THE PULMONARY ARTERIAL PRESSURE IN NORMAL ALBINO RATS AND THE EFFECT THEREON OF EPINEPHRINE

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(Received for publication, November 8, 1933)

In a recent publication (1) we described lesions in the pulmonary arterioles of rats which had lived for some time in compressed air. These lesions indicated the possibility of pulmonary hypertension. Accordingly, it was decided to make direct determinations of the blood pressure in the pulmonary artery of rats after varying periods of exposure to the conditions prevailing in previous experiments (1, 2). Since, so far as we can learn, there have been no observations on the pulmonary arterial pressure in rats, it was necessary to determine the average pressure in a series of normal animals.

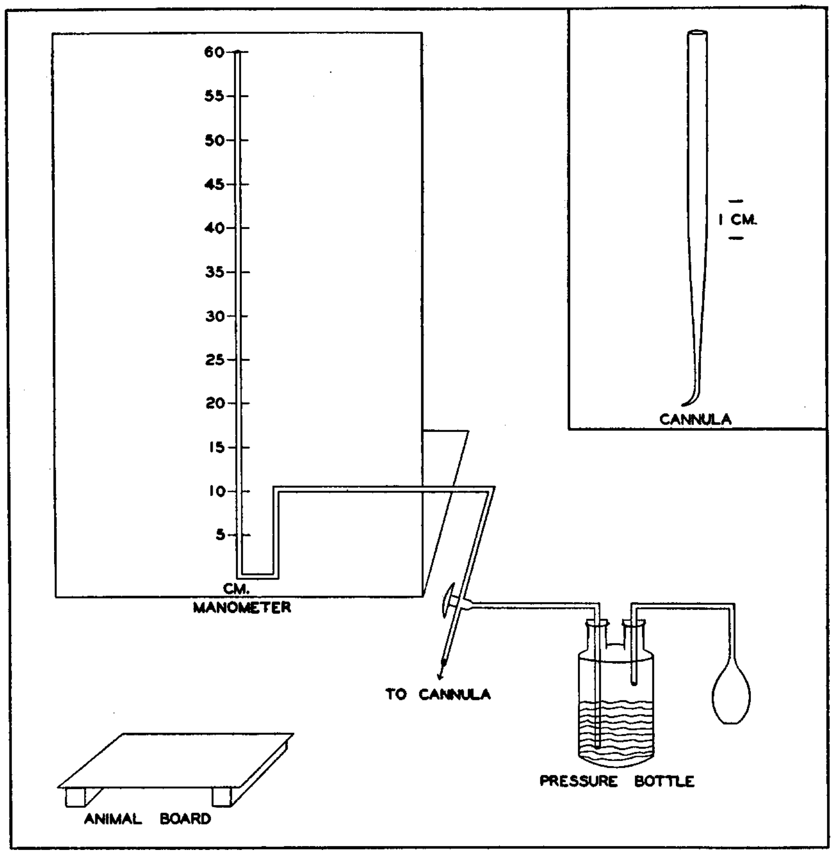
Methods

Albino rats from a standard colony were used. A total of thirty-four satisfactory determinations of the pulmonary arterial pressure was obtained. Some 70 per cent of the attempted readings proved successful after a suitable technique had been developed. The age of the majority of rats was between 4 and 5 months.

The pressures were determined directly on a water manometer (Text-fig. 1) by cannulating the pulmonary artery in a manner differing only slightly from the method described by Drinker and Went (3) for guinea pigs. The anatomical structure of the pulmonary arch in rats was such as to prevent the anchoring of a cannula as practiced by them. For this reason a small cannula was drawn from pyrex tubing (Text-fig. 1). The tip was turned from the shaft at a slightly obtuse angle. The end was ground on an emory wheel to a sharp, beveled point. The circumference of the tip increased abruptly as it approached the shaft, so that when the tip had pierced the arterial wall the increased circumference served as a wedge in the wall and thus prevented bleeding. The shaft was made long enough to be easily handled, ranging from 3 to 4 inches in length.

The cannula communicated directly with the water manometer through a three-way stop-cock (Text-fig. 1), one lead of which was connected with a pressure bottle containing a solution of methylene blue in normal saline. By means of a pressure bulb attached to this bottle the height of the column of saline could be readily adjusted until it was in approximate equilibrium with the pulmonary arterial pressure.

Preparation.—The rats were anesthetized by an intraperitoneal injection of a 0.5 per cent solution of nembutal (sodium-ethyl (1-methyl-butyl) barbiturate)



TEXT-FIG. 1. Diagrammatic sketch of experimental apparatus.

in normal saline. Rats weighing less than 200 gm. received 60 mg. per kilo of body weight, while rats over 200 gm. received 70 mg. per kilo. Satisfactory anesthesia was obtained in 10–15 minutes. The rat was then placed on its back on an animal board. A tracheal cannula was inserted and positive pressure artificial respiration with an electrical pump was started. After an appropriate adjustment had been determined in the early experiments, the stroke of the pump was not altered. The external jugular vein was then exposed to facilitate injection of heparin later. The thorax was opened by a longitudinal incision through the middle of the sternum from the tip of the xyphoid to the base of the neck. The thoracic walls were held apart by a self-retaining retractor. The thymus was dissected upward from the base of the heart and held back by a small clamp. Very little bleeding occurred when the incision was properly made through the middle of the sternum. Any bleeding points were temporarily clamped with hemostats. 3 or 4 minutes were allowed for clots to form in severed vessels before heparin was injected. A 0.6 per cent solution of heparin in normal saline was then injected, the number of cubic centimeters being determined by multiplying the weight in kilos by the factor 5.7. The usual quantity ranged from 1–1.5 cc. This amount of heparin was calculated to prevent the clotting of a quantity of cat's blood equal to twice the rat's blood volume. The latter was determined by assuming 85 cc. of blood per kilo of body weight.

Cannulation.—The cannula was filled with a 0.6 per cent solution of heparin and then connected to the manometer circuit by flexible rubber tubing. The water column was then raised to a height of 240–250 mm. The cannula was grasped in the right hand as a pencil, while the heart was gently retracted downward by a moist cotton pledget held in the left hand. In this way the pulmonary arch was exposed for a distance of 2–3 mm. distal to the pulmonic valve and the cannula was gently inserted with the tip directed toward the heart. When carried out successfully, the procedure required only a few seconds. The artificial respiration was discontinued for 5–10 seconds during the cannulation in order to steady the heart. As soon as the artery was entered, blood spurted into the tip of the cannula. The stop-cock was then turned so that the water column communicated freely with the cannula. If the water level tended to change immediately, it was readjusted as indicated until essentially in equilibrium with the pressure. Readings were then recorded at intervals of 15 seconds or 1 minute. In the first experiments the cannula was stabilized in plasticine, but since it frequently slipped out of the artery during the transfer from hand to plasticine, this method was abandoned. It was found more satisfactory for the operator to continue to hold it in place by hand.

Manometer readings were usually recorded in longhand; however, during experiments with epinephrine, in which marked changes in pressure occurred suddenly, it was found necessary to record the readings by camera at 5 second intervals according to the method described by Field and Drinker (4).

The results of all experiments in which cannulation was successful are shown in Table I. The average pulmonary arterial pressure for this series of thirty-four rats is seen to be 256 mm. H_2O.

The reliability of recording the pressure for only a few minutes is demonstrated by Table II, in which are presented the average pressure readings of fifteen rats that were recorded for periods ranging from 6

TABLE I

Rat No.	Age	Sex	Duration of experiment	Pulmonary arterial pressure, Average of, 1st 5 min.	Pulmonary arterial pressure, Average of, Total duration
	days		*min.*	*mm.* H_2O	*mm.* H_2O
10-31	126	M	54	279	276
10-12	140	F	38	279	284
10-10	140	F	35	256	256
10-39	129	M	20	263	260
10-33	126	F	18	257	267
10-34	128	M	13	284	273
10-40	131	M	12	244	247
10-36	128	M	10	250	249
10-51	334	F	10	303	309
10-41	130	F	9	284	261
10-54	155	M	8	253	255
10-60	159	M	8	276	276
10-76	125	F	8	229	225
10-32	126	F	7	228	223
10-19	143	F	6	277	278
10-45	133	M	6	259	258
10-17	141	F	5	267	267
10-53	154	M	5	272	272
10-58	157	M	5	312	312
10-61	159	M	5	266	266
10-66	—	—	5	265	265
10-69	125	F	5	255	255
10-70	125	M	5	299	299
10-71	125	M	5	201	201
10-72	125	M	5	187	187
10-73	125	F	5	183	183
10-74	125	F	5	220	220
10-23	133	M	4	—	281
10-35	128	M	4	—	219
10-52	334	F	4	—	243
10-59	159	M	3	—	239
10-62	159	M	3	—	275
10-65	305	M	3	—	233
10-63	303	M	2	—	291
Corrected average of series (34 rats).................				257	256

to 54 minutes. The pressures on the 1st minute and for the first 5 minutes after the water column was in equilibrium as well as for the total duration are shown. The difference between these readings is insignificant. The average pressure during the first 5 minutes after reaching the equilibrium was accepted as the standard in later experiments, because one was definitely able to ascertain that a constant level had been reached by then while further prolongation was unnecessary.

Accessory Factors.—The fact that sex, age, weight, and duration of anesthesia within reasonable limits bear no relationship to the pulmonary pressure is illustrated by the graphs in Text-fig. 2. The time

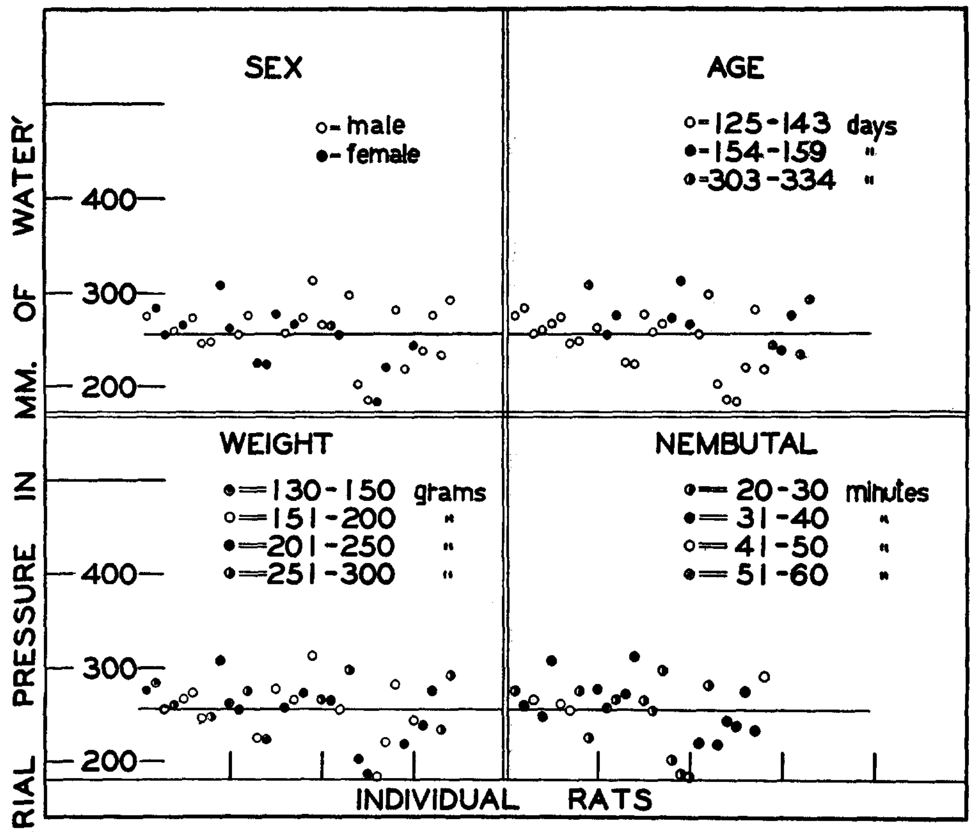
TABLE II

Rat No.	Duration of experiment	Pulmonary arterial pressure		
		Average of		
		1st min.	1st 5 min.	Total duration
	min.	*mm. H_2O*	*mm. H_2O*	*mm. H_2O*
10-31	54	270	279	276
10-12	38	281	279	284
10-10	35	268	256	256
10-39	20	290	263	260
10-33	18	258	257	267
10-34	13	280	284	273
10-40	12	242	244	247
10-36	10	259	250	249
10-51	10	280	303	309
10-41	9	289	284	261
10-54	8	270	253	255
10-76	8	238	229	225
10-32	7	235	228	223
10-19	6	275	277	278
10-45	6	272	259	258
Average (15 rats).............		267	263	261

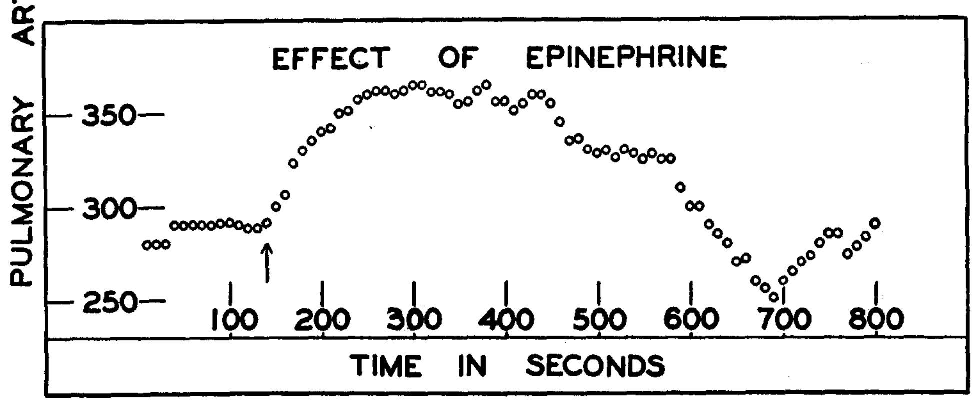
in the anesthesia graph represents the number of minutes elapsing between the injection of nembutal and the cannulation of the pulmonary artery.

The Effect of Epinephrine

The effect of epinephrine on the pulmonary pressure was studied in nine rats. An approximate 1:100,000 solution of epinephrine was used. It was administered intravenously in doses of 0.1–0.5 cc. The femoral and external jugular veins were used for injections.



Text-Fig. 2



Text-Fig. 3

Text-Fig. 2. These graphs illustrate the fact that the age, weight, and sex of the experimental animals, as well as the duration of anesthesia employed in this study bear no relationship to the pulmonary arterial pressure.

Text-Fig. 3. This graph shows the effect of epinephrine on the pulmonary arterial pressure in a representative experiment.

Epinephrine invariably caused an abrupt increased activity of the heart and a simultaneous elevation of the pulmonary pressure, the degree varying directly with the amount administered. A maximum pressure was soon reached but persisted for only a short time, gradually returning to normal. In the illustrated case 0.3 cc. of a 1:100,000 solution of epinephrine was injected into the femoral vein as indicated by the arrow (Text-fig. 3).

DISCUSSION

Three possible causes of error in making these determinations became apparent; namely, asphyxia, obstruction of the pulmonary circulation, and tension on the trachea. The first of these, when present, was usually caused by mucus or less frequently by a kink in the trachea at the junction with the cannula. Obstruction to the pulmonary circulation was due to faulty cannulation, resulting in either undue tension on the pulmonary arch or a disturbance of the normal relationships of the heart and mediastinal contents. Abnormal tension on the trachea probably caused its effect by altering the mediastinal relationships with impairment of the pulmonary circulation at the root of the lungs. All three of these accidents resulted in an abnormal temporary elevation of the pulmonary pressure to varying heights, followed by a sudden failure of the right side of the heart with a rapid fall in pressure ending in death unless remedied. After a little practice these difficulties were readily avoided. Early in the study it was realized that a cannulation was either immediately satisfactory in all respects or else it should be considered a failure and discontinued. When properly performed, no additional manipulation was necessary other than the adjustment of the water manometer as indicated. It was desirable to set the manometer a centimeter or two below rather than above the expected pressure. In this way a small quantity of blood was allowed to rise in the tip of the cannula. Cardiac pulsations could be followed here to ensure a patent cannula, while at times they were rather weak in the manometer.

The systemic blood pressure of rats under ether anesthesia has been determined in a series of 40 adults by Durant (5). The arithmetical mean in this group was 119 mm. Hg (1618 mm. H_2O). The ratio of the average pulmonary pressure in our experiments to the average systemic pressure of 113 mm. Hg (6) is 1:6 which is identical to the ratio 1:6 given by Fuhner and Starling (7) for dogs. A comparison of the average pulmonary pressure found in this study to the average systemic pressure of 119 mm. Hg reported by Durant in a larger series of rats gives a ratio of 1:6.3 which is in close accord with the above ratios.

CONCLUSIONS

1. A satisfactory method for the direct determination of the pulmonary arterial pressure in rats is described.

2. The arithmetical mean of the blood pressure in the pulmonary artery in a series of thirty-four normal albino rats under nembutal anesthesia is 256 mm. H_2O (18.8 mm. Hg).

3. Intravenous epinephrine causes an abrupt but briefly sustained rise in the pulmonary arterial pressure with a gradual return to normal.

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