The Advantages and Disadvantages of Circulatory and Liver Protection Therapy of Cattle

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Introduction

Disorders of the circulatory and liver function systems may occur in countless and etiologically very distinct cattle diseases in both adult cattle and calves. The functional disorders may develop through diseases of the circulatory organs, or the liver itself--that means a primary organic disease. Additionally there are numerous secondary disturbances of these organic functions which occur as the result of other organic and infectious diseases, as in connection with certain metabolic disturbances, deficiency diseases or poisoning. In addition to the basic therapy, therefore, in many cases additional symptomatic treatment is essential for the preservation of the circulatory and/or metabolic maintenance of liver function. Aside from the clear medical indications, in addition to the diagnostic and therapeutic possibilities, the selection and application of such therapeutic measures must be carefully weighed in the treatment of cattle. The secondary effects-the danger of injury from drugs and the economics of the treatment must also be considered.

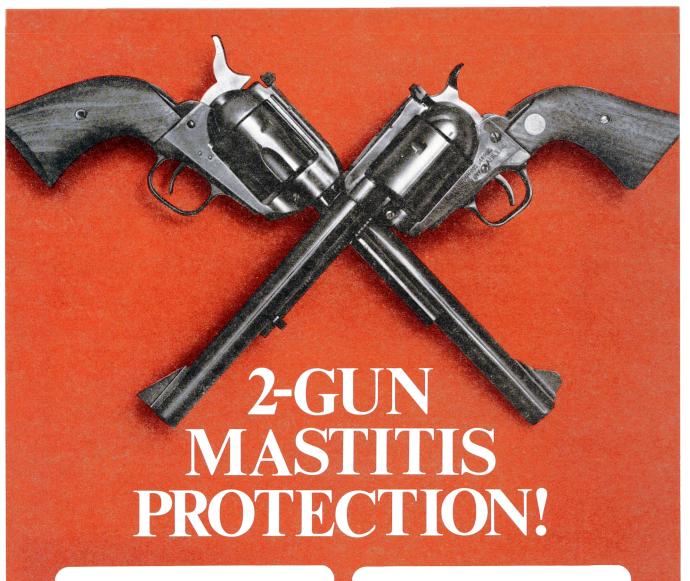
Treatment of Circulatory Disturbances

Very narrow boundaries have been established in the differentiation of the functional disturbances of the circulatory system in cattle, with the current state of large animal practice and the limited means of research possibilities in the field. The clinical examination on blood circulation in cattle (Rosenberger et al, 1977) includes, as a rule, only auscultation, the sound and pain percussion of the heart in addition to the pulse rate, and quality; the filling and color of the externally visible blood vessels (arteries, veins, capillaries) and the visible mucous membranes. The cellular and biochemical composition of the blood could also be investigated. In most large animal clinics, too, phonocardiographic, electrocardiographic and x-ray research on the heart or the control of the arterial and

English translation by LaVerne Koelsch Jones, Edmon Low Library Oklahoma State University, Stillwater, Oklahoma 74074 venous blood pressure are at this time, still not routinely carried out.

One may recognize and differentiate the most important functional disorders of the circulatory system with simple well known clinical research procedures, but an accurate relationship to the numerous etiological and pathogenetic different circulatory disturbances can, at times, only be made with difficulty. The therapeutic procedures depend, however, essentially on the localization (cardiac insufficiencies, central or peripheral circulatory deficiencies) and the origin (hypovolemia, endotoxicosis, anaphylaxis of the functional disturbances of the circulatory system. In addition to the mild forms of cardiac and circulatory insufficiencies, which only require a prophylactic "support" measure, those life threatening and urgent conditions of cardiac--or circulatory--failure take on immediate and specific clinical significance (Bouckaert and deMoor, 1967; Hapke, 1971 and 1975; Fishcer, 1976; Landauer and Kramer, 1976). The pathogenesis of these commonly designated regulatory disturbances, such as circulatory shock, has not yet been clarified in all particulars, nevertheless, on the basis of the latest research findings (Raab, 1975) the biochemical and clinical relationships are more intelligible. At the present time, the primary reason for circulatory dysfunction is believed to be a reduction of the conduction time volume, plus a diminished flow in the capillary and micro-circulation as well. The direct results of this diminished blood flow consists of an increased capillary penetration and dilatation, with blood stasis and intravascular coagulation (sludge-syndrome). This leads to oxygen deficiencies and excess acid in tissues, especially in the so-called shock organs (in cattle particularly spleen, liver and intestines) and precipitates a life endangering circulus vitiosus (vicious circle), which then leads to a decrease in the circulating blood volume, venous blood return, cardiac minute volume and blood pressure and thus to a compensating arterial constriction (table 1).

The differences in the individual forms of shock may be seen from a pathogenetic viewpoint (neurogenic, angiogenic shock, etc., Krause, 1954). One such classification, however,



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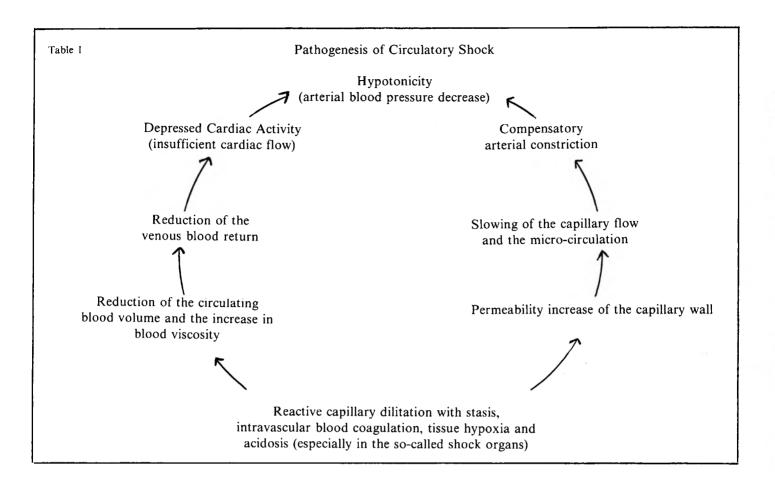
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Cardiogenic shock	Pericardial
	Myocardial
	Endocardial
	Heart Malformations
	Tumors of the heart region
	Electrolyte imbalance (Ca, Mg, K)
Hypovolemic shock	
Hemorrhagic shock	Massive external or internal bleeding
	Hemorrhagic diathesis (predisposition)
Dehydration shock	Severe enteritis
	Ileus (bowel obstruction)
Septic shock	Septicemic or pyemic-metastasizing infection
(Endotoxic shock)	Endogeneous intoxication syndrome
Anaphylactic shock	Antigen-antibody reactions
	Allergies
	Anaphylactic reactions

Table 3: Diagnosis and treatment of the various circulatory disturbances of cattle.

Types of circulatory disturbances	Cardiac	l characteristi function Pulse rate		efill time Capillaries	Vol.	Blood Hematocrit	Treatment
Cardiac insufficiency Acute	-	+	+	+	+	+	Mild form: calcium preparations in low dosage Severe form: immediately effective cardiac glycosides
Chronic	-	+	+	+	+	- Or +	Cardiac glycosides
Circulatory insufficiency Hemorrhagic shock	-	+	-	-	_	-	Blood transfusion Calcium preparations in low dosage
Dehydration shock	-	+	-	-	-	+	Circulatory supplement through infusio therapy with buffered hypotonic solutions
Endotoxic shock	-	+	-	+	+ or -	+	Basic therapy: i.v. infusion with buffered solutions Glucocorticosteroids in high dosages, i.e. cardiac glycosides
Anaphylactic shock	-	+	-	+ or +	+ or -	+	Basic therapy: i.v. infusion with buffered solutions and calcium prepar- ations in low dosage Glucocorticosteroids and/or antihistamines

- reduced; + raised; = unchanged

on the basis of polyfactorial shock sequences is unsuitable and will not prove out by clinical-diagnostic methods. The shock forms may be classified appropriately from an etiological view point, by which cardiologic, hypovolemic, septic and anaphylactic shock can be differentiated (Raab, 1975). A summary of the most frequent primary types of shock in cattle are given in table 2.

The differential diagnoses of the various circulatory disturbances of cattle depend, on one hand, on the recognition of the primary cause of the disease, and, on the other hand, on some characteristic circulatory parameters ascertained by examination (table 3). Since all forms of circulatory disturbances, almost without exception, are combined with a (not directly provable) decrease of the cardiac minute volume and an elevation of the cardiac rate, the use of elementary auscultatory findings of the heart function therefore are not differentially reliable. The auscultatory findings of the heart ordinarily indicate diagnostically recognizable changes (sinus brachycardia, rhythmic disturbances, endoor exo-cardiac background

sounds, etc.) only with the cardially limited circulatory disturbances. On the other hand, from the filling condition of the blood vessels, especially of the veins and "capillaries" (particularly the pre-capillary venules in the region of the episcleral vessels) one can derive useful differential diagnostic conclusions; by means of the technically simple hematocrit determination of the blood important additional knowledge can be obtained (table 3). Above all, in each case, an exact diagnosis about the kind and degree of the circulatory disturbance should be arrived at and treatment measures instituted for the fundamental differences in each type. Where the severe forms of heart failure in cattle as a rule are cause for the immediate disposal of the animal, in less serious cardiac conditions one may often favorably influence results through intravenously administered calcium preparations in small doses (for example: 100 ml. calcium gluconate) or through intravenously introduced and cautiously dosed cardiac glycosides (especially strophanthin preparations; table 3). The added action of the heart muscle and the toxic cardiac action of any calcium or cardiac

Table 4: Summary of the volume replacement possibilites in circulatory shock

Volume replacement	Molecular weight	Properties Fluid retention ml/g	Half-life period	Dosage ml/kg	Pharmacokinetics	Secondary actions
Crystalloid solutions Electrolyte solutions i.e. Aquifusal Sterofundin	low		minutes	5 - 20	Rapid dissemination into extracellular space, rapic ionic ex- change and renal excretion	Regulation of the disturbed fluid and electrolyte balance diuretic stimulation
Colloidal solutions Gelatin preparations i.e. Haemaccel Physiogel Plasmagel	30,000 to 35,000	14	3-4 hours	2 - 5	Predominantly renal excretion	Occasional allergic reactions
Dextran preparation i.e. Rheomacrodex Macrodex Longasteril	40,000 60,000 70,000	20-25	3-4 hours 6-8 hours	2 - 5	Elimination through decomposition and renal excretion	Occasional allergic reactions, disturbances of blood coagulation
Hydroxyethyl Plasmateril	450,000	14	8-12 hours	2 - 5	Enzymatic decomposition and renal excretion	Occasional allergic reactions
Whole blood	-		I-5 days	1 -2 each transfusion	Premature decomposition of the transfused erythrocytes	Occasional blood group incompatibility reactions; accelerator of blood coagulation

glycoside therapy of too high a dosage must be most carefully observed (Hapke et al, 1968; Lossnitzer, 1971; Hapke and Prigge, 1972; Schoner, 1977).

In cattle the prevention of shock after surgical intervention, severe injury or accident has great practical significance as does treatment of those cases of protracted disease and those where medical assistance is requested late in the course of the disease. With all kinds of hypovolemic shock moreover the volume replacement through blood transfusions or through transfusion therapy with hypotonic or isotonic, buffered crystalloid-or colloidal solutions are of the utmost importance. The specific properties and the dosages of the most important infusion solutions are brought together in table 4. With cattle the use of colloidal volume replacement solutions are usually prohibitive on economic grounds.

The basic rationale for the treatment of endotoxic and anaphylactic shock consists of the intravenous infusion of cyrstalloid or colloidal solutions, eventually plus glucocorticosteroids (Grinstein-Nadler and Bottoms, 1976) or antihistamines and beside medication, which is heart and

blood vessel effective. It is better to abstain from the use of adrenergic pharmaceuticals in cattle, given the present level of knowledge of circulatory diagnostics, with its danger of pharmacologically produced circulatory dysregulation or deterioration (Hapke, 1963). A medically induced blood pressure elevation in shock can cause the microcirculation to further deteriorate (Hapke, 1975).

Treatment of Liver Function Disturbances

Of the countless liver diseases which occur in cattle the icteric causing forms may be diagnosed by simple clinical procedures (table 5). On the other hand additional research procedures are essential for the diagnosis of the common anicteric acute and chronic liver diseases of cattle. These procedures, in relation to the acute hepatopathology, are chiefly the investigation of the urine (bile pigment excretion) and of blood (serum bilirubin, serum enzymes, bromsulfalein test), and, with the suspicion of the existence of a chronic liver disease, that of an exploratory laparotomy. The practicability and the limitation of hepatic diagnosis in cattle through simple testing procedures under practice

Table 5: Clinical classification and occurrence of the most important liver diseases in cattle.

Туре	of liver disease		Disease sy	vndromes Occurrence in
		Hemolytic icterus	Hemoglobinurea	Babesiasis, leptospirosis, chronic copper poisoning, feeding hemo- globinuria (cabbage, rape)
Acute	Icteric	Hepatic icterus	Hepatic insufficiency	Puerperal hepatic coma Toxic hepatic dystrophy
		Posthepatic icterus	Bile obstruction	Bile colic Solar dermatitis (hepatogenic Photosensitivity)
	Anicteric	Fatty liver Hepatitis parenchymatosis (Hepatic cell necrosis) Interstitial Hepatitis (Periportal lesions)	Metabolic disturbances Alimentary indigestion Abomasal displacement Endogenous intoxication syndrome Poisoning	Parturition paresis, acetonemia Rumen acidosis Displacement of the abomasum (left and right) Paralytic mastitis Puerperal intoxication Salmonellosis Arsenic, phosphorus, antimony, Carbon tetrachloride, lead, zinc
Chronic	Chronic interstitial hep Perihepatic fibrosa Hepatic necrosis Hepatic apostematosa Hepatic congestion Tumors of the liver	patitis	Liver parasites Liver abscesses Liver metastasis	Fascioliasis Purulent navel invection Bang's necrosis bacillus Necrotic rumenitis, pyemia, thrombosis of the caudal vena cava, traumatic liver perforation Hoflunder syndrome Mesentheleoma, carcinoma

conditions has been repeatedly reported (Grunder, 1971, 1974 and 1977; Rosenberger et al, 1977). The basis of the differential diagnosis of the most important liver diseases of cattle are grouped in table 6.

Due to a lack of systematic, controlled and adequate therapy studies the treatment of liver function disturbances in cattle up to the present has been largely empiric. The establishment of a basis for the treatment of liver diseases in cattle therefore is particularly urgent, since liver function disturbances with severe metabolic problems often occur in high producing cattle in connection with alimentary, metabolic, toxic and infectious disease conditions. Because of the more frequent use of rapid test procedures and simple photometric laboratory methods in veterinary practice in increasing number of cases are diagnosed. To be sure, a greater part of the milder liver function disturbances require no special treatment, since the liver, because of the great regenerative ability of its parenchyma, tends to normalize itself. Despite this, many such cases previously referred to as "liver protection therapy" are now treated. In this connection the safety of the therapeutic measures and the animal's tolerance in the treatment of those difficult cases with liver dysfunction must absolutely take precedence. However, the number of cases with liver affecting, or direct and indirect hepatotoxic drugs is inordinately large (Adam, 1972; Symonds, 1976), and the particular dangers of an additional medicinal injury to the already overburdened, functionally disturbed or degeneratively altered hepatic parenchyma must not be overlooked. Earlier research on experimentally induced liver damage in cattle (Grunder, Rosenberger and Timm, 1974) has clearly shown that powerful glucocorticosteriods and high doses of intravenously administered nutritive solutions may rather unfavorably influence the functionally disturbed liver.

With the present state of knowledge the following drugs are recommended in most of the established liver therapy (lipotropic substances, cholinechloride phospholipide, methionin, ornithin aspirates, organ extracts, etc.) *Treatment with ACTH is recommended for high producing cows suffering from fatty liver syndrome (Eness, 1975).

^{*} But this effectiveness has not been established.

Table 6: Differential diagnosis of the most important liver diseases in cattle.

Type of liver disease		Pathognomonic symptoms		
	Hemolytic icterus	Visible mucous membrane: pale yellow, lemon colored Circulatory weaknesses: cool skin, tachycardia of about 120/minute Urine: coffee colored (hemoglobinuria), bile pigment test positive Blood: anemic, serum blood tinged Liver function: greatly depressed (Serumbilirubin, enzyme, BSP)		
Acute hepatitis	Hepatic icterus (hepato-cellular parenchymatic or retention icterus)	Visible mucous membrane: dirty-yellow Liver percussion field: almost always enlarged and palpable Urine: tea to congac colored, bile pigment test positive Liver function: greatly depressed (Serumbilirubin, enzyme, BSP)		
	Congestive icterus (posthepatic, mechanical or obstructive iceterus)	Visible mucous membrane: pale yellow-pink, orange colored Bile colic with or without solar dermatitis Digestive system: motility halted, feces "balled up" Gall bladder area palpable Urine: unchanged, later tea colored, Urobilistix negative Liver function: greatly depressed (especially serum bilirubin and BSP) (In doubtful cases an exploratory laparotomy on the right side)		
	Anicteric hepatitis, fatty liver	None Urine: dark yellow to tea colored, methyline blue test usually positive Blood: non specific changes in cellular and albumin contents Liver function: slight to medium disturbance (serum bilirubin of 1 mg/100 ml, enzyme, especially SGOT, -GT, BSP slightly raised or normal)		
Chronic hepatitis	Fascial liver changes (liver cirrhosis) Abscesses of the liver Metastases of the liver	None Blood: occasional lymphocytosis Liver function: usually not clear changes (in doubtful cases: exploratory laparatomy)		

Favorable results have been found experimentally by treatment with combinations of sugar and amino-acid i.v. solutions in low doses (Grunder, Rosenberger and Timm, 1974) and accepted in bovine practice (Heinen, 1975; Hermisson, 1975, Grotzner, 1975; Wanderka, 1975). Treatment on the basis of the individual disease in acute hepatic disturbances in cattle can be found in table 7. One must bear in mind both the composition of, and the important differences in dosage, in the existing i.v. solutions for treatment of liver diseases.

The particular dangers of the present "liver protection therapy" consists of a polypharmacy with a great possibility of detrimental drug actions or reactions (Szabuniewiez et al, 1973), which places an additional burden on the already overstressed or disturbed metabolic functions of the injured liver. In this connection one must above all be mindful that

the greater part of the drugs administered must eventually be metabolized from the enzymes of the hepatic cells (Darnis, 1976). The direct therapeutic influence of the enzyme synthesis in the liver cells and the resulting improvement and acceleration of the metabolic functions offers, in the future, certain prospects for effective treatment possibilities in liver diseases.

Summary

Disturbances of the circulatory and liver function systems in cattle of all ages have great practical importance, since, in addition to the isolated primary disease of these organs, further secondary and symptomatic functional disturbances occur. The possibilities of diagnosis and differentiation of the circulatory disturbances have very narrow parameters in large animal bovine practice; therefore an etiological

Table 7: Treatment alternatives in acute liver diseases of cattle.

Type of liver disease	Cause	Treatment	Symptomatic	
Hemolytic icterus	Babesiosis Leptospirosis	Chemotherapy	Blood transfusion (½ - 1 1. citrated blood and 100 ml. calciumborogluconate i.v.)	
(Hemoglobinuria)	Copper poisoning Change in feed Feeding and hemoglobinuria		Cardiac glycosides in small doses I.V. therapy (see below)	
Hepatic icterus (Liver insufficiency)		e hepatotoxic feed and drugs mary diseases, particularly stabolic disturbances	I.V. therapy with dextrose and amino acid solutions (dosage: 1 - 2 ml./kg of body weight; with continuous i.v. drip 2 - 4 ml./kg of body weight daily) Regulation of the disturbed digestive functions	
Posthepatic icterus (Bile blockage)	1 1	Choleretika to restore the xploratory laparotomy and omy	Bile duct antibiotics Magnesium sulfate 100 - 300 g orally I.V. therapy (as above)	
Acute anicteric liver disease (fatty liver, liver	metabolic disturban	ary diseases, specifically	I.V. therapy with glucose and amino acid solutions	
degeneration, etc.)	Dietary feeding		Regulation and stimulation of the digestion of the rumen	

classification for types of shock, cardiological, hypovolemic, septic and anaphylactic shock, is entirely suitable. Therapeutic measures concerning circulatory volume, the microcirculation and the work of the heart itself are all part of the current research on the pathogenesis of circulatory shock. More research is necessary on the adrenergic drugs in cattle.

Only the icteric occurring forms of liver diseases in cattle can be diagnosed by simple clinical methods. Additional test methods or an exploratory laparotomy must be used for the diagnosis of all anicteric acute and chronic liver diseases. For want of a positive treatment basis for the so called "liver protection therapy" for cattle treatment, continues empiric. Complete harmlessness of the drugs and good hepatic tolerance should take precedence in all therapeutic measures. The most favorable clinical procedures in acute hepatopathology consists of combined sugar and amino acid based i.v. solutions in low doses.

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