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period is significant, up to 200% in some individuals. These alterations are probably not related to the presence or dose of ketamine, because similar changes have been noted after medetomidine alone. They also occur when animals are still unconscious. These findings suggest that cardiovascular control mechanisms are different in these three species.

Thus, the use of medetomidine-ketamine and atipamezole provides a new, potent, and safe method for chemical immobilization and reversal in various nondomestic animals. In ruminants and camelids, this method provides an effective, non-narcotic alternative for chemical restraint and reversal. In carnivores and primates, the small doses of ketamine required make the immobilization smoother and more easily reversible.

Although reliable dose recommendations for medetomidine-ketamine combinations have been established for various mammalian species, more work is needed, especially in equids, and in the more excitable ruminant species, such as antelopes. I am not aware of any studies in pinnipeds, elephants, or giraffes. Results in avian species are promising but more accurate dosage rates must be established for different species. A few isolated trials in fish indicate that the effects of medetomidine, medetomidine-ketamine combinations, and atipamezole resemble those seen in mammals and birds. There are no reports on the use of medetomidine or atipamezole in reptiles.

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STRESS AND CAPTURE MYOPATHY IN ARTIODACTYLIDS

Terry R. Spraker

STRESS

Stress is a commonly used word that has different meanings to different people (e.g., wildlife biologist, zoo veterinarian, high-intensity food production manager [poultry producer], researcher, animal rights activist). Breazile[2] has suggested a definition: "stress is an internal (physiologic or psychogenic) or environmental stimulus that initiates an adaptive change or a stress response in an animal." Therefore, any stimulus that alters the homeostatic state of an animal, whether internal or external, is a stressor, and the numerous reactions of the body to combat this alteration comprise the stress response. However, Moberg[9] has stated that an acceptable definition is not so easy to formulate. Some reasons include the following: (1) there are no good biological tests to measure stress; (2) contrary to Selye's hypothesis of a nonspecific response to all stressors,[10] there appear to be various responses to different stressors; (3) with regard to biological responses to stress (behavioral, autonomic, and neuroendocrine), there is a marked degree of interanimal variability; and (4) there has been a failure to correlate measures of stress and meaningful changes in the well-being of animals.

Breazile[2] has defined three forms of stress—eustress, neutral stress, and distress. Eustress is a stimulus that is beneficial to the animal. Neutral stress evokes responses that do not affect the animal's well-being, comfort, or reproduction. Distress might be harmful to the animal, but can cause responses within the animal that interfere with its reproduction, comfort, or well-being. In some cases, prolonged eustress or neutral stress may lead to distress. Prolonged distress may result in various disorders in animals, such as alteration in behavior activity, cardiovascular problems, hypertension, decreased feed conversion, gastric and intestinal ulceration, reproductive failure, electrolyte imbalance, urticaria, and immunological deficiencies.[2,3]

Fear, anxiety, perception of danger, novel environments, and crowded conditions are important physiological stressors that cause distress. These are usually perceived through vision, hearing, olfaction, and touch or pressure to the skin. These stimuli are assembled primarily in the hypothalamus and then project into limbic and neocortical areas. The limbic region appears to be the most important area of the brain that is activated. Next, impulses stimulate the neuroendocrine or autonomic nervous system. Stimulating the neuroendocrine and autonomic nervous system has many consequences. These physiological mechanisms are normal responses for maintaining homeostasis, and are not harmful unless the stressor is prolonged.[9]

Many stressors result in changed behavior. With a mild stressor, the animal may respond by moving, running, or vocalizing. Usually, acute stress increases feeding and chronic stress decreases feeding. In rab-

bits, following capture and release, it has been found that the animal runs a short distance, stops, and begins to eat. This may be a mechanism in the overall scheme of prey-predator behavior. Obviously, this is a poor response for the prey, but helpful for the predator. This unusual behavior has also been observed in bighorn sheep. The limbic system is the primary area of the brain that controls feeding; it involves endogenous opioids, cholecystokinin, and dopamine as neuromodulators.[1]

A well-known effect of chronic stress on humans and animals is a decrease in reproduction, which includes decreases in libido, fertility, implantation of fertilized ovum, and development of fetus.[2,6] This is a well-recognized problem in zoos. Attempts to control chronic stress because of its effect on reproduction is a driving force to improve zoo exhibits.

A recognized response to a stressor involves activation of the limbic system, which stimulates the hypothalamus to secrete adrenocorticotrophic hormone (ACTH)-releasing factor and causes the pituitary to release ACTH, which results in an increase in the synthesis and release of cortisol. This mechanism produces many metabolic alterations, including modulation of the immune system, gluconeogenesis, and development of gastric ulcers. Hyperglycemia produced by glucocorticoids is primarily caused by hepatic gluconeogenesis, inhibition of cellular uptake of glucose, and increased lipid and protein catabolism. Sequelae of these metabolic alterations associated with chronic stress include delayed wound healing, muscle atrophy, and immune deficiencies.[2,3]

Glucocorticoids have long been known to reduce immunity, which causes an animal to be more susceptible to disease. Many mechanisms result in modulation of the immune system. Steroids are known to cause a neutrophilia, probably a result of the release of marginated neutrophils into the blood. Steroids cause lysis and margination of T cells, monocytes, and eosinophils and decrease the proliferation of lymphoid cells.[2,3]

Lipocortins are released by specific cells in response to steroids. Biological actions of lipocortins include limiting the activation of leukocytes through the depression of phospholipase A_2, which results in the decreased production of prostaglandins, thrombaxanes, and leukotrienes. The inhibition of prostaglandin synthesis is also linked with gastric and duodenal ulceration.[2,3]

Activation of the autonomic nervous system as a result of a stressor results in increased stimulation of the sympathetic arm, with a corresponding decrease of the parasympathetic arm. Cannon[4] first explored this response to an acute stress, and named it the "flight-or-fight response." It is mediated through activation of the sympathetic nervous system, which results in a stimulation of the adrenal medulla and the release of epinephrine, norepinephrine, and encephalins. The primary functions of the sympathetic nervous system are the production of a positive isotropic effect on the heart, vasoconstriction of vessels of the kidney, digestive system, connective tissues, and skin, and a corresponding vasodilation of vessels to the brain, skeletal muscle, heart, and lungs. Catecholamines are catabolic and cause lipolysis and gluconeogenesis. Epinephrine and norepinephrine also inhibit gastrointestinal motility and secretions.[2,3]

Endorphin is a 31-amino acid peptide that is released simultaneously with ACTH from the pituitary gland. Encephalins are synthesized by medullary cells of the adrenal gland and are released with epinephrine and norepinephrine. These peptides modulate T-cell–dependent immunoglobin production, lymphocyte proliferation, and natural killer cells, and provide a link between the brain and immune system. Infectious agents such as viral, bacterial, or fungal organisms can result in the release of β-endorphins, thus causing an infection-induced analgesia.[2,3] Endorphins may also reduce pain suffered by prey that has just been captured by a predator.

The stress response includes many other factors, such as the release of renin from the juxtaglomerular apparatus of the kidney, vasopressin synthesis and release by the paraventricular nucleus of the hypothalamus, vasoactive intestinal peptide release through the sympathetic stimulation of the intestine, and substance P release through the sympathetic stimulation of nerves ending in tissues. The stress response is extremely complex, and probably has numerous other functions. Breazile[2,3] and Moberg[8,9] have written excellent reviews of the physiology of stress.

CAPTURE MYOPATHY

Capture myopathy (CM) is a syndrome that occurs in wild (free-ranging and captive) mammals and birds. In nature, CM is probably an inherent mechanism that hastens the death of an animal following capture by a predator, thereby reducing pain in the prey and conserving energy for the predator—a mechanism which is, in a way, beneficial to both. This condition is occasionally observed in domestic animals and humans. CM has been recognized for the last 30 to 35 years. A spectrum of names such as muscular dystrophy, capture disease, degenerative polymyopathy, overstraining disease, white muscle disease, leg paralysis, muscle necrosis, idiopathic muscle necrosis, exertional rhabdomyolysis, stress myopathy, transit myopathy, diffuse muscular degeneration, and white muscle stress syndrome has been given to this syndrome, but the most commonly used is capture myopathy.[5] CM has been described in many wild ruminants and occasionally in primates, seals, horses, cattle, sheep, dogs, and birds. CM is similar to a condition in humans called march myoglobinuria or exertional rhabdomyolysis, which is an acute rhabdomyolysis in untrained athletes or military recruits following heavy exercise, especially at high temperature.

Four clinical syndromes have been observed in animals, capture shock, ataxic myoglobinuric, ruptured muscle, and delayed-peracute. The clinical

signs, gross and histological lesions, and suggested pathogenesis of these syndromes are discussed.

Clinical Signs

Capture Shock Syndrome

Capture shock may be observed in recently trapped animals, and also occurs during immobilization. Animals with this syndrome usually die within 1 to 6 hours postcapture. Clinical signs include depression, shallow, rapid breathing, tachycardia, elevated body temperature, weak thready pulse (hypotension), and death. These animals have elevated serum aspartate aminotransferase (AST), creatine phosphokinase (CPK), and lactate dehydrogenase (LDH) levels. The most common postmortem lesions include congestion and edema of the lungs and severe congestion of small intestine and liver. Occasionally, frank blood and blood-tinged contents are found within the small intestine. Histological studies confirm the gross observations. Small areas of necrosis are occasionally found in skeletal muscle and the brain, liver, heart, adrenal glands, lymph nodes, spleen, pancreas, and renal tubules. These lesions are most pronounced if the animal has been hyperthermic. Small thrombi may occasionally be found in the capillaries in various organs.

Ataxic Myoglobinuric Syndrome

The ataxic myoglobinuric syndrome probably occurs most commonly. It can be seen several hours to several days postcapture. Clinical signs include ataxia, torticollis and myoglobinuria, and vary from mild to severe. Serum enzyme (AST, CPK, and LDH) and blood urea nitrogen (BUN) levels are elevated. Animals showing mild signs usually survive, whereas those with moderate to severe signs usually die. At necropsy, there are renal and skeletal muscle lesions. The kidneys are swollen and dark. The urinary bladder is empty or contains a small amount of brownish urine. Multifocal pale, soft, dry areas, accentuated by small white foci in a linear pattern, are usually found within the cervical and lumbar muscles and in the flexors and extensors of the limbs (Figs. 36–4 and 36–5). The lesions are bilateral but not symmetrical, and are subtle in animals that die within 1 to 2 days postcapture but pronounced in animals that survive longer. Animals with prolonged survival may have minute ruptures within the necrotic muscles.

Figure 36–4. Necrosis in the rear limb muscles.

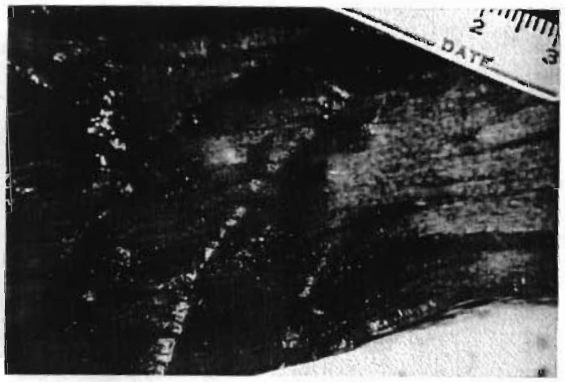

Figure 36–5. Necrotic fibers distributed throughout a muscle.

Histological lesions are primarily within the renal cortex and skeletal muscle. Renal lesions are characterized by dilatation of tubules, moderate to severe tubular necrosis, and protein (myoglobin) casts. Muscular lesions are characterized by acute rhabdomyolysis. Myocytes are markedly swollen, with loss of striations and fragmentation and cleavage of myofibrils. In many areas, sarcolemmal nuclei are pyknotic (Fig. 36–6). Sarcolemmal proliferation usually begins within 3 days postcapture.

Ruptured Muscle Syndrome

Animals with the ruptured muscle syndrome usually appear normal at capture but begin to manifest clinical signs 24 to 48 hours later. Commonly observed clinical signs include a marked drop in the hindquarters and hyperflexion of the hock. This is caused by unilateral or bilateral rupture of the gastrocnemius muscle. Serum enzyme levels (AST, CPK, and LDH) are extremely elevated. BUN levels are usually within normal limits or are only slightly elevated. Animals with this form of CM may survive for several weeks, but most die.

Gross lesions observed include massive subcutaneous hemorrhage of the rear limbs and multifocal, small to large, pale, soft lesions in forelimb, hindlimb, diaphragm, cervical, and lumbar muscles. Muscular lesions are similar to those described for the ataxic myoglobinuric phase, but are more severe and widespread. These lesions are bilateral but not symmetrical. Multiple, small to large ruptures may be found in necrotic muscles (Fig. 36–7). Commonly ruptured muscles include the gastrocnemius, subscapularis, middle and deep gluteal, semitendinosus, and semimembranosus muscles.

Histological lesions are predominantly located

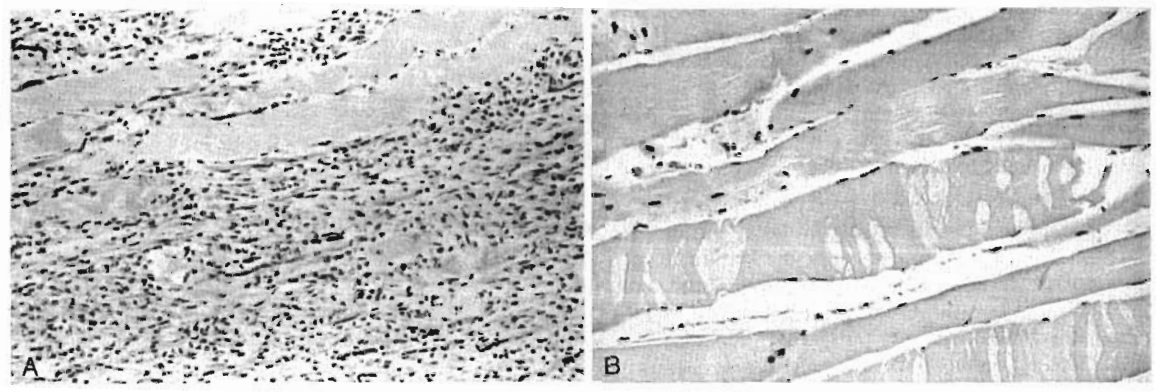

Figure 36–6. *A,* Loss of muscle striations and cleavage of myofibrils; *B,* pyknotic sarcolemmal nuclei (*A,* × 400; *B,* × 400).

within the skeletal muscles and are characterized by massive necrosis. Lesions are similar to those described for the ataxic myoglobinuric syndrome; however, with the latter, there are more sarcolemmal proliferation, fibrosis, and muscular regeneration. Histological lesions are similar to those described for selenium-vitamin E deficiency, except that there is less mineralization in CM.

Delayed-peracute Syndrome

The delayed-peracute syndrome is usually seen in animals that have been in captivity for at least 24 hours. These animals appear normal while undisturbed. If disturbed, captured, or suddenly stressed, they try to escape or run but stop abruptly, and stand or lie still for a few moments; their eyes begin to dilate, and they die within several minutes. This form of CM is rare. These animals die in ventricular fibrillation and have elevated AST, CPK, and LDH levels. Usually, there are no lesions or a few small pale foci within the skeletal muscle at necropsy. Histological lesions are characterized by a mild to moderate rhabdomyolysis throughout the skeletal muscle, especially in the hindlimbs.

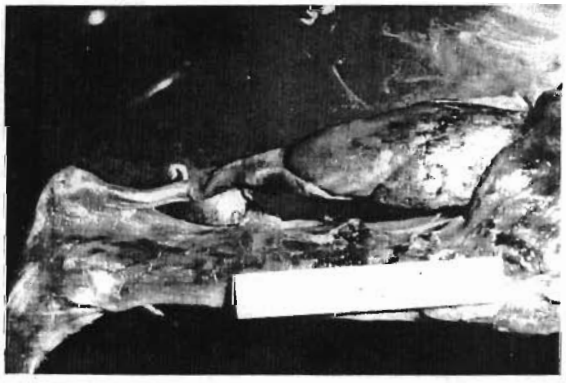

Figure 36–7. Necrosis and rupture of the gastrocnemius muscle.

Pathogenesis

The pathogenesis of CM is a dynamic and complex process involving at least three components: perception of fear, sympathetic nervous and adrenal systems, and muscular activity. The normal reactions of these components are discussed, followed by alterations in their biological functions.[7]

Normal Physiology

In the resting state, the sympathetic and parasympathetic nervous systems and adrenal medulla are continually active. This basal activity is called sympathetic-parasympathetic "tone," and allows for greater control of target organs. Sympathetic tone maintains constriction of most blood vessels to approximately half of their maximum diameter. By increasing sympathetic stimulation or adrenal medulla secretions, vessels can be constricted even more or, if activity is inhibited, vessels can be dilated. Exhaustion of sympathetic tone can lead to generalized vascular dilation, a drop in blood pressure, a decrease in blood flow to muscle, stagnation of blood flow in dilated capillaries, and generalized hypoxia, shock, and death. The adrenal medulla alone can maintain tone even when the sympathetic nervous system is eliminated, thus demonstrating the importance of the basal secretion of epinephrine and norepinephrine. In severe distress, the impact of adrenal exhaustion can result in severe hypotension, vascular collapse, and death.[7]

Danger, fear, or terror is acknowledged mainly through vision, olfaction, and auditory senses. These sensory stimuli enter the brain and are integrated by the hypothalamus, thalamus, and cerebral cortex. Activation of the hypothalamus alters activity of the autonomic nervous system, stimulating the sympathetic and inhibiting the parasympathetic nerves. Under certain circumstances, the sympathetic nervous system discharges almost as a complete unit. This activity is called mass discharge. It frequently occurs when the hypothalamus becomes activated by sudden fright, fear, or severe pain. This mass discharge is characterized by the following: (1) increase in arterial

pressure; (2) increased blood flow to active muscles concurrent with a decreased blood flow to organs that are not needed (e.g., kidney, digestive system, skin); (3) increased rate of cellular metabolism; (4) hyperglycemia; (5) increased glycogenolysis; (6) increased muscle strength; (7) increased mental activity; and (8) increased rate of blood coagulation. The summation of these events is called the sympathetic stress response or alarm reaction and enables an animal to perform more strenuous physical work or activity than otherwise possible.[7]

Another important function of the sympathetic nervous system is stimulation of the adrenal medulla. Preganglionic sympathetic nerve fibers pass from the intermediolateral neurons of the spinal cord to the adrenal medulla. Stimulation of these nerves results in a release of epinephrine and norepinephrine, which quickly diffuse into the blood. The adrenal medulla releases approximately 0.2 mg/kg/min of epinephrine and 0.05 mg/kg/min of norepinephrine in the resting state. When the adrenal gland is stimulated, approximately 80% is epinephrine and 20% is norepinephrine, but the relative proportions of these hormones change considerably under different physiological conditions. These hormones have similar effects on organs as those produced by direct sympathetic stimulation, except that biological effects last five to ten times longer. Norepinephrine is a generalized vasoconstrictor that results in an increase in peripheral resistance, thus causing an elevation in blood pressure. Norepinephrine also inhibits gastrointestinal motility and dilates the pupils of the eyes, but has little to no effect on heart. Epinephrine causes similar changes except it has a greater effect on the heart by increasing the rate and strength of contractions, but it causes only weak constriction of vessels within skeletal muscle. Because skeletal muscle vessels represent a major segment of vessels of the body, this difference is of special importance. Both hormones cause a decrease in renal blood flow, epinephrine by 40% and norepinephrine by 20%, thus predisposing to renal hypoxia.[7]

Catecholamines increase catabolism and thereby produce an increase in oxygen consumption, basal metabolic rate, heat production, and lactic acid formation. Epinephrine affects carbohydrate metabolism indirectly by stimulating the adenohypophysis to release ACTH through either a direct action on the pituitary or by activation of the hypothalamus. In either case, ACTH stimulates the adrenal cortex to secrete steroids, which promotes the synthesis of carbohydrates from proteins. Norepinephrine has little to no effect on carbohydrate metabolism. Epinephrine and glucocorticosteroids are important hormones that mobilize adipose tissue into free fatty acids, which represent easily available energy to cells. Glucocorticosteroids also induce an increase in the liver glycogen level, apparently by inhibiting the phosphorylation of glucose to glucose-6-phosphate; however, they have little effect on muscle glycogen. Researchers have demonstrated that corticoids reduce the animal's ability to resist infectious diseases (see earlier).[7]

Muscular activity is simultaneously activated in the fear response. Terror of pursuit and capture is perceived through the animal's senses and are integrated in the thalamus, resulting in activation of the motor cortex. Motor neurons of the spinal cord are then stimulated, causing the release of acetylcholine from neuromuscular junctions.

Skeletal muscle is composed of fibers ranging from 10 to 80 μ in diameter. Fibers in most muscles extend the entire length of the muscle and are innervated by one nerve ending, usually located near the middle of the fiber. Myocytes are composed of numerous myofibrils (actin and myosin filaments) suspended parallel to each other in sarcoplasm. Sarcoplasm contains potassium, magnesium, phosphate, enzymes, and numerous mitochondria. Contraction occurs when an action potential travels over the muscle fiber and causes the release of calcium into the sarcoplasm surrounding the myofibrils. Calcium is believed to uncover reactive sites or inhibit troponin-tropomyosin complexes in the actin filament, which results in a sliding over or ratcheting of the actin filament over the myosin filament. This process is the beginning of contraction but energy is needed in order for contraction to continue.[7]

The basic energy source for muscle contraction is adenosine triphosphate (ATP). The maximum amount of stored ATP in the muscle of a well-trained athlete only lasts 5 to 6 seconds, so ATP has to be continuously supplied to muscles. Three energy sources are active in muscle cells during activity: (1) phosphagen; (2) aerobic glycolysis; and (3) glycogen-lactic acid system. The phosphagen energy system is composed of phosphocreatine, which has a high-energy phosphate bond that can degrade and release enough energy to convert one ADP (adenosine diphosphate) to one ATP. This reaction may occur within a fraction of a second, so this energy is instantaneously available for use, as with stored ATP. With phosphocreatine and stored ATP, muscles can only contract maximally for 10 to 15 seconds. This system is used first, primarily for short bursts of muscle exertion.[7]

The second and most important source of energy is glycolysis, which proceeds slowly in the resting state. Glucose is stored as glycogen in liver and muscle. Glycogenolysis is the breakdown of stored glycogen to reform glucose by a process called phosphorylation. Epinephrine can specifically activate phosphorylase, resulting in the increased availability of glucose. Glucose is metabolized to pyruvic acid and hydrogen ions. Pyruvic acid is converted to acetyl coenzyme A and is incorporated into the citric acid cycle. Hydrogen ions are shunted through the electron transport chain (oxidative phosphorylation). The oxidation of hydrogen occurs through a series of enzymatically catalyzed reactions that split each hydrogen atom into a hydrogen ion and an electron, which reacts with dissolved oxygen to form hydroxyl ions and water. Of the 38 ATP molecules produced from a glucose molecule, oxidative phosphorylation accounts for 34. As long as adequate blood flow (oxygen and substrate) is provided, it can provide

energy for long periods of time. Aerobic glycolysis can usually meet all the body's ATP needs, except during heavy exercise or times of severe muscle exertion.[7]

When oxygen supplies are insufficient, anaerobic glycolysis may occur for a short time. This reaction is wasteful of glucose, only producing four ATPs/glucose, but is extremely important in muscle cells. A glucose molecule is split into two pyruvic acid molecules and hydrogen ions. Pyruvic acid reacts with nicotinamide adenine dinucleotide and hydrogen to form lactic acid. Lactic acid then diffuses into the extracellular fluids and cytoplasm of less active cells. Most of the lactic acid is converted back to glucose by the liver (Cori cycle). Heart and other tissues, to a lesser degree, can convert lactic acid to pyruvic acid and use it for energy. Under optimal conditions, anaerobic metabolism can provide an additional 30 to 40 seconds of maximal muscle activity in a well-trained athlete. Lactic acid build-up in muscle causes extreme fatigue.[7]

Two other factors occur at this time with respect to overall muscle activity, blood flow and heat production. During rest, blood flow through skeletal muscle averages 3 to 4 ml/min-/100 g of muscle, with 20 to 25% of capillaries being open. However, with strenuous exercise, this rate can increase to 50 to 80 ml/min/100 g of muscle. In the cat, the stimulation of sympathetic vasodilation fibers to skeletal muscle can increase blood flow by 400%. This marked increase of blood volume in muscle is accommodated by the filling of many dormant capillaries. When muscle activity begins, blood flow increases but is intermittent. Blood flow decreases as muscle contracts because of the compression of vessels and increases during relaxation, a process called the muscle pump. Because of the muscle pump, the total blood volume during exercise is, on average, equal to or just above the volume of blood in a resting muscle. Immediately following strenuous exercise, when the muscle is relaxed, up to 25% of the total blood volume can be in muscle mass, compared to 15% of the total blood volume at rest or during work.[7]

This muscle pump is active when the animal is running but is inactive when it is immobilized by physical or chemical restraint or is standing in a crate. In most situations (except during chemical immobilization), the muscles of most frightened animals that are not running are in a relatively isotonic state of contraction, which hinders blood flow into muscles. This leads to poor tissue perfusion, decreased heat dissipation, and hypoxia. Conversely, if an animal is chemically immobilized following pursuit, the muscles are relaxed and may allow more blood (an additional 10%) to flow into them. This can further reduce blood pressure, increase capillary pooling, decrease heat dissipation, and increase hypoxia to muscle, which all lead to focal necrosis.[7]

Heat production is another important process that occurs in muscles during exercise, and has at least four sources. Heat is produced when myofilaments slide together and when they relax. Glycogenolysis causes additional heat production. Heat is produced for about 30 minutes following exercise during the recovery phase of muscle. This "recovery" heat production is the result of chemical processes operating to restore muscle to resting equilibrium. An additional source of heat is the ambient temperature. When muscle is being worked or exercised, heat from the environment can flow into muscle cells. Excessive local heat can lead to tissue necrosis.[7]

Alteration of Normal Function

The pathogenesis of capture myopathy (CM) involves the exhaustion and ultimate failure of many active biological mechanisms whose primary function is to maintain homeostasis in a time of crisis. These reactions include activation of the sympathetic nervous system, resulting in "mass discharge," and the outpouring of biologically active substances (e.g., epinephrine, norepinephrine, endorphins, encephalins). Their primary function is to meet the metabolic requirements of the body by altering blood flow and increasing metabolism. The underlying pathogenesis of CM is identical to that of shock. Causes of shock include severe stress, fright, neurological factors, pain, trauma, massive hemorrhage, heart failure, severe burns, and infection. The fundamental hemodynamic mechanism of shock is a vicious cycle associated with reduced tissue perfusion and hypoxia, regardless of cause.

Capture Shock Syndrome

The pathogenesis of capture shock is probably identical to that of vasogenic-neurological shock. This can be initiated by many factors, including a strong and continuous stimulation of the sympathetic nervous system (with or without muscular activity). This sympathetic response is initially beneficial to the animal but, if prolonged, results in an increase in vascular capacity and a decrease in blood pressure. The normal blood volume is incapable of filling the circulatory system adequately. Prolonged sympathetic stimulation is followed by a phase of exhaustion of precapillaries caused by arteriolar receptors becoming refractory to continuous stimulation. However, postcapillary venous beds are not as refractory, because they can function normally at a lower pH. Constriction at this locus continues after the arteriolar spasm has abated. Capillary congestion and subsequent hypoxia result in reduced blood pressure, increased visceral pooling, decreased venous return, and decreased cardiac output. Circulatory shock leads to inadequate delivery of nutrients (glucose and oxygen) and removal of cellular waste products from tissues.

There are three stages of shock: (1) nonprogressive; (2) progressive; and (3) irreversible. In nonprogressive shock, the normal circulatory compensatory mechanisms eventually cause full recovery if the initiating causes are eliminated. In progressive stage, the animal steadily deteriorates until death. In irreversible shock, it has progressed to a point that no known treatment is adequate to save the animal's life. Factors in progressive shock lead to cardiovas-

cular deterioration. As the blood pressure drops, the flow becomes sluggish in small vessels; thrombosis of capillaries and small veins can occur, which exacerbates hypoxia. Tissue metabolism continues so that intracellular carbonic and lactic acid levels increase and diffuse into the blood. This acidity, combined with other deterioration products from ischemic tissues, leads to intravascular coagulation and thrombosis. When the arterial pressure falls substantially, the coronary blood flow decreases below that required for adequate nutrition of the myocardium. This decreased activity of the myocardium results in lower cardiac output. Progressive deterioration of the heart may take several hours and is usually not a major factor during the first several hours of shock, but subsequently becomes more important. Decreased blood flow to the brain can lead to coma and death, which usually occur in the later stages of shock. After several hours of generalized capillary hypoxia, the permeability of the capillaries gradually increases and large quantities of fluid escape into surrounding tissues.

With prolonged hypoxia, a generalized cellular deterioration occurs. The pathogenesis is believed to occur as follows. The active transport of sodium and potassium through cell membranes is greatly reduced because of a decrease in the intracellular pH. Sodium and chloride accumulate in the cell and potassium is lost to extracellular fluids. Mitochondrial activity is reduced. Lysosomes begin to rupture, releasing many enzymes that cause further intracellular deterioration. The cellular metabolism of nutrients (glucose) decreases. Hormone activity, especially of insulin, decreases. Tissue necrosis ensues, particularly in the liver, lung, skeletal muscle, and heart. During severe shock, cells adjacent to the arterial ends of capillaries are better nourished than cells adjacent to the venous ends of the same capillaries, which leads to the necrosis of tissues around venules. This is well demonstrated in the liver (central lobular necrosis). Such a lesion is common in the kidneys, resulting in tubular necrosis, uremia, renal failure, and death. The deterioration of pulmonary capillaries leads to edema.

Muscle hypoxia ensues because of decreased oxidative phosphorylation. When this occurs, cellular metabolism converts from aerobic to anaerobic glycolysis for the production of energy (ATP). If prolonged, anaerobic glycolysis leads to an accumulation of intracellular lactic acid and hydrogen ions. Poor blood flow decreases carbon dioxide removal, which reacts with water to form intracellular carbonic acid, thus lowering the intracellular pH. Capillary stagnation further reduces the effective circulating blood volume. Tissue hypoxia associated with the stagnation of blood is the factor that perpetuates shock. This cycle leads to a hemodynamic crisis, vascular collapse, and death.

Ataxic Myoglobinuric Syndrome

The pathogenesis of the ataxic myoglobinuric syndrome is actually a continuation of capture shock. Animals that have survived longer may now show clinical signs and postmortem lesions related to renal failure and muscle necrosis. The kidneys have suffered profound hypoxia because of vasoconstriction by the sympathetic nervous system and catecholamines. This leads to tubular necrosis. Excessive amounts of myoglobin exacerbate the necrosis, but this is probably not the primary cause. Tubular necrosis can be mild to severe, depending on the severity of the hypoxia. If tubular necrosis is severe, renal failure ensues.

Muscular lesions have progressed from mild to moderate by this stage. Muscular lesions are associated with hypoxia and deficient ATP, a result of the exhaustion of oxidative phosphorylation and aerobic glycolysis. Anaerobic metabolism is the primary source of ATP in this syndrome, resulting in severe intracellular acidosis. This produces alteration and destruction of enzyme systems and organelles, such as the sodium pump and mitochrondia. Cellular swelling also occurs, which further disrupts cellular function and allows the diffusion of intracellular components such as potassium, CPK, AST, and LDH into the blood. This proceeds to cellular necrosis. The primary causes of death in these animals include renal failure, azotemia, and acidosis.

Ruptured Muscle Syndrome

The pathogenesis of the ruptured muscle syndrome is a continuation of what has already been described. In this syndrome, the mechanisms combatting shock and azotemia have been successful, but the muscle lesions have now had time to progress. The muscles contain extensive areas of necrosis and rupture when forced to bear weight. The most common location for rupture is the proximal third of the gastrocnemius muscles. The primary causes of death are usually electrolyte imbalance, acidosis, and toxemia from massive necrosis of skeletal muscle.

Delayed-peracute Syndrome

The pathogenesis of the delayed-peracute syndrome can be theorized, based on observation, necropsy results, and basic physiology. A suggested explanation for this syndrome is the occurrence of moderately severe rhabdomyolysis in recently captured animals. Rhabdomyolysis causes hyperkalemia and acidosis, but not severe enough to result in overt clinical signs. When an animal is acutely stressed or captured again, there is a surge of epinephrine and norepinephrine from the adrenal medulla. Hyperkalemia causes functional abnormalities of the heart and skeletal muscle by lowering the resting electrical potential of membranes, thereby preventing repolarization. High levels of epinephrine on these altered membranes results in ventricular fibrillation and cardiac arrest. If these animals had not been recaptured and restressed, they probably would have lived.

Thus, CM is a condition that occurs in wild and captive animals. CM may be caused by many stressors, such as terror, capture (with or without chase), and restraint. CM is associated with the exhaustion

of normal physiological mechanisms that provide energy to perform work to escape. These mechanisms become exhausted at varying times, depending on the species of animal, type, and/or severity of the stressor, and environmental conditions (e.g., temperature, humidity), thus giving rise to the different syndromes of CM.

Treatment and Control

Prevention is the most effective means of managing CM. Under field conditions, the treatment of CM is usually unsuccessful. Numerous procedures may be carried out to reduce the prevalence of CM. However, CM may still occur, even with the most well-planned capture strategies. Factors that help prevent CM include the following:

1. Have a well-trained crew, with the minimal number of people to do the job. The crew should be trained in restraint and be able to notice early signs of CM.
2. Only capture on days that have acceptable environmental conditions for the species of animal that is being captured.
3. If trapping is done on a hot day, spray the animals with water to keep them cool. Spray against the hair to wet the skin, especially keeping the head, ears, and feet wet.
4. Keep noise and movement down to a minimum. Blindfolds are sometimes helpful. Make sure that blindfolds do not rub the cornea, because superficial ulcers can develop, and be sure that blindfolds do not cover the animal's nostrils.
5. When capturing an animal by chase, run animals as slowly and for as short a distance as possible. You have to know when to *stop*.
6. Whenever possible, use trapping techniques that lure the animal into the trap, instead of techniques that require chase.
7. Monitor the animal's body temperature during restraint. Have equipment available to treat hyperthermia early.
8. Giving multiple vitamins and vitamin-E/selenium is not harmful but probably does not help either. If the animals are on a range known to be deficient in vitamins, they should be trapped with lure traps and the deficient substance (e.g., selenium, copper, vitamin E) added to the bait. Treatment with antibiotics to help prevent secondary infections during this time of stress is suggested.
9. Animals should be transported in well-suited crates or trailers. Some animals are best transported alone, whereas others do better with two to three together.
10. Make sure "crate mates" are compatible. Do not place mature males together with females and neonates.
11. Food and water should be provided to meet the specific needs of the animal. During long trips, the transporting vehicle should stop and fresh water offered to animals. Shortly after capture, most animals are mildly dehydrated.
12. If chemical immobilization is used, well-trained personnel, and proper drugs, dosages, and delivery systems are necessary.
13. When releasing animals into new pens that already house animals, make sure that the resident animals do not harass the new arrivals.
14. When animals are trapped and placed in captivity, they should be left undisturbed (except for water and feeding) for 2 to 3 weeks. This allows time for skeletal muscle to heal and helps prevent the delayed-peracute syndrome of CM.
15. If the incidence of CM is greater than or equal to 2%, the trapping technique and protocol should be re-evaluated; a mortality rate greater than or equal to 2% during trapping is *not acceptable.*
16. The primary goal of treatment is the control of shock and hyperthermia. Equipment and drugs needed for the treatment of CM should be readily available at the time of capture, including the following:
    a. Make sure there is adequate ventilation. This can be a particular problem when using nets or ropes.
    b. Control excessive hemorrhage.
    c. Fluid therapy is used to restore blood pressure and volume, increase energy levels (glucose), and correct any acid-base and electrolyte imbalances.
    d. A number of drugs, including steroids, glucose, anticoagulants, cardiac and respiratory stimulators, vasoconstrictors, vasodilators, and vitamins and minerals can be given to animals suffering from CM.

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