

## THE EFFECT OF THIOPENTAL ON PERIPHERAL VENOUS TONE

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PRICE and co-workers<sup>1</sup> described hypotension during pressure breathing in subjects anesthetized with thiopental. The hypotension was attributed to lowering of cardiac output secondary to postarteriolar pooling of blood and reduced venous return. This interpretation has been supported by other studies<sup>2,3</sup> which show that central blood volume falls in the absence of pressure breathing in subjects deeply anesthetized with the barbiturate. Since capillary volume is small, the "post-arteriolar pooling" would be represented by an increase in the volume of blood in the systemic veins. Such an increase in volume would be caused by a reduction in venous tone because venous pressure is known to fall<sup>4</sup> during thiopental anesthesia. An increase in volume in the face of a decrease in transmural venous pressure could occur only if the veins had decreased ability to resist the distending force of the blood they contain.

The experiments to be reported here were done to see if thiopental anesthesia is associated with reduction in tone of the forearm veins.

### METHODS

Surgical patients without cardiovascular disease were studied in the anesthesia preparation room before their operations. The tests were done without premedication and with subjects lying supine. Venous tone was measured in the right forearm using a plethysmographic method<sup>5</sup> which will be described briefly in paragraphs below. Pressure was measured in the antecubital veins of the slightly dependent left arm and in a femoral artery with strain gauges. End-expiratory  $\text{CO}_2$  concentration was monitored intermittently throughout most experiments with a

Liston-Becker  $\text{CO}_2$  analyzer. The water level in the plethysmograph was measured with two partially immersed electrodes.<sup>6</sup> Pressures, plethysmographic water level and end-expiratory  $\text{CO}_2$  concentration were recorded using a Sanborn direct-writing oscillograph.

Control observations were made; then thiopental was given by continuous intravenous infusions or single injections in doses sufficient to reduce mean arterial pressure 10 to 15 mm. of mercury. The level of depression was adjusted by altering the dose so that experimental observations could be made with subjects breathing spontaneously with end-expiratory  $\text{CO}_2$  concentration near control levels. The total dose of thiopental varied from 400 to 900 mg. given over periods which ranged from 20 to 40 minutes. In 3 experiments ephedrine sulfate, 25 to 50 mg. was given intravenously during the infusion of thiopental and while the subjects were hypotensive. The thiopental infusions were continued at the same rate and observations were repeated after blood pressure became stable.

Venous tone was determined by obtaining venous pressure-volume curves using a modification<sup>7</sup> of the plethysmographic method previously described.<sup>5</sup> The forearm is enclosed in a tall plethysmograph and water is added so that the pressure it exerts on the arm is greater than venous pressure but less than arterial pressure. The arterial inflow drives venous pressure in the forearm to a height greater than that of the water. The difference between the pressure within the veins and the pressure surrounding them is the *transmural pressure*.<sup>8</sup> Under these conditions it is a low value (0.5 to 1.0 mm. of mercury) which is constant and also reproducible<sup>5</sup> following an induced change in pressure. The volume of blood in the veins at this low transmural pressure is also small and constant.<sup>9</sup> The origin of all venous pressure-volume curves is the venous volume which exists at this low level of transmural

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pressure. Since the volume and pressure values are small they are regarded for practical purposes as zero. To obtain the curves the transmural pressure in the forearm veins is increased from "zero" to 30 mm. of mercury in increments of 5.0 mm. of mercury by inflating a pneumatic cuff on the arm proximal to the plethysmograph. The increase in forearm venous volume caused by each increment of pressure is measured and recorded. The curves are constructed by plotting venous volume, in milliliters per 100 ml. of forearm tissue, against transmural pressure (fig. 1). The curves are convex toward the volume axis. If the veins become less distensible or increase their tone (fig. 2) the curve falls nearer the pressure axis; if they become more distensible or lose tone the curve falls near the volume axis. The final point on the curve, the volume at a transmural pressure of 30 mm. of mercury, is termed arbitrarily the *venous distensibility*. A high value is associated with reduced tone and a low value with increased tone. Since the venous pressure-volume characteristics are the same in both arms, the naturally occurring venous volume of the forearm is the volume coordinate of the point on the curve which corresponds to the venous pressure (equals transmural pressure) measured in the arm not in the plethysmograph. The natural volume is determined by drawing a

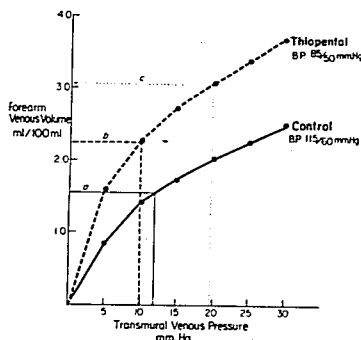


FIG. 1. Pressure-volume curves of forearm veins during the control period and during hypotension induced by thiopental.

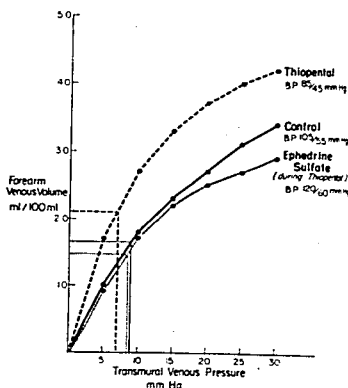


FIG. 2. Pressure-volume curves of forearm veins during the control period, during the hypotension induced by thiopental and following administration of ephedrine during intravenous infusion of thiopental.

perpendicular from the measured value on the pressure axis to the point of intersection with the curve (fig. 1).

Forearm volume changes were obtained by measuring changes in the height of the water in a vertical cylinder attached to the top of the plethysmograph. The diameter of the cylinder was such that maximal changes in limb volume raised the water level less than 5 mm. This increase in water level was not sufficient to cause a measurable error in transmural pressure in the veins. A long plethysmograph rather than the previously described tandem instrument<sup>5</sup> was used. With a long box the incompletely pressurized zone of tissue at the proximal end contributes only a negligible fraction to the total volume change within the plethysmograph unless the limb diameter is unusually large.

Mean pressure values were determined by electrical integration of the output of the strain gauges. Standard errors and probability values were computed according to methods described by Fisher.<sup>10</sup>

## RESULTS

The data from the 7 experiments are in table 1. Mean arterial pressure was reduced

TABLE 1  
VENOUS RESPONSES TO THIOPENTAL ADMINISTRATION

Experiment No.	Mean Arterial Pressure (mm. Hg)		Venous Pressure (mm. Hg)		Venous Distensibility (ml./100 ml.)		Venous Volume (ml., 100 ml.)	
	C	T	C	T	C	T	C	T
1	87	75	14.5	13.0	2.4	3.3	1.5	2.0
2	72	62	8.7	6.7	3.6	4.2	1.7	2.1
3	90	75	9.3	9.3	2.3	3.7	1.1	2.2
4	82	72	11.7	10.7	3.5	3.8	2.0	2.0
5	78	65	11.9	9.9	2.6	3.7	1.5	2.2
6	95	85	9.9	9.1	3.5	4.1	1.9	2.4
7	103	85	8.4	8.1	3.2	4.3	1.4	2.2
Mean	86.3	74.1	10.6	9.5	3.0	3.9	1.6	2.2
Mean difference	12.10		1.09		0.86		0.57	
Standard error	0.86		0.298		0.143		0.130	
Probability	<0.031		<0.02		<0.001		<0.01	

C refers to observations made during the control period; T, to observations during the hypotension induced by thiopental.

by an average of 12.1 mm. of mercury by administration of thiopental. Peripheral venous pressure fell in 6 and remained unchanged in 1 of the 7 tests. The average decrease was 1.1 mm. of mercury. Venous distensibility increased in each experiment. The average increase in forearm venous volume at a transmural pressure of 30 mm. of mercury was 0.9 ml./100 ml. of forearm tissue. Despite the fall in venous distending pressure the reduction in venous tone was sufficient to result in pooling of blood in the forearm in 6 of the 7 experiments. The average increase in venous volume of 0.6 ml./100 ml. represents a forearm blood volume increase of 35.6 per cent.

Figure 1 is taken from experiment 5. The distance on the ordinate from *a* to *b* represents the amount of blood which pooled in the forearm as a result of reduced venous tone. Figure 2 is representative of the results of 3 experiments in which epinephrine was given into a foot vein after the subject had been made hypotensive by thiopental. In each case venous tone and venous pressure as well as arterial pressure were restored to near the control levels, and the "pooled" blood was "pushed" from the forearm.

#### DISCUSSION

In previous unpublished experiments we were unable to release venous tone in the

extremities of resting supine subjects by administration of a ganglionic blocking drug or by epidural anesthesia. Warming the room from 83 to 95 F. did not change venous tone in normal subjects studied by Wood and Eckstein.<sup>5</sup> These facts led us to believe that the veins in the extremities of normal subjects resting comfortably in the supine position might have minimal tone and thus be capable of slight if any dilatation. The loss of tone in the first few of the thiopental experiments caused us to consider the possibility that venoconstriction existed during the control period, and that the reduction in tone was simply a sedative effect. We tested this possibility in the last 4 experiments by giving enough thiopental to produce sleep but not enough to lower blood pressure. No reduction in venous tone and no pooling were observed under these conditions. This observation is in accord with that of Etsten and Li,<sup>2</sup> who found that cardiac output was not reduced during light pentothal anesthesia. It may be that the large dose of thiopental reduces venous tone because of a direct effect on vascular smooth muscle rather than by a depressing action on the nervous system. In any event epinephrine appears to reverse this thiopental effect.

Figure 1 illustrates the possible result of increasing venous pressure during deep thiopental anesthesia. This could occur as a

result of such manipulations as positive pressure ventilation, changing the position of the patient or pressure on the abdomen. In figure 1 the intersection of line *c* with the ordinate indicates the volume of blood which would pool in the forearm if venous pressure were raised approximately 8 mm. of mercury above the control level. It would appear that the total venous return might be greatly reduced if venous pressure were increased by only a small amount and if all the veins responded as those in the forearm.

#### SUMMARY

Pressure-volume curves of forearm veins were obtained before and during hypotension induced by large doses of thiopental given intravenously. The results are consistent with the hypothesis that thiopental produces pooling of blood in the periphery of the body and this pooling is caused by loss of venous tone. The administration of ephedrine appears to reverse this effect of thiopental.

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thiazide may intensify digitalis action; administering potassium may prevent or abolish digitalis arrhythmias. The administration of calcium intravenously may induce digitalis intoxication while lowering of blood calcium by chelation with edathamil is a method of treatment of digitalis intoxication. (Modell, W.: *Clinical Pharmacology of Digitalis Materials*, *Clin. Pharmacol. Ther.* 2: 177 (Mar.-Apr.) 1961.)