# Shock – Pathophysiology and Treatment

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## Introduction

**Shock is a condition of severe hemodynamic and metabolic dysfunction, characterized by reduced tissue perfusion, impaired oxygen delivery, and inadequate cellular energy production.**

Many common disorders lead to shock, including those associated with severe heart failure, hypovolemia, peripheral vasoconstriction, thromboembolism, sepsis, hypoxia (caused by anemia, methemoglobinemia, carboxyhemoglobinemia), heat stress, severe hypoglycemia, and cyanide poisoning.

**Patient acute response to circulatory failure or shock fall into the following phases:**

1. **Activation of the autonomic nervous system** – sympathetic autonomic neural activity stimulation is immediate, and has the following effects:

   (a) Increased heart rate – beta-1 adrenergic receptor stimulation.

   (b) Increased myocardial contractility – beta-1 adrenergic receptor stimulation.

   (c) Increased cardiac output**.**

   (d) Increased peripheral vascular resistance – mediated by alpha-adrenergic arterial construction of skin, voluntary muscle, abdominal viscera, and kidneys.

   (e) Increase in alveolar ventilation – mediated by beta-2 adrenergic receptor stimulation.

   **These effects serve to maintain blood pressure, and increase heart, lung, and brain perfusion.**

2. **Release of epinephrine and norepinephrine from the adrenal glands** – further augments cardiorespiratory stimulation, and causes hyperglycemia, and elevation of plasma free fatty acids, which serve as an energy source during stress.

3. **Activation of the Renin-Angiotensin-Aldosterone System (RAAS)** – release of renin from the juxtoglomerular apparatus occurs in response to decrease pressure in the renal efferent arterioles, and adrenergic stimulation of the juxtoglomerular cells. Renin acts on a serum globulin called angiotensin, converting it to angiotensin I. Angiotensin I is in turn converted to angiotensin II by angiotensin converting enzyme (ACE) in the lungs. Angiotensin is a potent arteriolar constructor. Angiotensin also stimulates the release of aldosterone from the adrenal glands, which increases sodium and water reabsorption from the distal tubules in the kidneys, and also augments adrenaline secretion and stimulates ADH release.

4. **Release of Antidiuretic Hormone and Adrenocorticotrophic Hormone** – occurs in response to altered serum osmolality, baroreceptors stimulation and physiologic stress response mediated by the limbic system. Water retention and corticosteroid release follows.

5. **Tissue hypoxia** – occurs as a result of tissue vasoconstriction and reduced tissue perfusion, mediated by the neurohormonal responses mentioned above. Tissue hypoxia results in decreased ATP production, cell swelling, and the release of the metabolites of arachadonic acid, lysosomal enzymes, phospholipases and proteases, and oxygen free radicals. Complement and immune system activation may also occur in response to tissue invasion by bacteria or their toxins. These compounds produce a wide variety of effects, including significant pulmonary vasoconstriction, systemic vasodilatation, and increased capillary permeability. They are also associated with disruption of capillary endothelial integrity, platelet activation, and the development of disseminated intravascular coagulopathy.

6. **Cell and organ death** – occurs secondary to decreased tissue oxygen delivery, and tissue hypoxia. As shock progresses, marked decreases in systemic arterial blood pressure and cardiac output occur, forcing more tissues into anaerobic metabolism and lactic acid production. Microthrombi form in tissue vascular beds, slowing blood flow through tissues, leading to hyperviscosity of blood, hypercoagulation, and organ anoxia and death.

## Decompensation

The initial physiologic response to shock is that of compensatory increases in cardiorespiratory function in an attempt to maintain tissue perfusion and ventilation and oxygenation. As mentioned earlier, the end result is the uneven distribution of blood flow to microcirculatory bed. When there is disparity between the metabolic demands of tissue or illness that overwhelms the capacity of the circulatory system to meet these demands, decompensation occurs. Decompensation is more likely to occur in those patients where there is pre-existing cardiac, pulmonary or other organ impairments. Tissue oxygen debt resulting from reduced tissue perfusion is the primary underlying physiological mechanism that subsequently leads to organ failure and death.

**Arteriolar and venular constriction** in renal, mesenteric, and hepatic circulation causes ischaemic injury in these organs, cellular hypoxia, anaerobic metabolism, lactic acidosis, and release of cellular and bacterial mediators of inflammation. Sustained venuloconstriction, arteriolar dilation (caused by decreased pH, release of local vasodilator substances) increases capillary hydrostatic pressure, and contributes to regional extravasation of fluid into the interstitial space.

Continued activation of immunologic mechanisms, activation of arachadonic acid cascade and increased release of other mediators of shock, including histamines, kinins, bradykinin, serotonin, oxygen free radicals, and lysosomal enzymes, perpetuate maldistribution of blood flow away from central circulation, and contribute to loss of intravascular fluid volume, and tissue hypoxia and death.

Disruption to vascular wall integrity causes activation of clotting cascade, resulting in the deposition of fibrin thrombi throughout the vascular system, contributing to further ischaemia, hypoxia and acidosis. The coagulation activation eventually consumes clotting factors, resulting in systemic fibrinolysis and continued hemorrhage; symptoms of disseminated intravascular coagulopathy (DIC).

Following fluid therapy, patients with postoperative, post traumatic, and volume-depleted states, including dehydration, may remain hypovolemic, have increased interstitial water, decreased intracellular water, and increased total body water. This may or may not be manifested as peripheral or pulmonary edema.

## Clinical-Pathophysiological Correlations

**Symptoms of shock are indicative of decreases in tissue blood flow, exaggerated sympathetic autonomic responses, and the presence of circulating mediators of shock.**

**Symptoms of Patients with Circulatory Dysfunction**

- Tachycardia.
- Dry, clammy, pale, cold mucous membranes; mucous membranes may also be red and warm.
- Cyanosis due to low oxygen saturation, sluggish capillary blood flow.
- Slow capillary refill time due to vasoconstriction, and reduced blood volume.
- Initial euphoria mediated by increased sympathetic tone, followed by mental depression due to hypoxia and hypotension.
- Rapid pulses, becoming weak (decreased cardiac output).
- ECG changes include S-T segment slurring; ventricular premature depolarization's or ventricular tachycardia, especially following blunt chest trauma. Sinus tachycardia progressing to bradycardia is a poor prognostic sign.
- Reduced urine output, reduced urine sodium, acute renal failure.
- Depressed liver blood flow is characterized by centrilobular necrosis, with leakage of liver cytosol enzymes, and increasing blood clotting times.

## Goals of Fluid Therapy in Small Animal Medicine

**The primary goal of fluid therapy in illness is the delivery of oxygen to tissues**

The rationale for this goal is that oxygen delivery to tissues, and oxygen consumption are measurable parameters that determine whether a patient lives or dies. This has been proven in several multi-center randomized studies in human medicine. Time is the major factor that determines the outcome of intervention and therapy in patients with shock. When early, or primary events are ignored, temporal patterns are lost, and therapy is then directed to the consequences of, rather than the causes of, circulatory dysfunction.

In order to evaluate underlying circulatory mechanisms, it is necessary to describe the time course, or sequence of events that has occurred in a given patient, and to differential primary events from secondary or tertiary events.

Intravenous fluid therapy and circulatory support is aimed at achieving the following:

1. Immediate intravascular volume resuscitation
2. Immediate restoration of normal blood hemoglobin concentration
3. Immediate restoration of colloid oncotic pressure

4. Rehydration
5. Maintenance of fluid balance

Although cardiac and respiratory functions are directly measurable, tissue perfusion and oxygenation are not quantifiable. However, tissue perfusion and oxygenation are of greater consequence in terms of outcome. Inadequate tissue perfusion with either low of high blood flow, leads to tissue hypoxia, which, when extensive in degree or protracted time, produces organ dysfunction, multiple organ failure, and death. When the early manifestations of shock are alleviated by therapy that is insufficient to correct poor tissue oxygenation, the resultant oxygen debt may not be recognized until the appearance of organ failure, including ARDS, sepsis, acute cardiac failure, renal failure, hepatic failure, DIC or coma.

**Effective Use of Fluid and Transfusion Therapy**

Fluid therapy in small animal practice is usually directed at correcting a maldistribution of blood flow due to many conditions, including hypovolemia, dehydration, vascular space alterations, poor cardiac performance, and sepsis in order to optimize tissue oxygen delivery.

**Therapy of Shock**

Therapeutic objectives in the therapy of shock are outlined below, in order of temporal priority. At all times, the goals of fluid therapy are the achievement of supra-normal values of cardiac output, and oxygen delivery.

1. **Blood volume restoration.** Vigorous and rapid blood volume loading that does not produce pulmonary edema (pulmonary arterial pressures of greater than 20 mm Hg) is the first and most important therapy. It is easier to achieve the therapeutic goals with colloids than crystalloids, because colloids expand plasma volume without over-expansion of the interstitial water. In a study of human critical patients, only 20% of crystalloid remained in the intravascular space by the end of a 1-hour infusion, and 40 minutes later, almost all had gone into the interstitial space. In patients with peripheral edema, administration of colloids is preferred to increase colloid osmotic pressure. Diuretics may be used if volume expansion becomes a problem.

    - Isotonic crystalloids – 60-90 ml/kg/hr initially to achieve normalization of cardiac indices including heart rate, pulse pressure, mean arterial blood pressure, and urine output. Note that systolic and mean arterial pressures may be normal to high due to sympatho-adrenal mediated vasoconstriction.
    - Hypertonic saline in combination with dextran 70. Give 20%NaCl @ 1.5 ml/kg with dextran 70 @ 3 ml/kg intravenously over 5-15 minutes as a bolus. If using 7.5% NaCl administer at a rate of 4 ml/kg in combination with dextran 70 as above. Specific indications include patients with cranial trauma, chest trauma, and those patients with compromised pulmonary parenchyma due to existing pulmonary disease, pulmonary contusions, obstructive pulmonary disease, and poor cardiac function, i.e., patients at risk for developing pulmonary edema. Specific or relative contraindications for using colloids and hypertonic solutions include patients with clinical dehydration, or those with coagulopathies. Following initial volume resuscitation with hypertonic saline and colloids, patients should be provided with ad libitum access to free water, or should receive free water in their maintenance fluids.

- Hypertonic saline in combination with pentaspan is given as a bolus in a similar manner to hypertonic saline and dextran 70. Hypertonic saline is dosed at 4 ml/kg and pentaspan is dosed at 3-10 ml/kg.

2. **Maintenance of optimum hemoglobin concentration.** Packed red blood cells or whole blood is administered to maintain a hematocrit of approximately 27%. The rate of infusion should not exceed 20 ml/kg/hr unless patient. Blood products should not be administered concurrently with calcium-containing fluids as calcium may cause in-line clotting of the blood product.

3. **Maintenance of colloid oncotic pressure** may be achieved by using plasma products such as fresh frozen plasma, or by using synthetic colloids such as dextran 70 or pentaspan.

4. **Maintenance of cardiac output and tissue blood flow.** This is achieved through adequate intravascular volume resuscitation using crystalloids and colloids, and by the use of positive inotropic support. After the maximum effect of fluids has been obtained, administration of an inotropic agent such as dobutamine may be started. The starting dose is 2 μg/kg/min, and is titrated according to the patient status. Dobutamine produces marked increased in cardiac output and stroke volume, as well as decreases in systemic and pulmonary vascular resistances, and venous flow pressures. Hypotension can occur in patients that are inadequately volume resuscitated prior to commencement of therapy. Administration of vasopressor will produce greater increases in blood pressure than dobutamine, but do not improve tissue oxygen delivery to the same extent as dobutamine. For this reason, dobutamine is preferred over dopamine in the therapy of shock and circulatory dysfunction.

5. **Maintenance of pulmonary function and adequate gas exchange** involves the provision of oxygen supplementation by nasal catheter or oxygen-enriched air. Ensuring the patient has an optimal hemoglobin level is also critical in ensuring adequacy of gas exchange in the lungs. Mechanical ventilation is indicated in those patients where oxygen supplementation fails to increase $SpO_2$ above 80-85%.

6. **Maintenance of adequate mean arterial blood pressure.** Hypotension is defined as a mean arterial pressure below 70 mm Hg, and diastolic pressures less than 50 mm Hg. Alpha-adrenergic vasopressor intensify the uneven vasoconstriction produced by neural mechanisms. This uneven vasoconstriction raises blood pressure, but may further exacerbate the uneven microcirculatory flow present in patients with shock. The effect of dopamine and epinephrine, because they also have inotropic actions that improve cardiac performance, is a balance between favorable increase in blood, and unfavorable uneven maldistribution of blood flow. The smallest doses needed to maintain satisfactory blood pressure should be used, because no amount of vasopressor can make up for inadequate blood volume. Dopamine is used at a starting dose of 1-3 μg/kg/min.

7. **Maintenance of adequate urine volume** is achieved through management of hypovolemia and maldistribution of blood flow as outlined above. Oliguria or anuria are managed by the addition of furosemide at 2-4 mg/kg IV, mannitol at 0.5-1.0 gm/kg IV over 10 minutes, and dopamine at 1-3 μg/kg/min IV. The goal is urine output of 2-4 ml/kg/hr.

8. **Body temperature control** is achieved through normal tissue perfusion, and the provision of warm humidified air, and warming of intravenous fluids. The goal is a normal rectal temperature of 38.0-39.2°C.

9. **Manage disorders of cardiac rhythm** as they arise to ensure synergy of ventricular contraction.

10. **Manage sepsis** through ensuring adequate tissue perfusion and tissue oxygen delivery as outlined above. Selection of antibiotics should be based on culture and sensitivity from isolated organisms.

11. **Maintain normal blood glucose.**

**A note on Acid – Base Balance**

To correct an acid/base disturbance of metabolic origin such as occurs in shock states, we must effect a change on the serum bicarbonate concentration. This can be done by either the addition of bicarbonate to administered fluids, or by modifying chloride content of administered fluids, by changing to a fluid with less chloride in it, stimulating the kidney to retain more bicarbonate in order to make up the body 'quota' of anions to achieve electrolyte equilibrium. This may be done by changing from 0.9% NaCl to Hartman's solution, or by changing from Hartman's to 0.25%NaCl + 2.5% dextrose or PlasmaLyte – M. Induction of diuresis through fluid therapy, and/or the use of diuretics will increase renal excretion of chloride in preference to bicarbonate.

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