M.Sc. Experimental Surgery

EFFECTS OF HAEMODIALYSIS ON ENDOTOXIN AND HAEMORRHAGIC SHOCK

by

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CHAPTER 1

INTRODUCTION

Knowledge of the cause and management of shock have been subjects of intensive investigation and speculation since the history of medicine.

For many years, the treatment of hemorrhagic shock has been centered about the concept that the main defect in this syndrome is the blood loss and that ideal treatment is the replacement of this loss with adequate transfusions. Alongside with fluid replacement, vasopressors have been extensively used in the treatment of any form of hypotension, with the assumption that the fall in blood pressure is a valid measurement of the blood volume deficit.

In bacteremic shock, massive antibiotics and adrenocorticoids have been used extensively (MacLean, 1962) with some convincing results. In spite of the advent of antibiotics, the mortality rate of patients with coliform bacteremic shock is still over 65% (Adcock and Hakanson, 1960), (Spink, 1960). In some areas this percentage is even higher.

Our knowledge of the dynamics of shock is better than it was fifty years ago. There is recognition that the development of shock is a very complex phenomenon, not necessarily causally related to any one factor. Shock results from a multiplicity of influences, hormonal, renal, circulatory, biochemical, humoral and enzymatic.

With the growing acceptance of the view that catecholamines are

the major offenders in the refractory state of shock and in the irreversible phenomenon, many investigators (Lillihei, 1962), (Wilson, 1963), (Longerbeam, 1962), (Corday, 1960), are objecting to the indiscriminate use of vasopressors during haemorrhagic and endotoxin shock. Ganglionic blocking agents are receiving preference over sympathomimetics (Nickerson and Carter, 1959), (Hakstian, et al, 1961), (Thomas, 1958), (Gourzis, et al, 1961), (Baez, et al, 1952).

With so many conflicting opinions as to the best management of the shock syndrome, we decided to tackle the biochemical aspect of the problem.

Hence, our objectives were to correct the pH by dialysing lactic acid and other organic acids (pyruvic acid and phosphate), which play a part in the irreversible phenomenon. Since byproducts of bacteria can be dialysed into the rinsing solution, we believe that by ultrafiltration of these harmful substances, we may cure or prolong survival time in animals. Since histamine and catecholamines are incriminated in the irreversibility of shock, we thought that these substances could also be dialysable. Dialysis in itself helps to correct hypovolemia and by so doing we hoped to counteract peripheral vascular pooling and aggregation of cells that occurs during shock. (Wiggers, 1950), (Lars-Eric Gelin et al, 1961), (Cameron, 1962), (Shoemaker, 1962), (Nickerson, 1959), (Aust, 1957).

CHAPTER II

REVIEW OF LITERATURE

A. HISTORICAL PERCEPTIVES

There is no problem in the field of medicine which has elicited so much interest of physicians and surgeons throughout the ages as 'shock'. Celsus at the beginning of the Christian Era, in describing the effects of traumatic shock wrote:

> Now when the heart is penetrated, much blood issues, the pulse fades away, the colour is extremely pallid, cold and malodorous sweat bursts out as if the body had been wetted by dew; the extremities become cold and death quickly follows.

In 1497, Brunschweig (1933) commented on the collapse which followed severe gunshot wounds, but he attributed this condition to poisoning of the wound by gunpowder. Even Billroth (1859), one of the greatest surgeons of all time, believed that gunpowder poisoning was partly responsible for some of the symptoms of shock.

Puerperal sepsis in the large hospitals of Europe is vividly described in Devils, Drugs and Doctors (Haggard 1953). Books on colonization of the Orient give diagnostic descriptions of victims of cholera, dying of bacteremia and dehydration hypotension.

As we move through the centuries, we see that bleeders, barbers, surgeons and physicians all recognized this syndrome of haemorrhagic and endotoxin shock without calling it as such. This word 'shock' was first used in the English translation from the works of the French surgeon LeDran (1743), who during the same year wrote:

> The bullet thrown by gunpowder acquires such rapid force that the whole animal machine participates in shock and agitation.

Ambroise Pare (1582) pointed out this syndrome of shock which he called 'commotion' as he thought it was caused by 'falling from a high place on something solid and hard' or 'by blows causing contusions, such as those caused by a stone or a mass or a blow of a lance or an artillery blow or thunder falling near a person'. He referred to the pallor, cold sweat, indetectable pulse as 'Petite Morte'. The original of this text reads:

> D'avantage faut entendre qu'outre les susdites fractures, il se fait une autre disposition appelée Commotion. Ou ébranlement et concussion du cerveau, qui cause semblables accidents que les fractures du Crâne: laquelle Commotion se fair pour avoir tombé de haut en bas sur chose solide et dure, ou par coups orbes, comme de pierre, ou d'une masse, ou d'un coup de lance, ou l'air d'un coup D'Artillerie, ou du tonnerre tombant près de la personne, voire de la main, ou autres semblables.

Subsequently there sprung other workers in this field of shock in the 18th, 19th, and 20th Centuries, to mention only a few men like: (1) Bell (1812), (2) Abernathy (1804), (3) Hunter (1812), (4) Cannon (1917), (5) Harkins (1935), (6) Wiggers (1950). All these men have given tremendous contributions in the field of shock.

Abernathy (1804) in his 'surgical observations' described a patient admitted into St. Bartholomew's Hospital, with an 'aneurism of the femoral artery', for treatment of which he tied the external iliac artery. The description of this patient's ninth day post-operative condition is suggestive of bacteremic shock.

> His pulse beat...160 in a minute, his tongue was covered with a dark brown fur, he looked agitated, and purge took place, which was not restrained till the following night by a cordial and opiate mixture.

PHOTOGRAPH I

This woundman, a generation later than Brunschweigh, shows cannon balls impinging themselves, one upon the arm and the other upon the leg. This picture actually represents all the possible causes of shock as conceived by physicians and barbers of the 19th Century. A lance falling near the left foot of the 'man' is also seen. It is also noted that over the upper third of the thigh, an eruption is seen. This represents the "great pox", which was becoming an important cause of shock at the time. (Courtesy Bilroth "Historical Studies on Gun Shot Wounds", 1859.)

Herman Fischer (1870) corroborated with current opinion in Germany on the concepts of surgical shock as '...paralysirenden Einfluss einer plötzlicher und heftigen Nervenver Letzung auf die Herzthätigkeit'. Translated into English this reads: '(Shock) is caused by a sudden and violent injury of the nerves, with a paralysing influence on the action of the heart.'

B. MODERN CONCEPTS OF PATHOPHYSIOLOGY OF THE SHOCK SYNDROME

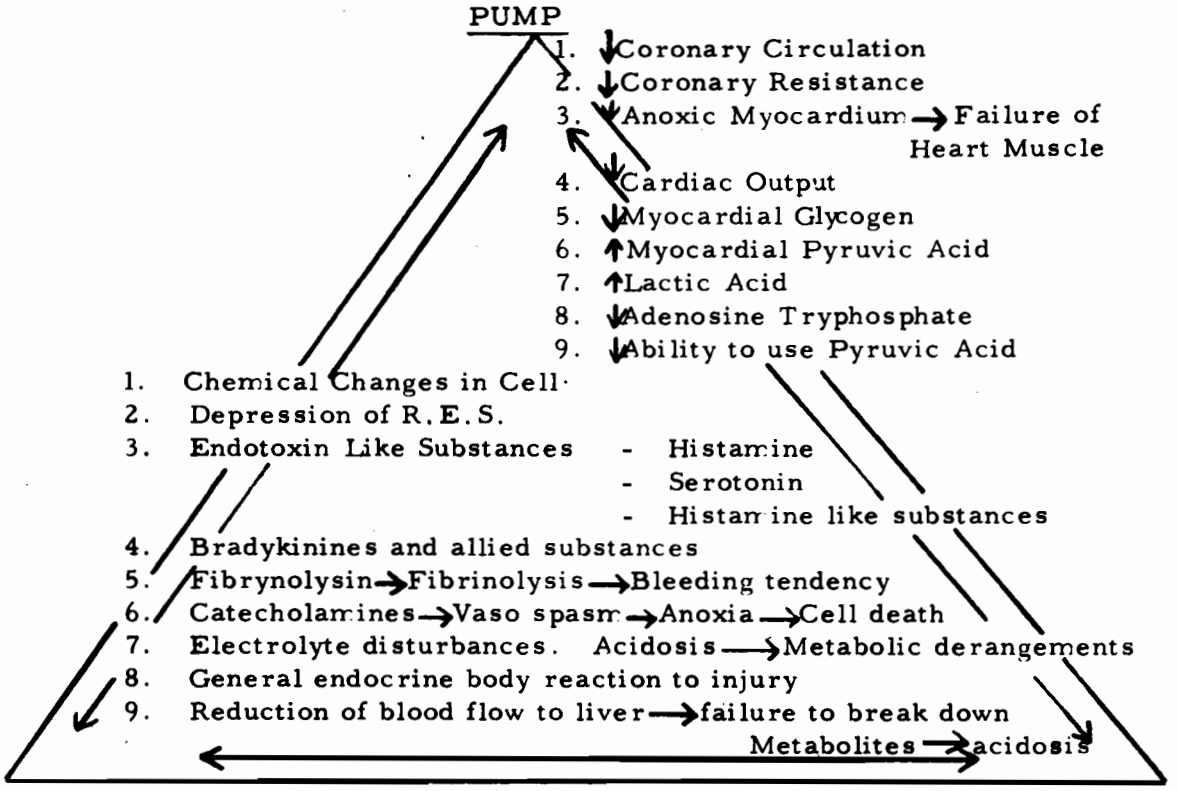
With the general progress over the last fifty years in the understanding of human biology, anatomy, physiology and biochemistry, the present concept of the pathophysiological mechanisms involved in the shock syndrome are clearer than they were during the time of Ambrose Pare (1582).

It is now more generally accepted by nearly all authorities on this subject that the factors which are principally concerned with shock or the target organs are: (1) the heart (Guyton, 1961, 1962) (Melcher, 1951). (2) the circulating volume (Fine, et al, 1955), (Blalock, 1930), (Phemister, 1927-28); (3) the peripheral vessels, arterioles, metarterioles, venules and capillaries (Wiggers, 1950), (Cameron, 1962), (Hardaway, 1959, 1961, 1962). In between these target organs, a host of physical, biochemical and metabolic changes occur, which lead to further depression of normal functions of the target organs, leading to irreversibility.

1. THE ROLE OF THE HEART

a) Failure of the Myocardium

The importance of the myocardium and its role in the development of the irreversible phenomenon in shock has been a subject of in-



CIRCULATING VOLUME

1. Reduced blood pressure
2. Reduced blood and/or plasma volume or not at all
3. Decreased venous return
4. Reduced oxygen supply to tissues
5. Circulating injurious substances from injured tissues (Burns or released by bacteria)

PERIPHERAL VESSELS

1. Regional peripheral resistance
2. Pooling and stasis in venules and capillaries of other organs
3. Decreased clotting time
4. Aggregation of cells → stasis → ↓ Tissues and cell perfusion → Cell death
5. Lecithinase → Possibility of endothelial disruption

DIAGRAM ILLUSTRATING BRIEF PATHOPHYSIOLOGY OF THE SHOCK SYNDROME

tensive investigation during the last decade. The shock state that accompanies severe myocardial infarction fortifies the theory that the failure of the pump mechanism is the primary cause of irreversibility. Increase in atrial pressure, diastolic ventricular and ventricular end diastolic pressure along with diminished ventricular stroke output (Crowell and Guyton, 1961, 1962), (Wiggers, 1942, 1947, 1950) give strong evidence of the importance of cardiac function in endotoxin and haemorrhagic shock. Izquieta and Pasternack (1946) observed depression of the ST segment during haemorrhagic and ischemic compression shock. Bloor (1958) and his associates observed the same abnormal electrocardiographic changes in haemorrhagic shock. Cardiac glycosides have been found to be beneficial in experimental traumatic shock (Keyl, 1956, 1957). This supports the important role of the myocardium in the production of irreversible haemorrhagic and endotoxin shock.

Kohlsteadht and Page (1944), Werle et al (1942) also support the theory that the primary failure of the myocardium is responsible for the irreversible phenomenon.

There are many different types of insults which can lead to myocardial deterioration in shock (Sarnoff, 1955). Nutritional deficiency, bacterial toxins, underlying heart disease (Guyton, 1961, 1962) may exert deleterious effects on the myocardium during shock. Many bacterial toxins, especially the endotoxins of the gram negative coliforms, have very toxic effects on the myocardium (Ross, 1957) .."Whatever the cause of a particular type of shock might be, death of a person finally ensues when the heart itself can no longer pump blood. In haemorrhagic shock, as well as many other types of shock, it is the heart itself that is the

primary and lethal deteriorating structure of the circulation and that deterioration which occurs in other parts of the circulation may vary well not be lethal at all." (Guyton, 1961)

According to the above theory, all other changes that accompany this phenomenon are secondary to myocardial failure.

On the other hand, (Weil et al, 1956), (Freedberg, 1944) (Zamecnik, 1947) and (Ebert, 1955a, 1955b) studying the venous pressures in dogs observed that the systemic venous pressure was either reduced or it remained the same during the experimental period. This indicates that congestive heart failure is not the cause of shock.

Sarnoff (1954), in his studies on haemorrhagic shock, observed that both the right and the left ventricles showed evidence of myocardial failure, dilitation of the heart and a decrease in the vigor and rapidity of arterial systole. Augmenting coronary flow, either mechanically or by administration of aramine, led to the decrease in right auricular pressure and dilatation of the heart. Melcher (1951) found, in dogs subjected to prolonged shock, areas of fatty infiltration and necrosis of cardiac muscle.

Hypovolemia and insufficient coronary blood flow leads to decrease in cardiac output, decrease in oxygen transport, oxygen availability and increase in oxygen debt and eventually to myocardial failure (Simeone et al, 1958a, 1958b), (Melcher and Walcott, 1951), (Weil, 1957), (Sarnoff, 1954), (Catchpole, 1955).

b) Decreased Coronary Circulation and Cardiac Output

Normally coronary blood flow as measured in the lower animals approximately constitutes four to five percent of the total cardiac

output. In human beings this would mean an average coronary flow of approximately 225 ml/minute (Guyton, 1962).

During haemorrhagic and endotoxin shock, there is a significant continuing decrease in coronary resistance with concommittant decrease in coronary circulation (Wiggers, 1950), (Eckenhoff et al, 1940, 1947), (Edwards, 1954), (Hackel and Goodale, 1955), (Opdyke, 1947), (Corday et al, 1960). This decrease in coronary flow leads to the generalized decrease in myocardial blood flow (Catchpole, 1955), (Churchill-Davidson et al, 1955). Decrease in coronary flow is accompanied by decrease in cardiac output and stroke volume (Osher, 1953), (Read et al, 1957), (Hackel and Goodale, 1955), (Hausner et al, 1940). Reduction in coronary flow has been associated with shock states regardless of cause and has been known to result in myocardial necrosis (Master et al, 1937), (Friedberg and Horn, 1939), (Melcher and Walcott, 1951). Normally about 65% of the oxygen in the arterial blood is removed before it circulates the coronaries. During shock, the oxygen saturation of arterial blood circulating the coronaries is greatly reduced. This leads to severe anoxia to the myocardium. Meneely (1946) postulated that prolonged anoxia of the myocardium can lead to increased permeability of the blood vessels in the heart, which would be an actual structural damage to the heart. Nobody has yet reduplicated Meneely's findings.

There is a progressive decline in cardiac output as shock reaches the terminal phase and a critical level of cardiac output, which, if lowered even slightly by withdrawal of blood, results in sudden death (Fine, 1947). There is temporary improvement in

cardiac output following transfusion (Wiggers, 1950).

c) Metabolic Effects of Shock on the Heart

Any prolonged hypotension leads to decreased oxygen consumption of the heart muscle. This is particularly prominent during the latter stage of shock. (Burdette, 1952). It has been shown that myocardial oxygen availability parallels closely the fall and rise in blood pressure seen in experimental haemorrhagic and endotoxin shock (Caliva, 1959). The prolonged anoxia causes many metabolic changes in the heart muscle. The myocardial extraction of lactate is increased during haemorrhagic shock (Edwards et al, 1954). Arterial concentration of pyruvate and lactate are increased during oligemic and normovolemic shock. Opdyke, (1947) also noticed reduction of myocardial extraction coefficient of pyruvate to negative values during shock, but sometimes there was increase in lactic acid (Burdette, 1950) and decreased adenosinetriphosphate (LePage, 1946).

Arterial glucose concentration is increased during olegemia, while myocardial glycogen drops. Myocardial pyruvate extraction is decreased while pyruvate in the coronary becomes higher than in the arterial blood.

None of these changes can be pointed out with certainty as the primary causes of the final state of irreversibility. There seems to be little doubt as to the synergistic effect of these pathophysiological mechanisms in precipitating irreversibility in shock.

2. EFFECT OF ENDOTOXIN AND HAEMORRHAGIC SHOCK ON PERIPHERAL VESSELS

a) Peripheral Resistance

"The animal had been bled to death, so that the vessels had an additional stimulus to produce contraction in them, as we know that all vessels in animals endeavour as much as possible to adapt themselves to the quantity of fluid circulating in them." (Hunter, J., 1812). Even as early as the beginning of the Nineteenth Century, prominent surgeons and physicians noticed the reaction of blood vessels to haemorrhagic shock. (Seelig and Lyon, 1909)

In haemorrhagic shock, the cardiovascular system tries to adjust itself in order to accommodate the smaller volume by increasing the peripheral resistance through generalized vasoconstriction. (Gessell, 1919), (Catchpole, 1955), (Erlanger, 1919), (Wiggers, 1950), (Cameron, 1962), (Lansing, 1962). This adjustment is brought about by vasomotor nerves situated in the walls of the capillaries. At the same time, increase in plasma catecholamines helps to maintain this vasomotor tone (Fine, 1962), (Vassant, et al, 1963), (Corday, 1960), (Wiggers, 1950), (Cameron, 1962). Catchpole (1955) noted that administration of l-nor-epinephrine during haemorrhagic shock did not lead to further peripheral vasoconstriction. However, there was a rise in blood pressure without increase in mean cardiac output. This is indicative of a differential increased resistance in different parts of the vascular beds. Wiggers (1950) observed the same phenomenon of differential vascular resistance. Vasodilation was noted to appear an hour before death (Fine, 1962).

Landgren and Neil (1951a, 1951b) demonstrated that stagnant hypoxia caused a heavy discharge of chemoreceptors and that this was correspondingly reduced by increasing systemic pressure. However, Field and Laverty (1958) do not subscribe to the theory of humoral vasoconstrictor material. Phemister and Hardy (1927, 1928) described vasodilator substances which develop in heparinized blood outside the body and therefore temporarily help tissue perfusion after reinfusion and thus increase cardiac output. The same authors believe that prolonged vasoconstriction that follows may be due to serotonin that is formed in the transfused blood or in the body of the animal during shock.

General vasoconstriction which occurs in all types of shock is aimed at redistribution of a large volume of blood to those structures whose function is vital for immediate survival. This vasoconstriction to other organs, if prolonged, may lead to the production of lethal factors or possibly to factors that lead to irreversibility (Cameron, 1962), (Alexander, 1955), (Adcock, 1960). Probably the haemorrhagic necrosis of the small bowel seen in fatal endotoxin and haemorrhagic shock may be due to intense vasoconstriction and oligemia of the gut (Lillehei, 1956, 1957), (Lillihei and MacLean, 1958). This may also be responsible for an increase in the hematocrit and Hemoglobin and a decrease in plasma volume (Lillihei and MacLean, 1958), (Fine et al, 1959).

The clinical situation of shock due to sepsis appears to be primarily related to the failure of peripheral vascular resistance. Gilbert et al, (1955) found in their patients that hypotension was not associated with decreased cardiac output, while peripheral resistance was reduced. These authors found that patients who received blood

contaminated with coliform bacilli or in septic abortion, exhibited these hemodynamic abnormalities. Hinshaw et al (1958) in animal experiments with Escherichia Coli endotoxin also noted a fall in peripheral resistance. Weil et al (1956) reported normal total peripheral resistance during the early phases of shock. This resistance, however, tended to decline as the animal progressed into shock (Hinshaw et al, 1958). This decline in peripheral resistance is probably due to the release of some parasympatholytic substance at the nerve endings. Vick and Hinshaw, (1960) believe this substance to be acetylcholine. There is a possibility also that this delayed vasodilatation in this type of shock may be due to accummulation of acid metabolites associated with a large oxygen debt (Hinshaw, 1958). On the other hand, Cannon and Bayliss (1919) claimed to have discovered a substance liberated from injured tissue, a histamine-like substance which on being absorbed circulated throughout the body, producing dilation and increased capillary permeability. Parsons and Phemister (1930) were unable to demonstrate any such vasodilation toxin coming by the blood stream from an injured area.

Zweifach et al (1956) noted that progressively increasing doses of endotoxin led to the decrease in the response of the terminal arterioles to epinephrine; at the same time the venules became more reactive. This physiological disturbance contributes to the stagnation of flow and peripheral pooling. Thomas (1956) and Zweifach (1956) claim that endotoxin intensifies the local vasoconstrictive action of epinephrine.

Species differences in reaction to endotoxin make this

subject more intriguing. Injection of endotoxin into a monkey leads to hypotensive changes which are not clearly understood (Ross, 1957) at the present stage in our knowledge of shock in primates. In the cat, venous pooling is noted primarily in the pulmonary vascular system and not in the splanchnic bed (Gilbert, 1960), while in the rat, marked liver congestion with haemorrhage suggests trapping of the blood in the splanchnic area. There is a similarity between the endotoxin vasomotor and vascular collapse with anaphylaxis. Probably this similarity is due to a common factor which depresses the reticuloendothelial system (Fine, 1959), (Frank, 1955), (Thomas, 1958). Studying the hemodynamics of patients with bacteremic shock, Vassant et al (1963) found that reduction in mean arterial pressure was accompanied by reduced cardiac output and increased peripheral resistance. This would indicate that the reduction in arterial pressure is due to a decline in cardiac output rather than due to arteriolar dilatation or so called 'vasomotor collapse'. Mean circulation time was prolonged, reflecting decreased velocity of blood flow. In gram negative shock patients, hypotension is associated with a marked reduction in cardiac output; vasodilation does not account for the hypotension (Vassant et al, 1963), (Wiggers, 1947, 1948). Deficit in venous return and venous pooling with decreased venous return account for the initial reduction in cardiac output (Weil, 1961), (Wiggers 1950), (Wiggers and Werle, 1942) and for the primary causes of bacteremic shock (Vassant et al, 1963).

b) <u>Venomotor Failure</u>

Venomotor failure also throws new light on the process of

blood pooling in shock. This is accounted as the primary cause in the reduction of venous return in haemorrhagic shock (Wiggers, 1950), (Alexander, 1955), (Zweifach, 1944), (Gelin et al, 1961). It seems that oscillatory behaviour of the vasomotor centres following haemorrhage (Guyton and Harnis, 1951) produces oscillations in venomotor tone as well as fluctuations in arteriolar tone (Green et al, 1943). The magnitude of venoconstriction evoked by haemorrhage indicates that this is a contributing factor in compensatory adjustments of the circulatory system. Venomotor tone tends to dissipate most markedly in critical hypotension (30 mm Hg). This is followed by muscular venules (Zweifach, 1944). It seems that venomotor failure heralds the period of irreversibility. Since there is little arteriolar dilatation (Alexander, 1955), (Wiggers, 1950) in endotoxin shock, this places upon the venomotor system a major responsibility for the hemodynamic failure of the circulation in shock. Alexander (1944) demonstrated that venomotor tone sharply rose with haemorrhage just as in arterioles, but it is not maintained with prolongation of hypotension. Failure of the venomotor mechanisms is an important factor in shock, as it leads to pooling and aggregation of blood in the venous system (Gelin et al, 1961), (Hardaway, 1961a, 1961b, 1962). This in turn leads to decreased cardiac output, decreased nutrient flow, anoxia, metabolic changes and then finally to the irreversible state of shock.

It is concluded that failure of the venomotor mechanisms is an important factor in shock.

c) Coagulation Mechanisms in Shock

Hewson (1846) noted that in bleeding human patients "the blood which issued last coagulated first". Turpini and Stefanini (1959) confirmed Hewson's findings, and in addition they found that during haemorrhagic and traumatic shock, hypercoagulability was followed by hypocoagulability, with a fall in clotting elements and an increase in fibrinolysin activation.

Endotoxin (Hardaway et al, 1959, 1961a, 1961b) and haemorrhagic shock have been shown to be associated with abnormalities in the coagulation mechanism (Hardaway and McKay, 1959, 1962a, 1962b) (Gans, 1960). Intravascular clotting and hypercoagulability of the blood has been a constant finding in all types of shock (Crowell and Read, 1955a, 1955b), (Crowell, 1960). However, it seems to be encountered to a greater degree in haemorrhagic than in endotoxin shock.

The author observed, while taking blood samples for chemistries and electrolytes, that when a dog had been in shock for 3½ hours, the blood was so hypercoaguable that more heparin had to be added in order to keep the blood in a liquid state. MacKay (1955, 1956) and his associates noted the same changes in coagulation of the blood after administration of incompatible blood transfusion.

The cause of decreased clotting during haemorrhage is obscure. Norepinephrine is known to cause significant drop in clotting time of dogs (Hardaway, 1962). Decrease may be again a protective mechanism aimed at staunching haemorrhage (Hardaway, 1962). In severe haemorrhage, the blood is so hypercoagulable that intravascular

coagulation takes place (Ehrlick, 1963). This results in the body's depletion of fibrinogen and prothrombin (Tagnon et al, 1946). With microcirculation reduced to these dangerous levels, perfusion to vital organs is markedly reduced and thus tissue death takes place especially in those areas which have a great need for continuous blood supply such as the kidney and the gastrointestinal mucosa. Irreversibility was correlated with a fall in prothrombin and fibrinogen which denoted intravascular coagulation and aggregation of cells (Hardaway, 196la, 1961b, 1962). Injection of thrombin produced the same intravascular phenomenon (Hardaway, 1960). It seems that death occurs due to tissue necrosis as a result of thrombi. The focal necrosis and haemorrhages that occur in the liver, kidneys, pancreas and sometimes in the heart following irreversible haemorrhagic and endotoxin shock are due to these vascular disturbances (Hardaway, 1959).

Hypercoagulability and survival are correlated, since hypocoagulability heralds the appearance of irreversibility (Hardaway et al, 1963). Probably autogenous heparin appears later and causes the hypocoagulability. Neutralization of this heparin-like substance by protamine seems to point to the fact that the substance is heparin, which is probably released by the liver (Hardaway et al, 1963). The same authors claim protection of the animal against lethal influences of haemorrhagic shock by administration of fibrinolysin, probably by dissolution of established clots in visceral capillaries and destruction of fibrinogen.

In splenectomized animals (Hardaway, 1962) the fibrinogen

levels were not only lower initially, but fell less. This was much more significant in permanent survivors. These findings suggest that there is less total fibrinogen converted into fibrin in splenectomized than in normal dogs. Splenectomy does seem to give some protection against irreversible haemorrhagic shock.

Besides the aggregation and sequestration of blood in the capillaries and venules, there are some enzymatic derangements which seem to take place as a result of prolonged tissue and cellular anoxia. Lecithinase is liberated in the anoxic areas of the circulation (Hardaway, 1963). This enzyme hydrolyses the cement of the endothelium, leading to more plasma loss into the extravascular spaces. This may be one of the causes of focal necrosis found in some organs following protracted endotoxin hypotension.

Whatever the actual pathological derangements are in peripheral vessels, there is no doubt that this part of the circulation has a role to play in the irreversible phenomenon of shock.

3. CIRCULATING VOLUME IN HAEMORRHAGIC AND ENDOTOXIN SHOCK

a) Vasovagal Syncope

Reduction in effective blood volume and venous return are important in the development of circulatory failure. Circulatory failure can occur without any external loss of blood, characterized by fall in right atrial pressure and slight increase in heart rate. Unpleasant smells, pain, psychic fright or physical trauma without any loss of blood, either internally or externally, may result in fainting. This form of shock is called vasovagal syndrome (Lewis,

1932). In this syndrome, peripheral resistance is markedly decreased, suggesting a reflex vasodilation as the dominant factor (Warren et al, 1945).

There is increase of flow through the muscles while that of the skin and the brain is decreased. Muscular blood flow is reduced by sympathetic nerve block. Sudden syncope which is followed by reduction of arterial pressure is due to reflex vagal slowing and/or dilatation of the blood vessels dominantly in the muscles.

b) Volume Changes During Haemorrhagic Shock

This type of shock results initially from reduction in blood volume. It was Keith (1919) who first demonstrated decreased volume of the circulating blood in shock. Although haemorrhage may be the inciting cause of this syndrome, the signs and symptoms, as well as the ensuing physiological and biochemical alterations, are not entirely the direct effect of the blood volume deficit per se. Some factors must enter the picture to produce these changes.

Between the initiating blood volume loss and the final end result, there are many compensatory reactions, many of which have a bearing on irreversibility. A chain of events occurs after haemorrhage and they are so linked together that a vicious cycle occurs. Haemorrhage and hypovolemia stimulate the activity of the sympathetic nervous system, which leads to increased production of epinephrine (Walker, et al, 1959), (Cameron, 1962), (Wiggers, 1950), (Harkins, 1935), Longerbeam, 1962), (Longerbeam et al, 1962), (Corday, 1960), (Shoemaker, et al, 1961), (Walton, et al, 1959).

This compensatory response leads to initial increase of

blood flow through the liver, increased portal vein pressure and increased resistance to flow across the liver, (Shoemaker, 1961) which gradually decreases due to regional resistance (Shoemaker, et al, 1961). This resistance in hepatic flow leads to increased portal vein pressure which in turn hinders blood flow from the splanchnic area. With generalized impairment in the circulation, there is impairment of the metabolic and biochemical functions of the liver. The interference with hepatic circulation eventually leads to aggregation of cells in hepatic sinusoids and small peripheral vessels and the same vicious cycle described before comes into play again, eventually leading to irreversibility.

Replacement of the blood volume deficit after protracted and severe haemorrhagic shock does not avert the phenomenon of irreversibility. Therefore decrease in blood volume which is postulated to be a sequellae of capillary permeability and/or blood loss does not appear to be the main factor in irreversibility.

c) Blood Volume Changes in Endotoxin Shock

It is generally believed that there is a reduction in the volume of circulating blood in all types of shock. In shock without haemorrhage, the diminuation of blood volume is attributed to passage of fluid from the blood into the tissues possibly as a result of some toxic substance (Blalock, 1930a, 1930b), which disrupts the peripheral vessels. Lillihei and MacLean (1958), on studies of blood volume in ninety dogs, reported an increasing plasma loss reaching an average of 35% immediately prior to death. Lillihei (1962)

working separately, also reported a similar plasma loss in irreversible haemorrhagic shock.

Penner and Bernheim (1942) working with shiga toxin noticed that after injection of the toxin into the dog, there was a rise in hemoglobin, red cell count, hematocrit reading and specific gravity of whole blood. The values of these parameters indicate a decrease in circulating blood volume.

Crenshaw, et al (1962), using S^{35} labelled sodium sulphate I^{131} and Cr^{51}, concluded that during acute haemorrhagic shock in dogs, there is a marked diminution in functional extracellular fluid volume. This is attributed to the defect in internal distribution of the extracellular fluid. In their experiments, the total functional extracellular fluid loss averaged 31%. These results were obtained from patients who had been admitted during acute haemorrhagic shock.

The average blood volume deficit in endotoxin and in haemorrhagic shock after transfusion in rabbits and dogs is 7.0% (Grable et al, 1963). In fact this team claims to have found no change or an increase in plasma volume before death.

It is possible that during haemorrhagic and endotoxin shock, substances such as histamine, proteases, kinins, polypeptides and other permeability factors are responsible for capillary permeability in shock - thus allowing the loss of circulating plasma volume (Miles, 1961), (Stetson, 1961). However, replacement of the same amount of fluid loss did not increase the survival rate. (Grable et al, 1963), (Lillehei, 1962).

On the other hand there are others who claim that plasma volume during endotoxin shock remains within normal range (Ebert and Astead, 1941). Gilbert (1960) found that during the early stages of uncomplicated endotoxin shock, there was no critical reduction in total blood volume. However, this reduction seems to be a contributory factor during the later stages of shock.

Intravenous injection of typhoid vaccine, produced no change in hematocrit of plasma volume as measured by T-1824 (Favorite and Morgan, 1942), (Gibson and Kopp, 1938). Altschule et al (1945) reported an increase in plasma volume in febrile conditions. Patients dying with shock from peritonitis or from a transfusion contaminated by gram-negative organisms were found to have normal blood volume and hematocrit (Emerson and Ebert, 1945), (Richards, 1943-44), (Stevens et al, 1953).

The correlation between plasma volume and irreversibility is still obscure. Death occured in dogs whose plasma volume deficit had been corrected (Lillihei and MacLean, 1958), and it has been shown in experimental peritonitis that plasma volume fall does not determine death or survival (Ebert, 1949), (Frank et al, 1955).

There are reasons to suspect that a fall in plasma volume must eventually occur. Histological evidence of edema in the intestine (Penner and Bernheim, 1942) seems to substantiate this loss. Studies with tagged I^{131} showed the highest concentration of this isotope in the intestine (Aust and Johnson, 1957, 1958), (Aust, 1959).

The later fall in plasma volume is probably due to increase in capillary permeability which has been pointed out previously.

There are experimental data which indicate that plasma volume falls during endotoxin shock. There is progressive rise in hematocrit as the dog sinks deeper into shock (Penner and Bernheim, 1942). Hematocrit increases closely parallel plasma losses (Lillehei and MacLean, 1958). Blood diarrhoea often starts one to three hours after endotoxin administration and continues until death. The author's own observations confirmed these findings.

Blood determinations made in patients with bacteremic shock following contaminated blood (Stevens et al, 1953) were within normal limits. Ebert and Stead (1941) investigating the hemodynamics of circulatory failure in acute infections did not find any significant blood volume reductions. Muelheims (1959) and his co-workers have demonstrated that after severe haemorrhage, the liver shows a decrease in red blood cell volume of about 50%.

Falling plasma volume reported in dogs is probably the result of dehydration or loss of fluid into the interstitial space or both. Braude et al (1955), working on rabbits and using endotoxin tagged with radio active sodium chromate, demonstrated that the distribution of radioactivity was greatest in the plasma for two hours, after which its highest concentration was found in the liver and the buffy coat (Braude, 1955a, 1955b).

Differences in figures on plasma volume changes in endotoxin shock may be due to differences in the techniques of estimating plasma loss. This problem of volume changes could be re-evaluated by using more than one species and standardizing the method of

measuring plasma volume using modern instruments such as the volemetron.

4. THE ROLE OF THE LIVER DURING SHOCK

a) Circulatory Changes

Two-thirds of the hepatic flow is from the portal vein and one-third is from the hepatic artery (Bard, 1956). Decrease of systemic blood pressure is followed by a decrease in both portal and hepatic artery circulation.

The liver plays a very important role during haemorrhagic and endotoxin shock. The hemodynamic events that follow haemorrhage or bacteremia are reflections of more dire consequences in the splanchnic vasculature than in any other system of the body. The increased hepatic vascular resistance to blood flow produces in effect, a physiologic dam (Hamrick, 1955), (Shoemaker, 1962), (Kuida et al, 1958). With increasing haemorrhage, the portal vein flow decreased almost linearly (Wiggers, 1946), (Shoemaker, 1961). The pooling of blood in the splanchnic area is probably due to the constriction of hepatic veins. Adminstration of E. Coli endotoxin is followed by an immediate decrease in blood pressure. This initial phase of hypotension is due to decreased venous return, caused by initial hepatic venous spasm followed by sequestration of blood and plasma in the intestine and a consequent decrease in cardiac output (Aust and Johnson, 1958), (MacLean, et al, 1956), (MacLean and Weil, 1956). Farber (1954) and his associates have shown that mechanical obstruction of hepatic veins causes hypotension and decreased venous return to the heart. This increase in portal vein pressure and intestinal

congestion encountered in haemorrhagic and endotoxin shock has been questioned by many investigators (Lillehei, 1956, 1957), (Lillehei and MacLean, 1958), (Schweiburg et al, 1957), (Frank et al, 1946), (Cohn and Parsons, 1950), (Johnson, 1958), (Zanetti, 1952). This constriction of hepatic veins resembles histamine shock (Hinshaw, 1960, 1961 and 1962), (Wiggers, 1950).

Previous measurements of the portal vein flow in acute shock recorded a decrease in flow but did not indicate a significant increase in mesenteric vascular resistance (Cull, et al, 1956), (Selkirk and Brecher, 1956), (Levy, 1958).

As the hepatic resistance increases and falling hepatic blood flow progresses, a critical situation arises where the diameter of the sinusoids produces alterations in the blood velocity. Exaggerated Rouleau formation occurs and leads to sludging or aggregation of red cells in the hepatic sinusoids (Gelin, 1956, 1961), (Gelin and Shoemaker, 1961), (Knisely et al, 1945). Congestion and hyperemia of the hepatic sinusoids take place in the pericentral area. Sludging of cells in hepatic sinuscids was also seen in burns (Gelin, 1956) and in haemorrhagic shock (Knisely, 1946), (Wiggers, 1950). However, Hamrich and Meyers (1955) believe that although there is sludging, there is no alteration in the oxygen consumption in the splanchnic area. It is this sequestration of blood in this area that gives rise to reduction in effective circulating volume (Shoemaker, 1962). Histological evidence of acute hyperemia and congestion of the liver have been observed both in man and experimental animals dying of shock.

b) Biochemical Derangements

As shock progresses from impending to the irreversible state, there is a depletion of glycogen stores. This is reflected by the hyperglycemia which is markedly prominent during the hypotensive period of shock (Beatty, 1945). It was Claude Bernard who was the first man to show that haemorrhage produces hyperglycemia. The glycogen release is activated by the sympathetic nervous system (Engel, 1952), (Wiggers, 1950), which also stimulates the adrenal medulla to liberate adrenaline and finally the activation of the liver to liberate glucose. Engel (1943) attributed the hyperglycemia to increased glucogenolysis. Wiggers (1950) is of the opinion that elevated levels of glucose are due to the failure of the liver to synthesize glycogen from glucose and lactic acid and that there is also a concomittant depression of the tissue's ability to utilize glucose efficiently. The liver's uptake of oxygen is decreased and its ability to deaminize amino acids and synthesize urea from dl-alanine and ammonium lactate is impaired (Wilhelmi, 1945), (Wiggers, 1950). The energy reserves represented by stores of A.T.P. and A.D.P. are diminished (Wiggers, 1950), (Levenson, 1961), (McShan et al, 1945), (Lepage, 1946). There is intracellular accumulation of creatinine, inorganic phosphates and other nitrogenous metabilites (Cowley et al, 1960), (Nelson and Seligson, 1953), (Fishman and Levine, 1948).

Due to the depression of the liver circulation, there is a loss of liver potassium and an increase in liver sodium chloride.

Prolonged haemorrhage leads to increase of liver potassium by 50% and decrease of liver sodium by 50%. Thus liver electrolyte derangement and the additional enzymatic disturbances lead to the accumulation of water in the liver (Darrow and Engel, 1945).

The biochemical changes in the liver, the depletion and the reduction of oxygen saturation in the portal system play an important role in the irreversible phenomenon (Lepage, 1946), (Frank et al, 1946), (Seligman et al, 1947). There is a reduction in the secretion of bile during shock. Bromsulpthalein clearance is diminished (Fine, 1947), (Wiggers, 1950), (Levenson et al, 1961). The congestion and discoloured state of the liver observed during haemorrhagic and endotoxin shock, especially in the latter, suggest that the liver must play some important role during the period of stress. The friable congested liver found at death from haemorrhagic shock suggests severe reduction of liver function during haemorrhagic shock.

c) Toxic Factors

Seligman et al (1947) found that by viviperfusion of the liver for five to nine hours with arterial blood from the donor, 88% of the dogs in haemorrhagic shock, irreversible to transfusion, recovered, while dogs which were perfused through the femoral artery had a 77% mortality rate. In the same year, Fine and Seligman (1947), working on dogs in which therapeutic transfusions had failed, obtained results similar to Seligman's group.

Frank et al (1946) prevented or delayed the onset of irreversible shock by increasing arterial blood flow to the liver.

Elliott (1951) reported higher survival rate on dogs which had received intravenous injections of sodium dehydrocholate. At the same time he noticed that by increasing arterial blood flow to the liver, he increased the survival rate of dogs subjected to haemorrhagic shock.

Chambers et al (1944) suggested the presence of a circulating toxin in haemorrhagic and torniquet shock. Certain toxins cause hepatic vein contraction in dogs and this results in arterial hypotension, hepatic congestion and increased portal vein pressure (Thomas and Essex, 1949). Shorr (1945) and his associates are of the opinion that shock is due to an endogenous vasopressor toxin, which is principally found in the liver. However, if a toxin is responsible for the lethal outcome of shock, it would be difficult to account for the healthy state of the donor dog, while the recipient dies in shock. There must be some neutralizing element in the donor dog which is not available in the recipient in spite of the free intermixture of the two blood streams (Fine, 1947). Shorr (1945) found that the toxin is elaborated by anoxic liver even in vitro and it is inactivated by healthy liver tissue. The same investigator and his team isolated reduced ferritin from shocked liver and claimed this material as the toxin responsible for irreversibility (Shorr et al, 1957).

These findings seem to indicate that the liver manufactures a toxin which is capable of paralysing the vascular tone. There may be a hepatic hormone which normally maintains vascular tone, which like hypertensinogen and fibrinogen, disappears as the hepatic cells become increasingly incompetent (Fine, 1952). On the other

hand, Prinzemetal (1944) claims that there is a principle in certain liver extracts which possesses power of decreasing mortality and increasing survival time in animals subjected to burn shock.

The important role of the liver during endotoxin shock is demonstrated by Seligman (1948) who injected radioactive (I^{131}) Serratia marcescens into rats. He found that the greatest radioactivity was in the liver.

5. THE ROLE OF THE INTESTINE IN IRREVERSIBLE HAEMORRHAGIC AND ENDOTOXIN SHOCK

There is considerable overlap in the mesenteric and hepatic changes that take place during shock. The anatomical and circulatory relationships of these two systems are well known.

The role of the intestine in irreversible haemorrhagic and endotoxin shock has been widely studied by many investigators (Blalock and Levey, 1937), (Blattberg et al, 1960), (Braude, 1955a, 1955b), (Lillehei, 1957, 1958, 1962). Preservation of blood flow to the gastrointestinal tract by cross circulation (Lillehei, 1957) has resulted in protection of 80% of dogs from going into irreversible shock. Blood diarrhea, edema, mucosal haemorrhages and necrosis of the small bowel, which are a sine qua non of the irreversible shock syndrome, were prevented by this form of treatment. It appears that the site of irreversibility is the gastrointestinal tract (Henly, 1958). The reduction of normal portal flow from the average of 31.6cc./min./kg. to 18.5cc./min./kg. (Henly et al, 1958), (Corday, 1960) during the hypotensive period may be responsible for the haemorrhagic necrosis of the bowel.

After administration of endotoxin, the liver weight rises

abruptly while the intestinal weight rises over a period of 4-6 hours until death ensues. (Aust and Johnson, 1958). The increase in the weight of these organs is probably due to plasma sequestration in the intestines (Hinshaw et al, 1958a, 1958b). MacLean (1956) and his associates have demonstrated a marked loss of fluid into the intestine following endotoxin shock with small bowel weight rising to as much as 196-770 grams in the hour following endotoxin injection. The fluid loss partly accounts for the hypotension observed. Aust and Johnson (1958) believe that endotoxin causes capillary permeability to the degree where leakages of large protein molecules in the intestinal spaces occur. This explains the edematous congested intestine that is found at autopsy of dogs dying of irreversible endotoxin and haemorrhagic shock (MacRay, 1958). The pathophysiological intestinal similarities between endotoxin, haemorrhagic and traumatic shock have led to the belief that all forms of shock have a bacterial or endotoxin etiology for the production of irreversibility (Fine, 1952, 1954, 1958), (Fine et al, 1959), (Jacob et al, 1954), (Schweinburg et al, 1954), (Lillehei, 1957), (Lillehei and MacLean, 1958).

On the basis of this hypothesis, Lillehei (1962) (Zweifach et al, 1958) sterilized the gut of dogs before subjecting them to haemorrhagic shock. This did not alter the course of irreversibility. At the same time, Fine (1952, 1955, 1962) reports better results in dogs pretreated with non-absorbable oral antibiotics, if given prior to the induction of haemorrhagic shock. He claims antibiotic treatment pre induction of shock increases the survival rate from 20% to 65%. Yet out of 192 blood cultures taken at intervals

during shock up to the time of death, only four positive cultures were found: two for clostridia and two for pseudomonas (Powers and Schloerb, 1958). Intestinal extirpation of the dogs prevented the plasma sequestration and 'pooling' into the intestine that follows bacteremic or endotoxin shock.

Lillehei (1957), Lillehei and MacLean (1958) and Fine et al (1959), while they disagree on the bacterial etiology of every form of shock, agree that the late phase of irreversible shock is probably mediated by bacterial endotoxins which cause the vascular changes that contribute to the irreversible phenomenon and then finally to the death of the animal.

Ravin (1958) and his co-workers have demonstrated the presence of endotoxin activity within 5-10 minutes of irreversible haemorrhagic shock.

Lillehei (1956) demonstrated that perfusion of the superior mesenteric artery either with or without an Eck fistula, thus perfusing the small bowel at near normal pressure, was more effective in preventing irreversible haemorrhagic shock than perfusion of the liver. The dogs which survived permanently did not show the mucosal congestion and necrosis which were noted in the control animals. Lillehei (1958) also claims that a 'hemin' pigment is present in higher concentration in the plasma of non-survivors than in the survivors and the pigment increases coincident with the development of irreversibility.

Deuterium oxide studies with endotoxin shocked dogs showed that the intestine and the liver took up sufficient deuterium

oxide from the blood in two minutes. This is consistent with the sequestration of plasma previously mentioned, that is noted in endotoxin shock (Bradle and Johnson, 1958). In their studies, they also demonstrated that after endotoxin administration, the normal flow rate value for the intestine was reduced from 1.2 ml./min./gm. to 0.4 ml./min./gm. This perhaps explains the basis for the necrotic haemorrhages of the small intestine in irreversible haemorrhagic and endotoxin shock.

The mucosal haemorrhagic necrosis which is seen in dogs dying from irreversible haemorrhagic and endotoxin shock can be compared to the pseudomembranous enterocolitis which occurs in some patients dying from various disease entities associated with shock (Penner and Bernheim, 1939a, 1939b). These authors conclude that pseudomembranous enterocolitis may be a sequellae of vascular spasm encountered during shock. This entity is not due to antibiotic therapy, since it was described before the advent of antibiotics. It must be concluded therefore that necrosis of the intestine may occur in shock just as it does in the kidney (Penner and Bernheim, 1939a, 1939b).

Ende (1958) reported several cases of intestinal necrosis in patients dying of severe heart failure and shock who at post mortem had no demonstratable mesenteric thrombotic vascular occlusion. Gastrointestinal mucosal ulcerations, the so-called stress ulcers (Boyd, 1961) and haemorrhages are a common finding at post mortem following severe shock.

Franco-Bowder (1959) and his associates working on a potent histamine liberator, polymixin B., induced mucosal haemorrhages and

erosions similar to those encountered in endotoxin and haemorrhagic shock. These authors concluded that histamine release from the peripheral body stores is the primary cause of vascular disturbances, which result in the intestinal lesions. In the monkey, which is much closer to man than the dog, intestinal haemorrhagic necrosis is rarely seen in endotoxin shock (Vick et al, 1963).

"It would seem that the small bowel is the locus minoris resistance during haemorrhagic and endotoxin shock. The additional intraluminal loss of blood and plasma as a result of peculiar susceptibility of the intestinal capillary bed to ischemia appears to be one of the significant lethal factors in haemorrhagic 'shock'". McRay (1958).

6. RENAL HEMODYNAMICS DURING SHOCK

Impairment of renal function is a common clinical finding which is associated with the shock syndrome. Anuria, proteinuria, oliguria, azotemia, uremia and sometimes hematuria are a reflection of severe disturbances in renal function (Bywaters, 1944), (Van Slyke, 1948), (Corcoran, 1943, 1945, 1947a, 1947b). These findings are commonly encountered in patients with bacteremic and haemorrhagic hypotension. Under normal conditions estimated blood flow to the kidney is 20-25% of totalcardiac output (Selkurt, 1945, 1946). On account of its copious blood supply and its labile vasomotor activity, the kidney plays an important role in homeostasis of the circulatory system.

The hypotension that occurs in shock leads to renal ischemia, which is probably the cause of the renal changes (Malcolm, 1905).

Hypotension causes reduction in renal blood flow (Moyer et al, 1955), (Cameron, 1962), (Wiggers, 1950), which in turn is accompanied by a decrease in glomerular filtration rate (G.F.R.). The excretion of potassium, inorganic phosphate and lactate is also severely impaired. These physiological derangements are accompanied by metabolic acidosis, since the increased production of acids cannot be compensated by their excretion and formation of ammonia to conserve base (Wiggers, 1950), (Cannon, 1917), (Wilson, 1963), (Clowes, 1961), (Crandell, 1959).

It is possible that some substances unrelated to the renin-angiotonin system (Corcoran, 1943), (Chambers and Zweifach, 1947) are rapidly liberated from the blood following endotoxin injection. These substances may be responsible for the renal vaso constriction within the first hour of endotoxin circulation (Wiggers, 1950). Increase in renin substrate of dog's blood increases after haemorrhage. (Hamilton and Collins, 1941, 1942), (Sarpestein et al, 1941, 1942), (Huidobro and Braun - Mendez, 1942), (Rau, 1949).

Franklin (1951) postulated that the vasoconstriction of the renal circulation which occurs is preferrential treatment of the brain and the heart. Histamine-like substances may be responsible for the kidney hyperemia, the persistent fall in systemic arterial blood pressure and the gradual decline in peripheral resistance (Vassant et al, 1963), (Spink, 1961), (Hinshaw and Bradley, 1959), (Hinshaw et al, 1957, 1961).

A proteolytic enzyme may be released from the juxtaglomerular apparatus or from the cortical epithelium. The enzyme, by reacting

with plasma globin forms angiotonin (hypertensin) (Wiggers, 1950). This results in tubular reabsorption depression (Pickering and Prinzmetal, 1940). Trip and Ogden (1948) believe that this vasoconstrictor substance is a byproduct of angiotonin.

Default of renal excretory mechanism seems to be the most important factor in man in the production of irreversibility in shock (Vick et al, 1963). Hinshaw and Bradley (1959) also working on clearance tests, observed the temporary decline of excretion ratios after administration of endotoxin. This temporary decrease suggests depression of renal tubular function secondary to vasoconstriction. The Tm P.A.H. values returned to preendotoxin levels while creatinine ratios showed irregular changes. The same investigators noted a fall in weight of the kidney after endotoxin injection (Hinshaw and Bradley, 1957). Other investigators (Selkurt, 1945, 1946), (Corcoran and Page, 1943, 1947), (Lawson et al, 1944), (Phillips et al, 1945), (Montague and Wilson, 1948), using clearance techniques have demonstrated impairment of renal blood flow during shock.

Blood studies on A. V. oxygen differences during haemorrhagic shock do not show any change; renal veins stay well oxygenated till the terminal phase of shock (Wiggers, 1950). Even when the glomerular filtration rate is less than 10% of normal, extraction ratios of para-amino-hippurate are maintained (Vick et al, 1963). Suprarenal aortic occlusion for eight hours in the African green monkey resulted in acute renal failure and yet the animals survived up to seven hours of haemorrhagic hypotension with no significant

renal sequellae (Cerilli et al, 1962).

On the other hand, Selkurt (1945a, 1945b, 1946) by clamping the renal vessels during haemorrhagic shock produced damage to the kidney tubules. The pathophysiological changes ranged from hydropic degeneration to parenchymatous (Moon, 1947) degeneration of renal tubules. In clinical shock these changes are heralded by scanty dark concentrated urine, containing albumin, hemoglobin, epithelial and red cells, as well as hyaline granular and pigmented casts (Martineau and Hartman, 1947).

As shock progresses to irreversibility, hemolysis and liberation of myoglobin takes place. This is more commonly encountered in shock arising from burns and crush injuries. The myoglobin is deposited into the kidney tubules. Such deposition may lead to complete blockage of nephrons and ultimately to circulatory failure (Bywaters, 1944), (Corcoran et al, 1943), (Corcoran and Page, 1943, 1945, 1947).

7. METABOLIC CHANGES

a) Carbohydrate Metabolism

The hypoglycemia that is encountered in endotoxin and haemorrhagic shock has been already mentioned. The interference in the functional efficiency of the enzyme systems concerned in oxydation, such as cytochrome oxidase and the succino-oxidase system is partly responsible for the derangements of carbohydrate metabolism during shock.

As the hypoxia continues, the ability of the liver to remove

lactate falls progressively and the arterial level of the lactate rises accordingly (Beatty, 1945). There is also an elevation of inorganic phosphate, lactic acid and depleted glycogen, A. T. P. (adenosinetriphosphate), phosphocreatinine and an abnormal accumulation of phosphopyruvic acid (Lepage, 1946). Beatty also found that in severe haemorrhage there is increase in the amount of glucose released by the liver, and in the arterial glucose level in spite of the rise in peripheral glucose utilization (Russell et al, 1944). The shift to anaerobic metabolism may lead to faulty energy production with breakdown of high energy organic phosphorus compounds to inorganic phosphorus (Engel, 1952). The most important factor which initiates this anaerobic metabolism during shock is tissue anoxia (Wilheim, 1948).

It is reasonable to postulate that the extraordinarily high lactic acid and low arterial pH that occurs during haemorrhagic shock may combine to upset the vital enzymatic processes. This may contribute eventually to cellular disorganization and death (Russell et al, 1944). The same authors think that the integrity of the enzyme systems is not seriously damaged since they show a rapid return to normal following transfusion. The development of irreversibility in haemorrhagic shock is not due to failure of the liver to metabolize lactic and pyruvic acids (Russel et al, 1944), (Drucker et al, 1958). When death occurs, it seems to arise from disorganization of the cellular and enzymatic processes (Drucker et al, 1958).

The return to normal (Seligman et al, 1947) of lactic and pyruvic acid after transfusion is interpreted as indicating that

metabolic acidosis is not the primary cause of irreversibility. Neverthe less, many investigators believe that while acidosis per se does not cause irreversibility, it is an important contributory factor since administration of alkalinizing agents increased the survival rate of dogs subjected to prolonged haemorrhagic shock (Levine et al, 1944), (Cannon, 1918), (Hardaway, 1961,,1962), (Milroy, 1917), (Wiggers and Ingram, 1946).

b) Protein Metabolism

Some of the metabolic disturbances of protein have been discussed. Each tissue metabolizes protein in its own fashion and there are differences in anabolic and catabolic rates amongst various tissues (Levenson et al, 1959). As a result of plasma loss in untreated haemorrhagic shock, hypoproteinemia occurs. There is increase in total free amino nitrogen during shock (Sayers et al, 1945), (Engel et al, 1943), (Russell et al, 1946).

An early rise in the level of amino nitrogen during haemorrhagic shock is indicative of a poor prognosis (Sayers et al, 1945), if the animal is not treated. As the animal progresses into shock, there is increased release of amino acids from muscle and other organs which are damaged as a result of reduced circulation. As the liver fails in metabolizing nitrogenous compounds, aminoacidemia takes place.

There is a release of various peptides and activation of certain proteolytic enzymes which are probably released from the muscle (Levenson et al, 1961). In severe late shock, elevation of blood ammonia is commonly observed (Cowley et al, 1960),

(Nelson and Seligson, 1953). This rise is partly due to hydrolysis of urea in the gut, absorption of the ammonia into the portal blood and decreased ability of the liver to form urea.

c) Tissue Metabolites

Tissue concentrations of glycogen, adenosine triphosphate, and phosphocreatinine were analysed (Wiggers, 1950). Samples were drawn from the liver, the kidney, brain and heart muscle. There was no depletion of these substances in the brain and muscle. The heart showed slight depletion of energy reserves, while the kidney and liver showed serious depletion. The conclusion drawn is that during shock, there is a preferential distribution of blood to the heart and the brain at the expense of the kidneys and the liver (Lepage, 1946).

The metabolic changes seen in shock may be a reflection of changes in the mitochondria of cells (Croxatto et al, 1951). There is claim that enzymatic hydrolysis of the peptides leucylglycine, leucyldiglycine and leucinamide acetate are increased following haemorrhage and traumatic shock in dogs and cats (Levenson, 1951). There is also a corresponding rise in lactic acid dehydrogenase (Vessell et al, 1951).

d) Acid Base Balance and Electrolytes

Hypovolemic shock is accompanied by reduction in alkali reserve, a marked metabolic acidosis (Cannon, 1919), (Milroy, 1917), (Wiggers, 1950) and a development of oxygen debt (Guyton, 1961). This metabolic acidosis is due to an increase in blood lactic and other organic acids. The reduction in the tissue perfusion leads to

anaerobic respiration which leads to accumulation of metabolites and a further reduction in alkali reserve. This leads to reduction in pH and an increase in plasma catecholamines (Manger et al, 1957). Animals treated with THAM: tris (Hydroxymethyl) aminomethane (Page and Olmstead, 1951) had a greater survival rate (Hardaway, 1962) than animals treated with saline alone (Smith and Moore, 1962). These authors observed that saline administration in highly acidotic dogs produced little change in the animal's acid-base status. There was, however, a fall in the serum potassium level in 75% of the dogs. Dextrose in water infusion showed no change in potassium, chloride and sodium levels.

Levine (1944) reports 62% survival rate in haemorrhagic shock animals treated with sodium bicarbonate supplemented with whole blood transfusions, while treatment with whole blood alone yielded 25% survival. All the control animals died.

In Hardaway's group (1962), the highest survival rate was observed when correction of the arterial blood pH was associated with oxygen delivery. Catecholamines were highest in those animals which did not receive buffer, indicating that acidosis per se in addition to hypotension may stimulate catecholamine production.

Acidosis which appears during haemorrhagic and endotoxin shock is not a direct cause of irreversibility, since its correction does not seem to prevent the irreversible trend (Hardawayet al 1962)(Cannon 1918)(Russell et al 1963).

The rapid metabolic acidosis which develops in haemorrhagic and endotoxin shock is partially compensated by a reduction in partial pressure of carbon dioxide in the blood (Hardaway et al 1962), (Root et al 1947), (Guyton 1962). Metabolic acidosis correlated well with survival and could be used as an effective criteria for prognosis (Root et al, 1947).

Electrolyte disturbances are known to occur during haemorrhagic and endotoxin hypotension. There is marked increase in plasma potassium due to movement of intracellular fluid into the blood stream to replace the fluid volume lost through haemorrhage. Plasma potassium may also rise as a result of cellular release of potassium associated with glycogen and protein tissue breakdown (Baetjer, 1935), (Zwemer and Scudder, 1937), (Root et al, 1947). The potassium levels reach their highest levels in eight hours. The more severe the haemorrhage, the higher the serum potassium concentration. Zwemer (1937) believes that histamine has something to do with increased potassium levels in the blood during shock, since injection of histamine is followed by increased potassium levels in extracellular body fluids. During hyperventilation, there is a drop in potassium levels (Hall and Reeser, 1963).

The high levels of serum potassium exert toxic effects on the heart (Manery and Solandt, 1943). Winkler et al (1938) noted during shock only minor electrocardiograph changes of potassium intoxication. These authors maintain that it is exceptional for death to be caused by cardiac arrest resulting from potassium auto-intoxication. They feel that such high toxic serum levels occur only pre-mortem. The tonic effects of potassium may be aggravated by hypocalcemia and acidosis which may be seen in shock (Levenson, 1961).

Plasma sodium and chloride may be normal or low during the early phase of shock. At this stage, sodium and chloride excretions are initially low, while potassium execretion is high. Sodium tends to accumulate in the injured tissues (Tabor et al,

1951). As the potassium leaves the cell, sodium and hydrogen enter, resulting in hyponatremia. Sodium and hydrogen immigration into the cell may also be accompanied by basic amino acids such as lysine (Fuhrman, 1960).

8. NEUROHUMORAL AND ENDOCRINE ASPECTS OF SHOCK

a) Miscellaneous Neurohumoral Substances

Any form of injury to the nervous system such as concussion, as well as prolonged hypotension, was found to lead to failure of the pressor response to angiotonin (Fine, 1961). Cannon and Rosenblueth (1937) found that denervation of animals in shock greatly augmented response to a variety of drugs. Treatment of animals with adrenergic blocking agents increased the rate of survival in animals subjected to shock (Wiggers, 1950). Nickerson and Carter (1959), using a Noble-Collip Drum, found that the vasodilator Hydralazine reduced the incidence of acute traumatic death, while Dibenzyline increased the overall survival, whether trauma was mild or severe.

Acidosis and hypoglycemia, as discussed before, are known to accompany shock (Cannon, 1918). Elevation of lactic acids and glucose is mediated by increased catecholamines in the plasma of shocked dogs (Fine 1961). The reduction of arterial pH is followed by depression of CO_2, which results in depression of ventricular isometric systolic tension. There is a corresponding decrease in the vessels' response to norepinephrine (Derby et al, 1960).

Page (1961) demonstrated that forced breathing of CO_2 produced hypotension and severe vascular refractoriness in dogs. Total sympathectomy prevented this refractoriness. It seems that CO_2 is a powerful stimulator of the autonomic ganglia.

It is postulated (Fine, 1961), (Wiggers, 1950), that humoral agents control vasomotor and venomotor tone of the peripheral vessels during shock. These same investigators believe that rhythmic contractions of the vascular smooth muscle or release of local substances may also be responsible for the adjustment of vascular tone during shock.

It is possible that some substances besides epinephrine and norepinephrine may be responsible for the vascular phenomenon. Environmental change of pH may be equally important in regulating peripheral vascular tone.

The kidneys, in response to a variety of stimuli, including haemorrhage, release some vasoconstrictor substances (Huidboro and Braun-Mendez, 1942). The same authors claim that the proteolytic enzyme renin is freed to act on alpha - 2- globulin to produce angiotensin, which has a powerful effect on vascular tone. Even CO_2 concentration can effectively change vascular tone. The sodium cation has been clinically noted as the chief offender in maintaining or increasing vascular tone in hypertension.

It is possible that these vasoactive substances have injurious effects to both peripheral vessels and the heart. In the plasma of shocked animals, other unidentified vasoconstrictor substances may be present (Page, 1961). Weinstein et al (1960)

identified what they considered to be a vasopressin in the blood of dogs subjected to haemorrhagic shock.

Freiden et al (1954) found that their hypophysectomized animals were extremely vulnerable even to slight haemorrhage. Administration of pitressin returned susceptibility to haemorrhage back to normal.

Angiotensin, synthesized at Cleveland Clinic and Ciba Pharmaceutical Co., is another vasoactive polypeptide whose pharmacological effects in shock are still under investigation (Page, 1961). Proteases liberated during tissue injury may be responsible for liberation of these vasoactive substances.

Sarpistein (1941) found that blood of normal animals with normal blood pressure contains activator with no renin, whereas post haemorrhage blood taken after long persisting low pressure contains demonstrable amounts of renin. These findings support the views that the kidney acts as an organ of internal secretion in order to preserve the homeostasis of the whole circulatory system by humoral mechanism (Levenson, 1961).

b) Epinephrine

It has already been pointed out that shock, fear and other situations of stress lead to an increase in production of catecholamines. In haemorrhagic and endotoxin shock the amount of endogenous circulating catecholamines becomes markedly increased (Corday, 1960), (Cameron, 1962), (Wiggers, 1950), (Longerbeam, 1962), (Harkins, 1935, 1941a, 1941b, 1941c). Watts (1956) is of

the opinion that the amount of endogenous catecholamines may be as high as 29 micrograms/l., decreasing to 7 micrograms/l. after restoration of the blood volume to normal by reinfusion. In spite of normovolemia and reduction in circulating catecholamines, the animals still went into irreversible shock and died (Greever and Watts, 1959).

Corday et al (1960) found that the peripheral levels of norepinephrine increased to a much greater extent than those of epinephrine, while epinephrine levels in adrenal vein plasma were more than the norepinephrine levels. This finding seems to indicate that the main source of norepinephrine level in the peripheral blood was extra adrenal, possibly sympathetic nerve endings. They postulated that the high peripheral norepinephrine levels may be due to decreased utilization, rather than due to activity of an extra-adrenal source.

Although there was no evidence to demonstrate adrenal cortical insufficiency during shock, necropsy findings have revealed that sequential histological changes develop in adrenal glands of animals and humans who have died as a result of various types of shock (Blalock, 1934), (Dunphy et al, 1941), (Davis, 1941, 1949),(Moon, 1942). In those animals that succumbed to shock comparatively early, petechial haemorrhages were found in the medulla and in the Zona reticularis and Zona fasciculata of the cortex (Wiggers, 1950). After a prolonged state of shock, focal necrosis and leucocytic infiltration have been reported (Selye, 1946). It is difficult to conclude as to whether these pathological changes are the cause or the consequence

of the circulatory failure responsible for death. Irreversible haemorrhagic shock can develop without any demonstrable histopathological changes in the adrenals. The author autopsied twenty dogs which had died in irreversible shock and no macroscopic or microscopic lesions were found in the kidney and the adrenals.

What part the adrenals play in the mechanism of shock is still not clear. Walker et al (1959) claim that they found increased corticosteroids in the adrenal veins of dogs subjected to acute blood loss.

c) Histamine

Histidine decarboxylase activity of certain animal tissues can be increased by stress, by injection or release of epinephrine or norepinephrine or by injection of E. Coli endotoxin - evidence pointing to an increase in the rate of histamine synthesis in the living animal (Schayer et al, 1960). These observations strongly suggest the hypothesis that histamine and the catecholamines form a balance concerned with circulatory homeostasis under conditions of stress and that a sufficient excess of either of the antagonists may lead to circulatory collapse. The events observed in the small blood vessels during shock support this hypothesis. There are similarities between the vascular actions of histamine and endotoxin (Kuida et al, 1958), (Gillbert et al, 1958), (Hinshaw et al, 1959), (Lillehei and MacLean, 1958), (Aust, 1959), (Dale 1929), (Hardy, 1959), (Stead and Warren, 1944).

The activity of histidine decarboxylase is increased by endotoxins. These observations suggest that the rate of histamine synthesis is accelerated in this kind of shock (Schayer, 1960a, 1960b). In addition, it is found that the stimuli such as stress, epinephrine, endotoxin, also lead to increased activity of the enzyme, which synthesizes histamine; the likelihood that histamine is an important shock toxin seems very strong. Schayer (1960a, 1960b) found that catecholamines increased the activity of histidine decarboxylase.

d) Serotonin

This neuroendocrine hormone is also associated with argentifinomas and it is a powerful vasoconstrictor (Walton, 1959). It is liberated from platelets. It seems that during haemorrhage, serotonin has a beneficial effect of causing an injured blood vessel to contract down on a forming platelet clot (Page, 1961). The role of serotonin during shock is not clear. It may be that this substance is a precursor or a more primitive form of epinephrine and norepinephrine.

e) Bradykinin

Bradykinin seems to be liberated during shock. This substance has been recently synthesized and it seems besides its pressor effects, to cause increased capillary permeability. The author observed during endotoxin shock a period where bradycardia was very marked. This usually occurred 5 - 30 minutes after administration of endotoxin. Goodwin and Richards (1960) found in the blood of protozoa-infected

animals a substance which was similar to polypeptides. The substance may arise from host parasite reaction.

f) Heparin

Hypercoagulability of the blood, which occurs in shock, has already been discussed (Crowell and Read, 1960), (Crowell, 1960). Large doses of heparin have been known to protect dogs from irreversible shock (Crowell and Read, 1955), (Crowell, 1960), (Hardaway et al, 1959, 1962).

9. PRESENT CONCEPTS ON THE TREATMENT OF SHOCK

a) Vasopressors

Vasopressors have been used in the treatment of shock for many years. However, at the present moment, controversial evidence regarding the efficiency of vasopressor agents in shock, is accumulating. During haemorrhagic shock or any form of stress, the body pours out its own endogenous catecholamines (Corday, 1960), (Cameron, 1962), (Wiggers, 1950), (Close, 1958), (Wiggers and Ingram, 1948), (Longerbeam, 1962), (Lillehei and MacLean, 1958), (Bronson et al, 1957), (Zweifach, B.W., et al, 1956). These workers argue that although initial vasoconstriction offers temporary benefits by augmenting the amount of blood which can be lost before critical changes in the blood pressure occur, there can be little doubt that the prolonged continuance of sympathogenic constriction is deleterious in that it accelerates the onset of the irreversibile state.

Clove et al (1957) claim 65% mortality rate in haemorrhagic shock dogs treated with norepinephrine as compared to 33% in controls. Vassant, Weil et al (1963), working on patients with bacteremic shock found that arterial resistance and not vasodilation was the underlying cause of reduced venous return. They also questioned the wisdom of using vasopressor agents, since their use would result in additional vasoconstriction. Administration of metaraminol in endotoxin shock to maintain 'normal' blood pressure enhanced the fatal reaction of the animal to endotoxin (Lillehei and MacLean, 1959).

Aramine (metaraminol bitartrate) may temporarily improve an increase of flow through the myocardium, but there is no correction of the carbohydrate metabolic disturbances that occur during hypotension and oligemia. Transfusion seems to correct some of those disturbances. Correcting the hypotension alone for which the vasopressors are principally used does not seem to accomplish much good. This supports the concept that hypotension alone is not necessarily harmful to the heart (Catchpole, 1955). Severe hypotension induced by spinal anesthesia produces no evidence of myocardial anoxia or gross metabolic derangements in human subjects (Hackel, 1960), (Hackel and Goodale, 1955).

Each organ has a characteristic vascular response to endogenous or exogenous catecholamines. Catchpole (1955) found that l-norepinephrine decreased coronary vascular resistance which was already decreased in haemorrhagic hypotension. Corday (1960) found that levarterenol caused increase in coronary flow above control values and peripheral coronary resistance diminished markedly.

The administration of sympathominetics causes a marked drop in the portal vein circulation. On the whole, total hepatic flow is diminished because the blood supply to the liver at this time becomes principally arterial in origin. Brunson et al (1957) believe that the incidence of liver necrosis has increased in the last ten years because of the extensive use of vasopressor drugs. The liver shows central necrosis, which is known to occur in shock alone. Other investigators (Braude et al, 1953), (Borden and Hall, 1951), (Hall and Gold, 1955), have found a high correlation between hepatic necrosis and the administration of sympathomimetic amines. Corday (1960) does not accept this concept, since 70% of the oxygen supply to the liver is supplied by the hepatic artery and flow of this vessel is almost equal to the normal flow after levarterenol administration.

Reduction of systemic blood volume is followed by reduction in renal blood flow with increased vascular resistance. Restoration of renal circulation to normal by levarterenol leads to further reduction in blood flow and increase in vascular resistance (Corday, 1960), (Watts, 1956), (Livesay et al, 1954). However, when small doses of epinephrine or levarterenol were administered, the excretion of urine increased, whereas large doses of these drugs led to reduction in the volume of urine (Langston and Guyton, 1958). Necrosis of the kidney following severe haemorrhagic and traumatic shock have been substantiated in man (Penner, 1940), (Sheehan, 1947, 1950), (Duff, 1941), (Lucke, 1946), (Bywaters, 1944), (Corcoran and Page, 1947), (Van Slyke, 1948), (Oliver et al, 1951).

The decrease in flow and increase in vascular resistance is disproportionally large in renal and splanchic circulations. The possibility that vasopressors may aggravate the ischemia of the intestine already produced by the shock cannot be ignored (Cone et al, 1957). These authors have recently reported the occurrence of intestinal necrosis in a young child with a pheochromocytoma, who died in hypertensive crisis. These observations support the theory that high concentration of catecholamines in the circulation exert deleterious effects on the gut and other organs. Penner and Bernheim (1939) produced ulcerations of the digestive tract in dogs by repeated injections of epinephrine.

Stimulation of the splanchnic nerve and injection of epinephrine and norepinephrine all produce vasoconstriction of the mesenteric vascular bed (Deal and Green, 1956), (Levy, 1958). Even sympathetic stimulation alone has been shown to produce mesenteric vasoconstriction (Bunch, 1898), (Bayliss and Starling, 1899), (Grayson and Swan, 1950).

Hardaway (1962), who has done some extensive work on coagulation of the blood during shock, observed that norepinephrine causes hypercoagulability of the blood, which leads to tissue anoxia, tissue necrosis and eventually to the irreversible phenomenon.

In spite of the growing evidence against the indiscriminate use of sympathomimetic drugs in the treatment of any form of hypotension, clinical evidence of the beneficial effects of vasopressors cannot be ignored (MacLean, 1962). The good effects of vasopressors resides in their ability to increase the perfusion of vital organs,

improve the venous return, (Rasking, 1953), (Shadle, 1955), (Weil, 1956), and enhance the myocardial function by increasing coronary flow and sometimes by direct stimulation of the myocardium itself (Lansing et al, 1962).

The increase in venous return to the heart with concommitant increase in cardiac output effected by sympathomimetics has been established experimentally (Rasking, 1953), (Shadle, 1955), (Weil, 1956). The vasopressors may also have a dilating effect on hepatic veins (Andrews, 1955). Catchpole (1955) and his co-workers claim that norepinephrine decreases coronary vascular resistance in haemorrhagic shock dogs and increase coronary blood flow. It seems according to these authors that sympathomimetics have a physiological action on the heart, the kidneys and the liver, especially in a patient with bacteremic shock. Norepinephrine used to treat haemorrhagic shock refractory to blood replacement has been employed with encouraging success (Lansing and Stevenson, 1958), (Lansing et al, 1957).

The use of vasopressors early in shock before vasomotor collapse has taken place and in dosages that maintain blood pressure just below normal has satisfactory results (Corday, 1960),,(Lansing et al, 1962). In cases where loss of blood is the initiating cause of shock syndrome, vasopressors alone cannot be used as substitutes for blood replacement. Epinephrine alone in the treatment of olegemic shock is not effective because it does not correct the metabolic abnormality while concurrently imposing a heavier burden

of work on the heart due to further increase in vascular resistance (Caliva et al, 1959). "Successful restoration of the blood pressure by a vasopressor must not be the signal for a period of complacency." (Lansing, 1962).

b) Ganglionic Blocking Agents

Vasoconstriction in response to sympathetic nervous system hyperactivity as cited before, may play a deleterious role in the development of the shock syndrome.

Nickerson and Carter (1959) have demonstrated rather convincingly that pretreatment of dogs with vasodilators may increase the percentage of animals surviving various procedures designed to induce shock. Zingg (1958) using his own method of inducing haemorrhagic shock and pretreating the experimental animals with .5 mg/kg hydralazine, claims 66% permanent survivors and 30% in the controls. Baez et al, (1952) claims 100% survival rate in dibenamine pretreated animals subjected to haemorrhagic, traumatic and endotoxin shock, while only 37.5% of his controls survived. On the whole, a significant increase in the survival rate of animals subjected to haemorrhagic, traumatic and endotoxin shock has been demonstrated by many investigators using different forms of vasodilators and ganglionic blocking agents (Hakstian et al, 1961), (Baez et al, 1952), (Beck, 1956, 1959), (Carruthers and Crowley, 1956), (Hershey et al, 1955), (Inglis et al, 1959), (Jacob et al, 1956), (Gourzis et al, 1961), (North et al, 1951), (Saltz, 1960).

Vick (1963) and his co-workers in studying the relative value

of hydrocortisone, metaraminol (aramine) and phenoxybenzamine (Dibenzyline) on endotoxin shocked monkeys and dogs found that Dibenzyline dramatically reversed the renal functions when given after the onset of shock. While aramine and hydrocortisone maintained the arterial blood pressure for a long time, they did not greatly influence renal hemodynamics.

Vasoconstriction in the presence of haemorrhage gives preferential treatment of blood supply to the vital centers, the heart and the brain. In sympathectomized animals, such preference is lost. All tissues of the body are accorded the same treatment as long as the vital centres receive sufficient blood supply. All tissues of the body probably receive an adequate amount of circulation and the aggravation of the shock condition is prevented (Freeman et al, (1938). Ganglionic blocking agents work on the same principle.

Baez (1958) and his associates postulate that the protection afforded by Dibenzyline may be due to changes it induces at a cellular metabolic level besides its sympatholytic action.

Chlorpromazine, another ganglionic blocking agent, has been shown to prolong the survival time of dogs in irreversible shock (Inglis et al, 1959). This group also observed increased mesenteric circulation after administration of chlorpromazine. The importance of mesenteric circulation in the irreversible phenomenon has already been discussed.

It was also noted that animals pretreated with ganglionic blocking agents showed less blood/kg. in the reservoir compared to the control group. This may mean that pretreated animals may reach

standard levels of hypotension with less blood loss than controls (Zingg, 1958).

c) Hydrocortisone and Corticosteroids

What part cortisone plays in haemorrhagic and endotoxin shock is still a matter of speculation. Administration of cortisone in pharmacologic dosage produces a decline in arterial pressure and an increase in cardiac output (Lillehei and MacLean, 1959) in patients with shock.

> Thus the beneficial effects of corticosteroid in the treatment of bacteremic shock may be due to increase in systemic flow which is accomplished without the penalty of added vasoconstriction.
>
> (Vassant, Weil et al, 1963).

Dibénzyline and corticosteroid seem to be synergistic in this regard of increasing cardiac output with vasodilation and thus improve tissue perfusion. Kurland and Freedberg (1951) observed a potentiation of pressor response to norepinephrine in normotensive patients after administration of A.C.T.H and cortisone. These authors conclude that hydrocortisone has a protective effect against lethal tissue-damaging effect of endotoxin. Some investigators (Zweifach, 1952), (Fritz and Levine, 1951), have demonstrated that in adrenolectomized animals, vascular response to norepinephrine is lost and it is restored only by topical application of adrenal extracts or by injection of cortisone. On the other hand, Hayes (1954) is of the opinion that in haemorrhagic shock there is a decreased minute volume of blood delivered to the kidneys and presumably to the adrenal glands, with a subsequent possible

reduction in the amounts of adrenal corticosteroids available in the circulation per unit time for peripheral tissue utilization.

However, nobody has yet demonstrated conclusively reduction in steroid output during hypotension. Since massive doses of cortisone are required to produce any substantial effects, it is quite likely that the levels of circulating corticosteroids are inadequate to maintain a satisfactory vascular response (Conolly, 1958). Cowley (1962) and his co-workers using D. Aldosterone in dosages ranging from .05 mg/kg. body weight to .1mg/kg reduced the mortality of haemorrhagic shock dogs by 45%. They believe that aldosterone protects the animals against renal shut down and haemorrhagic enteritis. Zweifach and Chambers (1942) using histamine and trauma to produce shock, prevented capillary hyperemia by administration of cortical extracts. Some investigators believe that the corticosteroids which influence intermediary metabolism are the most effective in preventing irreversible circulatory failure (Swingle et al, 1941, 1942), (Remington, 1942).

Selye and Dosne (1940) using corticosterone, found it effective in combating traumatic shock. However, Noble and Collip (1942) did not find practical benefits of cortical compounds in shocked animals. Fine and Seligman (1942) also observed no favourable effects of corticosteroids in treatment of haemorrhagic shock. These unfavourable effects of corticosteroids on haemorrhagic shock have been reported by other investigators (Howard and DeBakey, 1951), (Knapp and Howard, 1957).

Studies on adrenal cortices of dogs dying as a result of haemorrhagic shock showed depletion of total carboxyl containing lipoid and that administration of cortisone and A.C.T.H. increased the histologic evidences of damage to the adrenal cortices of dogs in irreversible haemorrhagic shock (Frank et al, 1955).

CHAPTER III

METHODOLOGY AND MATERIALS

1. ANIMALS

One hundred and thirty-four mongrel dogs without preference to sex and weighing between 18 - 26 kg. (average 22 kg.) were used in these studies. These dogs were subjected to different conditions of haemorrhagic and endotoxin shock and were divided into four main groups:

GROUP I: DIALYSIS OF NORMAL DOGS - 10 dogs

a) 5 without prophylactic antibiotics

b) 5 with prophylactic antibiotics

GROUP II: ENDOTOXIN SHOCK

a) Endotoxin and early dialysis with old and new coils - 28 dogs

1) 14 controls

2) 14 experimental

b) Endotoxin and early dialysis with new coils only - 10 dogs

c) Endotoxin and late dialysis with old and new coils - 15 dogs

1) 5 controls

2) 10 experimental

d) Endotoxin and histamine - 6 dogs

e) Endotoxin and mechanical effects of dialysis - 10 dogs

f) Endotoxin, morphine and early dialysis, with both new and old coils - 10 dogs

GROUP III: HAEMORRHAGIC SHOCK

a) Haemorrhagic shock and dialysis - 20 dogs

1) 10 controls

2) 10 experimental

b) Haemorrhagic shock and Dibenzyline - 20 dogs

1) 10 controls

2) 10 experimental

GROUP IV: DETERMINATIONS OF NORMAL ARTERIAL CHEMISTRIES - 5 dogs

All the dogs were fasted for twenty-four hours before they were subjected to any form of experimental procedure. Dogs which did not look healthy were discarded or used as donors for the blood necessary for priming of the dialysing artificial Kolff kidney machine. All attempts were made to avoid exciting the dogs as they were being transferred from the kennels to the anesthesia room. Most technicians skilfully mastered the art of cajoling a dog to the anesthetic table with very little struggling on the part of the animal. When the dog had completely won the confidence of the operator and his team, it was weighed on Weight Model 9281 (Toledo) Scale. Then the dog was securely tied around the mouth to prevent any accidental dog bites in the laboratory.

2. OPERATIVE METHOD AND ANESTHESIA

a) Method of Anesthesia

The left antero-medial aspect of the foreleg was shaved, so as to visualize the gross anatomical position of the cephalic vein. Since some dogs became excited by the sound of the automatic electric shaving machine, time for the dog to calm down was allowed before any anesthesia was administered. All dogs except the endotoxin and morphine group (Group II, (f)) were anesthetized with 30 mg/kg of intravenous nembutal. This was cautiously injected into the left cephalic vein with an 18 gauge needle. In cases where there was accidental infiltration of the nembutal in the tissues around the left cephalic vein, the right foreleg was used. In most cases the amount of anesthesia used was less than 30 mg/kg. Injection of the nembutal was discontinued as soon as the dog showed sufficient muscle relaxation with preservation of the corneal reflex. The binder around the mouth was loosened. The dogs were shaven in both groins and painted with tincture of merthiolate 1:200.

b) Operative Procedure and Operation Room Set-up

No aseptic technique was observed in our experiments. The animals were then transported to the operation room. The experimental dog was laid in a dorsal position on the Weight Model 9281 Scale, which is calibrated in both pounds and kilograms and can be opened and locked during the experimental procedure. This scale

enabled the operator to observe the weight of the experimental animal throughout the procedure. The control dog was laid down on a separate table beside the experimental dog. This facilitated constant observation of both dogs during the experiment.

Both dogs were intubated, but no pump or Bird Respirator was connected to the tube. A thermometer probe was inserted into the oesophagus to record temperatures in degrees centigrade. In order to prevent both the probe and the intubation tube from slipping, they were tied separately around the upper jaw. The probe was sometimes snuggly tied around one of the canines, while its other end was connected to one side of the Tele-thermometer. This is so constructed that two probes, one from each dog can be plugged in at the same time on each side of the Tele-thermometer box. (Fig. 2)

When the dogs were securely tied on the tables, both the right and the left femoral vessels were dissected out and clearly exposed through a longitudinal incision one inch long, made two centimeters below the inguinal ligament. Then 3 mg/kg heparin was injected into the right femoral vein by means of a 22 gauge needle. The right femoral vein was cannulated by a polyethylene tube, No. P.330. This was pushed as high as possible to the level of the inferior vena cava for recording venous pressures in centimeters of saline. The height of this manometer was adjusted to the level of the right auricle. The right femoral artery was also cannulated and connected to a mercury manometer and occasionally, by means of a three way stop-cock, to a Sandborn polygraph,

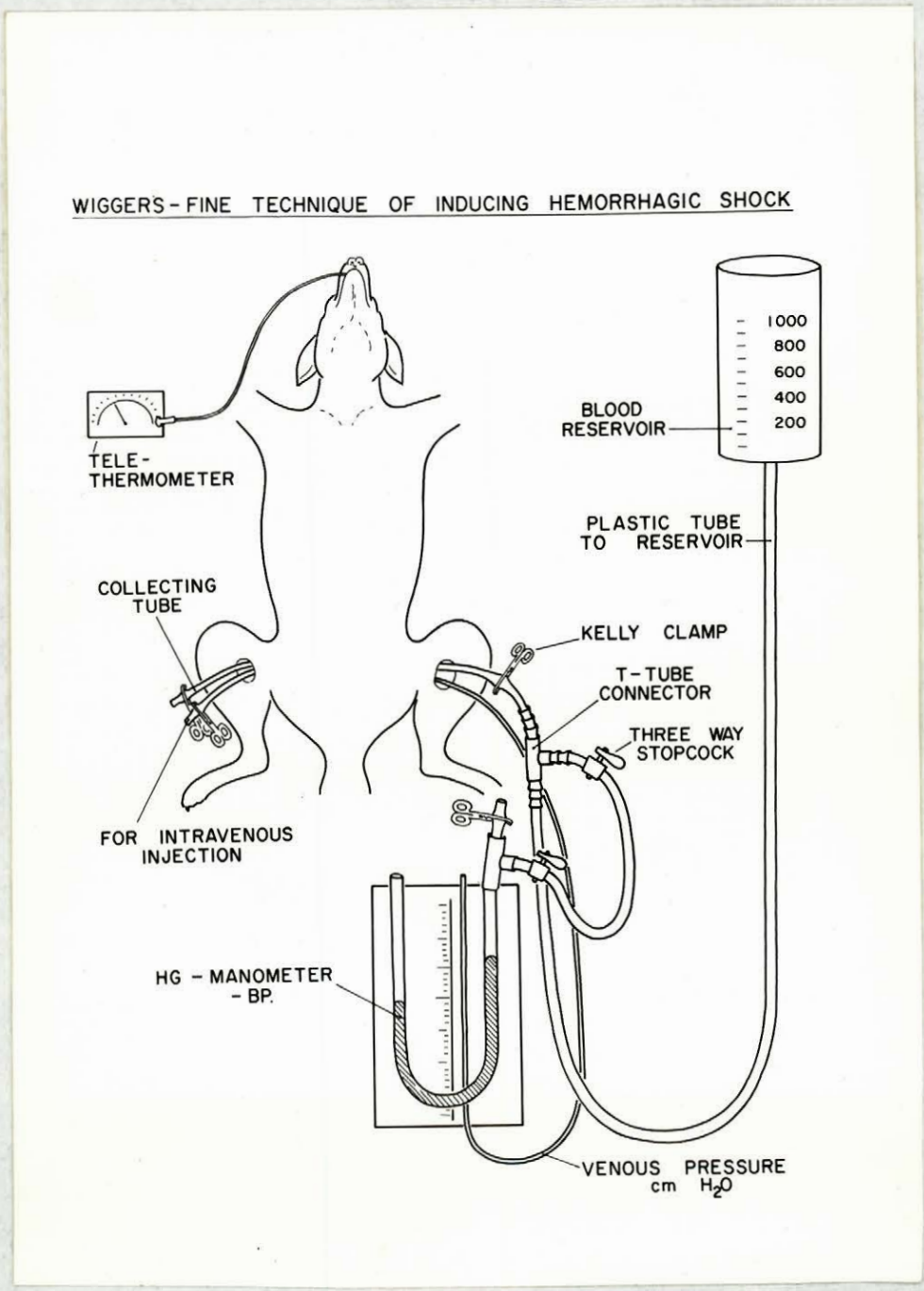


Fig. 2.--This illustrates the different apparatus used in the induction of haemorrhagic shock, using Wiggers-Fine Technique. In the case of Endotoxin shock, the reservoir was excluded from the set up.

for recording of mean arterial pressures and diastolic pressures respectively. (Photograph 2) The left femoral artery and vein were also cannulated with 'tapered' cannulae especially designed for hemodialysis tubing connections. These cannulae were first filled with normal saline to expel the air and then clamped with Kelly forceps to keep them filled with saline. Then they were inserted into the vessels. They remained clamped until hemodialysis began or when arterial samples of blood were being withdrawn. In the control dogs, the left femoral vessels were cannulated only when intravenous injections of endotoxin formed part of the experiment and when arterial blood chemistries and electrolytes were taken during the experimental period.

When all the cannulae were inserted in their proper places, the experimental dog was weighed again. It is obvious that the cannulae, Kelly clamps, the weight of the leashes and the pressure of the dog on the table all helped to increase the original weight of the dog alone. All articles on the scale contributing to this weight were recorded.

The control vital signs in both experimental and control dogs were noted. If any blood chemistries and electrolytes were studied, the control samples were taken at this period.

PHOTOGRAPH II

This picture illustrates a cannula with three way stop cock, which is connected to both a mercury manometer and a Sandborn Polygraph. A reservoir with 500 cc of blood is seen hanging on an adjustable pole at the foot of the dog. In the foreground is a tele-thermometer.

3. MATERIALS AND METHOD OF COLLECTING BLOOD SAMPLES FOR CHEMISTRIES AND ELECTROLYTES

a) The Anaerobic Method of Collection of Blood Samples for pH, pCO_2, and HCO_3

A 20 cc syringe was connected to the end of the arterial tapered cannula and 10 cc of blood was drawn and laid aside. The Kelly clamp was put back. In a few seconds another 20 cc syringe filled with 3 cc of heparin was connected to the cannula. No air was to be left in between the heparin and the nozzle of the syringe. After the syringe was connected to the cannula, the Kelly clamp was released and the arterial blood was allowed to flow slowly into the syringe. A little over 20 cc of blood was collected. Exercising every care not to introduce air into the syringe, 4 cc of blood from this syringe was squirted into a 10cc beaker. The outlet of the syringe was closed tightly by means of a special rubber cap to prevent air coming in and out of the syringe.

Meanwhile an assistant quickly pipetted 2 cc of blood from the 10 cc beaker. The blood was allowed to flow drop by drop into a centrifuge tube containing 5 cc of 11% trichloracetic acid that was kept in a refrigerator. The tube was covered with paraffin paper and taken back to the refrigerator till the lactic acid was determined. In the collection of these samples for lactic acid, avoidance of the fingers coming into contact with the delivery end of the pipette or the paraffin paper is of utmost importance. Fingers contain an appreciable amount of lactic acid.

Then finally 10 cc of the blood was drawn in a 20 cc silicone coated syringe and carefully squirted into a centrifuge tube. The assistant reinfused into the dog the first 10 cc of blood which had been withdrawn before all the blood samples were taken. After pipetting 100 mm of blood for hematocrit determinations, the rest of the sample of blood was centrifuged, and the supernatant serum used for determinations of electrolytes.

b) Hematocrit Determination

The Winthrobe method was used for the determinations of hematocrit. This consisted of filling a Winthrobe tube with heparinized blood to the 100 mm mark. This was spun at 3,000 revolutions per minute for thirty minutes. Then the height of the red cells was read and the packed cell volume expressed in percentage.

After samples for control electrolytes and chemistries were taken, haemorrhagic or endotoxin shock was begun.

4. METHOD AND MATERIALS OF INDUCING SHOCK

a) Haemorrhagic Shock

A reservoir with a capacity of 2,000 cc was employed. The inside part of the reservoir was silicone sprayed once a week. The right femoral artery was cannulated with a polyethylene tubing, 4 cm in diameter, attached to a plastic T tubing connector, one arm of which was connected to a blood reservoir, while the other was connected to a mercury manometer with a three way stop-cock. (Fig. 2)

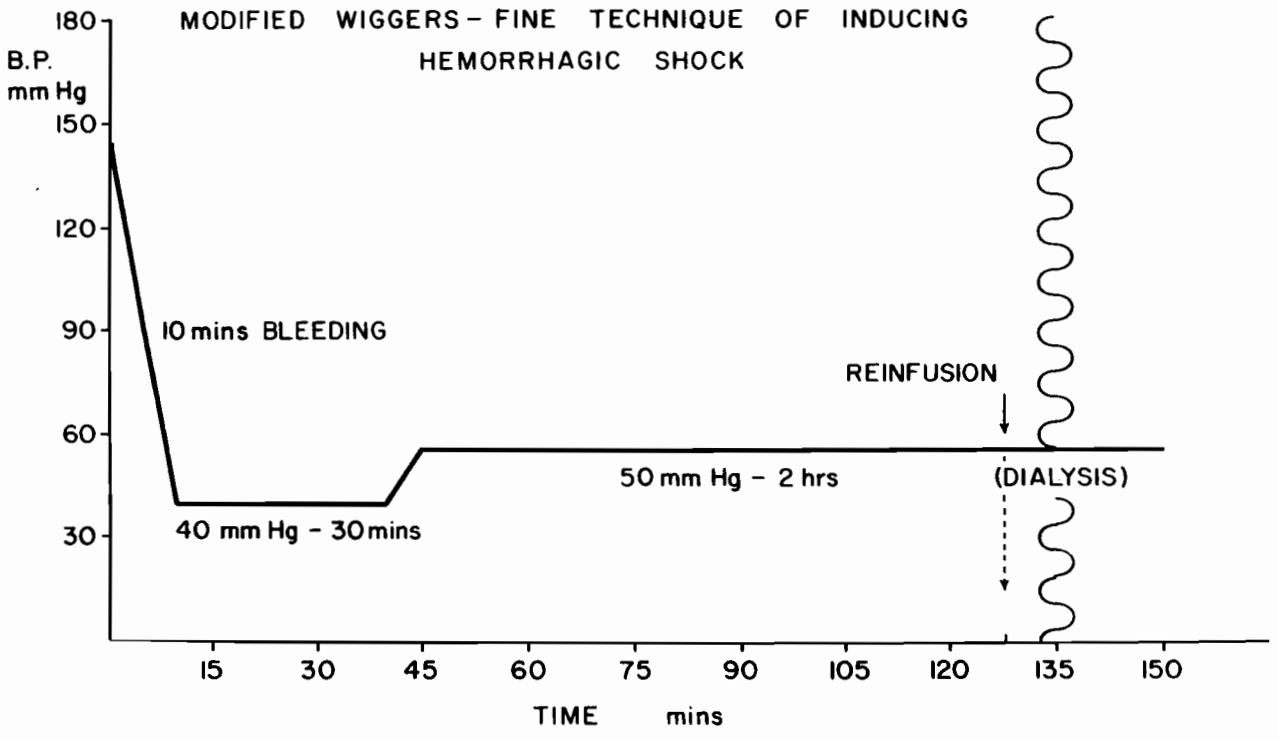


Fig. 3.--This diagram illustrates Wiggers-Fine Technique used in one series for production of haemorrhagic shock. The dog is bled into the reservoir for 10 minutes, till the blood pressure is down to 40 mm Hg. It is kept at this level for 30 minutes. At the end of 30 minutes, the reservoir is elevated, so that blood pressure reaches a level of 50 mm Hg. This level is maintained for 2 hours before reinfusion.

The tube connecting the blood reservoir with the T tubing connector is made of polyvynil material and has a bore of 8 cm in diameter. It measured 4½ yards long and thus enabled the reservoir to be elevated and lowered accordingly. A special adjustable intravenous pole for hanging the blood reservoir was used. This enabled the operator to adjust the height of the blood reservoir. Blood samples were usually collected from the left femoral artery.

In order to bring the dogs to irreversible shock, the modified Wiggers-Fine Technique was employed (Wiggers, 1950), (Fine, 1954). This method consists of bleeding the dog into a reservoir for ten minutes to bring the blood pressure to 40 mm Hg for thirty minutes. (Fig. 3) Blood pressure is maintained there by lowering or elevating the reservoir, as the case may be. After thirty minutes, the mean blood pressure is elevated to 50 mm Hg and kept there for two hours. At the end of the two hours, the blood is reinfused into the dog by means of a syringe intraarterially and then if the dog is to be dialysed, dialysis begins and is carried on for one hour.

Whenever blood samples were collected, they were drawn at 0 min., 30 min., 90 min., 150 min., 210 min., and 270 min. (See Table 4)

b) Endotoxin Shock

In this form of experimental shock, 3 mg/kg endotoxin was given intravenously for a period of one to five minutes. For the first thirty minutes, all vital signs were recorded every five minutes in both control and experimental dogs. This was done in order to avoid the possibility of missing the bradycardio-hypotensive period, which

usually occurred within five to thirty minutes after endotoxin injection. When this crucial period was over, the vital signs were recorded every ten minutes.

Blood samples for chemistries and electrolytes were collected in the same manner described above.

In both haemorrhagic and endotoxin shock, the weight of the experimental animal on the scale was determined every fifteen minutes during the course of the experiment. Weight determinations were useful. They served as a guide together with blood pressure and flow rates in replacement of fluid lost by the dog during the shock and hemodialysis periods.

Each dog received 4 mg/kg of protamine intravenously before it was sutured and taken to the recovery room.

5. PRINCIPLE OF THE ARTIFICIAL KIDNEY

This implies an exchange of two solutes through a semipermeable membrane - the blood on one side of a cellulose membrane and the rinsing (dialysing fluid) fluid on the other. (Figure 4) Diffusible substances of small molecular size, such as urea, creatinine, uric acid and phosphate freely traverse the membrane. Plasma proteins, protein-bound substances and viruses are held back.

Substances with smaller molecular weight are removed from the blood, if the volume of the rinsing fluid is large and if their concentration is greater in the blood than in the rinsing fluid. Electrolytes can pass through the membrane, guided by differences in concentration between those in the blood plasma and the electrolytes in the rinsing fluid. In this way, plasma electrolytes concentration

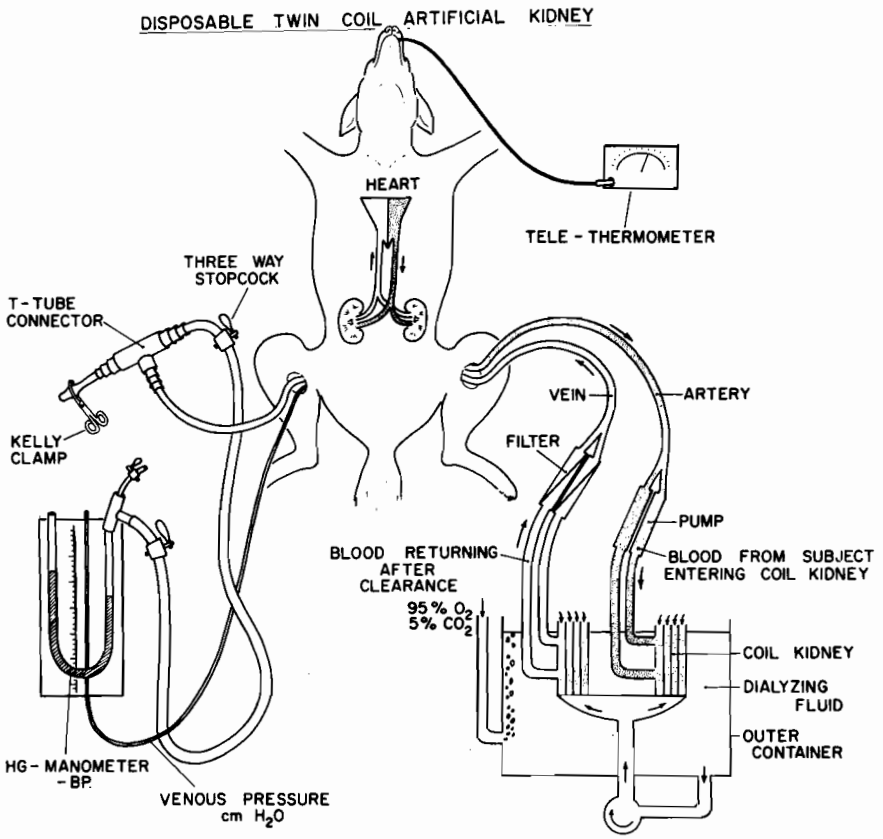


Fig. 4.--This diagram illustrates the principle and apparatus involved in the use of Kolff kidney for haemodialysis. The outer chamber, or tank, the dialyzing fluid, the inner container with the disposable coil kidney are shown on the right hand corner of the picture. The direction of the flow of blood during dialysis is shown by arrows.

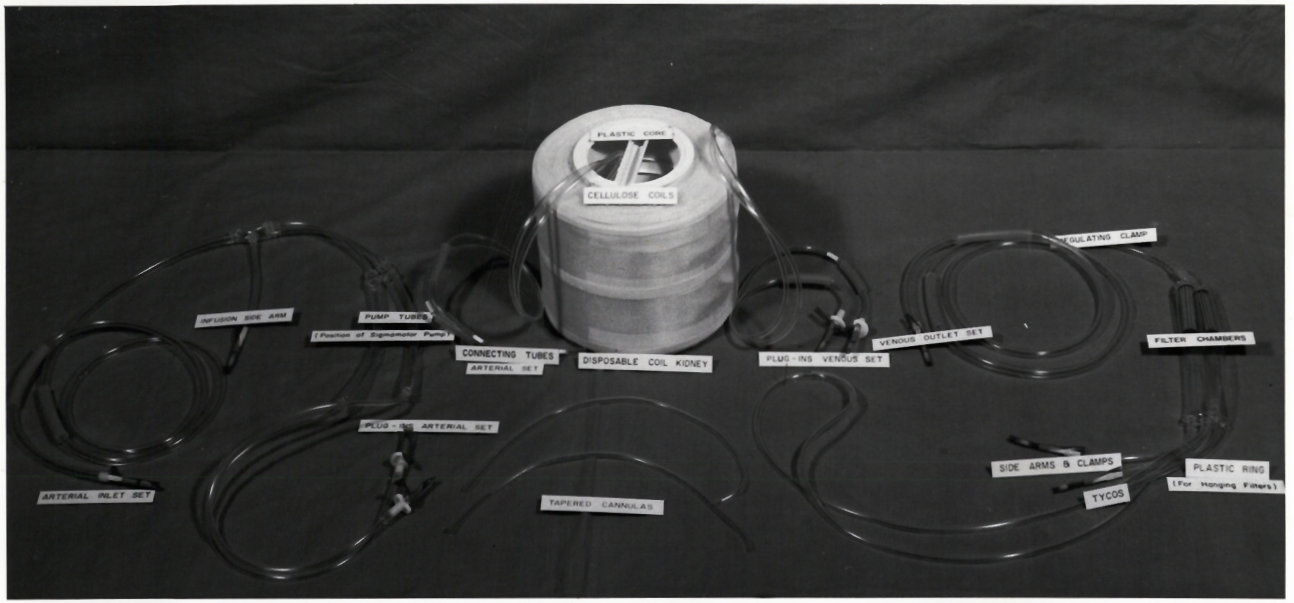
can be controlled. Dialysis can correct acidosis, hyperpotassemia or hypopotassemia within a few hours (Kolff, 1956). Acidosis in shock causes resistance of vessels to sympathomimetic drugs (Burget and Visscher, 1927). Sodium content can be adjusted to any predetermined level. Histamine and catecholamines are postulated to play an important role in the irreversibility of shock (Schayer et al, 1960a, 1960b), (Hinshaw, 1958), (Wiggers, 1950), (Harkins, 1926, 1941). Since these substances have small molecular weight, it is possible that they are dialysable. The molecular weight of histamine is 111, epinephrine 185 and that of norepinephrine is 169. Harmful bacterial products liberated during bacteremic shock may also be dialysable.

The rinsing fluid generally approaches the composition of normal plasma. The blood is usually drawn from the femoral artery and after it has been 'purified' by dialysis, it is returned to the femoral vein.

6. DESCRIPTION OF THE DISPOSABLE KIDNEY COIL

This disposable kidney coil is produced by Travenol Laboratories Inc. It is based on the kidney coil developed by William J. Kolff, of the Cleveland Clinic, Ohio (Kolff, 1956a, 1956b, 1957). The coil consists of two cellulose tubings enveloped in fiberglass screens or mesh. (Photograph 3) The fiberglass screens allow expansion of the cellulose tubes to a controlled maximum in diameter. The layers of the screens and tubing are sewn in a large roll, which is wrapped around the central cylinder. It is of interest to note that

PHOTOGRAPH III



This is the disposable Kolff kidney coil with all the tub-connections that are used during dialysis. The arterial set is on the left, while the venous one is on the right. In the centre are two tapered cannulas, which fit into the lumen of an artery, according to the size of its caliber.

when this method of dialysis was first introduced, an old fruit can was used as a central core (Kolff, 1956). There are two lengths of cellulose tubing in parallel arrangement, each measuring approximately 10.75 meters long, which is equivalent to a dialysing area of 19,000 sq. cm. This parallel arrangement makes it a 'twin' coil. Cellulose tubing has a flat diameter of 4.5 cm and the pore size of 24 angstrom. Its wall thickness is 1/1000 of an inch. The plastic central core around which both the fiberglass and the cellulose tubing are wrapped measures about 10 cm in diameter.

The patient's blood is circulated through the semipermeable cellulose membrane and leaves through the tubing to the venous side of the circuit, while the rinsing or dialysing fluid circulates on the outside. (Fig. 4) Rinsing fluid also circulates crosswise the fiberglass mesh. The rinsing fluid is pumped into the bottom of the can in which the coil is firmly fitted. The fluid flows up through the screening and over the top of the container and falls back into the tank.

Polyvinyl chloride tubings and nylon connecting pieces are used in this set-up. Polyvinyl tubings have the advantage of setting properties, so that less heparin than usual is used in the system.

Blood required for priming is approximately 1500 ml. At a flow rate of 200-400 ml of blood per minute, the average urea removed in the course of six hours is 60 - 90 grams. At this rate, urea clearance is about 140 ml per minute. The pressure required to pump the blood through the dialyser at this rate is approximately 160 mm Hg. The sygmamotor pump is so designed that it maintains the dialysing fluid flow at 3 - 5 liters per minute. At this rate of flow,

PHOTOGRAPH IV

DOG UNDERGOING HAEMODIALYSIS--The dog lying on the scale is undergoing dialysis. The tank with its plastic cover is seen near the wall. Inside the inner container is the kidney coil, held in place by a metal band. Beside the tank, on the right hand side, is a sygmamotor pump and switches for thermostat circulation and drainage of the dialysing fluid. A tycos anaeroid manometer and a bottle of saline connected to side arm are held up by an intravenous pole.

the ultrafiltrate is approximately 300 ml (2-6 pounds weight loss during dialysis). The outflow pressure could be increased to 250 mm Hg in which case there will be a loss of fluid of approximately 700 ml per hour or 6-8 pounds in one hour. The blood from the dog is pumped from the femoral artery into two tubes of the arterial set. These tubes pass through the sygmamotor pump so that substantially the same amount of blood in both tubes is pumped into the kidney coil.

After traversing the 90,000 sq. cm surface of the cellulose membrane, which is constantly being inundated by circulating rinsing fluid, blood leaves the coils through the venous end of the set (the periphery). Before the blood enters back into the dog through the femoral vein, it flows through two filter chambers of the venous set, where air bubbles are trapped and blood flows can be observed. (Photograph 3)

7. PERMANENT EQUIPMENT CONSISTS OF: (Photograph 4)

1. Sygmamotor pump

2. A 100 liter tank for rinsing fluid. The tank is made of stainless steel. It has a clear plastic cover or transparent lid, so as to prevent excessive steaming. There is a platform for the sygmamotor pump, a can or container for the dialysing unit (cellulose tubing and fiberglass screen). There is also a metal board on the side of the platform, where switches for drainage of the tank, circulation of the rinsing fluid, and thermostat are found. The tank has large inflow and outflow pipes for quick changing of rinsing fluid.

8. ADDITIONAL EQUIPMENT

Some of this equipment is needed during dialysis: 8 Kelly clamps, 20cc syringe and 'tapered' cannulae especially suited for dialysis tubing connections.

9. RINSING OR DIALYSING FLUID

The rinsing tank contains 100 liters of fluid. The temperature of this tank is thermostatically controlled by an electric heater, and kept at 37° - 39°C. (100° - 102°F.)

The dialysing fluid contains sodium chloride, sodium bicarbonate, potassium chloride, calcium chloride, magnesium chloride, glucose and lactic acid in concentrations shown in Table 1.

In clinical practice, to maintain the pH at 7.4 during dialysis, 90% O_2 with CO_2 is bubbled through the rinsing fluid. This method, besides maintaining a stable pH, has the advantage of oxygenating the blood during dialysis.

10. ASSEMBLING THE DIALYSING UNIT

The coil unit is removed from the plastic bag and firmly fastened into the inside container can. A flat steel belt is slid and fastened over the top of the coil to keep it in the can during dialysis. The tubes for the inflow and outflow are found in the hollow space of the central core. The arterial tubes have clear vinyl plastic ends with cotton plugs, while the venous tubings are attached to the periphery of the coil and terminate in 'male' connectors. A yellow band is attached to corresponding inflow and outflow tubes.

TABLE 1

COMPOSITION OF DIALYSING FLUID

COMPONENTS	G/100L	Na^+	K^+	Ca	Mg^{++}	Cl^-	HCO_3^-	GLUCOSE
NaCl	585	100				100		
$NaHCO_3$	252	30					30	
KCl	22.4		3			3		
$CaCl_2$	29.4			4		4		
$MgCl_2$	15.0				3	3		200
Total in meq/l		130	3	4	3	110	30	

Lactic Acid - 20 cc to adjust pH to approximately 7.4

The cotton plugs can be either removed by a small hemostat, or part of the plastic ends can be cut off by a sharp straight scissors. The green protectors from the plug-ins (male) on the arterial side are removed. The plug-ins are inserted into the 'female' cut-ends of the inflow tubes. Kinks in the tubings should be avoided at all cost.

The venous connecting tubes are usually sealed together. They require to be cut in the centre. The green covers on the plug-ins of the outflow tubes are removed and the plug-ins similarly inserted into the outflow tubes of the coil unit.

These connections may seem confusing at first, but closer examination will show that both the inflow and outflow connections have male and female tubing connections which cannot be easily confused.

The tubing connections should be wired to make doubly sure that an air leak does not occur. A tycos anaeroid manometer is tightly fitted into one of the side arms on the filter, especially designed for measuring pressure from the coil. The other two side arms on each filter chamber are clamped with Kelly forceps. (Photograph 4)

On the venous set, there is a plastic ring, sometimes green in colour, which is used for hanging the filter chambers in an upright position, with the filter chambers at the bottom and the tycos above. Clamps are placed on the arterial inlet tubing, the venous tubing and the infusion side arm, which is connected with an intravenous tubing to a bottle of 1000 cc 5% D/Normal Saline.

The rinsing tank is filled with 100 liters of warm tap water

(37°C.) which is circulated through the screening of the coil unit for about ten minutes. This water is removed from the tank and then filled with dialysing (rinsing) fluid.

11. PREPARATION OF THE RINSING FLUID

The NaCl, $NaHCO_3$ and KCL are poured into a separate container of hot water and thoroughly mixed till the salts are completely dissolved. Meanwhile the tank is being filled with warm tap water. When the water fills the tank to about 80 liters, the taps are closed.

Two hundred grams (200gm) of sugar is poured into the dialysing fluid tank. Then $CaCl_2$ and $MgCl_2$ are mixed in their own separate bucket and completely dissolved before they can be added to the rinsing solution. After addition of 20 cc of lactic acid to the rinsing solution, the solution of $MgCl_2$ and $CaCl_2$ is added to the tank. Lactic acid, besides adjusting the pH, also prevents precipitation of calcium into the bottom of the tank. The tank is filled to 100 liter mark and the temperature kept between 37° and 39°C.

As a final check for the isotonicity of the rinsing fluid, 5 cc of arterial blood is mixed with 5 cc of the rinsing fluid and spun at 200 rev/min. for fifteen minutes. If hemolysis does not occur, the solution is isotonic and satisfactory for use. If, however, hemolysis occurs, the solution should be discarded and a fresh solution should be made up.

In clinical practice, if the object of dialysis is hyperpotassemia, then one half of the usual potassium concentration is used in the dialysing fluid. It is also important to hydrate a dehydrated

patient before dialysis is done because of considerable ultrafiltrate that is removed in one hour.

In cases where dialysis is carried out for six hours, the rinsing fluid should be changed at least once.

It is also important to note that dialysing fluid must be prepared immediately prior to dialysis to prevent $Ca^{\bullet}$ and $Mg^{\bullet}$ from precipitating upon standing. Preparation of the solution of $MgCl_2$ and $CaCl_2$ in water with the temperature above 43°C (110°F) may also lead to the precipitation of $Ca^{\bullet}$ and $Mg^{\bullet}$ ions.

12. TESTING THE KIDNEY COIL

The circulating pump is switched on and observations are made on how the dialysing fluid circulates through the screen of the coil unit. The rinsing fluid circulates upwards and crosswise through the polygrass mesh. Care is taken that no testing of the kidney is done before the coil is wet.

The pump tubes of the arterial set are placed in the sigmamotor pump, with the plastic circular stops just outside the pump housing on the inflow side of the pump. The pump tubes must be properly placed in the holes of the pump housing or else they will not function properly. The tubing should not be pinched when the sigmamotor plates are closed.

The whole set is re-examined before priming the machine with 5% D/Normal Saline. Having made sure that the unit is airtight and that all equipment to be used during dialysis is nearby, the Kelly clamps on the side arm and on the arterial inlet are released

and the solution allowed to fill the inlet tubing by gravity. The Kelly clamp is put back when the inlet tubing is filled with 5% D/Normal Saline. In filling this tube, all bubbles of air must be expelled.

A special regulating screw clamp is snugly applied on the venous side of the tubing. This clamp is essential for the regulation of ultrafiltration pressure in the coil.

The sigmamotor pump is started very slowly, observing whether the pump tubings are receiving the same pumping strength of the sigmamotor machine. Oftentimes air is trapped in the pump tubes of the arterial set. These bubbles of air are easily removed by bending the outflow ends upwards. A slight downward bend of the plastic stops also helps in the removal of air from the pump tubes.

When this is done, 100 ml of heparinized blood from a donor dog is pumped through the unit. This is followed by 5% D/Normal Saline. Leaks can be detected by the appearance of blood in the dialysing or rinsing fluid. The sigmamotor pump should always be stopped before bottles of either blood or saline are empty to avoid introducing air into the system.

If no leak is noticed, running of the sygmamotor pump is continued, gradually increasing the speed till the flow rate reaches 200-400 ml of saline per minute. At this rate, the speed control plate of the pump is clamped with a Kelly forceps. The flow rate is determined by timing how long a 500 ml bottle of 5% D/Normal Saline takes to empty into the circuit at a horizontal flow in both filter chambers.

Another method used for measuring flow rate is to collect outflow from the kidney into a graduated one liter flask. After the circuit is primed with 5% D/Normal Saline, it is again primed with 1500 cc of fresh blood.

Every dialysis requires one or two donor dogs, which are weighed, heparinized, cannulated into the femoral artery and bled into a sterile one-liter empty bottle. The blood is kept in the refrigerator until the time it is needed for priming the kidney.

When the kidney is primed with blood and there are no air bubbles anywhere in the tubes, the arterial outflow tubing is connected to the femoral artery of the dog through the tapered cannula. The venous inlet is similarly connected to the venous cannula. Meanwhile, the clamp for adjusting the flow and the ultrafiltrate pressure is adjusted to maintain a pressure of 160-180 mm Hg. The Kelly clamps on the tapered cannulae are not released until another check is done on the circuit and its connections. Then the chief operator gives the sign to his assistant (if he has one) and the two Kelly clamps are removed simultaneously with the switching on of the sygmamotor pump.

The chief operator concentrates on the proper working of the whole machine, while the assistant keeps a constant check on the vital signs of the dog. Replacement of fluid lost by the dog is determined by the amount of weight the dog loses during dialysis, the blood pressure, the turgor and elasticity of the dog's skin. Hematocrit % is also helpful in determining the amount of fluid lost by the dog during ultrafiltration.

Dialysis was carried on for the whole hour in our experiments. Once dialysis starts, it should not be stopped to avoid settling out of erythrocytes in the dialyser.

Occasionally during the priming of the kidney machine with blood, the level of blood in one filter chamber may be higher than in the other and it may obstruct vision of flow. In order to overcome this inconvenience, a release of the Kelly clamp on the side arm to bleed the air, will bring the blood to the desired level. In cases where the level of the blood column is too high in the filters, forcing 10-20 cc of air into the chamber will reduce the level.

During the whole period of dialysis, a special attempt is made to maintain a constant volume of blood in the machine and thus avoid change in the blood volume of the dog-patient. The visibility of the rinsing fluid is important so that if there is a leak in the dialysing membrane, it will be seen immediately.

As blood is forced through the 19,000 sq. cm of cellophane surface, a hydrostatis pressure difference across the membrane is created so that ultrafiltration as well as dialysis take place. The ultrafiltration pressure of 250 mm Hg is preferable on the blood side than on the rinsing fluid. The reasons being that besides its efficiency in dialysing out harmful substances into the bath, in case of a leakage, blood coming into the bath can be easily seen, whereas rinsing fluid going into the blood is difficult to see. This may lead to over hydration of the dog and since the bath is not sterile, bacteria may be

introduced into the animal (where aseptic technique is an important factor). Ultrafiltration also has the advantage of counteracting the colloid osmotic forces of blood plasma that operate in the opposite direction.

13. PRECAUTIONS DURING DIALYSIS

1. At flow rate of 200-300 ml of blood per minute, a dog can bleed to death in a few minutes, if a broken tube or leak is not noticed. This stresses the necessity for the operator to keep a constant eye on both the machine and the patient.

2. Occasionally the arterial wall may be sucked into the opening of the catheter, a vacuum created and air sucked through some weak opening into the tubes. Therefore, care is always taken to see that no vacuum is formed.

3. The wall of the vein may also be sucked into the open end of the tapered cannula and may lead to obstruction of flow and if not corrected, to the bursting of the kidney coil. Perforation of a vein with the outflow catheter may lead to enormous hematomas.

4. Temperature of rinsing fluid should be watched carefully at all times.

5. Occasionally, if the pump tubes are not properly positioned in the sygmamotor pump, a perforation may occur and thus a leak is created in the system.

6. Dialysing (rinsing) fluid must be isotonic before starting the circulating pump to prevent hemolysis of the blood in the cellulose.

14. METHOD OF DETERMINATION OF BLOOD CHEMISTRIES

A) Lactic Acid (Barker, S. B. and Summerson, N.H., 1941)

Principle--Lactic acid is converted into acetaldehyde by treatment with concentrated sulfuric acid. The acetaldehyde is determined by its colour reaction with p. hydroxydiphenyl in the present of cupric ions. The colour is read in a photoelectric colourimeter with a filter having a peak transmission at 560 mμ.

Reagents:

1. 20% $CuSO_4$ .5 H_2O (200 grs. $CuSO_4$ to 1,000 ml H_2O)
2. 4% $CuSO_4$ .5 H_2O (take 100 ml of the above 20% solution and dilute to 500 ml)
3. 11% Trichloracetic Acid
4. Conc. Sulfuric Acid
5. 1.5% p-hydroxydiphenyl in 3% NaOH

Lactate std. 5 mg% in 0.25% Benzoic Acid

Make up from 5% std. solution and dilute 1:100

Use the following way:

0.1 ml to 4.5 ml of water (total volume) 2.5mg%

0.2 ml to 4.5 ml of water (total volume) 5 mg%

0.3 ml to 4.5 ml of water (total volume) 7.5mg%

0.4 ml to 4.5 ml of water (total volume) 10 mg%

0.5 ml to 4.5 ml of water (total volume) 12.5mg%

To prepare 5% lactic acid std. solution

If Lithium Lactate is used: Lithium Lactate M.W. = 96.012 gr

Lactate = 89.072 gr. per mole.

To prepare a solution containing 5 gr. of lactate in 100 ml, or 5 gr.% solution with regard to lactate

$x = 5 \times 96.012 = 5.39$ gr/liter, or 89.072

Weigh out 0.539 gr. of Li lactate and dissolve it in 0.25% Benzoic Acid and make up to100 ml in vol. flask.

Working standard (5 mg%)

Take 1 ml of the above standard solution and dilute to 100 ml with 0.25% Benzoic Acid.

Procedure in the Determination of Lactic Acid

1. Treatment of the protein free sample by copper sulfate calcium hydroxide procedure of Van Slyke to remove interfering materials, such as glucose.
2. Conversion of the lactic acid to acetaldehyde by controlled oxidation with sulfuric acid.
3. Colour development by treatment in concentrated acid solution with p. hydroxydiphenyl in the presence of added cupric ions, which enhance the colour development.

Reagents:

1. 11% Trichloracetic Acid. This should be freshly prepared every two weeks and stored in the refrigerator.
2. 20% Copper Sulfate Solution ($CuSO_4 \cdot 5 H_2O$)

3. Calcium Hydroxide (CaOH)
4. Concentrated Sulfuric Acid - Reagent Grade s.g.1.84
5. 4% Copper Sulfate Solution
6. 1.5% p. hydnoxydiphenyl in 3% Sodium Hydroxyde (NaOH)
7. Lactate Standard - 5 mg% Keep in refrigerator in 0.25% of Benzoic Acid.

Caution:

This method is extremely sensitive. Since all cells produce lactic acid, there is enough on the fingers to destroy the accuracy of the test. Therefore, it is advisable not to mix tubes by inverting with the centrifuge tube or touching the tips of the pipettes.

Method:

Take 2 cc of whole blood and add dropwise to 8cc of cold 11% T.C.A. Cover with paraffin paper, shake and centrifuge for five minutes. The supernatant fluid is stored in the deep freeze.

1. Place 1 cc of supernatant fluid in a centrifuge tube.
2. Add 3.5 cc of distilled water
3. Add 0.5 cc of 20% copper sulfate solution.
4. Add approximately 0.5 g calcium hydroxide (a little on the end of a spatula). Cover with paraffin paper and shake well. The solution in the tube should turn bright blue and if it is pale, add more calcium hydroxide.
5. A blank tube, containing water in place of supernatant, and a standard should be set up similarly.
6. Stand for at least thirty minutes, shaking occasionally and then centrifuge for thirty minutes.

7. A 1 cc aliquot of the supernatant is layered carefully on 6 cc of conc. sulfuric acid in a pyrex tube in an ice bath. Aliquots should be taken in duplicate.
8. Shake tubes quickly to mix under ice water. Localized heating due to uneven mixing will cause the oxidation of acetaldehyde to acetic acid.
9. Heat the tubes for five minutes in boiling water.
10. Cool to 30° C and add one drop of 4% copper sulfate solution. To this is added 0.1 cc diphenyl reagent. A white precipitate will form.
11. Mix carefully and stand at 28-30°C for thirty minutes with occasional shaking.
12. Heat in boiling water bath for ninety seconds.
13. Cool, transfer to colourimeter tubes, and read percent transmission on Coleman Junior at wavelength 560.

Standard Curve

0.0, 0.1, 0.2, 0.4, 0.6 cc lactate standard (5mg%) is pipetted into centrifuge tubes and water is added to make the volume up to 4.5 cc. Proceed as above in stages. These amounts correspond to 0.0, 2.5mg%, 5mg% and 15mg% lactate in whole blood and a straight line is obtained if the percent transmission is plotted versus concentration in mg% on semi-log paper.

B) pCO_2, pH and HCO_3 Determination

Principle in the determination of blood chemistries (Guyton, 1961), (Wright, 1961), (Davenport, 1961)--The Astrup (1955, 1956, 1957, 1958) method is one of the best and quickest methods available in the quick analysis of any acid-balance in the blood.

When blood comes in contact with carbon dioxide of specific partial pressure, it will take up or give off CO_2 until a state of equilibrium is reached. It was Peters and Van Slyke (1932) who first worked on the absorption curve for carbon dioxide in the blood.

Increase of partial pressure of carbon dioxide leads to a concomittant increase in the absorption of carbon dioxide and vice versa - CO_2 will be expelled if there is decrease in partial pressure.

Blood will take up CO_2 in the capillaries where the partial pressure is low under normal circumstances. The importance of this function of the blood cannot be overestimated.

Henry's law states "The content of gas physically dissolved in a liquid is proportional to the partial pressure of the gas above the liquid." This same law applies to blood and plasma with regard to CO_2. Changes brought about by chemical means are of more importance than the actual physical absorption or separation of CO_2.

The ability of the hydroxyl ion to combine with CO_2 to form a bicarbonate or vice versa is the most important chemical reaction in the

process of CO_2 exchange in the blood.

$$OH^- \uparrow CO_2 \qquad HCO_3$$

In accordance with the law of mass action, the relation between the concentrations of the components involved in this scheme is given by the following equation:

$$C_{OH} \, C_{CO_2} = K \cdot C_{HCO3}^-$$

Looking at this equation, it is evident that

1. An increase in CO_2 partial pressure or higher CO_2 partial pressure must also lead to an increase of HCO_3. In order to produce HCO_3, OH^- is also required and thus leads to the decrease of C_{OH^-}.

2. Similarly, a decrease of CO_2 (lower partial pressure) leads to a decrease in HCO_3^-; but when HCO_3^- dissociates, OH^- is produced and hence OH^- concentration will rise correspondingly.

3. This decrease of OH^- brought about by an increase of CO_2 is counteracted by the addition of OH^- ions, the ability of converting CO_2 into HCO_3^- will be improved correspondingly.

4. Knowing the concentration of OH^- ions and the partial pressure of CO_2, the concentration of HCO_3^- ions can be calculated.

Since the pH of an aqueous solution is specific also for the concentration of OH^-, according to the temperature, it is sufficient to know the pH of the blood sample and the partial pressure of CO_2 to be able to calculate the concentration of bicarbonate.

According to the Astrup Method, the partial pressure of CO_2 can only be determined indirectly. Astrup's Method allows the sample to equilibrate with a gas mixture whose CO_2 partial pressure has been predetermined. When the equilibrium is attained, the pH is determined

and then bicarbonate content is calculated under the conditions given below.

The plasma relationship between pH, $C_{HCO_3^-}$ and C_{CO_2} are covered by the Henderson-Hasselbalch equation:

$$pH = g.110 + \log \frac{(HCO_3^-)}{(CO_2 + H_2CO_3)}$$

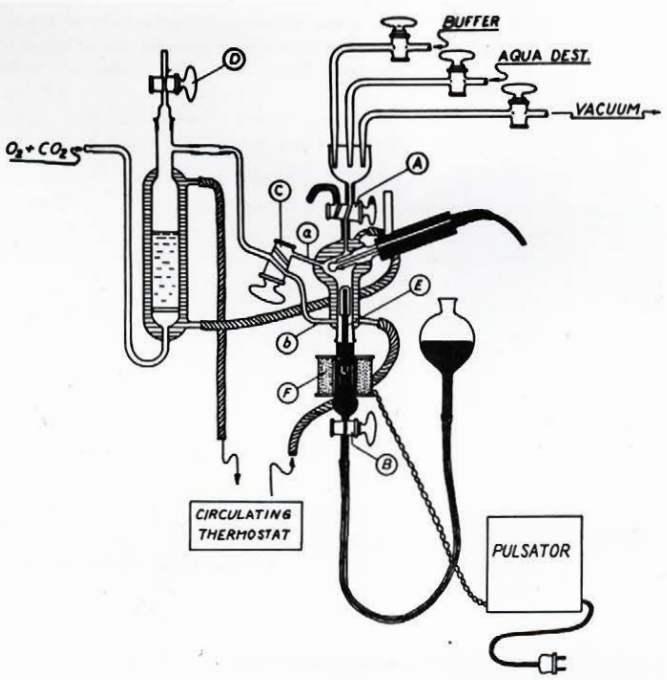
$$pH - 6.110 - \log \frac{(HCO_3^-)}{pCO_2 . 0.03}$$

In this equation, (HCO_3^-) means the bicarbonate concentration in millimols per liter and pCO_2 is the partial pressure of CO_2 in mm Hg.

The bicarbonate concentration at a pCO_2 of 40 mm Hg is called 'standard bicarbonate'. The standard bicarbonate then "Is the concentration of bicarbonate in the plasma, which is separated from the cells with the hemoglobin completely oxygenated, at a pCO_2 of 40 mm Hg and at a temperature of 38° C." (Astrup, 1958). The normal 'standard bicarbonate' in humans is 23± 2 meq/l. In dogs it ranges between 17-25 meq/l.

Astrup has achieved to establish the correlation between pCO_2 and pH for plasma at varying composition. A resulting set of curves, serves the purpose of finding the actual pCO_2 of blood at the moment of sampling.

The Van Slyke method of volumetric and manometric determination of total CO_2 is usually not followed by a pH determination, which is an important omission. The Astrup Method has bridged this important gap.



Arrangement for equilibrating plasma with gas mixtures of known compositions. For detailed explanation see text.

Fig. 5.--THE ASTRUP APPARATUS

Astrup Procedure

a) Apparatus

The Astrup apparatus (Fig. 5) consists of a chamber with two sides, one at the top, A, and the other at the bottom, b. A two way stop-cock, C, connects both side tubes with a moistening chamber, which contains distilled water enveloped by a water jacket kept at 38°C. A mixture of O_2 and CO_2 passing the moistening chamber is saturated with water vapor at the temperature of the water in the water jacket. From moistening the chamber, the gas mixture can be led to the electrode chamber through one of the side tubes and/or it can be allowed to escape through cock D, when two way cock C is closed. The chamber is provided with an agitator, E, operated by a coil, F, which is fed from a pulsator. The agitator moves up and down at a frequency of about three cycles per second. The downward movement is brought about by the attraction of the coil and the upward movement by the buoyancy.

A circulating thermostat (Photograph 5) and a pH meter are placed on either side of the Astrup apparatus. A cylinder of 10% CO_2 is kept in a horizontal position to "avoid decrease in the CO_2 concentration of the outflowing gas during use as the higher specific gravity of CO_2 relative to O_2 causes the CO_2 concentration in the lower part of the cylinder to decrease when standing upright." (Astrup, 1957)

b) Standard Buffer Solution

This solution is used for adjustment of the pH meter. The preparation consists of an M/15 phosphate, prepared from 200 M/15 primary

PHOTOGRAPH V

THE ASTRUP APPARATUS--This is the Astrup apparatus described in Fig. 4. The pH meter can be seen on the right hand side of the picture, close to the apparatus and the circulating thermostat is similarly situated on the left hand side of the apparatus.

potassium phosphate (9.078g dry KH_2PO_4 p.a. (Merck) dissolved in one liter of redistilled water) and 800 ml M/15 secondary sodium phosphate (11.8667 g Na_2HPO_4, $2H_2O$ p.a. (Merck) dissolved in one liter of redistilled water). The pH of this solution is taken to be 7.360 at 38°C. The buffer is best stored in a pyrex bottle provided with a sodalime tube.

c) Prodadure

It is beyond the scope of this brief description to go into the details of the Astrup procedure.

Arterial blood is anaerobically collected into a 20 cc syringe as described above. Half the sample is centrifuged under liquid paraffin. Equilibration of the plasma with O_2-CO_2 mixture is made. The gas mixture enters the measuring chamber through the upper side tube (a) and escapes through cock A. By means of the mercury, the plasma level is lowered so that the agitator is above the surface of the plasma each time it reaches its top position and a fresh film of plasma continuously comes into contact with the gas. The equilibration generally takes six to ten minutes. When this has been completed, cock C is closed and the plasma level is elevated to surround the electrode. The pH is then measured after two minutes.

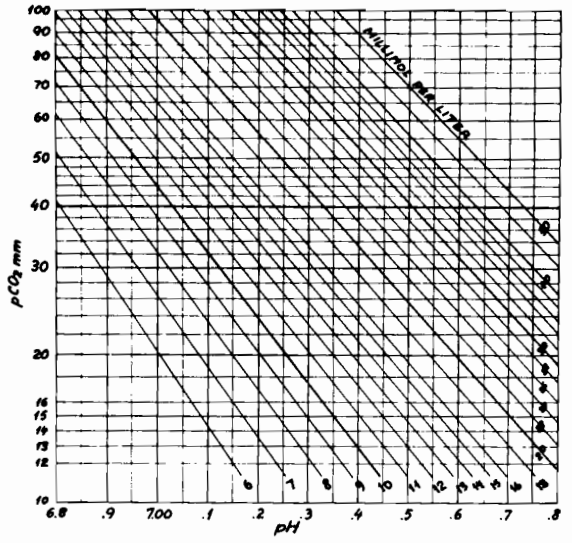
The pCO_2 in aqueous solution is calculated from the carbon dioxide concentration, measured as follows:

$$pCO_2 = \frac{(B-W \times \text{percent } CO_2}{100}$$

B = Barometric pressure in mm Hg

W = Vapour pressure of water at 38° C (= 50 mm Hg)

After the anaerobic introduction of the sample in the electrode chamber, the actual pH is measured. Then the plasma is equilibrated



Relation between pH and pCO_2 at bicarbonate concentrations in plasma of normal protein concentration. The figures at the lines signify bicarbonate concentrations measured in mMol/L.

Fig. 6

with an O_2-CO_2 mixture of known pCO_2 of approximately 40 mm Hg, the pH is measured again and the position of the pH-pCO_2 curve is found by using the diagram on Figure 6.

Finally, the pCO_2 is determined by means of the curve and the actual pH. Knowing the actual pCO_2 and the actual pH of the plasma sample, the total content of CO_2 can be calculated by means of the Henderson-Hasselbalch equation:

$$pH = pK_1 + \log \frac{(HCO_3)}{(CO_2 + H_2CO_3)}$$

The actual bicarbonate concentration expressed in mM/l can be calculated by inserting in this equation the pH value measured at 38°C, taking pK_1 to be 6.110 and replacing (pCO_2 + H_2CO_3) expressed in mM/l, by pCO_2 in mm Hg multiplied by 0.03. In short, the bicarbonate concentration and that of the physically dissolved CO_2 gives the total CO_2.

15. METHOD OF DETERMINATION OF SERUM ELECTROLYTES

A. Materials Used:

2 ml pipette, 100 ml volumetric flask, double distilled water, oxygen tank, propane tank and galvanometer scale. (Photograph 6)

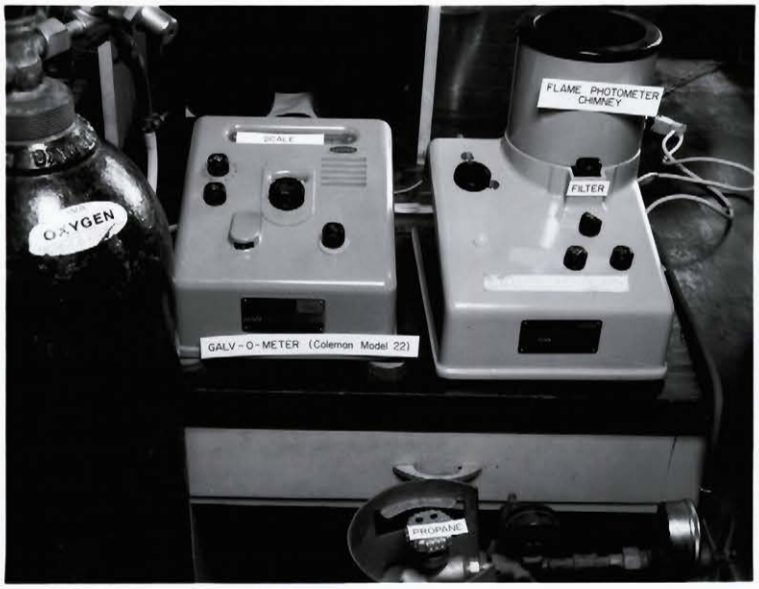
B. Method

1. Sodium--The method used for serum Na^+ estimation in our experiments is based on the original method adopted by Barnes: (Valley, 1962)

a) Pipette 0.5 ml of serum or plasma into a 100 ml volumetric flask.

b) Fill the flask with water to within 5 ml of the

PHOTOGRAPH VI



COLEMAN MODEL 22 FLAME PHOTOMETER.--This is used for determination of serum potassium and sodium. The propane tank is seen at the bottom of the photometer chimney and filter. The oxygen tank is on the left side of the photometer, while the reading scale is at the very top of the machine.

mark and then add 2 ml of 1% Sterox S.E. to make up to the volume with water.

c) Adjust machine with oxygen at 10.5 lbs. and propane at 5 lbs.

d) Set blank back to zero and stronger working standard at 150 meq/l on the galvanometer scale.

e) When the machine is stable, read the sample of serum directly from the scale.

f) When working, a beaker of the blank solution should be kept separate and used only for flushing through the atomizer.

Principle--In the excitation of electrones, each absorbs energy and releases it in light of specific wave length and the amount of light emitted is measured by photoelectric tubes.

Reagents

a) 1% Sterox S. E. in water

b) Na^+ Standard 0.75 meq/l Na^+ and 0.02% Sterox S.E. -- equivalent of 150 meq/l Na^+ in diluted serum or plasma.

c) 0.5 meq/l Na^+ and 0.02% Sterox S.E. -- equivalent of meq/l Na^+ in diluted serum or plasma.

d) Blank and cleaning reagent 0.02% Sterox S.E.

Caution--All reagents mentioned in Na^+ and K^+ techniques should be stored in pyrex or polythene bottles. Whenever water is mentioned, double distilled water is meant.

2. Potassium

a) Pipette 0.5 ml of serum or plasma into a 25 ml volumetric flask. Fill to within 10 ml of mark with water.

b) Pipette 5 ml of reagent 2 into the flask and make up the volume with water.

c) Adjust the flame photometer with 10.5 lbs. of O_2 and 5 lbs. of propane.

d) Set reagent 3 to zero and reagent 1 to 5 meq/l on the scale when the machine is stable.

e) Read the sample of serum or plasma directly from the scale. Between each reading of serum or plasma, flush the atomizer with reagent 4.

Reagents

a) K^+ Standard - 0.1 meq/l potassium, 25 meq/l sodium and 0.02% Sterox S.E.

b) 125 meq/l Sodium and 0.1% Sterox S.E.

c) Blank: 25 meq/l sodium and 0.02% Sterox S.E.

d) Cleaning reagent: 0.02% Sterox S.E.

3. Chloride

Method and Materials--This method is based on Folin-Wu:

a) To 0.2 ml of plasma add 1.8 ml of water.

b) Add 0.06 ml of the indicator and titrate with the mercuric nitrate with a microburette calibrated to 0.01 ml. One

ml should equal 100 drops. When filtration is done directly on plasma, the colour at first is salmon-red, changing to deep violet when the titration is begun, then becoming pale yellow or colourless. A sharp change to pale violet then, denotes the end point.

c) Carry out the titration on 2 ml of the standard chloride solution.

Principle--Plasma is titrated with a mercuric nitrate solution, using diphenylcarbazone as indicator, which gives a violet - blue complex with mercuric ions.

Mercuric chloride is formed and remains in solution, but it is so very slightly dissociated that sufficient mercuric ions to give this colour are only present when all the chloride is titrated and excess mercuric nitrate is added.

Reagents

a) Mercuric Nitrate solution, made by dissolving 3 grams of mercuric nitrate in a few hundred milliliters of water. The 20 ml of 2N. nitric acid is added to make up a litre of water. It is important to adhere to this formula strictly, otherwise the end point will not be sharp.

b) Diphenylcarbazone indicator. Dissolve 100 mg in 100 ml of 95% alcohol. Keep this solution in the dark in a refrigerator.

c) Standard chloride solution. Dissolve 585 mg NaCl, dried at 120°C in water and make up to one liter.

16. EXTRACTION AND BIOASSAY OF HISTAMINE

Principle

Guinea pig ileum is particularly sensitive to histamine and hence the contraction obtained and recorded on a rotating drum can be used for bioassay of unknown quantity of histamine in any extracts.

Procedure

The 'Bioassay Method' of C.F. Code (1956 Mayo Clinic) was used in our experiments.

1. Blood samples of 10 cc were taken at intervals of 2 secs., 10 secs., 30 secs., 1 minute, 2 minutes, 5 minutes, 10 minutes 1 hour, 2 hours, and 2½ hours.
2. The blood or a piece of tissue is weighed accurately on a balance.
3. Add 10 cc of 10% T.C.A. (Trichloroacetic Acid) and homogenize and centrifuge at 3,000 r.p.m. for fifteen minutes.
4. Take the supernatant fluid and pour it in a flask.
5. To the residue, add 5 cc of 5% T.C.A., mix and then centrifuge at 3,000 r.p.m. for fifteen minutes.
6. Pool with the first supernatant.
7. Extract, using air reflux and heat for 1½ hours. Extraction should be in flash evaporator using absolute alcohol 3x under pressure. The end product should be absolutely dry.
8. Dissolve in 10 cc tyroden solution and do the bioassay, using guinea pig's ileum and organ bath.

17. EXPERIMENTAL PROCEDURES ON DIFFERENT GROUPS OF DOGS

GROUP I: DIALYSIS OF NORMAL DOGS

a) Without Prophylactic Antibiotics--Five dogs were dialysed for one hour. After the completion of dialysis, the dogs' incisions were closed up with number I merselene sutures and taken to the recovery room. No prophylactic antibiotics were administered. Vital signs were recorded in the manner described above.

b) With Prophylactic Antibiotics--The five dogs in this group, after the end of the experiment were given 2 cc of Fortimycin intramuscularly. This was the only variable between these two groups of dogs.

GROUP II: ENDOTOXIN SHOCK

a) Endotoxin shock and early dialysis with old and new coils--Twenty-eight dogs were used in this group, fourteen experimental and fourteen controls. All the twenty-eight dogs were subjected to the same experimental procedure described above. Both groups of dogs received 3 mg/kg of endotoxin intravenously. In addition to the recording of vital signs, blood samples for chemistries, electrolytes and hematocrits were collected in ten experimental and ten control dogs. Dialysis was begun thirty to thirty-five minutes after the injection of endotoxin. No form of treatment was given to the control dogs. At the end of the experiment, prophylactic antibiotics, 2 cc of Fortimycin, was administered intramuscularly before the dogs were taken back to their cages.

b) Endotoxin Shock and Early Dialysis with New Coils Only--Ten dogs were used in this study. These dogs were dialysed thirty to thirty-five minutes after endotoxin administration. The important variable in this group, when compared with the above early dialysis, was the use of new coils only.

c) Endotoxin Shock and Late Dialysis with New and Old Coils--Fifteen dogs were employed in this group. The only difference between this group and the early dialysis is that, instead of dialysing these dogs thirty to thirty-five minutes after endotoxin injection, they were dialysed in three and a half to four hours after the administration of endotoxin. Electrolytes, chemistries and hematocrits were not determined.

d) Endotoxin Shock and Histamine--Six dogs were used in this group. After the usual infrainguinal ligament incision was made, and the femoral artery and veins well exposed, a polyethylene tube, 4 cm in diameter, was inserted into one of the femoral arteries. The catheter was pushed so high that its proximal tip was one inch above diaphragm. Specimens for whole blood and plasma histamine were taken at two seconds, ten seconds, thirty seconds, one minute, two minutes, one hour, two hours, and two and one half hours.

Plasma histamine levels were determined in one group of three dogs, while blood histamine levels were determined in the other three dogs.

For the extraction of histamine from these samples, the bioassay method of C.F. Code described above was used.

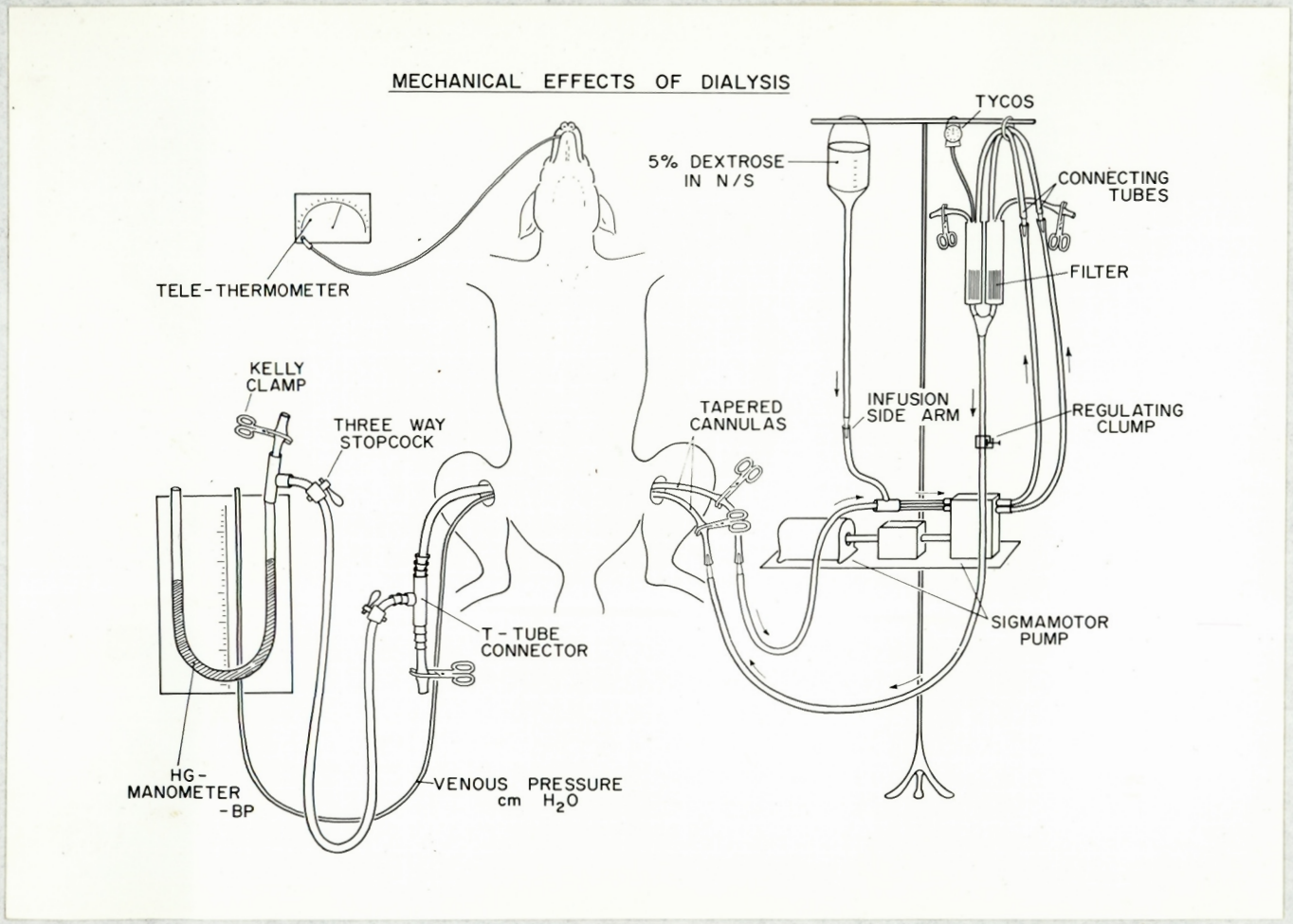


Fig. 7.--This diagram illustrates the set up of the apparatus used in 'Mechanical Effects of Dialysis'. It is noted that this set up is for all intents and purposes the same as Fig. 3 (Dialysis), except that in the former, the bath, the kidney coil and the dialysing fluid are absent - an important omission.

e) Endotoxin shock and Mechanical Effects of Dialysis--(Fig. 7) Ten dogs were employed in this group. The important difference between this group and the early and late dialysis groups is the absence of the kidney coil and the rinsing solution. This group is an important double control for the mechanical effects of dialysis during haemorrhagic and endotoxin shock. This is in effect an extracorporeal circulating system of hemodialysis. (Photograph 7)

The resistance to circulation was kept at a pressure of 100 mm Hg. Circulation was maintained for one hour. The weights of five dogs were continuously watched during the process of pumping. Blood chemistries, electrolytes and hematocrits were determined in five dogs.

f) Endotoxin, Morphine and Early Dialysis with Both New and Old Coils--This is the only group which did not receive nembutal. Ten dogs, five control and five experimental, were employed. Three milligrams per kilogram of body weight of morphine sulfate and .3 mg/kg of atropine were given intramuscularly one half hour before the endotoxin was administered intravenously. Samples for blood chemistries and electrolytes were not collected.

GROUP III: HAEMORRHAGIC SHOCK

a) Haemorrhagic Shock and Early Dialysis--There were ten experimental and ten control dogs used in this group. In order to shock the dogs, the modified Wiggers-Fine Technique was employed. Blood

PHOTOGRAPH VII

MECHANICAL EFFECTS OF DIALYSIS--This dog has been given .5 mg/kg Endotoxin and is undergoing 'Mechanical Effects of Dialysis'. The absence of the tank and its contents is noted, otherwise the rest of the connections are similar to the set up of dialysis.

chemistries, electrolytes, hematocrits and vital signs were determined in all the twenty dogs.

At the end of two and one half hours of shock, the blood was reinfused intraarterially into the dog by means of a syringe. Dialysis was begun soon after all the blood was back into the dog. Blood samples taken during dialysis were drawn through the three-way stopcock.

In five dogs, a polyethylene tubing 4 cm in diameter was pushed into the right auricle through the ipsilateral external jugular vein. Central venous pressures in centimeters of water were recorded simultaneously with inferior vena cava pressures.

b) Haemorrhagic Shock and Dibenzyline--The same method, Wiggers-Fine Technique, was used to bring this group of dogs into shock. There were twenty dogs in this series, ten experimental and ten control. It is to be noted that the latter group of dogs resembles the control group of haemorrhagic shock and dialysis.

The ten experimental dogs received .5 mg/kg of dibenzyline in 100 cc of normal saline intravenously after all the control parameters had been taken. One hour after the administration of dibenzyline, a second blood specimen for biochemistries and electrolytes was drawn. The dogs were then shocked for two and one half hours.

GROUP IV: DETERMINATION OF NORMAL ARTERIAL CHEMISTRIES

Five calm and docile dogs without any anesthesia were tied onto the operating table. All the dogs did not put up a struggle, since

since they had been hand picked on the basis of their tameness. By means of an 18 gauge needle, arterial blood samples for chemistries were drawn from the femoral artery. Compression was applied to the artery after withdrawal of the needle and the dog was sent back to the cage.

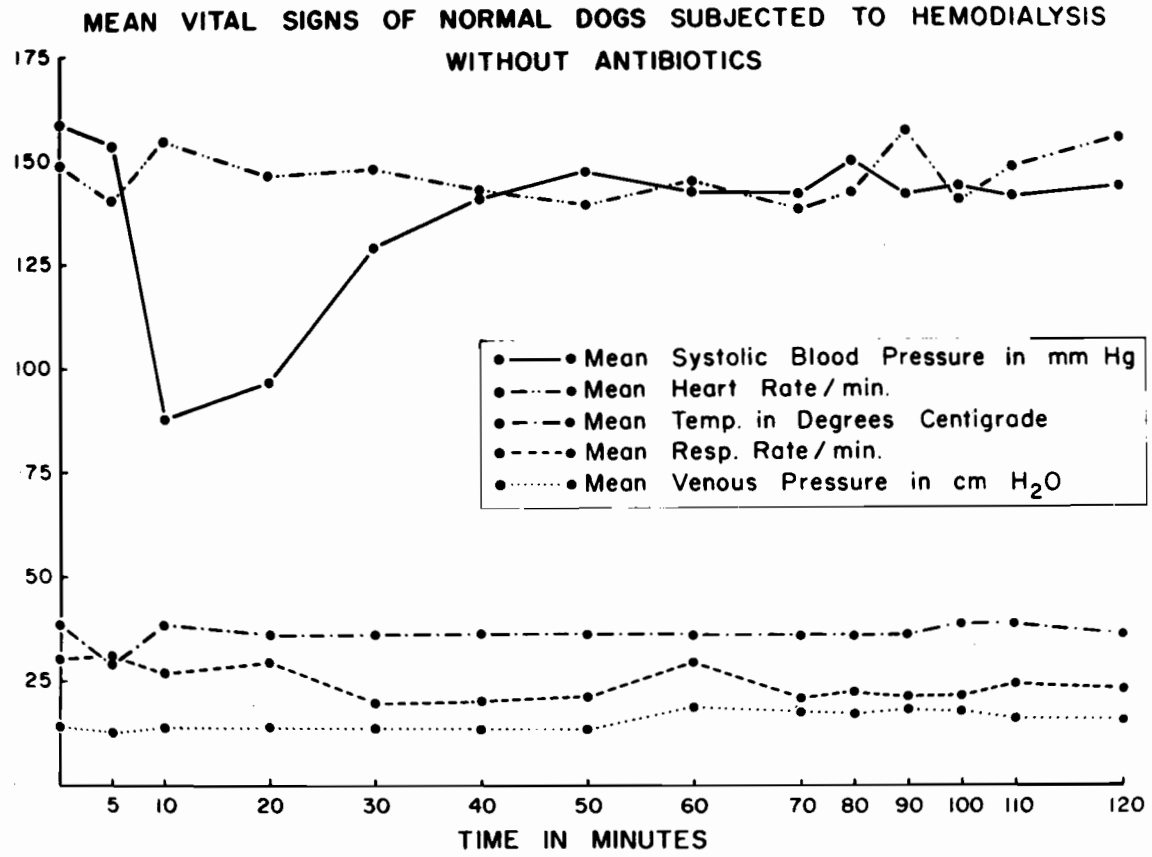


Fig. 8.--There is an initial drop in mean blood pressure, heart rate, temperature, respiratory rate and venous pressure during the first ten minutes of dialysis. Then for the next thirty minutes, all the parameters show a tendency to go back to normal levels and to stay stable till the end of dialysis.

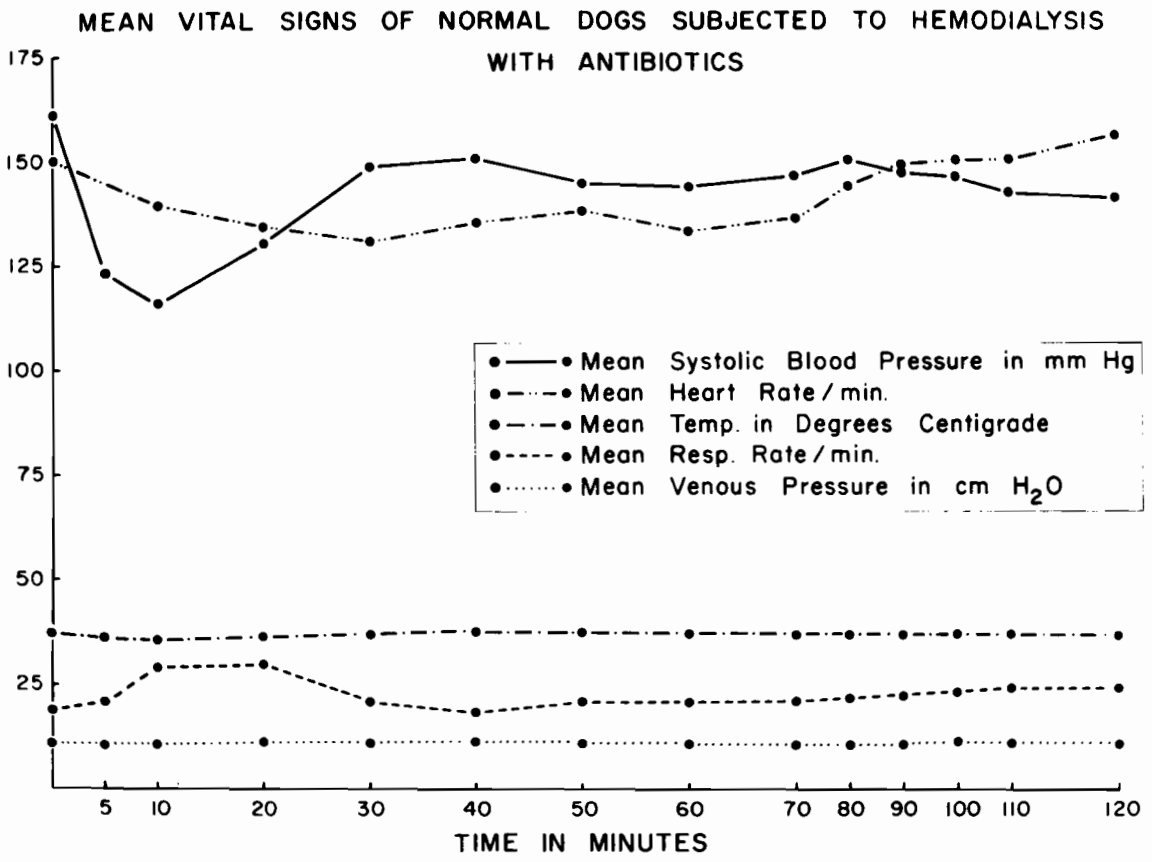


Fig. 9.--Except for the mean venous pressure and respiratory rate, the vital signs display the same tendencies observed in Fig. 8. The mean venous pressure in this group remained at practically the same level during the period of dialysis.

CHAPTER IV

RESULTS

GROUP 1:

A: DIALYSIS OF A NORMAL DOG WITH AND WITHOUT PROPHYLACTIC ANTIBIOTICS

1. EFFECTS OF DIALYSIS ON THE VITAL SIGNS OF A NORMAL DOG

a) Temperature--The mean normal temperature in a healthy dog lies between 36 - 37°C. In both groups of dogs there was a slight drop in temperature of an average 1.5°C at the beginning of dialysis. However, as a whole, after this initial drop, the temperature leveled off again till the end of the experiment. (Fig. 8 and Fig. 9)

b) Blood Pressure--There was usually a drop in systolic blood pressure, sometimes to levels as low as 50 mm Hg. Only one dog in the antibiotic group did not experience this period of hypotension. This same dog lived for five days. This phenomenon of initial hypotension following the beginning of dialysis was a common feature encountered in both groups.

c) Heart Rate--The average normal heart rate in a dog is 140 beats per minute. In both groups the values did not differ markedly and the heart rate seemed to remain at practically the same level throughout the experiment. There was a tendency towards tachycardia

during the last forty-five minutes of the experimental period.

d) Venous Pressure--The mean normal venous pressure of a dog is 6 - 6.5 cm of H_2O. The antibiotic group showed stable mean venous pressures, which remained at about 10 cm H_2O during the whole period of dialysis. The non antibiotic group showed higher mean venous pressures averaging 14 cm H_2O throughout the experimental period. The stability of venous pressures at some point during dialysis was noted in both groups. (Table 2)

e) Respiratory Rate--There was a tendency towards hypernea at the beginning of the experiment in the control dogs. During the later thirty minutes of the experiment, the respiratory rate returned to normal. The prophylactic group showed normal mean respiratory rates throughout the observation period.

At some point during dialysis, all the parameters were noted to be stable and to remain stable for a period of fifteen to thirty minutes. (Table 2) The temperature, blood pressure, heart rate, venous pressure and respiratory rate remained practically unchanged during this period. (Figs. 8 and 9) The time at which this physiological equilibrium occurred was different in each animal. (Appendices I and II)

There were no permanent survivors in the dogs that did not receive prophylactic antibiotics, while in the antibiotic group, four out of five dogs survived permanently. These survivors were subsequently used as donors in later experiments on hemodialysis.

TABLE 2

EFFECTS OF DIALYSIS ON VITAL SIGNS OF NORMAL DIALYSED DOGS WITH AND WITHOUT PROPHYLACTIC ANTIBIOTICS

TIME IN MINUTES		0	5	10	20	30	40	50
Temperature in Degrees Centigrade	C	37.3	29.3	37.2	36.7	36.7	36.5	36.1
	A	37.0	36.7	36.3	36.9	36.95	36.9	36.6
Blood Pressure in mm/Hg	C	157.6	152.8	88.4	96.0	128.0	138.0	146.0
	A	160.4	122.8	115.4	129.6	147.2	150.0	143.0
Heart Rate per Min	C	149.2	140	154.6	145.2	147.2	139.8	139.2
	A	149.4	141.5	138.8	132.8	130.0	134.0	137.2
Venous Pressure in cm. Water	C	14.1	12.7	13.3	14.4	14.5	12.8	13.0
	A	11.1	10.7	10.6	10.9	10.5	10.8	10.4
Respiratory Rate per Min.	C	30.0	30.6	27.4	24.2	19.0	19.6	21.4
	A	18.2	20.8	27.2	29.0	20.8	18.2	20.2

TABLE 2 (Cont'd.)

TIME IN MINUTES		60	70	80	90	100	110	120
Temperature in Degrees Centigrade	C	36.1	36.0	36.1	36.1	37.9	37.9	35.9
	A	36.2	36.2	36.2	36.2	36.4	36.4	36.3
Blood Pressure in mm./Hg	C	142.0	140.2	149.6	141.4	143.6	142	140
	A	142.6	145.6	149.6	146.2	145.6	142	141.4
Heart Rate per Min.	C	144	138	142	156.8	142	148.4	154.4
	A	132.4	135.8	143.2	146.6	149	150	155.2
Venous Pressure in cm. Water	C	17.6	16.5	16.3	16.6	16.5	14.5	15.7
	A	10.4	10.3	10.2	10.2	10.7	10.3	10.2
Respiratory Rate per Min.	C	29.8	21.8	23.0	21.2	22.4	24.6	22.8
	A	20.2	21.4	21.6	22.0	22.6	24.4	24.0

A = Dogs receiving antibiotics C = Control - no antibiotics

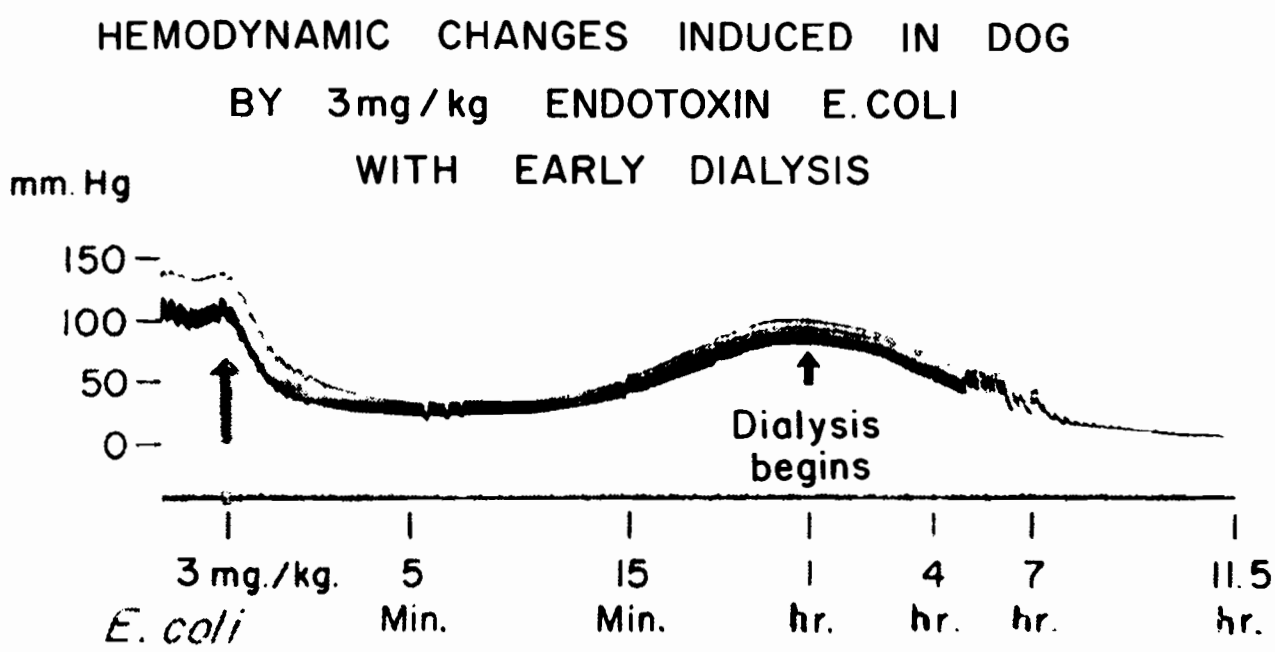


Fig. 10.--Administration of endotoxin is followed by a dramatic fall in blood pressure, which lasts for a period of thirty to sixty minutes. Then the blood pressure rises again to control levels and stays for another period of thirty to sixty minutes, after which it declines progressively till the death of the animal. The period of initial hypotension is sometimes accompanied by a marked bradycardia.

TABLE 3

COMPARATIVE VITAL SIGNS OF CONTROL AND EARLY DIALYSED DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade	C	37.51	37.32	36.8	36.5	36.49	36.08	36.0	35.86	36.11
	D	36.92	36.52	36.63	36.16	34.14	35.58	35.22	35.09	34.64
Blood Pressure in mm Hg	C	154	134	119	109	95	90	89	89	88
	D	110	109	115	110	109	103	99	93	88
Heart Rate per Minute	C	154.07	140	132.57	149.93	146	149.57	163	158.93	160.86
	D	146	137	125	133	142	148	146	147	150
Venous Pressure in cm Water	C	6.5	5.4	5.1	4.7	4.5	4.3	3.9	4.4	4.1
	D	6.2	4.6	3.3	3.8	4.4	4.2	4.5	4.5	4.4
Respiratory Rate per Minute	C	29.5	27.64	23.86	26.79	33.86	33.14	30.5	29.93	30.43
	D	26	33	37	37	32	30	27	26	25

TABLE 3 (Cont'd.)

TIME IN MINUTES		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade	C	36.03	36.3	36.2	36.1	36.0	35.5	34.9	34.6
	D	34.44	34.41	34.44	34.21	34.07	33.85	33.85	33.79
Blood Pressure in mm Hg	C	89	87	93	95	94	95	96	95
	D	88	88	91	95	99	102	103	105
Heart Rate per Minute	C	169.21	181.5	187.8	184.7	189.9	186.6	187.3	187.8
	D	154	161	165	162	162	160	160	160
Venous Pressure in cm. Water	C	4.5	3.9	5.5	6.2	6.5	6.7	5.9	5.6
	D	4.9	4.7	5.0	5.5	5.7	6.0	5.8	5.9
Respiratory Rate per Minute	C	26.7	27.79	27.6	27.0	25.1	24.1	25.1	24.5
	D	25	24	25	25	24	27	26	26

C = Control D = Dialysed

TABLE 4

MEAN ELECTROLYTES, CHEMISTRIES AND HEMATOCRIT OF CONTROL AND EARLY DIALYSED DOGS SUBJECTED TO 3MG/KG ENDOTOXIN E. COLI (DIFCO)

TIME IN MINUTES	0	30	90	150	210
CONTROL DOGS					
pH	7.37	7.33	7.33	7.32	7.34
pCO_2 in mm Hg	23.1	17.92	16.34	14.52	15.95
HCO_3 in meq/l	13.94	9.47	9.6	9.83	8.92
Lactic Acid in meq/l	3.01	4.99	5.68	6.22	5.72
Chlorides in meq/l	112	114	114	116	115
Sodium in meq/l	147	144	146	148	145
Potassium in meq/l	3.66	3.88	3.42	3.71	3.99
Hematocrit %	47	52	52	53	54

TABLE 4 (Cont'd.)

TIME IN MINUTES	0	30	90	150	210
DIALYSED DOGS					
pH	7.32	7.28	7.31	7.33	7.35
pCO_2 in mm Hg	25.8	22.5	21.7	20.2	15.9
HCO_3 in meq/l	15.01	12.01	11.8	11.7	10.4
Lactic Acid in meq/l	3.57	4.79	5.71	6.23	5.98
Chlorides in meq/l	110	110	109	110	116
Sodium in meq/l	147.7	147.6	138.1	146.2	143.0
Potassium in meq/l	3.63	3.39	2.9	2.95	3.26
Hematocrit %	49	43	43	44	45

TABLE 5

SURVIVAL TIME IN HOURS OF CONTROL AND EARLY DIALYSED DOGS SUBJECTED TO ENDOTOXIN

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Control Dogs	8	8	10	7.5	5	2.5	9	4.75	30	3.5	3.5	6	24	24
Dialysed Dogs	8	30	20	9.5	9.5	30	30	9.5	8.5	5	30	30	30	30

	Mean Number of Hours	Number of Permanent Survivors	Percent Survivors
Control Dogs	10.5	1	7%
Dialysed Dogs	20.0	7	50%

TABLE 6

PERCENT SURVIVAL OF CONTROL AND EXPERIMENTAL DOGS

TOTAL NUMBER OF DOGS, BOTH CONTROL AND EXPERIMENTAL, SUBJECTED TO 3 MG/KG ENDOTOXIN

	Total No. of Dogs	No. of Permanent Survivors	Percent Survival
Control	34	6	17.64
Experimental	39	19	48.71
Histamine Group	6	0	0

TOTAL NUMBER OF DOGS IN HAEMORRHAGIC SHOCK AND THEIR CONTROLS

	Total No. of Dogs	No. of Permanent Survivors	Percent Survival
Control	20	1	10%
Experimental	20	3	30%

TABLE 7

MEAN VITAL SIGNS IN EARLY ENDOTOXIN DIALYSED DOGS WITH OLD AND NEW COILS

TIME IN MINUTES	0	15	30	45	60	75	90	105	120
Temperature in Degrees Cent.	37.9	37.9	37.8	37.7	37.6	37.5	37.5	37.4	37.4
Blood Pressure in mm Hg	156	89	93	101	105	104	109	112	112
Heart Rate per Minute	190	106	135	161	162	167	175	178	173
Venous Pressure in cm Water	6.2	5.6	5.8	6.5	7.2	6.5	6.0	5.6	5.5
Respiratory Rate per minute	19.2	21.9	21.3	23.7	23.4	24.9	23.4	23.7	24.0

TABLE 7 (Cont'd.)

TIME IN MINUTES	135	150	165	180	195	210	225	240	270
Temperature in Degrees Cent.	37.1	37.0	36.8	36.7	36.4	36.1	36.0	35.9	35.8
Blood Pressure in mm Hg	109	108	107	106	105	102	100	100	101
Heart Rate per minute	170	170	172	173	172	172	171	180	182
Venous Pressure in cm Water	5.7	5.7	5.5	5.7	5.7	5.7	5.8	6.2	6.2
Respiratory Rate per minute	24.0	27.0	28.5	28.2	24.6	25.8	24.3	24.7	25.2

TABLE 8

EFFECTS OF LATE DIALYSIS ON VITAL SIGNS IN ENDOTOXIN DOGS WITH OLD AND NEW COILS

TIME IN MINUTES		0	15	30	45	60	75	90	105
Temperature in Degrees Centigrade	C	37.9	37.9	37.9	37.8	37.6	37.4	37.1	37.1
	D	38.1	38.1	38.1	37.8	37.6	37.5	37.5	37.4
Blood Pressure in mm Hg.	C	158	90	83	107	109	116	121	113
	D	152	103	107	109	124	132	124	120
Heart Rate per Minute	C	190	124	103	132	129	127	133	150
	D	180	131	122	163	168	171	180	181
Venous Pressure in cm Water	C	5.9	3.2	2.9	3.7	5.4	5.5	4.3	4.8
	D	6.2	4.3	4.2	5.7	6.6	6.0	5.4	4.8
Respiratory Rate per Minute	C	40	42	43	45	34	35	48	40
	D	21.3	20.4	18.9	20.7	22.7	22.8	24.3	20.7

TABLE 8 (Cont'd.)

TIME IN MINUTES		120	135	150	165	180	195	210	225
Temperature in Degrees Centigrade	C	37.2	37.1	36.8	37.2	37.2	37.0	37.2	36.3
	D	37.3	37.1	37.2	37.0	36.9	36.8	36.8	36.8
Blood Pressure in mm Hg	C	102	101	92	109	105	102	101	104
	D	116	111	109	108	101	102	98	97
Heart Rate per Minute	C	180	185	165	224	244	244	288	227
	D	201	198	216	223	215	219	208	201
Venous Pressure in cm Water	C	4.4	4.7	4.9	3.2	2.5	2.7	3.8	5.0
	D	4.8	4.2	4.4	4.3	4.4	4.3	4.3	4.3
Respiratory Rate per Minute	C	37	29	33	40	30	30	25	27
	D	20.4	22.8	23.1	20.7	20.4	20.4	20.4	21.9

C = Control D = Dialysed

TABLE 9

INFLUENCE OF EARLY AND LATE DIALYSIS ON THE VITAL SIGNS OF ENDOTOXIN DOGS
(OLD AND NEW COILS)

TIME IN MINUTES		0	15	30	45	60	75	90	105
Temperature in Degrees Centigrade	E	36.92	36.52	36.63	36.16	36.14	35.58	35.22	35.09
	D	38.1	38.1	38.1	37.8	37.6	37.5	37.5	37.4
Blood Pressure in mm Hg	E	152	109	115	110	109	103	99	93
	D	152	103	107	109	124	132	124	120
Heart Rate per Minute	E	146	137	127	133	142	148	146	147
	D	180	131	122	163	168	171	180	181
Venous Pressure in cm Water	E	6.2	4.6	3.3	3.8	4.4	4.2	4.5	4.5
	D	6.2	4.3	4.2	5.7	6.6	6.0	5.4	4.8
Respiratory Rate per Minute	E	26	33	37	37	32	30	27	26
	D	21.3	20.4	18.9	20.7	22.7	22.8	24.3	20.7

TABLE 9 (Cont'd.)

TIME IN MINUTES		120	135	150	165	180	195	210	225
Temperature in Degrees Centigrade	E	34.64	34.44	34.41	34.44	34.21	34.07	33.85	33.85
	D	37.3	37.1	37.2	37.0	36.9	36.8	36.8	36.8
Blood Pressure in mm Hg	E	88	88	88	91	95	99	102	103
	D	116	111	109	108	101	102	98	97
Heart Rate per Minute	E	150	154	161	165	162	162	160	160
	D	201	198	216	223	215	219	208	201
Venous Pressure in cm Water	E	4.4	4.9	4.7	5.0	5.5	5.7	6.0	5.8
	D	4.8	4.2	4.4	4.3	4.4	4.3	4.3	4.3
Respiratory Rate per Minute	E	25	25	24	25	25	24	27	26
	D	20.4	22.8	23.1	20.7	20.4	20.4	20.4	21.9

TABLE 9 (Cont'd.)

TIME IN MINUTES		240	255	270	285	300	315	330
Temperature in Degrees Centigrade	E	33.79						
	D	36.6	36.5	36.1	35.8	35.6	35.3	35.1
Blood Pressure in mm Hg.	E	105						
	D	88	93	97	94	92	97	93
Heart Rate per Minute	E	160						
	D	173	174	179	178	174	168	168
Venous Pressure in cm Water	E	5.9						
	D	4.9	5.0	5.0	5.2	5.1	5.8	5.9
Respiratory Rate per Minute	E	26						
	D	21.6	21.9	22.8	21.3	23.0	23.5	23.5

E = Early Dialysis D = Delayed Dialysis

TABLE 10

INFLUENCE OF THE MECHANICAL EFFECTS OF DIALYSIS ON THE VITAL SIGNS OF ENDOTOXIN DOGS

TIME IN MINUTES	0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade	37.86	37.76	37.70	37.55	37.55	37.25	37.15	36.75	36.63
Blood Pressure in mm Hg.	149.5	96.4	100.0	107.1	111.5	106.7	96.9	89.9	85.9
Heart Rate per Minute	163.2	105.1	136.4	137.2	164.7	169.6	175.8	183.7	185.7
Venous Pressure in cm Water	8.49	6.74	8.84	8.44	8.15	8.15	7.45	6.85	6.40
Respiratory Rate per Minute	29.1	26.6	23.2	27.1	28.9	26.2	27.9	28.6	26.8

TABLE 10 (Cont'd.)

TIME IN MINUTES	135	150	165	180	195	210	225	240	360
Temperature in Degrees Cent.	37.86	36.45	36.40	36.10	38.85	35.83	35.75	35.56	35.87
Blood Pressure in mm Hg	79.2	78.0	76.6	74.3	72.4	84.8	84.4	83.1	79.0
Heart Rate per Minute	190.2	198.5	189.3	192.8	139.4	176.9	172.9	190.4	178.1
Venous Pressure in cm water	5.75	5.60	5.90	6.95	7.15	7.28	6.48	6.16	6.16
Respiratory Rate per Minute	26.4	27.0	24.6	23.4	22.0	21.6	24.0	24.0	25.1

TABLE 11

COMPARATIVE TRENDS OF VITAL SIGNS OF ENDOTOXIN DOGS SUBJECTED TO EARLY DIALYSIS AND ITS MECHANICAL EFFECTS

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade	D	37.9	37.9	37.8	37.7	37.6	37.5	37.5	37.4	37.4
	M	37.86	37.76	37.70	37.55	37.55	37.25	36.75	36.75	36.63
Blood Pressure in mm Hg	D	156	89	93	101	105	104	109	112	112
	M	149.5	96.4	100.0	107.1	111.5	106.7	96.9	89.9	85.9
Heart Rate per Minute	D	190	106	135	161	162	167	175	178	173
	M	163	105.1	136.4	137.2	164.7	169.6	175.8	183.7	185.7
Venous Pressure in cm Water	D	6.2	5.6	5.8	6.5	7.2	6.5	6.0	5.6	5.5
	M	8.49	6.74	8.84	8.44	8.15	8.15	7.45	6.85	6.40
Respiratory Rate per Minute	D	19.2	21.9	21.3	23.7	23.4	24.9	23.4	23.7	24.0
	M	29.1	26.6	23.2	27.1	28.9	26.2	27.9	28.6	26.8

TABLE 11 (Cont'd.)

TIME IN MINUTES		135	150	165	180	195	210	225	240	270	360
Temperature in Degrees Centigrade	D	37.1	37.0	36.8	36.7	36.4	36.1	36.0	35.9	35.8	
	M	36.76	36.45	36.40	36.10	35.85	35.83	35.75	35.56		35.87
Blood Pressure in mm Hg	D	109	108	107	106	105	102	100	100	101	
	M	79.2	78.0	76.6	74.3	72.4	84.8	84.4	83.1		79.0
Heart Rate per Minute	D	170	170	172	173	172	172	171	180	182	
	M	190.2	198.5	189.3	192.8	139.4	176.9	172.9	190.4		178.1
Venous Pressure in cm Water	D	5.7	5.7	5.5	5.7	5.7	5.7	5.8	6.2	6.2	
	M	5.75	5.60	5.90	6.95	7.15	7.28	6.48	6.16		6.16
Respiratory Rate per Minute	D	24.0	27.0	28.5	28.2	24.6	25.8	24.3	24.7	25.2	
	M	26.4	27.0	24.6	23.4	22.0	21.6	24.0	24.0		25.1

D = Dialysed Group M = Mechanical Effects

GROUP II:

B: ENDOTOXIN SHOCK

2: EFFECTS OF ENDOTOXIN AND DIALYSIS ON VITAL SIGNS
(Tables 3, 7, 8, 9, 10, 11)

a) Temperature--In all the dogs that received 3 mg/kg of endotoxin, both dialysed and control, there was a marked and progressive fall in temperatures. The difference between the control temperature and that at the end of the experiment was sometimes 5° Centigrade. High mean temperatures were noted in the group of dogs subjected to endotoxin and delayed dialysis. There does not seem to be a definite correlation between progressive drop in temperature and survival. (Appendices III, V, VII, VIII)

b) Blood Pressure--There is also a general tendency for blood pressure to fall progressively as the dog goes into shock. Immediately after administration of endotoxin, there is a dramatic fall in blood pressure to levels sometimes as low as 60 mm Hg. This period may last for thirty-five minutes to one hour. (Fig. 10) Out of seventy-nine dogs that received endotoxin, forty manifested this dramatic phenomenon of endotoxin hypotension. Three dogs never recovered from this crucial period as they went downhill and died in 3½ hours.

The control dogs in the endotoxin series showed a general tendency of maintaining their blood pressure below 100 mg Hg till the end of the experimental period. The experimental dogs and three

dogs in the-mechanical-effects-of-dialysis group generally showed a gradual rise in pressure during the last hour of the experiment. (Appendix XII) There is some correlation between survival rate and the behaviour of blood pressure during the shock period. Animals which tended to keep their mean blood pressures above 100 mm Hg during the experimental period, survived longer than those dogs which remained severely hypotensive (65 mm Hg) for over 3½ hours. All the morphine endotoxin dogs which survived permanently maintained their blood pressures well above 100 mm Hg throughout the experiment. (Table 13). One morphine-endotoxin dog which had remained hypotensive for one hour compensated at the end and it survived permanently. (Appendix XV) Dogs undergoing dialysis also showed initial drop in blood pressure at the beginning of dialysis, as observed previously in normal dogs. However, usually the dialysed dogs showed blood pressure increase at the end of the experiment, especially permanent survivors.

c) Heart Rate--(Appendices II, III, V, VII, VIII, IX, X, XI, XII, XIII, XV) In all the endotoxin dogs there was a tendency towards tachycardia after 2½ hours in shock. (Tables 3, 7, 8, 9) some groups, notably the endotoxin—mechanical-effects-of-dialysis animals, the mean heart rate was as high as 244 beats per minute. (Table 10) Five to ten minutes after the injection of endotoxin, some dogs showed a marked bradycardia to values as low as eighty beats per minute. Thirty-seven endotoxin dogs out of a total of

seventy-nine exhibited this period of bradycardia. It was of interest to notice that this period usually coincided with the period of initial hypotension mentioned above. Early dialysis was usually commenced when both bradycardia and hypotension phases had passed. (Fig. 10)

d) Venous Pressure--There was a tendency to elevation of venous pressure to averages of 8.5 cm water at the beginning of the experiment. Examining the values of individual animals, it is noted that some dogs showed initial venous pressures of 5-6 cm water. Towards the end of experimental period, most survivors maintained a venous pressure of 5-6 cm H_2O. The dogs that died during the experimental period showed a terminal elevation of venous pressure to levels as high as 13 cm water. Some permanent survivors also manifested this terminal increase in venous pressures to values as high as 14 cm water.

e) Respiratory Rate--There was a tendency towards hyperpnoea in most dogs at the beginning of the experiment, as observed in the other groups of dogs. Hyperpnoea was aggravated by endotoxin administration. The mean respiratory rate tended to rise slightly in the middle of the experiment, but in the majority of cases the rate showed little variation until towards the end of our observations. Examination of individual respiratory rates shows that permanent survivors tend to compensate well by maintaining a normal respiratory rate (18-27) towards the end.

TABLE 12

THE INFLUENCE OF MECHANICAL EFFECTS OF DIALYSIS VERSUS EARLY DIALYSIS ON ELECTROLYTES, CHEMISTRIES AND HEMATOCRIT OF ENDOTOXIN DOGS

TIME IN MINUTES		0	30	90	150	210	270
Chlorides in meq/l	M	121	116	119.7	123.7	120.4	117.5
	D	110	110	109	110	116	
Sodium in meq/l	M	145.2	143	145.6	145	142.5	141.5
	D	147.7	147.6	138.1	146.2	143	
Potassium in meq/l	M	3.57	2.95	2.98	3.25	3.21	2.73
	D	3.63	3.39	2.90	2.95	3.26	
Hematocrit %	M	54	48.4	50.4	51.3	50.8	44.5
	D	49	43	43	44	45	
pH	M	7.35	7.31	7.30	7.33	7.36	7.27
	D	7.32	7.28	7.31	7.33	7.35	
pCO_2 in mm Hg	M	32.2	25.8	21.1	17.9	15.8	15.0
	D	25.8	22.5	21.7	20.2	15.9	
HCO_3 in meq/l	M	19.4	13.4	11.1	10.6	10.2	8.6
	D	15.01	12.01	11.8	11.7	10.4	
Lactic acid in meq/l	M	4.37	4.83	6.00	5.55	5.92	5.88
	D	3.57	4.79	5.71	6.23	5.98	

M = Mechanical Effects D = Dialysed Group

TABLE 13

EFFECTS OF ENDOTOXIN, MORPHINE AND DIALYSIS ON VITAL SIGNS

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade	C	37.9	38.1	38.1	38.1	37.2	37.4	37.3	36.7	36.7
	D	36.9	37.2	36.9	36.8	36.8	36.7	36.5	36.2	36.2
Blood Pressure in mm Hg	C	125	96	116	117	116	110	109	104	102
	D	115	82	86	84	86	87	80	90	89
Heart Rate per Minute	C	160	167	172	165	166	176	176	188	188
	D	144	104	151	152	156	159	158	161	149
Venous Pressure in cm Water	C	4.6	4.6	4.7	4.4	4.8	5.0	5.3	5.1	5.0
	D	5.0	4.3	4.3	4.1	4.5	4.6	5.4	5.3	6.0
Respiratory Rate per Minute	C	38	40	46	51	53	65	67	41	39
	D	39	30	31	29	22	23	24	23	20

TABLE 13 (Cont'd.)

TIME IN MINUTES		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade	C	36.4	36.9	36.9	36.3	36.3	36.3	36.1	35.8
	D	36.1	35.6	35.8	35.6	35.3	35.4	35.0	34.9
Blood Pressure in mm Hg	C	90	103	101	94	91	93	91	88
	D	91	92	91	92	90	87	83	81
Heart Rate per Minute	C	141	180	186	206	186	196	200	204
	D	161	145	165	168	165	165	166	166
Venous Pressure in cm Water	C	5.4	4.1	4.3	4.1	4.0	3.9	4.6	4.9
	D	5.9	5.9	6.8	7.1	7.1	7.3	7.6	8.6
Respiratory Rate per Minute	C	28	32	32	29	30	31	26	26
	D	24	24	22	21	21	20	20	22

C = Control D = Dialysed

TABLE 14

COMPARISON OF VITAL SIGNS OF CONTROL AND DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90
Temperature in Degrees Centigrade	C	37.37	37.29	37.14	37.04	36.50	36.09	35.49
	D	37.7	37.8	37.7	37.4	37.2	36.9	36.8
Blood Pressure in mm Hg	C	157.2	40	40	40	50	50	50
	D	142	40	40	40	50	50	50
Heart Rate per Minute	C	156	128.5	142.1	153.9	159.9	168.6	168.5
	D	155	137	163	173	208	217	215
Venous Pressure in cm Water	C	7.65	3.70	2.60	4.0	3.35	3.20	3.5
	D	6.7	2.7	2.1	2.3	2.2	2.5	2.4
Respiratory Rate per Minute	C	27.3	39.3	37.0	31.5	31.5	31.8	32.4
	D	35	30	28	30	29	29	26

TABLE 14 (Continued)

TIME IN MINUTES		105	120	135	150	165	180	195
Temperature in Degrees Centigrade	C	34.95	34.25	33.80	33.65	33.65	33.6	33.4
	D	35.5	36.0	35.9	35.8	35.2	34.9	34.9
Blood Pressure in mm Hg	C	50	50	50	50	50	50	96
	D	50	50	50	50	50	112	108
Heart Rate per Minute	C	167.2	171.2	172.8	169.4	164.4	155.3	168.1
	D	215	219	221	218	228	193	183
Venous pressure in cm Water	C	3.35	3.30	3.25	2.26	2.86	4.60	4.6
	D	2.6	2.5	2.4	2.8	2.9	4.6	4.7
Respiratory Rate per Minute	C	31.2	32.7	32.1	32.7	32.5	27.5	29.6
	D	26	28	28	27	27	28	28

C = Control D = Dialysed

TABLE 14 (Continued)

TIME IN MINUTES		210	225	240	255	270
Temperature in Degrees Centigrade	C	33.27	33.06	33.06	33.06	33.05
	D	35.0	34.8	34.7	34.55	34.0
Blood Pressure in mm Hg	C	96	107	107	107	102
	D	106	101	103	111.3	117
Heart Rate per Minute	C	142.8	155.6	155.8	155.0	
	D	163	163	162	158	150
Venous Pressure in cm Water	C	5.9	5.0	4.9	5.0	5.2
	D	8.3	5.3	5.5	5.5	5.6
Respiratory Rate per Minute	C	24.4	27.7	26.2	24.3	23.2
	D	25	26	25	24	24

C = Control D = Dialysed

TABLE 15

INFLUENCE OF DIALYSIS ON BLOOD ELECTROLYTES CHEMISTRIES AND HEMATOCRIT IN HAEMORRHAGIC SHOCK DOGS

TIME IN MINUTES	0	30	90	150	210	270
CONTROL DOGS						
pH	7.32	7.18	7.13	6.16	7.16	7.12
pCO_2 in mm Hg	36.13	15.0	15.40	16.33	22.63	
HCO_3 in meq/l	17.39	9.03	7.30	7.18	9.09	
Lactic acid in meq/l	4.06	10.2	15.32	14.71	9.41	
Chlorides in meq/l	113	115	113	116	117	
Sodium in meq/l	160	146	148	151	159	149
Potassium in meq/l	3.6	5.5	4.7	5.0	5.8	
Hematocrit %	44	47	51	53	58	61

TABLE 15 (Continued)

TIME IN MINUTES	0	30	90	150	210	270
DIALYSED DOGS						
pH	7.40	7.18	7.17	7.15	7.36	7.31
pCO_2 in mm Hg	30.7	20.5	16.4	18.6	23.3	21.7
HCO_3 in meq/l	18.2	7.9	7.4	7.2	11.6	12.4
Lactic acid in meq/l	2.8	9.3	10.0	9.7	6.5	7.0
Chlorides in meq/l	117	114	115	116	107	110
Sodium in meq/l	147.6	146.8	149.1	152.2	140.5	142.2
Potassium in meq/l	4.02	5.54	5.23	5.77	4.33	4.23
Hematocrit %	51	52	52	54	50	50

TABLE 16

EFFECTS OF DIBENZYLINE ON VITAL SIGNS OF DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90	105	120	135
Temperature in Degrees Centigrade	C	37.5	37.5	37.6	37.3	37.2	37.1	36.7	36.7	36.8	36.8
	D	37.7	37.7	37.5	37.3	37.2	37.1	37.1	36.7	36.5	36.3
Blood Pressure in mm Hg	C	149	40	40	40	50	50	50	50	50	50
	D	150	124	108	108	101	96	40	40	40	47
Heart Rate per Minute	C	181	188	183	212	215	202	202	194	208	220
	D	194	183	191	182	180	185	188	199	208	194
Venous Pressure in cm Water	C	4.6	3.0	2.0	3.0	2.1	2.2	3.2	3.3	3.4	3.4
	D	4.3	4.2	4.3	4.4	4.2	4.3	4.1	3.2	3.5	4.2
Respiratory Rate per Minute	C	22	23	22	24	25	21	21	20	21	21
	D	21	22	17	17	17	18	22	22	22	25

TABLE 16 (Continued)

TIME IN MINUTES		150	165	180	195	210	225	240	255	270	285
Temperature in Degrees Centigrade	C	36.5	36.0	35.7	35.0	34.8	34.7	34.6	34.4	34.4	33.6
	D	36.1	35.9	35.8	35.3	34.9	34.1	34.4	33.9		
Blood Pressure in mm Hg	C	50	50	80	81	101	117	114	112	107	92
	D	47	48	48	50	50	87	97	103		
Heart Rate per Minute	C	228	222	204	169	167	166	179	174	200	223
	D	213	213	209	196	178	176	203	182		
Venous Pressure in cm Water	C	3.4	3.3	4.3	6.2	7.0	6.6	6.7	6.6	6.6	6.2
	D	3.7	3.9	4.9	4.4	4.8	5.0	3.9	3.7		
Respiratory Rate per Minute	C	21	22	22	20	20	20	19	17	20	20
	D	26	26	25	25	23	24	26	27		

C = Control D = Dibenzyline

GROUP III:

C: HAEMORRHAGIC SHOCK

3: EFFECTS OF HAEMORRHAGIC SHOCK, DIALYSIS AND DIBENZYLINE ON VITAL SIGNS (Tables XIV, XVI)

a) Temperature--(Appendices XVI, XVII, XX) The same tendency of gradual temperature depression seen in the endotoxin group was also noted in the haemorrhagic group. The temperature in the latter group had the tendency to drop much lower than in the former group. There did not seem to be any difference in the behaviour of temperature between experimental and control animals. However, one dibenzyline-haemorrhagic shock animal maintained its temperature to an average of 38° C throughout the experimental period. This same dog was a permanent survivor. On the whole, animals which survived either permanently or the longest, tended to stabilize their temperatures at an average of 34° C.

b) Blood Pressure--Ten to fifteen minutes after reinfusion, the mean blood pressure in both experimental and control animals went up to levels above 100 cm Hg. The mean values were however higher in dialysed dogs than in the controls. (Table IV) The dibenzyline control dogs were almost identical to the haemorrhagic shock and dialysis control group of animals. After the administration of .5 mg/kg dibenzyline, there was a gradual fall of blood pressure to levels as low as 50 mm Hg in thirty minutes. (Figs. 11 & 12) Seven out of ten dogs in this series showed this tendency. All the three permanent

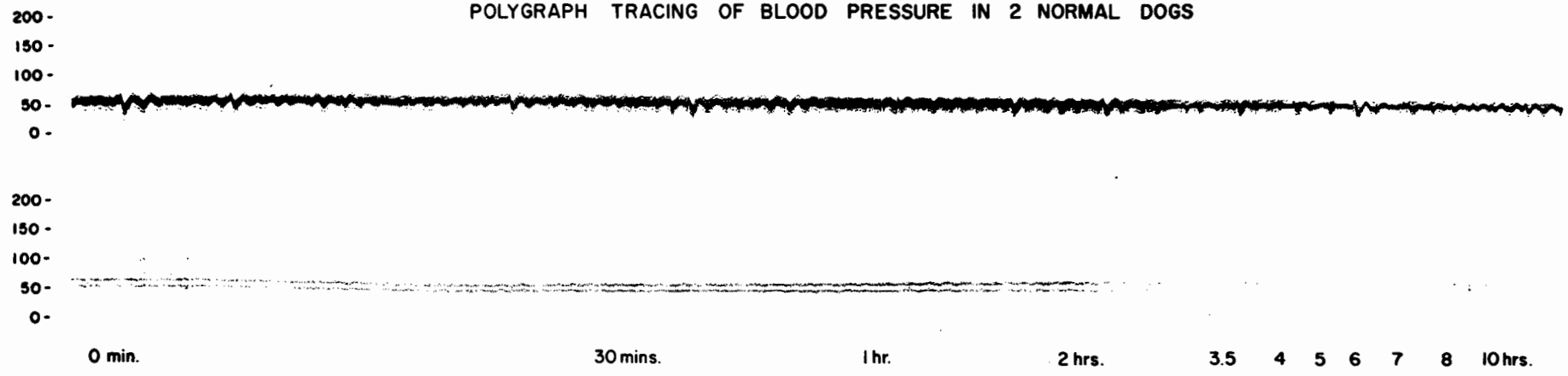


Fig. 11.--This is a normal polygraph tracing of two dogs which were not subjected to any form of experimental procedure. They were anesthetized with nembutal and their blood pressures were observed for over eight hours. Nembutal in pharmacological doses does not cause hypotension in a dog.

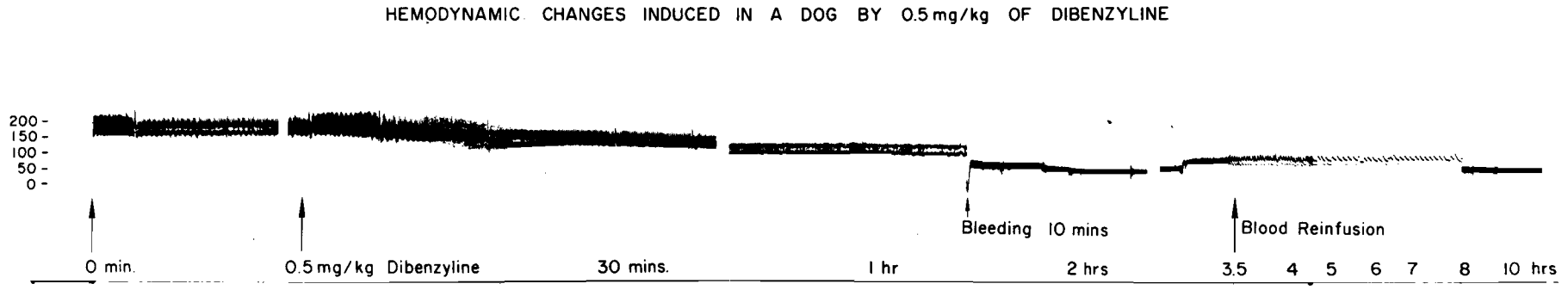


Fig. 12.--Administration of Dibenzyline (phenoxybenzamine) is accompanied by a gradual fall in blood pressure to levels as low as 50 mm Hg. In spite of this hypotension the other vital signs are not adversely affected.

survivors in this group had blood pressures below 100 mm Hg for the whole hour prior to the induction of the dogs into shock. They, however, showed elevation of their blood pressure above 100 mm Hg after reinfusion and maintained it to that level till the end of the experiment. One dibenzyline dog showed progressive fall of blood pressure after administration of the drug and died in three hours.

c) Heart Rate--There was a general tendency towards tachycardia as the animal went deeper into shock. This was seen in both control and experimental dogs. In fact the dialysed dogs' mean values were much higher than the control group. (Tables 14 and 16) The heart rate in this latter group went as high as 228 beats per minute. The dibenzyline dogs had mean heart rates lower than their control group. The seven dogs which died in less than five hours in this series showed a severe tachycardia, up to 300 beats per minute, fifteen to thirty minutes pre mortem. However, one dog, which survived permanently, also manifested a severe tachycardia, 300 beats per minute at the end of the experimental period.

d) Venous Pressure--There was an increasing depression of venous pressures from the normal average values of 6.5 cm water to levels as low as -2 cm water. Nine dogs in the haemorrhagic group showed venous pressures which were below zero degrees centigrade. One of these dogs was a permanent survivor. These subzero values usually appeared fifteen to twenty minutes after induction of shock. They remained at this level until reinfusion when the venous

pressure went up again to levels slightly below control values. Dialysed dogs manifested a tendency to increase venous pressures to normal values. As observed in the endotoxin dogs, there was always an elevation of venous pressures to averages of 16.5 cm water just before death.

e) Respiratory Rate--Some dogs were hyperpnoeic before the experiment was begun. Hyperventilation was a common feature of all dogs at the beginning of the bleeding period. One dialysed dog which died in 3½ hours had a respiratory rate of ninety per minute. There was a general tendency for the dogs to reach normal respiratory rates towards the end of the experimental period. All the nine permanent survivors in this group showed a tendency to adjust their respiratory rate to normal values. As a general rule, most dogs showed an increased respiratory rate in the middle of the experimental period. It is of interest to note that the dibenzyline dogs, except one, maintained a fairly normal respiratory rate (18-27) throughout the whole experimental period.

f) Blood Volume and Rate of Bleeding into the Reservoir--In all the control and experimental dogs, except the dibenzyline animals, the rate of blood flow into the reservoir had an average of 120-150 cc per minute, while the bleeding volumes averaged 40 cc/kg body weight. (Photograph VIII) At the end of induction of haemorrhagic shock, there was so much resistance in reinfusing the blood back into the dog that a 50 cc syringe had to be employed in order to reinfuse

the blood intraarterially. In the dibenzyline animals there was little resistance to reinfusion. It was also noted that most haemorrhagic shock dogs started autoreinfusion at the average time of seventy-nine minutes. In the dibenzyline group, six out of ten dogs did not reinfuse at all for 2½ hours. (Appendix XXII) (Table 20)

It is interesting to note that in all endotoxin and haemorrhagic shock dogs that were weighed, the average loss of weight during the experimental period was 1.5 kg.

4: EFFECTS OF TREATMENT ON SURVIVAL RATE (Tables 5, 6, 19, and Fig. 13)

a) Normal Dogs, Dialysis and Prophylactic Antibiotics--There were four out of ten (80%) permanent survivors in the dogs which received prophylactic fortimycin after haemodialysis. The average life span of the dogs which did not receive prophylactic antibiotics was 4.2 days. No dog in this group lived for more than five days.

b) Endotoxin Group--The total number of permanent survivors in the endotoxin group out of a total of seventy-three dogs (excluding six histamine dogs) was twenty-five. Of these dogs, six out of thirty-four controls were permanent survivors, while nineteen out of the thirty-nine experimental animals lived permanently.

In the endotoxin and early dialysis with new and old coils, there were eight permanent survivors out of twenty-eight paired dogs; one control and seven experimental. The mortality rate in the experimental group was fifty percent as compared to ninety-three percent in the control animals.

TABLE 17

BEHAVIOUR OF BLOOD ELECTROLYTES, CHEMISTRIES AND HEMATOCRIT FOLLOWING ADMINISTRATION OF DIBENZYLINE TO HAEMORRHAGIC SHOCK DOGS

TIME IN MINUTES	0	30	60	90	150	210	Res. Blood	270	330
CONTROL DOGS									
pH	7.36		7.17	7.17	7.16	7.17	7.34	7.29	7.45
pCO_2 in mm Hg	37.5		18.8	20.3	23.6	20.6	34.2	21.5	24.5
HCO_3 in meq/l	20.3		8.2	8.7	9.5	9.9	18.8	11.9	15.8
Lactic acid in meq/l	2.7		10.02	11.36	10.1	12.05	4.98	7.2	
Chlorides in meq/l	117	114		114	114	115	117	100	119
Sodium in meq/l	145	143		144	146	146	146	147	
Potassium in meq/l	4.1	5.4		5.5	5.8	6.1	6.4	5.0	6.0
Hematocrit %	46	45		43	49	52	43	54	52

TABLE 17 (Cont'd.)

TIME IN MINUTES	0	30	60	90	150	210	Res. Blood	270	330
DIBENZYLINE DOGS									
pH	7.42	7.38		7.3	7.29	7.32		7.29	
pCO_2 in mm Hg	34.4	27.7		21.1	22.3	26.1		26.4	
HCO_3 in meq/l	19.9	15.1		11.2	10.1	12.6		13.1	
Lactic acid in meq/l	2.57	4.27		8.4	7.63	4.61		6.07	
Chlorides in meq/l	113	112		111	114	113		112	
Sodium in meq/l	142	144		143	149	143		144	
Potassium in meq/l	4.0	3.6		4.2	4.1	4.4		4.6	
Hematocrit %	48	48		48	50	44		49	

TABLE 18

EFFECTS OF DIBENZYLINE, HAEMORRHAGIC SHOCK AND ENDOTOXIN SHOCK ON pH AND BICARBONATE AFTER CORRECTION OF PCO_2 TO 40 MM/Hg

TIME IN MINUTES	0	30	90	150	210	270
Endotoxin and Early Dialysis						
pH	7.20	7.16	7.18	7.19	7.12	
PCO_2	40	40	40	40	40	
HCO_3	20.5	17.5	18.0	19.0	17.5	
Lactic acid	3.57	4.79	5.71	6.23	5.98	
(Endotoxin and Early Dialysis) Control						
pH	7.25	7.17	7.1	7.12	7.14	
PCO_2	40	40	40	40	40	
HCO_3	22.5	17.5	14.0	15.0	16.0	
Lactic acid	3.01	4.99	5.68	6.22	5.72	
Endotoxin and Mechanical Effects of Dialysis						
pH	7.21	7.12	7.06	7.08	7.12	7.03
PCO_2	40	40	40	40	40	40
HCO_3	20	15	11.0	12.5	20	10
Lactic Acid	4.37	4.83	6.00	5.55	5.92	5.88

TABLE 18 (Continued)

TIME IN MINUTES	0	30	60	90	150	210	Res. Blood	270	300
Haemorrhagic Control Group									
pH	7.26	7.04		7.0	7.0	7.06		7.0	
PCO_2	40	40		40	40	40		40	
HCO_3	17	10.5		8.0	6.5	12.5		8.0	
Lactic acid	4.06	10.12		11.6	14.71	7.6		10.0	
Haemorrhagic Dialysis Group									
pH	7.34	7.06		7.0	7.0	7.22		7.17	
PCO_2	40	40		40	40	40		40	
HCO_3	27.5	11.5		8.0	8.2	20		17.0	
Lactic acid	2.8	9.3		10.0	9.7	6.5		7.0	
(Haemorrhagic) Dibenzyline Group Control									
pH	7.33		7.03	7.05	7.05	7.05	7.29	7.16	7.32
PCO_2	40	40	40	40	40	40	40	40	40

TABLE 18 (Continued)

TIME IN MINUTES	0	30	60	90	150	210	Res. Blood	270	300
(Haemorrhagic) Dibenzyline Group Control (Cont'd.)									
HCO_3	28.0		10	10.8	10.8	11.0	25	19.0	26.5
Lactic acid	2.7		10.02	11.36	11.1	12.05	4.98	7.2	
Haemorrhagic Dibenzyline Group									
pH	7.37	7.29		7.18	7.17	7.22		7.2	
PCO_2	40	40		40	40	40		40	
HCO_3	32.5	25.0		18.0	17.5	20		19	
Lactic acid	2.57	4.27		8.4	7.63	4.61		6.07	

pCO_2 in mm Hg HCO_3 and Lactic acid in meq/l

TABLE 19

COMPARATIVE CHART OF SURVIVAL TIME IN HOURS OF DOGS SUBJECTED TO DIBENZYLINE, ENDOTOXIN SHOCK AND HAEMORRHAGIC SHOCK

DOG NUMBER		1	2	3	4	5	6	7	8	9	10	11
Endotoxin Control Group		8	8	10	7.5	5	2.5	9	4.75	30▼	3	3.75
Endotoxin & Mech. Effects of Dialysis		3.5	10	7	28	10	10	10.5	9	3	9	
Delayed Dialysis		30▼	30▼	30▼	9	7.5	30▼	5	24	24	30▼	
Early Dialysis Old & New Coils		8	30▼	20	9.5	9.5	30▼	30▼	9.5	8.5	30▼	
Early Dialysis New Coils		30▼	24	30▼	24	30▼	30▼	30▼	24	30▼	30▼	
Endotoxin & Morphine	C	30▼	4	30▼	30▼	2						
	E	24	24	8	10	12						
Haemorrhagic Control Group		3	10	8	10	30▼	8	3.5	30▼	10	9	

TABLE 19 (Continued)

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	11
Haemorrhagic Dialysis Group	8	30*	8.5	20	4.5	3.5	30*	14	24	30*	
Haemorrhagic Dibenzyline	5	30'	30'	2.5	3	20	10	12.5	30	3.5	
Haemorrhagic Dibenzyline Control	3.5	11	20	9	12	9	4.5	7	24	30*	

C = Control

E = Experimental

TABLE 19 (Cont'd.)

DOG NUMBER	12	13	14	Mean	Number of Survivors	Survival Rate
Endotoxin Control Group	6	24	24	10.4	1	7%
Endotoxin and Mechanical Effects of Dialysis				10.1	1	10%
Delayed Dialysis Old and New Coils				20.4	5	50%
Early Dialysis Old and New Coils	30*	30*	30*	20.0	7	50%
Early Dialysis New coils only				28.2	7	70%
Endotoxin and Morphine C				19	3	60%
E				15.6	0	0%
Haemorrhagic Control Group				12.2	2	20%
Haemorrhagic Dialysis Group				17.2	3	30%
Haemorrhagic Shock Dibenzyline				14.0	3	30%
Haemorrhagic Shock Dibenzyline Control				13.0	1	10%

C = Control E = Experimental

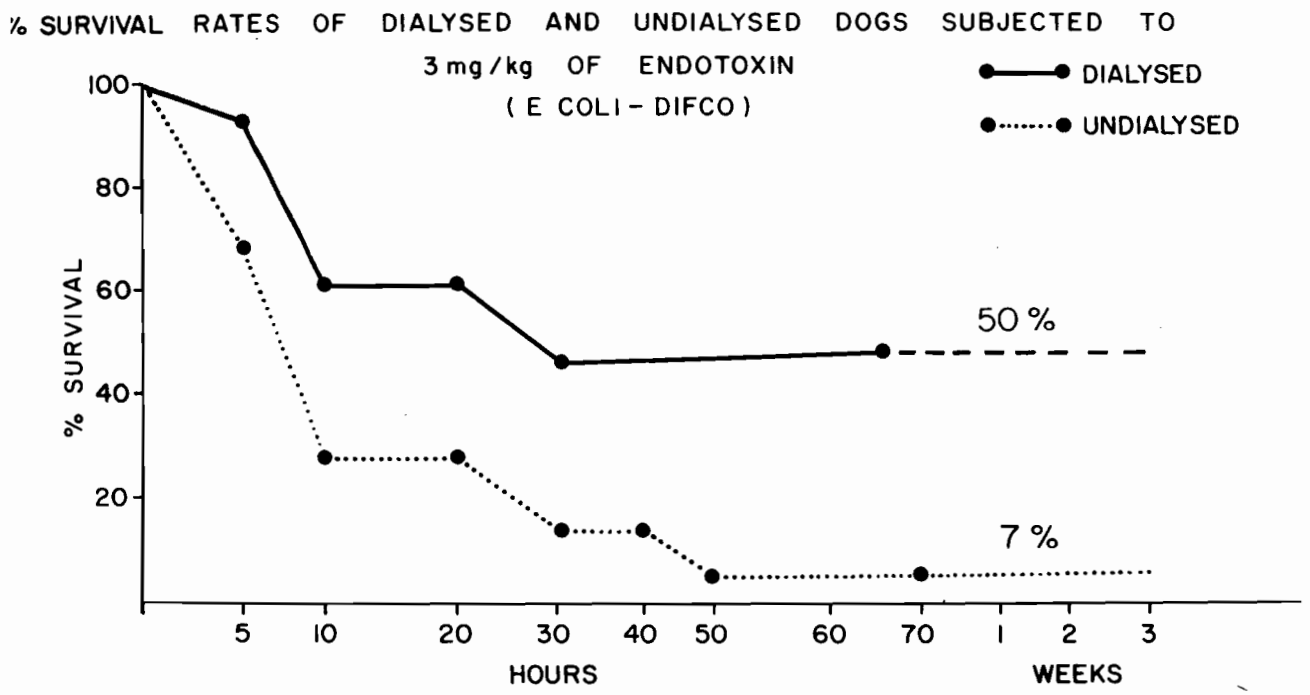
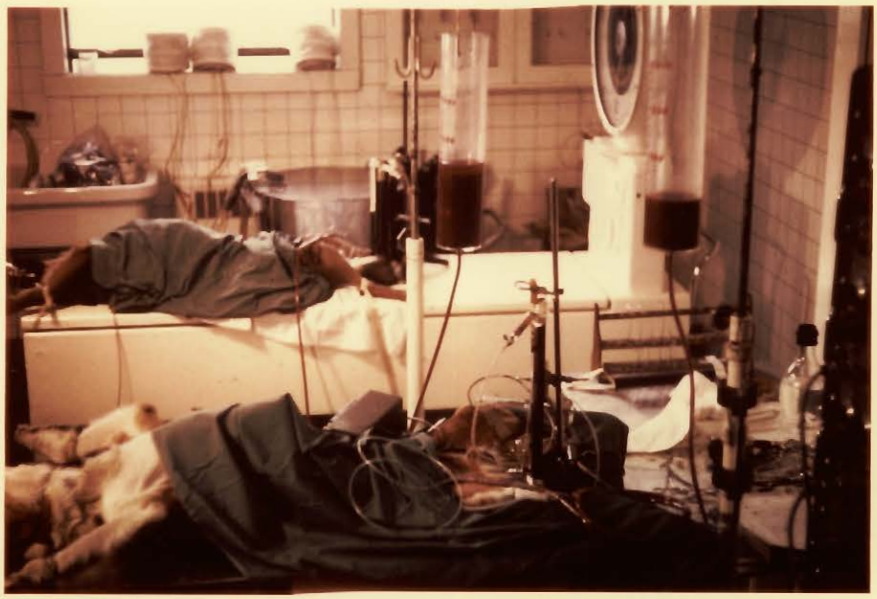


Fig. 13.--The highest mortality rate in both control and experimental dogs lies between one and ten hours. After this period, most dogs live permanently.

PHOTOGRAPH VIII



These two dogs have almost identical weights. Both dogs were subjected to Wiggers-Fine Technique of haemorrhagic shock. Both dogs have a blood pressure of 50 mm Hg. The dog on the Weight Scale Model 9281 (Toledo) has a bleeding volume of 1,100 cc of blood in the reservoir, while the dibenzyline dog in the foreground has a bleeding volume of 500 cc.

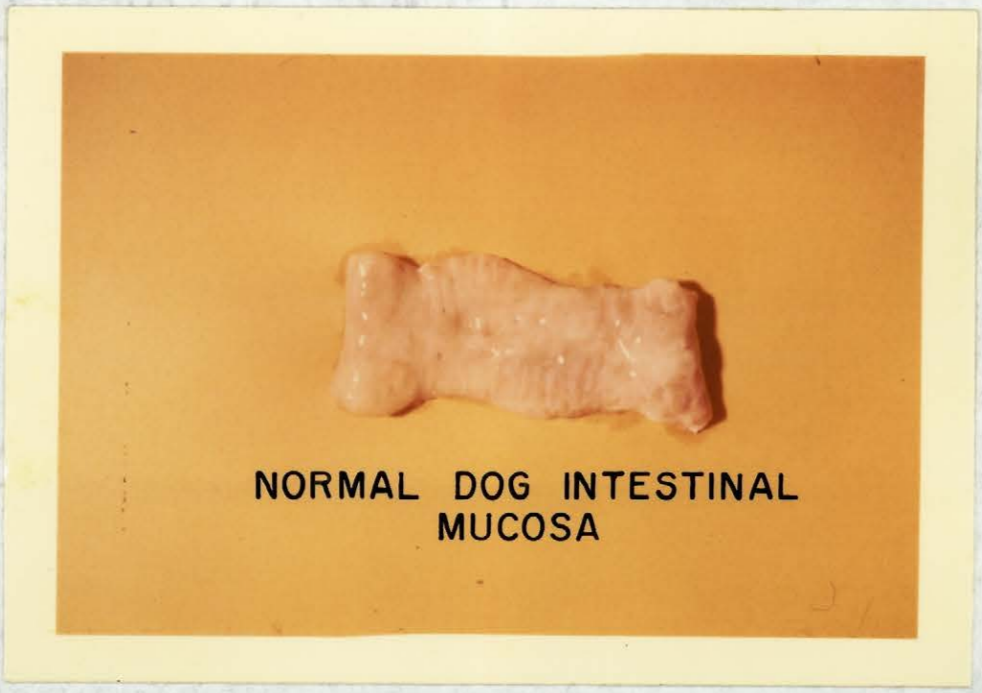
In the dogs that were dialysed early with new coils only, the survival rate was seventy percent out of a total of ten healthy mongrel dogs. Among the ten dogs out of fifteen that were dialysed $3\frac{1}{2}$-4 hours post endotoxin injection, five (50%) were permanent survivors while in the five control animals, there was only one (10%) permanent survivor. The survival rate of the mechanical-effects-of-dialysis dogs closely resemble that of all control dogs subjected to endotoxin. Out of ten dogs subjected to this procedure, only one lived up to twenty-eight hours. The mean survival time is almost identical with that in the control group of early dialysis; 10.1 hours and 10.4 hours respectively.

However, of the ten morphine dogs, four (40%) were permanent survivors. The experimental group had one (10%) permanent survivor out of five dogs, while the control dogs had three (60%) out of five permanent survivors.

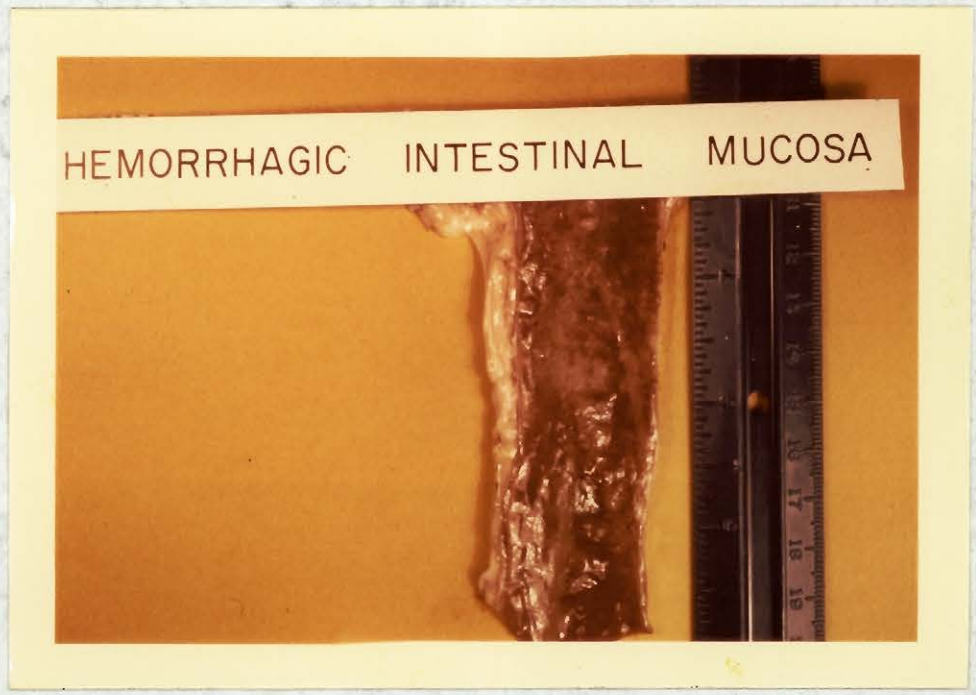
c) Haemorrhagic Group--Out of a total of forty dogs employed in this experiment, nine (22.5%) were permanent survivors. In the ten animals subjected to haemorrhagic shock and hemodialysis, three (30%) were permanent survivors, while only two (20%) of the ten control dogs in this group survived permanently.

The control group of the dibenzyline dogs which resembled the control of the haemorrhagic shock and dialysis dogs, had one (10%) permanent survivor out of ten dogs. The other ten animals which received .5 mg/kg of dibenzyline had three (30%) permanent survivors.

PHOTOGRAPH IX



PHOTOGRAPH X



A piece of small intestine was taken from a dog which lived 8 hours after endotoxin injection. The mucosa looks oedematous and haemorrhagic. The same pathological findings were observed in non survivors subjected to haemorrhagic shock.

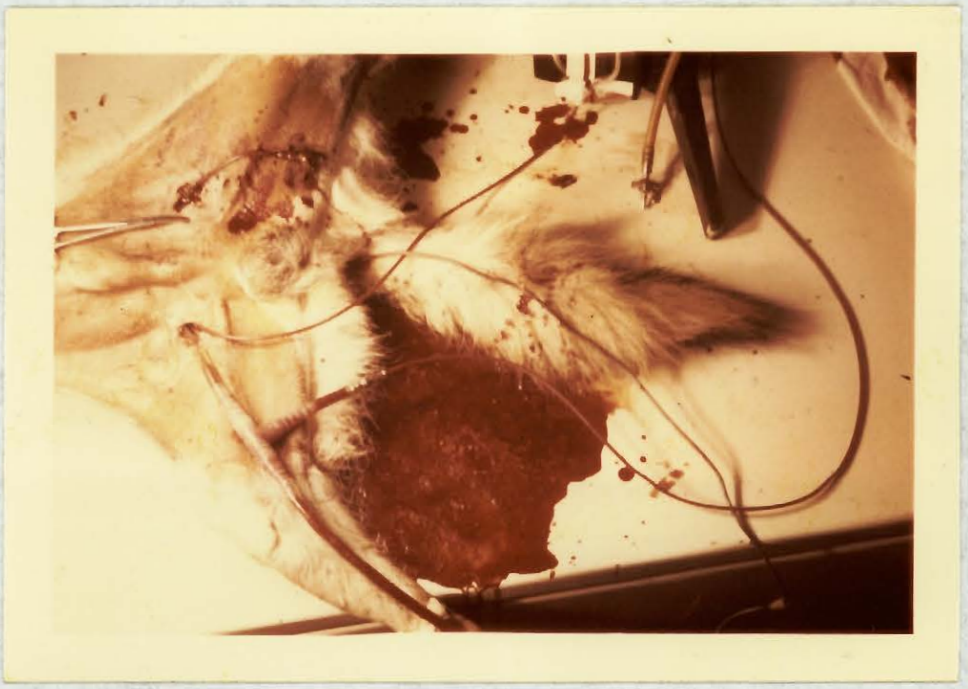
5: NECROPSY FINDINGS (Photographs IX and X)

All the ten normal dogs subjected to haemodialysis with or without antibiotics were autopsied. In those dogs which died and had not received antibiotics, the lungs were congested, haemorrhagic, soggy and covered with white-greyish mottled patches. The liver was also covered with these whitish lesions. These findings were highly suggestive of septicemia. Both large and small intestines were unremarkable. The permanent survivors who were donors, were also opened immediately after death, and no gross pathological lesions were noted in the viscera.

Ten of the endotoxin group that had died in shock were also autopsied. The significant findings were bluish purplish serosa of the small bowel from the upper jejunum to the ileum. On opening the small bowel, bloody yellowish fluid was found. The mucosa was oedematous, congested and haemorrhagic and some mucosal ulcerations were seen in some segments of the small bowel.

In the twenty haemorrhagic shock dogs, the same haemorrhagic phenomenon in the mucosa of the small intestine was noticed. In addition to these findings, the spleen was extremely contracted and rubbery in consistency. The five dibenzyline dogs that were autopsied did not show as much of a severe haemorrhagic necrosis of the bowel as the five control dogs. All the five permanent survivors that were sacrificed after thirty hours did not show these gross pathological

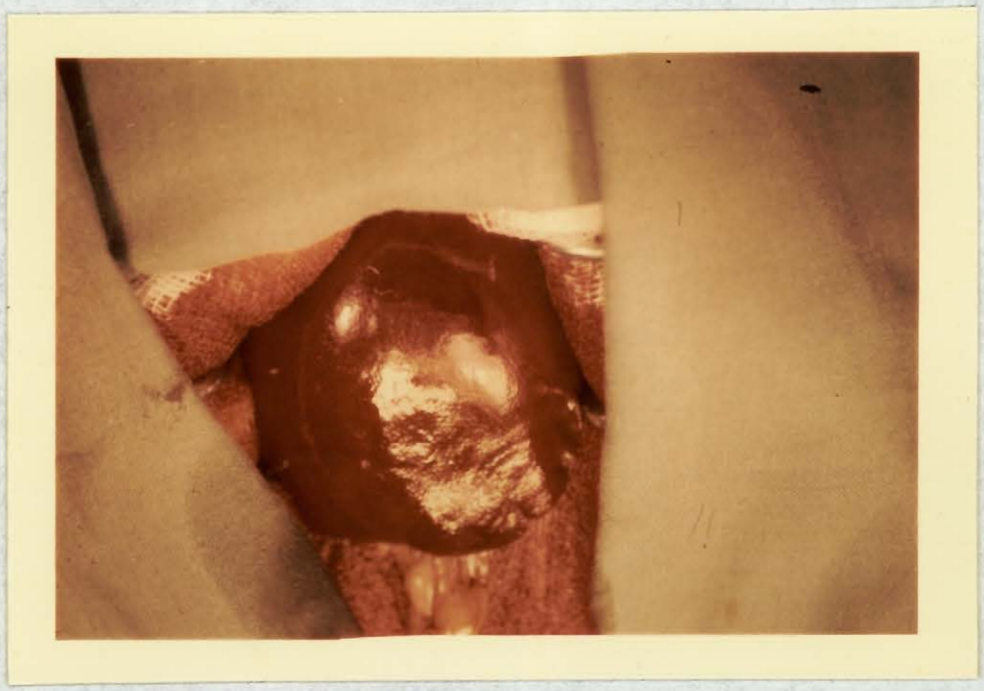
PHOTOGRAPH XI



BLOODY DIARRHOEA IN A HAEMORRHAGIC SHOCK DOG

This dog began having bloody diarrhoea after 2½ hours in haemorrhagic shock. The shed blood had already been reinfused into the dog.

PHOTOGRAPH XII



This is the appearance of a normal liver. Notice the beefy, reddish, healthy colouration of this organ.

PHOTOGRAPH XIII

After administration of 3 mg/kg of endotoxin to the same dog, the capsule becomes very tense. The liver becomes engorged with a tremendous amount of blood and it changes its normal colour to a blue-blackish appearance. These changes last for two hours or more.

changes.

Often some dogs would start having a bloody diarrhoea after $2\frac{1}{2}$-$3\frac{1}{2}$ hours in shock. (Photograph XI)

6: OTHER FINDINGS

Three histamine dogs, that were opened through a midline incision to visualize the liver, showed gross interesting changes in the liver as the dog went deeper into shock. The beefy-reddish appearance of the liver (Photograph XII) progressively became darker (Photograph XIII) to an almost black colour in one hour after the administration of endotoxin. The capsule became tense as the colour deepened. After two hours and a half of these observations, the liver did not seem to regain its normal colour.

7: EFFECTS OF ENDOTOXIN SHOCK AND DIALYSIS ON BLOOD CHEMISTRIES, ELECTROLYTES AND HEMATOCRIT IN DOGS

a) ELECTROLYTES (Tables 4 and 12) (Appendices IV, V, and VII)

In the endotoxin group, chemistries, electrolytes and hematocrits were determined in fourty-five dogs.

1. Chloride--The mean chlorides in both control and experimental dogs remained at practically the same level. There was a slight hyperchloremia at the end of $3\frac{1}{2}$ hours. Examining the individual values of the chloride anion, there is a general tendency of increasing plasma chloride as the dog goes deeper into shock. Nineteen dogs out of a total of forty-five endotoxin dogs showed this tendency of slight hyperchloremia with progressive shock.

2. Sodium--Plasma sodium shows the opposite tendency of the chloride anion in both dialysed and control dogs. Only six dogs in this series showed a slight increase in sodium cation as the dog sank deeper into shock. In fact, there was a progressive lowering of the mean sodium values in all the dogs.

3. Potassium--In dialysed dogs and in dogs subjected to endotoxin and mechanical effects of dialysis, there was a general fall of plasma potassium during the shock period. On the other hand, in the control group, there was a general increase in plasma potassium levels during the experimental period.

4. Hematocrit--Hematocrit levels increased with increasing shock except in dialysed dogs where the tendency at progressive falling or stabilization of hematocrits was observed. The mechanical-effects-of-dialysis dogs showed the same tendency.

b) CHEMISTRIES

1. pH --(Normal arterial blood chemistries are shown on Table 21.) The mean pH in all the endotoxin dogs which had been followed for three and a half hours was 7.33. However, in the endotoxin-mechanical-effects-of-dialysis dogs, that were followed for 270 minutes, the mean pH was 7.27. On the whole these dogs did not manifest an acidosis of significance.

TABLE 20

COMPARATIVE CHART OF TIME IN MINUTES BEFORE DOG STARTS REINFUSION

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Haemorrhagic Control Dogs	25	50	25	40	100	45	40	50	40	110	53
Haemorrhagic Dialysed Dogs	55	30	60	50	30	50	50	50	40	80	50
Dibenzyline & Haemorrhagic Shock Dogs	50	50	100	N.R.	N.R.	N.R	90	N.R	N.R	N.R	29
Haemorrhagic Shock Control Dogs	90	90	75	50	50	75	90	90	90	90	79

N.R. = No Reinfusion

TABLE 21

A. ARTERIAL BLOOD CHEMISTRIES OF NORMAL UNANESTHETIZED DOGS

DOG NUMBER	1	2	3	4	5
pH (Blood)	7.42	7.41	7.38	7.86	7.43
pH (Serum)	7.28	7.22	7.24	7.30	7.24
pCO_2 in mm Hg	32.3	27.8	32.0	37.2	28.0
Bicarbonate in meq/l	20.20	17.8	18.6	21.2	18.5
Lactic acid in meq/l	1.8	2.3	2.03	1.4	1.4

TABLE 21 (Continued)

ARTERIAL BLOOD CHEMISTRIES OF NORMAL UNANESTHETIZED DOGS
AFTER CORRECTION OF pCO_2 TO 40 MM, Hg

BB

DOG NUMBER	1	2	3	4	5
pH (Blood)	7.37	7.32	7.34	7.61	7.34
pH (Serum)	7.23	7.20	7.20	7.29	7.16
pCO_2 at 40 mm, Hg	40	40	40	40	40
Bicarbonate in meq/l	20.1	18.0	19.8	25.0	16.5
(Blood)	30	27.0	27.5	40.0	27.6
Lactic Acid in meq/l	1.8	2.3	2.0	1.4	1.4

However, in correcting the pCO_2 to 40 mm Hg, the pH becomes markedly lower from the average of 7.33 to 7.1, even as low as 7.0. The lowest mean pH was found in the haemorrhagic shock control dogs. (Table 18) On the whole, the dialysed dogs showed a higher pH than the controls. The controls on the other hand showed higher pH averages than the dogs subjected to endotoxin and the mechanical effects of dialysis.

2. pCO_2 -- The control dogs showed a reduction of pCO_2 from the control almost by half. This reduction was maintained throughout the experimental period. There is a similarity of mean pCO_2 in the endotoxin-mechanical-effects group and endotoxin control dogs. The mean pCO_2 in dialysed dogs was maintained at practically the same control value throughout the observation period.

3. Bicarbonate--There was a tendency in the control group to maintain its bicarbonate level at $9 \pm 1.f$ meq/l. Individual results showed that bicarbonate concentrations were markedly reduced during the first half hour of endotoxin shock. The endotoxin-mechanical-effects-of-dialysis dogs showed a marked depression of mean HCO_3^- during the experimental period. Dialysed dogs showed a fairly steady level of HCO_3^-. Even bicarbonate values of individual dogs showed this steady tendency. When the pCO_2 was corrected to 40 mm Hg, the bicarbonate values were much higher than the previous figures. (av. 6 meq/l)

4. Lactic Acid--There was a general tendency for gradual elevation of lactic acid from the control levels. Lactic acid in the endo-

toxin-mechanical-effect-of-dialysis dogs reflected the same tendency, as in the endotoxin control dogs. Dialysed dogs also showed a slight rise of lactic acid during the experimental period. The tendency towards elevation of lactic acid was noted in individual dogs as a whole.

In the endotoxin dogs, the chemistries were not markedly different from normal. However, when pCO_2 was corrected to 40 mm Hg, there was a drop in pH to very severe acidotic levels. On the whole, dialysed dogs seemed to retain higher pCO_2 values than the control dogs. Bicarbonate showed progressive depletion during shock. On correction of pCO_2 to 40 mm Hg, there was a tendency towards preservation of base bicarbonate to normal values. Lactic acidosis, although not very severe was observed in all dogs.

8: EFFECTS OF HAEMORRHAGIC SHOCK, DIBENZYLINE AND DIALYSIS ON BLOOD ELECTROLYTES, CHEMISTRIES AND HEMATOCRIT
(Appendices XIX, XXI, and XXIII)

a) ELECTROLYTES

1. Chloride--The two control groups in this series are almost identical. Mean chloride of the twenty dogs also manifested a tendency towards hyperchloremia at the end of 4½ hours. The mean values of chloride of this group markedly resembled the endotoxin control group. Dibenzyline dogs exhibit lower plasma chloride when compared with the controls. However, the dialysed haemorrhagic shock dogs did not have chloride mean values that were lower than the controls. In fact, the figures were very similar. On the whole, the dialysed endotoxin group showed lower mean plasma chloride than the dialysed haemorrhagic shock dogs.

2. Sodium--The mean plasma sodiumwas higher in the ten dogs which served as controls of the dialysed haemorrhagic shock dogs than in all the other thirty dogs in this group. There was little difference in plasma levels between the dibenzyline dogs and the dialysed haemorrhagic shock animals. Plasma values in this group generally resembled the endotoxin group.

3. Potassium--Potassium levels in control dogs showed a tendency to rise as the dog sunk deeper into shock, while dialysed haemorrhagic shock dogs manifested little changes from the control values. However, the dibenzyline dogs showed lower mean values by 2 meq/l of potassium throughout the experimental period. In all the endotoxin group, the potassium levels were much lower than in the haemorrhagic group.

4. Hematocrit--There was a general tendency in the elevation of hematocrit in the control dogs. While in the dibenzyline and the dialysed dogs, hematocrits seemed to remain fairly steady during shock. The hematocrit of the control in this group very much resembles the endotoxin and early dialysis control dogs. Both groups showed a general tendency towards hematocrit elevations as the dogs went into irreversible shock.

b) CHEMISTRIES

1. pH -- The pH in all the control dogs was extremely acidic for the first two hours. In one group of control dogs, the pH remained

at 7.1 plus a fraction until the end of the experiment. However, in the other ten control dogs, pH returned to preshock levels after reinfusion of the blood into the dog. While the ten dialysed haemorrhagic shock dogs also manifested a strong acidotic state for the first two hours, after reinfusion and dialysis, the pH went up markedly almost to control values after treatment. The dibenzyline group did not have a single mean pH which was below 7.2 throughout the whole experimental period. The pH remained at this high level during shock. It was also noted that in the endotoxin dogs, the pH reservoir blood was determined before reinfusion, the average was 7.34. Correcting the pCO_2 to 40 mm Hg, the control group showed a severe depression of pH to 7.0. However, in one control group of ten dogs, there was an elevation of pH to control levels at the end of the experiment. The control group that showed severe acidosis had two permanent survivors out of ten (20%) and mean survival hours of 12.2, while the other control group, which showed an elevation of pH to preshock levels at the end of 4½ hours, had one permanent survivor (10%) and an average survival time of 13 hours. The dibenzyline dogs, even after correction of pCO_2, did not show pH values below 7.1, while the dialysed haemorrhagic shock dogs still showed a slight elevation of pH during and after hemodialysis. The severity of the acidosis in corrected pH of the control in haemorrhagic dogs resembled the endotoxin-mechanical-effects-of-dialysis dogs.

2. pCO_2 -- In all the control dogs there was a tendency of marked reduction of pCO_2 from the control values. Sometimes these mean values were almost half the preshock values. It was noted that

pCO_2 was generally lowered by not less than 10 mm Hg during the period of shock. This same phenomenon was observed in dialysed haemorrhagic shock dogs. The dibenzyline dogs on the whole, while they reduced their pCO_2 by 5 mm Hg, were able to maintain it at the same level during the experiment. The pCO_2 values of dialysed endotoxin dogs very much resembled the dibenzyline haemorrhagic shock dogs. In the endotoxin animals, except for the dialysed group, the pCO_2 tended to be lower than in the haemorrhagic dogs. It was of interest to note that the blood reservoir pCO_2 did not fall below 33 mm Hg. (Table 18)

3. Bicarbonate--There was a progressive severe depression of bicarbonate in all dogs except the dibenzyline group, during the first 2½ hours of shock. There was a general tendency towards elevation of bicarbonate values after reinfusion and dialysis. Even the control dogs which were not dialysed showed this bicarbonate elevation towards the end of the experiment. One remarkable observation was that the dibenzyline group maintained their bicarbonate levels above 10 meq/l till the end. The reservoir pCO_2 stayed at the same control values.

Correcting pCO_2 to 40 mm Hg, the control haemorrhagic shock dogs show a severe depletion of base bicarbonate reserve to values as low as half the preshock levels. It was noted, even in the corrected bicarbonate concentration, that post reinfusion figures tended to be higher than the preceding shock values. Dibenzyline dogs preserved their base bicarbonate throughout the critical stages of shock. In this group there was no depletion of bicarbonate to levels as low as

those found in control dogs. Dogs subjected to dialysis showed an increase in base bicarbonate two times higher than the preceding values. Even in the endotoxin dogs, there was a general tendency of preservation of base bicarbonate throughout dialysis. It was also interesting to observe that in the endotoxin-mechanical-effects-of-dialysis dogs, which also received normal saline during the process, there was a progressive reduction of bicarbonate similar to the other control groups in endotoxin and haemorrhagic shock.

4. Lactic Acid--There was progressive elevation of lactic acid within half an hour to one hour of haemorrhagic shock. In the control dogs there was a reduction of lactic acid for the hour immediately following reinfusion of the reservoir blood into the dog. The dibenzyline dogs maintained a steady level of lactic acid. No value of lactic acid in this group exceeded 8.4 meq/l for 4½ hours. The experimental dogs showed a slight drop of lactic acid concentration following dialysis. Reservoir lactic acid was lower than the lactic acid in the dog. In contrast to the marked acidosis of the haemorrhagic dogs, the endotoxin animals manifested a low degree of lactic acidosis during shock; no values were higher than 6.0 meq/l in the endotoxin shock dogs.

CHAPTER V.

DISCUSSION.

An attempt has been made to demonstrate the efficacy of haemodialysis in the treatment of endotoxin and haemorrhagic hypotension. One hundred and thirty-four dogs were employed in this study. Seventy-nine were given 3 mg/kg body weight of endotoxin under various conditions of shock. Using a modified Wiggers-Fine technique, forty dogs were subjected to haemorrhagic shock, ten of which were dialysed.

The initial drop in blood pressure after initiation of dialysis is probably due to a decrease in venous return to the heart from the coil as a result of disparity in the volume of blood received by the dog and the volume of blood returning to the coil during the first few minutes of dialysis. It is possible that the femoral vein may be in spasm. This incipient drop in blood pressure after initiation of dialysis is seen in all dogs which undergo this form of treatment. When the animal has adjusted itself to this form of stress, the vital signs tend to level off to normal values. The period where all the parameters remained fairly constant is suggestive of a state of 'physiological equilibrium'. This is probably indicative of a period where perfusion of vital organs is satisfactory during dialysis.

It seems that regardless of what form of shock an animal is subjected to, there is a period where tachycardia is very much marked. This is usually seen after the animal has been in shock for two and one half hours. Tachycardia which was observed in many animals during shock was markedly less pronounced in dibenzyline dogs. Tachycardia is a compensatory circulatory mechanism. Since dibenzyline causes blood to be physiologically distributed in equal amounts to all parts of the body without preference to any particular organ, sufficient tissue perfusion and increased cardiac output may explain the relative absence of tachycardia in dibenzyline dogs subjected to haemorrhagic shock. As a whole, a tachycardia of over three hundred beats per minute indicates a poor prognosis. A progressively falling blood pressure is, in spite of transfusion, indicative of the irreversible stage. These two grave prognostic signs are also encountered in humans with bacteremic and haemorrhagic shock (Kinney et al, 1962), (Wilson, 1963). A dog whose systemic blood pressure stays above a hundred during dialysis and after reinfusion has a good chance of surviving longer or permanently. Probably the reason for this is that at this state the vital organs, notably the kidney, the intestines, the brain and the liver are well perfused and well oxygenated due to elimination of anoxia. The liver, by receiving sufficient nutrition, metabolises lactic acid efficiently and thus prevents occurrence of acidosis which enhances metabolic derangements that play an

important role in the irreversible phenomenon.

The initial dramatic period of hypotension which follows administration of endotoxin may be due to a sudden release of some vasoactive substance, possible histamine, but no significant amount of histamine in blood or plasma was extracted during this period. Perhaps a more sensitive technique is needed to exclude histamine as the cause of this dramatic post endotoxin injection hypotension. Schayer et al (1960 a, 1960 b) believe that histidine decarboxylase activity is markedly increased during the first two and one half hours of shock. Alican and Hardy (1961) found that this initial hypotension period of endotoxin shock was accompanied by elevation of portal vein pressure and an increase in thoracic duct lymph flow. The direct relationship between the hypotension itself and these physiological phenomena have not been established. Concomitant bradycardia is often noticed during this period. Heart rate may drop to levels as low as 80 beats/minute. It is possible that bradykinins and other allied kinins are released by endotoxin.

Administration of dibenzyline causes a dramatic fall of blood pressure not unlike that observed in endotoxin shock. The dibenzyline hypotension occurs ten to fifteen minutes after the administration of the drug. It is preceded by higher amplitudes on the polygraph tracing. This may be indicative of increased myocardial contractile strength which is partly responsible for

the increased cardiac output observed with this drug (Vassant et al, 1963), (Nicherson et al, 1959), (Vick et al, 1963).

Morphine as an 'anaesthetic agent' does not seem to cause as much hypotension as nembutal. This may explain why on the whole these dogs have higher blood pressure averages throughout shock than the nembutal dogs.

Hyperventilation is observed at the beginning of each haemorrhagic shock experiment and towards the end. This phenomenon is also observed with endotoxin administration. This initial hyperventilation is probably reflex in origin. The vasomotor respiratory centre attempts to adjust itself to the sudden onslaught by some noxious stimulus.

When the animal is already in shock or going into irreversible state another phase of compensatory hyperventilation is observed. The animal, in trying to compensate for the rising lactic acid, blows off CO_2. Thus the pCO_2 of haemorrhagic and endotoxin shock dogs is characterized by progressive fall as the dog sinks into irreversibility.

The dibenzyline dogs maintain a fairly constant temperature throughout the experimental period. The reason may be due to the less acidotic state of this group of dogs throughout the hypotensive period. In spite of the severe hypotension encountered in the dibenzyline dogs, there is less acidosis in this group than in the other groups of dogs subjected to the same pattern of hypotension.

Therefore the severity of hypotension in shock does not necessarily mean greater metabolic disturbances. There is no definite relationship between severe hypotension alone and the irreversible state. In spite of correction of hypotension by reinfusion of the shed blood and infusion of normal saline, 40% of the twenty haemorrhagic shock dogs went into irreversible state and died, while in endotoxin shock where thirty-four out of seventy-three dogs received no infusion at all, 66% survived permanently (Tables 6 and 19).

The venous pressures tend to rise at the beginning of each experiment from 10.7 to 14.1 cm of water (average 12.4) in normal dogs subjected to dialysis alone. In endotoxin shock dogs, the range of initial venous pressure is from 3.6 to 8.5 cm water (average 6.0) in both experimental and control dogs. In the haemorrhagic group of dogs, mean venous pressures ranged from 4.3 to 6.7 cm water (average 6.5). The depression of venous pressures in haemorrhagic shock sometimes to negative values may be a reflection of peripheral venomotor disturbances. Reinfusion of reservoir blood temporarily restored the venous pressure to normal levels, indicating that a temporary improvement in cardiac output and tissue perfusion follows restoration of blood volumes to normal.

The dogs, being lightly anaesthetized, were 'whining' at the beginning of the experiment. This grunting like respiration increased intraabdominal pressure (Val Salva Maneuver) and led to

rather elevated venous pressures. This also explains why the normal dogs subjected to haemodialysis alone showed the highest initial mean venous pressures. Terminal elevation of venous pressure is a reflection of decreasing venous return secondary to the failure of the 'pump' to function efficiently. It was also observed that some permanent survivors exhibited elevated venous pressures at the end of five hours. The reason for this was that the dogs were already recovering from shock and were ready to jump off the table. This behaviour was frequently observed in endotoxin-morphine permanent survivors.

The progressive fall of temperatures during haemorrhagic and endotoxin shock is summarized in the appendices. This progressive fall in temperature may be due to the dog's loss of heat to its ambient environment such as the scale and/or the room or it may be a reflection of decreased metabolic rate secondary to reduction of effective circulating blood volume to vital organs and thermoregulating centres of the brain. Temperatures of haemorrhagic shock dogs under the same experimental conditions showed a tendency to drop lower than the endotoxin dog's temperatures. This is suggestive of a metabolic rather than the environmental cause in the behaviour of temperature during shock (Vassant et al, 1963), (Longerbeam et al, 1963), since the both groups of dogs were exposed to the same environment during the experimental period.

That there is peripheral vascular resistance during haemorrhagic shock is shown by the great resistance to reinfusion of the reservoir blood into the dog after two and one half hours in shock. This is the reason why a 50 cc Luer Lock syringe had to be employed to reinfuse the dogs intraarterially. The resistance was hardly encountered in the dogs which were pretreated with dibenzyline. In fact, most of these dogs auto reinfused by mere elevation of the reservoir stand to a higher level.

This simple experimental observation stongly supports the arguments of those who advocate the use of ganglionic blockers during shock to overcome the vasospastic effects of endogenous catecholamines.

The average weight loss of a dog during five to six hours of haemorrhagic and endotoxin shock is 1.5 kg. This is probably due to evaporation and loss of water through the respiratory system. Out of ten dogs subjected to mechanical effects of dialysis, in spite of restoration of the weight lost during the experimental period, only 10% survived. This observation implies that replenishment of lost fluid alone does not alter the course of irreversibility.

The major blood changes in both haemorrhagic and endotoxin shock, particularly in the former, consists of decreases in arterial pH, pCO_2 and bicarbonate concentration with increases in the concentration of lactate. The pH of control arterial blood

varies between 7.28 and 7.44 (Dittmer, 1961) (Table 21) , averaging 7.33. During endotoxin shock, the pH of both experimental and control animals remained practically within normal limits ranging between 7.27 and 7.38 (average 7.34) while in haemorrhagic shock dogs, pH ranged between 7.12 and 7.38 (average 7.25). In the endotoxin group there was hardly any difference between the pH of dialysed dogs and that of the control dogs. The reason for this similarity may be that the dogs were not followed for a period of over five hours. Probably, if blood studies were made eight to ten hours after endotoxin administration, the pH might have shown significant acidotic levels. However Vassant, Weil et al (1963), working on patients with bacteremic hypotension, found no significant acidosis in these patients. Their blood pH value was also normal and the pCO_2 measurements showed no consistent values. Correcting the pCO_2 to 40 mm Hg the pH becomes highly acidic in both experimental and control dogs, ranging from 7.03 to 7.25 (average 7.14). The dialysed dogs do not show any significant correction of pH to normal values (Table 18).

After correction of pCO_2, haemorrhagic shock dogs show a very severe acidosis with the pH ranging from 7.0 to 7.37 (average 7.18). After initiation of dialysis there is a slight elevation of pH from 7.0 to 7.22. Dialysis does seem to counteract metabolic acidosis either by diluting the acids or by dialysing out lactic and phosphoric acids through osmolarity

gradient difference between the bath and the plasma.

Dibenzyline dogs show the least pH depression in haemorrhagic shock dogs. This attempt at maintaining a normal pH during haemorrhagic shock is perhaps indicative of the drug's ability to prevent aggregation of cells, improve tissue perfusion and counteract the formation and accumulation of metabolites. It seems that prevention of metabolic derangements and accumulation of tissue metabolites play one of the key roles in the irreversible phenomenon. Dibenzyline is antiadrenergic and therefore improves the tissue perfusion by relief of venous spasm, prevention of blood sequestration and collection of by-products of anaerobic metabolism.

It is also interesting to note that blood reservoir pH, pCO_2, bicarbonate and lactic acid were within normal limits (Table 18). This blood has not undergone the active anaerobic metabolism that goes on in a dog that is in shock.

Normal arterial pCO_2 in a dog ranges between 30.0 and 43.7 (average 36.4). There is general reduction of pCO_2 during haemorrhagic and endotoxin shock (Table 4). This is more marked in haemorrhagic shock dogs which did not receive any treatment. The general depression of pCO_2 was less marked in those dogs which were treated with dibenzyline. In both endotoxin and haemorrhagic shock dogs treated with dialysis there was less depression of

pCO_2 (Table 15). The increased pulmonary ventilation that occurs during shock is responsible for the general reduction of plasma pCO_2. The more severe the acidosis the more the animal hyperventilates in order to compensate. Reduction of pCO_2 leads to reduction in plasma bicarbonate concentration. The nature of the acid-base changes is shown by the graph on Figures 14 and 15 which show a positive relationship between bicarbonate concentration and lactic acid. This is indicative of the fact that the chief metabolite responsible for acidosis is lactic acid. As dibenzyline and dialysis correct acidosis to a degree, there is less reduction of pCO_2 in animals subjected to these two forms of treatment.

The same correlation between levels of lactic acid and pH were observed in both endotoxin and haemorrhagic shock dogs. The lower the pH the higher the lactic acid (Figs. 16 and 17). This finding confirms the previous observation that the chief cause of acidosis in these two forms of shock is lactic acid (Hardaway, 1962), (Cannon, 1918), although some other acid may help to aggravate the picture.

Bicarbonate of control arterial blood averaged 33.5 meq/l, ranging between 27.0 and 40 meq/l. During haemorrhagic and endotoxin shock, the values of bicarbonate show a general tendency towards reduction. However, in the dogs that were dialysed or pretreated with dibenzyline, there was a tendency

towards preservation of bicarbonate at higher levels. In the haemorrhagic shock dogs where bicarbonate is severly depressed at the end of two and one half hours, institution of dialysis raises the bicarbonate values to reasonably high values. This rise of bicarbonate following dialysis is significant when correlated with a concomitant rise in pH and depression in lactic acid. This finding is not so marked in control dogs. Dialysis does seem to correct metabolic acidosis during shock.

We can reasonably postulate that dialysis causes physiological preservation of base bicarbonate because the mechanical-effects-of-dialysis dogs, which also received saline, do not show this tendency of preservation of bicarbonate that is amply demonstrated in dialysed dogs (Tables 12, 15, 17, 18). This is more marked in endotoxin than haemorrhagic shock dogs. In the latter, dialysis does not seem to be capable of preserving bicarbonate. Dibenzyline, in this respect, is superior to dialysis.

Dibenzyline dogs show the slightest reduction of bicarbonate throughout the shock period. This was pointed out previously as due to better perfusion of all the organs of the body.

The lactic acid concentration of the blood of control animals varied from 1.4 to 2.3 meq/l. The increase in blood lactate that follows shock accounts for the acidosis that is encountered in this syndrome. This is more marked in haemorrhagic

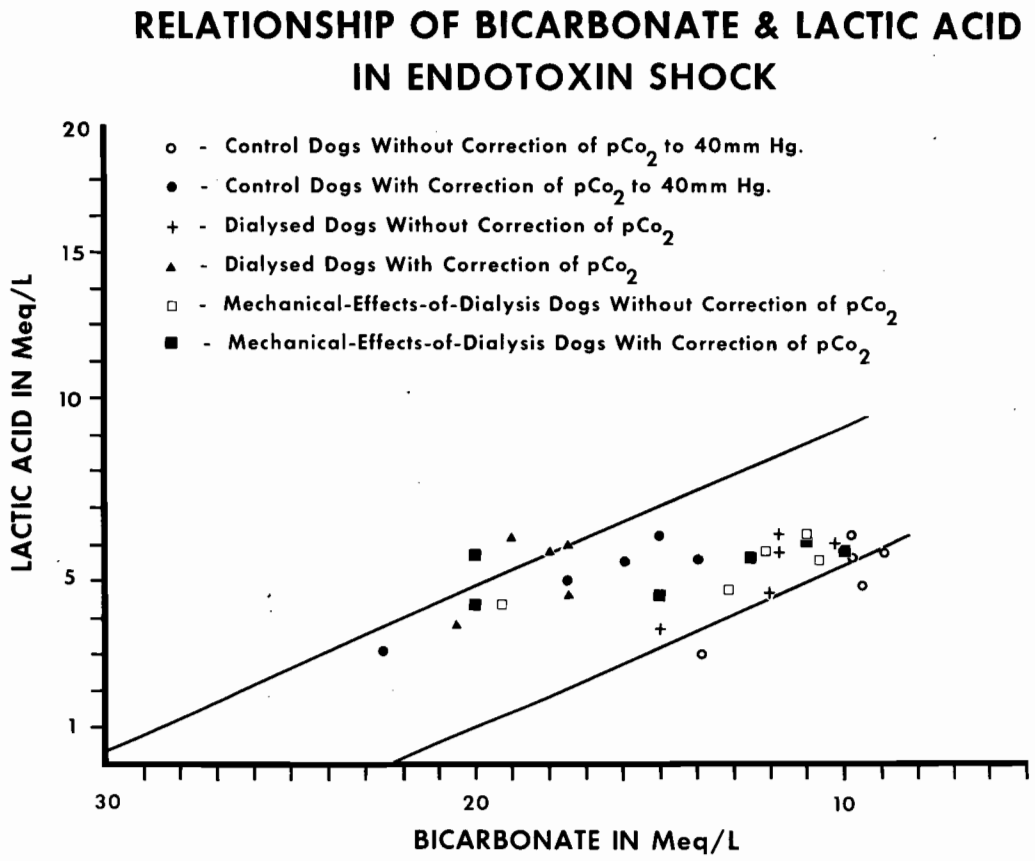


Fig. 14.-- This scattergram shows a positive relationship of bicarbonate to lactic acid in dogs subjected to endotoxin shock. Although pCO_2 is not corrected to 40 mm Hg that relationship is still well demonstrated - the lower the lactic acid the higher the bicarbonate.

than in endotoxin shock. This reflects the very severe lactic acidosis that is encountered in haemorrhagic shock. Prolongation of this state for over two and one half hours is fatal even though the acidosis and the hypovolemia are corrected. Endotoxin shock dogs show only a moderate increase in lactic acid during shock. This is probably due to the fact that the animals in this study were not in severe enough acidosis to reflect a marked change in lactic acid (Table 18). Following dialysis, there is a slight reduction of lactic acid in haemorrhagic shock dogs. Dilution effect of the saline may account for this fall since reservoir blood lactic acid was four times lower than the blood lactic acid. Since there is no marked lactic acidosis in endotoxin shock, dialysis does not produce any significant changes. Dibenzyline dogs were spared of severe lactic acidosis during the whole period of shock.

The progressive rise in hematocrit during shock is due to plasma loss (25% - MacLean and Weil, 1956), (7% - Grable et al, 1963). Whatever the amount of plasma lost, there is some progressive elevation of hematocrit during endotoxin shock. It is higher in haemorrhagic shock where some dogs show hematocrits as high as 63%. In dialysed haemorrhagic shock dogs, hematocrit tends to fall at the end of the experimental period while in endotoxin shock, hematocrit remains fairly constant. In both cases, this fall can be attributed to the infusion of 5% D/N.S.

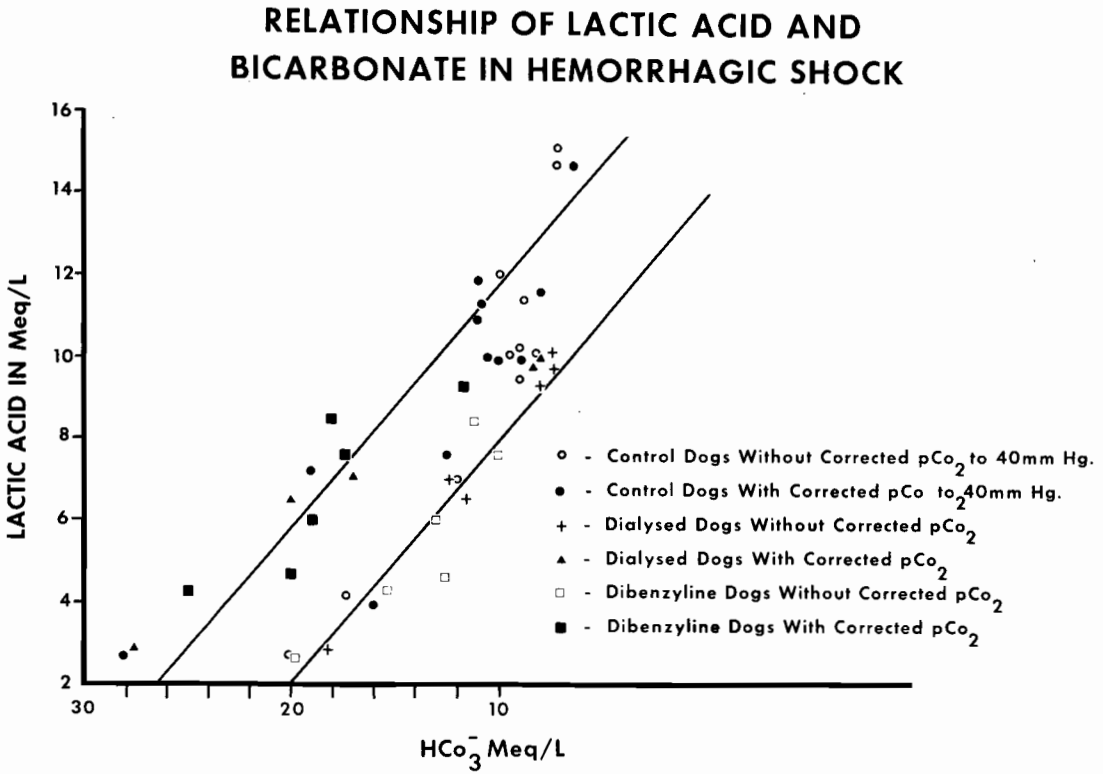


Fig. 15.--This graph is almost similar to Figure 14. It shows the same positive relationship between bicarbonate and lactic acid in haemorrhagic shock dogs. Lactic acidosis is very severe in this group of dogs and the depression of bicarbonate is quite marked even without correction of pCO_2 to 40 mm Hg. Elevation of bicarbonate is noted in dialysed and dibenzyline dogs.

during dialysis. Dibenzyline dogs show steady hematocrit values which are kept at levels close to normal throughout the experimental period. This observation supports the fact that dibenzyline prevents aggregation of cells and thus improves tissue perfusion.

The major changes in arterial blood electrolytes during shock are characterized by hyperkalemia and hyperchloremia in both control and experimental animals. This finding has been observed by other investigators in this field (Richards, 1943, 1944), (Wilson, 1963), (Wiggers, 1950), (Page, 1961). This is postulated to be due to emigration of the chloride and potassium ions from the cell to the extracellular space. There is general tendency towards hyponatremia as shock progresses. Dibenzyline and dialysis have a tendency to keep plasma sodium at normal constant values during shock.

The general fall in plasma potassium observed in dialysed and mechanical-effects-of-dialysis dogs is probably due to saline infusion while the hypokalemia may be the result of the dilution effect of 5% D/N.S. This reasoning is fortified by the fact that control groups which did not receive saline showed a general tendency towards hyperkalemia as pointed out before.

These changes in the blood constituents indicate the nature and the extent of some of the metabolic disturbances which occur when blood flow is slowed by decreasing the blood volume. Measurements of arterial pH, pCO_2 and lactate therefore

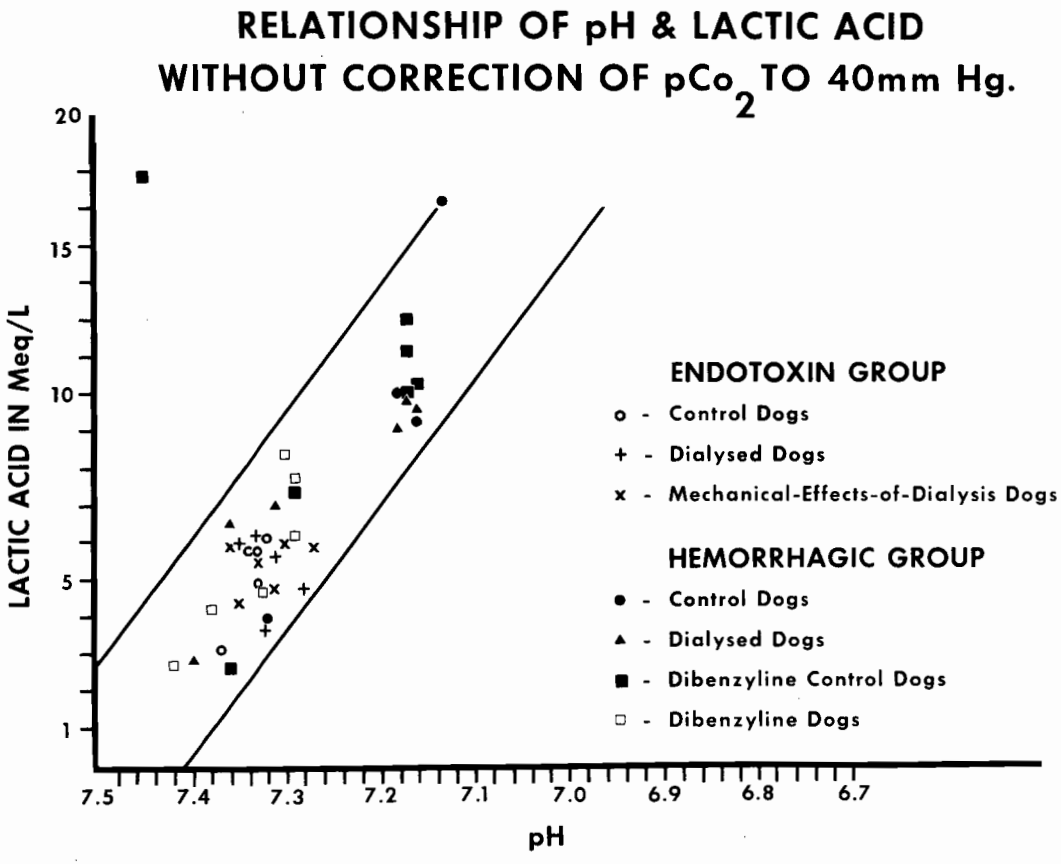


Fig. 16.--The rise in lactic acid is accompanied by pH depression and vice versa. Control dogs manifest a marked rise in lactic acid followed by depression of pH. Dialysed and dibenzyline dogs show comparatively low values of lactic acid.

provide further quantitative criteria not only for determining the depth or degree of shock, but also for testing at various stages the effectiveness of transfusion or any other therapeutic procedure.

One of the most interesting observations in these experiments is the correlation of survival time between the different groups of animals (Table 22). The survival time and percent survival rate in each experimental group of animals is summarized on Table 22. There is a definite correlation in survival time between the endotoxin control dogs and the endotoxin-mechanical-effects-of-dialysis animals. The former group had an average survival time of 10.4 hours while the latter averaged 10.1 hours. The two groups received 3 mg/kg endotoxin. Their main difference is that one group was subjected to the pumping effect of haemodialysis while the other group received no other form of trauma besides the endotoxin. Pumping the endotoxin shock dog without a kidney coil and bath or shocking the animal without any added insult have practically the same mortality rate. The survival rate of delayed dialysed dogs using old and new coils is 50% while that of early dialysed dogs with old and new coils is also 50%. This seems to point out that delayed dialysis does not seem to have a greater advantage over early dialysis in the treatment of endotoxin shock. The use of new sterile coils

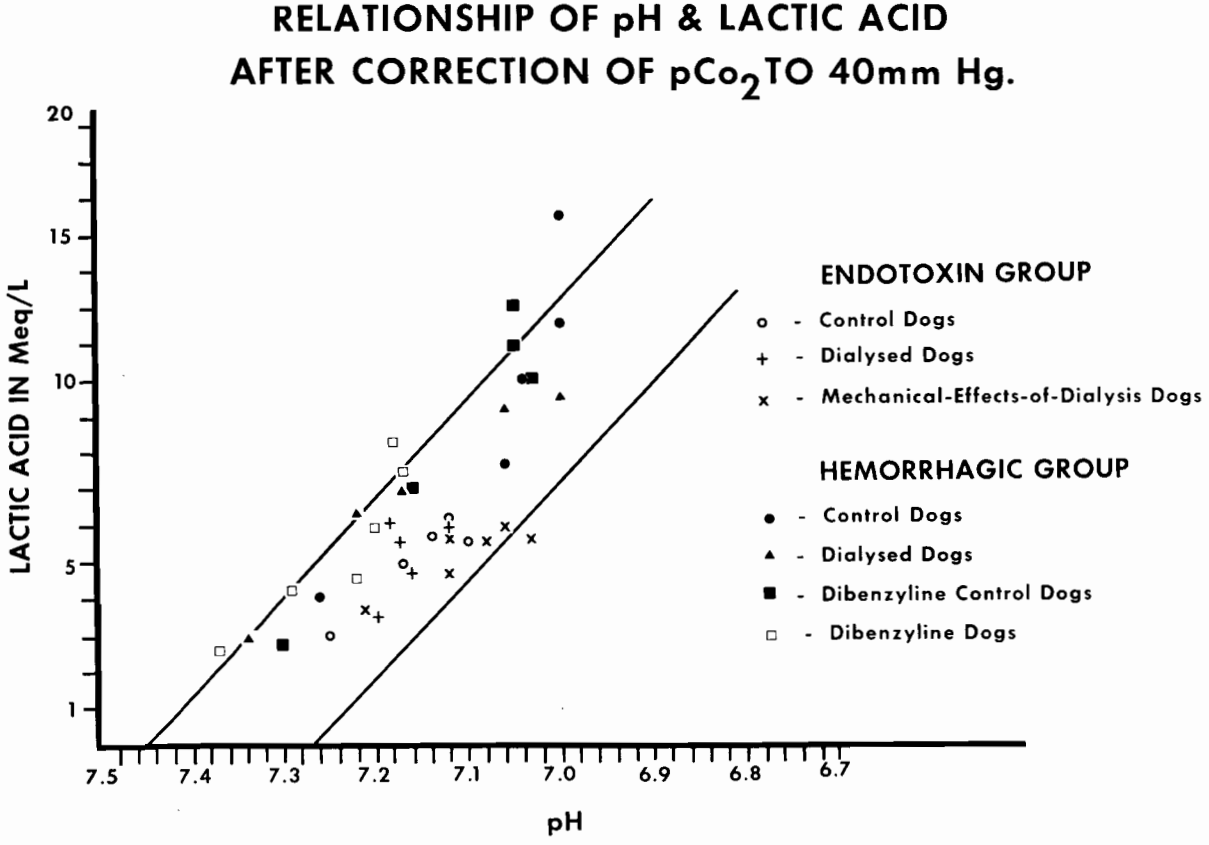


Fig. 17.--Even after correction of pCO_2 to 40 mm Hg, there is still a positive relationship between lactic acidosis and depression of pH. The control dogs in haemorrhagic shock show the highest concentrations of lactic acid. Dialysed and dibenzyline dogs show the least accumulation of lactic acid.

yielded 70% survival rate. The efficiency of the new kidney coil is reflected in the additional 20% survival rate. It is also noted that early dialysis or late dialysis have a mortality rate almost seven times as low as in the two control groups. These facts indicate that haemodialysis is of some value in bacteremic shock.

The fact that morphine-endotoxin-dialysed dogs had no permanent survivors while the controls had 60% survival rate is intriguing. It is very likely that morphine has a protective effect on a dog subjected to endotoxin. The dialysed dog was deprived of this protection as morphine was probably dialysed into the bath. Some pharmacological interaction between morphine and endotoxin, beneficial to the dog, may have been responsible for protecting the dogs from the lethal effects of endotoxin. A larger number of dogs is needed to interpret these findings statistically.

In the haemorrhagic shock dogs which were subjected to haemodialysis, only 30% survived while the controls in the same group had 20% survival rate. This is an interesting finding. It has been noted that haemorrhagic shock produces a marked state of lactic acidosis (Tables 15, 17 and 18) with marked depression of pH to levels as low as 7.0. We have also observed that in our experiments there is an apparent elevation of pH to 7.22 and base bicarbonate from 8.2 to 20 meq/l after dialysis

and a significant lowering of lactic acid from 9.7 to 6.5 meq/l coupled with an elevation of pCO_2 from 18 to 23 mm Hg. This is in contrast with the endotoxin group whose chemistries and electrolytes were practically within normal limits. In spite of hardly any acidosis during endotoxin shock, 50% of the early dialysed dogs died in irreversible shock, while the undialysed dogs in the same group had a mortality rate of 93%. In haemorrhagic shock, although correction of the pH is apparently accomplished by haemodialysis, yet the mortality rate is 70%.

Comparing the mortality rates of the endotoxin and haemorrhagic dialysed dogs and correlating them with the degree of chemical and electrolyte disturbances, it seems that while acidosis plays a role in the irreversible phenomenon of shock, it is not the chief actor on the stage since the drama can go on to the end with or without it. This conclusion is fortified by the observation of chemistries and electrolytes in dibenzyline treated dogs. Even though these dogs maintained their blood chemistries and electrolytes close to normal levels throughout shock, only 30% survived permanently.

The questions that come to our mind are: How do we account for better results of haemodialysis in the treatment of endotoxin shock? What are we dialysing in endotoxin shock which is not dialysable or absent in haemorrhagic shock? Could the substance or substances be catecholamines and/or histamine or could

this be some bacterial toxic product or is it the endotoxin itself that is dialysed out before it sauses irreversible damage to cells? It is possible that histamine and catecholamines are in greater concentration in endotoxin shock than in haemorrhagic shock. One important difference between these two groups is that dialysis, in spite of its correction of the acidotic state in haemorrhagic shock, does not seem to be of value in the treatment of this condition. One reason may be that when dialysis begins (two and one half hours after shock has begun), the animal is already in a state of irreversibility; thus at this stage this form of treatment appears to be an addition of another insult to injury.

CHAPTER VI.

SUMMARY AND COMMENTS.

1. One hundred and thirty-four dogs were employed in this series of experiments. One hundred and nineteen were subjected to experimental shock. Forty were subjected to haemorrhagic shock while seventy-nine dogs were given a lethal dose of E. Coli. Blood chemistries and electrolytes were determined in seventy dogs which were divided into: five normal, twenty-five endotoxin and forty haemorrhagic. Vital signs were recorded in all the dogs except five normal and six endotoxin dogs which did not require these parameters.

2. The review of literature on endotoxin and haemorrhagic shock was presented with special reference to the feasibility of employing haemodialysis in the treatment of these two forms of hypotension.

3. Dialysis is a relatively innocuous form of treatment which has been clinically employed for a wide variety of conditions which include: acute and chronic uremia, acute tubular necrosis, acute pancreatitis, acute glomerulo-nephritis, hemoglobinuric and myoglobinuric nephrosis, hepatorenal syndrome, acute renal failure supervening on existing renal disease, chemical nephrosis, salicylate and

barbiturate poisoning.

The artificial kidney can correct intractable oedema by ultrafiltration of 1,000-2,000 ml. in one hour (Kolff, 1954). Electrolyte derangements are encountered in many disease entities, many of which are associated with acute or chronic renal disease. Haemodialysis, if performed with enough caution, can restore electrolyte composition of blood plasma to normal more rapidly than can the natural kidney or any diuretic.

4. Haemodialysis was the principal form of treatment used in haemorrhagic and endotoxin shock. The results obtained with this form of treatment indicate that dialysis, if combined with antibiotics, cardiac glycosides and oxygen, has a place in the treatment of endotoxin shock.

It is also reasonable to conclude that if aseptic technique was used in conjunction with dialysis and antibiotics, more dogs could have survived the fatal effects of endotoxin.

5. Dibenzyline was used in a group of haemorrhagic shock dogs and its effect on blood chemistries and survival time has been discussed. Dibenzyline, while it produces hypotension by its sympatholytic action, also causes vasodilation of the vessels in those parts of the body where blood is most needed (heart, small intestine, liver and kidney). It appears that the greatest benefit rendered by dibenzyline in

haemorrhagic shock is in the opening up of the arteriolar portion of the circulation. This is so vital to tissue perfusion that even if shock is induced, anoxia does not take place so rapidly.

In spite of its apparent good effects on circulation, dibenzyline did not markedly improve the survival rate in animals subjected to haemorrhagic shock. It is possible that a larger dose than the one used in this series may give better results.

6. Morphine, for some obscure reason, seems to have some protective effect on dogs subjected to endotoxin shock. This observation needs more data to have some statistical value.

7. The major changes in blood chemistry and in acid-base balance which occur in haemorrhagic and endotoxin shock consist of progressive decreases in pH and arterial CO_2 content and progressive increases in the concentration of lactate and possibly phosphate. The metabolic acidosis, which is present during shock, is partly compensated for by a reduction in arterial CO_2.

There is no definite relationship between blood chemical derangements and survival in these series of experiments.

8. Dialysis has no place in the treatment of haemorrhagic shock. It could be useful if instituted before the onset of the irreversible stage.

CHAPTER VII.

CONCLUSION.

1. Dialysis of a normal dog without any secondary infection is compatible with life.

2. In endotoxin shock, haemodialysis, if instituted within five hours of infection, can prevent animals from going into irreversible shock. It is possible that some patients who are seen in the early phases of bacteremic shock may benefit from this type of treatment since the mortality in this form of hypotension is still high.

3. Endotoxin must release some toxic by-product, which contributes towards irreversibility and this substance or substances must be dialysable.

4. Combination of haemodialysis with antibiotics in treating endotoxin shock must yield better results than haemodialysis or antibiotics alone.

5. Haemodialysis is not an effective treatment of haemorrhagic shock. It may however be useful if used before irreversible changes have taken place.

6. Haemorrhagic shock produces a very severe acidosis, correction of which does not seem to alter the fatal trend in the majority of animals. Less metabolic derangements are encountered in endotoxin shock.

7. The major changes in the arterial blood chemistries and electrolytes after haemorrhage and endotoxin administration consist of decreases in the pH, pCO_2 and sodium and increases in lactate and potassium.

8. While metabolic acidosis is postulated to play an important role in the irreversible phenomenon, it does not seem to play a vital role, since its correction or absence does not necessarily reverse the fatal trend of shock.

9. Dibenzyline, while maintaining chemistries and electrolytes at near normal levels during haemorrhagic shock, does not increase the number of survivors.

10. Progressive fall in blood pressure in spite of dialysis or any form of treatment is indicative of a poor prognosis in any form of hypotension.

11. Replacement of fluid lost by the dog does not necessarily avert the irreversible trend.

12. Hypotension or olegemia alone cannot be responsible for the metabolic and electrolyte derangements in shock because dibenzyline dogs, in spite of their prolonged and severe hypotension, exhibit less metabolic derangements than the other group of dogs with higher blood pressures.

APPENDIX I

EFFECTS OF DIALYSIS ON MEAN VITAL SIGNS IN NORMAL DOGS WITHOUT PROPHYLACTIC ANTIBIOTICS

A	Time in Minutes		0	5	10	20	30	40	50
	Temperature in Degrees Centigrade		37.3	29.3	37.2	36.7	36.7	36.5	36.1
		R	36 - 38.5	36 - 38	35.5 - 38.5	35.5 - 38	35.5 - 38	35.5 - 37.5	34.5 - 37.5
	Blood Pressure in mm Hg		157.6	152.8	88.4	96.0	128.0	138.0	146.0
		R	130 - 170	134 - 170	60 - 134	50 - 150	70 - 150	86 - 174	115 - 176
	Heart Rate per Minute		149.2	140	154.6	145.2	147.2	139.8	139.2
		R	102 - 180	102 - 168	142 - 160	132 - 170	90 - 174	69 - 216	120 - 156
	Venous Pressure in cm Water		14.1	12.7	13.3	14.4	14.5	12.8	13.0
		R	9 - 24	5.5 - 24	5.5 - 24	6.5 - 16	7.0 - 24	8.0 - 17	9.0 - 18
	Respiratory Rate per Minute		30	30.6	27.4	24.2	19	19.6	21.4
		R	18 - 60	20 - 51	15 - 51	15 - 30	15 - 24	15 - 24	15 - 30

(Continued)

B	Time in Minutes (Cont'd.)		60	70	80	90	100	110	120
	Temperature in Degrees Centigrade		36.1	36	36.1	36.1	37.9	37.9	35.9
		R	34.5 - 37	34.5 - 37	34 - 37	34.5 - 37	34 - 37	34 - 37	34 - 37
	Blood Pressure in mm HG		142	140.2	149.6	141.4	143.6	142	140
		R	120 - 170	120 - 156	118 - 156	125 - 156	120 - 160	120 - 160	120 - 160
	Heart Rate per Minute		144	138	142	156.9	142	148.4	154.4
		R	120 - 156	120 - 156	120 - 160	134 - 180	120 - 168	134 - 170	134 - 200
	Venous Pressure in cm Water		17.6	16.5	16.3	16.6	16.5	14.5	15.7
		R	13 - 30	10 - 30	9 - 30	11.5 - 30	10.5 - 30	10 - 26	12.5 - 24
	Respiratory Rate per Minute		29.8	21.8	23.0	21.2	22.4	24.6	22.8
		R	15 - 60	15 - 34	15 - 32	8 - 32	8 - 32	8 - 40	8 - 40

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF NORMAL DIALYSED DOGS WITHOUT PROPHYLACTIC ANTIBIOTICS.

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	36.5	38.0	36.0	37.5	38.5	37.3
5	36.5	38.0	36.0	37.5	38.5	37.3
10	36.5	38.0	35.5	37.5	38.5	37.2
20	35.5	38.0	35.5	37.0	37.5	36.7
30	35.5	38.0	35.5	37.0	37.5	36.7
40	35.5	37.0	35.5	37.0	37.5	36.5
50	35.5	37.0	34.5	36.0	37.5	36.1
60	36.0	37.0	34.5	36.0	37.0	36.1
70	35.5	37.0	34.5	36.0	37.0	36.0
80	36.0	37.0	34.0	36.5	37.0	36.1
90	36.0	37.0	34.0	36.5	37.0	36.1
100	35.0	37.0	34.0	36.5	37.0	37.9
110	35.0	37.0	34.0	36.5	37.0	37.0
120	35.0	37.0	34.0	36.5	37.0	35.9

MEAN SYSTOLIC BLOOD PRESSURE IN MM HG OF NORMAL DIALYSED DOGS WITHOUT PROPHYLACTIC ANTIBIOTICS.

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	180	148	170	130	160	157.6
5	150	140	170	134	170	152.8
10	88	134	60	90	70	88.4
20	80	150	50	100	100	96.0
30	135	150	70	130	142	128.0
40	174	150	86	130	150	138.0
50	176	150	125	132	150	146.0
60	170	150	120	120	150	142.0
70	156	150	125	120	150	140.2
80	156	148	120	118	156	149.6
90	156	144	125	134	148	141.4
100	160	154	120	134	150	143.6
110	160	150	120	130	150	142.0
120	160	150	120	134	150	140.0

MEAN HEART RATE PER MINUTE OF NORMAL DIALYSED DOGS

WITHOUT PROPHYLACTIC ANTIBIOTICS.

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	144	180	152	168	102	149.2
5	144	132	154	168	102	140
10	144	142	160	156	171	154.6
20	132	132	160	132	170	145.2
30	174	90	160	132	170	147.2
40	216	69	144	120	150	139.8
50	156	126	144	120	150	129.2
60	156	150	144	120	150	144
70	156	120	144	120	150	138
80	156	120	144	130	160	142
90	144	180	156	134	170	156.8
100	144	120	144	134	168	142
110	144	150	144	134	170	148.4
120	144	150	144	134	200	154.4

MEAN VENOUS PRESSURE IN CM WATER OF NORMAL DIALYSED DOGS

WITHOUT PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	9.0	12.5	13.0	24	12.0	14.1
5	9.0	5.5	13.0	24	8.0	12.7
10	9.0	5.5	16.0	24	13.0	13.3
20	8.5	6.5	16.0	24	17.0	14.4
30	8.5	7.0	16.0	24	17.0	14.5
40	9.0	8.0	12.0	18	17.0	12.8
50	9.0	9.0	13.0	18	16.0	13.0
60	15	13.0	15.0	30	15.0	17.6
70	13	10.0	15.0	30	14.5	16.5
80	13	9.0	15.0	30	14.5	16.3
90	12	11.5	15.0	30	14.5	16.6
100	12.5	10.5	15.0	30	14.5	16.5
110	12.0	10.0	14.0	26	10.5	14.5
120	12.5	12.5	15.0	24	14.5	15.7

MEAN RESPIRATORY RATE PER MINUTE OF NORMAL DIALYSED DOGS

WITHOUT PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	20	60	28	24	18	30
5	20	51	28	24	30	30.6
10	20	51	28	24	15	27.4
20	24	30	28	24	15	24.2
30	24	18	20	18	15	19.0
40	24	21	20	18	15	19.6
50	24	27	12	30	15	21.4
60	32	60	12	30	15	29.8
70	34	18	12	30	15	21.8
80	32	30	8	30	15	23.0
90	32	30	8	24	12	21.2
100	32	30	8	30	12	22.4
110	40	30	8	30	15	24.6
120	40	30	8	18	18	22.8

APPENDIX II

EFFECTS OF DIALYSIS ON MEAN VITAL SIGNS IN NORMAL DOGS WITH PROPHYLACTIC ANTIBIOTICS.

A	Time in Minutes		0	5	10	20	30	40	50
	Temperature in Degrees Centigrade		37.0	36.7	36.3	36.9	36.95	36.9	36.6
		R	36.5 - 37.5	35.5 - 37.5	36.5 - 37.5	35.5 - 37.5	36.5 - 37.5	36.25 - 37.5	36 - 37.5
	Blood Pressure in mm HG		160.4	122.8	115.4	129.6	147.2	150.0	143.0
		R	150 - 170	50 - 170	55 - 162	58 - 158	120 - 160	134 - 160	100 - 160
	Heart Rate per Minute		149.4	141.5	138.8	132.8	130.0	134.0	137.2
		R	102 - 174	98 - 168	120 - 180	102 - 160	102 - 162	102 - 162	112 - 156
	Venous Pressure in cm Water		11.1	10.7	10.6	10.9	10.5	10.8	10.4
		R	8.5 - 13	6.5 - 14	7.5 - 14	8.5 - 14	8 - 14	8 - 16	8 - 14.5
	Respiratory Rate per Minute		18.2	20.8	27.2	29.0	20.8	18.2	20.2
		R	12 - 27	12 - 40	12 - 54	16 - 42	16 - 33	15 - 21	12 - 21

(Continued)

Time in Minutes (Cont'd.)		60	70	80	90	100	110	120
Temperature in Degrees Centigrade		36.2	36.2	36.2	36.2	36.4	36.4	36.3
	R	36 - 37.5	35.5 - 37	36 - 36.4	36 - 36.5	36 - 37.5	36 - 37.5	36 - 37.5
Blood Pressure in mm HG		142.6	145.6	149.6	146.2	145.6	142.0	141.4
	R	100 - 174	110 - 174	120 - 174	110 - 168	112 - 168	100 - 166	100 - 166
Heart Rate per Minute		132.4	135.8	143.2	146.6	149.0	150.0	155.2
	R	102 - 152	112 - 162	112 - 180	114 - 168	111 - 180	135 - 180	120 - 180
Venous Pressure in cm Water		10.4	10.3	10.2	10.2	10.7	10.3	10.2
	R	8 - 14.5	8 - 14.5	8 - 14.5	8.5 - 14.5	7.5 - 15	7.5 - 15	7 - 15
Respiratory Rate per Minute		20.2	21.4	21.6	22.0	22.6	24.4	24.0
	R	12 - 27	18 - 27	18 - 27	18 - 36	18 - 30	20 - 30	24 - 24

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF NORMAL DIALYSED DOGS WITH PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	37.0	37.5	36.5	36.5	37.5	37.0
5	36.5	37.5	35.5	36.5	37.5	36.7
10	36.5	37.5	35.5	35.5	36.5	36.3
20	36.5	37.5	37.5	36.5	36.5	36.9
30	36.2	37.5	37.5	37.0	36.5	36.95
40	36.0	37.5	37.5	37.0	36.5	36.9
50	36.0	37.0	37.5	36.0	36.5	36.6
60	36.0	37.0	35.5	36.0	36.5	36.2
70	36.0	36.5	36.0	36.0	36.5	36.2
80	36.0	36.5	36.0	36.0	36.5	36.2
90	36.0	36.5	36.0	36.0	36.5	36.2
100	36.0	36.0	37.5	36.0	36.5	36.4
110	36.0	36.0	37.5	36.0	36.5	36.4
120	36.0	36.0	37.5	35.5	36.5	36.3

MEAN SYSTOLIC BLOOD PRESSURE IN MM HG OF NORMAL DIALYSED DOGS WITH PROPHYLACTIC ANTIBIOTICS.

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	160	162	150	160	170	160.4
5	170	50	150	90	154	122.8
10	120	55	120	120	162	115.4
20	150	58	158	126	156	129.6
30	150	150	160	120	156	147.2
40	150	156	160	134	150	150.0
50	120	160	160	100	145	143.0
60	150	154	174	100	135	142.6
70	150	158	174	110	134	145.6
80	160	160	174	120	134	149.6
90	160	160	168	110	135	146.2
100	160	154	168	112	134	145.6
110	160	150	166	100	134	142.0
120	156	150	166	100	135	141.4

MEAN HEART RATE PER MINUTE IN NORMAL DIALYSED DOGS WITH PROPHYLACTIC ANTIBIOTICS.

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	174	171	102	132	168	149.4
5	168	170	98	112	160	141.3
10	138	180	120	120	144	138.8
20	102	150	150	102	160	132.8
30	112	134	162	102	140	130.0
40	112	144	150	102	162	134.0
50	112	154	150	114	156	137.2
60	112	152	152	102	144	132.4
70	123	138	162	112	144	135.8
80	120	180	160	112	144	143.2
90	140	168	166	114	145	146.6
100	144	180	160	111	150	149.0
110	140	150	180	135	145	150.0
120	146	180	180	120	150	155.2

MEAN VENOUS PRESSURE IN CM WATER OF NORMAL DIALYSED DOGS WITH PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	10	8.5	12.0	12.0	13.0	11.1
5	9.0	6.5	12.0	12.0	14.0	10.7
10	9.8	7.5	12.0	10.0	14.0	10.6
20	8.5	8.5	13.0	10.5	14.0	10.9
30	8.0	8.5	11.5	10.5	14.0	10.5
40	8.0	8.5	11.5	10.0	16.0	10.8
50	8.0	9.0	10.5	10.0	14.5	10.4
60	8.0	9.0	10.5	10.0	14.5	10.4
70	8.0	9.0	10.0	10.0	14.5	10.3
80	8.0	9.0	10.0	10.0	14.5	10.2
90	7.5	8.5	10.0	10.5	14.5	10.2
100	7.5	8.5	10.0	12.5	15.0	10.7
110	7.5	8.5	10.0	10.5	15.0	10.3
120	7.0	8.5	10.0	10.5	15.0	10.2

MEAN RESPIRATORY RATE PER MINUTE IN NORMAL DIALYSED DOGS WITH PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5	MEAN
TIME IN MINUTES						
0	27	12	24	12	16	18.2
5	40	12	24	12	16	20.8
10	54	12	24	30	16	27.2
20	33	42	30	24	16	29.0
30	18	21	33	21	16	20.8
40	18	21	15	21	20	18.2
50	18	20	12	21	16	20.2
60	18	20	12	27	24	20.2
70	18	20	18	27	24	21.4
80	21	18	18	27	24	21.6
90	20	18	18	36	24	22.0
100	20	21	18	30	24	22.6
110	20	24	24	30	24	24.4
120	24	24	24	24	24	24.0

SURVIVAL TIME OF DOGS SUBJECTED TO HAEMODIALYSIS

WITH AND WITHOUT PROPHYLACTIC ANTIBIOTICS

DOG NO.	1	2	3	4	5
No Antibiotic Group	4 Days	4 Days	4 Days	4 Days	5 Days
Antibiotic Group	4 Weeks	4 Weeks	4 Weeks	4 Weeks	5 Days

APPENDIX III

MEAN VITAL SIGNS OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO).

A	Time in Minutes	0	15	30	45	60	75	90	105	120
	Temperature in Degrees Centigrade	37.51	37.32	36.8	36.5	36.49	36.08	36.0	35.86	36.11
	R	35.5 - 40	34.5 - 39	32.5 - 39	32.5 - 39	31.5 - 40	31 - 39	31 - 39	31.5 - 39	31.5 - 40
	Blood Pressure in mm Hg	154	134	119	109	95	90	89	89	88
	R	118 - 190	40 - 170	20 - 168	22 - 170	30 - 155	20 - 140	20 - 140	20 - 144	18 - 150
	Heart Rate per Minute	154.07	140	132.57	139.93	146.07	149.57	163	158.93	160.86
	R	75 - 232	72 - 232	75 - 210	84 - 180	96 - 195	110 - 180	140 - 210	108 - 192	110 - 192
	Venous Pressure in cm Water	6.5	5.4	5.1	4.7	4.5	4.3	3.9	4.4	4.1
	R	3.5 - 11	3 - 8	2.5 - 14	2 - 10	2 - 9.5	1.5 - 11	1.5 - 8	1.5 - 9	1.5 - 7.5
	Respiratory Rate per Minute	29.5	27.64	23.86	26.79	33.86	33.14	30.5	29.93	30.43
	R	9 - 66	15 - 48	6 - 45	5 - 48	15 - 57	12 - 66	12 - 60	12 - 54	15 - 45

B	Time in Minutes (cont'd.)		135	150	165	180	195	210	225	240
	Temperature in Degrees Centigrade		36.03	36.3	36.2	36.1	36.0	35.5	34.9	34.6
		R	31.5 - 39.9	31.5 - 39.9	31.5 - 39.5	31.5 - 39	31.5 - 38.5	31 - 38.5	31 - 37	31 - 37
	Blood Pressure in mm Hg		89	87	93	95	94	95	96	95
		R	25 - 150	25 - 150	25 - 150	30 - 145	45 - 150	45 - 150	45 - 145	45 - 145
	Heart Rate per Minute		169.21	181.5	187.8	184.7	189.9	186.6	187.3	187.8
		R	112 - 212	112 - 240	120 - 270	132 - 268	130 - 280	120 - 275	120 - 280	130 - 270
	Venous Pressure in cm Water		4.5	3.9	5.5	6.2	6.5	6.7	5.9	5.6
		R	1.0 - 12	1 - 12	1.5 - 12	2 - 12.5	2 - 12.5	2 - 14.5	2 - 14	2 - 14
	Respiratory Rate per Minute		26.7	27.79	26.6	27.0	25.1	24.1	25.1	24.5
		R	15 - 45	18 - 45	18 - 40	18 - 45	6 - 42	6 - 39	18 - 36	18 - 42

R- Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF CONTROL DOGS

SUBJECTED TO ENDOTOXIN 3 MG/KG E. COLI (DIFCO)

A	DOG NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	35.5	38.2	38.75	36.75	38.0	39.0	37.5
	15	35.5	38.25	37.7	37.0	37.0	39.0	37.5
	30	32.5	39.0	38.0	37.25	35.5	38.0	36.5
	45	32.5	39.0	38.5	37.5	33.0	38.0	35.5
	60	31.5	39.0	38.5	37.5	32.5	39.0	35.0
	75	31.0	38.0	38.0	37.5	32.0	39.0	34.0
	90	31.0	38.5	38.0	37.0	32.0	39.0	34.0
	105	31.5	38.5	37.5	37.5	32.0	39.0	33.0
	120	31.5	38.5	37.5	37.5	32.0	39.0	33.0
	135	31.5	38.5	37.0	37.5	32.0	39.0	33.0
	150	31.5	38.5	37.0	37.0		39.0	33.0
	165	31.5	37.0	37.5	37.0		39.0	33.0
	180	31.5	37.5	37.5	37.5		38.5	32.5
	195	31.5	37.5	37.0	37.5		38.5	32.5
	210	31.0	36.5	37.0	36.5		38.0	32.5
	225	31.0	36.0	36.5	36.0		37.0	32.5
	240	31.0	36.0	36.5	35.0		37.0	32.5
	SURVIVAL TIME IN HOURS	24	10	7½	5	2'50"	9	4'45"

B

DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
TIME IN MINUTES								
0	37.5	38.0	37.5	36.0	40.0	35.5	37.0	37.51
15	37.5	38.0	37.5	36.0	40.0	34.5	37.0	37.32
30	36.0	38.0	39.0	36.0	39.0	35.5	35.5	36.8
45	37.5	39.0	39.0	35.0	39.0	34.5	33.0	36.5
60	39.5	38.0	40.0	36.2	38.0	34.5	33.2	36.49
75	36.5	38.0	39.0	36.2	38.0	34.5	33.0	38.08
90	36.0	38.0	39.0	36.0	38.0	34.5	33.0	36.0
105	36.0	38.0	39.0	36.0	38.0	33.5	33.0	35.86
120	36.0	38.0	40.0	36.0	38.0	33.5	35.0	36.11
135	36.0	38.0	39.9	36.0	38.0	33.0	35.0	36.03
150	36.0	38.0	39.9	36.0	38.0	33.0	35.0	36.3
165	36.0	38.0	39.5	36.4	38.0	33.0	35.0	36.2
180	35.5	38.0	39.0	36.0	38.0	33.0	35.0	36.1
195	35.5	38.0	38.5	36.0	38.0	33.0	35.0	36.0
210	35.5		38.5	35.5	37.5	32.5	35.0	35.5
225	35.5			35.5	37.0	32.5	34.5	34.9
240	35.5			35.5	36.0	32.5	34.0	34.6
SURVIVAL TIME IN HOURS	6	3½	3'50"	8	30	24	8	10.5

MEAN BLOOD PRESSURE IN MM HG OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO).

A DOG NO.	1	2	3	4	5	6	7
TIME IN MINUTES							
0	150	155	170	190	150	145	155
15	100	105	170	150	40	150	155
30	90	115	168	100	55	155	150
45	95	90	170	95	55	112	100
60	115	80	150	80	55	72	82
75	120	55	120	75	55	65	82
90	130	64	100	60	55	104	75
105	132	98	85	60	45	105	75
120	132	100	85	60	40	100	75
135	122	102	90	60	40	150	75
150	120	104	92	60		98	72
165	130	104	90	65		98	72
180	132	115	95	65		98	72
195	108	110	95	65		95	70
210	110	110	95	68		95	70
225	114	108	85	65		95	70
240	112	108	85	65		95	70
SURVIVAL TIME IN HOURS	24	10	7½	5	2'50"	9	4'45"

B

DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
TIME IN MINUTES								
0	175	158	166	140	150	130	118	154
15	164	152	170	154	120	140	104	134
30	160	122	158	154	130	90	20	119
45	170	105	150	154	140	80	22	109
60	155	100	100	100	128	90	30	95
75	155	95	80	98	124	120	20	90
90	115	95	80	95	120	140	20	89
105	105	94	78	95	120	140	20	89
120	102	90	78	92	125	144	18	88
135	102	85	78	118	130	150	25	89
150	100	84	78	118	120	150	25	87
165	100	85	78	118	120	150	25	93
180	100	85	72	100	120	145	30	95
195	98	90	70	112	118	150	45	94
210	98		74	112	115	148	45	95
225	99			112	115	145	45	96
240	100			100	115	145	45	95
SURVIVAL TIME IN HOURS	6	3	3'50"	8	30'	24	8	10.5

MEAN HEART RATE PER MINUTE OF CONTROL DOGS

SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO).

A DOG NO.	1	2	3	4	5	6	7
TIME IN MINUTES							
0	120	126	160	100	185	165	165
15	72	98	160	102	150	180	138
30	90	90	156	88	162	135	75
45	132	130	162	84	135	180	130
60	148	132	180	96	165	114	150
75	150	136	180	110	180	162	126
90	176	162	180	150	153	174	138
105	108	176	180	128	150	170	162
120	110	180	174	130	160	162	174
135	112	180	180	130	156	210	170
150	112	180	180	130		240	172
165	120	180	180	132		270	170
180	140	180	180	135		268	168
195	135	190	190	130		280	168
210	120	192	180	144		275	170
225	120	200	180	130		280	170
240	135	200	180	135		270	160
SURVIVAL TIME IN HOURS	24	10	7½	5	2'50"	9	4'45"

B

DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
TIME IN MINUTES								
0	120	232	75	156	130	210	213	154.07
15	132	232	84	132	140	160	180	140
30	210	180	75	165	100	180	150	132.57
45	162	168	100	150	98	178	150	139.93
60	195	164	114	140	108	180	159	146.07
75	162	150	120	138	150	180	150	149.57
90	210	150	147	140	160	180	162	163
105	192	150	189	140	170	132	148	158.93
120	192	180	180	162	172	132	132	160.86
135	210	192	162	162	170	212	120	169.21
150	210	195	162	240	170	212	120	181.5
165	220	230	160	240	170	200	120	187.8
180	214	225	170	238	175	178	132	184.7
195	222	232	172	270	170	180	130	189.9
210	210		180	260	168	212	128	186.6
225	220			240	170	220	130	187.3
240	220			240	168	220	130	187.8
SURVIVAL TIME IN HOURS	6	3½	3'50"	8	30'	24	8	10.5

MEAN VENOUS PRESSURE IN CM WATER OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO).

A

DOG. NO.	1	2	3	4	5	6	7
TIME IN MINUTES							
0	8.0	9.0	8.5	7.5	7.0	7.0	11.0
15	6.5	8.0	7.5	4.0	3.0	6.0	7.5
30	6.5	5.0	8.5	3.0	3.0	3.5	2.5
45	6.2	5.5	8.5	3.0	2.0	4.0	2.5
60	6.5	5.5	9.5	3.0	2.0	5.0	3.0
75	6.5	5.0	11.0	3.0	1.5	4.5	3.0
90	7.0	4.5	8.0	3.0	1.5	3.5	2.5
105	7.0	4.5	7.0	2.5	3.0	4.5	2.5
120	7.5	5.0	6.5	2.5	4.0	4.5	2.5
135	6.5	4.5	6.5	2.5	8.0	4.5	2.5
150	6.5	4.5	6.0	2.5		4.5	2.5
165	6.5	4.5	6.8	6.5		5.0	3.5
180	6.0	5.5	6.8	6.5		5.0	4.5
195	7.0	5.5	7.0	7.5		5.0	4.5
210	8.0	5.0	7.5	7.5		5.0	6.0
225	9.5	5.0	7.5	7.0		5.0	7.0
240	9.5	5.0	7.5	7.0		6.0	8.0
SURVIVAL TIME IN HOURS	24	10	7½	5	2'50"	9	4'45"

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	4.0	5.0	5.0	3.5	4.0	3.5	8.0	6.5
	15	6.5	3.5	4.5	3.5	8.0	3.5	4.0	5.4
	30	8.0	2.5	14.0	3.5	4.5	3.5	4.0	5.1
	45	7.5	2.5	10.00	2.5	4.5	3.5	4.0	4.7
	60	7.0	2.5	4.5	2.5	4.5	3.0	4.2	4.5
	75	5.0	1.5	5.0	2.5	4.0	3.0	4.2	4.3
	90	4.0	1.5	6.0	2.5	4.0	2.5	4.0	3.9
	105	4.0	1.5	9.0	2.5	6.5	2.5	4.0	4.4
	120	4.0	1.5	4.0	2.5	6.5	2.5	4.0	4.1
	135	4.0	1.0	4.0	2.5	12.0	1.5	3.5	4.5
	150	4.0	1.0	4.0	2.5	12.0	1.5	3.5	3.9
	165	4.0	4.5	10.5	3.0	12.0	1.5	3.5	5.5
	180	4.0	7.5	12.5	3.0	12.0	2.0	4.0	6.2
	195	4.0	8.5	12.5	3.0	14.5	2.0	4.0	6.5
	210	4.0		13.0	3.5	14.5	2.0	4.0	6.7
	225	4.0			3.5	14.0	2.0	4.0	5.9
	240	4.5			3.5	14.0	2.0	4.0	5.6
	SURVIVAL TIME IN HOURS	6	3½	3'50"	8	30'	24	8	10.5

MEAN RESPIRATORY RATE PER MINUTE IN CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO).

A	DOG. NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	42	18	39	40	66	15	27
	15	21	20	39	40	54	21	18
	30	21	21	18	28	45	18	18
	45	21	21	27	48	42	24	21
	60	24	20	21	50	42	33	57
	75	30	24	21	48	27	35	66
	90	30	24	15	36	30	39	60
	105	30	24	18	38	30	30	54
	120	30	24	18	38	30	36	45
	135	30	24	15	38	4	24	45
	150	27	24	18	38		26	45
	165	27	24	18	30		27	40
	180	27	18	21	27		24	45
	195	27	18	21	27		24	38
	210	27	24	21	30		24	38
	225	27	24	18	30		21	36
	240	18	24	18	30		27	42
	SURVIVAL TIME IN HOURS	24	10	7½	5	2'50"	9	4'45"

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	9	21	15	40	27	15	39	29.5
	15	15	15	18	24	39	15	48	27.64
	30	6	21	27	24	24	18	45	23.86
	45	5	24	28	24	30	18	42	26.79
	60	18	45	30	48	36	15	50	33.86
	75	12	33	27	54	18	21	45	33.14
	90	12	30	27	24	24	42	34	30.5
	105	12	30	27	24	21	42	36	29.93
	120	15	38	27	24	18	44	33	30.43
	135	24	38	30	27	18	27	33	26.7
	150	18	40	30	27	18	18	33	27.79
	165	18	40	36	27	18	21	33	27.6
	180	21	40	36	21	21	24	27	27.0
	195	22	6	42	24	21	24	33	25.1
	210	27		6	24	18	24	27	24.1
	225	27			24	18	24	27	25.1
	240	18			24	18	24	27	24.5
	SURVIVAL TIME IN HOURS	6	3½	3'50"	8	30+	24	8	10.5

APPENDIX IV

MEAN CHLORIDES IN MEQ/L OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	112	112	116	112	125	115	113	102	105	112	112
30	117	116	119	111	109	122	106	112	113	119	114
90	113	116	121	108	114	112	112	110	112	120	114
150	116	119	120	113	117	121	112	112	118	113	116
210	115	120	121	117	117		118	105	105	120	115
SURVIVAL TIME IN HOURS	8	24	10	7½	3½	3°50"	8	30	24	9	12.7

MEAN SODIUM IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	163	144	142	148	147	148	144	141	146	145	147
30	155	145	139	140.5	145	143	137.5	142	150	138	144
90	152	144	147	148.5	145	151	141.5	145.5	147	142	146
150	153	145	154	147	147	160	140	140	148	144	148
210	150	147	150	143	146		141	141	149	140	145
SURVIVAL TIME IN HOURS	8	24	10	7½	3½	3'50"	8	30'	24	9	12.7

MEAN POTASSIUM IN MEQ/L OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	2.1	3.77	3.7	4.67	3.8	4.4	3.4	3.3	3.9	3.6	3.66
30	2.8	3.85	4.0	3.45	4.3	4.6	4.3	3.1	4.5	3.9	3.88
90	2.1	3.47	3.4	2.95	3.95	4.0	3.3	3.7	3.3	4.0	3.42
150	2.4	3.47	3.5	3.0	4.9	4.8	4.05	3.6	3.6	3.8	3.71
210	3.0	3.57	5.1	3.57	5.4		3.7	3.7	3.4	4.5	3.99
SURVIVAL TIME IN HOURS	8	24	10	7½	3½	3°50"	8	30+	24	9	12.7

MEAN HEMATOCRIT % OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	47	55	50	45	37	57	45	44	44	45	47
30	50	57	55	48	54	65	44	47	49	50	52
90	55	58	55	47	50	61	38	49	51	55	52
150	57	60	58	46	50	63	40	45	55	53	53
210	60	65	59	50	47		43	46	60	57	54
SURVIVAL TIME IN HOURS	8	24	10	$7\frac{1}{2}$	$3\frac{1}{2}$	3'50"	8	30+	24	9	12.7

MEAN CHLORIDE, SODIUM, POTASSIUM IN MEQ/L AND HEMATOCRIT % IN CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

TIME IN MINUTES		0	30	90	150	210
Chlorides in meq/l		112	114	114	116	115
	R	102 - 125	106 - 122	108 - 121	112 - 121	105 - 121
Sodium in meq/l		147	144	146	148	145
	R	141 - 163	137.5 - 155	141.5 - 152	140 - 160	140 - 150
Potassium in meq/l		3.66	3.88	3.42	3.71	3.99
	R	2.1 - 4.67	2.8 - 4.6	2.1 - 4	2.4 - 4.9	3.0 - 5.4
Hematocrit %		47	52	52	53	54
	R	37 - 57	44 - 65	47 - 61	40 - 63	43 - 65

R = Range

MEAN pH OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	7.34	7.38	7.39	7.38	7.31	7.40	7.36	7.39	7.41	7.32	7.37
30	7.30	7.34	7.4	7.45	7.25	7.33	7.31	7.41	7.33	7.22	7.33
90	7.13	7.34	7.35	7.42	7.26	7.35	7.31	7.41	7.36	7.34	7.33
150	7.12	7.36	7.37	7.42	7.22	7.35	7.31	7.41	7.25	7.34	7.32
210		7.4	7.3	7.41	7.23		7.34	7.45	7.35	7.21	7.34
SURVIVAL TIME IN HOURS	8	24	10	7½	3½	3'50"	8	30'	24	9	12.7

MEAN pCO_2 IN MM Hg OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	25.0				26	23	17.4	24	23		23.1
30	24				13	12.5	18.5	17	22.5		17.92
90	24.2				19.8	10	12.5		15.2		16.34
150	11				20		11.4	10	20.2		14.52
210					21		10	17	15.8		15.95
SURVIVAL TIME IN HOURS	8	24	10	$7\frac{1}{2}$	$3\frac{1}{2}$	3'50"	8	30+	24	9	12.7

MEAN BICARBONATE OF CONTROL DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	13.1				13.4	14.9	11.2	15.0	15.0	15.0	13.94
30	7.5				7.5	7.9	10.3	12.0	12.6	8.5	9.47
90	10.5				10.0	6.3	8.3	8.6	11.0	12.5	9.60
150	5.6				10.5	7.0	7.8	13.0	13.0	11.9	9.83
210					9.9	6.9	7.1	12.0		8.7	8.92
SURVIVAL TIME IN HOURS	8	24	10	$7\frac{1}{2}$	$3\frac{1}{2}$	3'50"	8	30^{+}	24	9	12.7

MEAN LACTIC ACID IN MEQ/L OF CONTROL DOGS SUBJECTED TO ENDOTOXIN SHOCK 3 MG/KG E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	2.91	1.82	2.51	1.33	4.28	3.34	2.52	7.65	1.89	1.89	3.01
30	8.0	6.13	3.71	3.65	6.34	5.25	2.54	6.00	4.16	41.0	4.99
90	7.74	8.9	5.14	4.86	6.93	5.29	3.02	4.74	5.23	4.94	5.68
150	7.74	8.9	5.14	4.86	6.93	5.29	3.02	4.74	5.23	4.95	5.68
210		4.88		7.24		9.85	3.06	4.25	8.40	2.36	5.72
SURVIVAL TIME IN HOURS	8	24	10	7½	3½	3'50"	8	30+	24	9	12.7

MEAN pH, pCO_2, HCO_3 AND LACTIC ACID OF CONTROL DOGS

SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

TIME IN MINUTES		0	30	90	150	210
pH		7.37	7.33	7.33	7.32	7.34
	R	7.31 - 7.41	7.22 - 7.45	7.13 - 7.42	7.12 - 7.42	7.21 - 7.45
pCO_2 in mm Hg		23.1	17.92	16.34	14.52	15.95
	R	17.4 - 26.0	12.5 - 24.0	10 - 24.2	10 - 20.2	10 - 21.0
Bicarbonate in meq/l		13.94	9.47	9.60	9.83	8.92
	R	11.2 - 15	7.5 - 12.6	6.3 - 12.5	5.6 - 13.0	6.9 - 12
Lactic Acid in meq/l		3.01	4.99	5.68	6.22	5.72
	R	1.33 - 7.65	2.54 - 8.0	3.02 - 8.9	3.21 - 8.98	2.36 - 9.85

R = Range

MEAN pH, pCO_2, HCO_3 AND LACTIC ACID OF CONTROL DOGS

SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) WITH pCO_2 CORRECTED TO 40 MM HG

TIME IN MINUTES	0	30	90	150	210
pH	7.25	7.17	7.1	7.12	7.14
pCO_2 in mm Hg	40	40	40	40	40
Bicarbonate in meq/l	22.5	17.5	14.0	15.0	16.0
Lactic Acid in meq/l	3.01	4.99	5.68	6.22	5.72

APPENDIX V

MEAN VITAL SIGNS OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		36.92	36.52	36.63	36.16	34.14	35.58	35.22	35.09	34.64
	R	32 - 39.2	32 - 39.5	34.2 - 38	34 - 38	34 - 37.5	34.4 - 37	33.1 - 37	33 - 37	32.5 - 37
Blood Pressure in mm Hg		152	109	115	110	109	103	99	93	88
	R	110 - 180	28 - 165	50 - 160	58 - 158	64 - 170	65 - 175	52 - 150	40 - 160	38 - 160
Heart Rate per Minute		146	137	127	133	142	148	146	147	150
	R	132 - 165	96 - 175	66 - 180	100 - 162	104 - 180	120 - 170	120 - 175	120 - 172	120 - 180
Venous Pressure in cm Water		6.2	4.6	3.3	3.8	4.4	4.2	4.5	4.5	4.4
	R	3 - 14	1.5 - 12	1.5 - 7	1 - 7	1 - 9.5	1 - 8	2 - 8	1.5 - 10.5	1.5 - 8.5
Respiratory Rate per Minute		26	33	37	37	32	30	27	26	25
	R	6 - 42	6 - 75	6 - 52	18 - 80	15 - 78	15 - 70	15 - 60	15 - 60	15 - 36

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade		34.44	34.41	34.44	34.21	34.07	33.85	33.85	33.79
	R	32.5 - 36.5	32.5 - 36	32.5 - 36.5	32.5 - 35.5	32.5 - 35.5	32 - 35	32 - 35	32 - 35
Blood Pressure in mm Hg		88	88	91	95	99	102	103	105
	R	40 - 156	40 - 160	45 - 160	45 - 160	50 - 160	50 - 165	55 - 160	55 - 160
Heart Rate per Minute		154	161	165	162	162	160	160	160
	R	118 - 210	126 - 230	130 - 240	132 - 245	132 - 230	130 - 222	132 - 224	130 - 230
Venous Pressure in cm Water		4.9	4.7	5.0	5.5	5.7	6.0	5.8	5.9
	R	1.5 -	1 -	2 -	2 -	2 -	2.5 -	2.5 -	2.5 -
Respiratory Rate per Minute		25	24	25	25	24	27	26	26
	R	15 - 40	15 - 42	15 - 40	15 - 42	15 - 36	21 - 40	21 - 40	21 - 42

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

A

DOG NO.	1	2	3	4	5	6	7
TIME IN MINUTES							
0	37.5	37.0	36.5	37.5	39.25	32.0	38.75
15	37.5	37.0	35.5	37.0	39.5	32.0	38.5
30	38.0	37.5	35.5	37.5	36.2	35.5	38.0
45	38.0	37.5	35.25	37.5	36.2	37.2	37.0
60	37.0	37.5	35.1	37.7	35.7	37.5	36.5
75	37.0	36.0	35.5	37.5	35.25	36.5	36.5
90	36.9	35.5	33.1	36.5	35.0	36.5	35.1
105	36.5	35.25	33	36.5	35.0	36.5	35.1
120	35.5	34.75	32.5	36.5	34.7	36.5	34.1
135	35.5	34.75	32.5	36.0	34.0	36.5	34.1
150	35.5	34.75	32.5	36.0	34.0	36.0	34.5
165	35.5	34.5	32.5	36.5	34.0	35.5	34.0
180	35.5	34.5	32.5	35.5	33.5	35.0	34.0
195	35.0	34.5	32.5	35.5	33.5	35.0	34.0
210	35.0	34.0	32.0	35.0	33.5	35.0	33.5
225	35.0	34.0	32.0	35.0	33.5	35.0	33.5
240	35.0	34.0	32.0	35.0	33.0	35.0	33.5
SURVIVAL TIME IN HOURS	8	30+	20	9½	9½	30+	30+

B

DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
TIME IN MINUTES								
0	37.0	38.0	38.5	38.0	35.0	36.0	36.0	36.92
15	36.0	37.0	37.9	37.5	34.0	36.0	36.5	36.52
30	36.0	37.0	38.0	37.5	34.2	35.5	36.5	36.63
45	35.2	35.0	37.5	35.0	34.0	35.0	36.0	36.16
60	36.0	35.0	37.5	36.0	34.0	35.0	35.5	36.14
75	35.0	35.5	37.5	35.0	34.0	34.0	35.0	35.58
90	33.5	36.0	37.0	35.0	34.0	34.0	35.0	35.22
105	33.5	36.0	37.0	35.0	34.0	34.0	34.0	35.09
120	33.5	35.0	37.0	35.0	33.0	33.0	34.0	34.64
135	34.0	35.0	36.0	35.0	33.0	33.0	34.0	34.44
150	34.0	35.0	36.0	34.0	33.0	33.0	34.0	34.41
165	34.0	35.0	35.5	34.0	33.0	33.5	34.5	34.44
180	33.5	34.5	35.5	34.0	33.0	33.5	34.5	34.21
195	33.5	34.5	35.5	33.5	32.5	33.5	34.0	34.07
210	33.5	34.4	35.0	33.5	32.5	33.0	34.0	33.85
225	33.5	34.0	35.0	33.5	32.5	33.5	34.0	33.85
240	33.5	34.0	35.0	33.0	32.0	34.0	33.5	33.79
SURVIVAL TIME IN HOURS	9.5	9.5	5	30+	30+	30+	30+	20

MEAN BLOOD PRESSURE IN MM Hg OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

A	DOG NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	110	130	164	140	140	175	160
	15	28	130	165	110	122	115	165
	30	50	110	110	115	120	120	105
	45	58	92	128	120	104	120	125
	60	64	100	132	65	80	120	130
	75	75	110	122	65	67	120	112
	90	65	100	135	90	60	120	110
	105	70	92	142	80	54	110	110
	120	70	85	128	80	50	90	102
	135	72	85	128	75	48	65	108
	150	72	70	128	75	48	75	105
	165	72	60	130	80	50	85	105
	180	72	65	130	80	50	90	120
	195	70	75	135	85	55	100	130
	210	70	80	135	85	55	110	145
	225	68	90	135	85	55	120	145
	240	68	100	135	85	55	120	145
	SURVIVAL TIME IN HOURS	8	30+	20½	9½	9½	30+	30+

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	155	170	154	155	160	135	180	152
	15	30	60	104	152	130	135	100	109
	30	50	102	115	160	145	130	100	115
	45	62	80	118	158	150	150	120	110
	60	98	85	110	150	130	150	170	109
	75	68	82	100	140	122	149	175	103
	90	52	75	88	120	118	148	150	99
	105	40	62	84	102	126	160	144	93
	120	38	55	90	110	126	160	120	88
	135	40	55	80	90	120	156	130	88
	150	40	55	50	90	120	160	150	88
	165	45	55	50	100	130	160	150	91
	180	45	60	55	112	135	160	155	95
	195	50	60	55	110	140	160	155	99
	210	50	65	55	120	140	165	150	102
	225	55	60	55	130	140	160	150	103
	240	55	60	55	130	150	160	150	105
	SURVIVAL TIME IN HOURS	9.5	9.5	5	30*	30*	30*	30*	20.0

MEAN HEART RATE PER MINUTE OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

A	DOG NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	135	132	117	171	146	165	150
	15	96	155	120	171	145	175	165
	30	66	120	120	150	120	162	90
	45	104	108	120	150	132	162	100
	60	132	104	120	165	160	180	126
	75	132	150	120	168	148	150	135
	90	129	124	120	165	158	150	120
	105	120	150	132	165	172	150	129
	120	150	135	120	159	170	180	156
	135	148	132	132	160	144	180	154
	150	150	126	130	160	160	180	150
	165	150	130	130	165	160	180	150
	180	150	132	132	165	144	170	150
	195	160	132	132	165	150	165	155
	210	155	130	132	160	155	160	155
	225	150	132	132	160	155	150	155
	240	150	130	130	160	155	150	155
	SURVIVAL TIME IN HOURS	8	30'	20.0	9.5	9½	30'	30'

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	135	150	150	150	135	135	180	146
	15	150	150	132	156	99	135	100	137
	30	180	150	150	150	100	130	100	127
	45	147	150	150	154	120	150	120	133
	60	141	162	154	150	132	150	120	142
	75	132	168	160	160	132	148	170	148
	90	150	153	162	162	132	150	175	146
	105	159	156	160	150	120	149	150	147
	120	135	180	150	162	120	150	144	150
	135	156	210	165	180	118	160	128	154
	150	150	230	210	180	159	160	130	161
	165	150	240	220	180	160	160	135	165
	180	150	245	212	175	155	155	132	162
	195	155	230	212	160	150	150	144	162
	210	155	222	220	160	150	150	140	160
	225	160	224	210	165	155	158	138	160
	240	160	230	210	155	155	160	140	160
	SURVIVAL TIME IN HOURS	9.5	9.5	5	30*	30*	30*	30*	20.0

MEAN VENOUS PRESSURE IN CM WATER IN DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

A	DOG NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	5.5	3.0	5.0	3.5	11.5	5.0	14.0
	15	2.5	1.5	6.0	5.5	12.0	4.0	3.0
	30	3.5	1.5	7.0	2.5	2.0	4.0	2.0
	45	5.5	1.5	5.5	1.0	3.0	5.0	3.5
	60	4.5	1.0	5.5	1.5	6.0	5.0	9.5
	75	4.5	1.0	6.5	2.0	4.5	4.5	2.5
	90	5.5	2.5	6.5	2.0	3.5	5.0	4.5
	105	5.0	3.0	6.5	1.5	3.0	5.0	10.5
	120	5.0	3.5	5.5	1.5	3.0	6.0	7.5
	135	5.0	3.5	6.5	1.5	3.0	6.0	13.5
	150	5.0	2.0	6.5	1.5	3.0	5.0	13.5
	165	5.5	3.5	6.5	2.0	3.0	5.5	13.5
	180	5.5	3.5	6.0	2.0	4.5	5.0	13.5
	195	5.8	3.5	6.0	2.0	4.5	5.0	12.5
	210	6.0	3.5	6.0	2.5	4.5	5.0	12.5
	225	6.0	3.5	6.0	2.5	4.0	5.0	10.5
	240	6.0	3.5	6.0	2.5	4.0	5.0	10.5
	SURVIVAL TIME IN HOURS	8	30*	20.	9½	9½	30*	30*

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	6.5	8.0	6.5	7.0	3.0	5.0	4.0	6.2
	15	5.5	8.0	2.0	6.0	2.0	3.0	4.0	4.6
	30	3.0	5.5	2.0	3.0	2.0	4.0	4.5	3.3
	45	4.5	7.0	2.0	3.0	3.5	4.0	4.5	3.8
	60	4.0	6.0	2.0	3.0	4.0	4.5	5.5	4.8
	75	4.5	6.0	2.0	3.0	8.0	4.5	6.0	4.2
	90	3.4	7.0	2.0	3.0	8.0	4.5	6.5	4.5
	105	3.5	7.0	1.5	2.5	2.5	5.0	7.5	4.5
	120	3.0	7.0	1.5	2.5	2.5	5.0	8.5	4.4
	135	4.0	6.0	1.5	2.5	2.5	5.0	8.5	4.9
	150	4.0	6.0	1.5	1.0	4.0	5.0	8.0	4.7
	165	4.0	6.5	2.0	2.0	4.0	5.0	7.5	5.0
	180	5.5	6.5	4.5	3.5	4.5	5.5	7.5	5.5
	195	5.5	6.8	6.5	4.5	4.5	5.5	7.0	5.7
	210	6.0	7.0	8.5	5.5	4.5	5.5	7.0	6.0
	225	6.0	7.0	8.5	5.5	5.0	5.5	7.0	5.8
	240	6.0	7.0	8.5	6.5	5.0	5.5	7.0	5.9
	SURVIVAL TIME IN HOURS	9.5	9.5	5	30*	30*	30*	30*	20.0

MEAN RESPIRATORY RATE PER MINUTE IN DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

A	DOG NO.	1	2	3	4	5	6	7
	TIME IN MINUTES							
	0	21	21	18	27	40	33	15
	15	42	21	44	27	40	75	15
	30	60	21	22	22	48	62	72
	45	60	21	18	18	40	60	60
	60	28	18	15	27	68	21	18
	75	27	24	15	24	48	21	70
	90	18	42	15	27	48	21	24
	105	21	40	15	24	36	18	24
	120	24	33	15	24	36	30	24
	135	24	24	15	18	40	36	24
	150	22	27	15	18	42	21	24
	165	24	27	15	18	40	27	24
	180	24	27	15	21	42	27	21
	195	21	21	15	21	36	27	24
	210	27	24	21	24	40	30	24
	225	27	24	21	27	40	21	27
	240	27	24	21	24	42	24	24
	SURVIVAL TIME IN HOURS	8	30*	20.	9½	9½	30*	30*

B	DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN
	TIME IN MINUTES								
	0	12	6	42	21	39	60	12	26
	15	72	6	27	18	22	54	12	33
	30	60	6	30	18	40	51	12	37
	45	80	18	24	18	42	47	15	37
	60	54	27	21	15	78	47	18	32
	75	36	18	24	15	42	44	18	30
	90	39	18	24	15	24	60	15	27
	105	30	18	24	15	24	60	24	26
	120	36	18	24	15	24	27	21	25
	135	36	18	24	18	27	27	24	25
	150	36	18	33	15	27	27	24	24
	165	36	21	33	15	21	27	24	25
	180	30	24	33	21	24	24	21	25
	195	27	24	36	21	24	24	21	24
	210	27	24	30	27	24	27	27	27
	225	27	24	36	24	27	21	21	26
	240	24	24	36	21	27	24	24	26
	SURVIVAL TIME IN HOURS	9.5	9.5	5	30*	30*	30*	30*	20.0

APPENDIX VI

MEAN CHLORIDES IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	103	113	110	102	109	118	110	108	119	113	110
30	106	115	114	108	109	111	106	112	105	115	110
90	107	115	108	106	105	117	105	118	104	108	109
150	108	111	109	103	109	120	109	122	110	105	110
210		116	112	109	116	126	109	112	116	114	116
SURVIVAL TIME IN HOURS	8	30*	20	9½	9.5	30*	30*	30*	30*	30*	22.7

MEAN SODIUM IN MEQ/L OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	138	165	160	128	148	144	143.5	142.5	159.5	148	147.7
30	163	163	163	130	143.4	121	148	137.2	144	163	147.6
90	149	160	141	134	143.8	129.5	137	143	134.5	158	138.1
150	159	159	134	132	150	142.5	141.5	142	142	160	146.2
210		164	144	120	149	138	142	143	143	145	143
SURVIVAL TIME IN HOURS	8	30*	20	9½	5	30*	30*	30*	30*	30*	22.7

MEAN POTASSIUM IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXINE E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	3.6	3.3	2.1	4.6	3.47	4.17	4.15	3.3	4.25	3.4	3.63
30	4.3	3.8	2.95	3.5	3.45	3.0	3.3	3.0	3.38	4.2	3.39
90	3.1	2.6	1.95	2.7	2.7	3.9	2.95	2.7	3.5	2.9	2.9
150	3.1	2.6	2.4	2.8	3.25	3.47	2.95	2.5	3.42	3.0	2.95
210			2.1	3.2	4.55	3.82	2.9	2.3	3.4	3.8	3.26
SURVIVAL TIME IN HOURS	8	30▼	20	9½	5	30▼	30▼	30▼	30▼	30▼	22.7

MEAN HEMATOCRIT % IN DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	55	51	45	40	47	52	42	51	57	45	49
30	40	49	42	37	44	46	36	49	49	42	43
90	39	40	50	38	53	38	37	45	48	40	43
150	37	45	42	39	60	45	38	50	51	37	44
210	38	40	37	40	63	46	39	51	53	42	45
SURVIVAL TIME IN HOURS	8	30▼	20½	9½	5	30▼	30▼	30▼	30▼	30▼	22.7

MEAN CHLORIDE, SODIUM, POTASSIUM IN MEQ/L AND HEMATOGRIT %

OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

AND EARLY DIALYSIS

TIME IN MINUTES		0	30	90	150	210
Chlorides in meq/l		110	110	109	110	116
	R	102 - 119	105 - 115	104 - 117	103 - 122	109 - 126
Sodium in meq/l		147.7	147.6	138.1	146.2	143
	R	128 - 165	121 - 163	129.5 - 160	132 - 160	120 - 164
Potassium in meq/l		3.63	3.39	2.90	2.95	3.26
	R	2.1 - 4.6	2.95 - 4.3	1.95 - 3.9	2.4 - 3.47	2.1 - 4.55
Hematocrit %		49	43	43	44	45
	R	40 - 57	36 - 49	37 - 50	37 - 60	37 - 63

R = Range

MEAN pH OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	7.34	7.32	7.3	7.37	7.35	7.3	7.28	7.46	7.19	7.29	7.32
30	7.12	7.34	7.3	7.39	7.26	7.26	7.29	7.41	7.23	7.28	7.28
90	7.21	7.24	7.4	7.35	7.29	7.3	7.33	7.4	7.28	7.37	7.31
150	7.23	7.24	7.44	7.31	7.23	7.32	7.38	7.44	7.31	7.36	7.33
210	7.3	7.2	7.43	7.3	7.35	7.39	7.4	7.41	7.34	7.38	7.35
SURVIVAL TIME IN HOURS	8	30*	20	9½	5	30*	30*	30*	30*	30*	22.7

MEAN pCO_2 IN MM Hg OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	25.0	24.0			31.0	25.2	14.8	17.2	51.0	18.8	25.8
30	14.5				27.0	27.5	14.5	14.0	32.0	28.5	22.5
90	30.0	24.5			24.0	26.0	14.0	10	21.0	24.5	21.7
150	12.0	25.5			20.5	30.0	17.2	16.5	20.0	20.5	20.2
210		19.0			15.5	20.0	14.5	10.5			15.9
SURVIVAL TIME IN HOURS	8	30*	20	9½	5	30*	30*	30*	30*	30*	22.7

MEAN BICARBONATE IN MEQ/L OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	14.9	15.0			17.0	12.9	14.8	13.5	18.0	14.0	15.01
30	6.3	11.0			12.5	12.9	14.5	10.6	13.3	15.0	12.01
90	12.0	11.5			12.7	13.0	14.0	7.5	11.8	12.0	11.8
150	7.0	8.8			9.7	15.2	11.5	12.8	11.7	11.9	11.7
210	8.0	8.9			10.0	13.0	11.0	8.80	12.0	12.0	10.4
SURVIVAL TIME IN HOURS	8	30*	20	9½	5	30*	30*	30*	30*	30*	22.7

MEAN LACTIC ACID IN MEQ/L OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
0	3.49	1.68	1.81	4.24	3.64	3.75	3.96	8.16	3.5	1.49	3.57
30	9.82	3.73	2.69	6.15	5.38	3.67	3.85	5.66	3.4	3.62	4.79
90	8.65	5.96	3.07	6.65	4.38	4.16	3.85	8.57	4.3	6.56	5.71
150	9.9	7.48	3.29	8.75	6.23	6.23	4.89	5.I	4.7	5.82	6.23
210	9.8	8.15	2.69	8.23		5.12	5.20	6.43	4.5	3.75	5.98
SURVIVAL TIME IN HOURS	8	30*	20	9½	5	30*	30*	30*	30*	30*	22.7

MEAN pH, pCO_2, HCO_3 AND LACTIC ACID IN DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS

TIME IN MINUTES		0	30	90	150	210
pH		7.32	7.28	7.31	7.33	7.35
	R	7.19 - 7.46	7.12 - 7.41	7.21 - 7.4	7.23 - 7.44	7.2 - 7.43
pCO_2 in mm Hg		25.8	22.5	21.7	20.2	15.9
	R	14.8 - 51.0	14.0 - 32.0	10 - 30.0	12.0 - 30	10.5 - 20
Bicarbonate in meq/l		15.01	12.01	11.8	11.7	10.4
	R	12.9 - 18	6.3 - 15	7.5 - 14	7.0 - 15.2	8.0 - 13
Lactic Acid in meq/l		3.57	4.79	5.71	6.23	5.98
	R	1.68 - 8.16	2.69 - 9.82	3.07 - 8.65	3.29 - 9.9	2.69 - 9.8

MEAN pH, pCO_2, HCO_3 AND LACTIC ACID IN DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH pCO_2 CORRECTED TO 40 MM Hg

TIME IN MINUTES	0	30	90	150	210
pH	7.20	7.16	7.18	7.19	7.12
pCO_2 in mm Hg	40	40	40	40	40
Bicarbonate in meq/l	20.5	17.5	18.0	19.0	17.5
Lactic Acid in meq/l	3.57	4.79	5.71	6.23	5.98

SURVIVAL TIME IN HOURS OF EARLY DIALYSED ENDOTOXIN DOGS - OLD AND NEW COILS

DOG NO.	1	2	3	4	5	6	7	8	9	10
Number of Hours	8	30*	20	9.5	9.5	30*	30*	9.5	9.5	5

DOG NO.	11	12	13	14	MEAN NO. HOURS	PERMANENT SURVIVORS	PERCENT SURVIVORS
Number of Hours	30*	30*	30*	30*	20.0	7	50%

A P P E N D I X VII

COMPARATIVE VITAL SIGNS OF CONTROL AND EARLY DIALYSED DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

A	TIME IN MINUTES		0	15	30	45	60	75	90	105	120
	Temperature in Degrees Centigrade	C	37.51	37.32	36.8	36.5	86.49	36.08	36.0	35.86	36.11
		D	36.92	36.52	36.63	36.16	36.14	35.58	35.22	35.09	34.64
	Blood Pressure in mm Hg	C	154	134	119	109	95	90	89	89	88
		D	110	109	115	110	109	103	99	93	88
	Heart Rate per Minute	C	154.07	140	132.57	139.93	146	149.57	163	158.93	160.86
		D	146	137	125	133	142	148	146	147	150
	Venous Pressure in cm Water	C	6.5	5.4	5.1	4.7	4.5	4.3	3.9	4.4	4.1
		D	6.2	4.6	3.3	3.8	4.4	4.2	4.5	4.5	4.4
	Respiratory Rate per Minute	C	29.5	27.64	23.86	26.79	33.86	33.14	30.5	29.93	30.43
		D	26	33	37	37	32	30	27	26	25

B	TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240
	Temperature in Degrees Centigrade	C	36.03	36.3	36.2	36.1	36.0	35.5	34.9	34.6
		D	34.44	34.41	34.44	34.21	34.07	33.85	33.85	33.79
	Blood Pressure in mm Hg	C	89	87	93	95	94	95	96	95
		D	88	88	91	95	99	102	103	105
	Heart Rate per Minute	C	169.21	181.5	187.8	184.7	189.9	186.6	187.3	187.8
		D	154	161	165	162	162	160	160	160
	Venous Pressure in cm Water	C	4.5	3.9	5.5	6.2	6.5	6.7	5.9	5.6
		D	4.9	4.7	5.0	5.5	5.7	6.0	5.8	5.9
	Respiratory Rate per Minute	C	26.7	27.79	27.6	27.0	25.1	24.1	25.1	24.5
		D	25	24	25	25	24	27	26	26

C = Control

D = Dialysed

COMPARATIVE MEAN OF BLOOD CHEMISTRIES AND ELECTROLYTES

IN CONTROL AND EARLY DIALYSED DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

TIME IN MINUTES	0	30	90	150	210
CONTROL DOGS					
pH	7.37	7.33	7.33	7.32	7.34
pCO_2 in mm Hg	23.1	17.92	16.34	14.52	15.95
HCO_3 in meq/l	13.94	9.47	9.6	9.83	8.92
Lactic Acid in meq/l	3.01	4.99	5.68	5.22	5.72
Chlorides	112	114	114	116	115
Sodium	147	144	146	148	145
Potassium	3.66	3.88	3.42	3.71	3.99
Hematocrit %	47	52	52	53	54
DIALYSED DOGS					
pH	7.32	7.28	7.31	7.33	7.35
pCO_2 in mm Hg	25.8	22.5	21.7	20.2	15.9
HCO_3 in meq/l	15.01	12.01	11.8	11.7	10.4
Lactic Acid in meq/l	3.57	4.79	5.71	6.23	5.98
Chlorides	110	110	109	110	116
Sodium	147.7	147.6	138.1	146.2	143.0
Potassium	3.63	3.39	2.9	2.95	3.26
Hematocrit %	49	43	43	44	45

PERMANENT SURVIVALS AND NON SURVIVALS OF CONTROL AND EARLY DIALYSED DOGS

SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7
CONTROL DOGS							
Time in Hours	8	8	10	7.5	5	2.5	9
DIALYSED DOGS							
Time in Hours	8	30*	20	9.5	9.5	30*	30*

DOG NO. (Cont'd.)	8	9	10	11	12	13	14	MEAN HRS.	NO. OF P.S.	% SURVIVALS
CONTROL DOGS										
Time in Hours	4.75	30*	3.5	3.5	6	24	24	10.5	1	7%
DIALYSED DOGS										
Time in Hours	9.5	8.5	5	30*	30*	30*	30*	20.0	7	50%

Permanent Survivor - 30 Hrs.

TOTAL NUMBER OF DOGS BOTH CONTROL AND EXPERIMENTAL SUBJECTED TO 3MG/KG OF ENDOTOXIN

	TOTAL NO. OF DOGS	NO. OF P. SURV.	% SURVIVAL
CONTROL	34	6	17.64
EXPERIMENTAL	39	19	48.71
HISTAMINE GROUP	6	0	0

TOTAL NUMBER OF DOGS BOTH CONTROL AND SUBJECTED TO HAEMORRHAGIC SHOCK

	TOTAL NO. OF DOGS	NO. OF P. SURV.	% SURVIVAL
CONTROL	20	1	10%
EXPERIMENTAL	20	3	30%

A P P E N D I X VIII

MEAN VITAL SIGNS IN EARLY DIALYSED DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) WITH NEW COILS

A

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		37.9	37.9	37.8	37.7	37.6	37.5	37.5	37.4	37.4
	R	36 - 39	36 - 39	36 - 38.5	36 - 38.5	36 - 38	36 - 38.5	36.5 - 38	35.5 - 38.5	35.5 - 38.5
Blood Pressure in mm. Hg		156	89	93	101	105	104	109	112	112
	R	100 - 135	50 - 100	38 - 165	38 - 160	40 - 160	50 - 150	67 - 150	90 - 150	95 - 150
Heart Rate per Minute		190	106	135	161	162	167	175	178	173
	R	100 - 312	90 - 189	60 - 200	112 - 240	120 - 250	126 - 270	140 - 270	144 - 280	132 - 300
Venous Pressure in cm. Water		6.2	5.6	5.8	6.5	7.2	6.5	6.0	5.6	5.5
	R	1.5 - 13.5	2.0 - 13.0	1.0 - 12.5	2.0 - 12.5	2.5 - 12.5	2.5 - 15.5	2.5 - 12.5	1.5 - 12.5	1.5 - 12.5
Respiratory Rate per Minute		19.2	21.9	21.3	23.7	23.4	24.9	23.4	23.7	24.0
	R	15 - 24	15 - 36	12 - 36	18 - 27	18 - 27	21 - 39	15 - 27	21 - 27	12 - 27

B

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240	270
Temperature in Degrees Centigrade		37.1	37.0	36.8	36.7	36.4	36.1	36.0	35.9	35.8
	R	35.5-38.5	35.5-38	35.5-38	35.5-38	35-37.5	35-37.5	35-37.5	35-37.5	35-37.5
Blood Pressure in mm. Hg.		109	108	107	106	105	102	100	100	101
	R	65-150	65-155	65-155	65-155	65-155	65-160	65-160	65-167	65-160
Heart Rate per minute		170	170	172	173	172	172	171	180	182
	R	136-300	134-270	136-280	140-250	132-250	144-255	140-230	140-260	140-270
Venous Pressure in cm. Water		5.7	5.7	5.5	5.7	5.7	5.7	5.8	6.2	6.2
	R	2.0-10.0	1.0-13.5	1.0-12.5	1.5-12.5	1.5-12.5	2.0-12.5	2,0-12.5	3.0-12.5	3.0-12.5
Respiratory Rate per minute		24.0	27.0	28.5	28.2	24.6	25.8	24.3	24.7	25.2
	R	18-30	18-30	18 - 36	21-36	21-30	18-30	18-30	21-40	21-40

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH NEW COILS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	39.0	36.0	38.5	38.5	38.0	37.5	38.0	38.0	38.0	37.0	37.9
15	39.0	36.0	38.5	38.5	38.0	37.5	38.0	38.0	38.0	37.0	37.9
30	38.5	36.0	38.5	38.5	38.0	37.5	38.0	38.0	38.0	37.0	37.8
45	38.5	36.0	38.5	38.0	38.0	37.5	38.0	37.5	38.5	37.0	37.7
60	38.0	36.0	38.0	38.0	38.0	37.5	38.0	37.5	36.5	38.5	37.6
75	38.0	36.0	38.0	38.0	37.5	37.5	37.5	37.5	36.5	38.5	37.5
90	38.0	35.5	38.0	38.0	37.5	37.5	37.5	37.5	36.5	38.5	37.5
105	37.5	35.5	38.0	38.5	37.5	37.5	37.5	37.5	36.5	38.0	37.4
120	37.5	35.5	37.5	38.5	37.5	37.5	37.5	37.5	36.5	38.0	37.4
135	37.5	35.5	37.5	38.5	37.5	36.5	37.0	37.0	36.5	37.5	37.1

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
150	37.5	35.5	37.5	38.0	37.5	36.5	37.0	37.0	36.0	37.5	37.0
165	37.5	35.5	3555	38.0	37.5	36.5	37.0	37.0	36.0	37.5	36.8
180	37.5	35.5	35.5	38.0	36.5	36.5	37.0	36.5	36.0	37.5	36.7
195	37.0	35.0	35.5	37.5	36.5	36.0	37.0	36.0	36.0	37.5	36.4
210	35.5	35.0	35.5	37.5	36.5	35.5	36.0	36.0	36.0	37.5	36.1
225	35.5	35.0	35.0	37.5	35.5	35.5	36.0	36.5	36.0	37.0	36.0
240	35.5	35.0	35.0	37.5	35.5	35.5	36.0	36.5	35.5	37.0	35.9
270	35.5	35.0	35.0	37.5	35.5	35.5	35.5	36.5	35.0	37.0	35.8
SURVIVAL TIME IN HOURS	30*	24	30*	24	30*	30*	30*	24	30*	30*	28.2

MEAN BLOOD PRESSURE IN MM Hg OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH NEW COILS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes 0	140	165	148	175	165	135	145	190	135	165	156
15	50	75	75	140	55	90	100	80	45	75	89
30	50	100	52	150	38	95	112	165	95	75	93
45	80	125	80	140	38	98	108	160	100	80	101
60	90	125	95	135	40	100	108	160	100	95	105
75	100	135	90	105	50	100	100	150	100	112	104
90	100	135	100	105	67	112	100	150	110	112	109
105	105	135	100	100	90	112	100	150	110	115	112
120	95	130	100	100	95	112	120	150	100	115	112
135	65	130	120	100	95	100	120	150	100	112	109
150	65	112	120	98	100	100	120	155	100	112	108

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
TIME IN MINUTES											
165	65	110	112	98	100	100	110	155	112	112	107
180	65	100	112	98	100	100	100	155	112	115	106
195	65	95	115	95	100	98	100	155	112	115	105
210	65	65	115	95	100	98	100	160	112	112	102
225	65	70	100	95	98	98	98	160	100	110	100
240	65	75	100	95	98	98	90	167	100	110	100
270	65	75	112	95	98	98	90	160	100	110	101
SURVIVAL TIME IN HOURS	30*	24	30*	24	30*	30*	30*	24	30*	30*	28.2

MEAN HEART RATE PER MINUTE OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH NEW COILS

DOG NO.		1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes	0	100	150	250	240	144	204	174	312	180	150	190
	15	90	100	90	100	99	100	98	189	98	100	106
	30	60	118	180	200	96	100	120	189	120	165	135
	45	112	136	162	240	120	180	180	189	120	170	161
	60	120	136	162	250	140	150	174	180	132	172	162
	75	126	135	171	270	155	170	168	180	132	165	167
	90	180	150	171	270	150	160	170	185	140	170	175
	105	150	148	216	280	160	180	180	179	144	144	178
	120	150	148	192	300	155	180	144	180	132	146	173
	135	150	150	180	300	140	158	144	178	136	165	170
	150	150	150	180	270	150	160	148	190	134	170	170

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	144	148	180	280	155	170	150	180	136	172	172
180	140	144	180	250	180	180	155	185	140	174	173
195	132	144	172	250	180	180	160	185	144	168	172
210	140	144	172	255	178	155	162	180	144	170	170
225	150	150	172	230	190	200	162	179	140	140	171
240	140	150	170	260	180	222	170	168	138	168	180
270	140	150	180	270	162	215	220	172	140	170	182
SURVIVAL TIME IN HOURS	30*	24	30*-	24	30*-	30*	30*	24	30*	30*	28.2

MEAN VENOUS PRESSURE IN CM WATER OF DOGS SUBJECTED

TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH NEW COILS

DOG NO.		1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes	0	3.5	2.0	1.5	9.0	11.0	8.5	5.5	13.5	4.0	3.0	6.2
	15	3.5	2.0	2.0	3.5	11.0	13.0	5.5	7.5	4.0	3.5	5.6
	30	3.5	1.0	3.0	8.0	6.5	12.5	5.5	7.5	6.5	3.5	5.8
	45	3.5	2.0	4.5	9.5	6.5	12.5	5.5	10.0	6.5	4.0	7.2
	60	3.5	2.5	4.0	9.0	6.5	12.5	6.5	16.5	6.5	4.0	7.2
	75	3.5	2.5	3.5	5.5	5.5	15.5	6.5	12.5	6.0	4.0	6.5
	90	3.5	1.5	2.0	5.5	5.5	12.5	6.5	12.5	6.0	4.5	6.0
	105	3.5	1.5	1.0	5.0	5.5	12.5	6.0	10.5	6.0	4.5	5.6
	120	3.5	1.5	1.5	3.5	5.0	12.5	6.0	10.5	6.0	5.0	5.5
	135	3.5	2.0	3.0	3.5	5.0	12.5	5.5	10.0	6.5	5.5	5.7
	150	3.5	2.0	1.0	3.5	5.5	13.5	5.5	10.5	6.5	5.5	5.7

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	3.5	2.0	1.0	2.5	6.0	12.5	5.0	10.5	6.5	5.0	5.5
180	3.5	2.0	1.5	2.5	6.0	12.5	5.0	12.5	6.0	5.0	5.7
195	4.5	3.0	1.5	2.5	6.0	12.5	5.0	10.5	5.5	5.5	5.7
210	4.5	3.0	2.0	2.5	6.0	12.5	5.0	10.5	5.5	5.0	5.7
225	4.5	3.0	2.0	3.0	6.0	12.5	5.5	10.5	5.5	5.0	5.8
240	4.5	3.0	6.5	3.0	6.0	8.5	5.5	12.5	5.5	6.5	6.2
270	4.5	3.0	6.5	3.0	6.0	8.0	6.0	12.5	5.5	6.5	6.2
SURVIVAL TIME IN HOURS	30'	24	30'	24	30'	30'	30'	24	30'	30'	28.2

MEAN RESPIRATORY RATE PER MINUTE OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND EARLY DIALYSIS WITH NEW COILS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	24	15	21	18	21	21	18	21	15	18	19.2
15	30	15	36	18	15	21	24	27	15	18	21.9
30	36	12	24	18	15	21	24	24	21	18	21.3
45	24	18	36	21	18	30	27	24	18	21	23.7
60	24	30	24	21	18	30	27	21	18	21	23.4
75	30	39	21	21	21	30	21	21	21	24	24.9
90	27	30	15	21	18	27	24	27	21	24	23.4
105	27	24	21	21	21	27	24	50	21	21	23.7
120	27	24	21	18	27	30	24	30	18	21	24.0
135	21	18	21	33	21	27	30	30	18	21	24.0
150	30	18	30	33	24	30	30	27	21	27	27.0

DOG. NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	36	18	30	36	24	30	33	27	24	27	28.5
180	36	24	33	33	24	21	33	27	24	27	28.2
195	30	24	27	21	24	18	27	24	24	27	24.6
210	27	24	33	27	24	18	27	27	21	30	25.8
225	27	24	30	27	21	18	24	27	18	27	24.3
240	21	24	40	27	21	21	24	24	21	24	24.7
270	20	24	40	24	21	21	24	27	27	24	25.2
SURVIVAL TIME IN HOURS	30*	24	30*	24	30*	30*	30*	24	30*	30*	28.2

SURVIVAL TIME IN HOURS OF EARLY DIALYSED ENDOTOXIN DOGS - NEW COILS ONLY

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN NO. HOURS
Number of Hours	30*	24	30*	24	30*	30*	30*	24	30*	30*	28.2

NO. OF PERMANENT SURVIVORS	PERCENT SURVIVORS
7	70%

APPENDIX IX

MEAN VITAL SIGNS OF DOGS IN ENDOTOXIN SHOCK AND DELAYED DIALYSIS

A	TIME IN MINUTES		0	15	30	45	60	75	90	105	120	135	150
	Temperature in Degrees Centigrade		38.1	38.1	38.1	37.8	37.6	37.5	37.5	37,4	37.3	37.1	37.2
		R	36.5- 39	36.5- 39	36.5- 39	36.5 - 39	36.2 - 38.5	36 - 38.5	36 - 38.5	36 - 38	36 - 38	36 - 38.5	36 - 38.5
	Blood Pressure in mm Hg		152	103	107	109	124	132	124	120	116	111	109
		R	135 - 170	52 - 140	40 - 160	45 - 155	50 - 150	55 - 180	60 - 180	60 - 150	50 - 155	48 - 150	48 - 150
	Heart Rate per Minute		180	131	122	163	168	171	180	181	201	198	216
		R	108 - 270	81 - 300	72 - 300	52 - 270	111 - 270	96 - 240	98 - 240	120 - 220	120 - 300	156 - 230	150 - 300
	Venous Pressure in cm Water		6.2	4.3	4.2	5.7	6.6	6.0	5.4	4.8	4.8	4.2	4.4
		R	2.5 - 9.5	1.5 - 10.5	1.5 - 10.5	1.5 - 10.5	1.5 - 13.0	1.5 - 14.5	1.5 - 14.5	1.0 - 10.5	1.0 - 10	1.5 - 14	1.5 - 10
	Respiratory Rate per Minute		21.3	20.4	18.9	20.7	22.7	22.8	24.3	20.7	20.4	22.8	23.1
		R	6 - 60	9 - 33	6 - 30	6 - 60	12 - 50	12 - 54	12 - 57	12 - 27	12 - 27	12 - 42	12 - 39

B	Time in Minutes (Cont'd.)		165	180	195	210	225	240	255	270	285	300	315	330
	Temperature in Degrees Centigrade		37.0	36.9	36.8	36.8	36.8	36.6	36.5	36.1	35.8	35.6	35.3	35.1
		R	36 - 39	36 - 39	36 - 38.5	36 - 38.5	36 - 38.5	35.5- 38.5	35 - 38.5	34.5- 38.5	34 - 38	33.5- 38.5	33.5- 38	33 - 38
	Blood Pressure in mm Hg		108	101	102	98	97	88	93	97	94	92	97	93
		R	45 - 150	45 - 140	40 - 135	40 - 130	42 - 130	40 - 120	40 - 120	45 - 120	45 - 115	50 - 115	50 - 125	50 - 123
	Heart Rate per Minute		223	215	219	208	201	173	174	179	178	174	168	168
		R	154 - 350	162 - 300	156 - 300	132 - 270	132 - 270	190 - 252	100 - 252	105 - 260	110 - 246	114 - 231	120 - 231	110 - 240
	Venous Pressure in cm Water		4.3	4.4	4.3	4.3	4.3	4.9	5.0	5.0	5.2	5.1	5.8	5.9
		R	1.0- 10.5	2.0- 10.5	2.0- 10.5	2.0- 10.5	2.0- 10.5	3.0- 10.5	3.0- 11.5	2.5- 11.5	3.0- 10.5	2.5- 10.5	3.5- 9.5	3.5- 10.5
	Respiratory Rate per Minute		20.7	20.4	20.4	20.4	21.9	21.6	21.9	22.8	21.3	23.0	23.5	23.5
		R	12 - 27	12 - 27	12 - 27	12 - 27	12 - 30	12 - 30	12 - 36	12 - 36	12 - 30	12 - 39	12 - 39	12 - 39

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF DOGS DIALYSED 3½ - 4 HOURS

AFTER I.V. INJECTION OF 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG. NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	36.5	38.0	37.5	38.0	38.5	39.0	39.0	37.5	39.0	38.0	38.1
15	36.5	38.0	37.5	38.0	38.5	39.0	39.0	37.5	39.0	38.0	38.1
30	36.5	38.0	37.5	37.5	38.5	39.0	39.0	37.5	39.0	38.0	38.1
45	36.5	38.0	37.5	37.5	38.5	39.0	38.5	37.2	37.5	38.0	37.8
60	36.5	37.0	37.0	38.0	38.5	38.0	38.5	37.2	37.5	38.0	37.6
75	36.2	37.5	37.0	38.0	38.0	38.0	38.5	37.2	38.0	38.0	37.6
90	36.0	37.5	37.0	38.0	38.0	37.5	38.5	37.2	38.0	37.2	37.5
105	36.0	37.5	37.0	38.0	38.0	37.5	37.5	37.0	38.0	37.5	37.4
120	36.0	37.5	37.0	38.5	37.0	38.0	37.5	37.0	37.0	37.5	37.3
135	36.0	37.5	37.0	38.5	37.0	38.0	37.5	37.0	36.5	37.5	37.3
150	36.0	37.0	36.5	38.5	37.0	38.4	37.5	37.0	36.5	37.5	37.1
165	36.0	37.5	36.5	38.5	36.5	38.0	37.5	37.0	36.5	37.0	37.2

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes (Cont'd.)											
180	36.0	37.5	36.5	37.0	36.5	39.0	37.5	36.5	36.5	37.0	37.0
195	36.0	37.5	36.5	37.0	36.5	38.5	37.0	36.5	36.5	37.0	36.9
210	36.2	37.5	36.5	37.0	36.5	38.5	37.0	36.5	36.0	36.5	36.8
225	36.2	37.5	36.5	37.0	36.5	38.5	37.0	36.5	36.0	36.5	36.8
240	36.1	37.5	35.5	36.5	36.0	38.5	37.0	36.0	36.0	36.5	36.6
255	36.5	37.5	35.5	36.5	35.0	38.5	37.0	36.0	35.5	36.5	36.5
270	36.2	37.0	35.5	36.0	34.5	38.5	37.0	35.5	35.0	36.0	36.1
285	35.5	36.7	35.5	35.5	34.0	38.0	37.0	35.0	35.0	36.0	35.8
300	35.5	36.5	34.5	35.0	33.5	38.5	37.0	35.0	34.5	36.0	35.6
315	35.5	36.5	34.0	35.0	33.5	38.0		35.0	34.0	36.0	35.3
330	35.3	36.5	34.0	34.5	33.0	38.0		35.0	38.0	35.5	35.1
SURVIVAL TIME IN HOURS	30*	30*	30*	9	7½	30*	5	24	24	30*	22.0

MEAN BLOOD PRESSURE IN MM Hg OF DOGS DIALYSED 3½ - 4 HOURS

AFTER I.V. INJECTION OF 3 MG/KG of ENDOTOXIN E. COLI (DIFCO)

DOG. NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	162	140	140	160	135	165	155	150	140	170	152
15	130	125	140	90	52	100	110	65	130	100	103
30	160	125	140	40	48	125	100	90	130	105	107
45	155	130	140	45	48	130	100	100	130	115	109
60	150	130	150	112	50	140	105	110	140	150	124
75	140	180	155	140	55	140	110	110	145	145	132
90	130	120	150	130	60	140	115	110	135	145	124
105	125	100	135	100	60	145	140	110	130	140	120
120	110	90	135	110	50	130	155	110	125	140	116
135	108	80	130	110	48	125	140	105	120	150	111
150	108	70	130	112	48	120	125	105	120	150	109
165	105	65	135	115	45	120	120	105	120	150	108

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes (Cont'd.)											
180	110	60	140	110	45	110	120	85	120	112	101
195	112	60	135	115	40	120	120	85	130	100	102
210	115	60	130	115	40	110	120	85	100	100	98
225	120	65	130	115	42	110	120	85	100	90	97
240	60	85	120	70	40	120	120	85	80	95	88
255	70	100	85	112	40	110	120	85	110	100	93
270	95	100	90	120	45	120	90	90	115	100	97
285	115	90	110	80	45	110	90	85	115	98	94
300	115	80	100	70	50	112	90	85	115	98	92
315	125	80	100	100	50	115		90	115	98	97
330	123	80	95	80	50	110		90	115	98	93
SURVIVAL TIME IN HOURS	30*	30*	30*	9	7½	30*	5	24	24	30*	22.0

MEAN HEART RATE PER MINUTE OF DOGS DIALYSED 3½ - 4 HOURS AFTER I.V. INJECTION OF 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	192	108	180	270	180	150	180	138	132	270	180
15	150	31	99	90	150	102	300	138	112	90	131
30	120	72	99	126	159	126	300	90	144	100	122
45	170	72	210	144	162	120	270	156	150	180	163
60	162	120	201	150	180	160	270	156	111	168	168
75	150	96	162	201	178	180	240	156	108	240	171
90	180	98	165	210	180	210	222	150	150	240	180
105	185	120	160	216	180	220	210	162	160	200	181
120	165	120	175	210	210	300	220	162	180	214	201
135	166	180	195	192	210	222	230	156	214	210	198
150	180	180	180	228	195	300	240	150	290	212	216
165	154	180	198	250	210	350	240	159	300	190	223

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes (Cont'd.)											
180	180	168	168	270	170	282	250	162	300	200	215
195	162	168	210	265	156	300	270	162	290	222	219
210	180	132	258	240	168	180	260	168	270	224	208
225	180	132	198	225	180	160	270	162	270	230	201
240	150	114	198	252	156	90	210	168	150	240	173
255	138	120	210	252	156	100	210	168	162	220	174
270	154	120	150	260	156	105	210	240	158	240	179
285	168	114	180	180	150	110	210	246	210	216	178
300	150	114	170	168	150	120	210	231	210	220	174
315	150	120	150	180	130	120		231	210	222	168
330	155	120	162	240	120	110		168	210	230	168
SURVIVAL TIME IN HOURS	30*	30*	30*	9	7½	30*	5	24	24	30*	22.0

MEAN VENOUS PRESSURE IN CM WATER OF DOGS DIALYSED 3½ - 4 HOURS AFTER I.V. INJECTION OF 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	5.5	5.5	6.0	6.0	8.0	7.5	2.5	6.5	9.5	6.6	6.2
15	1.5	3.0	4.0	6.5	2.5	5.5	2.5	5.5	10.5	1.5	4.3
30	3.0	4.0	4.5	3.0	1.5	5.0	3.0	5.5	10.5	2.0	4.2
45	4.5	4.0	6.0	6.5	1.5	6.5	3.0	10.5	10.5	4.0	5.7
60	4.0	4.0	7.0	7.0	1.5	10.5	3.0	10.5	13.0	5.0	6.6
75	3.5	3.0	5.5	5.5	1.5	10.0	3.0	10.5	14.5	2.5	6.0
90	3.5	3.0	5.5	5.5	1.5	6.5	3.0	7.5	14.5	3.5	5.4
105	3.5	3.0	5.5	5.5	1.0	6.5	3.0	6.0	10.5	3.5	4.8
120	3.5	3.0	6.5	5.0	1.0	6.5	3.0	6.0	10.0	3.5	4.8
135	3.0	3.5	6.5	5.0	1.5	5.0	3.0	6.5	14.0	4.0	4.2
150	3.0	2.0	5.5	5.0	1.5	4.0	3.0	6.0	10.0	4.0	4.4
165	3.0	2.0	4.5	5.5	1.0	3.5	3.0	6.0	10.5	3.5	4.3

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
180	2.5	2.0	4.5	5.5	2.0	3.5	3.5	6.0	10.5	4.0	4.4
195	2.5	2.0	4.5	5.5	2.0	3.5	3.5	5.5	10.5	3.5	4.3
210	2.5	2.0	4.5	5.5	2.0	3.5	3.5	5.5	10.5	3.5	4.3
225	2.5	2.0	4.0	5.5	2.0	3.5	3.5	5.5	10.5	3.5	4.3
240	3.0	4.0	3.5	6.0	5.5	4.0	3.0	5.0	10.5	4.0	4.9
255	3.0	4.5	3.5	6.0	5.5	4.0	3.0	5.0	11.5	4.0	5.0
270	2.5	4.5	3.5	5.5	5.5	4.5	3.5	5.0	11.5	4.0	5.0
285	3.0	4.5	3.5	5.5	5.5	6.5	3.5	5.5	10.5	4.0	5.2
300	2.5	4.5	3.5	5.5	5.5	6.0	3.5	5.5	10.5	4.0	5.1
315	3.5	4.5	3.5	6.5	8.5	6.0		6.0	9.5	4.0	5.8
330	3.5	4.5	3.5	6.0	10.5	6.0		6.0	9.5	4.0	5.9
SURVIVAL TIME IN HOURS	30*	30*	30*	9	7½	30*	5	24	24	30*	22.0

MEAN RESPIRATORY RATE PER MINUTE OF DOGS DIALYSED 3½ - 4 HOURS AFTER I.V. INJECTION OF 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	18	6	36	60	21	12	15	15	12	18	21.3
15	33	12	27	21	27	12	12	21	9	30	20.4
30	21	6	27	18	30	12	18	21	9	27	18.9
45	60	6	24	18	27	12	18	15	9	18	20.7
60	45	12	21	50	24	12	18	15	12	18	22.7
75	30	12	27	54	24	12	21	15	12	21	22.8
90	21	15	21	57	24	12	27	33	12	21	24.3
105	18	15	24	27	24	12	27	18	21	21	20.7
120	18	18	24	18	27	12	27	15	24	21	20.4
135	18	42	21	15	27	12	24	21	24	24	22.8
150	18	39	21	15	27	12	30	27	18	24	23.1
165	18	15	24	21	27	12	27	21	18	24	20.7

DOG NO. (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
180	18	15	24	24	27	12	27	18	18	21	20.4
195	18	15	24	27	27	12	27	15	18	21	20.4
210	18	18	21	27	27	12	27	15	18	21	20.4
225	21	18	21	30	24	12	27	18	24	24	21.9
240	30	12	30	24	12	15	27	18	30	18	21.6
255	21	24	36	18	12	15	24	18	27	24	21.9
270	21	24	36	21	12	15	24	24	27	24	22.8
285	18	12	30	24	12	15	27	24	24	27	21.3
300	18	20	39	24	12	15	27	24	27	24	23.0
315	24	24	39	21	12	18		24	27	24	23.5
330	24	20	39	21	12	18		24	27	27	23.5
SURVIVAL TIME IN HOURS	30*	30*	30*	9	7½	30*-	5	24	24	30*	22.0

SURVIVAL TIME IN HOURS OF LATE DIALYSED ENDOTOXIN DOGS - OLD AND NEW COILS

DOG NO.	1	2	3	4	5	6	7	8	9	10	MEAN NO. HOURS
Number of Hours	30*	30*	30*	9	7.5	30*	5	24	24	30*	

NO. OF PERMANENT SURVIVORS	PERCENT SURVIVORS
5	50%

APPENDIX X

MEAN VITAL SIGNS OF ENDOTOXIN CONTROL DOGS (CONTROL TO LATE DIALYSIS)

A	TIME IN MINUTES		0	15	30	45	60	75	90	105	120	135	150
	Temperature in Degrees Centigrade		37.9	37.9	37.9	37.8	37.6	37.4	37.1	37.1	37.2	37.1	36.8
		R	36-39.5	36-39.5	36-39.5	36-39	34.2-39.0	34.2-39.0	34-38.5	34-38.5	34-38.5	34-38.5	34-38
	Blood Pressure in mm Hg		158	90	83	107	109	116	121	113	102	101	92
		R	125-185	30-130	40-120	45-160	50-160	65-140	55-145	55-150	32-145	30-135	20-140
	Heart Rate per Minute		190	124	103	132	129	127	133	150	180	185	165
		R	158-240	81-186	80-180	99-180	99-168	90-168	31-162	130-180	130-222	138-230	20-250
	Venous Pressure in cm Water		5.9	3.2	2.9	3.7	5.4	5.5	4.3	4.8	4.4	4.7	4.9
		R	1-12	1-6.5	1-6	2-6.5	2.5-10	2.5-10	2.0-7.5	2.5-7.5	2.5-7.5	2-11.5	1-12
	Respiratory		40	42	43	45	34	35	48	40	37	29	33
		R	12-90	15-90	15-90	18-95	15-70	15-68	24-90	24-66	21-48	10-64	6-71

B	TIME IN MINUTES (CONT'D.)		165	180	195	210	225	240	255	270	285	300
	Temperature in Degrees Centigrade		37.2	37.2	37.0	37.2	36.3	36.1	35.9	35.2	35.1	35.0
		R	36-38.5	36-38.5	36-38	36.5-38.5	35.5-37.5	35-37.5	35-37.5	35-35.5	35-35.5	35-35
	Blood Pressure in mm Hg		109	105	102	101	104	99	93	85	103	98
		R	75-150	60-160	60-150	60-150	65-150	62-130	40-140	30-120	62-128	40-130
	Heart Rate per Minute		224	244	244	228	227	228	171	144	180	205
		R	160-300	180-300	170-300	162-290	160-300	132-300	50-300	10-210	150-210	150-150
	Venous Pressure in cm Water		3.2	2.5	2.7	3.8	5.0	5.2	6.0	6.4	3.6	3.6
		R	4.5	4.5	5	6.5	10.5	10.5	12.5	14.5	5	5
	Respiratory Rate per Minute		40	30	30	25	27	30	19	21	26	25
		R	24-70	24-37	24-33	18-33	18-33	18-36	6-24	5-27	24-27	24-27

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF CONTROL DOGS SUBJECTED TO ENDOTOXIN 3 MG/KG OF E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	MEAN
Time in Minutes						
0	38.0	36.0	38.0	38.0	39.5	37.9
15	38.0	36.0	38.0	38.0	39.5	37.0
30	38.0	36.0	38.0	38.0	39.5	37.9
45	38.0	36.0	38.0	38.0	39.0	37.8
60	38.0	34.2	38.5	38.0	39.0	37.6
75	38.5	34.2	38.0	37.5	39.0	37.4
90	37.5	34.0	38.0	37.5	38.5	37.1
105	37.5	34.0	38.0	37.5	38.5	37.1
120	37.5	34.0	38.5	37.5	38.5	37.2
135	37.0	34.0	38.5	37.5	38.5	37.1
150	36.0	34.0	38.5	37.5	38.0	36.8

DOG NO. (Cont'd.)	1	2	3	4	5	MEAN
Time in Minutes						
165	36.0		38.5	36.5	38.0	37.2
180	36.0		38.5	36.5	38.0	37.2
195	36.0		38.0	36.5	37.5	37.0
210	36.5		38.5	36.5	37.5	37.2
225	36.0		37.5	36.5	35.5	36.3
240	36.0		37.5	36.0	35.0	36.1
255	35.5		37.0	36.0	35.0	35.9
270	35.0		35.5	35.5	35.0	35.2
285	35.0		35.0	35.5		35.1
300	35.0		35.0	35.0		35.0
SURVIVAL TIME IN HOURS	9	2½	30*	12	4½	11.6

MEAN BLOOD PRESSURE IN MM Hg OF CONTROL DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	MEAN
Time in Minutes						
0	125	150	170	160	185	158
15	30	90	130	118	80	90
30	40	60	120	115	90	83
45	45	60	130	130	160	107
60	50	65	130	140	160	100
75	68	65	140	140	165	116
90	110	55	145	145	138	121
105	112	55	135	150	112	113
120	100	32	135	145	100	102
135	105	30	135	135	98	101
150	80	20	140	125	95	92

DOG NO. (Cont'd.)	1	2	3	4	5	MEAN
Time in Minutes						
165	75		150	122	90	109
180	60		160	120	80	105
195	60		150	120	80	102
210	60		150	115	80	101
225	65		150	120	80	104
240	62		130	125	80	99
255	62		140	130	40	93
270	62		120	130	30	85
285	62		120	128		103
300	40		125	130		98
SURVIVAL TIME IN HOURS	9	$2\frac{1}{2}$	30*	12	$4\frac{1}{2}$	11.6

MEAN HEART RATE PER MINUTE OF CONTROL DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	MEAN
0	158	162	240	174	216	190
15	90	100	162	186	81	124
30	80	90	86	180	81	103
45	100	112	180	168	99	132
60	99	110	168	168	102	129
75	90	108	168	168	102	127
90	132	132	162	150	81	133
105	130	135	180	155	150	150
120	138	130	222	180	228	180
135	138	160	220	180	230	185
150	140	20	228	186	250	165

DOG NO. (Cont'd.)	1	2	3	4	5	MEAN
165	160		250	186	300	224
180	180		270	186	300	244
195	170		270	195	300	244
210	162		240	210	290	228
225	160		270	180	300	227
240	132		300	180	300	228
255	134		300	201	50	171
270	134		180	210	10	144
285	150		180	210		180
300	150		180	286		205
SURVIVAL TIME IN HOURS	9	2½	30*	12	4½	11.6

MEAN VENOUS PRESSURE IN CM WATER OF CONTROL DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	MEAN
Time in Minutes						
0	5.0	6.0	1.0	5.5	12.0	5.9
15	5.0	6.5	-1	3.0	2.5	3.2
30	4.0	6.0	-1	3.5	2.0	2.9
45	3.5	6.5	2.5	4.0	2.0	3.7
60	3.0	7.0	10.0	4.5	2.5	5.4
75	3.0	7.5	10.0	4.5	2.5	5.5
90	2.0	7.5	5.5	4.5	2.0	4.3
105	2.5	7.5	7.0	4.5	2.5	4.8
120	2.5	7.5	5.0	4.5	2.5	4.4
135	2.5	11.5	2.0	4.5	3.0	4.7
150	4.0	12.0	1.0	4.5	3.0	4.9

DOG NO. (Cont'd.)	1	2	3	4	5	MEAN
165	4.5		1.0	4.5	3.0	3.2
180	2.5		1.0	4.5	2.5	2.5
195	2.5		1.0	5.0	2.5	2.7
210	2.5		1.0	5.0	6.5	3.8
225	3.0		1.5	5.0	10.5	5.0
240	3.5		2.0	5.0	10.5	5.2
255	3.5		3.0	5.0	12.5	6.0
270	3.0		3.0	5.0	14.5	6.4
285	3.5		2.5	5.0		3.6
300	3.5		2.5	5.0		3.6
SURVIVAL TIME IN HOURS	9	2½	30*	12	4½	11.6

MEAN RESPIRATORY RATE PER MINUTE OF CONTROL DOGS SUBJECTED TO MG/KG OF ENDOTOXIN E. COLI (DIFCO)

DOG NO.	1	2	3	4	5	MEAN
Time in Minutes						
0	60	90	18	12	21	40
15	65	90	21	15	18	42
30	70	90	24	15	18	43
45	70	95	21	21	18	45
60	70	39	27	21	15	34
75	68	45	27	21	15	35
90	70	90	27	24	27	48
105	66	55	27	24	27	40
120	65	48	21	27	24	37
135	64	10	18	27	24	29
150	71	6	27	36	27	33

DOG NO. (Cont'd.)	1	2	3	4	5	MEAN
Time in Minutes						
165	70		30	36	24	40
180	37		30	30	24	30
195	33		24	30	33	30
210	30		21	18	33	25
225	33		24	18	33	27
240	27		30	18	36	30
255	24		24	21	6	19
270	27		27	27	5	21
285	27		27	24		26
300	24		27	24		25
SURVIVAL TIME IN HOURS	9	2½	30*	12	4½	11.6

A P P E N D I X XI

COMPARATIVE MEAN VITAL SIGNS OF CONTROL AND LATE DIALYSED DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO)

A	TIME IN MINUTES		0	15	30	45	60	75	90	105
	Temperature in Degrees Centigrade	C	37.9	37.9	37.9	37.8	37.6	37.4	37.1	37.1
		D	38.1	38.1	38.1	37.8	37.6	37.5	37.5	37.4
	Blood Pressure in mm Hg	C	158	90	83	107	109	116	121	113
		D	152	103	107	109	124	132	124	120
	Heart Rate per Minute	C	190	124	103	132	129	127	133	150
		D	180	131	122	163	168	171	180	181
	Venous Pressure in cm Water	C	5.9	3.2	2.9	3.7	5.4	5.5	4.3	4.8
		D	6.2	4.3	4.2	5.7	6.6	6.0	5.4	4.8
	Respiratory Rate per Minute	C	40	42	43	45	34	35	48	40
		D	21.3	20.4	18.9	20.7	22.7	22.8	24.3	20.7

B	TIME IN MINUTES (Cont'd.)		120	135	150	165	180	195	210	225
	Temperature in Degrees Centigrade	C	37.2	37.1	36.8	37.2	37.2	37.0	37.2	36.3
		D	37.3	37.1	37.2	37.0	36.9	36.8	36.8	36.8
	Blood Pressure in mm Hg	C	102	101	92	109	105	102	101	104
		D	116	111	109	108	101	102	98	97
	Heart Rate per Minute	C	180	185	165	224	244	244	228	227
		D	201	198	216	223	215	219	208	201
	Venous Pressure in cm Water	C	4.4	4.7	4.9	3.2	2.5	2.7	3.8	5.0
		D	4.8	4.2	4.4	4.3	4.4	4.3	4.3	4.3
	Respiratory Rate per Minute	C	37	29	33	40	30	30	25	27
		D	20.4	22.8	23.1	20.7	20.4	20.4	20.4	21.9

C	TIME IN MINUTES (Cont'd.)		240	255	270	285	300	315	330
	Temperature in Degrees Centigrade	C	36.1	35.9	35.2	35.1	35.0		
		D	36.6	36.5	36.1	35.8	35.6	35.3	35.1
	Blood Pressure in mm Hg	C	99	93	85	103	98		
		D	88	93	97	94	92	97	93
	Heart Rate per Minute	C	228	171	144	180	205		
		D	173	174	179	178	174	168	168
	Venous Pressure in cm Water	C	5.2	6.0	6.4	3.6	3.6		
		D	4.9	5.0	5.0	5.2	5.1	5.8	5.9
	Respiratory Rate per Minute	C	30	19	21	26	25		
		D	21.6	21.9	22.8	21.3	23.0	23.5	23.5

COMPARATIVE SURVIVAL TIMES IN HOURS OF DOGS SUBJECTED TO

3 MG/KG ENDOTOXIN WITH 'EARLY' AND LATE' DIALYSIS

A	DOG NO.	1	2	3	4	5	6	7	8	9
	Early Dialysis									
	0 - 35 Minutes	8	30*	20	9.5	9.5	30*	30*	9.5	8.5
	Controls	24	10	7½	5	2.50	9	4.45	6	3½
	Late Dialysis									
	3½ - 4 Hours	30*	30*	30*	9	7½	30*	5	24	24
	Controls	9	2½	30*	12	4				

B

DOG NO. (Cont'd.)	10	11	12	13	14	MEAN	PERMANENT SURVIVORS	% SURVIVAL
Early Dialysis 0 - 35 Minutes	5	30*	30*	30*	20	31.4	7	50%
Control	3.50	8	30*	24	8	10.5	1	7%
Late Dialysis $3\frac{1}{2}$ - 4 Hours	30*					22.0	5	50%
Controls						11.6	1	20%

30*- = Permanent Survivor

APPENDIX XII

MEAN VITAL SIGNS OF ENDOTOXIN DOGS SUBJECTED TO MECHANICAL EFFECTS OF DIALYSIS

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		37.86	37.76	37.70	37.55	37.55	37.25	37.15	36.75	36.63
	R	37.0-39.0	36.5-39.0	36.5-39.0	35.5-39.0	35.5-39.0	35.5-38.5	35.5-38.5	34.5-38.0	34.5-38.0
Blood Pressure in mm Hg.		149.5	96.4	100.0	107.1	111.5	106.7	96.9	89.9	85.9
	R	120-180	60-150	70-140	70-140	70-140	72-145	60-130	50-115	50-115
Heart Rate per Minute		163.2	105.1	136.4	137.2	164.7	169.6	175.8	183.7	185.7
	R	96-204	69-180	90-176	110-200	130-212	126-240	132-300	132-320	135-270
Venous Pressure in cm. water		8.49	6.74	8.84	8.44	8.15	8.15	7.45	6.85	6.40
	R	3.4-22.0	3.0-17.5	3.0-25.0	3.4-20.0	3.4-17.0	2.5-27.0	2.5-20.0	2.5-18.0	3.0-14.5
Respiratory Rate per Minute		29.1	26.6	23.2	27.1	28.9	26.2	27.9	28.6	26.8
		15-48	12-50	15-36	15-51	15-51	10-36	12-42	15-42	18-51

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240	360
Temperature in Degrees Centigrade		36.76	36.45	36.40	36.10	35.85	35.83	35.75	35.56	35.87
	R	34.5-38.0	34.5-37.5	34.5-37.5	34.0-37.5	34.0-37.5	33.5-37.5	33.5-37.0	33.5-37.0	33.5-36.5
Blood Pressure in mm. Hg.		79.2	78.0	76.6	74.3	72.4	84.8	84.4	83.1	79.0
	R	40-120	20-130	20-132	15-132	10-132	30-130	30-130	30-120	35-112
Heart Rate per Minute		190.2	198.5	189.3	192.8	139.4	176.9	172.9	190.4	178.1
		150-240	150-300	150-220	150-240	10-215	150-216	140-220	160-240	140-222
Venous Pressure in cm. Water		5.75	5.60	5.90	6.95	7.15	7.28	6.48	6.16	6.16
	R	3.0-13.0	3.0-12.5	3.5-12.5	3.0-11.5	2.5-12.0	3.0-14.0	3.0-10.0	3.0-10.0	3.0-10.0
Respiratory Rate per Minute		26.4	27.0	24.6	23.4	22.0	21.6	24.0	24.0	25.1
	R	18-51	18-51	18-33	18-30	6-30	2-30	18-30	18-30	21-30

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF DOGS SUBJECTED TO

3 MG/KG OF ENDOTOXIN (DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
0	38.0	37.5	38.0	38.1	37.0	38.0	37.5	37.0	39.0	38.5	37.86
15	37.5	36.5	38.0	38.1	37.5	38.0	37.5	37.0	39.0	38.5	37.76
30	37.5	36.5	38.0	38.0	37.0	38.0	37.5	37.0	39.0	38.5	37.70
45	36.5	35.5	38.5	38.0	36.5	38.5	37.5	37.0	39.0	38.5	37.55
60	36.5	35.5	38.5	38.0	36.5	38.5	37.5	37.0	39.0	38.5	37.55
75	36.0	35.5	38.0	37.5	36.5	38.5	37.0	37.0	38.0	38.5	37.25
90	36.0	35.5	37.5	37.5	36.0	38.5	37.0	37.0	38.0	38.5	37.15
105	36.0	34.5	37.5	36.5	36.0	37.5	37.0	36.5	38.0	38.0	36.75
120	36.5	34.5	37.0	35.1	36.2	37.5	37.0	36.5	38.0	38.0	36.63
135	37.5	34.5	37.0	35.1	36.5	37.5	37.0	36.5	38.0	38.0	36.76
150	36.5	35.0	36.0	34.5	36.5	37.5	37.0	36.5	37.5	37.5	36.45
165	36.5	34.5	36.0	34.5	36.5	37.5	37.0	36.5	37.5	37.5	36.40

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
180	36.0	34.0	36.0	34.0	36.5	36.5	36.5	36.5	37.5	37.5	36.10
195	35.0	34.0	35.5	34.0	35.5	36.5	36.5	36.5	37.5	37.5	35.85
210	35.0	33.5	35.5	34.0	35.5		36.5	36.0	37.5	37.0	35.83
225	34.5	33.5	35.5		35.5		36.5	36.5	37.0	37.0	35.75
240	34.0	33.5	35.5		35.5		36.5	35.5	37.0	37.0	35.56
360	34.0	33.5	35.5		35.5		36.0	35.0	36.5	36.0	35.87
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	3.5	10	7	28	10	10.1

MEAN BLOOD PRESSURE IN MM Hg OF DOGS SUBJECTED TO

3 MG/KG OF ENDOTOXIN (DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	180	130	155	150	145	160	150	120	145	170	149.5
15	69	95	150	125	90	85	90	120	60	80	96.4
30	100	70	140	125	110	90	85	115	75	90	100.0
45	125	70	140	125	128	90	90	115	80	108	107.1
60	122	70	140	130	128	95	110	110	95	110	111.5
75	82	72	145	120	128	90	110	110	100	110	106.7
90	60	72	130	125	80	60	112	110	110	110	96.9
105	62	65	100	95	80	50	115	110	110	112	89.9
120	62	50	90	80	80	50	115	110	110	112	85.9
135	60	45	70	50	75	40	120	100	120	112	79.2
150	60	45	80	20	75	30	120	98	130	112	78.0

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	65	40	80	20	75	30	115	98	132	112	76.6
180	62	38	70	15	75	30	115	98	132	108	74.3
195	50	38	70	10	75	30	115	98	130	108	72.4
210	50	30	75		75		115	95	130	108	84.8
225	50	30	75		75		112	95	130	108	84.4
240	50	30	75		75		112	95	120	108	83.1
360	50	35	70		70		100	95	112	100	79.0
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	10	7	28	10	10.1		

MEAN HEART RATE PER MINUTE OF DOGS SUBJECTED TO

3 MG/KG OF ENDOTOXIN (DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
0	180	156	186	204	96	170	180	150	145	165	163.2
15	69	180	180	120	72	80	90	60	110	90	105.1
30	132	144	176	110	210	90	160	110	112	120	136.4
45	126	126	156	110	150	200	170	170	144	120	137.2
60	132	132	150	200	200	212	179	162	150	130	164.7
75	132	126	160	240	210	222	164	155	155	132	169.6
90	132	138	156	300	210	204	166	158	150	144	175.8
105	132	135	210	320	200	198	178	160	160	144	183.7
120	135	204	220	270	204	195	180	144	155	150	185.7
135	204	214	234	240	180	190	190	150	150	150	190.2
150	210	208	300	210	210	200	182	160	150	155	198.5

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	212	212	180	214	210	220	185	150	150	160	189.3
180	200	240	184	220	216	220	188	150	160	150	192.8
195	130	141	180	80	215	10	170	150	168	160	139.4
210	200	162	174		216		175	168	170	150	176.9
225	140	180	180		220		168	170	170	155	172.9
240	200	240	180		210		174	179	160	180	190.4
360	190	200	168		222		165	175	140	165	178.1
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	3.5	10	7	28	10	10.1

MEAN VENOUS PRESSURE IN CM WATER OF DOGS SUBJECTED TO

3 MG/KG OF ENDOTOXIN (DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	16.5	6.5	22.0	3.4	7.5	5.5	6.5	4.5	5.0	7.5	8.49
15	8.5	3.0	17.5	3.4	6.0	5.5	6.5	4.5	5.0	7.5	6.74
30	17.5	3.0	25.0	3.4	6.5	6.0	7.5	5.0	6.5	6.0	8.44
45	20.0	3.5	20.0	3.4	6.5	6.0	7.5	5.0	6.5	6.0	8.44
60	12.5	11.1	17.0	3.4	6.5	6.0	7.5	5.0	6.5	6.0	8.15
75	12.5	8.5	27.0	3.5	6.5	2.5	7.5	5.0	2.5	6.0	8.15
90	11.0	9.5	20.0	4.0	6.5	2.5	7.0	5.0	2.5	6.5	7.45
105	6.5	10.0	18.0	4.0	6.0	2.5	7.0	5.5	2.5	6.5	6.85
120	6.5	9.5	14.5	4.0	6.0	3.0	7.0	5.5	3.0	5.0	6.40
135	4.5	7.5	13.0	3.5	6.0	3.0	6.5	5.5	3.0	5.0	5.75
150	4.5	6.5	12.5	3.5	6.0	3.0	6.5	5.0	3.5	5.0	5.60

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	4.5	6.5	12.5	3.5	6.0	6.0	6.0	5.5	3.5	5.0	5.90
180	6.5	6.0	11.5	10.5	6.0	8.5	6.0	6.0	3.0	5.5	6.95
195	6.5	6.0	11.5	12.0	6.0	10.5	6.0	6.0	2.5	4.5	7.15
210	8.5	4.5	10.5	14.0	6.0		6.0	6.0	3.0	6.5	7.28
225	8.5	4.5	10.0		6.0		6.0	6.5	3.0	6.5	6.48
240	8.5	4.5	10.0		6.0		5.0	6.5	3.0	6.0	6.16
360	8.0	4.5	10.0		6.5		5.0	6.5	3.0	6.0	6.16
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	3.5	10	7	28	10	10.1

MEAN RESPIRATORY RATE PER MINUTE OF DOGS SUBJECTED TO

3 MG/KG OF ENDOTOXIN (DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	18	48	27	18	42	42	27	36	18	15	29.1
15	33	50	18	15	12	36	30	36	18	18	26.6
30	27	33	16	15	15	36	36	18	18	18	23.2
45	21	51	21	15	40	30	33	18	21	21	27.1
60	30	51	21	15	40	30	21	27	21	28.9	
75	27	36	18	10	36	33	30	21	27	24	26.2
90	27	42	24	12	33	30	36	24	27	24	27.9
105	33	42	24	15	28	36	36	27	24	21	28.6
120	27	51	21	18	28	27	27	27	24	18	26.8
135	27	51	21	18	21	30	27	27	24	18	26.4
150	27	51	24	18	21	33	21	30	18	27	27.0

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	30	27	24	18	24	27	18	33	18	27	24.6
180	30	21	21	18	24	24	18	27	21	30	23.4
195	30	27	21	9	21	6	21	21	27	27	22.0
210	30	27	24	2	21		21	18	30	21	21.6
225	30	27	24		24		18	18	30	21	24.0
240	30	27	24		24		18	21	30	18	24.0
360	27	24	27		24		24	24	30	21	25.1
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	3.5	10	7	28	10	10.1

A P P E N D I X XIII

MEAN CHLORIDE IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	114	117	122	132	120	121
90	113	116	110	124	117	116
150	119	116	120	130	117	119.7
210	121	119	125		117	120.4
270	116	119				117.5
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN SODIUM IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	140	150	146	160	130	145.2
30	137	144	134	155	145	143.0
90	138	145	148	160	145	145.6
150	135	148	147		150	145.0
210	136	144	145		145	142.5
270	140	143				141.5
SURVIVAL TIME IN HOURS	10	10.5	9	2.5	9	8.4

MEAN POTASSIUM IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	3.3	3.1	3.1	4.25	4.1	3.57
30	3.2	2.5	2.75	3.2	3.1	2.95
90	3.1	2.5	2.6	4.1	2.6	2.98
150	3.5	3.0	2.8		2.8	3.25
210	3.6	2.25	3.7		3.3	3.21
270	2.95	2.5				2.73
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN HEMATOCRIT 5 OF DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	56	52	54	60	48	54.0
30	43	44	53	54	48	48.4
90	46	45	53	54	54	50.4
150	48	50	54		53	51.3
210	49	50	52		54	50.8
270	45	44				44.5
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN CHLORIDES, SODIUM AND POTASSIUM IN MEQ/L AND HEMATOCRIT % OF ENDOTOXIN DOGS SUBJECTED TO MECHANICAL EFFECTS OF DIALYSIS

TIME IN MINUTES		0	30	90	150	210	270
Chlorides in meq/l		121	116	119.7	123.7	120.4	117.5
	R	114-132	110-124	116-130	116-135	117-125	116-119
Sodium in meq/l		145.2	143	145.6	145	142.5	141.5
	R	130-160	134-155	138-160	135-150	136-145	140-143
Potassium in meq/l		3.57	2.95	2.98	3.25	3.21	2.73
	R	3.1-4.25	2.5-3.2	2.5-4.1	2.8-3.5	2.25-3.7	2.5-2.95
Hematocrit		54	48.4	50.4	51.3	50.8	44.5
	R	48-60	43-54	45-54	48-54	49-54	44-45

MEAN pH OF DOGS SUBJECTED TO 3MG/KG ENDOTOXIN

(DIFCO) E. COLI AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	7.34	7.43	7.37	7.33	7.30	7.35
30	7.28	7.37	7.38	7.24	7.29	7.31
90	7.25	7.38	7.18	7.42	7.25	7.30
150	7.25	7.36	7.42		7.29	7.33
210	7.28	7.34	7.45			7.36
270	7.26	7.28				7.27
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN pCO_2 IN MM Hg OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	35.0	22.0	38.0	38.5	27.5	32.2
30	31.0	22.0	22.5	25.0	28.5	25.8
90	25.5	17.0	22.0	16.5	24.5	21.1
150	22.5	16.2	15.0		18.0	17.9
210	19.5	14.5	13.5			15.8
270	18.0	12.0				15.0
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN HCO_3 IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	18.9	15.5	21.0	19.5	22.0	19.4
30	14.5	13.5	14.0	11.2	14.0	13.4
90	11.8	11.5	9.0	12.0	11.1	11.1
150	9.9	10.9	11.2		10.2	10.6
210	10.2	9.5	11.0			10.2
270	9.5	7.7				8.6
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN LACTIC ACID IN MEQ/L OF DOGS SUBJECTED TO 3 MG/KG ENDOTOXIN E. COLI (DIFCO) AND THE MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	3.14	5.87	5.61	3.74	3.50	4.37
30	3.51	6.55	6.55	5.14	2.99	4.83
90	3.79	6.40	7.48	6.74	5.61	6.00
150	3.97	6.10	7.58		4.56	5.55
210	4.00	6.64	7.11			5.92
270	4.30	6.45				5.88
SURVIVAL TIME IN HOURS	10	10.5	9	3.5	9	8.4

MEAN pH, PCO_2, HCO_3 AND LACTIC ACID
OF ENDOTOXIN DOGS SUBJECTED TO
MECHANICAL EFFECTS OF DIALYSIS

TIME IN MINUTES		0	30	90	150	210	270
pH		7.35	7.31	7.30	7.33	7.36	7.27
	R	7.30-7.42	7.24-7.38	7.18-7.42	7.25-7.42	7.28-7.45	7.26-7.28
pCO_2 in mm Hg.		32.2	25.8	21.1	17.9	15.8	15.0
	R	22.0-38.5	22.0-31.0	16.5-25.5	15.0-22.5	13.5-19.5	12.0-18.0
HCO_3 in meq/l		19.4	13.4	11.1	10.6	10.2	8.6
	R	15.5-22.0	11.2-14.5	9.0-12.0	9.9-11.2	9.5-11.0	7.7-9.5
Lactic acid in meq/l		4.37	4.83	6.00	5.55	5.92	5.88
	R	3.14-5.87	2.99-6.55	3.79-7.48	3.97-7.58	4.00-7.11	4.30-6.45

MEAN pH, PCO_2, BICARBONATE, AND LACTIC ACID WITH PCO_2 CORRECTED TO 40 MM Hg OF ENDOTOXIN DOGS SUBJECTED TO THE MECHANICAL EFFECTS OF DIALYSIS

TIME IN MINUTES	0	30	90	150	210	270
pH	7.21	7.12	7.06	7.08	7.21	7.03
pCO_2 in mm Hg	40	40	40	40	40	40
HCO_3 in meq/l	20	15	11.0	12.5	20	10
Lactic acid in meq/l	4.37	4.83	6.00	5.55	5.92	5.88

MEAN SURVIVAL TIME IN HOURS OF DOGS SUBJECTED TO 3 MG/KG OF ENDOTOXIN E. COLI (DIFCO) AND MECHANICAL EFFECTS OF DIALYSIS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN NO. HOURS	NO. OF PERMANENT SURVIVORS	PERCENT SURVIVORS
Number of Hours	10	10.5	9	3	9	3,5	10	7	28	10	10.1	1	10%

A P P E N D I X XIV

MEAN VITAL SIGNS OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		36.9	37.2	36.9	36.8	36.8	36.7	36.5	36.2	36.2
	R	35.5-38.0	36.5-37.5	36.5-37.5	36.0-37.5	36.0-37.5	36.5-37.1	36.0-36.9	25.5-36.5	35.5-36.5
Blood Pressure in mm Hg.		115	82	86	84	86	87	80	90	89
	R	100-130	60-100	60-110	60-112	68-115	75-105	65-95	65-120	70-110
Heart Rate per Minute		144	104	151	152	156	159	158	161	149
	R	120-165	90-150	120-200	120-208	120-198	120-200	126-180	126-195	120-192
Venous Pressure in cm. water		5.0	4.3	4.3	4.1	4.5	4.6	5.4	5.3	6.0
	R	3.5-7.0	3.0-7.0	2.0-7.0	2.5-6.0	2.5-6.0	3.0-6.0	3.5-8.0	3.5-8.0	3.5-8.5
Respiratory Rate per minute		39	30	31	29	22	23	24	23	20
	R	16-66	16-70	21-60	18-44	18-30	18-30	21-33	18-33	18-24

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade		36.1	35.6	35.8	35.6	35.3	35.4	35.0	34.9
	R	35.5-36.5	35.0-36.5	35.0-36.5	35.0-36.5	34.5-36.5	34.5-36.5	34.5-36.5	34.0-36.5
Blood Pressure in mm Hg.		91	92	91	92	90	87	83	81
	R	75-110	80-110	75-102	75-108	75-100	75-100	64-95	60-95
Heart Rate per Minute		161	145	165	168	165	165	166	166
	R	132-204	108-192	130-198	130-192	130-190	130-192	128-190	130-190
Venous Pressure in cm Water		5.9	5.9	6.8	7.1	7.1	7.3	7.	8.6
	R	4.5-8.5	4.5-8.5	4.5-10.0	5.5-10.0	5.5-10.0	5.5-10.0	5.5-10.0	5.0-14.5
Respiratory Rate per Minute		24	24	22	21	21	20	20	22
	R	18-30	18-27	18-27	18-24	18-24	18-24	18-24	18-27

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE

OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	37.5	38.0	36.7	35.5	37.0	36.9
15	37.5	37.5	37.5	36.5	37.0	37.2
30	37.5	37.5	36.5	36.5	36.5	36.9
45	37.5	37.5	36.0	36.5	36.5	36.8
60	37.5	37.5	36.0	36.5	36.5	36.8
75	37.1	37.0	36.5	36.5	36.5	36.7
90	36.9	36.5	36.5	36.0	36.5	36.5
105	36.5	36.5	35.5	36.0	36.5	36.2
120	36.5	36.5	35.5	36.0	36.5	36.2
135	36.5	36.5	35.5	35.5	36.5	36.1
150	35.0	35.5	35.5	35.5	36.5	35.6
165	35.0	35.5	35.5	35.5	36.5	35.8
180	35.0	35.5	35.5	35.5	36.5	35.6
195	34.5	35.5	35.5	34.5	36.5	35.3
210	34.5	35.0	35.5	34.5	36.5	35.4
225	34.5	35.0	34.5	34.5	36.5	35.0
240	34.0	35.0	34.5	34.5	36.5	34.9
SURVIVAL TIME IN HOURS	24	24	8	10	12	15.6

MEAN BLOOD PRESSURE IN MM Hg OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	112	100	110	130	122	115
15	100	60	80	70	100	82
30	80	80	98	60	110	86
45	60	75	98	75	112	84
60	68	75	98	75	115	86
75	75	90	90	75	105	87
90	65	90	75	75	95	80
105	65	90	120	80	95	90
120	70	90	110	80	95	89
135	75	95	110	80	95	91
150	80	95	110	80	95	92
165	90	95	102	75	95	91
180	90	95	108	75	90	92
195	90	90	95	75	100	90
210	95	90	75	75	100	87
225	95	90	75	64	90	83
240	95	90	70	60	90	81
SURVIVAL TIME IN HOURS	24	24	8	10	12	15.6

MEAN HEART RATE PER MINUTE OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	150	165	135	150	120	144
15	90	100	90	150	90	104
30	120	150	150	200	135	151
45	120	180	126	208	126	152
60	168	180	120	198	135	156
75	177	162	120	200	135	159
90	180	180	126	180	126	158
105	165	186	132	195	126	161
120	120	180	120	192	132	149
135	162	180	132	204	128	161
150	135	192	108	180	128	145
165	160	189	150	198	130	165
180	169	192	165	186	130	168
195	170	174	160	190	130	165
210	170	170	165	192	130	165
225	179	170	165	190	128	166
240	160	190	160	190	130	166
SURVIVAL TIME IN HOURS	24	24	8	10	12	15.6

MEAN VENOUS PRESSURE IN CM WATER OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	7.0	4.5	3.5	4.0	6.0	5.0
15	7.0	4.5	3.0	4.0	3.0	4.3
30	7.0	4.5	2.0	4.0	4.0	4.3
45	6.0	5.5	2.5	2.5	4.0	4.1
60	6.0	5.5	2.5	4.0	4.5	4.5
75	6.0	5.5	3.0	4.0	4.5	4.6
90	8.0	5.5	3.5	4.5	5.5	5.4
105	8.0	5.5	3.5	4.5	5.0	5.3
120	8.0	8.5	3.5	5.0	5.0	6.0
135	6.0	8.5	4.5	5.5	5.0	5.9
150	6.0	8.5	4.5	5.5	5.0	5.9
165	7.0	10.0	4.5	7.0	5.5	6.8
180	7.0	10.0	5.5	7.5	5.5	7.1
195	7.0	10.0	5.5	7.5	5.5	7.1
210	7.0	10.0	5.5	8.5	5.5	7.3
225	7.0	10.0	5.5	10.0	5.5	7.6
240	7.0	14.5	5.0	11.0	5.5	8.6
SURVIVAL TIME IN HOURS	24	24	8	10	12	15.6

MEAN RESPIRATORY RATE PER MINUTE OF MORPHINE - ENDOTOXIN DOGS SUBJECTED TO HEMODIALYSIS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	66	21	60	16	30	39
15	70	21	27	16	18	30
30	60	21	30	24	21	31
45	44	18	27	36	21	29
60	21	18	18	30	21	22
75	18	24	21	30	21	23
90	21	24	21	33	21	24
105	18	24	18	33	21	23
120	18	18	18	24	21	20
135	21	18	27	30	24	24
150	27	18	27	27	24	24
165	27	18	27	18	21	22
180	24	18	24	20	21	21
195	24	18	24	20	21	21
210	24	18	21	18	18	20
225	21	18	21	18	24	20
240	27	18	21	18	24	22
SURVIVAL TIME IN HOURS	24	24	8	10	12	15.6

APPENDIX XV

MEAN VITAL SIGNS OF MORPHINE - ENDOTOXIN DOGS

A TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		37.9	38.1	38.1	38.1	37.2	37.4	37.3	36.7	36.7
	R	37.5-39.0	37.5-40.0	37.5-40.0	37.5-39.0	35.5-39.0	36.5-39.0	35.0-39.0	35.0-38.0	35.0-38.0
Blood Pressure in mm Hg.		125	96	116	117	116	110	109	104	102
	R	100-150	60-135	102-132	110-132	105-130	80-135	75-135	60-135	50-130
Heart Rate per Minute		160	167	172	165	166	176	176	188	188
	R	132-192	135-204	132-222	132-213	135-210	126-210	126-210	126-214	120-210
Venous Pressure in cm Water		4.6	4.6	4.7	4.4	4.8	5.0	5.3	5.1	5.0
	R	1.5-10.0	1.5-9.0	1.5-9.0	1.0-9.5	1.0-9.5	1.0-9.5	1.5-9.5	1.5-9.5	1.5-8.5
Respiratory Rate per Minute		38	40	46	51	53	65	67	41	39
	R	21-72	21-100	21-140	21-140	24-140	24-200	33-200	30-72	27-72

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade		36.4	36.9	36.9	36.3	36.3	36.3	36.1	35.8
	R	33.5-38.0	36.5-38.0	36.5-38.0	35.5-37.5	35.5-37.5	35.5-37.5	35.5-37.5	34.5-37.5
Blood Pressure in mm Hg.		90	103	101	94	91	93	91	88
	R	30-120	90-120	80-128	60-120	55-110	50-110	40-110	30-112
Heart Rate per Minute		141	180	186	206	186	196	200	204
	R	6-200	147-204	162-204	195-222	150-225	180-210	180-215	188-222
Venous Pressure in cm Water		5.4	4.1	4.3	4.1	4.0	3.9	4.6	4.9
	R	1.5-10.5	1.5-7.5	1.5-7.5	1.5-7.0	1.5-6.5	1.5-6.5	1.5-8.0	1.5-10.5
Respiratory Rate per Minute		28	32	32	29	30	31	26	26
	R	10-36	27-36	27-36	18-34	24-34	24-36	9-36	5-36

R = Range

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF

MORPHINE-ENDOTOXIN DOGS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	39.0	37.5	37.5	37.5	38.0	37.9
15	40.0	37.5	37.5	37.5	38.2	38.1
30	40.0	37.5	37.5	37.5	38.2	38.1
45	40.0	37.5	37.5	37.5	38.2	38.1
60	39.0	37.5	35.5	37.5	36.5	37.2
75	39.0	37.5	37.5	37.5	36.5	37.4
90	39.0	37.5	37.5	37.5	35.0	37.3
105	38.0	36.5	36.5	37.5	35.0	36.7
120	38.0	36.5	36.5	37.5	35.0	36.7
135	38.0	36.5	36.5	37.5	33.4	36.4
150	38.0	36.5	36.5	36.5		36.9
165	38.0	36.5	36.5	36.5		36.9
180	37.5	36.0	35.5	36.0		36.3
195	37.5	36.0	35.5	36.0		36.3
210	37.5	36.0	35.5	36.0		36.3
225	37.5	35.5	35.5	36.0		36.1
240	37.5	34.5	35.5	35.5		35.8
SURVIVAL TIME IN HOURS	30*	4	30*	30*	2	19

MEAN BLOOD PRESSURE IN MM Hg OF

MORPHINE - ENDOTOXIN DOGS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	115	140	150	100	112	125
15	95	100	135	90	60	96
30	120	110	132	102	114	116
45	120	110	132	110	114	117
60	120	105	130	112	114	116
75	120	105	135	112	80	110
90	120	105	135	110	75	109
105	120	98	135	110	60	104
120	120	98	130	110	50	102
135	105	98	120	98	30	90
150	105	90	120	98		103
165	105	80	128	90		101
180	108	60	120	85		94
195	108	55	110	90		91
210	110	50	110	100		93
225	110	40	110	104		91
240	110	30	100	112		88
SURVIVAL TIME IN HOURS	30*	4	30*	30*	2	19

MEAN HEART RATE PER MINUTE OF

MORPHINE - ENDOTOXIN DOGS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	132	180	150	148	192	160
15	168	180	135	148	204	167
30	168	180	132	160	222	172
45	162	150	132	160	213	165
60	192	135	135	160	210	166
75	210	135	126	198	210	176
90	210	135	126	198	210	176
105	210	192	126	200	214	188
120	210	180	120	204	210	188
135	200	177	150	192	6	141
150	190	204	147	180		180
165	198	204	162	180		186
180	210	222	195	198		206
195	150	225	180	190		186
210	210	200	180	194		196
225	215	210	180	194		200
240	222	222	180	190		204
SURVIVAL TIME IN HOURS	30*	4	30*	30*	2	19

MEAN VENOUS PRESSURE IN CM WATER OF

MORPHINE - ENDOTOXIN DOGS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	1.5	8.0	1.5	10.0	2.0	4.6
15	2.5	7.5	2.5	9.0	1.5	4.6
30	2.5	7.5	3.0	9.0	1.5	4.7
45	1.0	7.5	2.5	9.5	1.5	4.4
60	1.0	6.5	2.5	9.5	4.5	4.8
75	1.0	6.5	2.5	9.5	5.5	5.0
90	1.5	6.5	2.5	9.5	6.5	5.3
105	1.5	5.5	2.5	9.5	6.5	5.1
120	1.5	5.5	2.5	7.0	8.5	5.0
135	1.5	5.5	2.5	7.0	10.5	5.4
150	1.5	4.5	3.0	7.5		4.1
165	1.5	5.0	3.0	7.5		4.3
180	1.5	5.5	2.5	7.0		4.1
195	1.5	5.5	2.5	6.5		4.0
210	1.5	5.0	2.5	6.5		3.9
225	1.5	8.0	2.6	6.5		4.6
240	1.5	10.5	5.0	6.5		4.9
SURVIVAL TIME IN HOURS	30*	4	30*	30*	2	19

MEAN RESPIRATORY RATE PER MINUTE OF

MORPHINE - ENDOTOXIN DOGS

DOG NUMBER	1	2	3	4	5	MEAN
Time in Minutes						
0	72	21	21	24	51	38
15	100	21	21	24	33	40
30	140	21	21	24	33	46
45	140	21	21	48	24	51
60	140	33	36	30	24	53
75	200	33	36	30	24	65
90	200	33	33	33	36	67
105	72	33	30	33	36	41
120	72	36	27	33	27	39
135	33	36	30	33	10	28
150	27	36	30	33		32
165	27	36	30	34	32	
180	18	30	33	34		29
195	24	33	30	34		30
210	24	36	30	34		31
225	27	9	36	30		26
240	33	5	36	30		26
SURVIVAL TIME IN HOURS	30▼	4	30▼	30▼	2	19

COMPARATIVE VITAL SIGNS IN MORPHINE - ENDOTOXIN DOGS CONTROL AND DIALYSED DOGS

A	TIME IN MINUTES		0	15	30	45	60	75	90	105	120
	Temperature in Degrees Centigrade	D	36.9	37.2	36.9	36.8	36.8	36.7	36.5	36.2	36.2
		C	37.9	38.1	38.1	38.1	37.2	37.4	37.3	36.7	36.7
	B lood Pressure in mm Hg.	D	115	82	86	84	86	87	80	90	89
		C	125	96	116	117	116	110	109	104	102
	Heart Rate per Minute	D	144	104	151	152	156	159	158	151	149
		C	160	167	172	165	166	176	176	188	188
	Venous Pressure	D	5.0	4.3	4.3	4.1	4.5	4.6	5.4	5.3	6.0
		C	4.6	4.6	4.7	4.4	4.8	5.0	5.3	5.1	5.0
	Respiratory Rate per Minute	D	39	30	31	29	22	23	24	23	20
		C	38	40	46	51	53	65	67	41	39

D = Dialysed C = Control

B. TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240
Temperature in Degrees Centigrade	D	36.1	36.6	35.8	35.6	35.3	35.4	35.0	34.9
	C	36.4	36.9	36.9	36.3	36.3	36.3	36.1	35.8
Blood Pressure in mm Hg.	D	91	92	91	92	90	87	83	81
	C	90	103	101	94	91	93	91	88
Heart Rate per Minute	D	161	145	165	168	165	165	166	166
	C	141	180	186	206	186	196	200	204
Venous Pressure in cm Water	D	5.9	5.9	6.8	7.1	7.1	7.3	7.6	8.6
	C	5.4	4.1	4.3	4.1	4.0	3.9	4.6	4.9
Respiratory Rate per Minute	D	24	24	22	21	21	20	20	22
	C	28	32	32	29	30	31	26	26

D = Dialysed C = Control

COMPARATIVE SURVIVAL TIME IN MORPHINE - ENDOTOXIN DOGS

CONTROL AND DIALYSED

DOG NUMBER		1	2	3	4	5	MEAN NO. HOURS	NO. OF PERMANENT SURVIVORS	PERCENT SURVIVORS
Number of Hours	D	24	24	8	10	12	15.6	0	0%
	C	30▼	4	30▼	30▼	2	19	3	60%

D = Dialysed C = Control

APPENDIX XVI

MEAN VITAL SIGNS IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90
Temperature in Degrees Centigrade		37.37	37.29	37.14	37.04	36.50	36.09	35.49
	R	36-38.5	34.5-38.5	34.5-39	33.5-39	33.5-39	33-38	33-38
Blood Pressure in mm Hg		157.2	40	40	40	50	50	50
	R	140-182	40-40	40-40	40-40	50-50	50-50	50-50
Heart Rate per Minute		156	128.5	142.1	153.9	159.9	168.6	168.5
	R	120-198	40-216	102-270	75-274	102-240	120-240	120-270
Venous Pressure in cm Water		7.65	3.70	2.60	4.0	3.35	3.20	3.5
	R	4.5-13.5	-1-10.5	-2-10	-2-20	-2-18	-2-18	-2-18
Respiratory Rate per Minute		27.3	39.3	37.0	31.5	31.5	31.8	32.4
	R	15-75	21-57	21-51	15-45	18-42	18-42	18-45

R = Range

B TIME IN MINUTES (Cont'd.)		105	120	135	150	165	180	195
Temperature in Degrees Centigrade		34.95	34.25	33.80	33.65	33.65	33.6	33.4
	R	33-37	33-36.5	32-36	31-36	31-36	31-35.5	31-35.5
Blood Pressure in mm Hg		50	50	50	50	50	50	96
	R	50-50	50-50	50-50	50-50	50-50	50-50	55-120
Heart Rate per Minute		167.2	171.2	172.8	169.4	164.4	155.3	168.1
	R	104-274	120-260	120-270	90-260	108-208	150-200	130-240
Venous Pressure in cm Water		3.35	3.30	3.25	2.26	2.86	4.60	4.6
	R	-2-18	-2-18	-2-18	-2-9	-2-9	1-9.5	2.5-10.5
Respiratory Rate per Minute		31.2	32.7	32.1	32.7	32.5	27.5	29.6
	R	18-45	18-45	18-45	18-45	18-45	6-45	21-36

C	TIME IN MINUTES (Continued)		210	225	240	255	270
	Temperature in Degrees Centigrade		33.27	33.06	33.06	33.06	33.05
		R	31-35	31.5-35	31.5-35	31.5-35	31.5-35
	Blood Pressure in mm Hg		96	107	107	107	102
		R	45-125	95-136	98-130	98-130	98-130
	Heart Rate per Minute		142.8	155.6	155.8	155.0	
		R	20-180	130-190	130-190	120-180	
	Venous Pressure in cem Water		5.9	5.0	4.9	5.0	5.2
		R	3.5-13.5	3.5-8.0	3.5-8.0	3.5-7.5	3.5-7.5
	Respiratory Rate per Minute		24.4	27.7	26.2	24.3	23.2
		R	4-36	21-33	18-33	18-27	21-27

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	37.0	37.2	36.0	37.5	37.0	38.5	37.5	38.0	38.0	37.0	37.37
15	37.5	37.2	34.5	37.2	37.5	38.5	37.5	38.0	38.0	37.0	37.29
30	37.5	36.5	34.5	36.5	38.9	39.0	37.5	37.5	37.5	36.5	37.19
45	37.5	36.5	33.5	36.0	38.9	39.0	37.5	37.5	37.5	36.5	37.04
60	37.0	35.5	33.5	35.5	38.9	39.0	36.0	37.5	37.5	36.0	36.50
75	37.0	34.9	33.0	35.0	38.0	37.0	36.5	37.5	37.5	36.0	36.09
90	36.0	34.9	33.0	34.5	38.0	37.5	35.5	36.0	35.5	34.0	35.49
105	36.0	34.5	33.0	33.5	37.0	36.5	35.0	36.0	35.0	33.0	34.95
120	36.0	33.5	33.0	33.5	35.0	36.5	35.0	35.0	34.0	33.0	34.25
135	36.0	33.5	33.0	32.5	35.0	36.0	34.0	35.0	33.0	32.0	33.80
150	36.0	33.5	31.0	32.5	35.0	36.0	33.0	34.5	33.0	32.0	33.65

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	36.0	33.5	31.0	32.5	35.0	35.5	33.0	34.5	33.0	32.5	33.65
180	35.5	33.5	31.0	32.5	34.5	35.4	33.0	34.4	33.5	32.5	33.6
195		33.5	31.0	32.5	34.5	35.5	33.5	34.5	33.5	32.5	33.44
210		33.5	31.0	32.0	34.5	35.0	33.5	34.5	33.0	32.5	33.27
225		33.0	31.5	32.0	34.5	35.0		34.0	32.5	32.0	33.06
240		33.0	31.5	32.0	34.5	35.0		34.0	32.5	32.0	33.06
255		33.0	31.5	32.0	34.5	35.0		34.0	32.5	32.0	33.06
270		33.0	31.5	32.0	34.0	35.0		34.0	32.5	32.0	33.05
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN BLOOD PRESSURE IN MM Hg OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	170	150	178	160	150	150	152	140	182	140	157.2
15	40	40	40	40	40	40	40	40	40	40	40
30	40	40	40	40	40	40	40	40	40	40	40
45	40	40	40	40	40	40	40	40	40	40	40
60	50	50	50	50	50	50	50	50	50	50	50
75	50	50	50	50	50	50	50	50	50	50	50
90	50	50	50	50	50	50	50	50	50	50	50
105	50	50	50	50	50	50	50	50	50	50	50
120	50	50	50	50	50	50	50	50	50	50	50
135	50	50	50	50	50	50	50	50	50	50	50
150	50	50	50	50	50	50	50	50	50	50	50

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	50	50	50	50	50	50	50	50	50	50	50
180	50	50	50	50	50	50	50	50	50	50	50
195		100	100	100	98	98	55	120	110	80	96
210		100	98	100	100	98	45	125	112	90	96
225		98	98	112	110	100		136	115	95	107
240		98	98	100	115	100		130	115	100	107
255		98	98	100	115	100		130	120	98	107
270		90	90	88	120	98		130	100	98	102
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN HEART RATE PER MINUTE OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	180	150	120	198	120	162	180	150	150	150	156
15	150	96	40	150	114	120	171	216	132	96	128.5
30	130	102	126	126	114	130	159	270	144	120	142.1
45	140	126	150	75	153	165	162	274	162	132	153.9
60	180	135	150	102	160	240	150	180	162	132	159.9
75	195	135	150	120	180	171	165	240	210	120	168.6
90	150	144	150	120	186	170	162	270	213	120	168.5
105	132	135	138	104	195	180	150	274	214	150	167.2
120	130	132	150	120	210	180	164	260	216	150	171.2
135	150	140	148	120	200	190	162	270	198	150	172.8
150	90	150	150	120	198	180	250	260	196	150	169.4

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	108	150	150	120	198	180	208	180	195	155	164.4
180	50	140	148	130	180	170	200	190	190	155	155.3
195		145	145	135	165	188	240	175	170	150	168.1
210		130	145	125	170	180	20	175	180	160	142.8
225		130	140	130	155	190		165	185	150	155.6
240		135	140	130	155	175		165	190	150	155.8
255		135	140	130	155	180		165	180	165	155.0
SURVIVAL TIME IN HOURS	2	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN VENOUS PRESSURE IN CM WATER OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	8.5	6.5	6.0	4.5	8.0	13.5	4.5	5.5	13.0	6.5	7.65
15	5.5	6.5	5.0	1.0	5.0	10.5	-1	-1	2.0	3.5	3.70
30	2.5	5.5	4.5	1.0	4.0	10.0	-2	-1	-1	2.5	2.60
45	2.0	5.5	4.5	1.5	4.0	20.0	-2	3.0	-1	2.5	4.0
60	2.0	4.5	3.0	1.0	4.0	18.0	-2	1.0	-1	3.0	3.35
75	2.0	4.5	2.0	1.0	3.5	18.0	-2	1.0	-1	3.0	3.20
90	2.0	4.0	4.5	1.5	3.5	18.0	-2	1.0	-1	3.5	3.5
105	2.0	4.0	4.5	1.0	2.5	18.0	-2	1.0	-1	3.5	3.35
120	2.0	4.5	3.0	1.0	2.5	18.0	-2	1.0	-1	4.0	3.3
135	2.0	4.0	2.0	1.0	2.0	18.0	-2	1.5	-1	5.0	3.25
150	2.0	4.0	1.0	1.0	2.0	9.0	-2	1.6	-1	5.0	2.26

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	8.0	4.0	1.0	1.0	2.0	9.0	-2	1.6	-1	5.0	2.86
180	9.0	4.5	1.5	1.5	2.0	9.5	8.5	3.5	1.0	5.0	4.6
195		6.5	2.5	4.5	3.5	8.5	10.5	3.0	2.5	5.5	4.6
210		6.5	4.5	3.5	3.5	8.5	13.5	3.5	3.5	5.5	5.9
225		6.5	4.5	3.5	4.0	8.0		3.5	4.5	5.0	5.0
240		6.5	4.5	3.5	4.0	8.0		3.5	4.5	5.0	4.9
255		7.0	4.0	4.0	4.5	7.5		3.5	4.5	5.0	5.0
270		7.0	4.0	4.0	5.5	7.5		3.5	4.5	5.5	5.2
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN RESPIRATORY RATE PER MINUTE IN CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	45	21	75	15	27	15	21	18	18	18	27.3
15	42	60	45	21	36	42	24	57	36	30	39.3
30	36	45	42	21	43	42	33	51	21	36	37.6
45	36	27	33	33	45	36	30	27	15	33	31.5
60	36	36	36	27	42	39	30	27	18	24	31.5
75	30	42	36	18	42	36	30	36	18	30	31.8
90	33	42	36	18	45	33	30	36	21	30	32.4
105	36	36	33	18	42	30	30	45	21	21	31.2
120	36	36	33	18	45	33	33	45	18	30	32.7
135	36	40	33	18	45	24	34	40	21	30	32.1
150	39	36	30	18	45	33	30	45	21	30	32.7

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	36	36	30	18	45	33	30	40	27	30	32.5
180	6	36	27	18	45	33	30	36	24	30	27.5
195		36	21	21	36	36	30	30	24	33	29.6
210		30	21	21	36	36	4	24	21	27	24.4
225		30	24	21	33	33		27	21	33	27.7
240		27	27	24	27	30		24	18	33	26.2
255		27	21	27	27	27		21	18	27	24.3
270		27	21	24	24	21		21	21	27	23.2
SURVIVAL TIME IN MINUTES	3	10	8	10	30*	8	3½	30*	10	9	12.2

APPENDIX XVII

MEAN CHLORIDES IN MEQ/L IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	114	119	119	103	111	109	119	116	117	107	113
30	115	115	115	108	120	112	119	115	114	114	115
90	112	114	114	112	118	112	120	114	111	107	113
150	113	117	119	113	112	113	125	116	120	115	116
210		121	124	112	116	115	114	114	125	112	117
270		121	124	112	116	115		114	125	117	117
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN SODIUM IN MEQ/L IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	158	156	162	155	163	156	119	145	142	145	150
30	150	145	156	146	164	151	119	145	143	143	146
90	156	145	154	157	156	156	120	148	150	141	148
150	164	151	156	158	155	161	130	146	146	143.5	151
210		156	158	155	164	156	160	144.5	149	144	154
270		154	156	153	160	152		144	147.5	147	151
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN POTASSIUM IN MEQ/L IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	3.5	2.7	3.2	3.6	4.5	2.7	3.92	3.3	4.4	4.37	3.6
90	4.3	3.2	5.0	4.4	3.6	3.7	6.95	4.8	6.3	5.07	4.7
150	5.2	3.2	6.0	5.7	4.2	3.6	6.0	5.0	6.4	4.7	5.0
210		5.0	5.6	5.8	3.8	4.0	5.0	5.1	7.6	5.15	5.2
270		4.8	5.4	5.6	3.6	4.2		5.0	7.4	5.22	5.22
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN HEMATOCRIT % OF DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	37	47	35	45	40	42	48	48	52	37	44
30	48	50	40	48	44	50	50	56	54	33	47
90	50	55	42	50	45	55	58	58	55	48	51
150	55	56	40	55	48	56	60	60	60	43	53
210		58	50	63	55	60	63	62	65	46	58
270		60	58	64	58	63		65	66	58	60
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

A CHART OF MEAN CHLORIDE, SODIUM IN MEQ/L, POTASSIUM IN MEQ/L, AND HEMATOCRIT % OF HAEMORRHAGIC CONTROL DOGS

TIME IN MINUTES		0	30	90	150	210	270
Chlorides in meq/l		113	115	113	116	117	117
	R	103-119	108-120	107-120	112-125	112-125	112-125
Sodium in meq/l		150	146	148	151	154	151
	R	119-163	119-164	120-156	130-164	144-164	144-160
Potassium in meq/l		3.6	5.5	4.7	5.0	5.7	5.2
	R	2.[illegible]-4.5	3.8-8.4	3.2-6.95	3.2-6.4	3.8-7.6	3.6-7.4
Hematocrit %		44	47	51	53	58	61
	R	35-52	33-56	38-58	40-60	46-65	54-64

MEAN pH OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	7.38	7.27	7.42	7.32	7.34	7.3	7.31	7.2	7.3	7.39	7.32
30	7.31	7.14	7.20	7.22	7.32	7.1	7.13	7.1	7.1	7.21	7.18
90	7.12	7.07	7.24	6.98	7.22	6.9	6.9	7.3	7.1	7.2	7.13
150	7.06	7.18	7.23	7.02	7.18	7.1	7.0	7.3	7.1	6.4	7.1
210		7.06	7.1	6.97	7.33	7.2		7.4	7.1	7.1	7.16
270		7.06	7.07	6.84	7.31	7.2		7.3	7.1	7.12	7.12
SURVIVAL TIME IN HOURS	3	10	8	10	30'	8	3½	30'	10	9	12.2

MEAN pCO_2 IN MM Hg OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	25.0	42.5	31.2	28.5	24.1	42.0	27.0	31.0	36.0	42.0	32.1
30		19.0	14.0	10.0		30.0	26.0	18.6	22.5	10.0	18.7
90		20.5	10.5	10.5		28.0	24.0	16.8	17.6	16.0	17.1
150		11.5	11.2	10.0	11.8	12.0	10.0	13.2	18.0	13.2	12.3
210		32.5	30.5	10.0	38.0	24.0		19.8	13.8	12.0	22.7
270		26.5	25.2	10.0	29.0	17.0		14.2	12.4	10.0	18.0
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN HCO_3 IN MEQ/L IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	20.5	19.1	18.0	15.0	18.0	20.0	14.0	14.5	17.8	11.2	16.8
30		6.2	7.5	6.0	19.0	8.0	9.0	6.8	8.4	10.4	9.03
90		6.4	6.5	10.0	6.8	6.5	6.5	10.5	7.0	5.8	7.30
150		6.3	7.5	10.0	6.2	7.5	5.0	9.6	6.9	5.7	7.2
210		9.2	10.5	10.0	19.0	8.5		13.5	6.3	7.1	10.4
270		8.4	8.5	10.0	17.5	7.0		11.5	6.3	6.1	9.40
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN LACTIC ACID IN MEQ/L IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	5.55	3.4	4.67	1.4	1.3	2.5	5.44	16.5	15.5	1.8	4.06
30	7.48	10.1	13.2	9.5	3.5	9.6	1.8	23.0	12.8	11.23	10.12
90	10.6	8.5	8.3	12.7	12.5	12.6	8.0	10.9	17.7	14.04	11.6
150	10.6	18.1	7.7	18.7	10.0	14.6	11.5	7.2	16.0	31.79	14.71
210		4.6	5.6	6.4	3.5	18.0	7.9	3.8		14.04	7.6
270		6.6	6.5	7.8	4.6	14.0	9.0	6.3		15.3	10.0
SURVIVAL TIME IN HOURS	3	10	8	10	30*	8	3½	30*	10	9	12.2

MEAN CHEMISTRIES OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270
pH		7.32	7.18	7.13	7.10	7.16	7.12
	R	7.2-7.42	7.1-7.32	6.9-7.3	6.4-7.3	6.96-7.4	6.84-7.3
pCO_2 in mm Hg		32.1	18.7	17.1	12.3	22.7	18.0
	R	24-42.5	10-30	10-28	10-18	10-38	10-29
HCO_3 in meq/l		16.8	9.03	7.3	7.2	10.4	9.4
	R	11.2-20.5	6.0-19	6.4-10.5	5.0-10	6.3-19	6.1-17.5
Lactic Acid in meq/l		4.06	10.12	11.6	14.71	7.6	10.0
	R	1.3-15.5	3.5-23	8.3-14.04	7.2-31.79	3.5-14.04	4.6-15.3

MEAN CHEMISTRIES IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK WITH CORRECTION OF pCO_2 TO 40 MEQ/L

TIME IN MINUTES		0	30	90	150	210	270
pH		7.26	7.04	7.0	7.0	7.06	7.0
	R						
pCO_2 in mm Hg		40	40	40	40	40	40
	R						
HCO_3 in meq/l		17	10.5	8.0	6.5	12.5	8.0
	R						
Lactic Acid in meq/l		4.06	10.12	11.6	14.71	7.6	10.0
	R						

APPENDIX XVIII

VITAL SIGNS IN DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90
Temperature in Degrees Centigrade		37.7	37.8	37.7	37.4	37.2	36.9	36.8
	R	36.2 39	-36.5- 39	36- 40	36- 40	36- 39.8	36- 38.5	36- 38
Blood Pressure in mm Hg		142	40	40	40	50	50	50
	R	122- 160	40- 40	40- 40	40- 40	50- 50	50- 50	50- 50
Heart Rate per Minute		155	137	163	173	208	217	215
	R	135- 180	99- 198	99- 258	100- 270	135- 350	135- 260	150- 270
Venous Pressure in cm H_2O		6.7	2.7	2.1	2.3	2.2	2.5	2.4
	R	3.5- 16.5	1.5- 5.5	-1- 5	-1- 5	-1- 4.5	-1- 5.5	-2- 5.5
Respiratory Rate per Minute		35	30	28	30	29	29	26
	R	12- 90	18- 54	15- 45	15- 48	15- 48	18- 36	15- 36

R = Range

B TIME IN MINUTES (Cont'd.)		105	120	135	150	165	180	195
Temperature in Degrees Centigrade		35.5	36.0	35.9	35.8	35.2	34.9	34.9
	R	35-38	35-37	35-37	34-37.5	34-36	34-36	34-36
Blood Pressure in mm Hg		50	50	50	50	50	112	108
	R	50-50	50-50	50-50	50-50	50-50	90-155	70-140
Heart Rate per Minute		215	219	221	218	228	193	183
	R	165-290	164-275	164-300	156-300	156-300	126-300	100-360
Venous Pressure in cm H_2O		2.6	2.5	2.4	2.8	2.9	4.6	4.7
	R	-2-5	-2-5	-2-4.5	1.1-4.5	1.2-4.5	2-8	1-8.5
Respiratory Rate per Minute		26	28	28	27	27	28	28
	R	15-36	21-36	21-36	21-30	21-36	15-51	6-50

C TIME IN MINUTES (Cont'd.)		210	225	240	255	270
Temperature in Degrees Centigrade		35.0	34.8	34.7	34.55	34.0
	R	34-36	34-36	32-36	32-36	32-36
Blood Pressure in mm Hg		106	101	103	111.3	117
	R	70-148	30-150	3-155	80-150	112-145
Heart Rate per Minute		163	163	162	158	150
	R	50-264	50-280	30-215	80-200	112-190
Venous Pressure in cm H_2O		8.3	5.3	5.5	5.5	5.6
	R	2-36.5	2.5-8	2.5-8.5	3-8.5	3.5-8
Respiratory Rate per Minute		25	26	25	24	24
	R	4-51	12-45	12-45	18-40	18-36

MEAN TEMPERATURE IN DEGREES CENTIGRADE OF DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	37.0	37.5	38.8	37.5	38.0	39.0	37.5	37.5	36.2	37.5	37.7
15	37.9	37.5	38.8	37.5	38.0	39.0	37.5	37.5	36.5	37.5	37.8
30	38.0	36.5	38.8	37.5	37.5	40.0	37.5	37.5	36.0	37.5	37.7
45	37.8	36.5	38.0	37.5	37.5	40.0	36.5	37.5	36.0	37.0	37.4
60	37.8	36.5	38.5	37.5	36.0	39.8	36.5	36.5	36.0	37.0	37.2
75	37.9	36.0	38.5	37.0	36.5	38.0	36.5	36.5	36.0	36.5	36.9
90	37.0	36.0	38.0	37.0	36.5	38.0	36.5	36.5	36.0	36.5	36.8
105	37.0	35.5	38.0	35.5	35.5	38.0	35.5	35.5	35.0	36.5	35.5
120	37.0	35.5	37.0	35.5	35.5	37.0	35.5	35.5	35.0	36.0	36.0
135	37.0	35.0	37.0	35.5	35.5	37.0	35.5	35.0	35.0	36.0	35.9
150	37.5	34.0	37.0	35.0	35.5	37.5	35.5	34.5	35.0	36.0	35.8

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	36.0	34.0	36.0	35.0	34.0	35.5	35.5	34.5	35.0	36.0	35.2
180	36.0	34.5	35.0	35.0	34.0	35.5	35.0	34.0	34.0	35.5	34.9
195	36.0	35.5	35.0	35.0	34.0	35.5	35.0	34.0	34.0	35.0	34.9
210	36.0	35.5	35.5	35.5	34.0	35.0	35.0	34.0	34.0	35.0	35.0
225	36.0	35.5	34.5	35.5	34.0		35.0	34.0	34.0	35.0	34.8
240	36.0	35.5	34.5	35.5	34.0		35.0	32.0	34.0	35.0	34.7
255	36.0	35.0	34.5	35.5	34.0		35.0	32.0	33.5	35.0	34.55
270	36.0	34.5	34.5	35.0	33.0		34.5	32.0	33.0	34.5	34.0
SURVIVAL TIME IN HOURS	8	30*	8½	20	4½	3½	30*	14	24	30*	17.2

MEAN BLOOD PRESSURE IN MM Hg OF DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	135	145	142	145	160	145	122	150	150	122	142
15	40	40	40	40	40	40	40	40	40	40	40
30	40	40	40	40	40	40	40	40	40	40	40
45	40	40	40	40	40	40	40	40	40	40	40
60	50	50	50	50	50	50	50	50	50	50	50
75	50	50	50	50	50	50	50	50	50	50	50
90	50	50	50	50	50	50	50	50	50	50	50
105	50	50	50	50	50	50	50	50	50	50	50
120	50	50	50	50	50	50	50	50	50	50	50
135	50	50	50	50	50	50	50	50	50	50	50
150	50	50	50	50	50	50	50	50	50	50	50

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	50	50	50	50	50	50	50	50	50	50	50
180	155	100	120	90	100	110	100	120	120	100	112
195	140	98	135	95	75	120	80	120	130	90	108
210	135	148	120	100	75	70	90	120	120	80	106
225	144	150	120	100	75		95	115	110	70	101
240	150	155	120	100	90		100	115	110	60	103
255	130	150	115	100	80		112	110	110	95	111.3
270	130	145	115	112	85		120	120	112	120	117
SURVIVAL TIME IN HOURS	8	30*	8½	20	4½	3½	30*	14	14	30*	17.2

MEAN HEART RATE PER MINUTE OF DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	135	150	150	180	150	168	150	180	156	135	155
15	150	150	120	180	150	198	105	99	132	90	137
30	180	156	138	180	150	225	258	99	134	105	163
45	180	162	150	200	162	250	370	100	150	110	173
60	180	180	168	240	222	250	350	135	169	186	208
75	219	198	168	252	213	248	300	170	135	260	217
90	204	198	168	248	212	270	270	180	150	244	215
105	170	200	170	200	212	255	290	240	165	250	215
120	164	198	210	164	220	250	275	230	216	258	219
135	164	168	214	175	210	256	300	210	210	300	221
150	156	168	270	180	210	270	300	225	200	200	218

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	156	168	270	180	214	256	280	300	189	270	228
180	126	158	150	150	220	150	300	210	162	300	193
195	144	152	150	144	210	100	360	162	188	200	183
210	144	150	150	135	210	50	264	162	180	180	163
225	132	150	150	140	220		280	180	150	175	163
240	130	150	150	140	215		200	168	150	160	162
255	130	150	140	140	200		180	160	155	155	158
270	120	150	135	130	190		175	150	148	150	150
SURVIVAL TIME IN HOURS	8	30*	8½	20	4½	3½	30*	14	14	30*	17.2

MEAN VENOUS PRESSURE IN CM WATER OF DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	7	5.5	4.5	4.5	3.5	6.0	7.5	5.5	6.5	16.5	6.7
15	2.0	2.0	2.5	2.0	3.0	3.0	1.5	3.5	5.5	2.0	2.7
30	2.0	2.0	2.5	1.0	-1	3.5	2.5	1.5	5.0	2.0	2.1
45	2.5	3.0	2.0	1.1	-1	3.5	3.0	1.5	5.0	2.0	2.3
60	3.0	3.0	1.5	1.1	-1	3.0	3.5	1.5	4.5	2.0	2.2
75	3.0	3.0	1.5	1.1	-1	4.0	3.5	2.0	5.5	2.0	2.5
90	3.5	3.0	1.5	1.1	-2	4.0	3.5	2.0	5.5	2.0	2.4
105	3.5	3.0	2.0	2.0	-2	4.5	3.5	2.0	5.0	2.0	2.6
120	3.5	3.0	2.0	1.1	-2	4.5	3.5	2.0	5.0	2.0	2.5
135	3.5	3.0	2.0	1.1	-2	4.5	3.5	2.0	4.5	2.0	2.4
150	3.5	3.0	2.0	1.1	1.5	4.5	3.5	2.0	4.5	2.0	2.8

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	3.5	3.0	2.0	1.2	2.5	4.5	3.5	2.0	6.5	2.0	2.9
180	6.5	5.5	3.5	5.5	2.5	8.0	4.0	2.0	6.5	2.0	4.6
195	5.5	5.5	3.5	5.5	1.0	8.5	4.5	2.5	6.5	3.5	4.7
210	5.5	9.5	3.5	5.5	2.0	16.5	4.5	2.5	6.5	6.5	8.3
225	5.5	7.5	3.5	5.5	4.5		4.5	2.5	6.5	8.0	5.3
240	5.5	6.5	3.5	5.5	6.0		4.5	2.5	6.5	8.5	5.5
255	5.0	6.5	3.0	5.5	7.0		5.5	3.0	6.0	8.5	5.5
270	5.0	6.5	3.5	5.0	8.0		5.0	3.5	6.0	8.0	5.6
SURVIVAL TIME IN HOURS	8	30*	8½	20	4½	3½	30*	14	14	30*	17.2

MEAN RESPIRATORY RATE PER MINUTE IN DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	15	54	12	15	21	90	44	18	18	60	35
15	54	24	40	21	21	24	48	18	24	30	30
30	45	27	15	27	42	27	18	21	24	30	28
45	33	30	15	24	33	27	48	24	27	36	30
60	24	30	15	33	30	27	48	24	27	36	29
75	27	30	18	33	30	30	36	24	21	36	29
90	24	30	15	24	30	30	30	24	21	36	26
105	21	30	15	24	30	30	30	24	21	36	26
120	21	30	21	24	36	30	30	24	21	30	28
135	21	30	21	24	36	30	33	27	24	30	28
150	27	30	21	24	30	30	30	24	21	30	27

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	21	30	24	24	36	30	30	27	21	30	27
180	15	36	24	21	30	15	36	51	21	27	28
195	21	50	24	24	30	6	36	45	18	24	28
210	15	51	21	16	27	4	36	40	18	24	25
225	12	36	21	16	27		36	45	18	24	26
240	12	24	21	16	21		36	45	24	24	25
255	18	21	21	18	24		27	40	21	24	24
270	18	18	18	21	21		27	36	27	27	24
SURVIVAL TIME IN HOURS	8	30▼	8½	20	4½	3½	30▼	14	14	30▼	17.2

APPENDIX XIX

MEAN CHLORIDES IN MEQ/L OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	108	114	113	122	120	116	122	122	114	114	117
30	107	111	115	117	105	122	115	117	114	114	114
90	108	112	119	122	110	124	115	115	116	107	115
150	110	114	125	128	109	120	119	115	114	109	116
210	105	100	110	106	109		110	110	102	110	107
270	109	107	111	109	110		113			111	110

MEAN SODIUM IN MEQ/L OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	167	146.5	144.5	146	143	141	147	148	148.	144.5	147.6
30	168	144	146	146	137	150	145	145	143	143.5	146.8
90	166	147	150	159	137	150	146	145	150	141	149.1
150	171	147	153.5	166	140	150	149	156	148	141	152.2
210	157	134	139	136	135		139	142	138	145	140.5
270	159	134.5	150	141			140			135.5	142.2

MEAN POTASSIUM IN MEQ/L OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	4.0	4.45	4.0	4.4	3.5	3.8	3.9	3.9	3.97	4.1	4.02
30	4.8	5.7	6.32	10.7	5.6	6.6	4.35	4.2	3.42	3.72	5.54
90	5.8	5.8	6.07	6.5	7.3	5.4	4.45	4.7	3.5	3.82	5.23
150	6.2	6.05	7.35	7.5	7.7	6.7	3.9	4.25	4.05	4.0	5.77
210	4.6	4.27	4.80	5.5	4.6		3.65	3.9	3.2	4.5	4.33
270	4.4	4.43	4.35	5.5			3.5			3.57	4.23

MEAN HEMATOCRIT % OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	45	47	53	56	44	55	57	48	55	50	51
30	40	44	52	66	48	58	55	48	49	44	52
90	42	53	59	68	48	65	54	44	49	40	52
150	40	60	67	72	56	68	63	42	42	42	54
210	37	60	47	59	40		52	55	50	52	50
270			44	52	42		50			51	50

A CHART OF MEAN ELECTROLYTES AND HEMATOCRITS IN DIALYSED DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270
Chlorides in meq/l		117	114	115	116	107	110
	R	108-122	107-122	107-122	109-128	102-110	107-113
Sodium in meq/l		147.6	146.8	149.1	152.2	140.5	142.2
	R	141-167	137-168	137-166	141-171	134-157	134.5-159
Potassium in meq/l		4.02	5.54	5.23	5.77	4.33	4.23
	R	3.7-4.45	3.42-10.7	3.5-7.3	3.9-7.7	3.2-5.5	3.5-5.5
Hematocrit %		51	52	52	54	50	50
	R	45-57	40-66	40-68	40-72	37-59	42-52

MEAN pH OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	7.27	7.45	7.4	7.39	7.38	7.50	7.44	7.37	7.38	7.44	7.4
30	6.9	7.1	7.3	7.15	7.11	7.20	7.36	7.28	6.22	7.2	7.18
90	7.12	7.1	7.2	7.07	7.09	7.16	7.29	7.24	7.24	7.21	7.17
150	7.1	7.1	7.2	7.0	7.14	7.15	7.28	7.13	7.16	7.22	7.15
210	7.2	7.3	7.3	7.22	7.22		7.39	7.30	7.37	7.27	7.36
270	7.2	7.5	7.3	7.2	7.19		7.38			7.42	7.31

MEAN pCO_2 IN MM Hg OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	40.5	24.0	34.5	26.0	24.6	10.0		53.0	35.0	29.0	30.7
30	52.8	19.8	13.2	21.0	13.4	8.0	14.0		10.0	22.0	20.5
90	17.5	13.9	16.7	18.5	15.0	8.0	18.0		21.5	18.5	16.4
150	18.0	24.0	10.0	20.0	11.5	24.0			23.5	18.0	18.6
210	29.8	21.5	18.0	21.8					22.0	26.5	23.3
270	35.5	17.5	16.0	13.5						26.0	21.7

MEAN HCO_3 IN MEQ/L OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	18.0	16.9	19.5	16.0	15.0	10.2		28.0	20.0	19.9	18.2
30	11.3	5.9	7.8	8.2	5.95	5.0	8.6		9.2	9.4	7.9
90	7.1	5.7	7.9	5.7	6.0	5.0	10.0		10.2	8.6	7.4
150	6.5	7.6	5.8	5.9	5.8	8.0			9.2	8.7	7.2
210	12.2	12.8	9.7	8.9					13.5	12.5	11.6
270	14.0	14.1	10.0	7.0						16.9	12.4

MEAN LACTIC ACID IN MEQ/L OF DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	1.6	1.7	2.9	4.3	2.27	4.73	2.69	1.44	2.43	7.74	2.8
30	7.5	12.7	6.3	9.38	17.34	10.74	6.23	6.80	8.14	7.80	9.3
90	8.3	16.6	8.3	14.23	10.32	3.50	6.95	11.55	6.34	8.75	10.0
150		14.0	5.7	10.57	8.95	9.64	6.65	8.15	14.73	8.32	9.7
210	7.7	6.5	5.9	6.41	5.69		5.70	7.0	7.69	6.66	6.5
270	6.7	5.4	10.3	9.47	6.37		6.1			4.42	7.0

A CHART OF MEAN CHEMISTRIES OF DIALYSED DOGS SUBJECTED TO HAEMODIALYSIS AND HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270
pH		7.40	7.18	7.17	7.15	7.36	7.31
	R	7.27-7.45	6.9-7.36	7.07-7.29	7.07-7.28	7.2-7.39	7.19-7.5
pCO_2 in mm Hg		30.7	20.5	16.4	18.6	23.3	21.7
	R	24-53	8-52.8	8-21.5	10-24	18-29.8	13.5-35.5
Bicarbonate in meq/l		18.2	7.9	7.4	7.2	11.6	12.4
	R	10.2-28	5.9-11.3	5.0-10.2	5.8-9.2	8.9-13.5	7.0-16.9
Lactic Acid in meq/l		2.8	9.3	10.0	9.7	6.5	7.0
	R	1.44-4.73	6.23-17.34	6.34-14.23	5.7-14.73	5.69-7.7	-4.42-10.3

A CHART OF MEAN pH, pCO_2, BICARBONATE AND LACTIC ACID OF DIALYSED DOGS SUBJECTED TO HAEMODIALYSIS AND HAEMORRHAGIC SHOCK WITH pCO_2 CORRECTED TO 40 MM Hg

TIME IN MINUTES	0	30	90	150	210	270
pH	7.34	7.06	7.0	7.0	7.22	7.17
pCO_2 in mm Hg	40	40	40	40	40	40
Bicarbonate in meq/l	27.5	11.5	8.0	8.2	20	17.0
Lactic Acid in meq/l	2.8	9.3	10.0	9.7	6.5	7.0

COMPARISON OF VITAL SIGNS OF CONTROL AND DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90
Temperature in Degrees Centigrade	C	37.37	37.29	37.19	37.04	36.50	36.09	35.49
	D	37.7	37.8	37.7	37.4	37.2	36.9	36.8
Blood Pressure in mm Hg	C	157.2	40	40	40	50	50	50
	D	142	40	40	40	50	50	50
Heart Rate per Minute	C	156	128.5	142.1	153.9	159.9	168.6	168.5
	D	155	137	163	173	208	217	215
Venous Pressure in cm H_2O	C	7.65	3.70	2.60	4.0	3.35	3.20	3.5
	D	6.7	2.7	2.1	2.3	2.2	2.5	2.4
Respiratory Rate per Minute	C	27.3	39.3	37.0	31.5	31.5	31.8	32.4
	D	35	30	28	30	29	29	26

C = Control D = Dialysed

B	TIME IN MINUTES (Cont'd.)		105	120	135	150	165	180	195
	Temperature in Degrees Centigrade	C	34.95	34.25	33.80	33.65	33.65	33.6	33.4
		D	35.5	36.0	35.9	35.8	35.2	34.9	34.9
	Blood Pressure in mm Hg	C	50	50	50	50	50	50	96
		D	50	50	50	50	50	112	108
	Hear Rate per Minute	C	167.2	171.2	172.8	169.4	164.4	155.3	168.1
		D	215	219	221	218	228	193	183
	Venous Pressure in cm H_2O	C	3.35	3.30	3.25	2.26	2.86	4.60	4.60
		D	2.6	2.5	2.4	2.8	2.9	4.6	4.7
	Respiratory Rate per Minute	C	31.2	32.7	32.1	32.7	32.5	27.5	29.6
		D	26	28	28	27	27	28	28

C

TIME IN MINUTES (Cont'd.) 6		210	225	240	255	270
Temperature in Degrees Centigrade	C	33.27	33.06	33.06	33.06	33.05
	D	35.0	34.80	34.7	34.5	
Blood Pressure in mm Hg	C	96	107	107	107	102
	D	106	101	103	111.3	117
Heart Rate per Minute	C	142.8	155.6	155.8	155.0	
	D	163	163	162	158	150
Venous Pressure in cm H_2O	C	5.9	5.0	4.9	5.0	5.2
	D	8.3	5.3	5.5	5.5	5.6
Respiratory Rate per Minute	C	24.4	27.7	26.2	24.3	23.2
	D	25	26	25	24	24

COMPARISON OF BLOOD CHEMISTRIES, ELECTROLYTES AND HEMATOCRIT IN CONTROL AND DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES	0	30	90	150	210	270
CONTROL DOGS						
pH	7.32	7.18	7.13	6.16	7.16	7.12
pCO_2 in mm Hg	36.13	15.0	15.40	16.33	22.63	
HCO_3 in meq/l	17.39	9.03	7.30	7.18	9.09	
Lactic Acid	4.06	10.12	15.32	14.71	9.41	
Cl^-	113	115	113	116	117	
Na^+	160	146	148	151	159	149
K^+	3.6	5.5	4.7	5.0	5.8	
Hematocrit %	44	47	51	53	58	61
DIALYSED DOGS						
pH	7.40	7.18	7.17	7.15	7.36	7.31
pCO_2 in mm Hg	30.7	20.5	16.4	18.6	23.3	21.7
HCO_3 in meq/l	18.2	7.9	7.4	7.2	11.6	12.4
Lactic Acid	2.8	9.3	10.0	9.7	6.5	7.0
Cl^-	117	114	115	116	107	110
Na^+	147.6	146.8	149.1	152.2	140.5	142.2
K^+	4.02	5.54	5.23	5.77	4.33	4.23
Hematocrit %	51	52	52	54	50	50

NUMBER OF HOURS OF PERMANENT SURVIVORS AND NON SURVIVORS OF CONTROL AND DIALYSED DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	% SURVIVAL
Control Dogs	3	10	8	10	8	30*	3½	30*	10	9	20%
Dialysed Dogs	8	30*	8½	20	4½	3½	30*	14	24	30*	30%

30* = Permanent Survivor

APPENDIX XX

MEAN VITAL SIGNS OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	15	30	45	60	75	90	105	120	135
Temperature in Degrees Centigrade		37.5	37.5	37.6	37.3	37.2	37.1	36.7	36.7	36.8	36.8
	R	34.1-39	32-39.5	32-39	32.5-38.5	32.5-38.5	32.5-38.5	32.2-38.5	32.2-38	32-38.5	32-38.5
Blood Pressure in mm Hg		149	40	40	40	50	50	50	50	50	50
	R	110-195	40-40	40-40	40-40	50-50	50-50	50-50	50-50	50-50	50-50
Heart Rate per Minute		181	188	183	212	215	202	202	194	208	220
	R	135-216	135-300	99-300	108-300	112-300	102-300	102-270	102-270	120-260	120-300
Venous Pressure in cm Water		4.6	3.0	2.0	3.0	2.1	2.2	3.2	3.3	3.4	3.4
	R	1.1-8.5	-1-8.5	-1-4.5	-1-7.5	-1-7.5	-1-7.5	-1-8.0	-1-8.5	-1-8.5	-1-8.5
Respiratory Rate per Minute		22	23	22	24	25	21	21	20	21	21
	R	12-60	12-30	15-30	15-36	18-36	15-36	12-36	12-36	12-33	15-33

TIME IN MINUTES (Cont'd.)		150	165	180	195	210	225	240	255	270	285
Temperature in Degrees Centigrade		36.5	36.0	35.7	35.0	34.8	34.7	34.6	34.4	34.4	33.6
	R	32-38.2	32-38.2	32-37.5	30.1-37.0	30.1-37	30.1-37	30.1-37	30-36.5	30-36.5	30-35.5
Blood Pressure in mm Hg		50	50	80	81	101	117	114	112	107	92
	R	50-50	50-50	50-150	30-150	10-150	65-155	45-150	30-150	30-150	45-150
Heart Rate per Minute		228	222	204	169	167	166	179	174	200	223
	R	150-312	150-280	150-275	50-225	10-350	117-300	50-270	20-300	102-290	102-312
Venous Pressure in cm Water		3.4	3.3	4.3	6.2	7.0	6.6	6.7	6.6	6.6	6.2
	R	-1-8.5	-1-8.5	-1-9.0	2-11.5	3.5-13	3-13	3-13.5	3.5-13	3.5-13	3.5-13
Respiratory Rate per Minute		21	22	22	20	20	20	19	17	20	20
	R	12-36	12-39	6-38	6-36	3-36	6-30	9-24	6-30	12-30	12-30

R = Range

MEAN TEMPERATURES IN DEGREES CENTIGRADE OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	38.5	34.1	36.0	38.0	39.0	36.0	39.0	38.5	38.0	38.0	37.5
15	38.5	32.0	36.0	38.5	39.5	36.5	39.0	38.5	38.0	38.0	37.5
30	38.2	32.0	36.5	38.5	39.0	38.5	39.0	38.5	38.0	38.0	37.6
45	38.2	32.5	36.1	37.5	38.5	38.0	38.5	38.5	38.0	37.5	37.3
60	38.5	32.5	36.0	37.0	38.5	38.0	38.5	37.5	38.2	37.5	37.2
75	38.5	32.5	36.1	37.0	38.0	38.0	38.5	37.5	37.5	37.0	37.1
90	38.0	32.2	36.1	37.0	38.0	38.0	38.5	36.0	37.5	37.0	36.7
105	38.0	32.2	36.0	37.0	37.0	38.0	38.0	36.0	37.5	37.0	36.7
120	38.0	32.0	36.0	37.0	37.5	38.0	38.5	36.0	37.5	37.0	36.8
135	38.0	32.0	35.5	37.5	37.5	38.2	38.5	36.0	37.5	37.0	36.8
150	37.0	32.0	35.5	37.5	37.0	38.2	38.0	36.0	37.5	36.5	36.5

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	33.0	32.0	34.0	37.5	37.0	38.2	38.0	36.0	37.5	36.5	36.0
180	33.0	32.0	34.0	37.5	37.5	37.5	37.0	35.5	36.5	36.5	35.7
195	32.0	30.1	33.5	36.0	37.0	37.0	37.0	35.5	36.0	35.5	35.0
210	32.0	30.1	33.5	36.5	37.0	37.0	35.0	35.5	36.0	5.0	34.8
225		30.1	33.5	36.0	37.0	36.5	35.0	35.5	35.0	34.0	34.7
240		30.1	33.5	35.5	37.0	36.5	34.5	35.0	35.0	34.0	34.6
255		30.0	33.5	35.5	36.5	36.0	34.5	35.0	35.0	34.0	34.4
270		30.0	33.0	35.0	36.5	34.0		34.0	35.0	34.0	34.0
285		30.0	33.0	35.0	35.5	34.0		34.0	35.0	33.0	33.6
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30*	13

MEAN BLOOD PRESSURE IN MM Hg OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	195	165	135	170	162	170	110	140	130	112	149
15	40	40	40	40	40	40	40	40	40	40	40
30	40	40	40	40	40	40	40	40	40	40	40
45	40	40	40	40	40	40	40	40	40	40	40
60	50	50	50	50	50	50	50	50	50	50	50
75	50	50	50	50	50	50	50	50	50	50	50
90	50	50	50	50	50	50	50	50	50	50	50
105	50	50	50	50	50	50	50	50	50	50	50
120	50	50	50	50	50	50	50	50	50	50	50
135	50	50	50	50	50	50	50	50	50	50	50
150	50	50	50	50	50	50	50	50	50	50	50

DOG NUMBER (Cont'd,)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	50	50	50	50	50	50	50	50	50	50	50
180	50	100	120	120	55	150	50	50	50	50	80
195	30	120	125	120	60	150	50	50	50	50	81
210	10	125	132	130	75	150	70	110	115	90	101
225		130	140	130	65	155	65	115	145	110	117
240		132	135	128	60	150	45	120	145	110	114
255		135	130	128	60	150	30	120	145	110	112
270		135	130	130	55	150	30	75	145	110	107
285		135	130	130	50	150		45	50	45	92
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30*	13

MEAN HEART RATE PER MINUTE OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	210	135	162	216	180	159	180	150	208	204	181
15	135	180	144	180	222	300	186	162	210	162	188
30	120	150	210	210	300	99	100	165	210	270	183
45	147	300	200	280	300	127	108	150	212	300	212
60	144	138	210	270	300	282	112	152	268	270	215
75	210	126	210	268	280	300	120	168	240	102	202
90	210	150	228	270	270	210	132	180	268	102	202
105	180	132	215	240	270	210	138	186	269	102	194
120	200	150	220	260	250	210	144	240	289	120	208
135	220	150	210	240	240	210	300	213	300	120	220
150	222	150	225	280	240	240	210	225	312	180	228

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	280	150	220	280	280	210	216	186	220	180	222
180	225	150	144	180	275	210	230	180	240	210	204
195	50	100	145	180	174	210	225	222	222	162	169
210	10	104	150	210	180	150	230	120	350	164	167
225		117	155	210	160	150	225	180	300	166	166
240		107	150	210	225	150	50	270	240	210	179
255		104	144	228	180	150	20	240	300	220	174
270		102	150	222	210	150		267	290	210	200
285		102	150	230	240	150		300	312	300	223
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30▼	13

MEAN VENOUS PRESSURE IN CM WATER OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	2	4.5	4.0	5.5	5.0	7.5	3.5	8.5	1.1	4.0	4.6
15	1	2.5	2.5	-1	1.0	5.5	5.0	8.5	1.1	4.0	3.0
30	1	4.0	3.0	-1	1.0	4.5	1	3.0	-1	4.0	2.0
45	-1	2.5	7.5	-1	7.0	4.5	1	4.0	1	4.0	3.0
60	-1	3.0	7.5	1	-1	4.0	-1	3.5	1	4.0	2.1
75	-1	3.5	7.5	1	-1	4.0	-1	3.5	1	4.5	2.2
90	-1	4.5	8.0	1.5	3.0	5.5	-1	5.5	1	4.5	3.2
105	-1	5.0	8.5	2.0	3.5	4.5	-1	5.5	1	4.5	3.3
120	-1	6.0	8.5	2.0	3.5	4.5	-1	5.5	1	4.5	3.4
135	-1	6.2	8.5	2.5	3.0	4.5	-1	5.5	1	4.5	3.4
150	-1	6.2	8.5	2.5	3.0	5.0	-1	5.5	1	4.5	3.4

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	-1	5.0	8.5	2.5	3.0	5.0	-1	5.5	1	4.5	3.3
180	5.5	5.2	9.0	4.5	3.0	5.0	-1	5.5	2.0	4.5	4.3
195	11.5	5.5	9.5	4.5	4.5	6.5	6.0	6.0	2.0	6.0	6.2
210	12.5	5.0	8.5	4.5	3.5	6.5	7.0	6.0	3.0	13.0	7.0
225		5.5	9.0	4.5	3.5	6.5	8.5	6.0	3.0	13.0	6.6
240		5.5	9.5	4.0	3.5	6.5	8.5	6.0	3.0	13.5	6.7
255		5.0	9.0	4.0	3.5	6.5	8.5	6.0	3.5	13.0	6.6
270		5.0	8.0	4.5	3.5	6.0		6.0	3.5	13.0	6.6
285		5.0	8.0	4.5	3.5	6.0		6.0	3.5	13.0	6.2
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30*	13

MEAN RESPIRATORY RATE PER MINUTE OF CONTROL DOGS

SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	12	18	18	60	15	15	24	15	21	18	22
15	24	18	27	30	30	12	30	21	21	18	23
30	24	18	27	30	27	15	18	15	27	18	22
45	36	18	27	27	27	15	18	21	36	18	24
60	36	18	18	27	24	24	21	27	36	18	25
75	24	18	18	27	18	21	18	15	36	18	21
90	24	18	18	30	15	18	21	12	36	18	21
105	21	18	15	30	12	18	21	12	36	18	20
120	21	18	18	30	15	18	24	12	33	21	21
135	21	18	18	27	15	15	27	15	33	21	21
150	21	18	18	27	12	15	30	12	36	24	21

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	21	18	18	27	12	18	30	12	39	24	22
180	6	18	18	30	12	24	36	12	38	24	22
195	6	18	18	30	9	24	36	12	27	24	20
210	3	18	15	27	12	18	36	27	24	24	20
225		6	15	30	12	18	15	27	24	30	20
240		9	15	24	12	18	12	27	24	24	19
255		12	12	18	12	15	6	27	24	30	17
270		18	12	21	15	18		24	24	30	20
285		18	12	21	15	21		24	24	30	20
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30▼	13

APPENDIX XXI

MEAN CHLORIDES IN MEQ/L OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	116	108	112	116	119	120	113	123	114	125	117
30	114	104	104	117	121	115	118	110	116	121	114
90	120	107	104	134	114	115	120	108	110	112	114
150	114	107	107	123	123	112	110	111	116	113	114
210		110	103	113	123	117	108	123	118	116	115
270		111	108	119	116	114	119	116	133		117
330									100		100
390									119		119

MEAN SODIUM IN MEQ/L OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	149	140	144	146	149	140	141	150	148	145	145
30	150	135	135	148	146	140	142	142	148	145	143
90	154	139	136	146	154	136	145	143	149	139	144
150	156	140	136	151	155	138	144	142	150	144	146
210		142	136	152	155	146	145	139	155	145	146
270		137	135	154	151	150	145	147	149		146
330								147			147
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30*	13

MEAN POTASSIUM IN MEQ/L OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	4.2	6.7	3.1	2.9	4.1	3.8	4.85	3.6	4.0	3.7	4.1
30	6.9	6.8	5.1	3.8	5.9	5.2	6.2	6.0	4.1	4.2	5.4
90	6.5	4.9	5.9	3.6	6.4	5.4	7.4	7.2	4.35	3.6	5.5
150	7.0	4.6	5.6	3.9	7.2	5.75	7.9	7.7	4.5	3.9	5.8
210		5.5	6.9	4.8	9.15	5.7	8.2	7.6	4.5	4.4	6.1
270		5.85	7.4	8.9	5.55	5.1	8.35	5.5	5.5		6.4
330								4.4	5.7		5.0
390									6.0		6.0
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30▼	13

MEAN HEMATOCRIT % OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	52	42	36	49	50	49	48	48	49	41	46
30	61	40	30	44	51	51	47	40	43	42	45
90	52	39	24	42	58	48	43	43	41	39	43
150	64	38	30	45	63	54	55	50	44	42	49
210		40	39	55	68	61	51	53	53	50	52
270		41	42	67	55	66	52	52	52		43
330								54	54		54
390									52		52
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30[F]	13

MEAN CHLORIDES, SODIUM, POTASSIUM IN MEQ/L AND HEMATOCRIT % OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270	330	390
Chlorides in meq/l		117	114	114	114	115	117	100	119
	R	108-125	104-121	104-134	107-123	103-123	108-133	100-	119-
Sodium in meq/l		145	143	144	146	146	146	147	
	R	140-150	135-150	136-154	136-156	136-155	135-154	147-147	
Potassium in meq/l		4.1	5.4	5.5	5.8	6.1	6.4	5.0	6.0
	R	2.9-6.7	3.8-6.9	3.6-7.4	3.9-7.9	4.4-8.2	5.1-8.9	4.4-5.7	6 -
Hematocrit %		46	45	43	49	52	43	54	52
	R	36-52	30-61	24-58	30-64	39-68	41-67	54-	52-

MEAN pH OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	7.34	7.34	7.32	7.50	7.38	7.34	7.30	7.33	7.31	7.45	7.36
60	6.86	7.17	7.08	7.25	7.07	7.27	7.31	6.97	7.25	7.45	7.17
90	7.06	7.19	7.05	7.29	6.92	7.29	7.2	6.96	7.33	7.46	7.17
150	6.86	7.18	7.04	7.31	6.91	7.30	7.18	7.05	7.30	7.45	7.16
210	6.70	7.09	7.02	7.31	7.0	7.29	7.29	7.21	7.29	7.45	7.17
Res. Blood	7.29						7.3			7.45	7.34
270		7.19	7.20	7.36	7.11	7.39	7.29	7.32	7.39	7.43	7.29
330									7.42	7.48	7.45
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30+	13

MEAN pCO_2 OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	46.0	39.0	33.0	22.0	38.0	41.0	33.0	41.0	48.0	33.5	37.5
60	30.0	14.5	22.0	15.5	10.0	13.5	19.5			25.0	18.8
90	39.0	13.8	25.0	19.5	10.0	12.0	18.2	30.0	19.0	16.5	20.3
150	43.0	13.5	25.5	20.5	10.0	16.0	15.5	31.0	44.0	16.8	23.6
210	10.0	10.0	27.5	23.5	28.5	21.5	11.0	24.5	27.0	22.0	20.6
Res. Blood	36						33			33.5	34.2
270		16.0	26.0	24.0	25.0	20.0	12.0	20.0	25.0	25.5	21.5
330									24.5		24.5
SURVIVAL TIME IN HOURS	$3\frac{1}{2}$	11	20	9	12	9	$4\frac{1}{2}$	7	24	30*	13

MEAN HCO_3 OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	23.0	20.0	16.5	17.5	21.5	21.5	18.0	20.8	22.9	21.0	20.3
60	5.0	6.8	7.3	8.2	5.0	8.0	11.0	5.0		17.9	8.2
90	10.5	6.9	7.4	10.5	5.0	6.5	9.0	7.0	11.0	13.5	8.7
150	7.0	6.7	7.3	11.2	5.0	9.4	7.4	7.8	20	13	9.5
210	8.0	5	7.5	12.5	7.3	11.1	7.5	10.4	13.5	15.5	9.9
Res Blood	16.8						16			23.5	18.8
270		7.4	10.5	14.0	8.3	13	7.8	11.3	15.8	19	11.9
330									15.8		15.8
SURVIVAL TIME IN HOURS	$3\frac{1}{2}$	11	20	9	12	9	$4\frac{1}{2}$	7	24	30*	13

MEAN LACTIC ACID OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	2.35	2.32	3.27	4.45	4.35	1.57	2.96	2.15	1.89	1.71	2.7
60	18.09	11.42	10.11		17.04	6.92	5.63	11.79	6.59	2.63	10.02
90	14.98	11.42	11.23	12.68	19.37	10.92	7.36	14.33	7.47	3.84	11.36
150	13.0	14.52	14.23		20.33	4.47	7.32	9.35	3.24	4.43	10.1
210	22.61	17.91	14.79		18.11	10.85	7.17	6.36	7.14	3.48	12.05
Res. Blood	16.31						4.78			3.84	4.98
270		11.42	7.48	6.97	12.78	4.44	8.37	4.67		2.09	7.28
SURVIVAL TIME IN HOURS	3½	11	20	9	12	9	4½	7	24	30*	13

MEAN pH, pCO_2 IN MM Hg, BICARBONATE AND LACTIC ACID IN MEQ/L OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	60	90	150	210	Res. Blood	270	330
pH		7.36	7.17	7.17	7.16	7.17	7.34	7.29	7.45
	R	7.3-7.5	6.86-7.45	6.92-7.46	6.86-7.45	6.7-7.45	7.29-7.45	7.11-7.43	7.42-7.48
pCO_2 in mm Hg		37.5	18.8	20.3	23.6	20.6	34.2	21.5	24.5
	R	22-48	10-30	10-39	10-44	10-28.5	33-36	12-26	24.5-
Bicarbonate in meq/l		20.3	8.2	8.7	9.5	9.9	18.8	11.9	15.8
	R	16.5-23	5-17.9	5-13.5	5-20	5-15.5	16-23.5	7.4-19	15.8-
Lactic Acid		2.7	10.02	11.36	10.0	12.05	4.98	7.2	
	R	1.57-4.45	2.63-18.09	3.84-19.37	3.24-20.33	3.48-22.61	3.84-6.31	2.09-12.78	

MEAN pH, pCO_2 IN MM Hg, BICARBONATE AND LACTIC ACID IN MEQ/L OF CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK WITH pCO_2 CORRECTED TO 40 MM Hg

TIME IN MINUTES	0	60	90	150	210	Res Blood	270	330
pH	7.33	7.03	7.05	7.05	7.05	7.29	7.16	7.32
pCO_2 in mm Hg	40	40	40	40	40	40	40	40
Bicarbonate in meq/l	28.0	10	10.80	10.80	11.00	25	17.0	26.5
Lactic Acid	2.7	10.02	11.36	11.1	12.05	4.98	7.2	

APPENDIX XXII

MEAN VITAL SIGNS OF DIALYSED DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

A

TIME IN MINUTES		0	15	30	45	60	75	90	105	120
Temperature in Degrees Centigrade		37.7	37.7	37.5	37.3	37.2	37.1	37.1	37.7	36.5
	R	34-39	33.5-39.5	33.5-39	33.2-39	32.5-39.2	32.5-39.2	32-39	32-39	31.5-39.5
Blood Pressure in mm Hg		150	124	108	108	101	96	40	40	40
	R	100-190	90-165	60-160	60-165	50-155	40-140	40-40	40-40	40-40
Heart Rate per Minute		194	183	191	182	180	185	188	199	208
	R	132-264	120-300	90-330	120-300	102-270	120-275	126-280	132-280	90-300
Venous Pressure in cm Water		4.3	4.2	4.3	4.4	4.2	4.3	4.1	3.2	3.5
	R	1.5-10.5	2-9.5	2-9.5	1.5-9.5	1.5-8.5	1.5-8.5	-1-8.5	-1-7.5	-1-8.5
Respiratory Rate per Minute		21	22	17	17	17	18	22	22	22
	R	6-60	6-60	9-24	12-24	12-24	12-24	15-24	6-36	2-36

B

TIME IN MINUTES (Cont'd.)		135	150	165	180	195	210	225	240	255
Temperature in Degrees Centigrade		36.3	36.1	35.9	35.8	35.3	34.9	34.1	34.4	33.9
	R	31.5-39	31.5-38.5	31.5-38.0	31.5-38.5	30.5-38	30.5-38	30-38	30-38	30-38
Blood Pressure in mm Hg		47	47	48	48	50	50	87	97	103
	R	30-50	30-50	35-50	30-50	50-50	50-50	30-110	85-112	88-120
Heart Rate per Minute		194	213	213	209	196	178	176	203	182
	R	50-270	142-240	100-300	50-280	120-290	50-280	6-300	140-280	150-220
Venous Pressure in cm Water		4.2	3.7	3.9	4.9	4.4	4.8	5.0	3.9	3.7
	R	-1-10.5	-1-11.0	-1-12.5	-1-13.0	-1-14.0	-1-15.0	-1-15.0	-1-7.5	-1-8.0
Respiratory Rate per Minute		25	26	26	25	25	23	24	26	27
	R	15-45	21-45	21-42	18-42	15-45	6-42	12-42	18-42	18-42

R = Range

MEAN TEMPERATURE OF DOGS SUBJECTED TO .5 MG/KG DIBENXYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	39.0	34.0	38.0	37.0	37.0	37.5	39.0	36.5	39.5	39.0	37.7
15	38.5	33.5	38.0	37.0	37.0	37.5	39.0	37.5	39.5	39.0	37.7
30	38.5	33.5	38.0	37.0	37.0	36.5	39.0	37.5	39.0	39.0	37.5
45	38.0	33.3	37.5	37.5	36.5	36.5	39.0	37.1	39.0	39.0	37.3
60	38.5	32.5	37.5	36.5	36.0	36.5	39.0	37.0	39.0	39.2	37.2
75	38.5	32.5	37.5	36.5	36.0	36.0	39.0	36.5	39.0	39.2	37.1
90	38.5	32.0	37.5	38.5	36.0	36.0	38.5	36.0	39.0	39.0	37.1
105	38.5	32.0	37.5	36.0	35.5	36.0	37.5	36.0	39.0	39.0	36.7
120	38.5	31.5	36.5	36.0	35.5	36.0	37.0	35.5	39.5	39.0	36.5
135	38.5	31.5	36.0	36.0	35.5	36.0	36.5	35.5	39.0	38.5	36.3
150	38.0	31.5	36.0	36.0	35.5	36.0	36.5	35.1	38.5	38.0	36.1
165	38.0	31.5	36.0		35.0	35.5	36.0	35.0	38.5	37.5	35.9

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
180	37.0	31.5	35.0		35.0	35.5	36.6	36.0	38.5	37.5	35.8
195	37.0	30.5	35.0			35.5	35.5	36.0	38.0	35.0	35.3
210	36.5	30.5	34.0			34.5	35.5	36.0	38.0	34.5	34.9
225	36.0	30.0	34.0			34.0	35.5	35.5	38.0	32.0	34.1
240	35.0	30.0	33.0			34.0	35.5	35.5	38.0		34.4
255	34.0	30.0	33.0			33.5	34.0	35.0	38.0		33.9
SURVIVAL TIME IN HOURS	5	30*	30*	$2\frac{1}{2}$	3	20	10	$12\frac{1}{2}$	30*	$3\frac{1}{2}$	14.7

MEAN BLOOD PRESSURE OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	160	140	140	190	120	150	175	165	100	160	150
15	155	100	130	160	90	100	105	145	90	165	124
30	135	92	90	140	60	98	90	135	80	160	108
45	150	90	90	125	60	98	100	120	80	165	108
60	155	88	90	118	50	95	100	120	70	120	101
75	140	88	85	110	40	88	100	120	75	115	96
90	40	40	40	40	40	40	40	40	40	40	40
105	40	40	40	40	40	40	40	40	40	40	40
120	40	40	40	40	40	40	40	40	40	40	40
135	50	50	50	30	40	50	50	50	50	50	47
150	50	50	50	30	40	50	50	50	50	50	47

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	50	50	50		35	50	50	50	50	50	48
180	50	50	50		30	50	50	50	50	50	48
195	50	50	50			50	50	50	50	50	50
210	50	50	50			50	50	50	50	50	50
225	100	100	80			80	95	110	98	30	87
240	100	112	90			85	95	110	100		97
255	112	120	95			88	95	110	102		103
270	112	150	98			88	95	110	102		108
285	112	150	100			80	95	120	102		108
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

MEAN HEART RATE OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	168	132	210	138	240	232	177	201	180	264	194
15	150	114	150	130	120	240	300	165	189	270	183
30	180	120	192	154	90	180	330	180	210	274	191
45	180	120	170	174	180	184	300	165	144	200	182
60	210	102	180	180	180	196	270	160	150	180	180
75	210	120	210	174	162	200	270	165	150	180	185
90	222	150	210	150	162	210	280	210	126	160	188
105	222	132	225	174	180	210	280	250	150	168	199
120	214	140	270	90	165	230	300	270	150	240	208
135	220	140	230	50	170	230	240	270	180	200	194
150	222	142	240		200	236	250	210	240	180	213

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
165	220	144	180		100	240	250	220	270	300	213
180	214	146	180		50	280	270	200	264	280	209
195	220	120	210			280	210	240	200	290	196
210	240	130	180			280	200	240	180	50	178
225	250	130	180			300	210	240	156	6	176
240	180	140	180			280	222	270	156		203
255	180	150	180			170	220	220	156		182
270	180	150	180			180	240	180	150		180
285	200	150	198			210	240	180	150		189
SURVIVAL TIME IN HOURS	5	30▼	30▼	2½	3	20	10	12½	30▼	3½	14.7

MEAN VENOUS PRESSURE IN CM WATER OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLENE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	4.5	1.5	10.5	4.5	2.0	2.0	5.5	4.5	2.5	5.5	4.3
15	4.5	2.0	9.5	4.0	2.0	2.0	5.0	4.0	2.5	6.5	4.2
30	5.0	2.0	9.5	4.0	3.0	2.0	4.5	3.5	2.5	6.5	4.3
45	5.5	1.5	9.5	7.0	2.5	1.5	4.5	3.5	2.5	6.0	4.4
60	5.0	1.5	8.5	6.0	2.5	1.5	4.5	2.5	4.0	5.5	4.2
75	5.0	1.5	8.0	6.0	2.5	1.5	4.5	2.5	2.5	8.5	4.3
90	5.0	-1	8.0	5.5	2.5	1.5	3.5	5.5	2.0	8.5	4.1
105	3.5	-1	7.5	5.5	1.5	-1	3.0	5.5	2.0	5.5	3.2
120	2.0	-1	7.5	5.5	2.0	-1	3.0	6.5	2.0	8.5	3.5
135	2.5	-1	7.5	10.5	2.0	-1	2.5	6.5	2.0	10.0	4.2
150	2.0	-1	7.5		2.5	1.0	2.5	5.5	2.0	11.0	3.7

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	2.0	-1	7.5		2.5	1.0	3.0	6.0	2.0	12.5	3.9
180	2.0	-1	7.5		10.5	1.0	3.5	6.0	2.0	13.0	4.9
195	2.0	-1	7.5			1.0	3.5	6.0	2.0	14.0	4.4
210	2.5	-1	7.5			1.0	4.5	6.0	3.0	15.0	4.8
225	2.5	-1	7.5			1.0	4.5	6.5	4.0	15.0	5.0
240	2.5	-1	7.5			1.0	5.0	6.5	3.0		3.9
255	2.5	2.0	8.0			1.0	5.0	6.5	2.5		3.7
270	2.5	2.5	8.0			1.0	5.0	5.5	3.0		3.8
285	2.5	2.5	7.5			1.0	5.0	5.5	3.0		2.9
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

MEAN RESPIRATORY RATE PER MINUTE OF DOGS SUBJECTED TO .5MG/KG DIBENZYLENE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	24	10	60	6	18	18	12	24	18	15	21
15	24	12	60	6	24	15	15	18	18	18	22
30	24	12	9	18	24	18	18	18	18	12	17
45	24	12	12	18	24	15	15	18	18	15	17
60	24	15	12	18	24	15	15	21	12	15	17
75	24	15	15	18	24	18	18	18	12	15	18
90	24	30	15	18	24	18	21	24	24	18	22
105	30	30	15	6	24	18	21	24	36	18	22
120	30	30	15	2	24	18	21	27	36	21	22
135	45	24	15		24	24	21	24	27	21	25
150	45	24	24		24	24	21	24	27	24	26

DOG NUMBER (Cont'd.)	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
165	42	24	24		24	27	21	27	21	24	26
180	42	24	24		24	27	18	21	24	24	25
195	45	24	24			24	24	18	24	15	25
210	42	24	24			24	27	21	15	6	23
225	42	24	24			27	24	18	12		24
240	42	24	21			27	21	18	30		26
255	42	24	21			27	24	18	30		27
270	42	24	21			24	21	18	30		26
285	40	24	24			24	21	18	27		25
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

APPENDIX XXIII

MEAN CHLORIDES IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	116	117	113	119	112	104	117	108	119	107	113
60	109	122	106	114	119	110	116	108	113	107	112
90	105	122	110		120	104	109	109	112	112	111
150	112	120	115		123	104	110	111	112	118	114
210	110	118	111			110	112	116	111		113
270	107	117	102				116	118	112		112
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

MEAN SODIUM IN MEG/L OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	140	150	151	139	139	141.5	141	142	140	140	142
60	137.5	150	150.5	147.5	148	140	145	142	142	140	144
90	137.5	141	145		149	145	144	138	142	144	143
150	140.5	144	145		150	141	148	140	143	145	149
210	139.5	145	144			144	150	140	141		143
270	145	144	143			147	145	142		144	
SURVIVAL TIME IN HOURS	5	30'	30'	2½	3	20	10	12½	30'	3½	14.7

MEAN POTASSIUM IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	3.9	3.45	4.6	4.3	4.35	4.07	3.5	3.6	3.9	4.0	4.0
60	3.72	4.15	3.1	3.5	3.5	3.5	3.2	3.15	3.8	3.95	3.6
90	6.65	4.0	3.45		4.0	3.3	4.7	3.6	3.9	4.2	4.2
150	5.85	3.7	3.45		4.35	3.43	4.15	3.55	4.0	4.9	4.1
210	6.3	4.8	3.65			3.55	4.3	3.85	4.6		4.4
270	6.4	4.5	3.8				4.7	4.2	4.3		4.6
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

MEAN HEMATOCRIT % OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	39	46	44	57	48	47	57	43	44	51	48
60	48	46	44	55	64	45	51	43	41	43	48
90	42	42	40	52	71	44	56	41	43	47	48
150	51	47	41		74	43	56	41	43	56	50
210	47	48	39			40	54	43	40		44
270	47	53	43				56	46	45		49
SURVIVAL TIME IN HOURS	5	30*	30*	2½	3	20	10	12½	30*	3½	14.7

MEAN ELECTROLYTES AND CHEMISTRIES AND HEMATOCRIT % OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270
Chlorides in meq/l		113	112	111	114	113	112
	R	104-119	106-122	105-122	104-120	110-118	102-118
Sodium in meq/l		142	144	143	149	143	144
	R	139-151	137-150	137-149	140-150	139-150	144-147
Potassium in meq/l		4.0	3.6	4.2	4.1	4.4	4.6
	R	3.5-4.45	3.2-4.15	3.3-6.65	3.43-5.85	3.65-6.3	3.8-6.4
Hematocrit %		48	48	48	50	44	49
	R	39-57	41-64	41-71	41-74	39-54	43-56

R = Range

MEAN pH OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	7.36	7.28	7.30	7.44	7.73	7.40	7.38	7.41	7.43	7.46	7.42
60	7.27	7.32	7.34	7.43	7.36	7.33	7.40	7.35	7.52	7.45	7.38
90	7.27	7.24	7.35	7.12	7.21	7.35	7.39	7.30	7.44	7.33	7.3
150	7.26	7.22	7.28	7.24	7.17	7.30	7.35	7.31	7.39	7.38	7.29
210	7.25	7.24	7.31	7.31		7.30	7.35	7.31	7.43		7.32
270	7.28	7.16		7.29			7.38		7.35		7.29
SURVIVAL TIME IN HOURS	30*	30*	2½	5	3	20	10	12½	30*	3½	14.7

MEAN pCO_2 IN MM Hg OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	29.5	43.5	36.0	21.5	13.8	41.0	33.5	35.5	34.5	30.0	31.9
60	29.0	28.5	34.4	16.8	10	45.0	30.0	34.5	17.0	21.0	26.6
90	22.3	24.5	24.8	10	10	36.0	20.5	18.0	12.5	21.5	20.0
150	22.0	23.0	36.0	10	10	35.0	25.5	20.0	23.0	19.0	22.4
210	17.0	23.0	30.0			36.0	28.0	24.0	19.0		26.0
270	20.0	26.5					34.0		25.0		26.4
SURVIVAL TIME IN HOURS	30[T]	30[T]	2½	30[P]	3	20	10	12½	30[P]	3½	14.7

MEAN HCO_3 IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG OF DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	16.7	19.8	18.0	15.2	20.2	24.2	19.2	21.5	23.0	21.0	19.9
60	13.5	14.5	16.0	12.2	5	22.0	18.2	18.5	15.0	15.5	15.1
90	11.0	11.0	15.0	5	5	19.0	13.1	10.2	10.2	12.2	11.2
150	10.8	10.0	10.0	5	5	16.5	14.5	11.0	14.5	12.4	10.1
210	8.9	10.0	10.0			17.0	15.5	12.7	13.8		12.6
270	10.6	9.9					17.5		14.5		13.1
SURVIVAL TIME IN HOURS	30*	30*	2½	30*	3	20	10	12½	30*	3½	14.7

MEAN LACTIC ACID IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG OF DIBENZYLINE AND HAEMORRHAGIC SHOCK

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Time in Minutes											
0	1.67	1.58	3.0	1.24	2.0	2.24	1.77	3.06	2.31	6.78	2.57
60	3.78	3.53	4.6	2.29	8.61	2.25	2.78	4.61	2.98	7.3	4.27
90	4.05	5.43	7.5	17.47	9.13	9.64	8.89	7.82	7.38	6.69	8.4
150	6.25	4.66	5.5	6.51	8.71	5.93	16.6	8.66	7.38	6.08	7.63
210	5.47	4.21	6.0	5.36		7.20	3.93	7.23	6.66		4.61
270	3.42	4.40		11.76			3.89		6.90		6.07
SURVIVAL TIME IN HOURS	30*	30*	2½	30*	3	20	10	12½	30*	3½	14.7

MEAN CHEMISTRIES IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK

TIME IN MINUTES		0	30	90	150	210	270
pH		7.42	7.38	7.3	7.29	7.32	7.29
	R	7.28-7.73	7.27-7.52	7.12-7.44	7.17-7.39	7.24-7.43	7.16-7.38
pCO_2 in mm Hg		34.4	37.7	31.1	22.3	26.1	26.4
	R	13.8-43.5	10-45	10-36	10-36	17-36	20-34
HCO_3 in meq/l		19.9	15.1	11.2	10.1	12.6	13.1
	R	15.2-24.2	5-22	5-19	5-16.5	10-17	9.9-17.5
Lactic Acid in meq/l		2.57	4.27	8.4	7.63	4.61	6.07
	R	1.24-6.78	2.25-8.61	4.05-17.47	4.66-16.6	3.93-7.23	3.42-11.76

R = Range

MEAN pH, pCO_2 IN MM Hg, LACTIC ACID AND BICARBONATE IN MEQ/L OF DOGS SUBJECTED TO .5 MG/KG DIBENZYLINE AND HAEMORRHAGIC SHOCK WITH pCO_2 CORRECTED TO 40 MM Hg

TIME IN MINUTES	0	30	90	150	210	270
pH	7.37	7.29	7.18	7.17	7.22	7.20
pCO_2 in meq/l	40	40	40	40	40	40
HCO_3 in meq/l	32.5	25.0	18.0	17.5	20	19.0
Lactic acid in meq/l	2.57	4.27	8.4	7.63	4.61	6.07

COMPARATIVE MEAN OF BLOOD CHEMISTRIES AND ELECTROLYTES IN CONTROL DOGS SUBJECTED TO HAEMORRHAGIC SHOCK AND .5 MG/KG DIBENZYLINE

TIME IN MINUTES	0	30	90	150	210	270
CONTROL DOGS						
pH	7.36	7.17	7.17	7.16	7.17	7.29
pCO_2 in mm Hg	37.5	18.8	20.3	23.6	20.6	21.5
HCO_3 in meq/l	20.3	8.2	8.7	9.5	9.9	11.9
Lactic Acid in meq/l	2.7	10.02	11.36	10.1	12.05	7.2
Chlorides in meq/l	117	114	114	114	115	117
Sodium in meq/l	145	143	144	146	146	146
Potassium in meq/l	4.1	5.4	5.5	5.8	6.1	6.4
Hematocrit %	46	45	43	49	52	43
DIBENZYLINE DOGS						
pH	7.42	7.38	7.3	7.29	7.32	7.29
pCO_2 in mm Hg	34.4	27.7	21.1	22.3	26.1	26.4
HCO_3 in meq/l	19.9	15.1	11.2	10.1	12.6	13.1
Lactic Acid in meq/l	2.57	4.27	8.4	7.63	4.61	6.07
Chlorides in meq/l	113	112	111	114	113	112
Sodium in meq/l	142	144	143	149	143	144
Potassium in meq/l	4.0	3.6	4.2	4.1	4.4	4.6
Hematocrit %	48	48	48	50	44	49

SURVIVAL TIME IN HOURS OF DIBENZYLINE DOGS AND THEIR CONTROLS

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	No. P.S.	MEAN No. HRS.	% SURVI-ALS
CONTROL	3.5	11	20	9	12	9	4.5	7	24	30*	1	13	10%
DIBENZYLINE	5	30*	30*	2.5	3	20	10	12.5	30*	3.5	3	14	20%

P.S. = Permanent Survivor = 30*

TIME IN MINUTES BEFORE THE DOG STARTS REINFUSION

DOG NUMBER	1	2	3	4	5	6	7	8	9	10	MEAN
Dibenzyline and Haemorrhagic Shock Dogs	50	50	100	N.R.	N.R.	N.R	90	N.R.	N.R.	N.R.	29
Haemorrhagic Shock Control Dogs	90	90	75	50	50	75	90	90	90	90	79

N.R. = No Reinfusion

BIBLIOGRAPHY

1. Abel, F.L. "Effect of Hemorrhage on Peripheral Blood Flow", Physiologist, 3 (3):4, 1960.

2. Abernathy, R.S., Halverg, F. and Spink, W.W., "Studies on the Mechanism of Chlorpromazine Protection Against Brucella Endotoxin in Mice", Journ. Lab. and Clin. Med. 49:708, 1957.

3. Abernethy, J. "Surgical Observations", Paternoster Row: Longmans and Rees, p. 210, 1804.

4. Adcock, L.L., and Hakanson, E.Y. "Vascular Collapse Complicating Septic Abortion", Am. Journ. Obst. and Gynec., 79:516, 1960.

5. Alexander, B. "Tissue Thiamine in Haemorrhagic Shock", Journ. Clin. Invest., 23:259, 1944.

6. Alexander, R.S. "Venomotor Tone in Haemorrhage and Shock", Circulation Res., 3:181, 1955.

7. Alican, F. and Hardy, J.A. "Mechanisms of Shock as Reflected in Studies of Lymph of Abdominal Organs", Surg. Gyn. and Obt. 113:743, 1961.

8. Altemeier, W.A., and Culbertson, W.P. "Progress Reports to the National Research Council on Studies in Sepsis and Irreversible Shock", June, 1958, p. 145.

9. Altschule, M.D., et al. "Circulation and Respiration During an Episode of Chill and Fever in Man", J. Clin. Invest., 24:585, 1945.

10. Anderson, A., and Kolff, W.J. "Artificial Kidney in the Treatment of Uremia Associated with Acute Glomerulonephritis (With a Note on Regional Heparinization)," Ann. Int. Med., 51:476, 1959.

11. Anderson, M.M., Stewart, J.D., Hubbard, R.S. et al. "The Effect of Variation in Hepatic Blood Flow on the Course of Shock", Surg. Forum, 6:499, 1954.

12. Andrews, W.H. "The Action of Adrenaline, L-Noradrenaline, Acetylcholine and Other Substances on the Blood Vessels of the Perfused Canine Liver," J. Physiol., 128:413, 1955.

13. Antopol, W. "The Production of the Shwartzman Phenomenon by Means of Bacterial Extracts", J. Infect. Dis., 61:331, 1937.

14. Astrup, P. "Ultra-Micro Methods for Determining pH, pCO_2 and Standard Bicarbonate in Capillary Blood", London: Ciba Foundation Research Forum, 1958.

15. Astrup, P. "A Simple Electrometric Technique for Determination of Carbon Dioxide Tension in Blood Plasma, Total Content in 'Separated' Plasma at a Fixed Carbon Dioxide Tension, (40 mm Hg)", Scan. J. Clin. Lab. Invest., 8:33, 1957.

16. Astrup, P. "On the Recognition of Disturbances in the Acid-Base Metabolism", Danish Med. Bull., 2:136, 1955.

17. Astrup, P. "Apparatus for Anaerobic Determination of the pH of Blood at 38 Degrees Centigrade", Scand. J. Clin. Lab. Invest., 8:20, 1956.

18. Aust, J.B., and Johnson, J.A., and Visscher, M.B. "Plasma Sequestration in Endotoxin Shock", Surg. Forum: Clinical Congress of the American College of Surgeons (Phila.), 8:8, 1957.

19. Aust, J.B., and Johnson,J. A. "Blood Flows to Various Tissues in Endotoxin Shock", Surg. Forum, 9:34, 1958.

20. Aust, J.G. "Distribution Kinetics of Various Substances in Endotoxin Shock", Fed. Proc., 18:5, 1959.

21. Baetjer, A. "The Diffussion of Potassium From Resting Skeletal Muscles Following a Reduction in Blood Supply", Am. J. Physiol. 112:139, 1935.

22. Baez, S., et al. "Dibenzyline Protection Against Shock and Preservation of Hepatic Ferrition Systems", Am. J. Physiol., 192:175, 1958.

23. Baez, S., Zweifach, B.W. and Shorr, E. "Protective Action of Dibenamine Against the Fatal Outcome of Haemorrhagic and Traumatic Shock in Rats", Fed. Proc., 11:7, 1952.

24. Baratz, R.A. and Ingraham, R.C. "Capillary Permeability During Hemorrhagic Shock in the Rat", Proc. Soc. Exp. Biol. and Med., 89:642, 1955.

25. Bard, P. Medical Physiology, 10th Edition, St. Louis: C.V. Mosby, 1956.

26. Barker, S.B. and Summerson, N.H. "Tthe Colorimetric Determination of Lactic Acid in Biological Materials", J. Biol. Chem., 138:535, 1941.

27. Bayliss, W.M. and Starling, E.H. "The Movements and Innervation of the Small Intestine", J. Physiol., 24:99, 1899.

28. Beatty, C.H. "The Ability of Liver to Change Blood Glucose and Lactate Concentration Following Severe Hemorrhage", Am. J. Physiol., 144:233, 1945.

29. Beck, L.V. and Reddick, T.F. "Chlorpromazine Counteraction of Trauma Induced Death", Proc. Soc. Exp. Biol. and Med., 92:851, 1956.

30. Beck, L.V. and Alexander, W.R. "Protection Afforded Mice Against Torniquet Trauma Induced Mortality by Ganglion Blocking Drug Chlorisondamine Dimethochloride", Proc. Soc. Exp. Biol. and Med., 101:786, 1959.

31. Bell, J. Discourse on the Nature and Cure of Wounds, 3rd Edition, James Clarke Cowgate, Edinburgh, 1812.

32. Bernard, C. Lecons sur le Diabete et la Glycogenese Animal , Paris: Bailliere, 1877.

33. Billroth, T. Historical Studies on the Nature and Treatment of Gunshot Wounds from the Fifteenth Century to the Present Time, Berlin: Universitats-Klinikum, 1859.

34. Blalock, A. and Bradburn, H.B. "Distribution of Blood in Shock and after Histamine", Arch. Surg., 20:26, 1930.

35. Blalock, A. "Pathological Changes in Shock", Arch. Surg., 29:837, 1934.

36. Blalock, A. and Levy, S.E. "The Effect of Hemorrhage, Intestinal Trauma and Histamine on the Position of the Blood Stream," Am. Journ. of Physiol., 118:734, 1937.

37. Blalock, A. "Experimental Shock: The Cause of Low Blood Pressure Produced by Muscle Injury", Arch. Surg., 20:959, 1930.

38. Blattberg, B., Maldonade, C. and Levy, M. "Intestinal Perfusion in Hemorrhagic Shock", Circultion Res., 8:920, 1960.

39. Bloor, B.M. et al. A.M.A. Arch. Surg., 1:55, 1955.

40. Boba, A. and Converse, J.G. "Ganglionic Blockage and Its Protective Action in Hemorrhage", Anesthesiology, 18:559, 1957.

41. Boyd, W. Textbook of General Pathology, 7th Edition, Lea and Febiger, Philadelphia, 1961.

42. Borden, C.W. and Hall, "Fatal Transfusion Reactions From Massive Bacterial Contamination of Blood", New Eng. J. Med., 245:760, 1951.

43. Bradle, J.A. and Johnson, J.A. "Blood Flows to Various Tissues in Endotoxin Shock", Surg. Forum, 9:34, 1958.

44. Braude, A.I., et al. "Studies with Radioactive Endotoxin. I. The Use of Ca^{51} to lable Endotoxin of Escherichia Coli," J. Clin. Invest., 34:830, 1955.

45. Braude, A.I., "Studies with Radioactive Endotoxin. II. Correlation of Physiologic Effects in the Distribution of Radioactivity in Rabbits Injected with Lethal Doses of E. Coli Endotoxin Labled with Radioactive Sodium Chromate", J. Clin. Invest., 34:858, 1955.

46. Braude, A.I., et al. "Overwhelming Bacteremic Shock Produced by Gram Negative Bacilli. Report of Four Cases with One Recovery", Michigan University Bulletin, 19:23, 1953.

47. Brunson, J.G., Eckman, P.L. and Campbell, J.B. "Increasing Prevalence of Unexplained Liver Necrosis", New Eng. Journ. Med., 257:52, 1957.

48. Brunschweigh, H. "Historical Studies on the Nature and Treatment of Gunshot Wounds from the 15th Century to the Present Time", Translated by C.P. Rhoads, New Haven, Conn., 1933.

49. Bunch, J.L. "On the Origin, the Course and Cell-Connections of the Viscero-motor Nerves of the Small Intestine", J. Physiol., 22:357, 1898.

50. Burdette, W.J. "Oxygen Consumption of Cardiac Muscle During Shock", Am. J. Physiol., 168:575, 1952.

51. Burdette, W.J. "Studies on the Metabolism of Cardiac Muscle from Animals in Shock", Yale J. Biol. Med., 23:411, 1950.

52. Bywaters, E.G.L. "Ischemic Muscle Necrosis: Crushing Injury, Traumatic Edema, Crush Syndrome, Traumatic Anuria, Compression Syndrome: Type of Injury Seen in Air Raid Casualties Following Burial Beneath Debris", J.A.M.A., 124:1103, 1944.

53. Bywaters, E.G.L. "Renal Lesions - Crush Injury", J.A.M.A., 124:1103, 1944.

54. Caliva, F.S., Napodano, R. and Zurek, R., et al. "The Effects on Myocardial Oxygen Availability of Hemorrhagic Hypotension and its Reversal by Various Agents, Including l-Norepinephrine", Am. Journ. Med. Sc., 238:308, 1959.

55. Cameron, R.G. "Hemorrhage and Shock", Florey, General Pathology, Philadelphia and London: W.B. Saunders Co., 1962.

56. Cana, F.S. et al. "The Effects on Myocardial Oxygen Availability of Hemorrhagic Hypotension and Its Reversal by Various Agents, Including l-Norepinephrine", Am. J. Med. Sc., 238:308, 1959.

57. Cannon, W.B. "Acidosis in Cases of Shock, Hemorrhage and Gas Infection", J.A.M.A., 70:531, 1918.

58. Cannon, W.B. "Acidosis in Shock", Great Brit. Med. Res. Committee No. 25, Special Report Series, 1919.

59. Cannon, W.T. and Rosenblueth, A. Automatic Neuroeffector Systems, New York: MacMillan, 1937.

60. Cannon, W.B. and Bayliss, W.M. Brit. Med. Res. Comm., Special Report Series No. 26, 1919.

61. Catchpole, B.N., Hackel, D.B. and Simeone, F.A. "Coronary and Peripheral Blood Flow in Experimental Hemorrhagic Hypotension Treated with l-Norepinephrine", Ann. Surg., 142:372, 1955.

62. Cerilli, G.J., Geever, E.F. and Gagnon, J. "The Effects of Suprarenal Aortic Occlusion and Hemorrhagic Hypotenstion on the Renal Function of Primates", Journ. Surg. Research, 2 (4):233, July, 1962.

63. Chambers, R.B. et al. "Peripheral Circulation During Torniquet Shock Syndrome in the Rat", Ann. Surgery, 120:791, 1944.

64. Chambers, R.B. and Zweifach, B.W. "Vasotropic Substances in Shock", Am. J. Physiol, 150:239, 1947.

65. Churchill-Davidson, H.C. et al. "The Effects of Adrenaline, Noradrenaline and Methedrine on Renal Circulation During Anaesthesia", Lancet, 2:803, 1951.

66. Close, A.S. et al. "Effect of Norepinephrine on Survival in Experimental Acute Hemorrhagic Hypotenstion", Surg. Forum, 8:22, 1958.

67. Close, S.A. et al. "The effects of Norepinephrine on Survival in Experimental Acute Hypotension", Surgical Forum, 8:22, 1957.

68. Clowes, G.H.A. Jr., Sagba, G.A. et al. "Effects of Acidosis on Cardiovascular Junction in Surgical Patients", Ann. Surgery, 154:524, 1961.

69. Code, C.F. and McIntire, F.E. "The Quantitative Determination of Histamine", In Methods of Biochemical Analysis, Vol. III. New York: Iterscience Publishers Inc., 1956, p. 49. (David Glock, Editor.)

70. Cone, T.E. Jr. et al. "Pheochromocytoma in Children", Pediatrics, 19:44, 1957.

71. Connolly, J.E. et al. "The Use of Intravenous Hydrocortisone in Hemorrhagic Shock", Surg. Forum, 9:17, 1958.

72. Corcoran, A.C. et al. "Crush Syndrome", Ann. Surg., 118:871, 1943.

73. Corcoran, A.C. and Page, I.H. "Effects of Hypotension Due to Hemorrhage and of Blood Transfusion on Renal Function in Dogs", J. Exp. Med., 78:205, 1943.

74. Corcoran, A.C. and Page, J.H. "Crush Syndrome; Post Traumatic Anuria: Observations on Genesis and Treatment", J.A.M.A., 134:436, 1947.

75. Corcoran, A.C. and Page, J.H. "Crush Syndrome", Arch. Surg., 51:93, 1945.

76. Corday, E. and Williams, J.H. "Effect of Shock and Vasopressor Drugs on the Regional Circulation of the Brain, Heart, Kidney and Liver", Am. Journ. Med., 29:228, 1960.

77. Corruthers, G.F. and Gowdey, C.W. "The Effect of Chlorpromazine Given with Reinfusion on the Mortality Rate from Standardized Hemorrhagic Shock in the Rat", Can. J. Bioch. and Physiol., 34:217, 1956.

78. Cowley, R.A. et al. "Hemorrhagic Shock in Dogs Treated with Extracorporeal Circulation. A Study of Survival Time and Blood Chemistry Levels", Surg. Forum, 11:110, 1960.

79. Cowley, R.A. et al. "Hemorrhagic Shock in Dogs Treated with D-Aldosterone. A Study of Survival Rate", Surg. Forum, 8:22, 1962.

80. Crandell, W.B. and Stueck, G.B. Jr. "Acid-base Balance in Surgical Patients", Ann. Surg., 149:342, 1959.

81. Crenshaw, C. et al. "Changes in Extracellular Fluid During Acute Hemorrhagic Shock in Man", Surg. Forum, 8:6, 1962.

82. Crowell, J.W. and Guyton, A.C. "Evidence Favoring a Cardiac Mechanism in Irreversible Hemorrhagic Shock", Am. Journ. Physiol., 201:893, 1961.

83. Crowell, J.W. and Guyton, A.C. "Further Evidence Favoring a Cardiac Mechanism in Irreversible Hemorrhagic Shock", Am. Journ. Phys., 203 (2):248, Aug., 1962.

84. Crowell, J.W. and Read, W.L. "In Vivo Coagulation - A Probable Cause of Irreversible Shock", Am. J. Physiol., 183:565, 1955.

85. Crowell, J.W. and Read, W.L. "Prevention of Irreversible Shock by Heparin", Fed. Proc. 14:33, 1955.

86. Crowell, J.W. "The Influence of Shock on the Clotting Mechanism. Conference on Recent Progress and Present Problems in the Field of Shock", Walter Read Army Institute of Research, Washington, D.C., 1960.

87. Craxatto, R., et al. "The Effects of Different Types of Shock on the Enzymic Activity of Plasma", Bol. Soc. Biol. Santiago, 8:110, 1951.

88. Cull, T.E. et al. "Arterial Inflow Into the Mesenteric and Hepatic Vascular Circuits During Hemorrhagic Shock", Am. J. Physiol., 185:365, 1956.

89. Dale, H.H. "Croonian Lectures on Some Chemical Factors in Control of Circulation", Lancet, 1:1179, 1929.

90. Darrow, D.C. and Engel, F.L. "Liver Water and Electrolytes in Hemorrhagic Shock", Am. J. Physiol., 145:32, 1945.

91. Davenport, H.W. The A.B.C. of Acid-Base Chemistry, Chicago, Illinois: University of Chicago Press, 1961.

92. Davis, H.A. "Shock and Allied Forms of Failure of the Circulation", New York: Gruna and Stratton, 1949.

93. Davis, H.A. "Pathology of Shock", Arch. Surg., 42:939, 1941.

94. Deal, C.P. Jr. and Green, H.D. "Comparison of Changes in Mesenteric Resistance Following Splanchnic Nerve Stimulation with Responses to Epinephrine and Norepinephrine", Circulation Res., 4:38: 1956.

95. Derby, T.D. et al. "Effects of Metabolic Acidosis on Ventricular Isometric Systolic Tension and the Response to Epinephrine and Levarterenol," Circulation Res. 8:1242, 1960.

96. Dittmer, D.S. "Blood and Other Body Fluids," Biological Handbooks, Fed. Am. Soc. Exp. Biol., 1961.

97. Donahue, J.K. and Parkins, W.M. "Pathology of Shock", Proc. Soc. Exp. Biol. and Med., 32:1249, 1935.

98. Drucker, W.R. et al. "Metabolic Aspects of Hemorrhagic Shock", Surg. Forum, 9:49, 1958.

99. Duff, G.L. and Murray, E.G.D. "Bilateral Cortical Necrosis of the Kidneys", Am. J. M. Sc., 201:428, 1941.

100. Dunphy, J.E. et al. "Pathology of Shock", Surg. Gynec. and Obst., 72:823, 1941.

101. Ebert, R.V. et al. "The Mechanisms of Shock in Peritonitis", Surgery, 25:339, 1949.

102. Ebert, R.V. and Astead, E. "Circulatory Failure in Acute Infection", J. Clin. Invest., 20:671, 1955.

103. Ebert, R.V. and Stead, E.A. Jr. and Gibson, J.G. "Response of Normal Subjects to Acute Blood Loss with Special Reference to Mechanism of Restoration of Blood Volume", Arch. Int. Med. 68:578, 1941.

104. Ebert, R.V. et al " A study of Hypotension (Shock) Produced by Meningococcus Toxin", Circulation Res., 3:378, 1955.

105. Eckenhoff, J.W. et al. "The Coronary Circulation in the Dog", Am. J. Physiol., 131:43, 1940.

106. Edwards, W.S. et al. "Studies on Myocardial Metabolism. III. Coronary Blood Flow, Myocardial Oxygen Consumption and Carbohydrate Metabolism in Experimental Hemorrhagic Shock", Journ. Clin. Invest., 33:1646, 1954.

107. Ehrilich, E.W. et al. "Effect on the Coagulation Mechanism of Graded Hypovolemia Due to Hemorrhage in Dogs", Surg. Forum, 8:24, 1963.

108. Elliott, H.B. "The Effect of Intravenous Sodium Dehydrocholate on the Mortality Rate Following Hemorrhagic Shock", Surgery, 29:829, 1951.

109. Emerson, C.P. Jr. and Ebert, R.V. "A Study of Shock in Battle Casualties", Ann. Surg., 122;745, 1945.

110. Ende, N. "Infarction of the Bowel in Cardiac Failure", New Eng. J. Med., 259:879, 1958.

111. Engle, F.L. and Engel, M.G. "Mechanism of Adrenal Cortex Stimulation", Am. J. Physiol., 147:165, 1946.

112. Engle, E.L. "The Significance of the Metabolic Changes During Shock", Amm. N. York Academy Sc., 55:381, 1952.

113. Engle, E.L. "Metabolic Aspects of Hemorrhage and Traumatic Shock", Tran. of the 2nd Conference on Shock and Circulatory Homeostasis, Josiah Macy Jr. Foundation, 1852.

114. Engel, E.L. et al. "Biochemical Studies on Shock: I. The Metabolism of Amono Acids and Carbohydrate During Hemorrhagic Shock in the Rat," J. Exp. Med., 397:410, 1943.

115. Erlanger, J. et al. "Studies in Secondary Traumatic Shock", Am. J. Physiol., 49:90, 1919.

116. Essex, H.E. and Thomas, W.D. "Response of Hepatic Venous Circulation to Certain Substances Given Intravenously," Proc. Staff Meeting Mayo Clinic, 25:34, 1950.

117. Farber, S.J. et al. "Shock Produced by Obstruction of Venous Return to the Heart in the Dog", Am. J. Physiol., 176:325, 1954.

118. Favorite, G.O. and Morgan, H.R. "Effects Produced by Intra-Venous Injections in Man of Toxic Antigenic Material Derived from Eberthella Typhosa, Clinical Hematological, Chemical and Serological Studies", J. Clin. Invest., 21:599, 1942.

119. Field, L.W. and Laverty, R. "Nervous and Humoral Responses to Acute Blood Loss in the Rat", J. Physiol., (London), 143: 213, 1958.

120. Fine, J. et al. "Specific Role of the Liver in Hemorrhagic Shock: Report of Progress to Date", Ann. Surg., 126:1002, 1952.

121. Fine, J., Rutenberg, S. and Schweinburg, F.B. "The Role of the Reticulo-Endothelial System in Haemorrhagic Shock", Journ. Exp. Med., 110:547, 1959.

122. Fine, J. "The Bacterial Factor in Traumatic Shock", Springfield, Ill.: Thomas, 1954.

123. Fine, J. et al. "Bacterial Factor in Traumatic Shock", New Eng. J. Med., 260:214, 1959.

124. Fine, J. "Comparison of Various Forms of Experimental Shock", Shock, Pathogenesis and Therapy, An International Symposium, 1962. (Ciba)

125. Fine, J. and Seligman, A.M. "On the Specific Role of the Liver in Hemorrhagic Shock", Ann. Surg., 126:1002, 1947.

126. Fine, J. et al. "D.C.A. in Hemorrhagic Shock", Surgery, 12:1, 1942.

127. Fine, J. "Host Resistance to Bacterial Infection in Traumatic Shock", Brit. J. Anaesth., 30:485, 1958.

128. Fine, J. et al. "In: The Biochemical Response to Injury", Edited by H. B. Stoner and C. J. Threlfall. Oxford: Blackwell, 1960.

129. Fine, J. et al. "The Bacterial Factor in Traumatic Shock", New Eng. J. Med., 260:214, 1959.

130. Fine, J. et al. "The Bacterial Factor in Traumatic Shock", Am. New York Academy Sc., 55:429, 1952.

131. Fine, J. Shock and Circulatory Homeostasis, New York: Macy, 1955.

132. Fine, J. "Relation of Bacteria to Failure of Blood Volume Therapy in Traumatic Shock", New Eng. J. Med., 250L889, 1954.

133. Fine, J. "Recent Progress and Present Problems in the Field of Shock", Fed. Proc., 20 (9):75, 1961.

134. Fischer, H. "Shock", In Volkmanns Klin Vort, No. 10 (Chir. No. 5), Leipzig: Von Breitkipf und Hartel, 1870.

135. Fishman, W. H. and LeVeen, H. H. "A Method of Partitioning Liver Proteins and Its Application to the Study of the Effects of Acute Hemorrhage in the Dog", Am. Surg., 127.

136. Franco-Bowler, S. et al. "Induction of Acute Gastric Lesions by Histamine Liberators in Rats", Journ. of Allergy, 30:1, 1959.

137. Frank, H. A. et al. "Traumatic Shock: Course of Hemorrhagic Shock in Dogs Treated by Peritoneal Irrigation or by Artificial Kidney". Am. Journ. Physiology, 168:140, 1952.

138. Frank, H. A. et al. "The Prevention of Irreversibility in Hemorrhagic Shock by Viviperfusion of the Liver", J. Clin. Invest., 25:22, 1946.

139. Frank, E.D. et al. "Effect of Antibiotics on Hemodynamics of Hypovolemic Septic Shock", Am. J. Physiol., 182:166, 1955.

140. Frank, H.A., Jacob, S. et al. "Effects of A.C.T.H. and Cortisone in Experimental Hemorrhagic Shock", Amer. Journ. Physiol., 180:282, 1955.

141. Frank, H.A., Seligman et al. "Traumatic Shock XIII. The Prevention of Irreversibility in Hemorrhagic Shock by Vivi-perfusion of the Liver", J. Clin. Invest., 25:22, 1946.

142. Franklin, K.J. "Aspects of the Circulation's Economy", Brit. Med. J., 1:1410, 1951.

143. Freedberg, A.S. et al. "The Cardiovascular Dynamics in Shock Due to Infection", J. Clin. Invest., 23:930, 1944.

144. Freeman, N.E. "Decrease in Blood Volume After Prolonged Hyperactivity of the Sympathetic Nervous System", Am. Journ. Physiol., 103:185, 1933.

145. Freeman, N.E. et al. "The Effect of Total Sympathectomy on the Occurrence of Shock from Hemorrhage", Journ. Clin. Invest., 17:359, 1938.

146. Friedberg, C.K. and Horn, H. "Acute Myocardial Infarction not Due to Coronary Artery Occlusion", J.A.M.A., 112:1675, 1939.

147. Frieden, J. et al. "Decreased Resistance to Hemorrhage in Neurophysectomized Dogs", Circulation Res., 2:214, 1954.

148. Fritz, I. and Levine, R. "Action of Adrenal Cortical Steroids and Nor-epinephrine on Vascular Responses of Stress in Adrenalectomized Rats," Am. J. Physiol., 165:456, 1951

149. Fuhrman, F.A. "Electrolytes and Glycogen in Injured Tissues", In: The Biochemical Response to Injury, Edited by H.B. Stoner and C.J. Threlfall. Springfield: Thomas, 1960.

150. Gans, H. and Drivit, W. "Effect of Endotoxin Shock on the Clotting Mechanism of Dogs", Ann. Surg., 152:69, 1960.

151. Gassel, H. S. et al. "Blood Volume Changes in Shock", Am. J. Physiol., 50:31, 1919.

152. Gelin, L. E. "Hematorheological Disturbances in Surgery", Address, Acta Chir. Scand., 1961.

153. Gelin, L. E. "Studies in Anemia of Surgery", Acta Chir. Scand., Suppl., 210, 1956.

154. Gelin, L. E. and Shoemaker, W. C. "Hepatic Blood Flow and Microcirculation Alterations Induced by Dextrans of High and Low Viscosity", Surgery, 49:713, 1961.

155. Giannelli, S. Jr. et al. "Use of Vasopressor Agents in Hemorrhagic Shock - Effect on Posthemorrhagic Hemodilation", Ann. Surg., 156(1):41, 1962.

156. Gibson, J. G. and Dopp, I. "Studies in the Physiology of Artificial Fever. I. Changes in the Blood Volume and Water Balance", J. Clin. Invest., 17:219, 1938.

157. Gilbert, R. P., Hinshaw, L. et al. "Effects of Histamine, Five Hydroxytryptamine and Epinephrine on Pulmonary Hemodynamics with Particular Reference to Arterial and Venous Segment Resistances", Am. Journ. Physiol., 194:165, 1958.

158. Gilbert, R. P. "Mechanisms of the Hemodynamic Effects of Endotoxin", Physiological Reviews", 40:245, 1960.

159. Gilbert, R. P. et al. "Hemodynamics of Shock Due to Infection", Stanford Med. Bull., 13:239, 1955.

160. Goodwin, L. G. and Richards, W. H. G. "Pharmacologically Active Peptides in the Blood and Urine of Animals Infected with Babesia Rodhaini and Other Pathogenic Organisms", Brit. J. Pharmacol., 15:152, 1960.

161. Gourzis, J.T., Hollenberg, M.W. and Nickerson, M. "Involvement of Adrenergic Factors in the Effects of Bacterial Endotoxin", Journ. Exp. Med., 114:595, 1961.

162. Grable, E., Israel, J., Williams, J. and Fine, J. "Blood Volume in Experimental Endotoxin and Hemorrhagic Shock", Ann. Surg., 157;561, 1963.

163. Grayson, J. and Swan, H.J.C. "Action of Adrenalin, Noradrenalin and Dihydroergocomine on the Colonic Circulation", Lancet, 1:488, 1950.

164. Green, H.D. et al. "Quantitation of Vasomotor Activity", Proc. Soc. Exp. Biol. and Med., 53:228, 1943.

165. Greever, C.J. and Watts, D.T. "Epinephrine Levels in the Peripheral Blood During Irreversible Hemorrhagic Shock in Dogs," Circulation Res., 7:192, 1959.

166. Griffin, J.C. Jr., et al. "The Effect of Norepinephrine (Levophed) on Survival in Standard Olegemic Shock", Surg. Forum, 9:4, 1958.

167. Griffith, F.A. and Pierce, R.G. "The Outflow of Blood from the Liver as Affected by Variations in the Condition of the Portal Vein and Hepatic Artery", Am. J. Physiol., 35:87, 1914.

168. Guyton, A.C. Textbook of Medical Physiology, Philadelphia and London: W.B. Saunders Co., 1962.

169. Guyton, A.C. Dynamics of the Heart in Shock, Fed. Proc., 9:51, 1961.

170. Guyton, A.C. and Harris, J.W. "Pressoreceptor-Automatic Oscillation: A Probable Cause of Vasomotor Waves", Am. J. Physiol., 35:87, 1914.

171. Hackel, D.B. "Effects of l-Norepinephrine on Cardiac Metabolism of Dogs in Hemorrhagic Shock", Proc. Soc. Exp. Biol. and Med., 105;780, 1960.

172. Hackel, D.B. and Goodale, W.T. "Effects of Hemorrhagic Shock on the Heart and Circulation in Intact Dogs", Circulation, 11:628, 1955.

173. Haggard, H. "Devils, Drugs and Doctors", Cardinal Edition, 1953.

174. Hakstian, R.W., Hampson, L.G. and Gurd, F.N. "Pharmacological Agents in Experimental Hemorrhagic Shock", A.M.A. Arch. Surg., 83:335, 1961.

175. Hall, K.D., and Resser, F.H. Jr. "Serum Potassium Levels in Hyperventilated Dogs", Proc. Soc. Exp. Biol. and Med., Vol. 3 (2):251, 1965.

176. Hall, W.H. and Gold, D. "Shock Associated with Bacteremia: Reviews of 35 Cases", Arch. Int. Med., 96:403, 1955.

177. Hamilton, A.S. and Collins, D.A. "The Homeostatic Role of a Renal Humoral Mechanism in Hemorrhage and Shock", Am. J. Physiol., 136:275, 1942.

178. Hamilton, A.S. and Collins, D.A. "Renin-Angiotonin System in Shock", Am.J. Med. Sc., 202:914, 1941.

179. Hamrick, L. and Myers, J. "Effect of Hemorrhage on Hepatic Blood Flow and Splanchnic Oxygen Consumption of the Dog", Circ. Res., 3:65, 1955.

180. Hardaway, Col. R.M. and McKay, D.G. "Intravascular Thrombi and the Intestinal Factor of Irreversible Shock", Ann. Surgery, 150:261, 1959.

181. Hardaway, Col. R.M. et al. "Vascular Spasm and Disseminated Intravascular Coagulation", Arch. Surg., 83:173, 1961.

182. Hardaway, Col. R.M. and Drake, Capt. D.C. "Prevention of Irreversible Hemorrhagic Shock", Ann. Surg., 157:39, 1963.

183. Hardaway, Col. R.M. et al. "Endotoxin Shock: A Manifestation of Intravascular Coagulation", Ann. Surg., 154:791, 1961.

184. Hardaway, Col. R.M. "Role of Intravascular Clotting in the Etiology of Shock", Ann. Surg., 155:325, 1962.

185. Hardaway, Col. R.M., Neimes, R.E. et al. "Role of the Canine Spleen in Irreversible Hemorrhagic Shock", Ann. Surg., 156: 503, 1962.

186. Hardaway, Col. R.M. and Weiss, F.H. "The Role of Intracapillary Clotting in the Etiology of Shock", A.M.A. Arch. Surg., 83:851, 1961.

187. Hardaway, Col. R.M., Watson, H.E. and Weiss, F.H. "Alterations in Blood Coagulation Mechanism After Intra-Aortic Injection of Thrombin", A.M.A. Arch. Surg., 81:985, 1960.

188. Hardaway, Col. R.M., Brune, W.H., Geever, E.F. et al. "Studies on the Role of Intravascular Coagulation in Irrersible Hemorrhagic Shock", Ann. Surg., 155:421, 1962.

189. Hardaway, Col. R.M. "Studies on pH Changes in Endotoxin and Hemorrhagic Shock", Journ. Surg. Res., 1:278, 1961.

190. Hardaway, Col. R.M. "Disseminated Intravascular Coagulation: A Cause of Shock", Ann. Surg., 149:462, 1959.

191. Hardaway, Col. R.M. "Effect of pH Control and Increased O_2 Delivery on the Course of Hemorrhagic Shock", Ann. Surg., 156:503, 1962.

192. Hardaway, Col. R.M. et al. "Prevention of Irreversible Hemorrhagic Shock with Fibrinolysin", Ann. Surg., 159:39, 1963.

193. Hardaway, Col. R.M. et al. "Role of Norepinephrine in Irreversible Hemorrhagic Shock", Ann. Surg., 156(1):57, 1962.

194. Hardaway, Col. R.M. et al. "Studies on the Relationship of Bacterial Toxins and Intravascular Coagulation of Pseudomembranous Enterocolitis", J. Surg. Research, 1:121, 1961.

195. Hardy, F.J. "The Mechanism of Histamine Edema", Fed. Proc., 18:62, 1959.

196. Harkins, H.M. "The Bleeding Volume in Severe Burns", Ann. Surg., 102:444, 1935.

197. Harkins, H.M. "Recent Advances in the Study and Management of Shock", Surgery, 9:231, 1941, 9:447, 1941, 9:607, 1941.

198. Hausner, E. et al. "Control of Coronary Blood Flow in the Heart-Lung Preparation", Am. J. Physiol., 131:43, 1940.

199. Hayes, M.A, "Shock and the Adrenocortex", Surgery, 35: 174, 1954.

200. Henly, W.S., Overton, R.C. et al. "The Effect of Hemorrhagic Shock on Intestinal Blood Flow," Surg. Forum, Clinical Congress of the American College of Surgeons, (Phila), 9:25, 1958.

201. Hershey, S.B., Guccione, II, and Zweifach, B.W. "Beneficial Action of Pretreatment with Chlorpromazine on Survival Following Graded Hemorrhage in the Rat", Surg. Gyn. and Obst., 101;431, 1955.

202. Hewson, W. The Works of William Hewson, F.R.S. London: G. Gulliver, Edition., Sydenham Soc., 1846.

203. Hinshaw, L.B. et al. "Role of Histamine in Endotoxin Shock", Proc. Soc. Exp. Biol. Med., 104:379, 1960.

204. Hinshaw, L.B. et al. "Mechanism of Histamine Release in Endotoxin Shock", Am. Journ. Physiol., 200:987, 1961.

205. Hinshaw, L.B., Bradley, G.M. "Effect of Endotoxin on Renal Function in the Dog", Am. Journ. Physiol; 196:1127, 1959.

206. Hinshaw, L.B. et al. "Effect of Endotoxin on Renal Function in the Dog", Am. Journ. Physiol., 191:230, 1957.

207. Hinshaw, L.B. "Effect of Endotoxin on Kidney Function and Renal Hemodynamics in the Dog", Am. Journ. Physiol., 201: 144, 1961.

208. Hinshaw, L.B. "Circulatory Responses to a CO_2 Buffer Following Lethal Injections of Endotoxin", Am. Journ. Physiol., 200(4):751, 1961.

209. Hinshaw, L.B. "Vascular Changes Associated with Development of Irreversible Endotoxin Shock", Am. Journ. of Physiol., 202(1):103, 1962.

210. Hinshaw, L.B. et al. "Changes in Total Peripheral Resistance in Endotoxin Shock", Proc.Soc. Exp. Biol., and Med., 108:24, Oct., 1961.

211. Hinshaw, L.B., Gilbert, R.P., Kuida, H. and Visscher, M.B. "Peripheral Resistance Changes and Blood Pooling After Endotoxin in Eviscerated Dogs", Am. Journ. Physiol., 195: 631, 1958.

212. Hinshaw, L.B., Jordan, M.M. and Vick, J.A. "Histamine Release and Endotoxin Shock in the Primate", J. Clin. Invest., 42:981, 1962.

213. Hinshaw, L.B., Gilbert, R.P., Kuida, H. and Visscher, M.B. "Role of Hepatosplanchnic Pooling Following Lethal Injection of Endotoxin in the Dog, Cat, Rabbit and Monkey", Fed. Proc., 17:71, 1958.

214. Hinshaw, L.B. and Bradley, G.M. "Alterations in Kidney Weight Produced by Escherichia Endotoxin", Am. Journ. Physiol., 189:329, 1957.

215. Howard, J.M. and De Bakey, M.E. "Treatment of Hemorrhagic Shock with Cortisone and Vitamin B_{12}", Surgery, 30:161, 1951.

216. Huidobro, F. and Braun-Mendez, E. "The Secretion of Renin by the Intact Kideny", Am. Journ. Physiol., 137:47, 1942.

217. Huidobro, F. and Braun-Mendez, E. "Renin-Antiotonin Mechanism after Hemorrhage", Am. Journ. Physiol., 137:47, 1942.

218. Hunter, J. A Treatise on the Blood, Inflammation and Gunshot Wounds. London: Borough and Sherwood, Neely and Jones, 1812.

219. Inglis, F. G. and Hampson, L. G. et al. "Effect of Chlorpromazine on Survival Time and Mesenteric Blood Flow in Experimental Shock", Ann. Surg., (Phila), 1949(1):43, Jan., 1959.

220. Izquieta, M. J. N. and Pasternack, B. "Electrocardiographic Changes in Hemorrhage and Ischemic Compression Shock", Proc. Soc. Exp. Biol. and Med., 61:407, 1946.

221. Jacob, S. et al. "Antiadrenergic and Antihistaminic Treatment in Hemorrhagic Shock in the Dog and the Rat", Am. J. Physiol., 186:79, 1956.

222. Jacob, S. et al. "Bacterial Action in Development of Irreversibility to Transfusion in Hemorrhagic Shock in the Dog". Am. Journ. Physiol., 179:523, 1954.

223. Johnson, P. C. and Selkurt, E. E. "Intestinal Weight Changes in Hemorrhagic Shock", Am. Journ. Physiol., 193:135, 1958.

224. Keith, N. M. Brit. Med. Res. Comm., Special Report Series, XXVII, 1919.

225. Keyl, A. C. and North, W. C. "Cardiac Glycosides in Traumatic Shock", J. Pharmacol. and Exp. Therapy, 119:229, 1957.

226. Keyl, A. C. and North, W. C. "Cardiac Glycosides in Tumbling Shock", Fed. Proc., 15:446, 1956.

227. Kinney, J. M. and Wells, R. E. "Problems of Ventilation after Injury and Shock", J. Trauma, 2(4):370, July, 1962.

228. Knapp, R. W. and Howard, J. M. "Studies on the Effect of Hydrocortisone on Irreversible Hemorrhagic Shock in the Dog", Surgery, 42:919, 1957.

229. Knisely, M. H., Eliot, T. S. and Bloch, E. H. "Sludged Blood in Traumatic Shock: I. Microscopic Observations of Precipitation and Agglutination of Blood Flowing Through Vessels in Crushed Tissues", A.M.A. Arch. Surg., 51:220, 1945.

230. Kolff, W. J. "Dialysis in Treatment of Uremia: Artificial Kidney and Peritoneal Lavage", Arch. Int. Med., 94:142, 1954.

231. Kolff, W. J. et al. "Results in Patients Treated with Coil Kidney (Disposable Dialyzing Unit)", J.A.M.A., 161:1433, 1956.

232. Kolff, W. J. "The Artificial Kidney - Past, Present, Future", Circulation, 15:285, 1957.

233. Kolff, W. J. and Leonards, J. R. "Reduction of Otherwise Intractable Edema by Dialysis or Filtration", Clev. Clin. Quart., 21:61, 1954.

234. Kohlsteadt, K. G. and Page, I.H. "Terminal Hemorrhagic Shock, Circulatory Dynamics, Recognition and Treatment", Surgery, 16:430, 1944.

235. Kuida, H., Hinshaw, L. B. et al. "Effect of Gram-Negative Endotoxin on Pulmonary Circulation", Am. Journ. Physiol., 192:335, 1958.

236. Kurland, G.S. and Freedberg, A.S. "Potentiating Effect of A.C.T.A. and Cortisone on Pressor Response to Intravenous Infusion of l-Norepinephrine", Proc. Soc. Exp. Biol. and Med., 78:28, 1951.

237. Landgren, S. and Neil, E. "Chemoreceptor Impulse Activity Following Hemorrhage", Acta. Physiol. Scand., 23:158, 1951.

238. Landgren, S. and Neil, E. "The Contribution of Carotid Chemoreceptor Mechanisms to the Rise of Blood Pressure Caused by Carotid Occlusion", Acta. Physiol. Scand., 23:152, 1951.

239. Langston, J. B. and Guyton, A.C. "Effect of Epinephrine on the Rate of Urine Formation", Am. Journ. Physiol., 192:131, 1958.

240. Lansing, A. M. and Stevenson, J.A.F. "Mechanism of Action of Norepinephrine in Hemorrhagic Shock", Am. Journ. Physiol., 193:289, 1958.

241. Lansing, A.M., Stevenson, J.A.F.and Gowdery, C.W. "The Effect of Noradrenaline on the Survival of Rats Subjected to Hemorrhagic Shock", Can. Journ. Biochem. and Physiol., 35:93, 1957.

242. Lansing, A.M. et al. "The Use of Vasopressor Agents in the Treatment of Shock", A Symposium on Shock, 2(4):386, 1962.

243. Lawson, H.D. et al. "The Renal Circulation in Shock", J. Clin. Invest., 23:381, 1944.

244. LeDran, H.F. "A Treatise or Reflections Drawn From Practice on Gunshot Wounds", (Translated) London: Clarke, 1743. (As cited by Scudder, J. Shock: Blood Studies as a Guide to Therapy, Philadelphia: J.B. Lippincott Co., 1940.)

245. LePage, G.A. "Biological Energy Transfortations During Shock as Shown by Tissue Analysis", Am. J. Physiol., 146:267, 1946.

246. Levenson, S.M. et al. "Nutritional and Metabolic Aspects of Shock", Fed. Proc., 20(3):99, 1961.

247. Levenson, S.M. and Watkin, D.M. "Protein Requirement in Injury and Certain Acute and Chronic Diseases", Fed. Proc., 18:1155, 1959.

248. Levine, R. et al. "Influence of Levarteronol on Portal Venous Flow in Acute Hemorrhage", Circulation Res., 6:587, 1958.

249. Levy, M.N. and Brins, S.H. "Influence of l-Norepinephrine Upon Cardiac Output in Anesthetized Dogs", Circulation Res., 5:85, 1957.

250. Levy, M.N. "Influence of Levarterenol on Portal Venous Flow in Acute Hemorrhage", Circulation Res., 6:587, 1958.

251. Lewis, F.J. et al. "Artificial Kidney: Clinical Uses", Lancet, 72:1, Jan., 1952.

252. Lewis, T. "Vasovagal Syncope and the Carotid Sinus Mechanism," Brit. Med. J., 1:873, 1932.

253. Lillehei, R.C. and MacLean, L.D. "The Intestinal Factor in Irreversible Endotoxin Shock," Ann. Surg., 148:513, 1958.

254. Lillehei, R.C. and MacLean, L.D. "Physiological Approach to Successful Treatment of Endotoxin Shock in the Experimental Aminal," A.M.A. Arch. Surg., 78:464, 1959.

255. Lillehei, R.C., Longerbeam, J.K. and Rosenberg,J.C. "The Nature of Irreversible Shock: Its Relationship to Intestinal Changes," Shock, Pathogenesis and Therapy, An International Symposium (Ciba), 1962.

256. Lillehei, R.C. "The Prevention of Irreversible Hemorrhagic Shock in Dogs by Controlled Cross Perfusion of the Superior Mesenteric Artery," Surg. Forum, 7:6, 1956.

257. Lillehei, R.C. "Prevention of Irreversible Hemorrhagic Shock in Normal and Eck Fistula Dogs by Controlled Cross Perfusion of the Superior Mesenteric Artery," Am. J. Physiol., 187:614, 1956.

258. Lillehei, R.C. "The Relationship of Increased Plasma Hemoglobin and the Appearance of an Abnormal Plasma Hemin and Pigment to the Development of Irreversible Hemorrhagic Shock in Dogs," Clinical Research, 6:131, 1958.

259. Lillehei, R.C. "The Intestinal Factor in Irreversible Hemorrhagic Shock," Surgery, 42:1043, 1957.

260. Livesay, W.R. et al. "The Cardiovascular and Renal Hemodynamic Effects of Aramine," Am. Heart J., 47:745, 1954.

261. Long, C.N.H. "Activation of Cortex," Fed. Proc., 6:461, 1947.

262. Longerbeam, K.L. "The Nature of Irreversible Shock, A Hemodynamic Study," Surg. Forum, 8:1, 1962.

263. Lotz, F., Beck, L. and Stevenson, J.A.F. "The Influence of Adrenergic Blocking Agents on Metabolic Events in Hemorrhagic Shock in the Dog," Can. J. Bioch., 33:741, 1946.

264. Lucke, B. "Lower Nephron Nephrosis (Renal Lesions of the Crush Syndrome of Burns, Transfusions and Other Conditions Affecting Lower Segment of the Nephron)," Mil. Surgeon, 99:371, 1946.

265. MacLean, L.D. and Weil, M.H. "Hypotension (Shock) in Dogs Produced by Escherichia Coli Endotoxin," Circulation Res., 4:546, 1956.

266. MacLean, L.D., Weil, M.H., Spink, W.W. and Visscher, M.B. "Canine Intestinal and Liver Weight Changes Induced by E. Coli Endotoxin," Proc. Soc. Exp. Biol. and Med., 92:602, 1956.

267. MacLean, L.D. "Bacteremic Shock: Pathogenesis and Treatment," Surg. Gynec. and Obst., 115:307, 1962.

268. Malcolm, J.D. "A Lecture on the Condition of the Blood Vessels During Shock," Lancet, 2:573, 1905.

269. Manery, J.F. and Solandt, D.Y. "Studies in Experimental Traumatic Shock With Particular Reference to Plasma Potassium Changes," Am. J. Physiol., 138:499, 1943.

270. Manger, W.M. et al. "Plasma Concentration of Epinephrine and Norepinephrine in Haemorrhagic and Anaphylactic Shock," Am. J. Physiol., 190:310, 1957.

271. Martineau, P.C. and Hartman, F.W. "Renal Lesions After Burns," J.A.M.A., 134:429, 1947.

272. Master, A.M. et al. "Sudden Profound Acrocyanosis as the Presenting Sign in Myocardial Infarction," J. Mt. Sinai, 4:21, 1937.

273. McKay, D.G. et al. "Alterations in Blood Coagulation Mechanism After Incompatible Blood Transfusion," Am. J. Surg., 89:583, 1955.

274. McKay, D.G. et al. "Pathologic Study of Intravascular Coagulation Following Incompatible Blood Transfusion in Dogs. II. Intraaortic Injection of Incompatible Blood," Am. J. Surg., 91:32, 1956.

275. McRay, J.M. Jr. et al. "The Role of the Small Intestine in Hemorrhagic Shock," Surg. Forum, 9:37, 1958.

276. McShan, W.H. et al. "Biological Energy Transformations During Shock as Shown By Blood Chemistries," Am. J. Physiol., 145:93, 1945.

277. Melcher, G.W. and Walcott, W.W. "Myocardial Changes Following Shock," Am. J. Physiol., 164:832, 1951.

278. Meneely, G.R. et al. "Ischemic and Anoxemic Damage to Myocardial Capillaries and Its Relation to Shock, Angina Pectoris and Myocardial Infarction," Fed. Proc., 5:226, 1946.

279. Miles, A.A. "Local and Systemic Factors in Shock," Fed. Proc., 20:141, 1961.

280. Milroy, T.W. "The Reaction Regulator Mechanism of the Blood Before and After Hemorrhage," J. Physiol., 51:259, 1917.

281. Montague, F.E. and Wilson, F.L. "Effect of Epinephrine and Shock on Sodium Para-Amino Hippurate Extraction by Rabbit Kidney," Am. J. Physiol., 159:581, 1949.

282. Moon, V.H. Shock: Its Dynamics, Occurrence and Management, Philadelphia; Lea and Febiger, 1942.

283. Moon, V.H. "Renal Disturbances in Shock," J.A.M.A., 134:425, 1947.

284. Moyer, J.H. et al. "Renal Hemodynamic Response to Vasopressor Agents in the Treatment of Shock," Circulation, 12:96, 1955.

285. Muelheims, G. et al. "Red Blood Cell Volume and Distribution After Bleed-out in the Rat as Determined by Cr^{51} Labelled Blood Cells," Am. J. Physiol., 196:173, 1959.

286. Nelson, R.M. and Seligson, D. "Studies on Blood Ammonia in Normal and Shock States," Surgery, 34:1, 1953.

287. Nickerson, M. ""Factors of Vasoconstriction and Vasodilation in Shock," Journ. Michigan Med. Soc., 54:45, 1955.

288. Nickerson, M. and Carter, S.A. "Protection Against Acute Trauma and Traumatic Shock by Vasodilators," Can. J. Biochem. and Physiol., 37:1161, 1959.

289. Nickerson, M. "Drug Therapy of Shock," Shock, Pathogenesis and Therapy, An International Symposium (Ciba). Edited by K.D. Bock Springer, Verlag, Berlin, 1962.

290. Nickerson, M. and Gourzis, J. "Blockade of Sympathetic Vasoconstriction in the Treatment of Shock," Journ. of Trauma, 2:399, 1962.

291. Noble, R.L. and Collip, J.B. "A.C.E. in Tumbling Shock," Quart. J. Exp. Physiol., 31:187, 1942.

292. North, W.C. and Wells, J.A. "Protective Effects of Certain Drugs Against Shock Induced by the Noble-Collip Drum," J. Pharmacol. and Exper. Therapy, 103:356, 1951.

293. Oliver, J. et al. "The Pathogenesis of Acute Renal Failure Associated With Traumatic and Toxic Injury, Renal Ischemia, Nephrotoxic Damage and the Ischemuric Episode," J. Clin. Invest., 30:1305, 1951.

294. Opdyke, D.F. and Foreman, R.C. "A Study of Coronary Flow Under Conditions of Hemorrhagic Hypotension and Shock," Am. J. Physiol., 148:726, 1947.

295. Osher, W.J. "Pressure-Flow Relationship of the Coronary System," Am. J. Physiol., 172:403, 1953.

296. Page, I.H. "Some Neuro Humoral and Endocrine Aspects of Shock," Fed. Proc., 20(9):75, 1961.

297. Page, I.H. and Olmsted, F. "The Influence of Respiratory Gas Mixtures on Arterial Pressure and Vascular Activity in 'Normal' and Hypertensive Dogs," Circulation, 3:801, 1951.

298. Pare, A. "Sympotomatology of Shock," Les Oeuvres d'Ambroise Pare, Vol. II, Paris: Dupuye, 1582.

299. Parsons, E. and Phemister, B.B. "Haemorrhage and 'Shock' in Traumatized Limbs; Experimental Study," Surg. Gynec. and Obst., 51:196, 1930.

300. Penner, A. and Bernheim, A.I. "Studies in the Pathogenesis of Experimental Dysentery Intoxication," J. Exp. Med., 76:271, 1942.

301. Penner, A. and Bernheim, A.I. "Acute Post Operative Enterocolitis," Arch. Path., 22:966, 1939.

302. Penner, A. and Bernheim, A.I. "Acute Post Operative Esophageal Gastric and Duodenal Ulceration," Arch. Path., 28:129, 1939.

303. Penner, A. and Bernheim, A.J. "Acute Ischemic Necrosis of the Kidney," Arch. Path., 30:465, 1940.

304. Penner, A. and Bernheim, A.J. "Experimental Production of Digestive Tract Ulcers," J. Exp. Med., 70:435, 1939.

305. Peters, J.P. and Van Slyke, D.D. Quantitative Clinical Chemistry: Interpretations, London: Billiere, Tindal and Cox, 1932.

306. Pickering, C.W. and Prinzmetal, M. "Effect of Renin on Urine Formation," J. Physiol., 98:314, 1940.

307. Phillips, R.A. et al. "Effects of Acute Hemorrhagic and Traumatic Shock on Renal Function of Dogs," Am. J. Physiol., 145:314, 1945.

308. Phemister, D.B. and Handy, J. "Vascular Properties of Traumatized and Clotted Bloods," J. Physiol., 64:155, 1927.

309. Powers, L.H. and Schloerb, P.R. "Intestinal Factor in Irreversible Hemorrhagic Shock," Surg. Forum, Clinical Congress of the American College of Sureions, (Phila) 9:40, 1958.

310. Prinzemetal, M. et al. "A Principle From the Liver Effective Against Shock Due to Burns," J. Clin. Invest., 23:795, 1944.

311. Rashking, W.J. et al. "Venous Return as Affected by Cardiac Output and Total Peripheral Resistance," Am. J. Physiol., 175:415, 1953.

312. Rau, G.C. "Hypertensinogen Content of Blood After Hemorrhage," Am. J. Physiol., 156:454, 1949.

313. Ravin, H.A. et al. "Host Resistance in Hemorrhagic Shock. XIV. Induction of the Schwartzman Reaction by Shock Plasma and Tissues," Proc. Soc. Exp. Biol. and Med., 97:436, 1958.

314. Read, R.C. et al. "Coronary Flow and Resistance in the Dog During Total Body Perfusion," Surg. Forum, 7:286, 1957.

315. Remington, J.W. et al. "Adrenal Steroids and Circulatory Failure," Endocrinology, 30:692, 1942.

316. Richards, E.W. "The Circulation in Traumatic Shock in Man," Harvey Lect., 39:217, 1943, 1944.

317. Root, W.J. et al. "Disturbances in the Chemistry and in Acid-Base Balance of the Blood of Dogs in Hemorrhagic and Traumatic Shock," Am. J. Physiol., 149:52, 1947.

318. Ross, C.A. "Cardiovascular Response of Unanesthetized Rats During Traumatic and Endotoxin Shock," Proc. Soc. Exp. Biol. and Med., 96:582, 1957.

319. Russell, J.A. et al. "The Role of the Peripheral Tissues in the Metabolism of Protein and Carbohydrate During Hemorrhagic Shock in Rats," J. Exp. Med., 79:1, 1944.

320. Russell, J.A. and Long, C.N.H. "Amino Nitrogen in Liver and Muscle of Rats in Shock After Hemorrhage," Am. J. Physiol., 147:175, 1946.

321. Russell, M.N. et al. "Evaluation of Tris (Hydroxymethyl) Aminomethane (THAM) in Experimental Hemorrhagic Shock," Surgery, 54:86, 1963.

322. Saltz, N.J. "The Effect of Ganglionic Blockage on Survival After Tourniquet Shock," A.M.A. Arch. Surg., 81:618, 1960.

323. Sarnoff, S.J., Case, R.B. et al. "Insufficient Coronary Flow and Myocardial Failure as a Complicating Factor in Late Hemorrhagic Shock," Am. J. Physiol., 176:439, 1954.

324. Sarnoff, S.J. et al. "Myocardial Failure as a Complicating Factor in Late Hemorrhagic Shock," Am. J. Physiol., 167:439, 1954.

325. Sarpestein, L.A. et al. "Renin-Angiotonin Mechanism in Shock," Proc. Soc. Exp. Biol. and Med., 48:505, 1941.

326. Sarpestein, L.A. et al. "Renin-Angiotonin Mechanism in Shock," Proc. Soc. Exp. Biol. and Med., 50:320, 1942.

327. Sartorius, H. "Treatment Results and Indications of Hemodialysis," Muenchen Med. Wsehr, 102:839, 1960.

328. Sayers, G.M. et al. "The Cholesterol and Ascorbic Acid Content of the Adrenal, Liver, Brain and Plasma Following Hemorrhage," Endocrinology, 37:96, 1945.

329. Schayer, R.W. "Relationship of Induced Histidine Decarboxylase Activity and Histamine Synthesis to Shock From Stress and From Endotoxin," Am. J. Physiol., 198:1187, 1960.

330. Schayer, R.W. "Relationship of Stress-Induced Histidine Decarboxylase to Circulatory Homeostasis and Shock," Science, 131:226, 1960.

331. Schweinburg, R.B. et al. "Host Resistance in Hemorrhagic Shock: IX. Demonstration of Circulating Lethal Toxin in Hemorrhagic Shock," Proc. Soc. Exp. Biol. and Med., 95:646, 1957.

332. Schweinburg, F.B. et al. "Bacterial Factor in Experimental Hemorrhagic Shock. Evidence for Development of a Bacterial Factor Which Accounts for Irreversibility to Transfusion and for the Loss of the Normal Capacity to Destroy Bacteria," Am. J. Physiol., 179:532, 1954.

333. Seelig, M.G. and Lyon, E.P. "The Condition of the Peripheral Blood Vessels in Shock," Journ. Am. Med. Ass., 3:45, 1909.

334. Seligman, A.M. et al. "Chemical Alteration of Polysaccharide from Serratia Marcescens. I. Tumor-Necrotizing Polysaccharide Tagged With Radioactive Iodine," J. Nat. Cancer Inst., 9:13, 1948.

335. Seligman, A.M. et al. "Hemorrhagic Shock Treated by Viviperfusion of the Liver," J. Clin. Invest., 26:530, 1947.

336. Seligman, A.M. et al. "Traumatic Shock XV. Carbohydrate Metabolism in Hemorrhagic Shock in the Dog," J. Clin. Invest., 26:536, 1947.

337. Selkurt, E.E. "Intestinal Shock and the Protective Role of the Liver," Am. J. Physiol., 197:281, 1959.

338. Selkurt, E.E. and Brecher, G.A. "Splanchnic Hemodynamics and Oxygen Utilization During Hemorrhagic Shock in the Dog," Circulation Res., 4:693, 1956.

339. Selkurt, E.E. "Renal Blood Flow and Renal Clearance During Hemorrhagic Shock," Am. J. Physiol., 145:699, 1945.

340. Selkurt, E.E. "Renal Clearances and Blood Flow," Am. J. Physiol., 144:395, 1945.

341. Selkurt, E.E. "Renal Clearances and Blood Flow," Am. J. Physiol., 145:376, 1946.

342. Selye, H. and Dosne, C. "Corticosterone and A.C.E. in Shock," Lancet, 2:70, 1940.

343. Selye, H. "Alarm Reaction," J. Clin. Endocrinology, 6:117, 1946.

344. Seneviratne, R.D. "Endotoxin (Dysentery and Cholera)," Journ. Path. Bact., 60:609, 1948.

345. Sheehan, H.L. "Symmetrical Cortical Necrosis of the Kidneys," Brit. Med. Journ., 2:1327, 1950.

346. Sheehan, H.L. "The Pathology of Shock in Obstetrics," Trans. Int. Congress.Obst. and Gyn., 4:151, 1947.

347. Sherry, S. "Homeostatic Mechanisms and Proteolysis in Shock," Fed. Proc., 20:909, 1961.

348. Shipley, R.E. and Helmet, O.M. "Sustained Pressor-Principle of Kidney - References to Earlier Work," Am. J. Physiol., 153:341, 1948.

349. Shoemaker, W.C. et al. "Hepatic Blood Flow in Hemorrhagic Shock," Surg. Forum, 9:30, 1958.

350. Shoemaker, W.C. et al, "The Role of the Liver in Development of Hemorrhagic Shock," Surg. Gynec. and Obst., 112:327,1961.

351. Shoemaker, W.C. et al. "Hepatic Vascular Response to Epinephrine," Am. J. Physiol., 201;58, 1961.

352. Shoemaker, W.C. "Recent Additions to the Knowledge of the Cause and Management of Shock," S. Clin. North Am., 3:13, 1962.

353. Shorr, E. "Intermediary Metabolism and Biological Activities of Ferritin," Harvey Lect., 50:112, 1954-55.

354. Shorr, E. et al. "On Occurrence Sites and Modes of Origin and Destruction of Principles Affecting Compensatory Vascular Mechanisms in Experimental Shock," Science, 102:489, 1945.

355. Simeone, F.A. et al. "The Effect of l-Norepinephrine Upon the Myocardial Oxygen Tension and Survival Rate in Acute Hemorrhagic Hypotension," Surgery, 44:168, 1958.

356. Simeone, F.A. "Shock and Blood Pressure," Surg. Gynec. and Obst., 108:740, 1959.

357. Smith, L.L. and Moore, F.D. "Refractory Hypotension in Man - Is This Irreversible Shock?" N.E. Journ. Med., 267:15, 1962.

358. Spink, W. and Vick, J. "Supplementary Role of Hydralazine in Reversal of Endotoxin Shock With Metaraminol and Hydrocortisone," Proc. Soc. Exp. Biol. and Med., 106:280, 1961.

359. Spink, W. "Pathogenesis and Management of Shock Due to Infection," Arch. Int. Med., 106:433,1960.

360. Spink, W. "A Labile Factor in Experimental Endotoxin Shock: Cross Transfusion Studies in Dogs," Journ. Exp. Med.,

361. Stead, E.A. and Warren, J.W. "Effect of Injection of Histamine Into Brachial Artery on Permeability of Capillaries of Forearm and Hand," Journ. Clin. Invest., 23:279, 1944.

362. Stetson, C.A. "Mechanisms of Action of Bacterial Toxins and Certain Critical Tissue Factors in Shock," Fed. Proc., 20:206, 1961.

363. Stevens, A.R. et al. "Fatal Transfusion Reactions From Contamination of Stored Blood by Cold Growing Bacteria," Ann. Int. Med., 39:1228, 1953.

364. Swingle, W.W. et al. "DCA in Circulatory Failure," Am. J. Physiol., 132:249, 1941.

365. Swingle, W.W. et al. "Adrenal Steroids and Circulatory Failure," Am. J. Physiol., 136:567, 1942.

366. Tabor, H. et al. "Distribution of Administered Fluid in Mice Subjected to Tourniquet Shock," Am. J. Physiol., 167:517, 1951.

367. Tagnon, H.J. et al. "The Occurence of Fibrinolysis in Shock With Observations on the Prothrombin Time and the Plasma Fibrinogen During Hemorrhagic Shock," Am. J. Med. Sc., 211:88, 1946.

368. Thomas, L. "Role of Epinephrine in the Reactions Produced by the Endotoxin of Gram-Negative Bacteria," Journ. Exp. Med., 104:865, 1956.

369. Thomas, L. "Physiologic and Pathologic Alterations Produced by the Endotoxins of Gram-Negative Bacteria," A.M.A. Arch. Int. Med., 102:452, 1958.

370. Thomas, W.D. and Essex, H.E. "Observations on the Hepatic Venous Circulation With Special Reference to the Sphincteric Mechanisms," Am. J. Physiol., 158:303, 1949.

371. Tripp, E. and Ogden, E. "Renal Pressor Principle," Am. J. Physiol., 153:336, 1948.

372. Turpini, R. and Stefani, M. "The Nature and Mechanism of Hemostatic Breakdown in Course of Experimental Hemorrhagic Shock," J. Clin. Invest., 38:53, 1959.

373. Van Slyke, D.D. "Effect of Shock on the Kidney," Ann. Int. Med., 28:701, 1948.

374. Varley, H. and Heinemann, W. Practical Clinical Biochemistry, London: Medical Books, 1962.

375. Vassant, N.U., Weil, M.H. et al. "Hemodynamic Studies on Clinical Shock Associated With Infection," Am. J. Med., 34(4):461, 1963.

376. Vessell, E.S. et al. "Plasma Lactic Acid Dehyrogenase Activity in Experimental Hemorrhagic Shock," Proc. Soc. Exp. Biol. and Med., 101:644, 1959.

377. Vick, A.V. et al. "The Effect of Treatment of Endotoxin Shock on Renal Hemodynamics and Survival," Surgery, 54:78, 1963.

378. Vick, J.A. and Hinshaw, L.B. "Role of Intestine in Endotoxin Shock," Proc. Soc. Exp. Biol. and Med., 109:200, 1962.

379. Vick, J.A. and Hinshaw, L.B. "Adrenergic and Cholinergic-Like Effects of Endotoxin on the Cardiovascular System of the Dog," Physiologist, 3:170, 1960.

380. Walker, W.F. et al. "Adrenal Medullary Secretion in Hemorrhagic Shock," Am. J. Physiol., 197:773, 1959.

381. Walton, R.P. et al. "Sympathetic Influences During Hemorrhagic Hypotension," Am. J. Physiol., 197:223, 1959.

382. Warren, J.V. et al. "Effect of Venesection and Pooling of Blood in Extremities on Atrial Pressure and Cardiac Output in Normal Subjects With Observations on Acute Circulatory Collapse in Three Instances," J. Clin. Invest., 24:337, 1945.

383. Watts, D.T. "Arterial Blood Epinephrine Levels During Hemorrhagic Hypotension in Dogs," Am. J. Physiol., 184:271, 1956.

384. Weil, M.H. et al. "Influence of Acidosis on Effectiveness of Vasopressor Agents," Circulation, 16:949, 1957.

385. Weil, M.H., Hinshaw, L.B., Visscher, M.B., Spink, W.W. and MacLean, L.D. "Hemodynamic Effects of Vasopressor Agent (Metaraminol) on Hypotension in Dogs Produced by Endotoxin," Proc. Soc. Exp. Biol. and Med., 92:610, 1956.

386. Weil, M.H. et al. "Studies in the Circulatory Changes in the Dog Produced by Endotoxin from Gram-Negative Micro-organisms," J. Clin. Invest., 35:1191, 1956.

387. Weil, M.H. et al. "Studies on the Mechanism of Shock Produced by Gram-Negative Bacteria," Jr. Am. Physician, 69:131, 1961.

388. Weinstein, H. et al. "Vasopressin in Blood: Effect of Hemorrhage," Endocrinology, 66:712, 1960.

389. Wiggers, C.J. Physiology of Shock, New York: Commonwealth Fuhd, 1950.

390. Wiggers, C.J. "Myocardial Depression in Shock: A Survey of Cardiac Dynamic Studies," Am. Heart J., 33:633, 1947.

391. Wiggers, C.J. and Werle, J.M. "Cardiac and Peripheral Resistance Factors as Determinants of Circulatory Failure in Hemorrhagic Shock," Am. J. Physiol., 136:421, 1942.

392. Wiggers, C.J. "Hemorrhagic - Hypotension Shock in Locally Anesthetized Dogs," Am. J. Physiol., 143:126, 1945.

393. Wiggers, H.C., Ingraham, R.C. et al. "Vasoconstriction and the Development of Irreversible Hemorrhagic Shock," Am. Journ. Physiol., 153:511, 1948.

394. Wiggers, H.C. and Ingraham, R.C. "Value of Alkalinizing Agents in Hemorrhagic Shock," Am. J. Physiol., 146:431, 1946.

395. Wiggers, H.C. et al. "The Influence of Prolonged Vasoconstriction on the Transition From Impending to Irreversible Shock," Fed. Proc., 6:226, 1947.

396. Wilhelmi, A.E. et al. "Some Aspects of the Nitrogen Metabolism of Liver Tissue From Rats in Hemorrhagic Shock," Am. J. Physiol., 144:674, 1945.

397. Wilson, J.N. "The Management of Acute Circulatory Failure," Surg. Clin. of N. America, 43:469, 1963.

398. Winkler, A.W. et al. "Studies in Experimental Traumatic Shock," Am. J. Physiol., 124:478, 1938.

399. Winkler, A.W. et al. "Electrocardiographic Changes and Concentration of Potassium in Serum Following Intravenous Injection of Potassium Chloride," Am. J. Physiol., 124:478, 1938.

400. Wright, S. Applied Physiology, Revised by C.A Keele and E. Neil, London: Oxford University Press, 1961.

401. Zamecnik, P.C., Nathanson, I.T. et al. "Physiologic Action of Clostridium Welchii (Type A) Toxins in Dogs," J. Clin. Invest., 26:394, 1947.

402. Zanetti, M.E. "Significance of Elevated Portal Vein Pressure in Etiology of Hemorrhagic Shock," Am. J. Physiol., 171:538, 1952.

403. Zingg, W. et al. "Effect of Hydralazine on Survival of Dogs Subjected to Hemorrhagic Shock," Surg. Forum, 9:22, 1958.

404. Zweifach, B.W. "Transaction on the First Conference on Shock and Circulatory Homeostasis," New York: Josiah Macy Jr. Foundation, Edited by H.D. Green, 1952.

405. Zweifach, B.W., Nagler, A.L., and Thomas, L. "The Role of Epinephrine in the Reactions Produced by the Endotoxins of Gram-Negative Bacteria," Journ. Exp. Med., 104:881, 1956.

406. Zweifach, B.W. and Metz, D.B. "Regional Differences in Response of Terminal Vascular Bed to Vasoconstrictive Agents," Am. J. Physiol., 182:155, 1955.

407. Zweifach, B.W., Gordon, H.A. et al. "Indicating that Germ Free Animals (Rats) Do Develop Irreversible Hemorrhagic Shock," Journ. Exp. Med., 107:437, 1958.

408. Zweifach, B.W. and Chambers, R. "Cortical Extract and Capillary Engorgement," Anat. Rec., 84:461, 1942.

409. Zwemer, R. and Scudder, J. "Potassium Changes in Experimental Shock," Am. J. Physiol., 119:427, 1937.