Experimental Studies on Fluid Replacement in Puppies: With Special Reference to Central Venous Pressure

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INTRODUCTION

Along with the recent elucidation of the physiology of body fluid and the progress in blood transfusion and fluid replacement, death due to hemorrhage or loss of body fluid has become a rarity. Especially, since blood chemical determinations have been widely carried out in clinical practice, adequate deficit therapy is performed against the loss of fluid and operative results markedly improved. However, in the determination of circulating blood volume to provide the basis for the dose of fluid administration, few simple methods enabling continous monitoring are available.[2,3] Although some methods are now available to calculate blood volume directly by dye dilution techniques or by radioactive methods[4,5] with the use of tagged red cells or plasma, they are not adequate for continuos monitoring of the blood volume changes. In the fiedls of pediatric surgery, especially in newborns and infants, advanced dehydration may occur due to vomiting or diarrhea. In hypotonic dehydration, circulatory plasma volume markedly decreases, leading to shock. Therefore, early discovery of loss of blood volume are imperative.

Following the introduction of central venous pressure monitoring in patients after thoracotomy by Hughes[28] and McGovern and the popularizing of this technique by Wilson and his associates, Borow[3] reported a series of patients in whom such monitoring was carried out for a wide variety of general surgical problems. Mostert[35] also considered central venous pressure to be more adequate than determination of blood volume using RISA for the evaluation of circulatory dynamics. Recently, increased use has been made of central venous pressure as a guide to blood volume changes although most observers agree that the two are not quantitatively related.[4,5,9,19,21,34,53,54] When cardiovascular function is stable, the central venous pressure will vary directly with alterations in blood volume.[33]

When blood volume and vascular dynamics are stable, the central venous pressure will vary inversely with cardiac pump action. Changes in vascular tone may also affect the central venous pressure independently.[52] Since the reason for the existence of the venous system as the reservoir system in the whole vascular system is due to its large capacitance, moderate changes of blood volume would scarcely

cause changes in central venous pressure. However, beyond the limit of the capacitance of the venous system, central venous pressure would suddenly rise. The present study was, therefore, undertaken to determine the reliability of central venous pressure measurement as a method of assessing increase of blood volume following overinfusion in puppies.

METHODS

Puppies weighing 500 to 1,500 grams were selected for the study. Except in group I, the puppies were anesthetized with intravenous Sodium Thiopental (17.5 mg. per kilogram body weight) and they were fixed on a table in a supine position. The catheter for the determination of arterial blood pressure was inserted from one femoral artery to abdominal aorta. The catheter for the measurement of central venous pressure was inserted from the right external jugular or right femoral vein to a point close to the right atrium to connect with water manometer. In the dogs for the assessment of pulmonary arterial pressure, succinylcholine chloride (2 mg. per kilogram body weight) was intramuscularly injected and followed by intratracheal intubation. After connecting the tube with infant circle type anesthetic apparatus, pure oxygen was given through inhalation, along with manual artificial respiration. After thoracotomy at the 4th intercostal space, pericardium was opened and the catheter for pressure determination was inserted into the pulmonary artery, and the chest closed. Pulmonary arterial pressure was determined with a water manometer. A catheter was inserted into the remain femoral vein for fluid infusion and administration of drugs. Physiological saline with addition of heparin at a concentration of 20 mg. per litre was used for infusion. One dose of infusion was 50 ml. per kilogram body weight, except for some animals in group II. The saline was injected through single shot from a syringe at the rate of 20 to 30 ml. per minutes after initial observations of arterial pressure, central venous pressure, and pulmonary arterial pressure. The measurements were repeated every 5 minutes after infusion for 30 minutes. When all parameters had returned to preadministration level, the animals were reinfused with the same dose of heparinized saline to observe the changes in pressures. Finally, the dogs, all of which showed signs of pulmonary edema, were sacrificed and the lungs excised and weighed. Experiments were carried out in the following 6 groups.

Group I. In three small puppies with body weight of 500 grams and in five moderate puppies with body weight above 1 kilogram, alterations in central venous pressure after infusion of saline (50 ml. per kilogram body weight) were compared. In group I., experiments were carried out without anesthesia, to compare the influence of anesthetics with anesthetized dogs of group II and subsequent groups.

Group II. Using puppies of body weight above 1 kilogram, 50 ml./kg. of saline was given in five animals and 100 ml./kg. in another six animals to study the

difference in fluctuation of central venous pressure.

Group III. Puppies with body weight above 1 kg. were dehydrated with the following three methods.

(1) In 3 dogs, laparotomy was followed by ligation of the pyloric portion of the stomach to induce obstruction and the abdomen was closed. Due to vomiting, state of dehydration occurred postoperatively.

(2) In 6 animals, laparotomy was followed by incision of part of the anterior wall of the stomach and the abdomen was closed. Postoperatively, peritonitis led to dehydration.

(3) In 3 dogs, jejunal fistula was made to allow the orally ingested food and the intestinal juice to be excreted from it out of the body.

In all the experiment, dogs with 3 to 5 % loss of body weight during 2 to 5 days after operation were used, to study the alterations in central venous pressure accompanying saline infusion of 50 ml./kg.

Group IV. In 5 puppies with body weight of more than 1 kg., changes in central venous pressure and pulmonary arterail pressure were compared after infusion of 50 ml./kg.

Group V. In 5 puppies weighing more than 1 kg., isoproterenol, 0.4 μg./kg. per minutes, intravenously, was administered over 10 min. period, followed by infusion of 50 ml./kg. to compare the changes in the central venous pressure and the pulmonary arterial pressure.

Group VI. In 5 puppies with body weight of more than 1 kg., phenoxybenzamine, 0.2 mg./kg., was slowly injected intravenously. After stabilization of the arterial pressure, changes in central venous pressure and pulmonary arterial pressure accompanying infusion of 50 ml./kg. were measured.

RESULTS

Group I. As shown in Fig. 1, the group of puppies with body weight of 500 grams showed average rise of central venous pressure of 7 cm H_2O after infusion. In puppies weighing over 1 kg., average rise was 4.2 cm H_2O. After the peak, the pressure values in both groups decreased and finally were close to starting values. Since the animals were not under anesthesia, central venous pressure rose upon every crying. After the second injection, the central venous pressure of the dogs weighing 500 grams suddenly rose by more than 10 cm H_2O, and the fall of the pressure was delayed. In puppies of 1 kg. body weight, the peak of the pressure after second infusion reached to 7.5 cm H_2o higher level than the starting level. After 20 minutes, however, the pressure fell towards the base-line. Among three dogs of 500 grams, one died of pulmonary edema during secondary infusion.

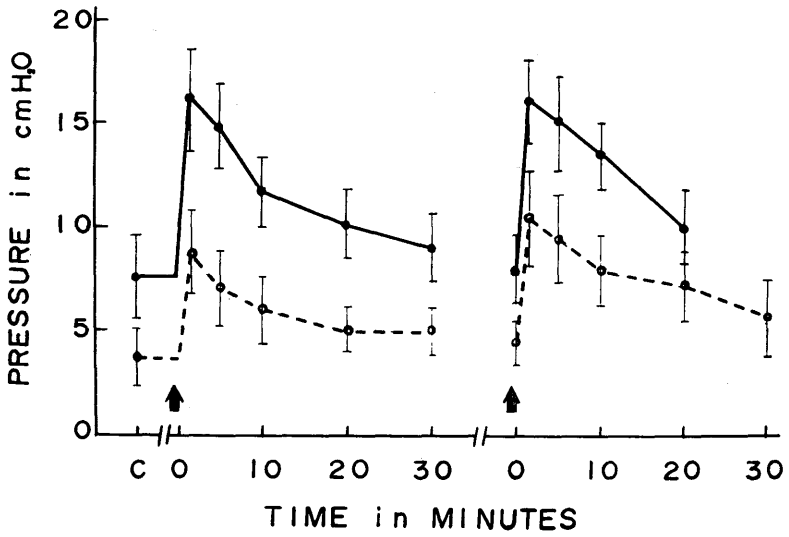

Fig. 1. Comparison of changes in central venous pressure after infusion between small puppies (solid line connecting solid circles) and large puppies (broken line connecting open circles). Bars show standard error. Arrows indicate infusion of saline (50 ml./kg.).

Group II. When the dose of saline was increased twice to 100 ml./kg., central venous pressure suddenly rose by more than 20 cm H_2O even in puppies of more than 1 kg. body weight (Fig. 2). The fall in pressure after the peak occurred

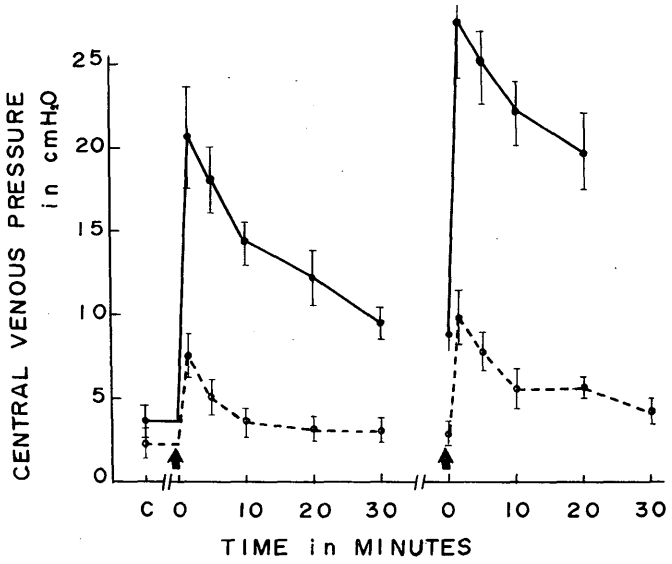

Fig. 2. Comparison between central venous pressure of the dogs infused 100 ml./kg. of saline (solid line connecting solid circles) and it of the dogs given 50 ml./kg. (broken line connecting open circles).

slowly, but the pressure did not return to control level 30 minutes afterward. Among 6 animals, 2 died of pulmonary edema and 2 died of acute heart failure. In 2 surviving animals, second infusion was done. After the peak of more than 25 cm H_2O, both animals died of heart failure. In the group given 50 ml./kg. of saline, the changes in central venous pressure were similar to that in group I. A return towards the base-line was noted after 10 minutes.

Group III. As shown in Fig. 3, in all three kinds of dehydrated dogs, approximately similar course of alterations in central venous pressure was noted after infusion. After second infusion, however, the rate of elevation of central venous pressure in the dehydrated animals was higher than in the control group (Group II). Among 6 puppies with peritonitis, 2 died of acute heart failure.

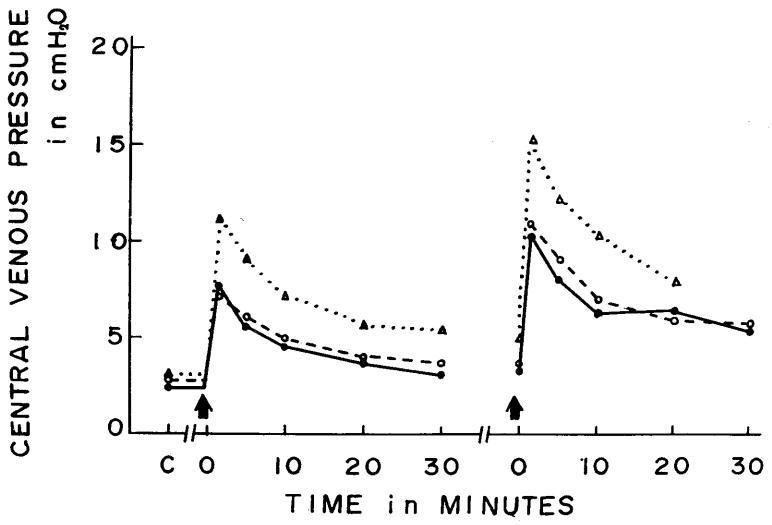

Fig. 3. Alterations in central venous pressure after infusion in a state of dehydration. Solid line shows central venous pressure in puppies performed pyloric stenosis, broken line indicates central venous pressure in dogs made jejunostomy, and dotted line represents central venous pressure in dogs developed peritonitis.

Group IV. As presented in Fig. 4, elevation of central venous pressure was about 5 cm H_2O after infusion of 50 ml./kg., while pulomonary arterial pressure rose by 12 cm H_2O, more than twice as much in the rate of elevation. Especially after the second infusion, pulmonary arterial pressure rose by 17 cm H_2O, more than 2.5 times as high as the peak of central venous pressure. The recovery towards the preadministration level didn't took place during 30 minutes after the infusion.

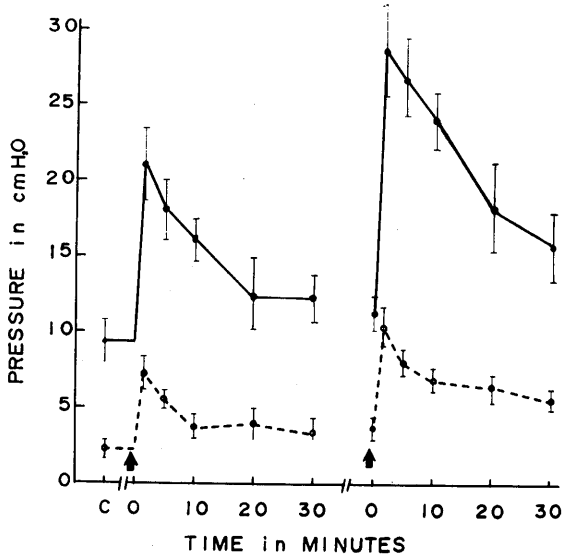

Fig. 4. Comparison between changes in central venous pressure (broken line) and changes in pulmonary arterial pressure (solid line) after infusion 50 ml./kg.

Group V. As shown in Fig. 5, the peak of central venous pressure was the same as it in Group IV, but decreased more rapidly closed to the preinfusion level. Such a tendency was more distinct after the second infusion. Pulmonary arterial

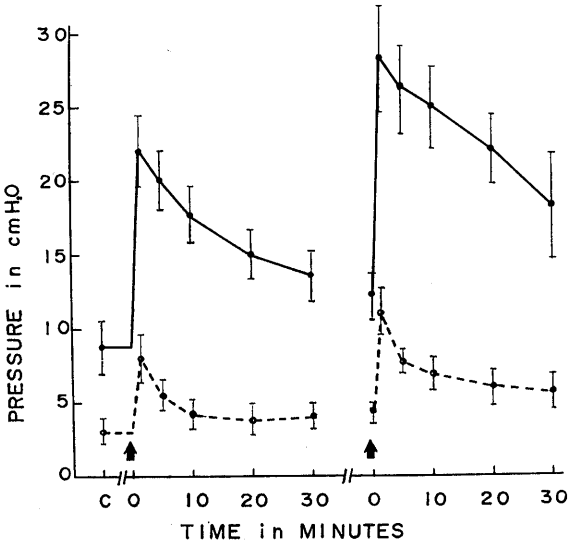

Fig. 5. Effect of infusion following preadministration of isoproterenol. Solid line shows changes in pulmonary arterial pressure and broken line indicates alterations in central venous pressure.

pressure showed a delay in the fall of post-peak pressure as compared with the control (Group IV). Even after 30 minutes, the pressure stayed 6 to 8 cm H_2O higher than the base line.

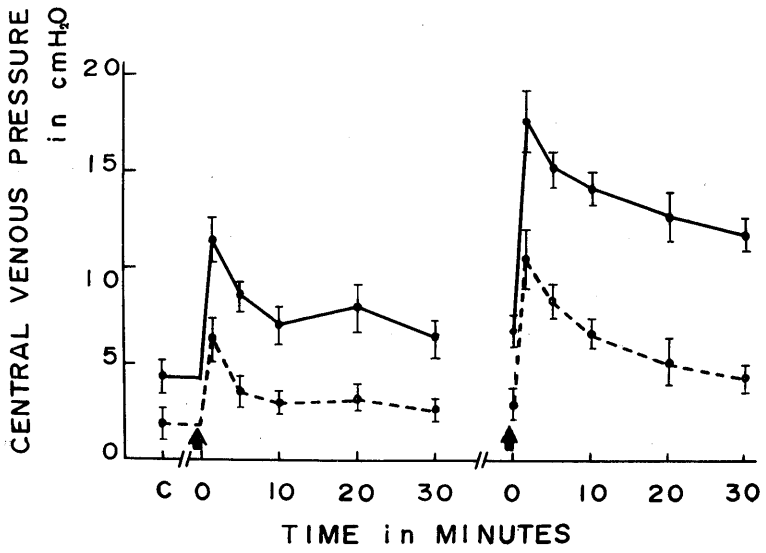

Fig. 6. Influence of infusion following pretreatment with phenoxybenzamine. Solid line shows pulmonary arterial pressure and broken line indicates central venous pressure.

Group VI. In puppies previously given phenoxybenzamine, arterial, central venous and pulmonary arterial pressures fell mildly. As shown in Fig. 6, rate of elevation of pulmonary arterial pressure following infusion of saline 50 ml./kg. was markedly lower than in the control group (Group IV). The central venous pressure returned to preinfusion level more slowly than in the control (Group IV).

DISCUSSION

Venous return in approximately the same amount as cardiac output is obtained despite a small pressure gradient, based on the facts the the blood stream is directed only to the direction of the heart on account of venous valves, the increase of the venous diameter with a decrease of flow resistance as the distance to the heart becomes smaller, and the influence by a negative intrathoracic pressure (-6 to -2.5 mm.Hg.). Since the venous system is a low pressure one, various factors give a deep influence.[32] Arterial pressure also influence the venous pressure via the capillaries (Vis a tergo). Veins are not a system of passive tubes; the smooth muscle in their walls can be activated by the sympathetic nerves. In hypovolemic

shock, despite the fall of arterial pressure and expected fall of central venous pressure, actual value of central venous pressure might stay within normal range, as the result of stimulation of the sympathetic nerveus system due to shock, leading to rise of the tonus of venous wall in a reflex.[1)13)] Consequently, administration of peripheral vasoconstrictor results in a rise of venous pressure and treatment of adrenergic blocking agents or anesthetics causes a fall of venous pressure (Vis a latere).[14)15)29)] Cardiac pump action also influences central venous pressure. Hudopeth et al.[26)] explained that it is better to look upon the central venous pressure as index of the function of the right ventricle and as reflecting the ability to the heart to handle the volume of blood being returned to it at that very moment (Vis a fronte). It is well known that in cardiac failure the high central venous pressure is due to not only to decreased cardiac function but also to generalized reflex venoconstriction.[43)]

Since such a variety of factors influences on venous pressure, the trend of serial central venous pressures and the response to fluid administration are often much more significant than the actual level of an isolated central venous pressure recording. Borow et al. emphasized that in general, central venous pressure ranging from 0 to 5 centimeters indicated hypovolemia and a definite indication for fluid administration. Central venous pressure of 6 to 12 centimeters suggests possible hypovolemia and usually these patients receive a trial of fluid administration. If central venous pressure above 15 centimeters indicates heart failure, fluid administration should be curtailed.

When circulatory blood volume is estimated from central venous pressure, distensibility of the venous wall gives a very intense influence.[42)] Burch[6)7)] is of the opinion that venous tone represents the action of squeezing the blood in the vein to the cardiac side, in an inverse relationship with venous distensibility. Since the distensibility of the venous system is great, it is able to contain 65 to 75 % of the total blood volume.[44)] Therefore, moderate increase in blood volume accompanying fluid infusion within limitation of venous capacitance dose not influence on the central venous pressure. In children, however, the danger of overtransfusion should never be forgotten in fluid therapy. In order to clarify the limitation of venous capacitance in children, an experimental study was carried out using puppies.

The plasma volume of puppies was assumed to be 5% of the body weight.[37)] This volume, 50 ml. per kilogram body weight, was chosen as one dose for infusion. In order to achieve a rapid increase of circulatory blood volume, injection of fluid was compared within 1 to 2 minutes. In our experiment physiological saline was used, because it is used widely in the field of pediatric surgery and it is possible to be infused quite rapidly. However, since the crystalloid solution stays in the blood vessel only for a short time, this is not adequate for long tern observation.[47)] Pate[38)] and Beattie[2)] found recovery of the central venous pressure after rapid

transfusion of the whole blood within 5 to 10 minutes. Also in our experiment main alterations in central venous pressure ended within approximately 5 to 10 minutes after infusion of saline.

In the experimental result in group I, even if the dose of fluid per unit body weight is identical, the rate of elevation of central venous pressure was higher in smaller puppies, probably due to smaller venous capacitance. Even in puppies with body weight above 1 kilogram, doubling the dose of fluid to 100 ml./kg. will bring the animal into the state beyond the limitation of the capacitance of the venous system. Central venous pressure suddenly rise to the level above 20 centimeters of water. Two of the 6 animals died of pulmonary edema while the remaining 4 expired of acute cardiac failure. In puppies with body weight between 1 and 1.5 kilograms, 50 ml./kg. infusion caused a transient rise of central venous pressure followed by return to the normal level 5 to 10 minutes later. The peak of central venous pressure immediately after infusion was low in the group treated with anesthetic agent (Group II) and the group preadministrated with α-receptor blocker (Group VI), suggesting the participation of the depressement of the venous tone. It is generally accepted that after administration of adrenergic blocking agents[41] or anesthetics[16][49] central venous pressure more faithfully reflects the circulating blood volume.

In some animals in group II given 100 ml./kg. and the smaller puppies in group I, the fall of the elevated central venous pressure was delayed for more than 20 minutes. According to Beattie,[2] increase in the blood volume by 100 % through transfusion caused a transient rise of venous pressure followed by a fall 10 to 15 minutes later. From a Guyton's report, adjustment of the circulatory system following very rapid transfusion is not due to innervation, because this phenomenon is seen in denervated or spinal anesthetized animals as well. Accordingly, delay of decrease in central venous pressure in our experimental groups is thought to be due to development of cardiac incompetence and overdistension of the reservoir system.

Changes of central venous pressure accompanying infusion in dehydrated puppies (Group III) were not much different from those in normals. Decrease of extracellular fluid in association with dehydration induces a fall of circulatory blood volume but is probably compensated by venous tone. After the second infusion central venous pressure rose abnormally and two of the 6 animals died of cardiac failure. Pierce et al.[40] performed rapid transfusion in dogs in hemorrhagic shock and found acute cardiac failure in a high proportion. However, this occurred only rarely upon administration of crystalloid solution. Massive transfusion of whole blood results in overload to the heart, since it stays in the vascular system for long time.[27] Upon the use of 50 ml./kg. of saline the central venous pressure shows only a transient peak even if infusion was performed rapidly.

As evident from the results of experiment in group IV, pulmonary arterial pressure

elevates more than double as high as central venous pressure. The distensibility of the pulmonary vascular bed is great and its resistance low.[10] Consequently, the perfusing pressure in the pulmonary circulation is only about one seventh of that is present in the greater circulation. The capacity of the pulmonary vascular bed when dilated is such that a large percentage of the total blood volume could be contained. A sudden increase of circulatory blood volume drives the blood within the venous system into the right atrium through the Frank-Starling mechanism. On the contrary, certain time is required while the blood passes through the pulmonary capillary bed, so that the pulmonary arterial pressure rises markedly despite a large distensibility of the pulmonary arterial system. Thomas[50] conducted overtransfusion in dogs to measure the pressures in various parts of the heart besides the central vein. The best agreement with the degree of hypervolemia was seen in the systolic pulmonary arterial pressure.[46][51][55] As compared with the method of measurement of central venous pressure,[54] the technic for the measurement of pulmonary arterial pressure was more difficult. It can be seen also from our data that pulmonary arterial pressure is more useful for the detection of hypervolemia and pulmonary edema than central venous pressure. Alleviation of pulmonary hypertension following infusion through preadministration of phenoxybenzamine is probably due to the dilating action on the pulmonary vascular system. Nickerson[36] pointed out the usefulness of α-adrenergic blockade for the detection of occult hypovolemia and for the prevention of development of pulmonary edema after administration of large amount of fluid. This agent is also quite effective in the treatment of shock, diminishing arteriolar contraction and improving of peripheral circuation.[22] While 0.1 to 0.2mg./kg. of phenoxybenzamine appeared to be effective in the prevention of pulmonary edema after overtransfusion, administration of doses more than 0.5 mg./kg. decreased progressively ventricular contractile force and cardiac output.[22]

On the other hand, isoproterenol which belongs to β-adrenergic stimulator also has an action of intensifying myocardial contraction and dilating peripheral blood vessels.[8][18][30] In the experimental results in group V, the rise of central venous pressure following fluid infusion was somewhat lowered by administration of isoproterenol, while pulmonary arterial pressure rose. At a concentration below 5 μg./min., the inotropic effect of isoproterenol becomes maximum but the vasodilator effect is still insufficient.[12] Since the concentration of isoproterenol used in our experiment was 4 μg./min., augmentation of the cardiac pump action facilitates the return of the blood in the venous system into the heart.[17] However, reduction of vascular tone of the pulmonary and venous systems is incomplete and the output from the right ventricle is increased, leading to the rise in pulmonary arterial pressure.

SUMMARY

In puppies weighing 500 to 1,500 grams, 50 ml./kg. saline was rapidly infused and the following results were obtained.

(1) With the use of the same amount of fluid per unit body weight, the rate of elevation of central venous pressure was higher in smaller puppies.

(2) With the infusion of 50 ml./kg. saline, a transient rise of central venous pressure was found in puppies weighing above 1 kg. Double amount of fluid caused cardiac failure.

(3) In dehydrated dogs, changes in central venous pressure after infusion of initial dose of saline were similar to those in controls, but after the second infusion, the pressure rose higher and two of six died due to cardiac failure.

(4) It was revealed that pulmonary arterial pressure rose more than twice as much as central venous pressure.

(5) Administration of isoproterenol caused a moderate rise of pulmonary arterial pressure after saline infusion.

(6) Administration of phenoxybenzamine depressed an increase in pulmonary arterial pressure following fluid infusion.

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