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An Analysis of Cardiopulmonary Hemodynamics During Hemorrhagic Shock in Dogs

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ABSTRACT

Utilizing the standard Wiggers' method, hemorrhagic shock was induced in ten anesthetized dogs by bleeding to a mean arterial pressure (MAP) of 50 mmHg for 2 hr and then to 30 mmHg for 1 hr, followed by reinfusion of the shed blood. The experimental protocol was designed to evaluate the effect of hemorrhagic shock on sequential pulmonary hemodynamic changes in relation to those of cardiac and systemic circulation. All selected cardiopulmonary hemodynamic parameters were recorded throughout the experiment on a multi-channel poly-oscillograph monitor. Total pulmonary resistance (TPuR) started rising early in hemorrhagic shock and was found to rise to a level that was 10-fold greater than pulmonary arteriolar resistance (PAR). This meant that, 90% of TPuR came from the venous side of the pulmonary vascular bed. Persistently raised TPuR even after reinfusion was linked to early death of the experimental animals. Myocardial contractility (max dp/dt mmHg/sec) which is one of the indices for cardiac performance was found to be severely depressed at terminal stage ($p<0.001$). Both total pulmonary and peripheral resistances were found to have an inverse relationship to ventricular performance which was measured by left ventricular stroke work (LVSW) and right ventricular stroke work (RVSW). There is a high suspicion that reinfusion or resuscitation following prolonged hypovolemic shock may aggrevate the hemorrhagic shock effects by facilitating the distribution of accumulated blood-borne toxic substances to various target organs and that, this has been linked with the early and sustained pulmonary hemodynamic disturbance found in these experiments.

The initial mechanism which triggers circulatory collapse in the postreinfusion period of hemorrhagic shock is still unknown. However, it is clear that shock is a disease involving multiple organ systems causing alterations in many physiological and biochemical processes, including those of the lung, heart and microcirculation, any one or a combination of which can lead to eventual irreversibility to treatment[8]. Most of the experimental studies on hemorrhagic shock for many years have been forcusing on heart and lung is shock, but until now, it has not yet been clear as to which one of the two organs contributes most to the irreversibility of shock.

The lung and the heart were first implicated in hemorrhagic shock by Wiggers (1945) when he said that severe and prolonged hemorrhagic hypotension led to death from respiratory or myocardial failure and called them lethal factors[38]. His experiments went further to suggest that, persistent low blood pressures damaged the myocardium and that was a major factor in the failure of blood transfusion in advanced stages of shock. However, recent reports say that in the early stages of shock, cardiac performance is relatively stable but a gradual cardiac impairment becomes important in the late stages of shock and that it is only as a preterminal or ter-

minal event that the relatively resistant myocardium fails[4,18,20]. Until now, it has not yet been possible to pin point the main cause of the myocardial failure in shock and as such its relative importance in the progression to irreversibility[20].

In his clinical and experimental analysis, Shoemaker (1974) found that pulmonary hemodynamic disturbance (increased pulmonary vascular resistance) was the earliest hemodynamic response to trauma and hemorrhage, it preceded the appearance of systemic hypotension and provided a means for early identification of the patients who subsequently die[31]. Nevertheless numerous other available literature suggest that prolonged hemorrhagic shock produces morphological and functional changes in the lungs but these resulting changes are not significant in determining irreversibility[1,25,29]. Several etiological factors have been implicated for these pulmonary changes[25,34] but, the primary underlying mechanisms responsible remain unproved. Moreover, there is little information about pulmonary circulatory changes during hemorrhagic shock. This study was undertaken in order to know sequential pulmonary hemodynamic changes in relation to those of cardiac and systemic circulation.

MATERIAL AND METHODS

Ten healthy adult mongrel dogs of either sex weighing 8 — 12 kg and unselected by age were first sedated with intramuscular injection of 15 — 20 mg/kg Ketaral (2—0-methylamino-Cychlohexanone-hydrochloride). Later, anesthesia was induced with Sodium pentobarbital (25 mg/kg, intravenously), trachea cannulated with a cuffed endotracheal tube and respiration maintained on a Mark 7 respirator (Bird Corporation Palm Springs, California). Every dog was fastened overnight prior to the experiment and was given a small amount of water in its cage.

Cutdowns were performed to introduce Polyethylene Catheters of varying internal diameters into both femoral arteries and veins, one carotid artery and one jugular vein. Systemic mean arterial pressure in the abdominal aorta was monitored by a catheter placed via the right femoral artery. Catheter in the right femoral vein monitored central venous pressure. The left femoral artery was used for bleeding the animal and was connected to a reservoir bottle containing about 100 milliliters of acid citrate dextrose anticoagulant solution in saline solution. The right femoral vein was cannulated for subsequent transfusion. A number 5 French Swan-Ganz Balloon Tipped Flow-Directed thermodilution catheter was inserted via the external jugular vein and advanced into the pulmonary artery, for measurement of pulmonary artery and pulmonary wedge pressures and for determination of cardiac output. Cardiac output was measured by injection of 3 ml of iced Saline into the proximal part of the catheter and was computed by a cardiac output computer (Model No. 9510 Edwards Laboratories, California) using the thermodilution technique. The thermistor of the flow directed catheter was placed into the pulmonary artery by a balloon floatation method, using the pressure pulse wave form as a guide to position. Left ventricular pressure and the rate of rise of left ventricular pressure (max dp/dt) were monitored by a catheter inserted through the common carotid artery and advanced into the left ventricle. Pressure pusle wave form was also used as a guide to position. Lead II of the electrocardiogram was monitored throughout the experiment. Heparin, 200 U/kg was administered intravenously in every dog after placement of the catheters. Then all catheters, except those from the left femoral artery and vein, were connected with strain gauge transducers to measure the intravascular pressures. Pressures were recorded throughout the experiment on a multichannel direct ink-writing polygraph monitor oscillograph (Polygraph 142—8, San-Ei Instrument Company, Tokyo). A simplified schematic overview of the experimental setup is given in Fig. 1.

A thirty minute control period of baseline measurements was allowed during which arterial and venous blood samples were drawn for control hematocrit, pH, pO_2, pCO_2 and base determination. The pH, base and blood gas partial pressures were measured on an acid-base analyser (Acid Base Laboratory , ABL_2, Radiometer A/S, Copenhagen). Hemodynamic control measurements were also recorded on the polygraph monitor during this period.

Hemorrhage in the dogs was initiated via the left femoral artery catheter at a rate of about 50 ml/min and collected in a plastic blood-

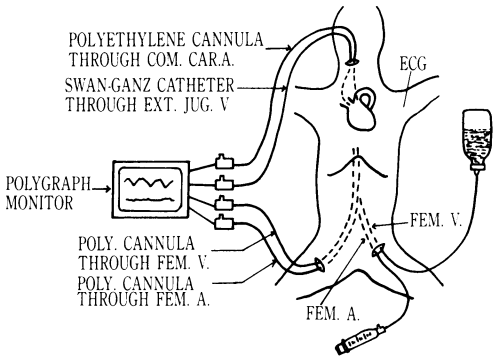

Fig. 1. Schematic diagram of experimental setup showing the cutdown and cannulation of blood vessels with catheters and their connection to the Polygraph monitor. Connection to cardiac output computer not shown.

reservoir bottle, according to the Wiggers' standard method[38]. Mean arterial pressure was lowered from control values to 50 mmHg and maintained at this level for 2 hr, not infrequently by means of additional small withdrawals of blood during the early period. After this period, the mean arterial pressure was further lowered to 30 mmHg by careful phlebotomy and maintained at this level for a period of 1 hr. The administration of small blood infusions towards the end of this period sometimes was necessary. This three hours period of hypovolemia was considered as a period of oligemic shock. The total volume of blood withdrawn during this period ranged from 350 ml to 450 ml. The whole shed blood, maintained at room temperature, was reinfused via the left femoral vein at a rate of less than 50 ml/min. The mean arterial pressure returned almost to control values immediately after reinfusion. The animals were followed up for an additional period until the mean arterial pressure dropped between 20 mmHg to 30 mmHg. This end stage of normovolemia was termed the terminal stage of normovolemic shock, whereas the recovery period immediately after reinfusion was identified as the compensated stage. The experiment was terminated at the terminal stage. Catheters were irrigated with Normal Saline containing heparin, 50 U per milliliters at hourly intervals, to prevent blockade of the catheters by blood clot formation.

Hemodynamic measurements in mean and dynamic values were recorded at specific regular

$$\text{(a) Total Pulmonary (TPuR) Resistance} = \frac{\text{Mean Pulmonary Artery Pressure} \times 1{,}332}{\text{Cardiac Output L/min}} \quad \text{dynes-sec/cm}^5$$

$$\text{(b) Pulmonary Arteriolar (PAR) Resistance} = \frac{\text{Mean pulmonary Artery Pressure} - \text{Mean Pulmonary Capillary Wedge Pressure} \times 1{,}332}{\text{Cardiac Output L/min}} \quad \text{dynes-sec/cm}^5$$

$$\text{(c) Total Peripheral (TPR) Resistance} = \frac{\text{Mean Arterial Pressure} - \text{Mean Central Venous Pressure} \times 100}{\text{Cardiac Output L/min}} \quad \text{Abitrary Units}$$

$$\text{(d) Right Ventricular Stroke Work (RVSW)} = \frac{\text{Cardiac Output} \times \text{Mean Pulmonary Artery Pressure} \times 1{,}332}{10^7} \quad \text{Joules/sec.}$$

$$\text{(e) Left Ventricular Stroke Work (LVSW)} = \text{Left Ventricular Stroke Volume} \times \text{Mean Arterial Pressure} \times 1.333 \times 10^3 \times 1.02 \times 10^{-6} \times 10^{-2}\text{Kpm}$$

$$\text{(f) Left Ventricular Stroke Volume (LVSV)} = \frac{\text{Cardiac Output} \times 1{,}000 \text{ (ml)}}{\text{Heart Rate (B/min)}} \quad \text{ml/B/min}$$

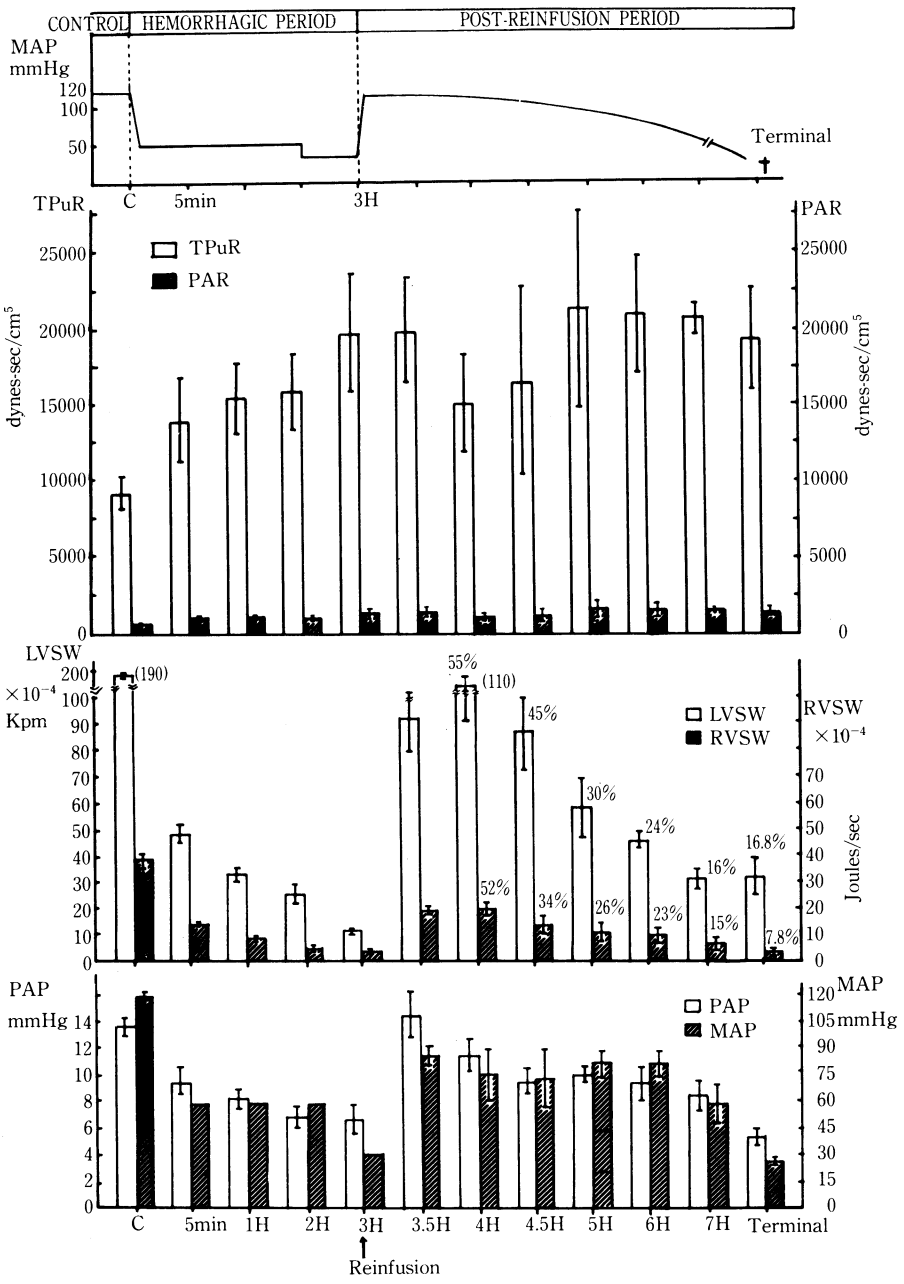

Fig. 2. Systematic comparison among cardiorespiratory hemodynamic values during hemorrhagic and postreinfusion period.
Hemodynamic changes observed in a series of anesthetized dogs subjected to Wiggers' standard method of hemorrhagic shock. These included Total Pulmonary Resistance (TPuR), Pulmonary Arteriolar Resistance (PAR), Right Ventricular Stroke Work (RVSW), Left Ventricular Stroke Work (LVSW), Pulmonary Arterial Pressure (PAP) and Mean Arterial Pressure (MAP). The upper most graph shows the experimentally controlled MAP and the expected behaviour of MAP after reinfusion. Each value is a mean from five to ten dogs. Small vertical bars indicate SEM. C = control and H = hour.

time intervals throughout the experiment. Hematocrit was determined hourly. Special hemodynamic parameters were chose for analysis and were calculated as follows[3,6,10,22,36].

Each dog in this experiment served as its own control by using the pre-experiment measurements. Statistical analysis for the hemodynamic parameters was done by using the student t-test for paired groups with $p<0.05$ considered significant.

The dogs were sacrificed at the terminal stage and immediately autopsied. Tissue samples for histopathological and electron microscopic investigation were obtained from heart, lung, liver, kidney, adrenal, pancreas, spleen, stomach, ileum and colon. Morphological findings are not reported in this paper.

RESULTS

A systematic comparison among selected cardiorespiratory hemodynamic parameters was attempted. Results are here by presented as grouped on the following figures. Parameters on Fig. 2 will be presented first.

(a) Linking of total pulmonary resistance (TPuR)* and pulmonary arteriolar resistance (PAR)* in hemorrhagic and postreinfusion period.

Five min after the mean arterial pressure (MAP) was brought to 50 mmHg by hemorrhage, both the TPuR and PAR values rose above the control (pre-experiment) values, but the rise was not a significant one. Two hr later with MAP at 50 mmHg, the values for TPuR and PAR continued to rise significantly ($p<0.05$). One hr after the MAP was further brought down to 30 mmHg, TPuR and PAR values both rose much higher than before ($p<0.01$). One hr after reinfusion (4H), both TPuR and PAR underwent an insignificant drop in values, and thereafter, both values started to rise again and remained significantly raised throughout the remaining postreinfusion period up to the terminal stage ($p<0.05$).

On comparing the two parameters in terms of resistance values, TPuR was found to rise to a level that was 10-fold greater than PAR at any one point both during the hemorrhagic and postreinfusion periods. This meant that, PAR contributed only 10% to the TPuR and 90% of TPuR came from the venous side of pulmonary vascular bed.

(b) Left ventricular stroke work (LVSW) and right ventricular stroke work (RVSW) in hemorrhagic and postreinfusion period.

Early in hemorrhagic period, five min after MAP was dropped to 50 mmHg, both LVSW and RVSW fell significantly below the control values ($p<0.01$). Both parameters continued to fall and reached their lowest values at the end of the hemorrhagic period with MAP at 30 mmHg. LVSW and RVSW started to rise toward pre-experimental values following reinfusion and by the end of the first postreinfusion hr (4H), they returned only to 55% and 52% of the control values respectively. Subsequent to this, both LVSW and RVSW started to fall and continued up to the terminal. During this fall of values, it was noted that RVSW fell at a faster rate than the LVSW. At two hr after reinfusion (5H), RVSW had follen to 26% of control values where as LVSW fell to 30%. At terminal stage, RVSW had follen to 7.8% while LVSW had follen to 16% of control values.

(C) Pulmonary arterial pressure (PAP) and mean arterial pressure (MAP) during hemorrhagic and postreinfusion period.

The pre-experimental average of MAP of all the dogs used in this experiment was about 120 mmHg. Five min after the MAP was lowered to 50 mmHg by hemorrhage, PAP fell significantly below control values ($p<0.01$) and continued to fall throughout the hemorrhagic period. Thirty min after reinfusion, PAP rose to a value greater than control, but MAP failed to return to control levels and rose only to 71% of pre-experimental values. Thereafter, both PAP and MAP started to fall gradually with a slight rise at the second and third hr of postreinfusion period, but then continued to fall until the terminal stage.

Next presentation is about the data on Fig. 3.

(a) Linking of total peripheral resistance (TPR) and total pulmonary resistance (TPuR) in hemorrhagic and postreinfusion period.

With MAP at 50 mmHg in the first five min of hemorrhagic period, TPR dropped slightly and was 85% of control values whereas TPuR rose

* TPuR and PAR may further be converted to metric resistance units by multiplying with a convertion factor 0.06 which was not used in the given formulae.

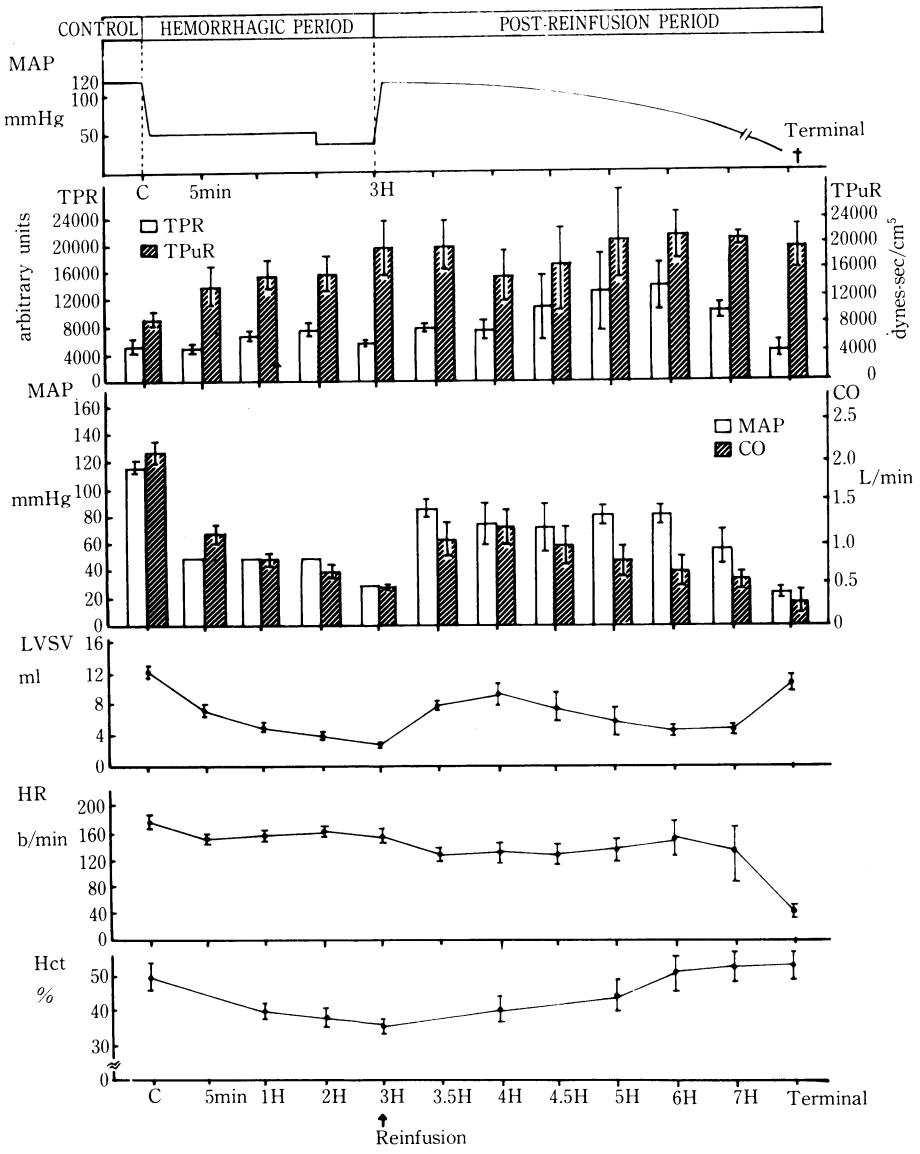

Fig. 3. Systematic comparison among cardiorespiratory hemodynamic values during hemorrhagic and postreinfusion period.
Hemodynamic changes observed in a series of anesthetized dogs subjected to Wiggers' standard method of hemorrhagic shock. These include Total Peripheral Resistance (TPR), Total Pulmonary Resistance (TPuR), Mean Arterial Pressure (MAP), Cardiac Output (CO), Left Ventricular Stroke Volume (LVSV), Heart Rate (HR) and Hematocrit (Hct). The upper most graph shows the experimentally controlled MAP and the expected behaviour of MAP after reinfusion. Each value is a mean from five to ten dogs. Small vertical bars indicate SEM. C = control and H = hour.

significantly ($P<0.05$) and was 151% of control values. At the end of two hr with MAP at 50 mmHg, both TPR and TPuR rose significantly above pre-experimental values but TPuR was 170% of control values while TPR was 140%. One hr later with MAP further dropped to 30 mmHg, TPR had an insignificant drop and was only 191.5% of control values whereas TPuR rose much higher and was 214% of pre-experimental values ($p<0.05$). One hr after reinfusion (4H), TPR rose slightly while TPuR dropped slightly but remained at an elevated level. Throughout the entired postreinfusion period, TPuR remained persistently raised while TPR started to rise gradually reaching higher values than in the hemorrhagic period.

Towards the terminal, TPR started to drop gradually and was 80% of control values at terminal stage. On the other hand, TPuR remained higher with reinfusion and was 210% of pre-experimental values at terminal stage.

On trying to compare the two parameters, these results show that TPuR started to rise early in the hemorrhagic period and was rising more faster than TPR.

(b) Mean arterial pressure (MAP) and Cardiac output (CO) in hemorrhagic and postreinfusion period.

During the whole hemorrhagic period, CO fell as MAP was lowered to specific levels by hemorrhage ($P<0.001$). Like MAP, CO failed to return to control levels with reinfusion and the maximum recovery was at one hr (4H) after reinfusion when CO was only 58% of the pre-experimental value. In the remaining postreinfusion period, CO and MAP both fell down gradually, but it was noted that, CO fell more faster than MAP. At terminal stage, CO was 13% while MAP was 20% of control values. There was a continued fall in CO in the postreinfusion period despite relatively high blood pressure values (MAP) as compared to the hemorrhagic period.

(c) Left ventricular stroke volume (LVSV), heart rate (HR) and hematocrit (Hct) in hemorrhagic and postreinfusion period.

These three parameters can easily be interpreted by comparing them with upper graphs especially with the upper most graph for MAP. LVSV fell as MAP was brought down by hemorrhage and raised momentarily with reinfusion before starting a gradual fall toward the terminal. The last raised LVSV value at terminal stage is a paradoxical one and was due to severe bradycardia (see HR graph below).

Results for HR changes were very variable but a significant fall in HR was noted immediately after reinfusion ($p<0.05$) and at terminal stage ($p<0.001$).

Hematocrit fell with hemorrhage and rose gradually with reinfusion and remained at high value even at terminal stage.

Fig. 4(a) and 4(b) show hemorrhagic shock effect on ten individual experimental dogs from which the mean values were calculated. Of all the dogs used in the experiment, 30% died in the hemorrhagic period, 20% died during retransfusion, and 50% in the postreinfusion period. The figures show a correlation between early pulmonary hemodynamic disturbance (eg raised Total Pulmonary Resistance (TPuR)) and early death of the experimental animals. Total Peripheral Resistance (TRR) is included here for comparison and more explanation is given below the figures.

Fig. 5 presents a typical response on hemorrhage and reinfusion on dog No. 6 by oscillographic tracings. The figure clearly demonstrates how myocardial contractility was affected in this experiment. Explanation is given on the accompanying footnote of the figure with other parameters included.

DISCUSSION

① Pulmonary and systemic resistance.

These studies have shown that, a major part of TPuR (90%) comes from the venous side of the pulmonary vasculature (Fig. 2). In their experiment, Cook and Webb[2] also found increases in pulmonary venous resistance during hemorrhagic shock. Increases in TPuR were found to occur early in hemorrhage and remained at a persistently raised level until the terminal stage. These findings are in much agreement with those reported by Shoemaker[31] and at the same time in line with other reports[2,5,21,28,32,33]. All of the dogs had high TPuR throughout the hemorrhagic and postreinfusion period and 50% of them died before reaching the terminal stage. Because of this, it was thought that persistently raised TPuR after reinfusion is of threatening prognostic value.

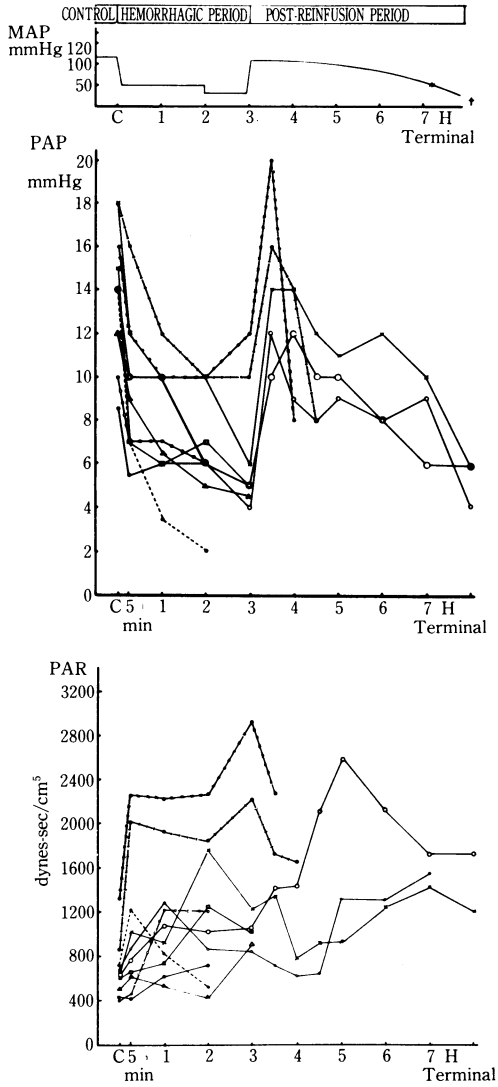

Fig. 4(a). Different individual dog reaction to hemorrhagic shock.
Pulmonary hemodynamic changes observed in a series of anesthetized dogs subjected to Wiggers' standard method of hemorrhagic shock. These include Pulmonary Arterial Pressure (PAP) and Pulmonary Arteriolar Resistance (PAR). The correlation between early severe pulmonary hemodynamic disturbance and early death of the experimental dogs is well depicted here. The upper most graph shows the experimentally controlled MAP and the expected behaviour of MAP after reinfusion. C = control and H = hour.

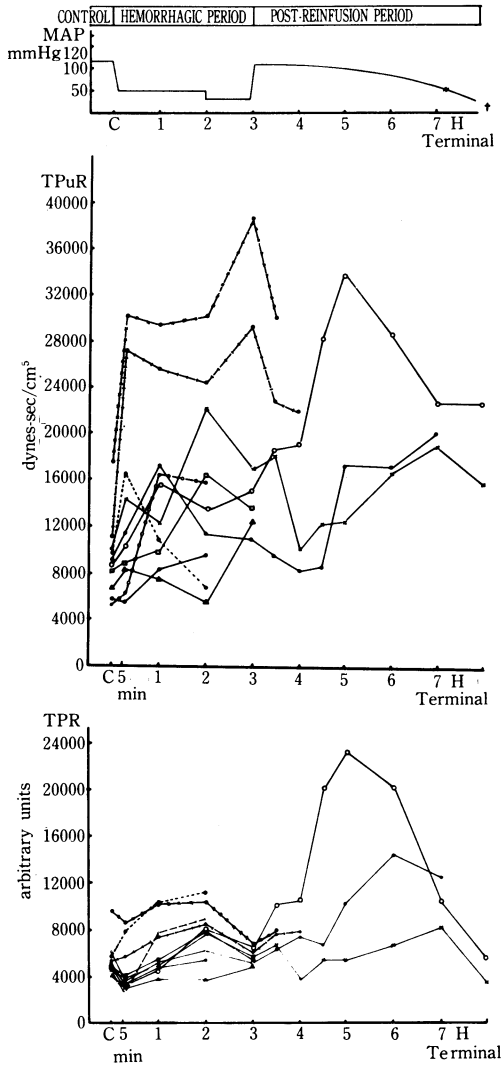

Fig. 4(b). Different individual dog reaction to hemorrhagic shock.
Total Pulmonary Resistance (TPuR) is compared with Total Peripheral Resistance (TPR) as observed in a series of anesthetized dogs subjected to Wiggers' standard method of hemorrhagic shock. Almost all of the experimental dogs had an early and persistently raised TPuR throughout the experiment where as higher values of TPR were mostly observed in the post-reinfusion period. Respective effect of these parameters on after load is well described in the discussion section. The upper most graph shows the experimentally controlled MAP and expected behaviour of MAP after reinfusion.
C = control and H = hour.

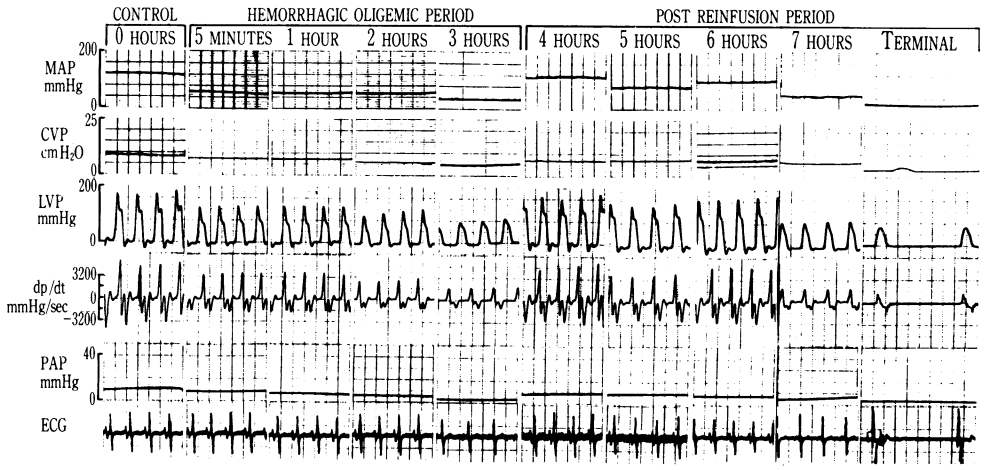

Fig. 5. Dog No. 6: Polygraph monitor oscillographic tracings showing the effect of hemorrhagic shock on myocardial performance and hemodynamics. Cardiac function is seen to deteriorate with a decrease in cardiac contractility as depicted by a falling in maximum rate of rise (max dp/dt mmHg/sec) of left ventricular pressure at the 2nd and 3rd hr of hemorrhage ($p<0.01$) and from 4th hour to terminal stage of the postreinfusion period ($p<0.001$). Hemorrhagic shock effect on Mean Arterial Pressure (MAP), Central Venous Pressure (CVP), Left Ventricular Pressure (LVP), Pulmonary Arterial Pressure (PAP), and Electrocardiogram (ECG) are also shown. Note also the development of severe bradycardia (ECG) towards the terminal stage, which is another sign for myocardial depression. Chart speed 25 mm/sec.

Persistent rise of TPuR serves as an early indicator to the development of shock lung[5]. The mechanisms leading to the development of this syndrome are still controversial and complex but, the latest observed events have been shown to occur in the capillary endothelium, with a shift of fluid from the intravascular into the interstitial space[5,9,32,34]. The initial event appears to be an increase in pulmonary capillary membrane permeability resulting in the accumulation of interstitial edema[26,34]. The cause of the altered permeability is unclear and is the subject of intense debate and research. Humoral and cellular (platelet and leuchocyte) factors appear to be the principal mediator of permeability edema[34]. A variety of stimuli including hemorrhagic shock may initiate the formation of cellular microaggregates that are subsequently cleared by pulmonary microcirculation. The pulmonary microemboli may partially or completely obstruct portion of the vasculature, resulting in uneven perfusion, and may release vasoactive or toxic humoral substances[9,26,31,34]. Histamine, Kinins, Prostaglandins, ATP, fibrin degradation products, complement fragments, and proteolytic lysosomal enzymes may damage the capillary endothelial membrane and cause permeability edema[28,34]. When this occurs impairment of venous return which is the primary abnormality of hemorrhagic shock becomes more severe because, the fluid in the interstitial space may compress the vasculature and increase pulmonary resistance, thereby further decreasing blood flow[5,12]. As TPuR continues to increase, afterload (impedance against which a ventricle pumps) to the right ventricle is increased leading to right sided myocardial dysfunction[12,20].

TPR was shown to rise slowly in the hemorrhagic period and maximum values were reached in the postreinfusion period (Fig. 3 and Fig. 4(b)). These results agree with many other reports on peripheral resistance[21,31,32,39]. The increased TPR which is a characteristic feature of hemorrhagic shock, of cardiogenic shock and of the later stages of sepsis is almost certainly due to the release of vasoactive substances which include catecholamines, renin-angiotensin II and corticosteroids[1,13,16]. Persistently raised TPR causes afterload to the left side of the heart, thus bringing additive effect to myocardial failure. Therefore, increased TPuR and TPR in hemorrhagic shock causes increased afterload to both sides of the heart which brings about an accumulated reduction in cardiac performance as

a whole.

② Left and right ventricular performance.

Results show that both LVSW and RVSW were depressed during hemorrhagic and postreinfusion period and that, after reinfusion, RVSW deteriorated at a faster rate than LVSW towards the terminal (Fig. 2). This happened because TPuR, which directly affects the right ventricle was more raised than TPR which directly affects the left ventricle (compare Fig. 2 and Fig. 3). In other words, vascular resistance showed an inverse relationship to ventricular performance.

From Fig. 5 it was shown that, the max dp/dt of left ventricular pressure, which is a well established measure of myocardial contractility[23,37], was severely depressed at terminal stage. ECG changes of fatal cardiac arrhythmias were also observed at this stage. Similar results have also been reported by other workers[4,11,20,22].

The findings reported herein clearly established that cardiac performance progressively deteriorates with increasing duration of hemorrhagic shock. No single factor has been incriminated as the main cause of heart failure in hemorrhagic shock, but the majority of the explanation given from experimental and clinical observations appears to be decreased myocardial contractility[11,20,23,32]. Excessive catecholamine stimulation can damage the heart, and this is said to be related to the myocardial zonal lesions seen by electron microscopy following hypovolemic shock[14,20,27]. Metabolic acidosis, hypoxia, and myocardial depressant factor (MDF), are among the factors reported to reduce myocardial contractility[18,20,25]. More recently, ß-endorphin and enkephalins said to be released during stress, have also been implicated as cardiodepressant substances[7,20]. Further work is needed to determine which of these factors predominate.

③ Other hemodynamic parameters.

CO which transiently increased by retransfusion was subsequently and gradually further depressed in spite of elevation of MAP near normal. This is because, increased plasma levels of vasoactive substances which are found late in shock increase capillary permeability which favours transudation of fluid from the plasma into tissue spaces thus causing decreased effective circulating blood volume which leads to decreased CO with increased shock effects[17,21]. The relatively elevated MAP seems to be supported at near normal levels by great increase in TPR (Fig. 3).

Hematocrit was found to rise with prolonged shock after reinfusion. This is due to the fact that, continued loss of intravascular fluid into the interstitium causes hemoconcentration which in turn leads to an increase in blood viscosity and therefore a higher resistance to blood flow[21,24]. This point can well be appreciated by a careful analysis of the Poiseuille's relationship which states;

$$\text{Flow} = \frac{\pi\ (P_1 - P_2)r^4}{8\ell\eta}$$

where $P_1 - P_2$ is the pressure gradient across vessels of length ℓ and radius r, η is the viscosity of the perfusion fluid.

Since most of the detrimental effects following hemorrhagic shock seem to occur during the postreinfusion period, the authors would like to theorise that, reinfusion or resuscitation following prolonged hypovolemic shock may facilitate easy transfer or distribution of blood-borne toxic substances which accumulated during the hemorrhagic period[36] to various target organs due to an increase in effective circulating blood volume. Moreover, this venous blood full of toxins on returning to the heart, first gets into contact with the right side of the heart and the lung before it is distributed to the systemic circulation. The authors therefore suspect that, this first contact could be the cause of early and sustained pulmonary hemodynamic disturbance observed in these experiments.

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