand by adding a second linear resistance in parallel with the Vol-O-Flo pneumotachograph used originally. As long as the frequency characteristics of both resistances remain equal, the same fraction of the total air moved should pass through the Vol-O-Flo pneumotachograph each time. As initial choices for linear parallel leak paths, two other pneumotachographs were used, one of the Fleisch variety (Instrumentation Associates, Inc., New York, New York) and one made locally from 400 mesh Monel wire screen. The Vol-O-Flo has a total $R = 10 \times 10^{-3}$ inches H_2O/lpm whereas the resistances of the Fleisch and the wire-screen devices are approximately 2.3×10^{-3} inches H_2O/lpm and 1.6×10^{-3} inches H_2O/lpm respectively.

The values of ΔP shown in Figure 13 were measured with the

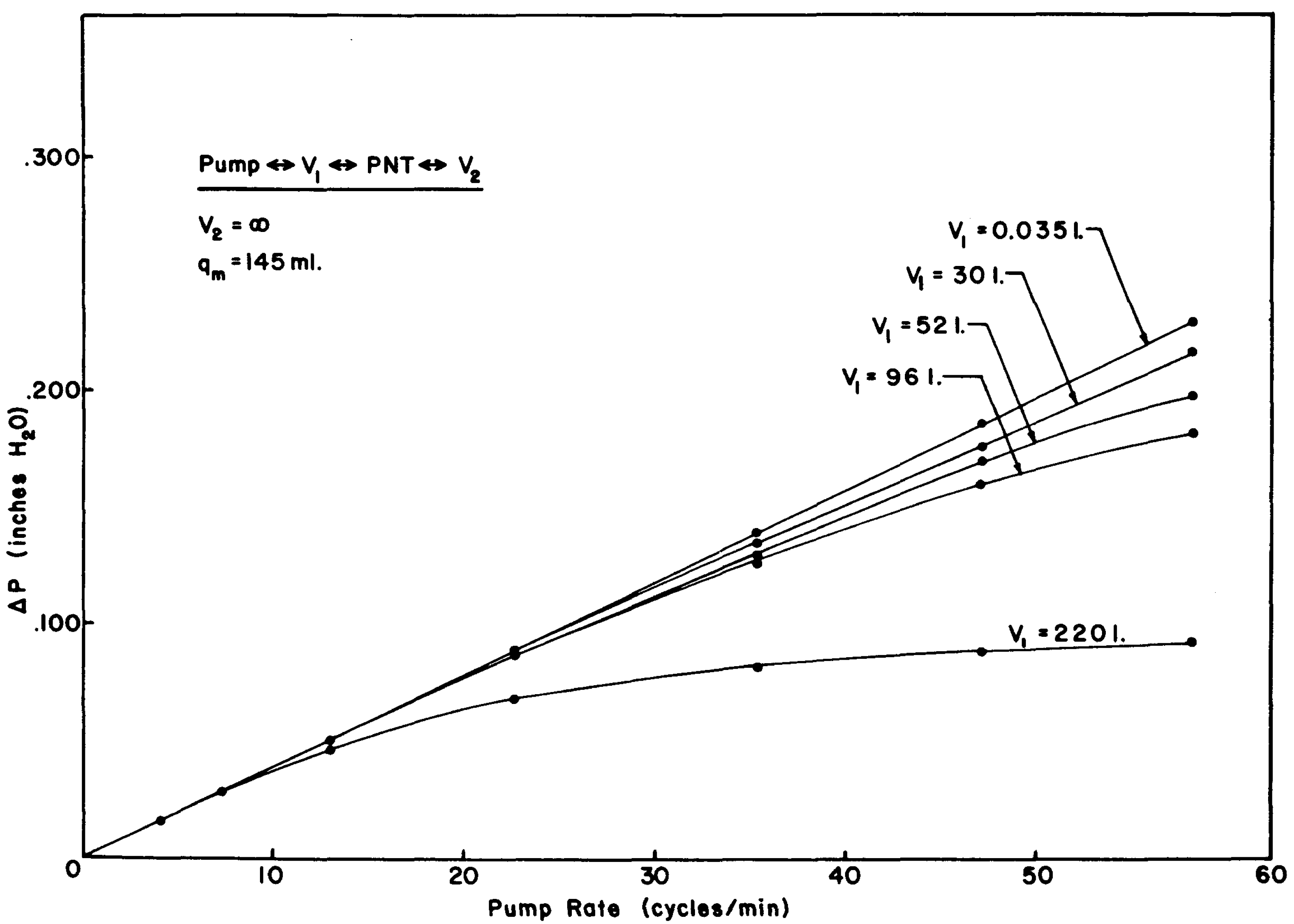


Fig. 12 The Effect of V_1 on the Frequency Response of the Pneumotachograph System.

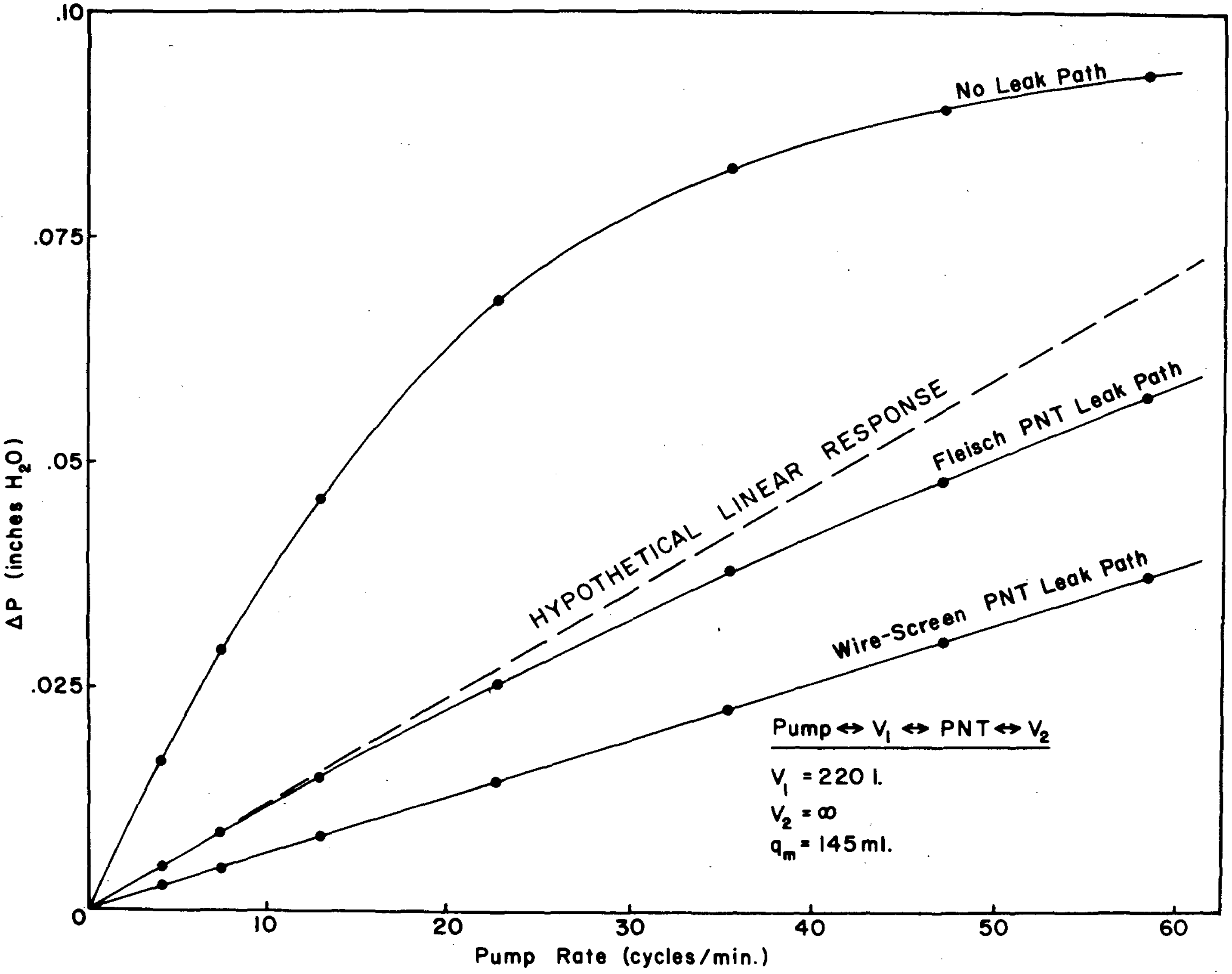


Fig. 13 The Effect on Frequency Response Caused by Reducing R by Adding Other Pneumotachographs in Parallel With the Vol-O-Flo Pneumotachograph.

Vol-O-Flo pneumotachograph. When no leak path was present, the same non-linearity was obtained as was shown in Figure 12. When the Fleisch pneumotachograph was added as a parallel leak path from the chamber, the amplitude of ΔP measured with the Vol-O-Flo was decreased but the linearity of response was greatly improved. Decreasing the value of R still further by using the wire-screen pneumotachograph again decreased the measured amplitude but a linear response was obtained over the frequency range of interest.

Based on the success of this test, an attempt was made to produce a substitute leak path that would be equal in performance to the wire-screen pneumotachograph but less expensive to manufacture. Various numbers of layers of fiberglass filter material were placed in a piece of 2-inch I. D. copper tubing and this was then used as a leak path. The results in Figure 14 show that with 8 or 10 layers of fiberglass the total resistance of this system was still too high and some non-linearity occurred. When the resistance was reduced by using only 6 layers of fiberglass, linear results were obtained. Further reduction in the number of layers of fiberglass caused a sag in the response curve at low frequencies, presumably due to some difference in frequency characteristics between the two resistive elements. These results indicate that the manufacture of a suitable leak path involves a certain amount of trial and error experimentation. If the resistance of the leak path is too high, drop-off in response at higher frequencies can occur, whereas if too little resistance is used, other frequency effects can occur. Thus, one must be very careful if this system is used to obtain linear results. In addition to being dependent on the number of layers of fiberglass, the resistance is, of course, also dependent on the amount of compression to which these layers are subjected. If replacement of one of these leak paths should ever be necessary, a considerable amount of time would be required to obtain another with similar characteristics.

The methods utilizing reduction of V_1 and R both have a basic fault in that one end of the pneumotachograph is open to room atmosphere, with its constant small changes in pressure. Under these

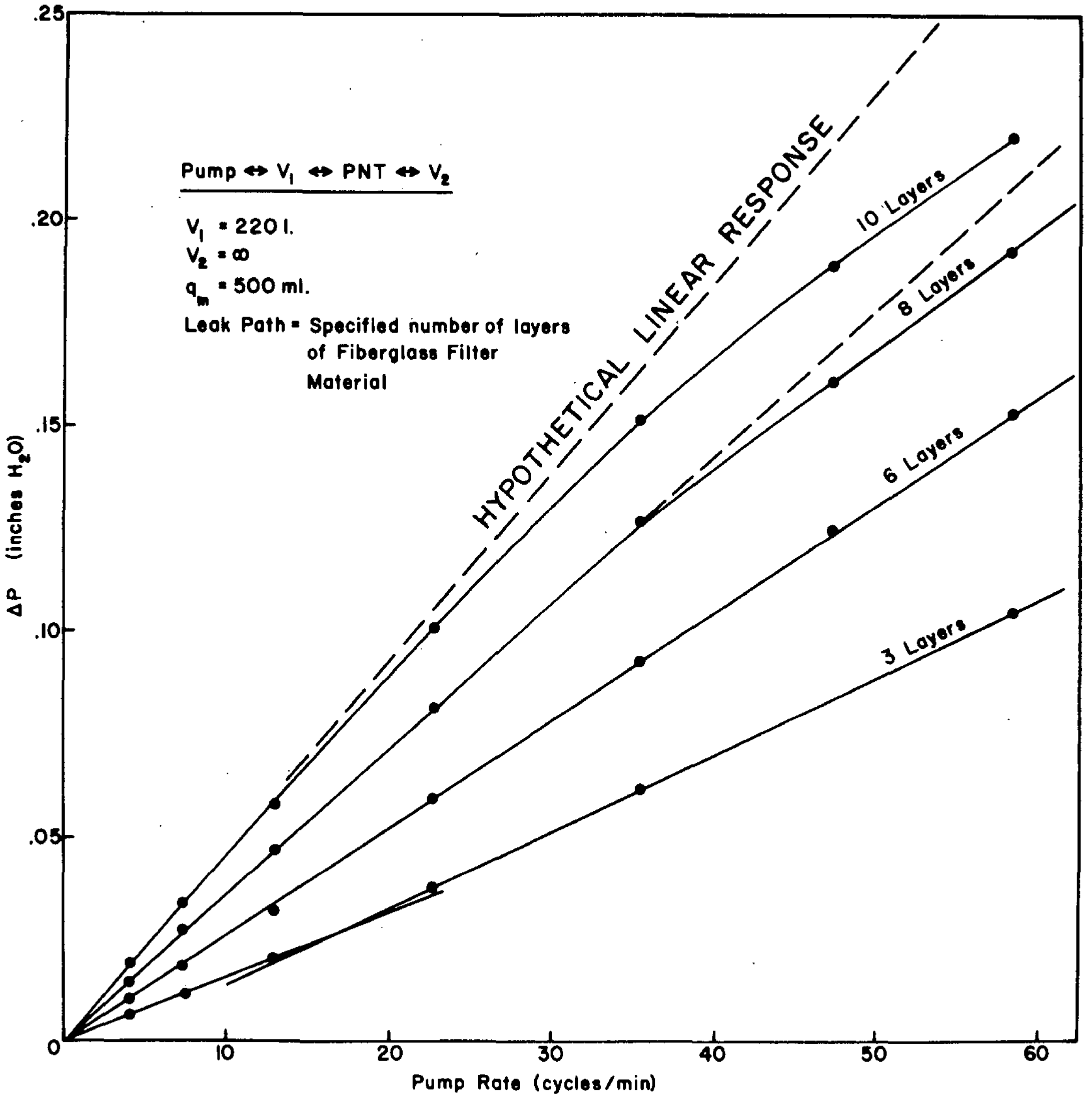


Fig. 14 Frequency Response Obtained When Using a Parallel Leak Path Containing Different Numbers of Layers of Fiberglass Filter Material.

conditions, a very erratic zero flow trace is obtained which becomes superimposed on the flow signals desired and can lead to considerable distortion. Another problem with using this system for an aerosol exposure apparatus is that with the pneumotachograph open to room atmosphere, the only barrier between the contaminated air in the aerosol exposure chamber and the room atmosphere is the rubber seal around the dog's nose described on page 38. Although this is designed as an air-tight seal, no margin of safety would be provided should a leak occur. For both of the above reasons, a completely sealed system is preferable. The following section describes the investigation of a system where V_2 is changed from an $\approx \infty$ volume to an enclosed volume of finite size.

4. Effect of V_2

The effect of V_2 was examined by maintaining V_1 at a value of 220 liters and using the Vol-O-Flo pneumotachograph without an auxiliary leak path. An empty 96-liter chamber was connected to the other end of the Vol-O-Flo pneumotachograph to serve as V_2. Once results had been obtained with $V_2 = 96$ liters, measured amounts of water were added to the chamber in order to decrease the air volume in the chamber, V_2, by known amounts. Representative data are plotted in Figure 15. As the size of V_2 was progressively decreased, the results became more nearly linear until at $V_2 = 36$ liters, linearity was achieved. Further reduction in V_2 resulted in a loss of amplitude but not in linearity. From the mathematics presented earlier, it can be shown that the range over which linearity is obtained increases with a decrease of V_2. However, there is a practical limit on the decrease in V_2 and that is the sensitivity with which ΔP can be measured since this also decreases with decreased V_2. For the present application, it has been found that a value of $V_2 =$ 25 liters produces signals that are easily measurable with the Statham PM 197 transducer.

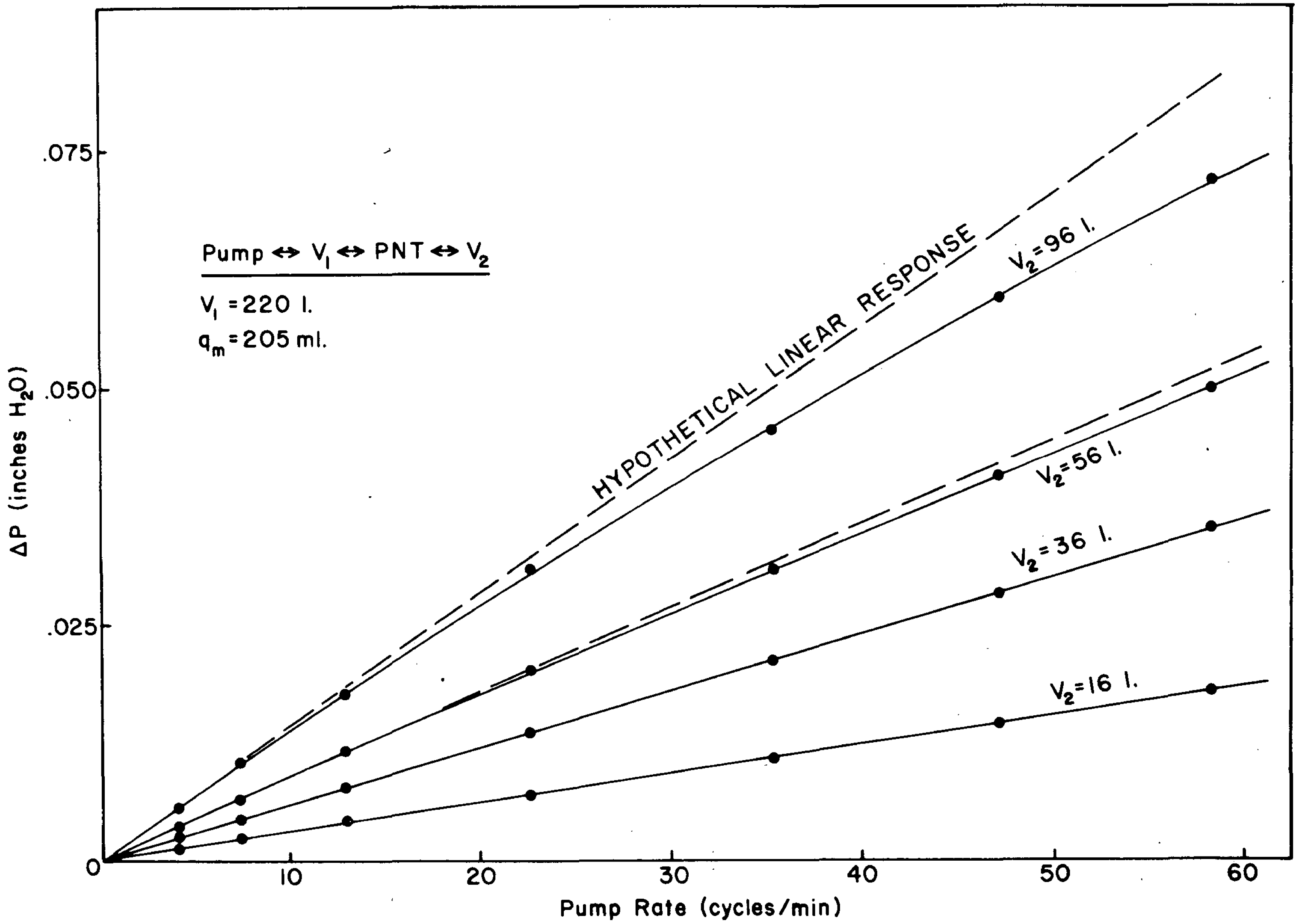


Fig. 15 The Effect of V_2 on the Frequency Response of the Pneumotachograph System.

FINAL DESIGN AND CALIBRATION

Results of the performance of 3 systems have been presented. Since System II never performed satisfactorily, the final choice for use with the exposure plethysmograph was between Systems I and III. System III was chosen because it was a sealed system that was not significantly affected by temperature or changes in laboratory pressure and because flow rate information could be easily obtained in addition to tidal volume and respiratory frequency data. The following information relates how System III was incorporated into the design of the exposure apparatus.

Adjustment of V_2 proved to be quite satisfactory for producing a linear response in System III over the frequency range of interest (< 60 cycles/minute) and no attempt was made to include an adjustment of R in the final design. Values of $V_1 = 149$ liters and $V_2 = 25$ liters were chosen for the final system. Figure 16 shows the relationship of these two chambers to the dry box containing the aerosol exposure apparatus and the transfer box used for moving the shielded aerosol generator assembly from the isotope preparation area to the exposure room. The pneumotachograph can be seen in the tubing connecting V_1 and V_2. A gate valve has been inserted on the plethysmograph side of the pneumotachograph so that the pneumotachograph can be isolated from the plethysmograph to obtain a zero flow signal even with a dog in the plethysmograph.

The walls of the plethysmograph were constructed from 3/8-inch thick Plexiglas. With this construction, the zero flow trace obtained with the valve open was more erratic than with the valve closed even though the other openings in the plethysmograph were sealed. Apparently changes in the ambient pressure in the exposure room caused the chamber walls to move in and out slightly which, in turn, moved air through the pneumotachograph. To minimize this problem, a horizontal and vertical brace was added to each side wall as can be seen in Figure 16. This added chamber rigidity also increased the magnitude of the observed values of ΔP by approximately 10 per cent.

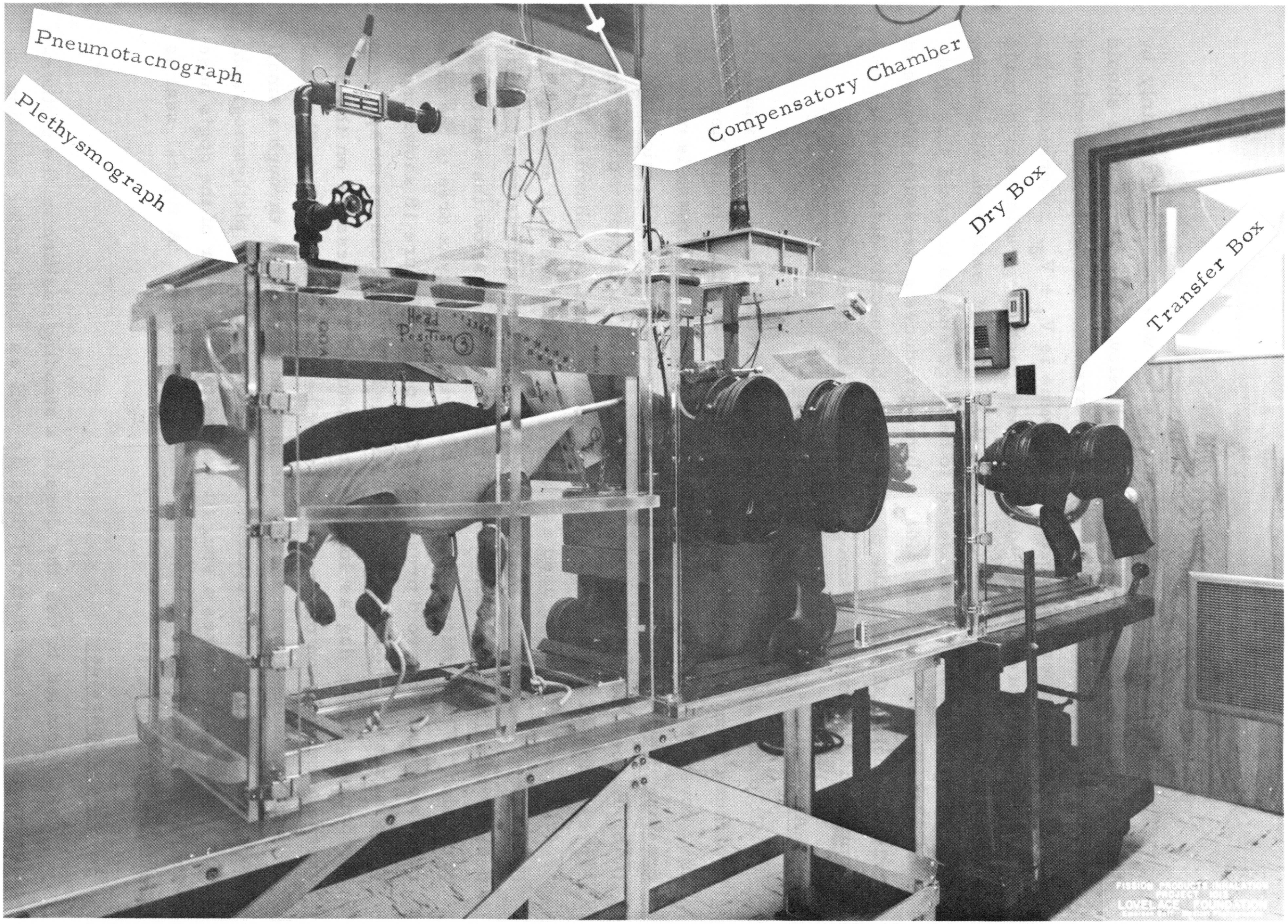


Fig. 16 General View of the Entire Exposure Apparatus With a Dog in Position in the Plethysmograph. The Compensatory Chamber, V_2, is Directly Above the Plethysmograph.

The size of the plethysmograph chamber was determined mainly by the size of the sling apparatus described below. However, one should also remember that with this particular system, the animal is enclosed in a sealed chamber whose effective volume is $V_1 + V_2$. Consequently, there is an overpressure produced during each inspiration which could alter the animal's breathing pattern if it were of sufficient magnitude. The present system is considered to be large enough to avoid this problem since a 200 milliliter tidal volume produces a pressure change of only 0. 5 inch H_2O within the plethysmograph. Specific details on several components of this plethysmograph system are given below.

A. Air Seal

To obtain an air seal around the dog's nose at the point at which it protrudes from the plethysmograph, its nose and part of its head are first covered with a specially made latex mask. This mask is made by brushing 3 or 4 coats of Lotol liquid latex (Naugatuck Chemical Div., U. S. Rubber Co., Naugatuck, Conn.) on a hand carved wooden form representing an average beagle's nose dimensions, as shown in Figure 17. Gauze strips to be used as ties for the mask, are also embedded in the rubber. After the mask is dry, it is coated with talcum powder, peeled from the mold, and a small hole is made to allow the nostrils to protrude. The portion of the mask covering the larynx area of the neck is also cut away to avoid pressure at this point. Figure 18 shows one of these masks as it looks in place on a dog. This mask causes no apparent discomfort to the dog as long as it produces no pressure on the soft cartilaginous portion of the nose directly behind the nostrils. The final air seal is obtained by inserting the masked dog's nose through a small hole in a sheet of rubber attached to the front wall of the plethysmograph. The rubber sheet makes a snug fit around the posterior of the dog's nose and a good rubber-to-rubber air seal is obtained. A typical seal is pictured in Figure 19.

B. Sling Apparatus

It was decided to use the dogs in a standing position in the plethysmograph. Unanesthetized dogs as well as those under sedation or

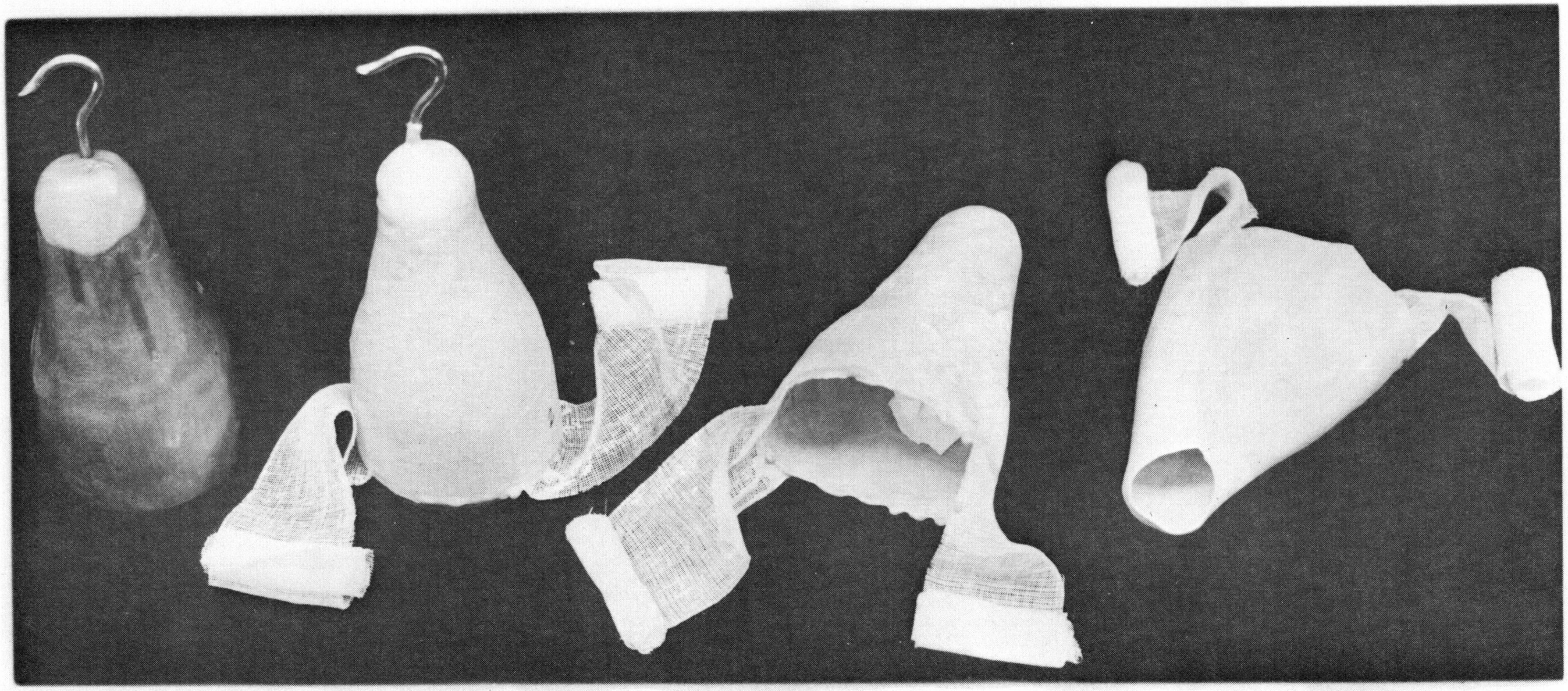


Fig. 17 Steps in the Construction of Molded Latex Masks. Mold at Left Was Carved From Balsa Wood and Coated With Several Coats of Spar Varnish Prior to Use.

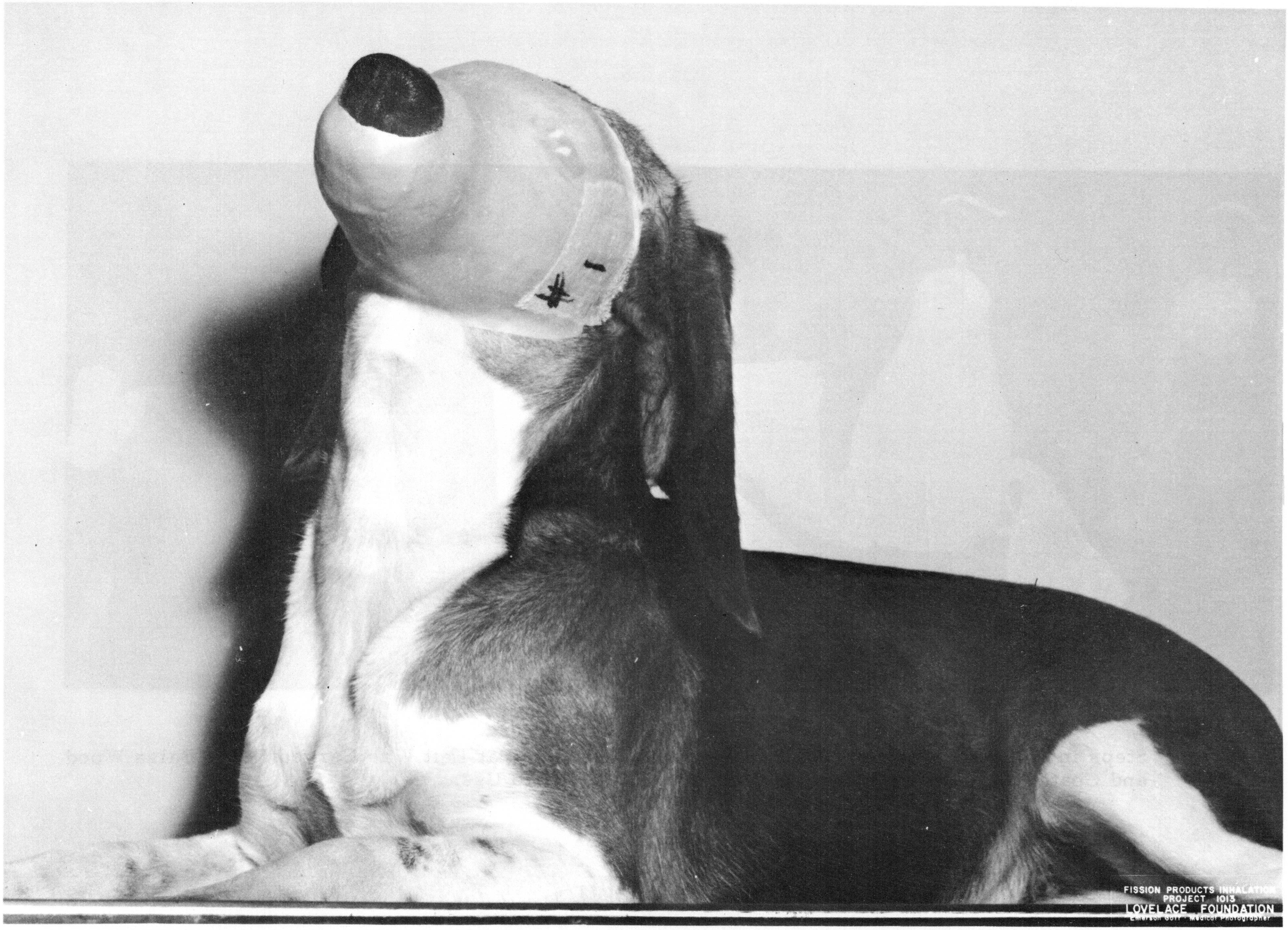
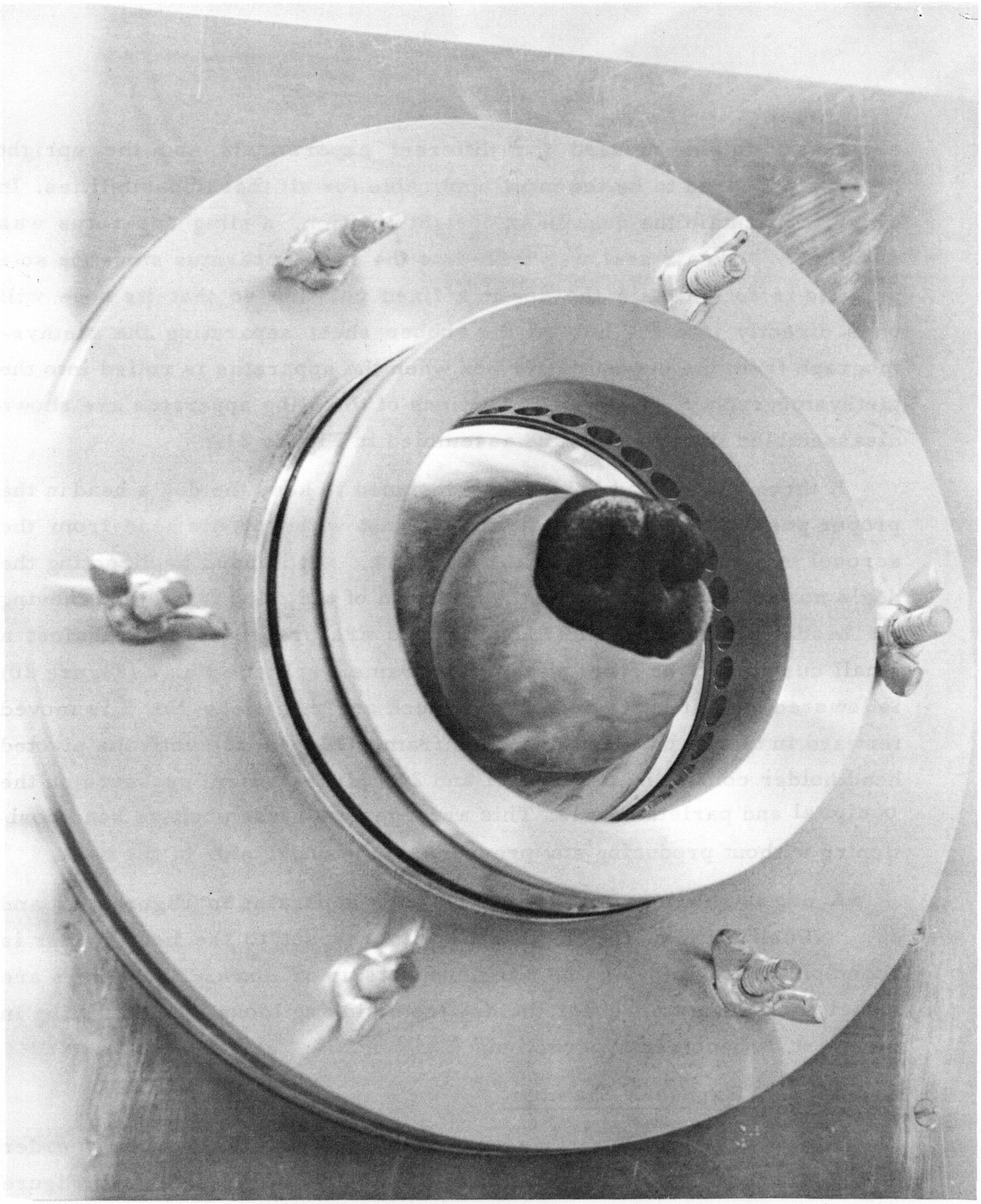


Fig. 18 Latex Mask as it Looks in Place on a Dog.



'ig. 19 Close-Up View of the Dog's Nose in the Exposure Position With the Conical Exposure Chamber Removed. Note the Rubber Air Seal Around the Posterior of the Dog's Nose and the Circle of Holes Which, in Turn, Are Connected to the Overflow Filter System.

anesthesia might be used for different experiments and the upright position appeared to be the most applicable for all these possibilities. In order to maintain the dogs in an upright position, a sling apparatus was designed. No air seal was built into the sling apparatus since its sole purpose is to maintain the dog in a fixed position so that its nose will pass directly into the hole in the rubber sheet separating the plethysmograph from the exposure dry box when the apparatus is rolled into the plethysmograph. The various portions of the sling apparatus are shown disassembled in Figure 20 and assembled in Figure 21.

A three-piece head holder was designed to keep the dog's head in the proper position and insure that he could not withdraw his head from the aerosol exposure chamber during exposure. It is used by directing the dog's nose through the hole in the front end of the sling frame and moving the head forward until the frontal bones are pressed firmly against a small cushion on the front plate of the frame. Piece No. 2 (Figure 20) is lowered until it rests on the dog's neck and then piece No. 3 is moved forward in tracks built into the sling frame (Figure 21) until the pivoted head holder consisting of pieces 1 and 2 produces a firm pressure on the occipital and parietal bones. This arrangement gives positive head positioning without producing any pressure on the under side of the neck.

A dog is shown in position in the sling apparatus in Figures 22 and 23. Positioning of the dog's body with respect to the head holder is accomplished by moving the sling supports up or down. The legs are loosely tied down to prevent the dog from kicking loose from the sling in the event he becomes hyperactive.

C. Aerosol Exposure Chamber

The gloves and glove rings were removed from the dry box in order that a clearer view of the aerosol system could be presented in Figure 24. The aerosol generator and overflow filters are enclosed in the lead shield which has wheels for movement into the transfer box. Immediately above the aerosol generator is a cylindrical mixing chamber which is connected to the conical exposure chamber shown in position over the

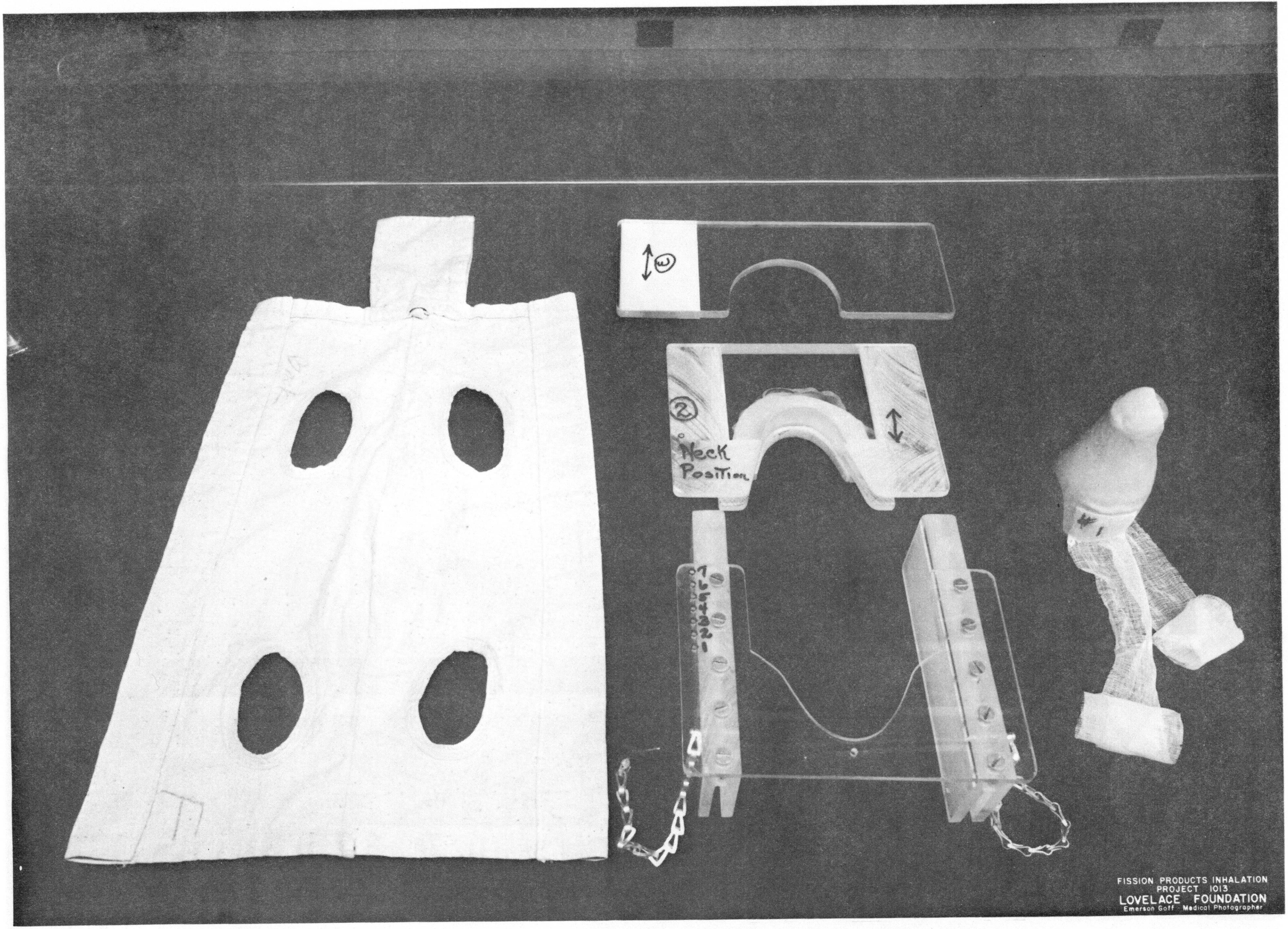


Fig. 20 Disassembled Components of the Sling Apparatus.

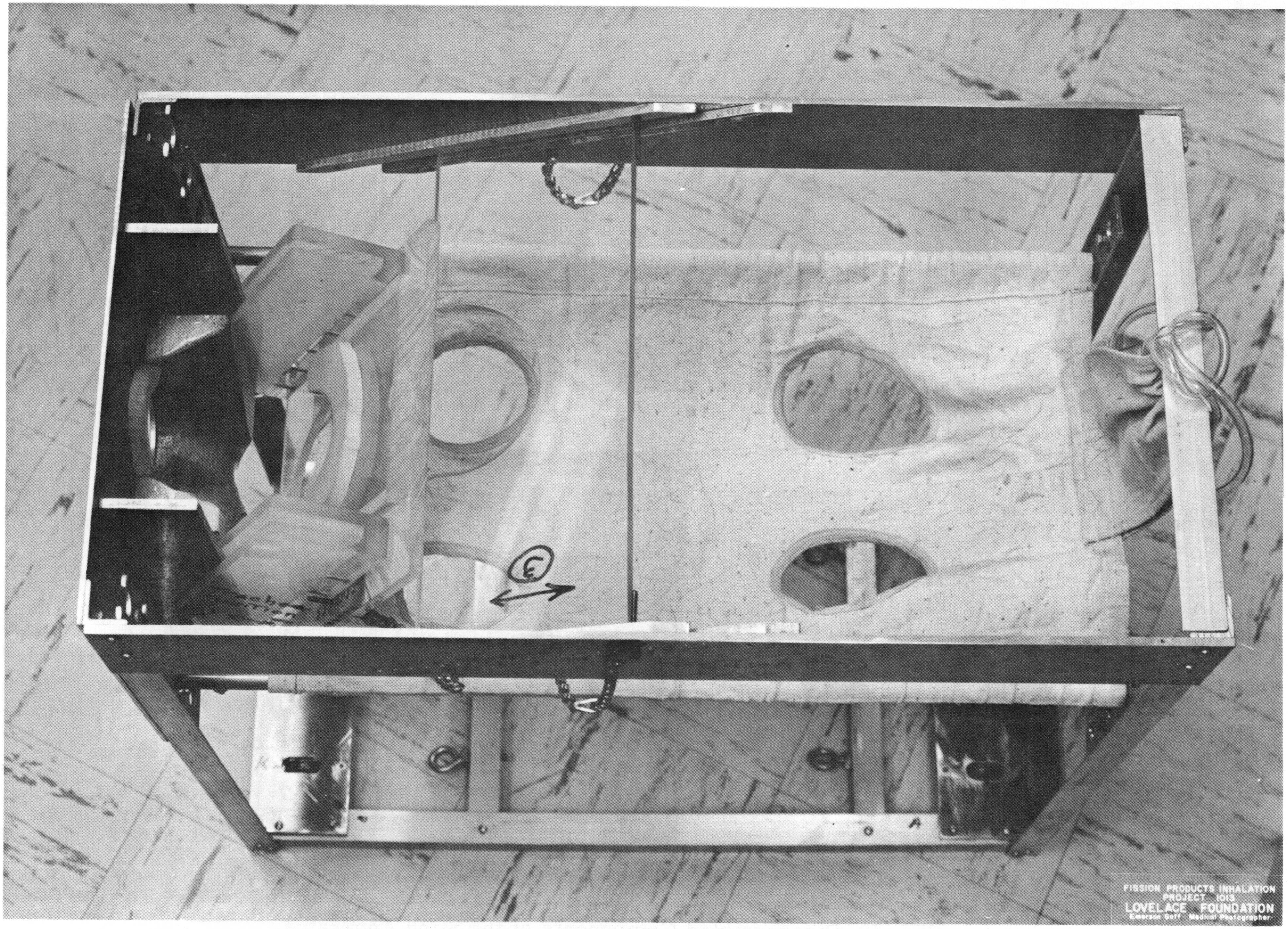


Fig. 21 Assembled Sling Apparatus With Adjustable Head Holder in Place.

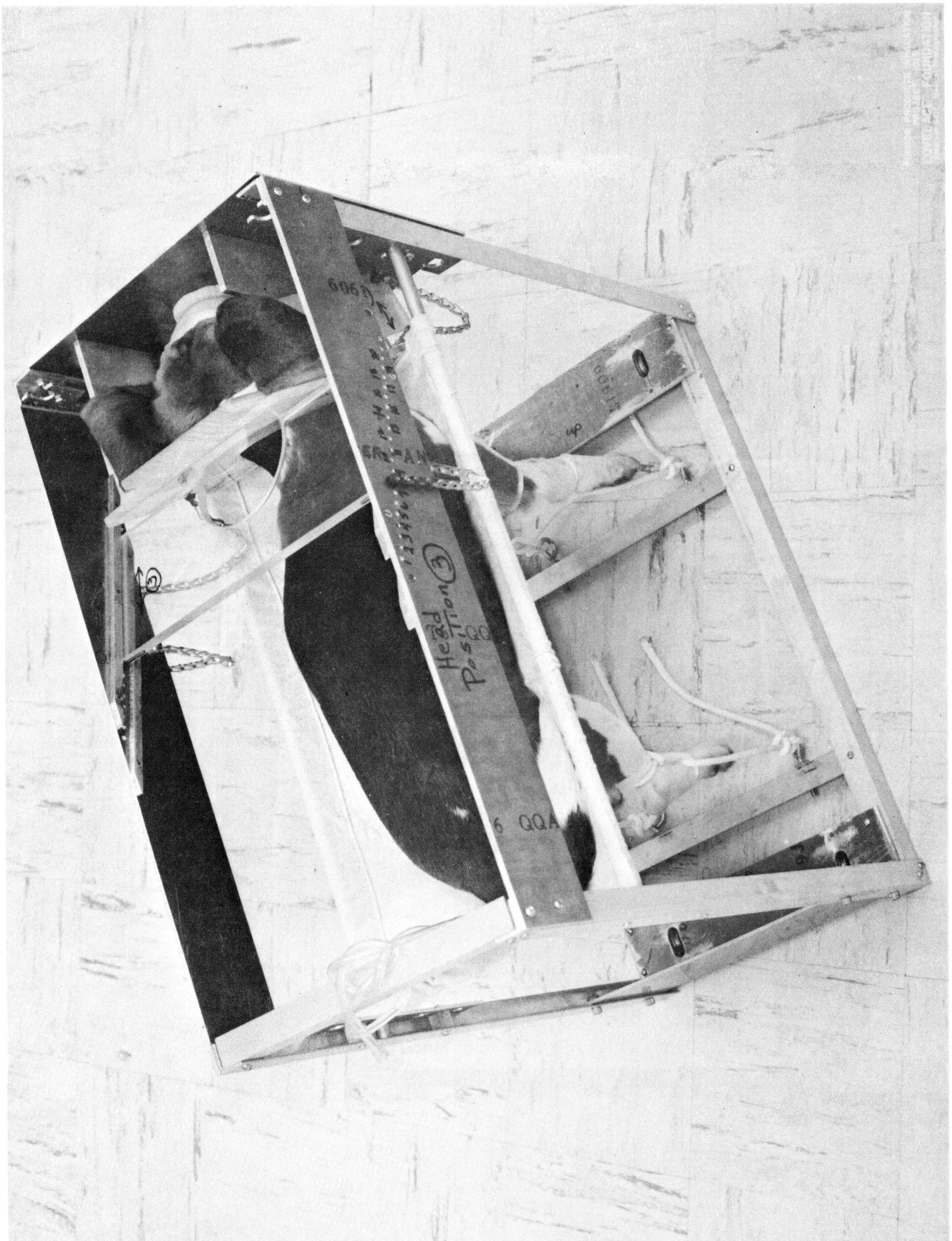


Fig. 22 Rear View of a Dog in Position in the Sling Apparatus.

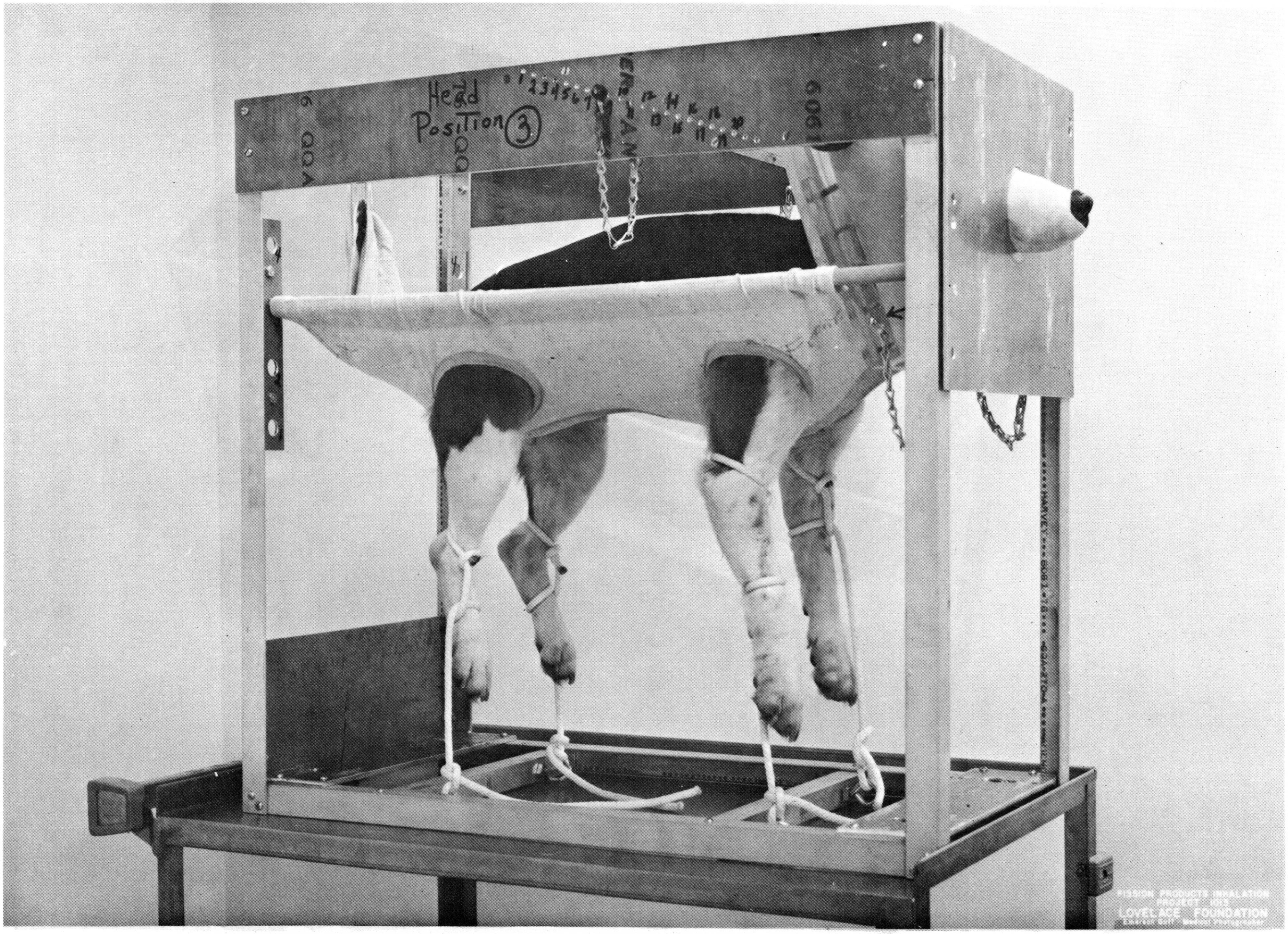


Fig. 23 Front View of a Dog in Position in the Sling Apparatus.

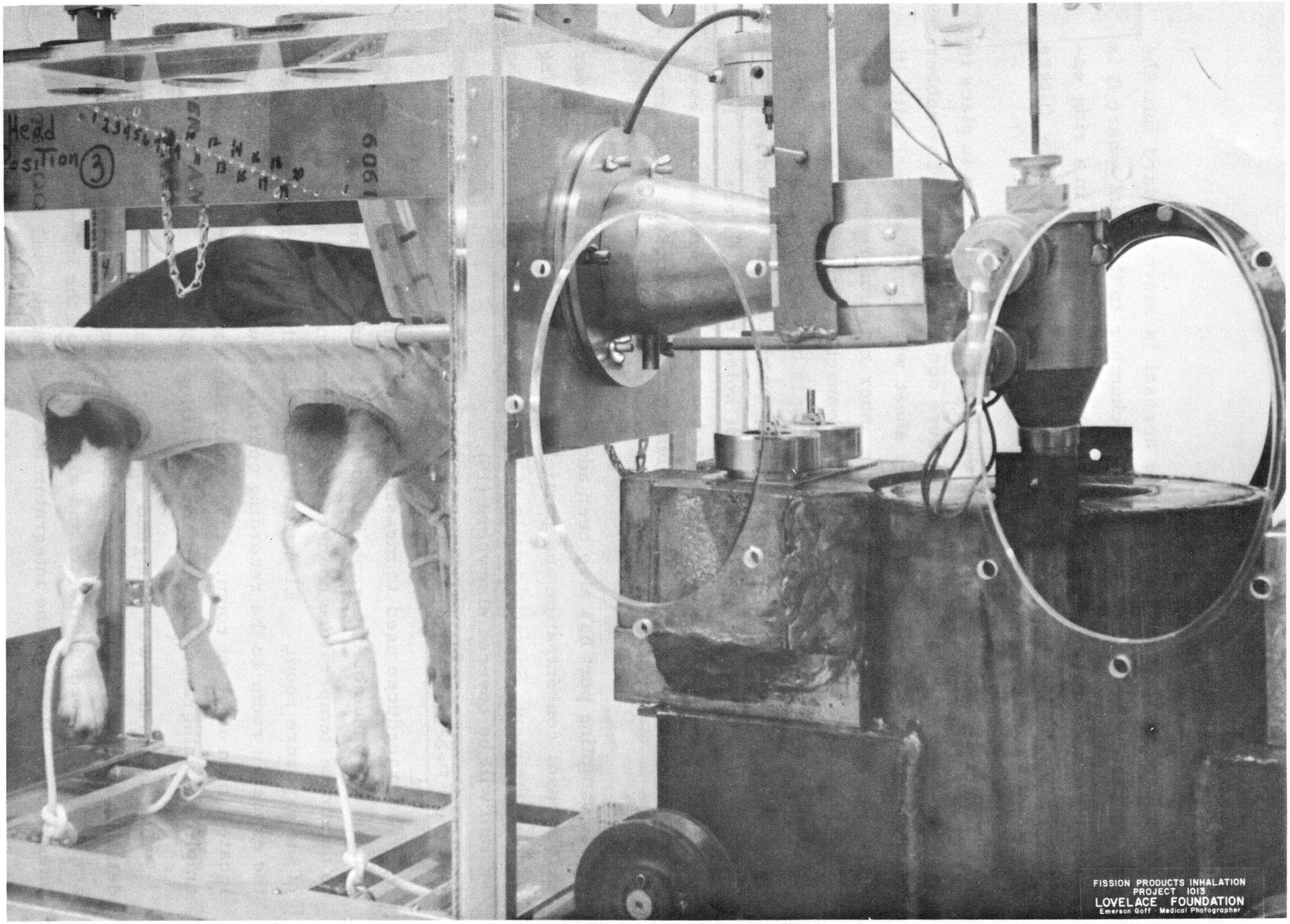


Fig. 24 A View of the Aerosol System With the Exposure Chamber in Place over the Dog's Nose. The Tubing Used to Connect the Exposure Chamber With the Overflow Filters Situated in the Shield is not Present in this Picture.

dog's nose. After production, the aerosol is moved upward into the mixing chamber and down the exposure chamber to the point where it is continuously drawn off through a series of holes located in a ring encircling the posterior portion of the dog's nose into two overflow filters for removal of any remaining aerosol.

Figure 19 shows a close-up of the dog's nose as it looks in place in the exposure apparatus with the exposure cone removed. The rubber mask is visible as well as the rubber sheet which makes a seal with it. Note the series of holes around the inner circumference of the ring behind the dog's nose which, in turn, is connected to the overflow vacuum system. With this arrangement, the dog is constantly exposed to fresh aerosol since the latter is continuously produced and moved past the dog's nose and out through the series of holes to the filters. In the present design, 37 liters of contaminated air pass through the cone every minute of exposure. To date, the length of each exposure has been 10 minutes.

A sampling port has also been added to the mixing chamber in order that aerosol concentration and particle size data can be obtained during each experiment. Specific details of the aerosol generating and sampling system will be covered elsewhere (19).

D. Data Procurement Apparatus

The transducer used to measure the differential pressure developed across the pneumotachograph has been enclosed in a small wooden box to minimize temperature changes and is shock-mounted near the ceiling of the exposure room. Electrical leads from the transducer pass from the exposure room to the recording console shown in Figure 25 which is located in an adjacent room. The recording console contains a carrier amplifier, integrator and Visicorder oscillograph.

The integrator was designed and built locally and is described in detail in another report (20). The flow signal emerging from the carrier amplifier is recorded directly and also serves as the input signal to the integrator. Drift in the integrator has been minimized by including a

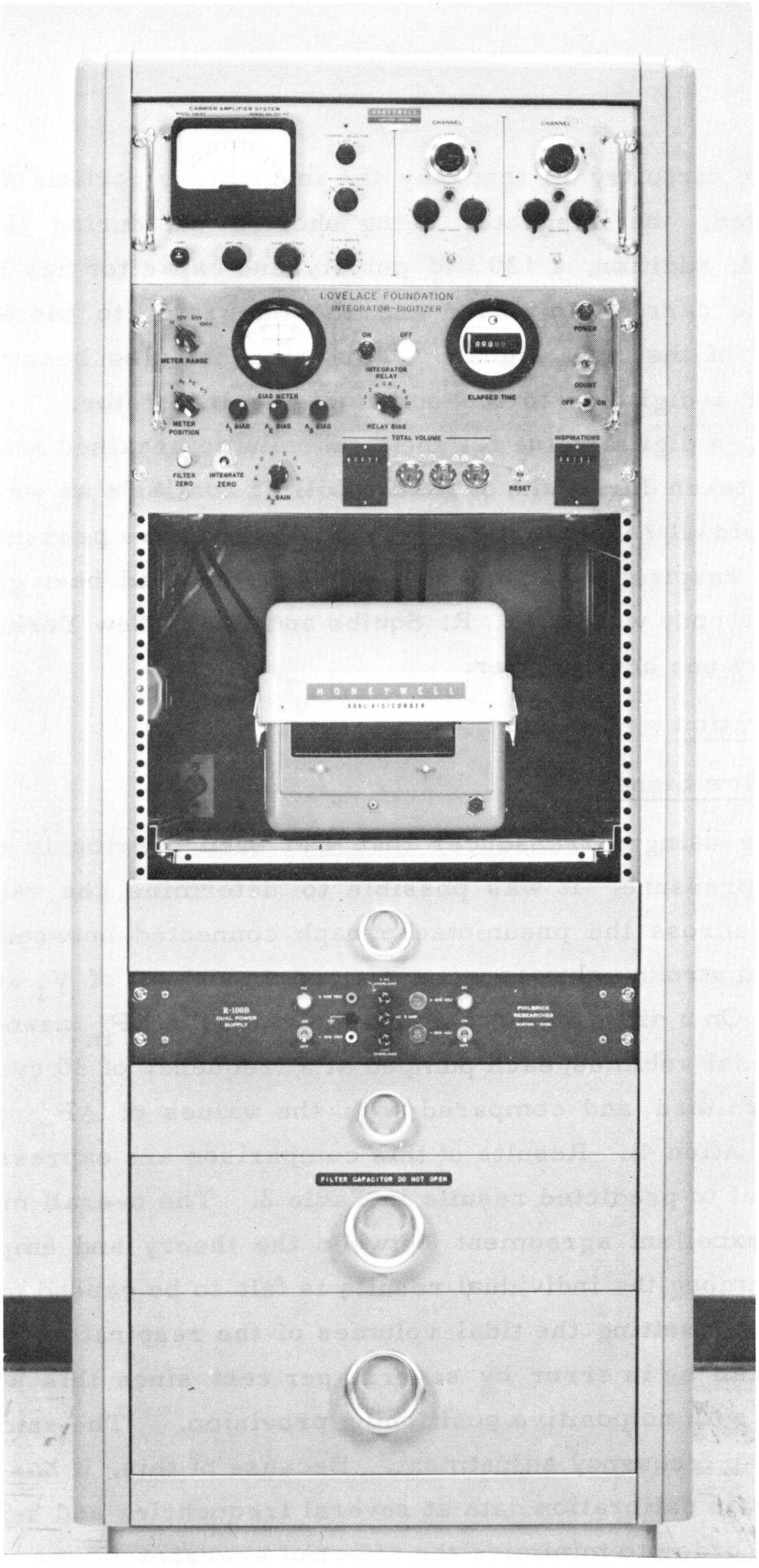


Fig. 25 Instrumentation Console Containing Carrier Amplifier, Integrator and Visicorder Oscillograph.

relay in the circuitry so that only the inspiratory portion of each breath is integrated, the integrator being shorted out during the expiratory portion. In addition, a 120 μfd polystyrene capacitor has been inserted between the carrier amplifier and the integrator to block out any dc component of the input signal. Provision has also been made for the addition of a digitizer to the output of the integrator. When this is completed, a digital value for the total volume breathed and the number of breaths taken during the exposure will be available as well as tracings of the individual respirations. Typical traces are presented in Figure 26 for the respiratory pump and for a dog that had been given 0.25 mg Vetame/lb. body weight (E. R. Squibb and Sons, New York, N. Y.) approximately one hour earlier.

E. Calibration

1. Flow Signal

By using a transducer that had been previously calibrated in terms of pressure, it was possible to determine the values of ΔP_m developed across the pneumotachograph connected between V_1 and V_2 when known stroke volumes were pumped in and out of V_1 at known frequencies. On 3 different occasions, the values of ΔP_m associated with 6 different tidal volumes, each pumped at a frequency of 20 cycles/minute, were determined and compared with the values of ΔP_m predicted by theory (Equation 4). Results of this comparison are expressed as ratios of empirical to predicted results in Table 2. The overall mean of 0.996 indicates excellent agreement between the theory and empirical data. Variation among the individual results is felt to be caused mainly by the uncertainty in setting the tidal volumes of the respiratory pump. Any one value can be in error by several per cent since this adjustment is continuous with no positive positioning provision. The same holds true for the pump frequency adjustment. Because of this, it has been necessary to obtain calibration data at several frequencies and several stroke volumes in order to minimize the effect of aberrant values.

Once it had been determined that the values of ΔP_m obtained were in

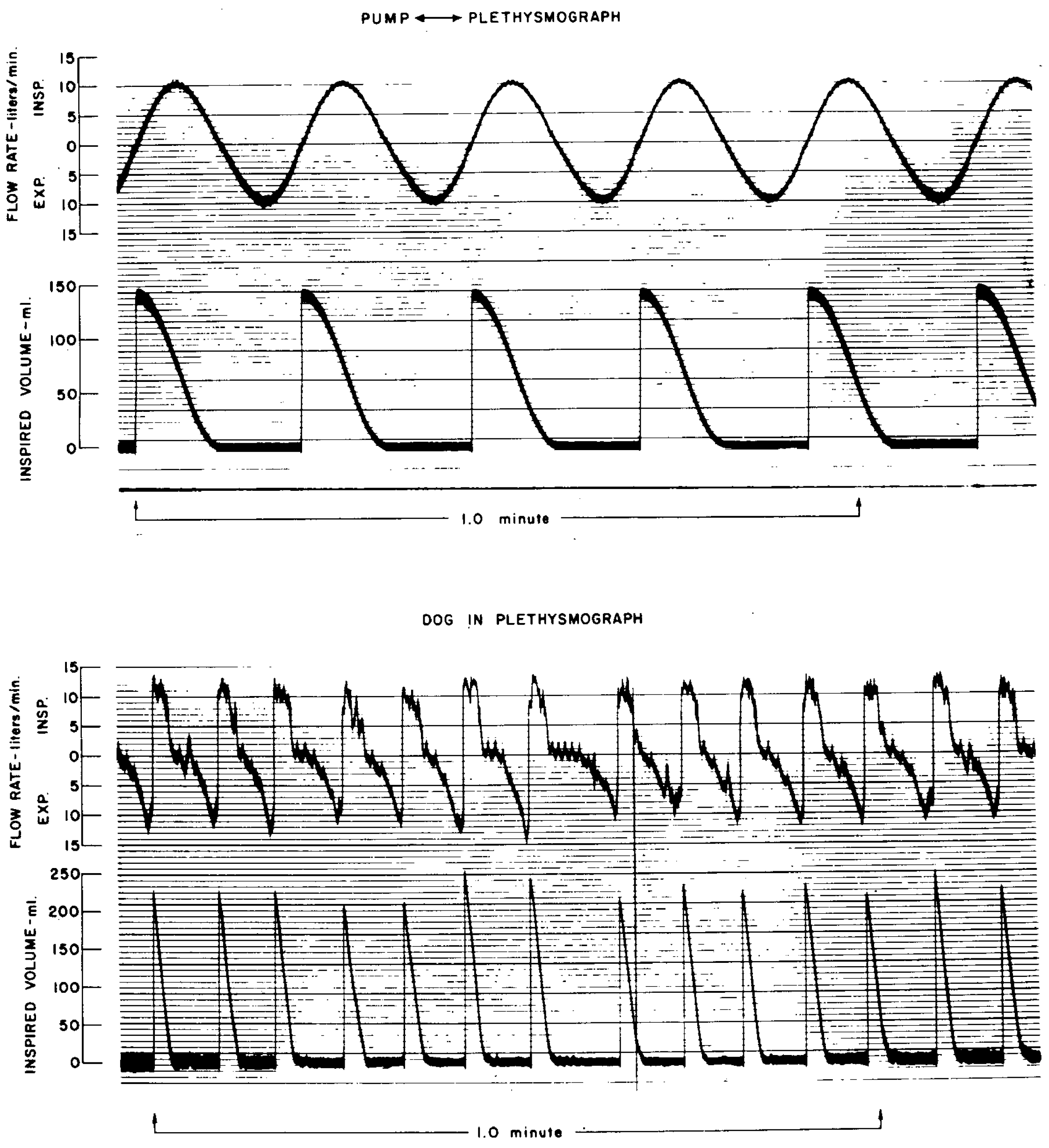


Fig. 26 Typical Records of Flow Rate and Tidal Volume Obtained With the Respiratory Pump and With a Dog.

TABLE 2

COMPARISON OF EMPIRICAL VALUES OF ΔP_m WITH THOSE PREDICTED BY EQUATION 4.

Tidal Volume - ml.	Ratio of Empirical to Theoretical Values		
	A	B	C
80	0.95	1.15	0.90
145	0.93	1.04	0.95
205	0.99	1.03	0.97
265	0.99	1.02	0.99
320	1.00	1.04	0.97
380	1.00	1.00	1.00

A, B & C indicate different series of experiments
Overall mean ratio = 0.996

agreement with those predicted by theory, a flow calibration was obtained that made it possible to convert recorder deflection to flow rate directly without intermediate conversion to pressure units. The pneumotachograph was first calibrated for unidirectional flow response and then used to calibrate the peak flow rates produced by the respiratory pump. By pumping known volumes directly in and out of the pneumotachograph at different frequencies, it was possible to obtain values of peak flow rate per cycle per minute (lpm/cpm) for each tidal volume used. After the pump was calibrated in this manner, it was connected to the plethysmograph chamber, V_1, and the pneumotachograph was inserted into the tubing connecting V_1 and V_2. The same values of tidal volume that were used to calibrate the pump were used to calibrate the plethysmograph. For each of these tidal volumes, the peak recorder deflection corresponding to the peak unidirectional flow through the pneumotachograph was obtained for 7 different pumping frequencies between 4 and 52 rpm. For each tidal volume used, a linear relationship between frequency and deflection was obtained, the slope of which yielded a value of mm deflection/cpm. The calibration factor was then calculated from any pair of values obtained with the same tidal volume:

$$\text{Calibration Factor} = \frac{\text{Pump Calibration (lpm/cpm)}}{\text{System Response (mm/cpm)}} = \text{lpm/mm.}$$

Five different tidal volumes were used on each of 4 different days to obtain the 20 values of the flow calibration factor given in Table 3. An analysis of variance at the 0.05 level of significance indicated that there were no significant differences between the results obtained on different days or between the results obtained with the 5 tidal volumes used. Thus, the flow signal response has been found to be free from any spurious frequency or volume effects in the range of interest.

2. Volume Signal

The volume signal from the integrator was calibrated by plotting recorder deflection versus pump tidal volume as shown in Figure 27. It can be seen that the response of the volume system is also linear indicating that the calibration factor obtained from the slope of the line

TABLE 3

PLETHYSMOGRAPH FLOW SIGNAL CALIBRATION FACTOR.

	lpm/mm			
Tidal Volume - ml.	A	B	C	D
80	0.512	0.512	0.502	0.522
145	0.518	0.496	0.508	0.507
205	0.503	0.495	0.503	0.499
265	0.497	0.500	0.503	0.503
320	0.498	0.503	0.505	0.495

A, B, C & D indicate experiments on different days.

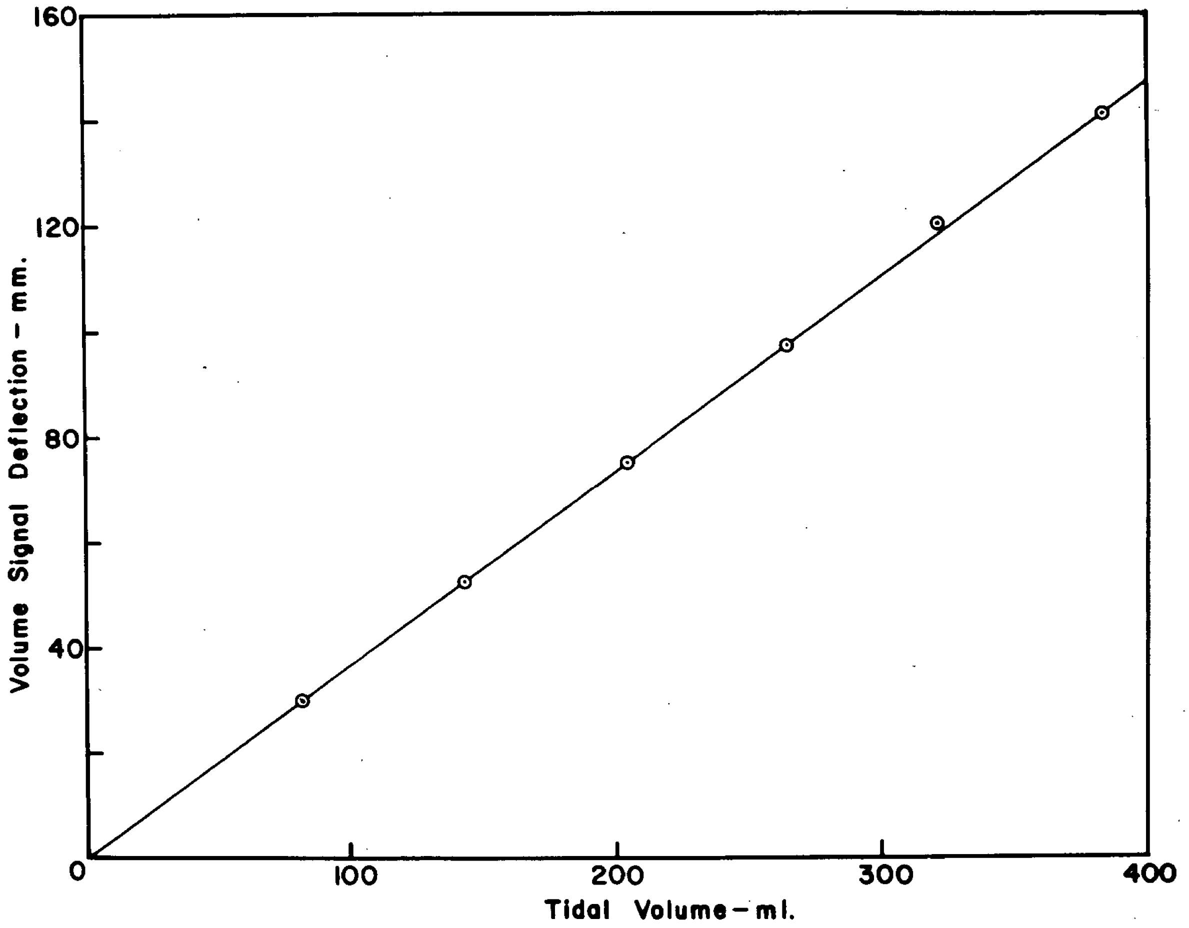


Fig. 27 A Typical Calibration Curve for the Volume Signal. (f = 23 rpm)

(ml/mm) is not influenced by the magnitude of the tidal volume. As the frequency of pumping is increased from 4 to 52 cpm for any given tidal volume, a total increase of approximately 3 per cent has been noted in the resulting recorder deflection. This apparently is the result of a loss in performance in the integrator at the low frequency end. Also, the sinusoidal action of the pump may present a worse picture of the frequency response than would a dog with its steeper rise and fall times in its flow signal. By using an intermediate frequency for calibration, this frequency effect should be negligible for the present application of the equipment.

3. Correction Factors

From equation 4 on p. 27, it can be seen that ΔP_m is directly proportional to the ratio $\frac{V_2}{V_1 + V_2}$. Under the calibration conditions listed above, V_1 = 149 liters and $\frac{V_2}{V_1 + V_2} = 0.144$. However, when a 10 kg dog is placed within the plethysmograph, the value of V_1 is reduced to 139 liters and $\frac{V_2}{V_1 + V_2} = 0.152$, an increase of 5.6 per cent. This increase in ΔP_m occurs when a dog is used instead of a respiratory pump and must be included in the calibration factors.

A second correction which must be made involves the temperature and humidity of the inspired gas. Each body volume change measured with the plethysmograph corresponds to an air volume at body temperature and pressure, saturated with H_2O (BTPS), but for deposition studies, one needs to know the volume of inspired air in terms of the temperature, pressure and humidity present in the aerosol exposure chamber since the companion aerosol concentration data are obtained under these conditions. Probes were inserted into the exposure chamber to obtain temperature and relative humidity readings while a dog was

c. The respiratory information is obtained without using any valving arrangement at the animal's nose.

d. A latex mask covers all of the dog's nose inside the aerosol exposure chamber except a small area around the nostrils. This feature eliminates a considerable amount of external contamination and hence minimizes post-exposure ingestion, a factor that can adversely affect deposition data.

e. The seal between the plethysmograph and the aerosol exposure chamber is made by inserting the masked nose of the dog through a small hole in a sheet of latex connected to the wall of the plethysmograph thus producing a tight rubber-to-rubber contact without requiring the use of an inflatable collar as is common with baby and small animal plethysmographs.

f. Provision is made for collecting the aerosol at a point posterior to the dog's nostrils. The aerosol is continuously produced and moved past the dog's nose so that fresh aerosol is available for each inspiration.

g. Each exposure can also be quantified in terms of aerosol concentration and particle size distribution by samples taken from the exposure chamber during each experiment.

present and an aerosol was being generated. The chamber air temperature was found to be about 1° C cooler than room temperature and the relative humidity was 45 per cent. From these data, the following correction factor was derived:

$$\frac{V_{(BTPS)}\left(P_b - P_{w_{310^\circ}}\right)}{T_1} = \frac{V_{(ATP)}\left(P_b - 0.45\ P_{w_{294^\circ}}\right)}{T_2}$$

$V_{(BTPS)}$ = Inspired air volume at body temperature and pressure, saturated.

$V_{(ATP)}$ = Inspired air volume at chamber temperature, pressure and humidity.

P_b = Barometric pressure.

P_w = Vapor pressure of H_2O at specified temperature.

T_1 = 310° A

T_2 = 294° A

From this, $V_{(ATP)} = 0.89\ V_{(BTPS)}$. Thus, all volume and flow data must be reduced by the factor 0.89 if the results are desired in terms of the conditions present in the aerosol exposure chamber.

SUMMARY

The performance of three systems utilizing pressure, volume and flow rate transducers respectively have been evaluated for use with a whole body plethysmograph incorporated in an apparatus for exposing dogs by inhalation to radioactive aerosols. The results obtained indicated that the flow rate transducer system was the most satisfactory. Features of the finalized design are as follows:

a. Inspiratory and expiratory flow rates, tidal volume and respiratory rate can be monitored throughout the exposure period.

b. All data are recorded on a strip chart recorder and provision has been made for the addition of output signals which give the **values** for total respirations and total volume inspired in digital form.

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