liberated from the tissues, induced the hyperreactivity to Ach. The validity of this conclusion rests upon the assumption that metabolic products of endotoxin or secondary substances formed by endotoxin in the blood would be capable of rapid induction of alteration of vascular reactivity to Ach. We had to assume further that such products were not fixed rapidly and firmly to the tissues but were present in an active form in the blood and transferable to the recipient. These assumptions appeared reasonable in view of the observations of other authors that secondary pyrogenic products of endotoxin produced in rabbits a significantly faster rise in temperature than the original endotoxin, and that these products were transferable passively with blood(4).

Summary. Transfer of rabbit blood incubated with endotoxin *in vitro* or *in vivo* to a recipient rabbit or a heart-lung preparation induced hyperreactivity of pulmonary blood vessels to acetylcholine after a latent period comparable to that observed after injection of endotoxin. We could not demonstrate the presence of metabolic products of endotoxin or secondary substances capable of inducing immediate alteration of vascular reactivity to acetylcholine after passive transfer to a recipient animal.

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Hemodynamic Effects of Pericardial Tamponade.* (31562)

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Resuscitation and management of patients in shock from blood loss and traumatic injuries complicated by bleeding into the pericardial cavity (tamponade) pose a difficult problem which has prompted a number of investigations of experimental tamponade in animals(1-6). However, there is a lack of information concerning the quantitative relationship between the stress imposed (*i.e.*, pressure or fluid volume in the pericardial cavity) and the resulting hemodynamic changes in pericardial tamponade. The purpose of the present investigation was to examine the hemodynamic adjustments in splenectomized dogs when the volume of fluid pumped into the pericardial cavity remained unchanged as compared with the adjustments observed when the fluid pressure in the cavity was kept constant.

Materials and methods. Eight successful experiments were completed on mongrel dogs (8.4-17.1 kg body weight) which were splenectomized and prepared with implanted pericardial catheters at least 10 days prior to performing the experiments. The catheter was tied securely into the pericardium, exteriorized through the thoracic wall and the distal

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end sealed and sewed under the skin so that it could be readily exposed at any later time when needed for the experiment by making a small skin incision.

The experiments were done under sodium pentobarbital anesthesia (33 mg/kg i.v.). The pericardial catheter was first tested for patency and then connected to an infusion-withdrawal pump (Harvard Apparatus Co., Dover, Mass.) through a 3-way stopcock and to a reservoir of isotonic saline at 37°C from which fluid could be pumped into the pericardial cavity. When not in use for pumping in or removing fluid, the side arm of the stopcock was used for recording the pressure in the pericardial cavity. Simultaneous recordings of central venous pressure and arterial pressure were also obtained.

Oxygen consumption was measured with the Benedict-Roth apparatus and intubation of a short rubber tube with a tight mask. Cardiac output was determined with the indocyanine indicator method(7). The central mean circulation time and central blood volume were also calculated. Total peripheral resistance was calculated from the cardiac output and mean arterial pressure measurements.

Simultaneous measurements of plasma volume with I^{131}-albumin (RISA, obtained from Abbott Laboratories, Oak Ridge, Tenn.) and total red cell volume with Cr^{51} (Rachromate, Abbott Laboratories, Oak Ridge, Tenn.) were made during the control period and at the mid-point of tamponade(8). Hematocrit values were obtained with the micro-centrifuge method and corrected by the factor of 0.97 for trapping(9). The plasma protein level (g%) was determined with the Refractive Index method(10).

Results. 1. *Pericardial and central venous pressure.* As shown graphically in Fig. 1, the mean pericardial and central venous control pressures were slightly below zero. With the onset of tamponade they increased to a positive value of approximately 13-14 cm saline. The pericardial pressure was generally slightly higher than the central venous pressure in both the constant pressure (CP) and constant volume (CV) experiments of 4 dogs each. During the 2-hour period of the CV tamponade, both pericardial and central venous pressures decreased to near zero. In the CP experiments such a decrease was not observed because of the further introduction of saline.

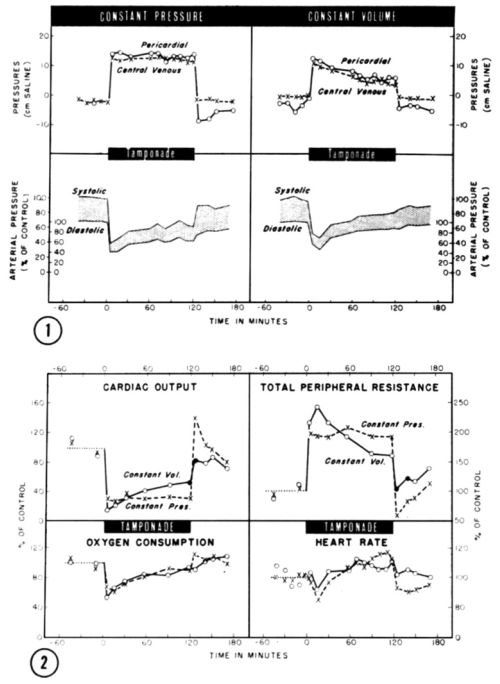


FIG. 1. Effect of constant pressure (CP) and constant volume (CV) pericardial tamponade on pericardial, central venous and arterial pressure. Symbols (O,X) represent mean values of 4 experiments.

FIG. 2. Influence of CP and CV pericardial tamponade on cardiac output, total peripheral resistance, oxygen consumption and heart rate. Symbols same as Fig. 1. Darkened circles are used whenever $P < 0.05$ in t test.

2. *Arterial pressure.* As the pericardial and central venous pressures were elevated immediately following the onset of tamponade, both arterial pressure and pulse pressure showed a marked reduction from the control values. The maintenance of constant pericardial and central venous pressures did not allow as much recovery of the arterial pressure as in the CV experiments where the arterial pressure returned almost to the control level during the 2-hour period of tamponade (Fig. 1). The pulse pressure showed only a limited recovery during CP tamponade but increased markedly after the tamponade was released. This differs from CV experiments where the pulse pressure gradually returned toward normal and did not show a marked increase following the removal

of the saline.

3. *Cardiac output.* As shown in Fig. 2, the cardiac output decreased and total peripheral resistance increased at the onset of tamponade in both series of experiments. The CV experiments showed a continuous recovery of both the cardiac output and peripheral resistance during tamponade and both returned to near control levels after release. The CP experiments showed almost no recovery of either cardiac output or total peripheral resistance during the 2-hour period, but following the release the cardiac output rose to 140% of control and the peripheral resistance decreased to near 50% of control. During the subsequent hour these values gradually approached control levels. In both series of experiments the heart rate showed an initial drop, followed by a progressive increase attaining a maximum value of approximately 110-120% of control at the termination of the tamponade. The heart rate returned approximately to control values during the post tamponade period.

4. *Oxygen consumption.* The oxygen consumption fell to approximately 50% of the control at the onset of the tamponade in both the CV and CP experiments (Fig. 2). In both series of experiments the oxygen consumption returned to almost 90% of the control value during 2 hours of tamponade. Following release the control values were once again attained.

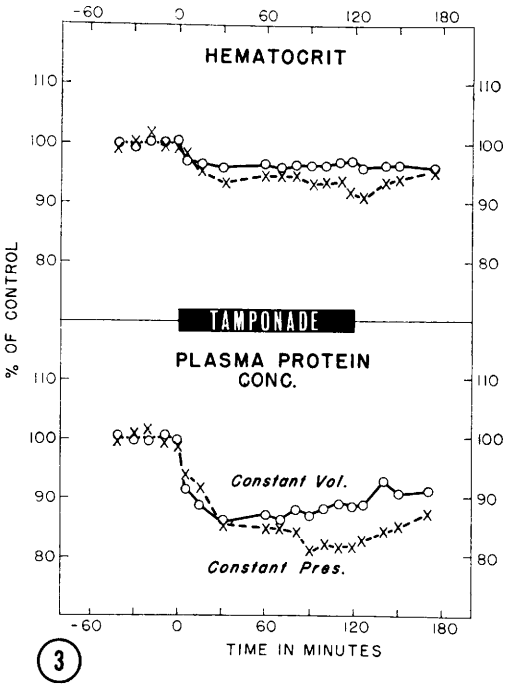
5. *Plasma protein concentration and hematocrit.* Immediately after the onset of both CP and CV tamponade, plasma protein concentration and hematocrit fell in a parallel manner, with the changes being slightly greater in the CP experiments (Fig. 3). These changes occurred mainly in the first 30 minutes. During the remaining 90 minutes and also after release, there was little change in hematocrit values. There appears to be a slight recovery of the plasma protein concentration in the CV experiments during the remainder of the 2-hour period and also following release. This recovery is not evident in the CP experiments except during the post tamponade period.

6. *Total blood volume.* The plasma volume, cell volume, total blood volume, and circulating total plasma protein data are presented in

TABLE I. Blood Volume and Total Circulating Plasma Protein Changes in CP and CV Tamponade.

	Constant pressure (n = 4)				Constant volume (n = 4)			
		Tamponade		Difference		Tamponade		Difference
	Control	Expected*	Measured	Meas.—Exp.*	Control	Expected*	Measured	Meas.—Exp.*
Plasma volume (ml/kg)	48.3 ± 2.2†	46.6 ± 2.2	54.2 ± .9	+7.6 ± 4.7	47.5 ± 3.2	46.1 ± 3.2	50.3 ± 2.8	+4.2 ± 2.5
Red cell volume (ml/kg)	29.7 ± 3.3	28.5 ± 3.2	28.6 ± 3.7	+ .1 ± .8	32.0 ± 1.6	30.9 ± 1.6	30.2 ± 1.5	− .7 ± .7
Total blood volume (ml/kg)	78.0 ± 3.2	75.4 ± 3.5	82.8 ± 3.2	+7.4 ± 4.4	79.5 ± 2.3	77.0 ± 2.2	80.5 ± 1.7	+3.5 ± 2.11
Total plasma protein (g/kg)	2.97 ± .09	2.86 ± .09	2.81 ± .07	− .05 ± .45	2.78 ± .28	2.70 ± .27	2.57 ± .30	− .13 ± .13

* Corrected for loss by blood sampling.
† Values represent mean ± S.E.M.



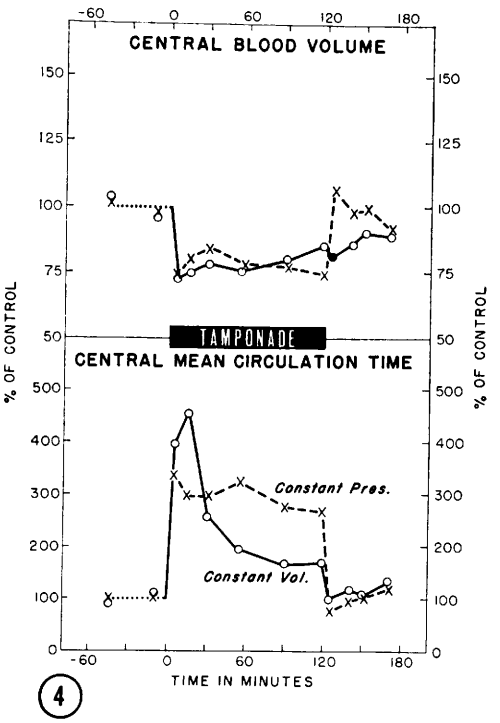


FIG. 3. Effect of CP and CV pericardial tamponade on hematocrit and plasma protein concentration. Symbols same at FIG. 1.

FIG. 4. Influence of CP and CV pericardial tamponade on central blood volume and central mean circulation time. Symbols same as Fig. 1. Darkened circles are used whenever $P < 0.05$ in t test.

Table I, where the control values are compared with those during tamponade. The total blood volume (ml/kg) increased by a greater degree in the CP than in the CV experiments. The change can be attributed to the expansion of the plasma volume from hemodilution. The decrease in cell volume is accounted for by sampling loss. The total circulating plasma protein decreased somewhat during the tamponade when compared to the control values.

7. *Central blood volume.* As seen in the upper half of Fig. 4, the central blood volume dropped 25% below the control value immediately upon the onset of tamponade, but recovered somewhat in the CV experiments during the 2-hour period and also after release, but never returned to the control value. In the CP experiments there was almost no recovery during the tamponade period, but following release the central blood volume increased to a value greater than the control and then gradually decreased during the remainder of the post tamponade period. The lower part of Fig. 4 shows the central mean circulation time, which increased in both series, the recovery being greater in the CV than in the CP experiments. With pressure maintained constant, there was much less recovery during tamponade followed by a recovery to near control values upon release.

Discussion and conclusions. The increase in pericardial and central venous pressures is sufficient to impede venous return to the right atrium and thereby produces a striking drop in cardiac output (Fig. 2). In addition there is a moderate reduction in heart rate during the first 15 minutes of the tamponade (Fig. 2), which also contributes to the reduction in cardiac output. Despite the increase in total peripheral resistance, the reduced blood flow results in an immediate and marked drop in arterial pressure. This decrease activates the baroreceptor mechanisms producing an increase in heart rate which eventually exceeds the control values. The oxygen consumption

drops initially because of the reduced blood flow but recovers during the course of the experiment almost to the control value. Since the recovery of oxygen consumption was greater than that of the cardiac output, the oxygen extraction from the blood must have increased, especially in the constant pressure experiments. Coincident with the onset of the tamponade there is an increase in respiratory rate and minute volume. A comparison of the two series of experiments shows that in the CV experiments, the pericardial and central venous pressures continuously and gradually decline during tamponade, allowing recovery of the reduced cardiac output by approximately 40%. As the cardiac output and arterial pressure recover, the total peripheral resistance also decreases progressively in the CV experiments. By contrast, in the CP experiments the pericardial and central venous pressures remain elevated and the reduced cardiac output and the elevated total peripheral resistance do not change throughout the course of the experiment. The arterial pressure also recovers to a lesser extent in the CP experiments. The decrease in both pericardial and central venous pressures during tamponade may be explained by two possible causes. Firstly, there may be a leakage or absorption of fluid from the pericardial cavity. Secondly, there may be a change in the size or shape of the heart or pericardium as an adaptation to the increased pressure. With one exception, the volume recovered from the pericardium was less than the volume pumped in, showing that some leakage or absorption occurred. This loss in volume could only be a partial explanation of the reduction in pericardial and central venous pressures, since the volume of saline required to maintain constant pressure was much larger than the *unrecovered* volume.

The reduced arterial and mean capillary pressure presumably facilitated entrance of fluid from the tissues with expansion of the plasma volume (Table I) and reduction in arterial hematocrit and plasma protein concentration (Fig. 3). It should be noted that the volume of fluid lost (unrecovered) from the pericardial cavity during tamponade was on the average 17 ml in the CP experiments and 27 ml in the CV experiments. In the former the plasma volume rose an average of 80 ml and in the latter by an average of 55 ml. Hence it is apparent that the amount of fluid escaping from the pericardial cavity during tamponade does not account for the observed hemodilution. In fact the plasma volume increased more in the CP experiments where the pericardial loss was smaller, indicating that the mean capillary pressure is lower in these experiments. The determining factor may be an increase in the pre/post capillary resistance ratio resulting from increased sympathetic activity(11,12). The fact that the peripheral resistance also is higher in the CP experiments is in agreement with a preferential constriction of the precapillary segment. The fluid influx involves a protein-free fluid since the total circulating plasma proteins (g/kg) do not change appreciably. The fall in central blood volume in the face of a rise in total blood volume suggests that pericardial tamponade causes a redistribution of regional blood volume.

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