Mouse Preparation for Pharmacodynamics Studies

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A method is described for recording an essentially undamped arterial pulse pressure in the mouse using methyl-2-cyanoacrylate physiological adhesive to secure a 22 gauge needle shaft in the carotid artery for cannulation. A miniaturized pneumotachograph screen for recording respiratory exchange in the mouse is described. Pulse pressure, ECG, and respiratory exchange tracings are shown.

PREVIOUS methods for recording directly the arterial pulse pressure of the mouse have been handicapped by low frequency response of the hydraulic and electronic systems utilized (1–6). Through the use of a large bore, hard plastic cannula, and a small displacement strain gauge pressure transducer in conjunction with rapid response electronics, an essentially undamped pulse pressure was obtained.

This report deals with simple techniques and instruments adapted for the direct recording of physiological measurements in the anesthetized mouse.

Preparation.—Female ICR mice from the Walter Reed colony weighing 25–35 Gm., aged 6–7 weeks, were used. Sodium pentobarbital (75 mg./Kg.) was administered intraperitoneally for anesthesia. The mouse was secured to the operating surface in a supine position using masking tape at each appendage and either side of the muzzle to secure the ears and whiskers to the table. The left femoral vein was exposed. A 27-gauge needle shaft, attached to a 15 μl. polyethylene cannula, was inserted into the vein and secured in position using methyl-2-cyanoacrylate monomer[1] as an adhesive. Drugs were introduced into this cannula in volumes of 10 μl. or less and flushed into circulation with 30 μl. of 0.9% NaCl solution. Additional doses of anesthetic (150–300 mcg.) were administered as needed through this cannula.

Cannulation of the Trachea.—The ventral neck area was exposed by a 3 cm. longitudinal incision. The strap muscles were exposed by separating the submaxillary glands by blunt dissection. (The fused ends of melting point capillaries worked well as dissecting probes.) The trachea was exposed by blunt dissection of the strap muscles. A tracheotomy was performed below the larynx, and a polyethylene tube large enough to fit snugly was inserted into the trachea.

Carotid Artery Cannulation.—The right carotid artery was visualized through the tissue and isolated to include the vagus nerve and as much fascia as possible using curved forceps for blunt dissection. The artery, nerve, and supporting fascia were stabilized using a single backtie which was secured to the table with beeswax. The exposed artery was supported by a melting point capillary. A 22-gauge needle shaft attached to a saline-filled vinyl cannula (B. D., No 442T) was inserted into the artery. The arterial wall was fixed to the cannula tip with the monomer adhesive.

All operative procedures were carried out with the aid of an illuminated magnifier.

ECG Leads.—Recording needle electrodes were implanted in the left hind leg and right foreleg; a needle electrode was implanted in the right hind leg as a ground lead.

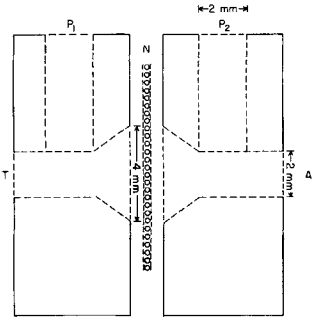


Fig. 1.—Diagram of pneumotachograph screen. Broken lines outline axes and size of holes bored in 4 mm. thick acrylic plastic. Nylon woven screen (N) in cemented between plastic halves. P_1 and P_2 lead to transducer. T leads to mouse tracheal cannula. A opens to ambient pressure. Over-all dimensions: 8 × 8 × 8 mm.

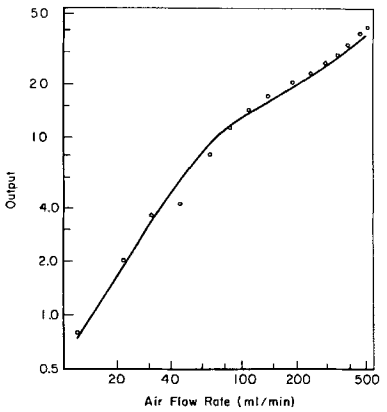


Fig. 2.—Calibration curve of pneumotachograph screen. Output voltage is in arbitary units.

Received July 22, 1966, from the Pharmacology Department, Walter Reed Army Institute of Research, Washington, D. C. 20012.

Accepted for publication August 15, 1966.

A portion of this work dealing with direct measurement of arterial pressure was reported in *Federation Proc.*, **24**, 365(1965).

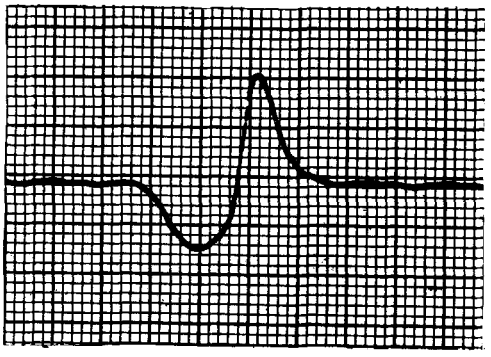
[1] Supplied through the courtesy of Ethicon, Inc., Somerville, N. J. For a description of the properties of this material see: Coover, H. W., Joyner, F. B., Shearer, N. H., and Wicker, T. H., *Soc. Plastics. Eng. J.*, **15**, 413(1959).

Respiratory Exchange Measurements.—The tracheal cannula was attached to a pneumotachograph screen which was made from a nylon screen cemented between two pieces of acrylic plastic. (See Fig. 1.) The two chambers of the pneumotachograph screen were connected by polyethylene tubing to the two sides of a Sanborn 270 differential gas pressure transducer which was activated by a Sanborn 350-1100 carrier preamplifier.

Arterial Pulse Pressure Measurements.—The arterial cannula was attached to a Sanborn 267B differential pressure transducer which was activated by a Sanborn 350-1100 carrier preamplifier.

ECG Recording.—The ECG impulses were amplified by a Phipps and Bird balanced biological preamplifier. The output of this first stage amplification was fed into a Sanborn 350-3200 ECG preamplifier.

All recordings were made on a Sanborn 964 polygraph at 50 mm./sec. and monitored on a fast sweep oscilloscope.



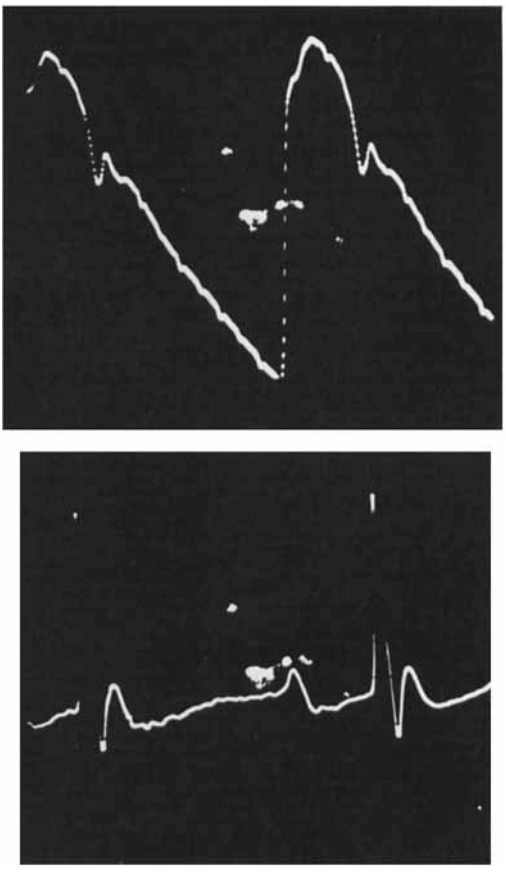


Fig. 3.—Tracings of physiological measurements of the mouse. Key: Bottom left, respiratory exchange cycle (chart speed: 50 mm./sec.); peak inspiration reached 55 ml./min.; peak expiration rate was 80 ml./min. Top right, pulse pressure curve (sweep time: 200 msec.); diastolic pressure is 60 mm. Hg; systolic pressure is 90 mm. Hg; heart rate is 550/min. Bottom right, ECG tracing (sweep time: 200 msec.).

The calibration curve of the improvised pneumotachograph screen-transducer assembly is shown in Fig. 2. A typical recording of respiratory cycle is shown in Fig. 3 (bottom left). Pulse pressure and ECG oscilloscope tracings are shown in Fig. 3, top right and bottom right, respectively.

REFERENCES

(1) McMaster, P. O., *J. Exptl. Med.*, **74**, 29(1941).

(2) Pradhan, S. N., Achinstein, B., and Shaw, M. J., *Federation Proc.*, **14**, 380(1955).

(3) Pradhan, S. N., Achinstein, B., and Shaw, M. J., *J. Pharmacol. Exptl. Therap.*, **113**, 44(1955).

(4) Pradhan, S. N., Achinstein, B., and Shaw, M. J., *Am. J. Physiol.*, **184**, 599(1956).

(5) Pradhan, S. N., Achinstein, B., and Shaw, M. J., *Arch. Intern. Pharmacodyn.*, **120**, 1(1959).

(6) Wu, H. C., and Visscher, M. B., *Am. J. Physiol.*, **153** 330(1948).