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Research Article

OBSERVATIONS ON AUTONOMIC PARTICIPATION IN PULMONARY ARTERIOLAR RESISTANCE IN MAN[1]

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It has been generally believed that the autonomic nervous system plays an insignificant role in the regulation of pressure within the pulmonary or lesser circulation. In 1939, Hamilton (1) studied the effect of various drugs upon the pulmonary arterial and venous pressures in unanesthetized dogs. He concluded that there was no evidence of autonomic control of the pulmonary circulation. Dirken and Heemstra (2), however, in 1948 found that resection of part of the sympathetic trunk increased pulmonary blood flow in rabbits. They found that vagotomy had no effect upon pulmonary flow.

Without knowledge of the pulmonary venous or "capillary" pressure, one cannot ascertain whether changes in pulmonary arterial pressure are due primarily to a change in cardiac output or to a variation in pulmonary arteriolar resistance. Until recently, the study of autonomic regulation of pulmonary blood flow in man could not be undertaken because of the lack of a satisfactory method of measuring pulmonary venous pressure, except in an occasional case of atrial septal defect. In 1948, Hellems and co-workers (3) described a method for determining pulmonary "capillary" pressure and have since given adequate proof that this pressure varies with the pulmonary venous pressure (4). When the pulmonary artery pressure, pulmonary "capillary" pressure, and cardiac output are determined simultaneously, the pulmonary arteriolar resistance may be calculated (5).

With the foregoing in mind, it was decided to determine the effect of the autonomic blocking agent, tetraethylammonium chloride (TEAC), upon the pulmonary arteriolar resistance in man; this report describes the results of such studies.

MATERIAL

It was thought that patients having pulmonary hypertension would be more likely to show a lowering of pulmonary pressure following autonomic blockade by tetraethylammonium because the effect of such blockade is much more pronounced in the systemic circulation when hypertension is present (6). A total of 15 patients were studied. Five were normal; two had pulmonary emphysema; two, congestive heart failure; one, active pneumonia; three, hypertensive vascular disease; one, bronchiectasis; one, diaphragmatic hernia with cor pulmonale.

METHOD

The majority of the patients were studied in the fasting condition. Cardiac catheterization was performed by the method of Cournand and Ranges (7). A double lumen catheter was used in order that pulmonary "capillary" pressure and pulmonary arterial pressure could be measured simultaneously. Pulmonary "capillary" pressure was obtained by the method of Hellems and his associates (3). The catheter was advanced into a branch of the pulmonary artery as far as possible, so that the branch was occluded and the pressure distal to the point of occlusion was obtained. The Hathaway blood pressure recording apparatus and Hathaway strain gauges were employed. Simultaneous electrocardiograms, ballistocardiograms, brachial arterial, pulmonary arterial, and pulmonary "capillary" pressures were recorded by means of a five channel optical oscillograph.

Cardiac outputs were determined by the direct Fick method. Two minute samples of expired air were collected in Douglas bags, analyzed in the Haldane apparatus, and measured in a Tissot spirometer. Duplicate samples were analyzed for CO_2 and O_2 and required to check within 0.03%. Pulmonary artery and brachial artery blood samples of 12 cc. each were obtained during the collection of expired air. The blood samples were collected slowly over a period of 45 to 60 seconds. Blood samples were analyzed for CO_2 and O_2 in the Van Slyke manometric apparatus. Duplicate samples were required to check within 0.2 volume %.

Resting cardiac outputs were obtained usually after the catheter had been in place 15 to 30 minutes or more. The mouthpiece for air collection was inserted before

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control records were obtained. After the blood and gas samples for the resting cardiac output had been collected, the subjects were given 5 or 6 mg. of tetraethylammonium chloride per kilogram body weight intravenously. The effect upon the brachial and pulmonary arterial blood pressures was observed by means of a cathode ray oscilloscope incorporated in the Hathaway pressure recording apparatus. When the maximum effect upon the blood pressures had been obtained, usually within three to five minutes, blood and gas samples for a second cardiac output were collected. Pressure recordings were obtained immediately before and immediately after the collection of blood samples. It would have been desirable to obtain another cardiac output after the effect of TEAC was dissipated, but the fact that the pulmonary arterial pressure remained low for the period of observation—20 to 30 minutes, or more—precluded this determination.

Mean pulmonary arterial, brachial arterial and pulmonary "capillary" pressures were determined by use of a Keuffel-Esser compensating polar planimeter.

Pulmonary arteriolar resistance was calculated by the formula:

TABLE I

Effect of intravenous TEAC upon mean pulmonary artery pressure, mean pulmonary "capillary" pressure and upon cardiac output

Patient	Before TEAC				After TEAC			
	P.A. mean	P.C. mean	C.O.	Rate	P.A. mean	P.C. mean	C.O.	Rate
	mm. Hg	*mm. Hg*	*L/min.*		*mm. Hg*	*mm. Hg*	*L/min.*	
1. C.C. 46 c.m. Normal (Convalescent)	17.0	12.4	4.95	64	14.5	9.5	5.1	100
2. M. C. 73 w.m. Normal (Convalescent)	13.1	9.7	3.50	80	14.9	10.1	4.12	96
3. O. B. 37 c.m. Normal (Convalescent)	14.5	7.2	5.50	74	17.1	10.2	4.91	92
4. J. H. 62 c.m. Hypertensive vascular disease	13.5	6.4	5.18	70	13.7	6.8	4.57	104
5. S. J. 60–? c.m. Hypertensive cardiovascular disease	25.0	13.8	4.45	75	18.6	13.4	3.05	100
6. I. W. 29 c.f. Postpartum myocardosis Heart failure	25.4	18.4	4.91	114	23.6	20.9	3.68	140
7. W. B. 54 c.m. A.S. Heart disease Heart failure	27.6	18.9	3.83	76	20.2	14.6	3.54	74
8. B. M. 57 c.f. Emphysema	28.0	10.5	4.03	90	25.6	9.0	3.01	86
9. J. B. 62 w.m. Emphysema (?) Lung tumor	25.5	14.8	4.24	84	17.9	16.0	2.41	76
10. G. A. 59 w.m. Diaphragmatic hernia Cor pulmonale	41.5	15.6	4.85	97	32.9	12.1	4.21	105
11. J. S. 75 w.m. Hypertensive vascular disease	26.4	—	4.33	86	22.1	—	3.21	98
12. B. A. 21 c.f. Normal (Convalescent)	17.6	—	4.70	109	18.3	—	5.05	118
13. W. M. 49 c.m. Bronchiectasis	23.2	—	5.80	84	15.7	—	6.18	78
14. L. J. 19 c.m. Bronchopneumonia	23.8	—	8.80	72	22.4	—	10.1	76
15. J. M. 22 c.m. Normal (Convalescent)	19.6	—	6.64	71	15.3	—	7.33	90

TABLE II

*Effect of TEAC intravenously on pulmonary arteriolar resistance**

Patient	Before TEAC Pulm. res.	After TEAC Pulm. res.	Net effect	Per cent effect	Initial P.A. press.
	dynes sec. cm.$^{-5}$	*dynes sec. cm.$^{-5}$*		%	*mm. Hg*
1. C. C. 46 c.m. Normal (Convalescent)	74.26	78.35	+ 4.09	+ 5.5	17.0
2. M. C. 73 w.m. Normal (Convalescent)	77.6	93.1	+ 15.5	+19.9	13.1
3. O. B. 37 c.m. Normal (Convalescent)	106.1	112.3	+ 6.2	+ 5.8	14.5
4. J. H. 62 c.m. Hypertensive vascular disease	109.2	119.9	+ 10.7	+ 8.9	13.7
5. S. J. 60–? c.m. Hypertensive cardiovascular disease	165.2	136.3	− 28.9	−17.4	25.0
6. I. W. 29 c.f. Postpartum myocardosis Heart failure	113.9	58.6	− 55.3	−48.5	25.4
7. W. B. 54 c.m. A.S. heart disease Heart failure	181.5	126.4	− 55.1	−30.3	27.6
8. B. M. 57 c.f. Emphysema	347.0	440.8	+ 93.8	+27	28.0
9. J. B. 62 w.m. Emphysema (?) Lung tumor	201.7	62.9	−138.8	−69.1	25.5
10. G.A. 59 w.m. Diaphragmatic hernia Cor pulmonale	426.8	394.9	− 31.9	− 7.4	41.5
11. J. S. 75 w.m. Hypertensive vascular disease	487.2	550.2	+ 63.0	+12.9	26.4
12. B. A. 21 c.f. Normal (Convalescent)	299.3	289.6	− 9.7	− 3.2	17.6
13. W. M. 49 c.m. Bronchiectasis	319.7	203.0	−116.7	−36.5	23.2
14. L. J. 19 c.m. Bronchopneumonia	216.1	117.2	− 38.9	−18.0	23.8
15. J. M. 22 c.m. Normal (Convalescent)	235.9	166.8	− 69.1	−29.2	19.6

* In subjects 11–15, the pulmonary resistance figures represent total pulmonary resistance rather than pulmonary arteriolar resistance.

$$R = \frac{PA - PC}{CO} \times 1332$$

where R = arteriolar resistance in dynes sec. cm.$^{-5}$.
PA = mean pulmonary artery pressure mm. Hg.
PC = mean pulmonary "capillary" pressure mm. Hg.
CO = cardiac output in cc. per sec.

Total peripheral resistance was determined according to the formula:

$$R = \frac{BA}{CO} \times 1332$$

where R = total peripheral resistance in dynes sec. cm.$^{-5}$.
BA = mean brachial arterial pressure mm. Hg.
CO = cardiac output in cc. per sec.

RESULTS

(*1*) *Mean pulmonary artery pressure.* Of 15 patients studied, mean pulmonary artery pressure was lowered by TEAC in 11, of whom all but one had pulmonary hypertension before TEAC (Table

I). The other four patients had normal mean pulmonary artery pressures, and no decline was observed after TEAC.

(2) *Pulmonary arteriolar resistance.* Ten patients had satisfactory determinations of the pulmonary "capillary" pressure. Four of the 10 had normal mean pulmonary arterial pressures between 13 and 17 mm. Hg and normal pulmonary "capillary" pressures between 6 and 12 mm. Hg (5). In each of these four subjects, the administration of TEAC produced a slight rise in pulmonary arteriolar resistance (Table II). Since there may be a 5% error in the direct Fick method of determining cardiac output, and since occasionally variations as great as 10% may be found in the resting subject (8), changes in resistance and output of less than 10% are considered insignificant.[4] In three of the four subjects the rise was so slight as to be negligible. An example of this is shown in Figures 1a and 1b. Figure 1a is taken from the record of C. C., a normal subject, before the administration of TEAC. Here the mean pulmonary artery pressure was 17.0 mm. Hg; the mean pulmonary "capillary" pressure was 12.4 mm. Hg; the mean brachial artery pressure was 116.8 mm. Hg. The ballistocardiogram was normal. At this time the cardiac output was 4.95 liters per minute, and the pulmonary resistance 74.26 dynes sec. cm.$^{-5}$. Figure 1b shows pressures recorded from the same subject seven minutes after 5 mg. TEAC per kilogram body weight intravenously. Here the mean pulmonary artery pressure was 14.5 mm. Hg; the mean pulmonary "capillary" pressure was 9.5 mm. Hg; and the mean brachial artery pressure was 106.2 mm. Hg. The cardiac output had risen to 5.1 liters per minute. The pulmonary arteriolar resistance rose slightly to 78.35 dynes sec. cm.$^{-5}$. Note the change in the ballistocardiogram.

[4] In a small series of duplicate cardiac outputs by the Fick method, we have found a mean error of 3.2% and a maximum error of 7.5%.

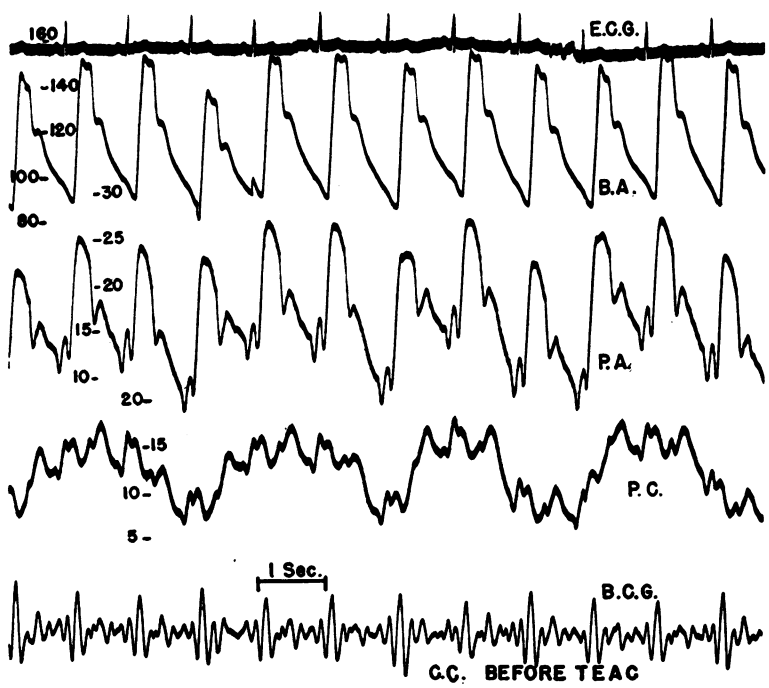

FIG. 1a. TAKEN FROM THE RECORD OF C. C., A NORMAL SUBJECT, BEFORE THE ADMINISTRATION OF TEAC

Here the mean pulmonary artery pressure was 17.0 mm. Hg; the mean pulmonary "capillary" pressure was 12.4 mm. Hg; the mean brachial artery pressure was 116.8 mm. Hg. The ballistocardiogram is normal. At this time the cardiac output was 4.95 liters per minute, and the pulmonary resistance 74.26 dynes sec. cm.$^{-5}$.

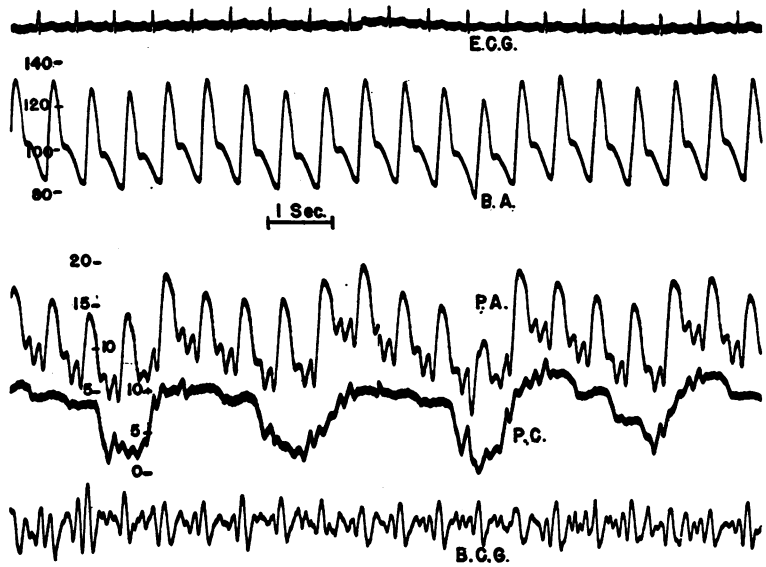

FIG. 1b. SHOWING PRESSURES RECORDED FROM THE SAME SUBJECT SEVEN MINUTES AFTER 5 MG. TEAC PER KILOGRAM BODY WEIGHT INTRAVENOUSLY

Here the mean pulmonary artery pressure was 14.5 mm. Hg; the mean pulmonary "capillary" pressure was 9.5 mm. Hg; and the mean brachial artery pressure was 106.2 mm. Hg. The cardiac output had risen to 5.1 liters per minute. The pulmonary arteriolar resistance rose slightly to 78.35 dynes sec. cm.$^{-5}$. Note the change in the ballistocardiogram.

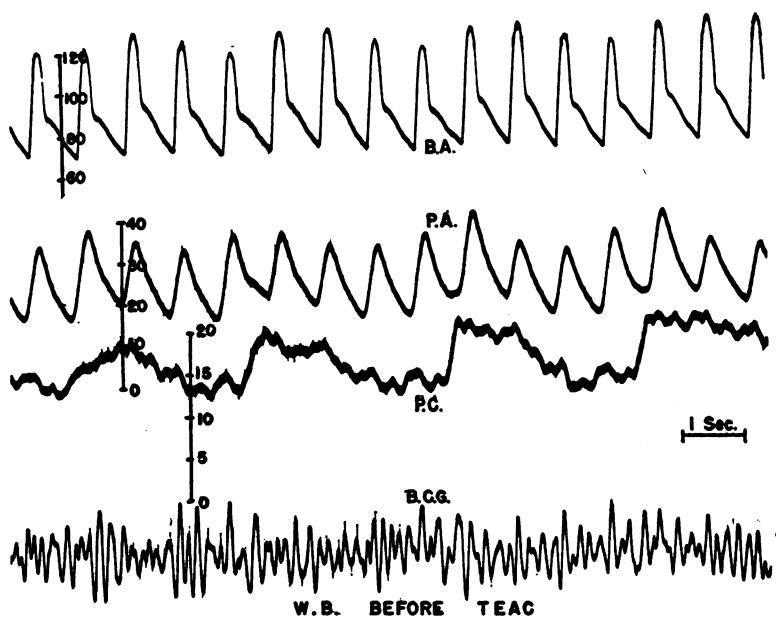

FIG. 2a. TAKEN FROM THE RECORD OF PATIENT W. B.

Before TEAC the mean pulmonary artery pressure was 27.6 mm. Hg; the mean pulmonary "capillary" pressure was 18.9 mm. Hg; the mean brachial artery pressure was 92.3 mm. Hg.

Among the remaining six cases, all of whom had pulmonary hypertension, TEAC produced a significant decline in pulmonary arteriolar resistance in four of the six (Table II). An example of decline in pulmonary arteriolar resistance after TEAC is seen in Figures 2a and 2b. This is taken from the record of patient W. B. Before TEAC, (Figure 2a) the mean pulmonary artery pressure was 27.6 mm. Hg; the mean pulmonary "capillary" pressure was 18.9 mm. Hg; the mean brachial artery pressure was 92.3 mm. Hg. In Figure 2b is seen a record taken 11 minutes after 5 mg. TEAC per kilogram body weight intravenously. The mean pulmonary artery pressure was 20.2 mm. Hg; the mean pulmonary "capillary" pressure was 14.6 mm. Mg; the mean brachial artery pressure was 70.1 mm. Hg. The cardiac output before TEAC was 3.83 liters per minute, and after TEAC was 3.54 liters per minute. Pulmonary arteriolar resistance fell from 181.5 dynes sec. cm.$^{-5}$ before TEAC to 126.4 dynes sec. cm.$^{-5}$ after TEAC.

(*3*) *Cardiac output.* The effect of TEAC upon cardiac output was variable, as demonstrated by a significant fall in output after TEAC in eight of the 15 cases, a significant rise in three cases, and no significant change in the remaining four. These changes in output bore no consistent relationship to the coincident changes in rate (Table I). In this connection, it is interesting to note the effect of TEAC upon the ballistocardiogram (Table III), which was recorded in 11 of the 15 subjects. Five of the ballistocardiograms were initially normal. Four of these five ballistocardiograms became definitely abnormal. An example of this is shown in Figures 1a and 1b. Four of the five patients with normal ballistocardiographic patterns showed a rise in cardiac output after TEAC, although the rise was considered significant in only two of these cases.

(*4*) *Peripheral resistance.* The effect of TEAC on the total peripheral resistance observed in 14 of the 15 cases, was noteworthy (Table IV). All

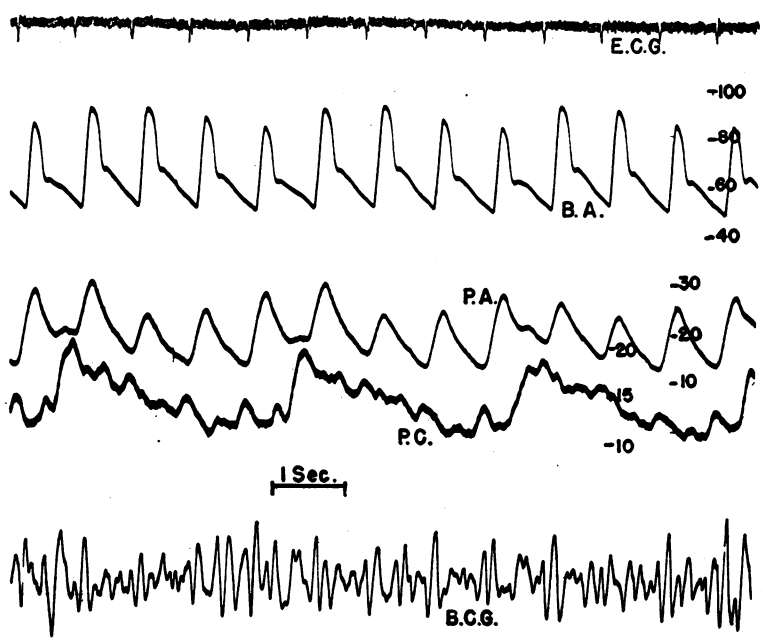

FIG. 2b. TAKEN 11 MINUTES AFTER 5 MG. TEAC PER KILOGRAM BODY WEIGHT INTRAVENOUSLY

The mean pulmonary artery pressure was 20.2 mm. Hg; the mean pulmonary "capillary" pressure was 14.6 mm. Hg; the mean brachial artery pressure was 70.1 mm. Hg. The cardiac output before TEAC was 3.83 liters per minute, and after TEAC was 3.54 liters per minute. Pulmonary arteriolar resistance fell from 181.5 dynes sec. cm.$^{-5}$ before TEAC to 126.4 dynes sec. cm.$^{-5}$ after TEAC.

TABLE III

Effect of intravenous TEAC upon the ballistocardiogram

Patient	Before TEAC		After TEAC	
	BCG	Cardiac output (Fick)	BCG	Cardiac output (Fick)
		L/min.		*L/min.*
1. C. C. 46 c.m. Normal (Convalescent)	Normal	4.95	Abnormal	5.1
2. S. J. 60–? c.m. Hypertensive vascular disease	Abnormal	4.45	Abnormal	3.05
3. I. W. 29 c.f. Postpartum myocardosis Heart failure	Abnormal	4.91	Abnormal	3.68
4. W. B. 54 c.m. A.S. Heart disease Heart failure	Normal	3.83	Abnormal	3.54
5. M. C. 73 w.m. Normal (Convalescent)	Abnormal	3.50	Abnormal	4.12
6. B. M. 57 c.f. Emphysema	Abnormal	4.03	Abnormal	3.01
7. J. S. 75 w.m. Hypertensive vascular disease	Abnormal	4.33	Abnormal	3.21
8. B. A. 21 c.f. Normal (Convalescent)	Normal	4.70	Abnormal	5.05
9. W. M. 49 c.m. Bronchiectasis	Abnormal	5.80	Abnormal	6.18
10. L. J. 19 c.m. Pneumonia	Normal	8.80	Normal	10.1
11. J. M. 22 c.m. Normal (Convalescent)	Normal	6.64	Abnormal	7.73

14 cases showed a rather marked drop in mean brachial arterial pressure after TEAC; in four cases, this decline was due to a decrease in cardiac output; in the remaining ten the change was due to a decline in peripheral resistance. The individual change in total peripheral resistance appeared to be unrelated either to the change observed in pulmonary arteriolar resistance or to the initial level of brachial artery pressure.

Complications

The only complication of cardiac catheterization encountered in this study, other than that of local thrombophlebitis, was that of transient right bundle branch block following the introduction of the catheter into the right ventricle. This was observed in three subjects, only one of whom was used in this study. In two instances, the patients had normal hearts. (In all three instances this complication persisted following withdrawal of the catheter.) The right bundle branch block disappeared within four hours in one case, and by the following morning in the other two. This complication has been previously observed in patients with heart disease by Cournand (9) and by Goldman in Bing's laboratory (10). This is considered not to be a serious complication (10).

DISCUSSION

Hellems, Haynes and Dexter (4) have presented ample evidence that the method employed by them and in this study for obtaining pulmonary "capillary" pressure in man is valid, and that pulmonary "capillary" pressure is practically identical with pulmonary venous pressure. Pressures on the occluded arterial and occluded venous sides of the pulmonary "capillary" network have been measured by them in dogs (3) and in

TABLE IV

Effect of intravenous TEAC upon mean brachial artery pressure and upon total peripheral resistance

Patient	Before TEAC				After TEAC					
	B.A. pressure	B.A. mean pressure	Cardiac output	TPR	B.A. pressure	B.A. mean pressure	Cardiac output	TPR	Net effect	Per cent effect
	mm. Hg	*mm. Hg*	*L/min.*	*dynes sec. cm.$^{-5}$*	*mm. Hg*	*mm. Hg*	*L/min.*	*dynes sec. cm.$^{-5}$*		%
1. C. C. 46 c.m. Normal (Convalescent)	155/90	116.8	4.95	1,885.6	135/90	106.2	5.1	1,664.2	−221.4	−11.7
2. M. C. 73 w.m. Normal (Convalescent)	156/60	98.2	3.50	2,242.3	126/60	86.4	4.12	1,676.0	−566.3	−25.2
3. O. B. 37 c.m. Normal (Convalescent)	130/70	94.5	5.50	1,373.2	140/85	111.7*	4.91	1,818.1	+454.9	+33.1
4. J. H. 62 c.m. Hypertensive vascular disease	160/90	118.4	5.18	1,826.7	125/78	92.5	4.57	1,617.6	−209.1	−11.4
5. S. J. 60–? c.m. Hypertensive cardiovascular disease	200/110	148.3	4.45	2,663.4	135/90	103.9	3.05	2,722.5	+ 59.1	+ 2.2
6. I. W. 29 c.f. Postpartum myocardosis Heart failure	112/65	82.5	4.91	1,342.9	95/62	75.1	3.68	1,631.0	+288.1	+21.4
7. W. B. 54 c.m. A.S. Heart disease Heart failure	128/70	92.3	3.83	1,926.0	90/50	70.0	3.54	1,580.3	−345.7	−17.9
8. B. M. 57 c.f. Emphysema	180/90	114.3	4.03	2,266.7	130/80	88.7	3.01	2,355.1	+ 88.4	+ 3.8
9. J. B. 62 w.m. Emphysema (?) Lung tumor	140/80	116.3	4.24	2,192.1	75/58	60.5	2.41	2,006.2	−185.9	− 8.4
10. G. A. 59 w.m. Diaphragmatic hernia Cor pulmonale	180/90	130.5	4.85	2,150.4	155/80	111.6	4.21	2,118.5	− 31.9	− 1.5
11. B.A. 21 c.f. Normal (Convalescent)	110/65	75.5	4.70	1,283.8	75/48	51.6	5.05	816.5	−467.3	−36.3
12. W. M. 49 c.m. Bronchiectasis	116/55	72.0	5.80	992.1	75/40	55.2	6.18	713.9	−278.2	−28.0
13. L. J. 19 c.m. Bronchopneumonia	140/70	79.8	8.80	742.7	90/55	62.0	10.1	490.6	−234.1	−32.3
14. J. M. 22 c.m. Normal (Convalescent)	148/80	101.6	6.64	1,222.9	130/75	91.9	7.33	1,001.9	−221.0	−18.0

* Mean B.A. pressure dropped to 89.9 mm. Hg six minutes after TEAC, but cardiac output was not measured at this time.

human subjects having atrial septal defects (4) with the finding of close agreement in the two pressures in both groups. Blood saturated with oxygen is obtained from the catheter recording pulmonary "capillary" pressure, indicating that there is no contamination with unsaturated pulmonary artery blood (4). Recent pulmonary "capillary" pressure recordings taken with a more sensitive recording apparatus show "A," "C" and "V" waves like those seen in jugular pulse tracings (11).

It is known that the tetraethylammonium ion blocks transmission in autonomic ganglia, both sympathetic and parasympathetic (12). The depressor effect of tetraethylammonium on systemic systolic and diastolic blood pressures results from the inhibition of vasoconstrictor tone (13).

The effect of tetraethylammonium upon pul-

monary arterial pressure was studied in three hypertensive patients by Frisk (14). He found a prolonged lowering of pulmonary arterial pressure after tetraethylammonium and concluded that this effect was due to a lowered peripheral resistance and a pooling of blood in the periphery. Greene and Bunnell also studied the effect of TEAC upon pulmonary arterial pressure (15). These workers found a fall in pulmonary artery pressure in almost every case studied. In contrast to Frisk, these investigators concluded that the drop in pressure was too great to be explained by the observed changes in cardiac output. As a result, they believed that neurogenic vasoconstrictor tone in the pulmonary vascular tree was responsible. However, neither of these groups of workers determined the pulmonary "capillary" pressure, and, therefore, final conclusions regarding the site of action of TEAC in lowering pulmonary arterial pressure cannot be drawn from their observations.

In the present study, however, the effect of TEAC upon pulmonary arteriolar resistance was determined, thus separating vasomotor changes from alterations in cardiac output as the cause of changes in pressure in the pulmonary artery. Although a sustained fall in pulmonary artery pressure was observed in 11 of 15 subjects receiving TEAC intravenously, in only four of the ten cases in whom pulmonary resistance was calculated was the drop due to change in pulmonary arteriolar resistance. In the other cases, the decline was due to a change in cardiac output, either primarily or as a result of peripheral pooling. The decline in pulmonary arteriolar resistance after TEAC in four of six cases of pulmonary hypertension indicated that in some such cases the increase in pulmonary arteriolar resistance is mediated in part, at least, through the autonomic nervous system. In cases I. W. and J. B., the pulmonary arteriolar resistance fell to normal levels after TEAC. The failure of pulmonary arteriolar resistance to decline following TEAC in all four subjects without pulmonary hypertension suggests that the autonomic nervous system may not be an important factor in the maintenance of normal pulmonary arteriolar resistance. More normals should be studied, however.

The effect of TEAC upon the ballistocardiogram is of interest. In four of five cases, the pattern became definitely abnormal after TEAC. TEAC is said to have a direct action upon the heart (14) in animals, increasing work capacity and reducing auricular pressures of the failing heart in the heart-lung preparation (13). Hoobler and his colleagues state, however, that no direct cardiac effect may be anticipated in the human subject (13). The changes in ballistocardiographic pattern observed here, and seen also by other workers in this laboratory (16), imply that there may be a direct action of TEAC upon the human heart after intravenous doses of 5 mg. to 6 mg. per kilogram body weight.

SUMMARY AND CONCLUSIONS

1) In 11 of 15 subjects, intravenous administration of TEAC produced a sustained fall in mean pulmonary arterial pressure.

2) In four patients with normal pulmonary artery pressure, TEAC intravenously did not lower pulmonary arteriolar resistance.

3) In four of six cases with pulmonary hypertension, TEAC intravenously caused a significant decrease in pulmonary arteriolar resistance.

4) The results suggest that in some cases of pulmonary hypertension, at least one component of the increased pulmonary arteriolar resistance is mediated through the autonomic nervous system.

5) The effect of TEAC upon the cardiac output was variable. The development of an abnormal ballistocardiographic pattern after TEAC in four of five subjects suggests a direct cardiac action of the drug in man.

6) Decline in mean brachial arterial pressure was seen in each of 14 subjects after intravenous TEAC. In four of these subjects, however, the fall in pressure was due to a decline in cardiac output rather than to a decrease in total peripheral resistance.

BIBLIOGRAPHY

1. Hamilton, W. F., Woodbury, R. A., and Vogt, E., Differential pressures in lesser circulation of the unanesthetized dog. Am. J. Physiol., 1939, **125**, 130.
2. Dirken, M. N. J., and Heemstra, H., Agents acting on the lung circulation. Quart. J. Exper. Physiol., 1948, **34**, 227.
3. Hellems, H. K., Haynes, F. W., Dexter, L., and Kinney, T. D., Pulmonary capillary pressure in animals estimated by venous and arterial catheterization. Am. J. Physiol., 1948, **155**, 98.

4. Hellems, H. K., Haynes, F. W., and Dexter, L., Pulmonary capillary pressure in man. J. Applied Physiol., 1949, **2**, 24.
5. Dexter, L., Pulmonary circulatory dynamics in health and disease, at rest. Bull. New England M. Center., 1949, **11**, 240.
6. Larsson, Y., and Frisk, A. R., Tetraethylammonium bromide for producing blockade of the autonomic ganglia. Acta med. Scandinav., 1947, Supp. 196, 212.
7. Cournand, A., and Ranges, H. A., Catheterization of right auricle in man. Proc. Soc. Exper. Biol. & Med., 1941, **46**, 462.
8. Cournand, A., *in:* Third Conference on Factors Regulating Blood Pressure. Josiah Macy, Jr. Foundation, New York, 1949.
9. Cournand, A., Personal communication.
10. Goldman, I. R., Blount, S. G., Friedlich, A. L., and Bing, R. J., Electrocardiographic observation during cardiac catheterization. Bull. Johns Hopkins Hosp., 1950, **86**, 141.
11. Dexter, L., Personal communication.
12. Acheson, G. H., and Moe, G. K., The action of the tetraethylammonium ion on the mammalian circulation. J. Pharmacol. & Exper. Therap., 1946, **87**, 220.
13. Hoobler, S. W., Moe, G. K., and Lyons, R. H., The cardiovascular effects of tetraethylammonium in animals and man with special reference to hypertension. Med. Clin. N. America, 1949, **33**, 805.
14. Frisk, A. R., Hammarström, S., Lagerlöf, H., Werkö, L., Björkenheim, G., Holmgren, A., and Larsson, Y., Effect of tetraethylammonium in arterial hypertension. Am. J. Med., 1948, **5**, 807.
15. Greene, D. G., and Bunnell, I. L., Vasomotor tone in the lesser circulation, and its inhibition by tetraethylammonium chloride. J. Clin. Invest., 1950, **29**, 818.
16. Braunstein, J., Personal communication.