Mean Circulatory Filling Pressure Measured Immediately After Cessation of Heart Pumping

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When the heart stops, the arterial pressure falls and the venous pressure rises until after 30–50 seconds the two pressures almost reach equilibrium. This equilibrium pressure, which presumably is equal to the pressure in all portions of the circulatory system, has in previous studies from this laboratory (1-3) and in this present study been called the 'mean circulatory filling pressure.' The term 'mean systemic pressure' as used by Starling (4) has not been used because the word 'systemic' now has the connotation of applying to the peripheral circulatory system alone rather than the entire circulatory system. Also, the terms 'hydrostatic mean pressure' as used by Bolton (5) and 'static blood pressure' as used by Starr (6) have not been employed in this discussion because to many physiologists the word 'static' means 'unchanging' and it has been shown many times that the autonomic reflexes continue to cause marked changes in pressures throughout the circulatory system even after the heart stops pumping (1-7).

Another reason for using the term 'mean circulatory filling pressure' is that, even though the pressures throughout the circulatory system under dynamic conditions are widely variant, there is a mean integrated pressure in the circulatory system all of the time. If one takes into consideration the different elasticity coefficients of the different blood vessels and also takes into consideration the different volumes of the different beds, then the mean integrated pressure of the circulatory system at any given instant can be shown mathematically to be exactly equal to the mean circulatory filling pressure should the heart stop beating and all pressures come to equilibrium instantaneously. Therefore, use of a term which implies that there is a continuously present mean pressure in the circulatory system has many advantages in emphasizing the importance of this pressure.

The mean circulatory filling pressure as it exists in the body at any given instant cannot possibly be measured because life is dependent on dynamic circulatory conditions. On the other hand, it has been pointed out by all investigators who have measured the mean circulatory filling pressure that shortly after the heart stops beating, intense vasoconstriction begins throughout the circulatory system (4, 6, 7). Consequently, in order to estimate accurately the mean circulatory filling pressure as it exists at any given moment, it is essential that measurement of this value be made within a few seconds after the heart stops beating or, in other words, before significant changes in vasomotor tone can take place as a result of reflexes. In order to make such rapid measurements it is necessary to establish rapidly equilibrium of the circulatory pressures by artificial means, for the rate of blood flow from the arteries to the veins is too slight for rapid equilibrium to occur. Except for the preliminary measurements reported from this laboratory (1-3, 7), the mean circulatory filling pressure has never been determined within the short interval of time after the heart stops beating and before reflex vasomotor constriction begins. In the present study, attempts which are believed to have been successful have been made to make such measurements under a number of different conditions.

METHODS

One hundred five dogs anesthetized with sodium pentobarbital and heparinized with 3 mg/kg of heparin have been used in these experiments. Pressures were measured with special recording mercury manometers.
within was measured from a catheter inserted into the right crossing. Also, special zero adjustments on the manometers were provided so that measurements accurate within 1 mm Hg could be made. The venous pressure was measured from a catheter inserted into the right atrium through an external jugular vein, and the arterial pressure was measured from a femoral or carotid catheter. The zero pressure level was considered to be one third the A-P thickness of the chest posterior to the anterior sternal surface. This is the zero level recommended by Eyster (8), and it has been found in this laboratory (7) to represent approximately the best estimation of the anatomical position of the right atrium in the chest of the dog.

In most of the experiments the heart was stopped by initiating ventricular fibrillation with a 110-volt 60-cycle alternating current stimulus applied to two needle electrodes placed anterior to the heart in the skin of the chest wall. After measurements were made the hearts were defibrillated with high voltage, high amperage, 60-cycle current delivered through large electrodes placed anteriorly and posteriorly on the chest. This procedure has been described and critically analyzed previously (9). In 15 experiments the hearts were stopped by vagal stimulation. This procedure always gave lower measurements for mean circulatory filling pressure than did fibrillation of the heart. Because of the tendency for the heart to dilate and perhaps other effects of vagal stimulation to occur, the higher values obtained by fibrillation have been considered to be more accurate and are the ones presented unless otherwise stated. In 21 dogs the flow of blood ceased, a special perfusion pump of the roller propulsion type was built to require only 20 cc of blood for priming. This was used to pump blood from a catheter inserted into the aorta through a femoral or a carotid artery to a catheter in an external jugular vein. The most crucial factor in the entire determination of mean circulatory filling pressure was the catheter inserted into the aorta. For repeated success the tip of the catheter must lie almost exactly at the point at which the aorta passes through the diaphragm. Elsewhere the vessel usually collapses around the orifice of the catheter.

In order to prevent interference by vasomotor reflexes with the measurements of mean circulatory filling pressure, in many of the animals total spinal anesthesia was instituted with 200 mg of procaine or 150 mg of metycaine in 20 cc of saline, and continuous infusions of epinephrine at varying infusion rates were begun. Such animals, as detailed previously (10–12), are totally devoid of all vasomotor reflexes, and the vasomotor tone of the circulatory system may be changed at will by varying the rate of epinephrine infusion.

The over-all procedure for the measurement of the mean circulatory filling pressure was as follows: the heart was fibrillated, and at the same instant the perfusion pump was started. The kymograph was operated at a rapid rate in order to make measurements more accurate. The arterial pressure began falling, and the venous pressure began rising. Within 2–6 seconds these two pressures became equal, and, because the pump was continuing to operate, the arterial pressure actually fell below the venous pressure. The mean circulatory filling pressure was considered as that value at which the two pressures crossed each other. Measurements in which equilibrium did not occur within 6 seconds were considered void because studies have indicated that significant increase in vasomotor tone begins to occur between approximately 6 and 10 seconds after the heart stops beating (7).

### RESULTS

**Critique of the Method for Measuring Mean Circulatory Filling Pressure.** Repeated measurements of the mean circulatory filling pressure. In 29 dogs in which the vasomotor and physical factors of the circulatory system were maintained under relatively constant conditions, repeated measurements of the mean circulatory filling pressure were made as illustrated in figure 1. As many as 20 such measurements were made in some of these animals. As long as the function of the circulatory system, as estimated by arterial pressure, remained approximately constant throughout the experiment, the repeated measurements of the mean circulatory filling pressure never varied more than 1 mm Hg.
from the average of all the values obtained in the respective animal. However, when the repeated processes of fibrillation and defibrillation were instituted in rapid succession, the arterial pressure fell progressively in five dogs a total of 18-52 mm Hg while the mean circulatory filling pressure fell concurrently a total of 1-2 mm Hg. For each mm Hg fall in the mean circulatory filling pressure, the arterial pressure fell an average of 28 mm Hg with a standard deviation of ±6.7 mm Hg.

Effect of anesthesia on mean circulatory filling pressure. When the mean circulatory filling pressure was determined with the dog under light anesthesia, he often began gasping for breath just as soon as the heart was fibrillated, and, because of chest and abdominal contractions, the venous and arterial pressures rose and fell spasmodically in a manner that made it impossible to measure the mean circulatory filling pressure. Consequently, moderate anesthesia, though not extreme anesthesia, was necessary to prevent respiratory interference with the measurement of mean circulatory filling pressure. Once the anesthesia was sufficient for adequate measurement of mean circulatory filling pressure, additional increments of anesthesia did not cause depression of the mean level of the circulatory filling pressure until the anesthesia became sufficient also to depress the arterial blood pressure.

Effect of curare on the measurement of the mean circulatory filling pressure. Six dogs were curarized during the course of measurement of the mean circulatory filling pressure. It was found that curare given to dogs under light anesthesia removed the respiratory effects on the measurement of the mean circulatory filling pressure in the same manner as did shifting the degree of anesthesia from light anesthesia to moderate anesthesia. On the other hand, in three dogs in which the anesthesia was already sufficient for adequate measurement of the mean circulatory filling pressure, curarizing the dogs did not change the measured value of the mean circulatory filling pressure.

Effect of operative fluid loss on measurement of the mean circulatory filling pressure. In many of the experiments in order to keep the operative loss of blood at essentially zero, the incisions for catheterization and cannulation were made by means of electrocautery. Even with these precautions approximately 20 cc of blood was needed to fill the rubber tube in the special roller perfusion pump. This blood was supplied from a donor animal in many instances. However, in order to determine whether or not donor blood was necessary, the following experiment was tried in three instances: After fibrillating the hearts of these three animals, the arterial and venous pressures were brought to equilibrium rapidly in the usual manner, and then the pump was stopped. While the mean circulatory filling pressure was being recorded on the kymograph, rapid injections of 30 cc of Tyrode's solution were made. In none of these instances did the injection of this quantity of fluid into the circulatory system cause sufficient rise in the mean circulatory filling pressure for this to be measured on the kymographic record. It was concluded that the precaution of using donor blood is unnecessary.

Determination of whether or not pumping blood from the arterial system to the venous system brings the entire circulatory system to complete equilibrium. In 15 experiments after fibrillation of the hearts and after the pump had brought the arterial and venous pressures to complete equilibrium, the pumping was stopped, and the kymograph was allowed to continue running. Within the first 5 seconds after the pumping stopped, the mean circulatory filling pressure remained continually within 1 mm Hg of the value at which the arterial and venous pressures first came to equilibrium. In seven dogs used for such measurements the natural reflexes of the circulatory system had been removed, as discussed under 'methods.' In these dogs the mean circulatory filling pressure, as measured on the kymograph, remained within 1 mm Hg of the crossing point of the arterial and venous pressures for at least 10 seconds following the initial establishment of equilibrium between these two pressures. When continuous recordings were made in these animals for several minutes beyond this first establishment of the equilibrium, the recorded mean circulatory filling pressure never rose above the value of the first equilibrium point, thus illustrating that fluid from areas other than the arteries and veins does not continue to flow into the
arteries and veins in sufficient volume to affect the measurement of mean circulatory filling pressure after initial establishment of equilibrium.

**Normal Mean Circulatory Filling Pressure.** In 18 dogs, shortly after each experiment was begun and while the mean arterial blood pressure under sodium pentobarbital anesthesia was definitely in the normal range of 110–140 mm Hg, the mean circulatory filling pressure was measured a total of 31 times. The average value of these measurements was 6.3 mm Hg with a standard deviation of ±0.94 mm Hg.

When vagal stimulation was used to stop the heart the values averaged approximately two-thirds those measured following fibrillation.

**Effect of Total Spinal Anesthesia on the Mean Circulatory Filling Pressure.** In five dogs the mean circulatory filling pressure was measured immediately after instituting total spinal anesthesia. The average mean circulatory filling pressure was 4.9 mm Hg with a standard deviation of ±0.7 mm Hg. The arterial pressure under these same conditions averaged 45 mm Hg with a standard deviation of ±11 mm Hg.

**Comparison of Mean Circulatory Filling Pressure in the Normal and in the Areflex Animal.** In five dogs the mean circulatory filling pressure was measured immediately after beginning the experiment, and then total spinal anesthesia, as described under 'methods,' was instituted. Following this, constant infusion of epinephrine at a rate sufficient to cause the arterial pressure to return to the original control level was begun. The mean circulatory filling pressure was again measured. In these five dogs it was found that the mean circulatory filling pressure in the areflex dog having a normal arterial pressure varied from 0–2 mm Hg greater than that in the normal animal.

**Effect of Vasomotor Tone on Mean Circulatory Filling Pressure.** In five dogs total spinal anesthesia was instituted, and then epinephrine at varying rates of infusion was given. Figure 2 illustrates the effect of different rates of infusion of epinephrine on the mean circulatory filling pressure. It will be noted from this figure that initial increments of epinephrine infusion caused a marked, progressive increase in the mean circulatory filling pressure. However, as the rate of infusion of epinephrine became extreme, the mean circulatory filling pressure approached an asymptotic maximum which, in the illustrated experiment, was approximately 16 mm Hg. The other four experiments showed identically the same results but with asymptotic maxima of 14, 18, 16, and 14 mm Hg, respectively.

**Leakage of Fluid From the Circulatory System When the Mean Circulatory Filling Pressure Is High.** In 10 normal dogs and in three areflex dogs normal saline or Tyrode’s solution equal in quantity to \( \frac{1}{2} - \frac{3}{4} \) normal blood volume was injected rapidly into the circulatory system. Following this, the arterial blood pressure, the venous pressure, the hematocrit, and the mean circulatory filling pressures were measured progressively for an ensuing 20 minutes to an hour. The same experiment was performed an additional three times in areflex dogs using whole blood equal in quantity to approximately one-third the blood volume. Figure 3 illustrates the course of the arterial blood pressure, the mean circulatory filling pressure, and the hematocrit following
Mean circulatory filling pressure

Figure 2. Effect of continuous injection of epinephrine (at different infusion rates) on the mean circulatory filling pressure and the arterial pressure.

Figure 3. Effect of rapid infusion of Tyrode's solution on the mean circulatory filling pressure, arterial blood pressure, and the hematocrit.

An infusion of 50 cc/kg of Tyrode's solution. Precisely the same effects were observed in all of the animals receiving saline or Tyrode's solution except for minor quantitative differences. Also, it was especially interesting to note that the effects on the various pressures were the same when blood was used instead of saline or Tyrode's solution in five additional experiments. The mean circulatory filling pressures following such infusions fell toward an asymptotic level which was very near the original control value, and these curves obeyed the same negative exponential formula, with half-times of 2-3 minutes, as was recorded previously for arterial pressure, venous pressure, and hematocrit. Assuming that there was neither sequestration nor loss of red blood cells from the circulatory system during the course of these experiments, the hematocrit changes were indicative of changes in blood volume. From the curves of Figure 3, it seems apparent that at the same time that the mean circulatory filling pressure was falling, there was a concurrent loss of fluid from the circulatory system, and that, as the mean circulatory filling pressure reapproached the normal control value, the rate of fluid loss from the circulatory system progressively diminished.

DISCUSSION

It is unfortunate that most of the previous measurements (5-7) of mean circulatory filling pressure ('static pressure,' 'mean systemic pressure') have been contaminated by vasomotor reflexes, for this makes most of these measurements of value only for relative purposes. Actually, the mean circulatory filling pressure of the circulatory system as measured within the first few seconds after the heart stops beating is only about one-half the same pressure measured 30 seconds or more after the heart stops beating. It has also been surprising to note how low this mean circulatory filling pressure is. Indeed, in the present studies, it was found to be an average of 6.3 mm Hg and even lower than this when measured by stopping the heart with vagal stimulation instead of fibrillation. This is only 1.4 mm Hg above the value found for the mean circulatory filling pressure in animals subjected to total spinal anesthesia, which animals, presumably, had almost minimal vasomotor tone.

The true importance of the mean circulatory filling pressures is yet to be elucidated. Actually, this value is determined by the ratio of fluid volume to the physical status of the circulatory system. The physical status in turn is determined by vascular elasticity, vascular plasticity, vascular tone, vascular dimensions, and external vascular pressure. Obviously, the greater the mean circulatory filling pressure, the greater will be the filling pressures of at least some parts of the circulatory system.
even under dynamic conditions, and this undoubtedly affects the operation of the circulatory system.

It was noted in the above results that whenever massive infusions are given to a dog, the mean circulatory filling pressure rises immediately and then falls along a negative exponential curve to approach almost the original control value for mean circulatory filling pressure. Because mean circulatory filling pressure is a direct function of blood volume, it is obvious that the increase in mean circulatory filling pressure is one of the more primary effects occurring in the circulatory system following an infusion and that other changes in the circulatory system, such as increases in arterial and venous pressures, probably result from the generalized increase in mean circulatory filling pressure. Therefore, though the exact relationship of mean circulatory filling pressure to other pressures has not been worked out, it seems obvious from the present experiments that the mean circulatory filling pressure is one of the many factors which enter into the determination of venous and arterial pressures.

It has also been pointed out in the above experiments that, as long as the fluid volume is excessive as the result of an infusion, there occurs active leakage of fluid from the circulatory system, but this leakage ceases as the mean circulatory filling pressure reapproaches normal. It has been found that the rate of decrease in mean circulatory filling pressure is approximately proportional to the elevation of mean circulatory filling pressure above normal. This is what would be predicted mathematically if the rate of fluid leakage from the circulatory system were a direct function of elevated mean circulatory filling pressure. Therefore, it appears that this is an automatic mechanism for the regulation of blood volume. That is, when there is excess blood volume, fluid leaks from the circulation rapidly at first and progressively more slowly as normal blood volume is approached. This same mechanism has been pointed out many times previously in connection with studies on venous and arterial pressures following infusions (10, 11, 13, 14).

The fact that continuous infusion of maximal quantities of epinephrine failed to elevate the mean circulatory filling pressure above a maximal value of 16–18 mm Hg has a very important implication regarding clinical venous pressures. Because the mean circulatory filling pressure is the pressure to which venous pressure rises when the heart stops completely, it is apparent from the theory of limits that this same level of 16–18 mm Hg is an upper limit to which the central venous pressure could be elevated by simultaneous heart failure and maximal vasoconstriction caused by epinephrine. This is the same limit found previously following a maximal Cushing reflex (7). On the other hand, after fluid infusion, the level of the mean circulatory filling pressure may be elevated to any height, depending on the quantity of infusion. Therefore, it appears that some of the very high venous pressures recorded in clinical heart disease must depend at least to some extent on other factors, such as fluid retention, besides simply failure of the heart and increased vasomotor tone.

It should be emphasized that each measurement which has been made in this study, for technical reasons, has been a composite measurement of both the mean pulmonary circulatory filling pressure and the mean peripheral circulatory filling pressure. However, because the pulmonary circulatory system involves only approximately one-fifth the total circulatory volume, the mean pulmonary circulatory filling pressure would probably have to be at least 4 mm Hg different from the mean systemic circulatory filling pressure in order to affect the composite measurement by as much as 1 mm Hg. Because it is unlikely that 4 mm Hg difference does exist under normal conditions, and, because the measurements are not accurate within less than 1 mm Hg, it is probable that the over-all measurement of mean circulatory filling pressure represents fairly accurately and mainly the mean peripheral circulatory filling pressure. Yet, there are some conditions such as left heart failure or pulmonary stenosis in which this generalization is undoubtedly untrue. Indeed, when the circulation was stopped in the present experiments by pulmonary artery constriction, a catheter passed beyond the constriction always measured a much lower mean pulmonary circulatory filling pressure than the mean filling pressure in the peripheral system.
SAUMARY

The pumping of blood by the heart of some 100 or more dogs was stopped suddenly by a) fibrillating the heart, b) strong stimulation of both vagi, or c) suddenly occluding the pulmonary artery by pulling a plastic loop which had been placed around the artery several weeks prior to experimentation. Immediately after heart pumping had ceased, blood was pumped by a perfusion pump from the aorta into an external jugular vein. In normal dogs, the mean circulatory filling pressure measured in this manner averaged 6.3 mm Hg with a standard deviation of ±1 mm Hg. Total spinal anesthesia caused this mean circulatory filling pressure to fall to an average of 5 mm Hg. Increasing the vasomotor tone (by injecting continuously maximal quantities of epinephrine) increased the mean circulatory filling pressure up to an average value of approximately 16 mm Hg. When heart pumping was stopped slowly by gradually pulling the plastic tube constrictor around the pulmonary artery, the maximal mean circulatory filling pressure which developed while the animals initiated their own sympathetic reflex activity averaged 13 mm Hg. Infusion of various quantities of fluid immediately prior to measuring the mean circulatory filling pressure caused elevation of the mean circulatory filling pressure, the elevation recorded being a function of the total quantity of fluid injected. When the mean circulatory filling pressure was acutely elevated by such fluid infusions, this pressure progressively fell back toward the control level along a negative exponential curve.

REFERENCES