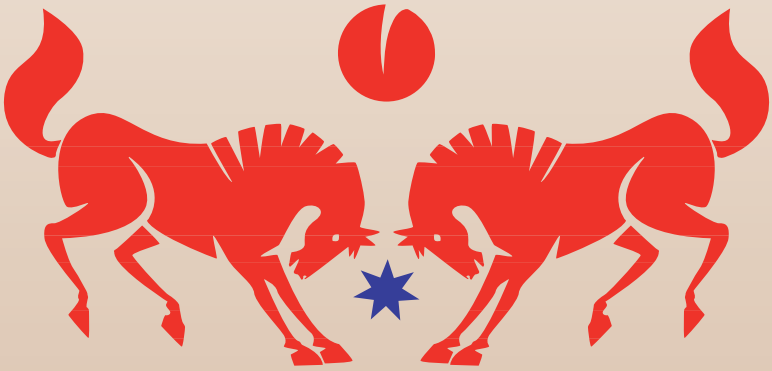
BULL POWER

NATIVE 100 % RAW TAURINE

ENERGY FEED

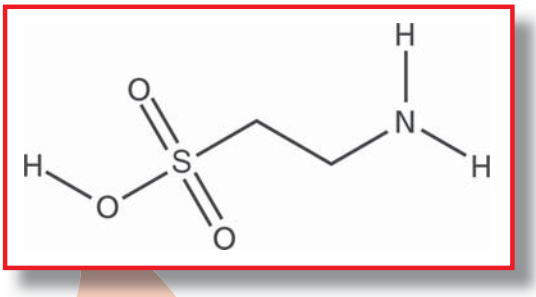


Granules 25 g sachet
40 sachets box

Tablet 100 mg – 100 tablets bottle

La taurina (dal latino <*http://it.wikipedia.org/wiki/Lingua_latina*> taurus, toro <http://it.wikipedia.org/wiki/Bos_taurus> , dato che è stata scoperta nella bile <http://it.wikipedia.org/wiki/Bile> del toro dagli scienziati austriaci Friedrich Tiedemann <http://it.wikipedia.org/w/index.php?title=Friedrich_Tiedemann&action=edit&redlink=1> e Leopold Gmelin <http://it.wikipedia.org/wiki/Leopold_Gmelin>) o acido 2-amminoetanosulfonico, è una sostanza chimica acida abbondante in molti tessuti di diversi animali <http://it.wikipedia.org/wiki/Metazoa> .

La Taurina è presente unicamente nel regno animale, i cibi vegetali non possiedono questo amminoacido.



AZIONI DELLA TAURINA

Gioca un ruolo importante nelle normali funzioni di cervello, cuore, colecisti, occhi e sistema vascolare. La Taurina è un importante componente degli acidi biliari e possiamo identificarla come un "detergente del colesterolo".

Tra le principali azioni della taurina ricordiamo le sue virtù antiossidanti; sensibilizza il sistema immunitario; è un agente detossificante migliorando la solubilità di certe sostanze e favorendone l'eliminazione per via renale.

L'ammino gruppo della taurina può reagire con carbossiacidi di tossine formando legami amidici; simile al neurotrasmettitore GABA. Regola il trasporto di ioni intra ed extra cellulare, stabilizza elettricamente le membrane cellulari. Modula l'attività del cAMP, che attiva importanti enzimi coinvolti nella contrattilità muscolare.

L'assunzione di taurina con la dieta stimola la formazione di una sostanza, il taurocolato che incrementa la secrezione di colesterolo nella bile e migliora il metabolismo lipidico epatico. Esercita un'azione positiva anche nel metabolismo degli zuccheri ed è un coadiuvante dell'insulina.
I sui livelli plasmatici aumentano dopo un intenso sforzo fisico a dispetto della riduzione degli altri amminoacidi (impegnati nel metabolismo neoglucogenetico).

EFFETTI DOVUTI A DEFICIENZE DI TAURINA

Prolungata deficienza di Taurina nel gatto e nel cane può portare a cardio-miopatie dilatative (DCM), una condizione in cui il cuore si allarga a causa di un suo assottigliamento e indebolimento.
Carenze di Taurina possono portare inoltre a degenerazioni o lesioni della retina. All'interno della retina, la taurina può aiutare a stabilizzare le membrane cellulari.

I gatti, a differenza dei cani e degli stessi esseri umani, non sono in grado di sintetizzare Taurina, motivo per cui è essenziale il regolare apporto della stessa con la dieta. La Taurina non è accumulata dall'organismo dei gatti, rendendo minimi i rischi di sovra dosaggio.

LA TAURINA COME INTEGRATORE NELL'ATTIVITA' SPORTIVA

Tra i benefici della taurina c'è un incremento della performance cardiaca durante l'esercizio. Studi effettuati hanno dimostrato un importante incremento del volume di sangue pompato dal cuore ad ogni battito.

Studi dimostrano l'efficacia nel ridurre lo stress ossidativo sui linfociti e la perossidazione lipidica che interviene nel cavallo sportivo ed altresì nei cani da corsa in conseguenza dell'attività prolungata.

BULL POWER

PROPRIETA'

L'amminoacido non partecipa alla sintesi delle proteine, anche per codesta ragione BULL POWER può essere assunto in qualsiasi momento della giornata.
Da utilizzarsi con Calcio, Magnesio ed un buon mix di vitamine.

DOSI

A discrezione del medico Veterinario e / o dell' Alimentarista.

CONFEZIONI

Pets : Flacone da 80 compresse da 100 mg ;

Cavalli : Astuccio da 40 buste da 25 g granuli.

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Effects of dietary fat and L-carnitine on plasma and whole blood taurine concentrations and cardiac function in healthy dogs fed protein-restricted diets.

Sanderson SL, Gross KL, Ogburn PN, Calvert C, Jacobs G, Lowry SR, Bird KA, Koehler LA, Swanson LL.

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OBJECTIVE: To evaluate plasma taurine concentrations (PTC), whole blood taurine concentrations (WBTC), and echocardiographic findings in dogs fed 1 of 3 protein-restricted diets that varied in fat and L-carnitine content. ANIMALS: 17 healthy Beagles. DESIGN: Baseline PTC and WBTC were determined, and echocardiography was performed in all dogs consuming a maintenance diet. Dogs were then fed 1 of 3 protein-restricted diets for 48 months: a low-fat (LF) diet, a high-fat and L-carnitine supplemented (HF + C) diet, or a high-fat (HF) diet. All diets contained methionine and cystine concentrations at or above recommended Association of American Feed Control Officials (AAFCO) minimum requirements. Echocardiographic findings, PTC, and WBTC were evaluated every 6 months. RESULTS: The PTC and WBTC were not significantly different among the 3 groups after 12 months. All groups had significant decreases in WBTC from baseline concentrations, and the HF group also had a significant decrease in PTC. One dog with PT and WBT deficiency developed dilated cardiomyopathy (DCM). Taurine supplementation resulted in significant improvement in cardiac function. Another dog with decreased WBTC developed changes compatible with early DCM. CONCLUSIONS AND CLINICAL RELEVANCE: Results revealed that dogs fed protein-restricted diets can develop decreased taurine concentrations; therefore, protein-restricted diets should be supplemented with taurine. Dietary methionine and cystine concentrations at or above AAFCO recommended minimum requirements did not prevent decreased taurine concentrations. The possibility exists that AAFCO recommended minimum requirements are not adequate for dogs consuming protein-restricted diets. Our results also revealed that, similar to cats, dogs can develop DCM secondary to taurine deficiency, and taurine supplementation can result in substantial improvement in cardiac function.

CARDIOVASCULAR CONDITIONS
Inherited problems in cats - confirmed and suspected

Feline cardiomyopathies

The first report describing acquired cardiac lesions which culminated in congestive heart failure was published in 1970. Over the subsequent decade, various reports were published detailing the gross anatomical and histological features of the feline cardiomyopathies. At that time, cardiomyopathy was detected in 8.5% of cats that underwent post-mortem examination. In addition, it was found that the classification system described in human beings suitably differentiated the disease groups described in cats, namely; Dilated Cardiomyopathy (DCM), Hypertrophic Cardiomyopathy (HCM), Restrictive Cardiomyopathy (RCM), Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), Unclassified Cardiomyopathy (UCM) and persistent moderator band cardiomyopathy. Initially, DCM and HCM were reported to be the most prevalent of the feline cardiomyopathies. However, in 1987, Pion and colleagues discovered a causal relationship between decreased plasma taurine levels and feline myocardial failure. With the supplementation of commercial cat food with taurine, the incidence of feline 'DCM' has decreased. Today, the most prevalent feline cardiomyopathy is HCM.

Hypertrophic Cardiomyopathy

HCM accounts for approximately 27% of all feline cardiac disease. In 1999, Kittleson and colleagues identified a family of Maine Coon cats with HCM and an autosomal dominant mode of inheritance, where 100% penetrance was demonstrated. Further studies have demonstrated left ventricular hypertrophy in a closed colony of Persian cats, a familial predisposition for HCM and aortic thromboembolism (AT) in a family of (American) domestic shorthaired cats, and a predisposition to severe HCM in the Ragdoll breed. In addition, a family of American shorthaired cats has been identified with a familial tendency for HCM and/or abnormal motion of the mitral valve. In all these studies the pattern of inheritance was consistent with that of an autosomal dominant trait. In addition, there are anecdotal reports of the disease occurring with an increased incidence in many other breeds (see breed predispositions above). Polymorphisms of both the feline TnT gene and the feline myosin regulatory light chain gene (MYL2) have been identified. Furthermore, it has been found that Myomesin (an M-band sarcomeric protein) was decreased or absent in Maine Coon cats with HCM, compared to control cats. Recently it has been discovered that some Maine Coon or Maine Coon cross cats with HCM have a mutation of the Myosin Binding Protein C. In addition, a different mutation of the same gene has also been identified in Ragdoll Cats with HCM, although as yet, it is not known what proportion of Ragdolls with HCM has this mutation.

Feline HCM is a highly heterogeneous disease and therefore, the associated clinical signs are highly variable. Since many cats are asymptomatic (cause no signs of ill health), apparent unexpected sudden death may occur. In others, stress may induce breathing difficulties due to acute pulmonary oedema or pleural effusion. Other reported clinical signs include rapid breathing, anorexia, vomiting, fainting or paralysis, which is typically of the hind limbs, lethargy and occasionally ascites (fluid on the abdomen).

Restrictive Cardiomyopathy

The term restrictive cardiomyopathy (RCM) is applied to cases of cardiomyopathic disease that restricts the diastolic ventricular function (relaxation) and excludes HCM. Pathologically, there are two forms described, one affecting the

myocardium only, and one affecting the endomyocardium (which is more common). There are no sex predilections, and the age of affected cats is highly variable, but typically middle to old aged animals are affected. RCM has not been reported as an inherited disease. However, it has been hypothesised that endomyocardial fibroelastosis (EMF), a fibrosis thickening of the endocardium may be a form of RCM. An increased incidence of EMF has been reported in the Burmese and possibly the Siamese breeds.

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Dilated Cardiomyopathy

Since the discovery of taurine deficiency in cats, the incidence of DCM has decreased, with now only ~3% of cats with cardiomyopathy suffering from systolic myocardial failure (DCM). Whilst some of these cats remain taurine deficient, either through poor diet, or metabolic anomalies, others appear to suffer from a familial DCM. In addition, isolation of parvoviral DNA (e.g. from Feline Panleukopenia Virus) has been isolated from cats hearts with DCM, and it has been hypothesised that some cases may be caused by an infectious myocarditis. It remains unclear as to whether the reported 'breed predispositions' to DCM (ie the Burmese and Abyssinian and Siamese breeds) are truly at an increased risk of primary DCM, have an increased taurine requirement or whether feeding differences in these breeds previously predisposed them to DCM.

Moderator Band Cardiomyopathy

Increased numbers or enlarged moderator bands (fibrous stands spanning the heart chambers) have been reported in various breeds of cats. There is anecdotal evidence that Burmese cats may be predisposed to the development of a large bridging moderator band, whilst Siamese cats may be predisposed to the development of multiple moderator bands spanning the ventricle.

HCM discussed on Susan Little's website www.catvet.homestead.com - Selected Inherited Diseases of the Cat.

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Congenital heart defects

A variety of congenital heart defects have been reported in cats. These may occur by themselves or in combination with other congenital abnormalities. Congenital heart defects can develop as a result of toxic, environmental, genetic, nutritional or chromosome related abnormalities. In cats, the estimated incidence of congenital heart disease is 0.2-1%. The most commonly reported abnormality is an atrioventricular defect (a hole between two or more of the cardiac chambers), this group of diseases included ventricular septal defects, atrial septal defects and endocardial cushion defects. Malformation of the atrioventricular (mitral and/or tricuspid) valves is the second most commonly reported congenital cardiac disease in the cat, followed by endocardial fibroelastosis (see Restrictive Cardiomyopathy: a predisposition to this disease has been reported in the Burmese and Siamese breeds, see specific breed predispositions), patent ductus arteriosis, aortic stenosis (a predisposition has been reported in the Siamese breed), and tetralogy of fallot (a combination of pulmonic stenosis, right ventricular hypertrophy, ventricular septal defect and dextrorotation of the aorta). Pulmonic stenosis has been reported occasionally in the cat.

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Congenital portosystemic shunt

It has been reported that Colour Point Persian cats are predisposed to a vascular anomaly by which the blood from the intestines bypasses the liver, a so called portosystemic shunt. They may therefore develop signs of hepatic encephalopathy caused by the systemic accumulation of ammonia, and numerous other neurotoxins. Most affected kittens have clinical signs from ~10-12 weeks of age, typically presenting with intermittent visual disturbances, pupillary dilation, ataxia, behavioural changes (eg. aggression), seizures, lethargy, depression, and ptyalism (excessive salivation). Stunted growth occurs rarely in cats. There is not usually any clear relationship between clinical signs and recent feeding. Diagnosis is made on finding raised bile acids in the blood and visualising the shunting vessel with ultrasound or contrast radiography. Medical and/or surgical treatment options are available.

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Peritoneopericardial diaphragmatic hernia (*)

Not truly a cardiac disease, peritoneopericardial diaphragmatic hernia (PPDH) is a congenital abnormality by which the abdominal cavity, directly communicates with the pericardium (the sac that the heart sits in). Colour point Persians and Persian cats have frequently been identified with peritoneal pericardial diaphragmatic hernia. Anecdotally, British Short hair cats and blue colour or colour point cats may be at an increased risk.

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Myocardial failure in cats associated with low plasma taurine: a reversible cardiomyopathy.

Pion PD, Kittleson MD, Rogers QR, Morris JG.

Thousands of pet cats die each year with dilated cardiomyopathy, the cause of which is unknown. Although taurine is present in millimolar concentrations in the myocardium of all mammals, taurine depletion has not previously been associated with a decrease in myocardial function in any species. In this study, low plasma taurine concentrations associated with echocardiographic evidence of myocardial failure were observed in 21 cats fed commercial cat foods and in 2 of 11 cats fed a purified diet containing marginally low concentrations of taurine for 4 years. Oral supplementation of taurine resulted in increased plasma taurine concentrations and was associated with normalization of left ventricular function in both groups of cats. Since myocardial concentrations of taurine are directly related to plasma concentrations and low plasma concentrations were found to be associated with myocardial failure in cats, a direct link between decreased taurine concentration in the myocardium and decreased myocardial mechanical function is proposed

Nutrition and cardiomyopathy: lessons from spontaneous animal models.

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Spontaneously occurring dilated cardiomyopathy in dogs and hypertrophic cardiomyopathy in cats are common diseases and are vastly underutilized as models of human cardiac disease. The goals of nutrition are no longer limited to a low-sodium diet, as research is now showing that nutrients can modulate disease and be an important adjunct to medical therapy. Deficiencies of certain nutrients can contribute to cardiomyopathies, as with taurine, but some nutrients-such as n-3 fatty acids, carnitine, and antioxidants-may have specific pharmacologic benefits. Dogs and cats with spontaneous cardiomyopathies are an exciting and promising model for studying nutritional modulation of cardiac disease.

Nutritional and Herbal Therapies in the Treatment of Heart Disease in Cats and Dogs

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Nutritional supplements such as L-carnitine and taurine have been found to be beneficial in dogs and cats with certain cardiac diseases. However, not all animals with cardiac disease respond to nutritional supplementation, which means that further work must be done to identify causes of cardiac disease. Herbal therapies have been used in dogs and cats based on information available from their use in humans. This paper reviews the possible benefits and side effects of L-carnitine, taurine, and herbal supplements.

Nutritional problems in cats: taurine deficiency and vitamin A excess.

Hayes KC.

Two nutritional problems of the cat are reviewed. One represents a deficiency of taurine, the other vitamin A toxicity. Taurine deficiency in cats is insidious because the progressive retinal degeneration induced may go unnoticed until the damage is advanced and irreversible. Both rods and cones undergo degeneration along with the underlying tapetum lucidum. The hyperreflective focal lesion is easily observed in the area centralis with an ophthalmoscope and has been previously identified as feline central retinal degeneration. This lesion is not reversed by taurine supplementation, even though the remaining retina may be saved from further degeneration. The cat requires dietary taurine, found in meat and fish, because it cannot synthesize enough to meet demands for bile acid conjugation and tissue metabolism, especially those of muscle and central nervous system. Vitamin A toxicity is not commonly observed in cats but may occur if cats are fed beef liver in which appreciable vitamin A is stored. Cats exhibit muscle soreness and hyperesthesia, especially along the neck and forelimbs where bony exostoses of cervical verterbrae and longbones are common. The diagnosis is readily made from radiographs. The response to removal of vitamin A from the diet is generally rapid and, unless the toxicity has been chronic in young kittens, recovery is generally satisfactory

Supportive and Symptomatic Care for Dogs and Cats with Hepatic FailureRobert M. Hardy, DVM, MS, DACVIM
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HEPATIC THERAPY

General objectives for therapy of hepatic failure revolve around attempts to eliminatecausative agents, if known, to suppress or eliminate mechanisms that potentiate the illness, toprovide optimal conditions for hepatocellular regeneration, and to control manifestations ofcomplications that develop. Clinical manifestations of hepatic failure are often similar in acuteor chronic hepatic failure, differing primarily in the severity and number of complications thatdevelop. Little controlled work has been done on therapy of spontaneous hepatic diseases in thedog or cat. Most therapeutic recommendations are based on conclusions obtained from trials inexperimental animals or humans.

Specific Therapy for Hepatic Failure

Therapy for hepatic diseases may be either specific (directed at a causative agent) orsupportive and symptomatic (directed at the signs of failure regardless of the cause). At present,there is little in the way of specific therapy available for the majority of known hepatic diseases.This is because the cause for many is not identified or known. If the cause is known. it has nospecific treatment (viruses), or it is no longer present when the disease is diagnosed (cirrhosis).Clinicians are compelled to treat the manifestations of hepatic failure symptomatically in anattempt to prolong the patient's life until sufficient repair and regeneration occurs to sustain life. Even if complete recovery is not possible, as is often the case, by utilizing appropriatetherapeutic manipulations, many animals can remain asymptomatic for months or years. Wherespecific therapy is available, it should obviously be utilized.

Supportive And Symptomatic Therapy

Regardless of the cause for hepatic failure in dogs and cats, most cases will receivesupportive and symptomatic therapy in addition to any specific drugs that may be indicated.Such care is designed to reduce or eliminate the severity of clinical signs while providing optimalconditions for hepatic regeneration. Even if cures are not possible, improvement in the patient'squality and quantity of life can be attained in many instances. In addition to rest and dietarymodifications, a number of drugs may be given to patients in hepatic failure to reduce majorcomplications that develop.

Dietary Modifications

Dietary therapy is the single most important means of modifying the clinical course ofmost spontaneous liver diseases in dogs and cats. Dietary modifications are going to be mosteffective in animals with subacute or chronic diseases because these patients will often be willingto voluntarily consume sufficient quantities of nutrients and calories to meet their body'smaintenance needs as well as those necessary for hepatic repair and regeneration.Animals withacute severe liver disease usually are unwilling to consume any food at all and must be force-fedor given parenteral hyperalimentation to meet their caloric needs.Dietary therapy involves adjusting the diet so that optimal quantities and types ofnutrients are provided to the animal.The intake of the animal must be balanced with its ability tometabolize these foodstuffs with a failing liver. Protein restriction and modification is of majorimportance.The goal is to minimize the alterations in nitrogen metabolism induced by hepatic3failure. Appropriate adjustments in the type and quantity of protein ingested by the patient willlead to a reduction in blood ammonia and a return of circulating branched-chain to aromaticamino acid ratios towards normal.The type and quantity of protein, as well as the frequency offeeding, are all important in reducing clinical signs of hepatic failure.Cottage cheese is a high quality protein source for animals in hepatic failure. Dogsusually find this food more palatable than cats. Cottage cheese contains no additives, is easilyand completely digested and has a good ratio of branched-chain to aromatic amino acids.Thebeneficial effects of cottage cheese are related to the fact that it undergoes less putrifaction andammonia production by intestinal bacteria during digestion, and that there is a reduction in ureasepositive bacteria within the colon when it is fed. Cottage cheese is superior to intravenous caseinhydrolysates in terms of both nitrogen retention and stabilization of plasma amino acid ratios.The lack of food additives in cottage cheese is important as many commercial pet foods containadditives that are metabolized by intestinal bacteria to potent hepatotoxins.The efficientdigestion of cottage cheese within the small bowel results in little residues being available forcolonic bacteria to metabolize. Decreasing intestinal residues reduces both the numbers ofcolonic bacteria and the toxic waste products of their metabolism. Low residue diets alsodecrease intestinal ammonia production by reducing desquamation of intestinal epithelium.Reduced intestinal cell turnover also results in less protein loss through intestinal lymphatics. Food should be provided to patients with hepatic failure three to four times per day. Hepaticfailure patients have reduced ability to handle normal quantities of dietary substrate. By dividingthe total daily nutrient intake into several smaller meals, these patients will maintain theirappetite and intake which will speed their recovery.Dogs with hepatic failure should receive approximately 1 gm/lb/day (2 gm/kg/day) ofhigh biologic value protein.This amount should be adequate for maintenance needs as well asthat needed for repair and regeneration of the liver, without leading to signs of encephalopathy.Cats have a significantly higher protein need and should receive sufficient good quality protein toprovide 30 per cent of their caloric needs as protein. In estimating the protein requirements ofpatients it is important to know the serum albumin concentration. Severe protein restriction inhypoalbuminemic patients may further deplete serum albumin concentrations and lead to ascitesor edema. If clinical signs improve on reduced protein diets but serum albumin concentrationsdo not, the protein content of the diet should be supplemented. The author recommendsincreasing the protein available by 0.25 gm/lb/day (0.5 gm/kg/day) at weekly intervals until eitherprotein anabolism is evident or signs of encephalopathy develop. It is not necessary to increasethe protein beyond 2.5 gm/lb/day (5 gm/kg/day). A commercially available reduced protein dietwhich works well in many dogs and cats with hepatic failure is canine or feline k/d. If animalswill eat enough to meet their caloric needs, this diet will provide sufficient protein for theirmetabolic demands. In some animals, even this reduced protein diet cannot be tolerated and anultra-low protein prescription diet, u/d, for dogs, or s/d for cats, must be utilized. Although thisdiet may not totally meet the protein needs of the liver failure patient, it may allow them tosurvive longer and more comfortably than with other available diets.An easily digested carbohydrate source should form the basis for the bulk of the requireddaily calories for animals with hepatic failure.The carbohydrate source chosen should be easilydigested so that minimal residues remain in the colon where intestinal flora may convert them tovolatile fatty acids.An inexpensive and useful carbohydrate source that meets these needs isboiled white rice.A high carbohydrate diet provides an easily assimilated source of nonproteincalories, which spares body tissues from catabolizing muscle protein for energy, and reduces thecatabolism of dietary nitrogen for energy.4Fats should be given so that they comprise 6 per cent of the dietary calories on a dryweight basis.This will be accomplished by supplying 0.51 gm/lb/day (1.32 gm/kg/day) of fat inthe diet. Fats are necessary to supply essential fatty acids, fat soluble vitamins (A, D, E, K), andimprove

palatability. Excessive fat supplementation may worsen signs of encephalopathy if thefat source contains large quantities of short chain fatty acids, e.g., coconut oil. However, shortchain fatty acids are primarily derived from dietary carbohydrates and to some extent aminoacids, not ingested fats. In general, milk fat, and seed oils are not sources of short chain fattyacids. Another reason for moderate fat restriction is that patients with hepatic failure may havereduced intestinal bile salts which are important for normal fat assimilation. If excessive fats arefed the animal may develop fat malassimilation and steatorrhea. Vitamin and mineral supplementation can be important, especially when diets areformulated at home. Hypovitaminosis is common in liver failure and is caused by multiplefactors. Decreased intake associated with anorexia is of major importance. In addition,increased physiologic demands, accelerated intestinal losses, malutilization and impaired storagecapacity all combine to increase dietary needs for vitamins. Vitamins most often deficient inhumans with hepatic failure include folic acid, B6, B12, thiamin, A, E, riboflavin, nicotinic acid,and pantothenic acid. In addition, the minerals zinc and cobalt are often deficient. Vitamins B6and B12 are particularly important for normal cell regeneration. Cats normally have 2 to 8 timesthe needs of dogs for B-complex vitamins. It is recommended that daily B-complex vitaminrequirements for dogs and cats be doubled. Vitamin C has recently been shown to be reduced inthe blood of dogs with experimental hepatic insufficiency and it should be supplemented at 12mg/lb/day (25 mg/kg/day). Zinc acetate has been supplemented in cirrhotic humans with chronic hepaticencephalopathy, and in short term studies, patients receiving zinc supplementation hadsignificantly improved neurologic status. Blood urea nitrogen concentrations returned to normalfollowing zinc supplementation, implying that zinc deficiency impaired the efficiency of the ureacycle. The recommended dosage for zinc in dogs and cats is 2.2 mg/lb/day (5.0 mg/kg/day). Vitamin and mineral supplements that contain copper should be avoided. This is particularlyimportant for dogs that have copper storage defects or in animals with chronic cholestasis. Ofthe fat soluble vitamins, K and D are the most important. If hemorrhagic tendencies develop inassociation with prolonged cholestasis, parenteral vitamin K1 0.5 to 1.5 mg/lb/day (1 to 3mg/kg/day,) IM may help to return clotting parameters to normal in a few days. Ifcoagulopathies are a result of chronic hepatocellular failure, parenteral vitamins will not beutilized by the failing liver. Fresh whole blood is necessary to stabilize clotting abnormalities inthis situation. The routine use of lipotropic agents containing methionine in dogs and cats in hepaticfailure should not continue. Metabolites of oral methionine can induce signs of hepaticencephalopathy quite easily in experimental dogs. It also acts synergistically with short chainfatty acids and ammonia to induce coma. Recently, it has been shown that methionine can alsoinduce a severe Heinz body hemolytic anemia in cats at dosages of 0.25 to 0.5 mg/lb/day (0.5 to1 gm/kg/day. Lipotropic drugs are of proven value only in cases in which confirmed deficienciesexist. Animals receiving a nutritious diet with adequate quantities of protein have no need formethionine supplementation which may actually worsen signs of disease. For animals that are totally anorectic, nutritional support may be supplied by forcefeeding one of several nutritionally complete liquid diets formulated for use in humans. Theycan be force-fed by syringe or administered through a nasoesophageal catheter or pharyngostomy5tube. Isocal has been used as the sole source of nutrition in experimental dogs that had portalcaval shunts surgically constructed (Eck fistula dogs). The dogs maintained normal weight, andserum albumin concentrations and had no central nervous signs, while those eating standard dogchow continued to deteriorate. Although the liver of Isocal-treated dogs continued to atrophy,the dogs appeared clinically normal. This diet has a relatively high ratio of carbohydrate pergram of protein, which has a protein sparing effect on the body. The author has experience withsimilar diets, Ensure-HN and Impact, which are used commonly in anorectic cats with idiopathiclipidosis. These formulations provide one calorie per milliliter of diet and are an efficient anduseful method of providing oral alimentation to patients in liver failure that will not eat on theirown. For cats, taurine will need to be supplemented at 50 mg/day to these human enteral diets. Several benzodiazepine derivatives may be tried as appetite stimulants for anorectic cats. These drugs are not as effective in dogs. Benzodiazepine compounds stimulate the hunger centerin the brain and can cause voracious feeding in normal cats. Of the available compounds,oxazepam is the most potent, followed by lorazepam, which is more potent than diazepam. Dosages as low as 0.05 mg/lb (0.1 mg/kg) increased food intake by 50 per cent, while 0.12 mg/lb(0.3 mg/kg) caused a 72 percent increase in food intake in normal cats. This effect occurred evenwhen the drug was given 12 hours prior to feeding. Dosages of 4.5 mg/lb (10 mg/kg) resulted insleepiness and ataxia. Diazepam was not as effective, but dosages of 0.12 mg/lb (0.3 mg/kg)caused a 39 per cent increase in food intake and 0.45 mg/lb (1.0 mg/kg) caused an 82 per centincrease in feeding. In the author's experience, diazepam stimulates a very transient interest ineating in cats with hepatic failure, and usually makes them sleepy even at 1.5 to 3 mg total dose. Oxazepam deserves more clinical evaluation in anorectic cats with liver failure to see if it willshorten the time necessary for forced feeding.

Drugs in Hepatic Failure

The liver is quantitatively the most important organ involved with drug metabolism,although the kidney, brain and other organs make significant contributions. For many drugsmetabolized in the liver, their duration and intensity of action may be increased in the presence ofliver disease. However, not all enzyme systems are equally affected by hepatic failure. Anumber of therapeutic agents cause nonspecific induction of hepatic drug metabolizing enzymes,and their metabolism may actually be increased, even in the presence of liver failure. There is notest of liver function that can be run to determine if a given drug will be metabolized normally ina patient with liver failure. As a general rule, most commonly used drugs are well tolerated bypatients with hepatic failure and can be prescribed, as long as animals are monitored for signs oftoxicity.

Antibiotics

Adequate hepatic function does not seem to be a critical factor in the handling of mostantibiotics by patients with liver failure. They are generally given at standard recommendeddosages and dosage intervals. Antibiotics are indicated as specific treatment for primarybacterial hepatitis, hepatic abscesses, bacterial cholangitis, or cholecystitis, and are of great valuein the suppression of intestinal bacteria that are responsible for many of the signs of hepaticencephalopathy (see Complications of Hepatic Failure).6The selection of antibiotics to be used for the treatment of nonhepatic infections shouldbe made with caution. It is best to avoid drugs that require hepatic inactivation or excretion sincethey may reach toxic levels if the failing liver is unable to effectively remove them from thecirculation. Conversely, for treating specific infections of the liver, drugs that are metabolizedand eliminated by the liver are ideal since very high tissue concentrations will develop. All tetracyclines are concentrated in the liver and excreted in bile. Biliary concentrationmay reach 5 to 32 times the serum concentration. Parenteral preparations are known to be toxicin high dosages in humans. A reversible lipidosis occurs in dogs given chlortetracycline, whichis the most hepatotoxic of the group. Tetracyclines also suppress hepatic protein syntheses andthus impair albumin synthesis and enzyme activity in the liver. Prolonged use of these drugshave been associated with decreased vitamin K absorption in man. Because they generally causeanorexia in dogs and cats and have toxic side effects, they are poor choices for animals withhepatic failure. Penicillins, and their newer derivatives, ampicillin and amoxicillin, reach high tissueconcentrations in the liver. They are primarily renally excreted, and are quite safe to use inanimals in hepatic failure. Hetacillin requires conversion to ampicillin by the liver, so this wouldnot be a good choice for animals in liver

failure. Cephalosporins also do not require hepaticmetabolism for biologic activity and are useful for treating systemic infections in patients withliver failure.Chloramphenicol is conjugated by the liver and then excreted by the kidney.Concentrated hepatic tissue and biliary levels are attained. Disadvantages to chloramphenicoloutweigh the potential benefits.The drug is a potent inhibitor of hepatic microsomal enzymesystems and thus inhibits the clearance of many other drugs and waste products producedendogenously. Its half-life is often prolonged in chronic liver disease and may augment its toxicpotential. It also produces anorexia and reversible erythroid hypoplasia both in dogs and cats andthus cannot be recommended for use.Lincomycin, clindamycin, and erythromycin estolate are all cleared by the liver or knownto be hepatotoxic and should be avoided in patients with liver disease because it may potentiatetheir toxicity.

Sedatives, Anticonvulsants, Anesthetics and Analgesics

Sedatives should be avoided in hepatic failure, since their use is commonly associatedwith the development of hepatic coma. Phenobarbital is primarily excreted by the kidney and isthe safest hypnotic. Convulsive states are best controlled using short acting compounds likediazepam (Valium) or chlordiazepoxide (Librium) at reduced dosages.There is potential forhepatotoxicity associated with the use of both phenytoin and primidone.They should not be usedto control seizures in animals with evidence of preexisting liver disease.Avoid analgesics, anesthetics and barbiturates in patients with hepatic failure. Ifanalgesia is required, meperidine, codeine, butorphenol, oxymorphone, or combinations ofdiazepam and ketamine are better tolerated than morphine. Start with smaller dosages that youwould normally use and give more if necessary, rather than give a relative overdose to start with.Of all the inhalent anesthetics, halothane has been frequently incriminated in cases of fulminanthepatic failure in humans following repeated exposures. Similar experiences in dogs or cats areextremely rare. Halothane in combination with hypoxia and metabolic acidosis may behepatotoxic. Because of its relative safety compared to other anesthetics, the author has noconcern about using halothane for anesthetizing metabolically fragile patients in hepatic failure.

Anabolic Androgenic Steroids

Several reports have attributed beneficial effects to the use of androgenic anabolicsteroids in the treatment of chronic liver disease in humans. Drugs evaluated includetestosterone propionate, methandrostenolone, testosterone, methenolone enanthate, andnorethandrolone. Administration of these drugs generally was continued for many months.Thebulk of clinical studies indicates a trend in favor of a positive effect for anabolic steroids in thecourse and prognosis of patients with cirrhosis and possibly other liver diseases. Anabolicsteroids appear to stimulate both hepatic RNA synthesis and protein synthesis in the regeneratingliver, and protect against the induction of fatty liver. One interesting report concerns the use ofnorethandrolone at 120 mg once daily for severe alcoholic fatty liver in humans.The lipidosiswas dramatically reversed in 2 weeks of this treatment.This effect was not observed when 25mg of daily testosterone was used.These compounds warrant clinical evaluations in cirrhosisand idiopathic lipidosis. Regardless of the drug used, for anabolic steroids to be effective,sufficient non-protein calories must be taken in to meet metabolic demands or no anabolic effectswill be seen. Methyltestosterone has been shown to have a mild toxic effect on the dog liver andshould be avoided.

Glucocorticoids

The use of glucocorticoids in hepatic failure remains a controversial subject.They haveproven efficacy only in human chronic active hepatitis and primary biliary cirrhosis.Theirpotential for use in canine chronic active hepatitis and feline cholangitis/cholangiohepatitis iscommon but confirmed evidence for benefit is lacking.The potential benefits to steroid useinclude increased appetite, reductions in serum bilirubin concentrations, reductions intransaminases, lessened BSP retention, and increased serum albumin concentrations. Glucocorticoids also have a mild choleretic effect, and might be useful in diseases associatedwith cholestasis. In spite of these many potential benefits, they are also known to have manydisadvantages. Glucocorticoids fail to prevent the progression of most acute liver diseases tochronic phases; they may increase the chance of intercurrent infections developing; theygenerally do not increase life expectancy; they fail to alter the histology of most liver diseases;and they can aggravate the management of ascites by promoting sodium retention Previouslystable cirrhotic dogs may deteriorate rapidly following the administration of steroids. Recentinformation indicates they also increase the incidence of peptic ulceration in cirrhotic men. Ingeneral, patients in which steroids may have a beneficial effect are those with prolonged anorexiaand weight loss in which increased food intake would be beneficial and those with suspectedimmune mediated hepatobiliary diseases.The dosage and type of glucocorticoid used may be more important in patients withhepatic failure than with other steroid responsive diseases. Short-acting steroids should bechosen; prednisone or prednisolone are the drugs of choice. Prednisone must be converted to itsactive form, prednisolone, by the liver.This should make prednisolone the best choice foranimals in liver failure, but most pharmacologic studies of this problem have concluded thebenefits of one drug over the other are minimal.Another important factor to consider in the useof steroids is that their half-life is often prolonged in animals with liver failure. Unless thedosage is reduced or the dosage interval is increased from those usually considered, signs of8iatrogenic hyperadrenocorticism may develop. Maintenance dosages in dogs may be as low as0.2 mg/kg/day.Ursodeoxycholic acid (Actigall) This naturally occurring bile acid appears to have unique hepatoprotective effects againstother more toxic bile acids. It is known that some bile acids have the potential to be hepatotoxicin high concentrations as would occur in cholestasis of any kind. The hydrophobic, lipophilicbile acids, chenodeoxycholic acid and deoxycholic acid have the greatest potential to causeinjury.They are known to increase in the circulation in chronic liver diseases. Conversely, thehydrophilic, lipophobic bile acid, ursodeoxycholic acid, has just the opposite effects. When usedchronically by the oral route, ursodiol results in decreased concentrations of hepatotoxic serumbile acids and may modify the rate of progression of chronic cholestatic liver diseases. Ursodiolis proposed to exert this hepatoprotective effect via three mechanisms; 1) hypercholeresis, 2) adirect protective effect or by displacement of hydrophobic bile acids from the circulation, and 3)immunomodulation. Only anecdotal evidence has appeared in the veterinary literature about thisdrug. It does not apparently induce any toxic side effects, however, documented evidence ofefficacy is still lacking as well.The current recommended dosage for both dogs and cats is 10 to15 mg/kg once daily orally (300 mg capsules, $1.96 ea in 1998).

Drugs to Control Hepatic Fibrosis

One of the most significant pathologic changes occurring in chronic liver diseases is thedevelopment of fibrosis. Both increased synthesis and decreased degradation of collagen occursin cirrhosis. If causative agents can be identified early in the course of chronic diseases, fibrosismay be completely reversible. However, at some point in the progression of chronic liverdiseases, fibrosis becomes self-perpetuating, even if the causative agent is removed.Immunologic factors appear to play a role in the development and progression of fibrosis in manychronic liver diseases.

Colchicine

Of all the experimental antifibrotic drugs available, colchicine appears to have the mostpotential. Colchicine is an alkaloid, antimitotic agent. This drug has unique anti-inflammatoryproperties but is only licensed for use in gouty arthritis. It binds to microtubule protein andinterferes with the function of mitotic spindles, which can arrest cell division. Colchicineprevents transcellular movement of collagen in fibroblasts and stimulates a two- to 10-foldincrease in collagenase activity. Preliminary clinical trials in human cirrhotics indicate thathistologic progression was halted and mortality was decreased by 25 per cent over a 53 monthperiod of study. In addition, serum albumin concentrations consistently increase in cirrhotichumans receiving colchicine. Therapeutic trials in primary biliary cirrhosis also show benefit. Serum albumin concentrations again increase, while those of bilirubin, cholesterol and ALTdecreased, and mortality was reduced by 50 per cent after 4 years. Only one clinical report of itsuse in dogs has been published. A 4 year old cirrhotic dog was treated for 7 months (0.014mg/lb/day or 0.03 mg/kg/day orally). The dog had deteriorated with the administration ofsteroids but improved clinically after colchicine was started. No toxicity was observed. Reported signs of acute toxicity in humans include nausea, vomiting, diarrhea and abdominalpain. These signs may be reduced by administering the drug intravenously. Chronic toxicity9includes agranulocytosis, aplastic anemia, myopathy and alopecia. The author has evaluatedcolchicine in several dogs with severe chronic liver disease. They showed no clinicalimprovement, but periods of evaluation were less than one month.

D-penicillamine

D-penicillamine is another drug which may be used to modify hepatic fibrosis. Largedosages given to cirrhotic rats (140 mg/lb/day or 300 mg/kg/day) induced significant reductionsin hepatic fibrosis. This dose is much higher than currently recommended for the dog (5 to 7mg/lb/day or 10 to 15 mg/kg/day), and would not likely be tolerated.

THERAPY FOR COMPLICATIONS OF HEPATIC FAILURE

A number of potentially serious complications of hepatic failure may develop in anygiven patient. It is often one or more of these complicating factors that causes the death of thepatient. It is important for clinicians to recognize these complications early in their course andmanage them vigorously if any degree of success is to be obtained.

Hepatic Coma

Hepatic coma is a serious complication of hepatic failure. It is seen most often in youngdogs and cats with congenital portal systemic shunts. Occasionally, an older dog or cat withchronic liver failure will manifest encephalopathic signs as well. In adult animals, signs ofencephalopathy are much less dramatic and often are those of depression, lethargy, vomiting anddiarrhea. The goal of therapy is to control the pathophysiologic mechanisms responsible forinducing the encephalopathy, while the liver attempts to regenerate sufficient tissue to maintainlife. This is accomplished by reducing the entry, production and absorption of gastrointestinal"toxins" and by administering systemic drugs which counteract the effects of the absorbed toxins. The mainstays of therapy for encephalopathy involve reduction of protein intake, suppression or elimination of urease containing intestinal bacteria, and catharsis. In addition, steps must be taken to recognize and eliminate any precipitating factors which may have inducedthe encephalopathy. For animals exhibiting signs of encephalopathy all oral intake of foodshould cease until CNS signs abate. This is particularly important for protein. Cessation of foodintake eliminates dietary sources of ammonia, toxic amines, aromatic amino acids, and shortchain fatty acids which induce encephalopathy. Next, complete catharsis of the colon should beundertaken. Emptying the colon rapidly decreases numbers of colonic bacteria and removespotentially toxic by-products of bacterial metabolism. Although warm water enemas are mostoften used, a more effective method combines substances which impair ammonia production orabsorption in the enema solution. Using a 10 per cent povodone iodine solution as the enemafluid, or adding liquid neomycin sulfate (22 mg/kg) to the enema fluid, results in more efficient, rapid suppression of colonic bacteria, which generate the majority of the blood ammonia. Enemas should be repeated until no fecal material in evident in the evacuated fluid. Another drug which is highly effective in lowering blood ammonia concentrations whenadded to enema fluid is lactulose (1-4-beta-galactosidofructose (Cephulac). Lactulose is asemisynthetic disaccharide which is not metabolized by mammalian intestinal disaccharidases. When this undigested sugar reaches the colon, intestinal bacteria hydrolyze it to lactic, acetic andformic acids, which dramatically lower colon pH. In addition to the pH effect, when large10quantities of unabsorbed solutes are produced in the colon an osmotic diarrhea results. Bloodammonia concentrations are lowered because of several unique attributes of lactulose. Byproductsof lactulose fermentation produce what is termed ionic trapping of ammonia within thecolon. In an acid environment, ammonia (NH_3) accepts a proton to form ammonium (NH_4^+). Ammonium is much less diffusible than ammonia. Thus, ammonium ions remain within thecolon and are excreted rather than being absorbed. This effect occurs at colon pH's of 6.2 or lessand is most noticeable if the colon pH is 5.0 or lower. In addition to ionic trapping, lactulose apparently inhibits ammonia generation by colonicbacteria through a process known as catabolite repression. By providing a carbohydrate source tointestinal bacteria, less proteolysis, peptide degradation and deamination of bacterial proteinsoccurs. This results in significantly less ammonia being generated by colonic bacteria than theywould produce under other circumstances, and this effect is independent of the pH effect. Lactulose containing enemas are much more effective than warm water enemas in reducing bloodammonia concentrations and improving clinical signs. Lactulose is diluted with warm water (30per cent lactulose, 70 per cent water) and given as a retention enema. Approximately 10 to 15ml/lb (22 to 33 mg/kg) is infused and retained in the colon for 20 to 30 minutes beforeevacuation. The pH of the evacuated fluid is measured and if greater than 6.0, another lactuloseenema should be administered. Improvement in neurological status can occur in 2 hours inhumans. As soon as patients are able to tolerate oral liquids, attempts should be made to "sterilize" the gut. Non-absorbable intestinal antibiotics are used to suppress potent urea splitting intestinalflora, which contribute significantly to blood ammonia concentrations. The antibiotic used mostcommonly for this purpose is neomycin sulfate, although kanamycin, vancomycin, andparomomycin may be used interchangeably. The recommended dose for use in dogs and cats isten mg/lb (22 mg/kg) three to four times daily. Other beneficial effects of the use of oralantibiotics are to decrease bacterial deamination of amino acids, and reduce the production ofaromatic amino acids, circulating false neurotransmitters, and short chain fatty acids by gutbacteria. Occasional rare complications to the chronic use of neomycin are oto- andnephrotoxicity, severe diarrhea, and intestinal malabsorption. A number of other systemicallyabsorbed antibiotics may be used in animals with hepatic failure as alternatives toaminoglycosides. One which has received a great deal of interest is metronidazole (Flagly). Metronidazole is active against many of the urease-positive, gram negative anaerobes which arepotent generators of ammonia in the intestinal tract. Most clinical studies have indicated thatmetronidazole is equal in effectiveness to neomycin in controlling blood

ammoniaconcentrations.The recommended dose is nine mg/lb (20 mg/kg) given every eight hours.Toxicity to metronidazole in man, includes nausea, ataxia, dizzyness and paresthesias, and indogs CNS signs may develop as well. Because of the potential for neurotoxicity and decreasedelimination in liver failure, and it may be preferable to administer metronidazole at 5 mg/lb (10mg/kg) TID to animals with encephalopathy. Many animals will also respond to other antibioticssuch as ampicillin, which are effective against intestinal anaerobes. These animals improveclincially while receiving antibiotics but develop signs of illness when antibiotics are stopped.This likely corresponds to the effects the drug has on GI flora, an effect that stops soon after it isdiscontinued.Oral lactulose may be used as an alternative to, or in conjunction with, intestinalantibiotics in the management of hepatic coma. Most surveys indicate that lactulose alone orneomycin alone provides clinical improvement in 80 per cent of humans with chronicencephalopathy. An additional group of patients will benefit from the combination of neomycin11and lactulose since these are sometimes synergistic. Because these two drugs control intestinalammonia formation by different mechanisms, this should not be surprising. It is interesting, thatneomycin does not impair the effectiveness of lactulose in most patients. Since lactulose requiresmetabolism by intestinal bacteria and neomycin kills bacteria, one would think that oralantibiotics would be contraindicated for maximal effectiveness of lactulose. This is not the case.Neomycin inhibits bacterial degradation of lactulose in less than one-third of patients. Lactuloseis degraded by lactulosophilic bacteria of which Bacteroides spp predominate. Bacteroides sppare fairly resistant to the effects of neomycin.To determine whether lactulose degradation isoccurring in animals receiving both drugs, measure stool pH after 7 to 14 days of combinedtherapy. If the stool pH is lower than 6.0 then the lactulose is being metabolized and neomycin isnot impairing its effectiveness. If the stool pH remains around 7.0, lactulose will be ineffectiveand should be discontinued. Lactulose is dosed so that a decrease in fecal pH is produced, butdiarrhea is avoided. Usually cats require 2.5 to 5 ml three times daily and dogs require 2.5 to 25ml three times daily. If watery diarrhea develops, the dosage should be reduced.Alternative methods of controlling hepatic encephalopathy may be tried, but are not likelyto be as effective as lactulose and neomycin. Attempts may be made to repopulate the colon withlactose fermenting, nonurease containing bacteria such as lactobacilli. Unfortunately,supplementing the diet with lactobacillus-containing drugs or yogurt in quantities sufficient tomaintain desirable flora in adequate numbers has not had much clinical success.Specifically formulated intravenous solutions containing primarily branched chain aminoacids as the nitrogen source have been marketed for use in the therapy of acute hepaticencephalopathy (Hepatamine).These solutions are designed to help normalize plasma aminoacid patterns by decreasing muscle catabolism.Decreasing muscle breakdown reduces theconcentration of circulating aromatic amino acids which are considered to be important in thegenesis of hepatic encephalopathy. Experimental work in encephalopathic dogs indicated thatuse of these preparations resulted in marked improvement in neurological status. However, themajority of the published results in humans with chronic encephalopathy does not support that itprovides significant benefit over other well balanced amino acid solutions. Clinicians must beextremely cautious when using inexpensive intravenous protein hydrolysates in animals inhepatic coma. Such solutions have extremely high ammonia concentrations, 1500 to 1900ugm/dl, and may rapidly worsen the clinical status of the patient. Stored blood may also bedangerous in this regard.Another drug which may be considered for use in encephalopathic dogs or cats that fail torespond to traditional therapy is l-dopa (Larodopa, Roche). L-dopa is a precursor tonorepinephrine and dopamine, and when given orally, it raises cerebral dopamine concentrations.It has been used with some success in humans with acute hepatic coma. Patients usually respondby regaining full consciousness in 6 to 12 hours. Unfortunately, responses may be transient eventhough therapy is continued. The recommended dosages, based on those used in man, would bean initial dose of 15 mg/lb followed by 3 mg/lb every 6 hours. No information regarding thesafety or efficacy of l-dopa in animals is available.A new parenteral benzodiazepine antagonist, flumazenil (Mazicon, 0.1 mg/ml, 5 ml vials,$6.00/ml, Hoffmann-LaRoche), has recently become available for clinical use. It is primarilyused in humans to treat benzodiazepine overdosage. However, since some of the signs of hepaticencephalopathy appear related to binding of "neurotoxins" to the benzodiazepine-barbiturate-GABA receptors in the CNS, this drug may reverse the "down regulation" of neural receptorsassociated with PSE. It is indicated for the acute management of encephalopathy, not, long-termcontrol. Current dosage recommendations are 0.03 mg/kg IV as needed to reverse signs of12encephalopathy.Oral cation exchange resins such as cholestyramine have been used in humans andexperimental animals to decrease the absorption of endotoxins from the intestines.Reticuloendothelial function of the liver is known to be impaired in cirrhosis and predisposespatients to bacterial infections. Cholestyramine binds bacterial endotoxin and prevents it frombeing absorbed systemically. No dosage is available for dogs and cats.Additional supportive measures may be necessary in the management of animals withhepatic encephalopathy. Parenteral fluid therapy is often required for several days in patientswith hepatic failure, and the fluid you choose to use can be an important therapeutic decision.Animals with chronic liver failure are often hypokalemic, alkalotic and prone to sodiumretention.The ideal fluid should be supplemented with potassium, be low in sodium and be nonalkalinizing.Sodium bicarbonate is given only if metabolic acidosis develops and is severe (pHis less than 7.1). Fluids containing lactate may be ineffective as alkalinizing agents since theliver is the site of conversion for lactate to bicarbonate and glucose. Either half-strength saline(0.45 per cent), or half-strength saline plus 2.5 per cent dextrose are good choices for fluid needsin the liver failure animal. These fluids should be supplemented with approximately 20 meq/l ofpotassium chloride. Glucose supplementation is beneficial in preventing hypoglycemia, indecreasing peripheral catabolic processes, and in decreasing brain ammonia concentrations.

Ascites and Edema

Ascites is a fairly common complication of chronic hepatic failure, while peripheraledema is very infrequent. Ascites, although varying in severity, is not necessarily harmful.Moderate amounts have minimal physiologic importance. When ascites is severe (marked by thepresence of respiratory distress or hypotension), therapy should be directed at reducing thevolume pharmacologically or mechanically, and also towards measures that will improve hepaticfunction. Patients with advanced hepatic failure and ascites may not have significant diuresisuntil improvement in hepatic function occurs.Low sodium diets and diuretics are the most commonly used means of controlling ascitesformation . If these methods fail, mechanical measures such as peritoneovenous or portal cavalshunting procedures may be tried. Low sodium diets and diuretics form the basis formanagement of most cases. Salt restriction must be severe in cirrhotic animals in order toeffectively manage ascites, and may require reductions in sodium intake that are much belowthose used in congestive heart failure. Commercially available low sodium diets (k/d, h/d, HillsPrescription Diets) may be tried initially, but if a poor response is noted, home-formulated dietsshould be tried. Ultra low sodium intake is on the order of 7 mg/lb/day (15 mg/kg/day) in dogs.Active sodium reabsorption by the kidney plays a major role in the development andperpetuation of cirrhotic ascites. Potent "loop" diuretics are useful in many cases in preventingthis reabsorption and inducing a diuresis. Either furosemide (1 to 2 mg/kg every 8 to 12 hours)or ethacrynic acid may be used. If a significant diuresis does not develop in 4 to 7 days, theinitial dose is doubled. If there is no response to this increased dose, an aldosterone antagonistshould be added to the therapy. A number of complications can develop following furosemideadministration in cirrhotic patients, nearly all of which are dose related.The most

important areelectrolyte disturbances (hypokalemia, hypochloremia, and hyponatremia), hypovolemia, andhepatic coma. Periodic serum electrolyte profiles need to be evaluated in animals receivingpotent diuretics for any period of time. In addition, animals must be monitored carefully to avoidinducing dehydration.13Some animals fail to respond to furosemide. This probably reflects the fact that serumaldosterone levels are very high in many cirrhotics. Hyperaldosteronism causes significantreabsorption of sodium in the distal tubules. Since furosemide promotes sodium excretionprimarily from the loop of Henle, much of the sodium that reaches the distal tubules isreabsorbed under the influence of aldosterone, negating furosemide's diuretic effect. Aldosteroneantagonists should be used in animals whose ascites is refractory to furosemide. Ascitic humancirrhotics who are refractory to furosemide, nearly all respond when spironolactone (Aldactoneor Aldactone-A) or triamterene are added to the diuretic regime. Spironolactone should beadministered at 0.5 to 1 mg/lb twice daily. Response may take several days to be noted. Ifneither a diuresis nor a decrease in ascites is noted, the dosage of spironolactone should bedoubled. In humans, dosages of spironolactone may be 6 to 20 times the usual recommendeddoses before an appropriate diuresis is produced.. In humans, it is possible to predict those thatare likely to need large doses of spironolactone by measuring the UNa/UK ratio. Patients likelyto respond poorly to low dosages of aldosterone antagonists have UNa/UK ratios of less than l.0,while in those that have good initial responses, the ratio is greater than 1.0. Potassiumsupplements should not be given to patients receiving aldosterone antagonists as this may lead tohyperkalemia. Do not attempt to remove ascites through pharmacologic means too vigorously. Asciticfluid has a maximal rate of mobilization of 700 to 900 ml/day in humans. Any net fluid lossbeyond this is at the expense of plasma water. Patients are not normally allowed to lose morethan 200 to 300 ml of net water loss per day (0.2 to 0.3 kg/day weight loss). Diuretics should bestopped once ascites is no longer clinically evident. If it reoccurs after drug withdrawal, thelowest dosage necessary to control ascites build-up should be continued indefinitely. If serumalbumin concentrations can be raised, ascites will often spontaneously regress. If two weeks of salt restriction and appropriate diuretic use do not result in significantreductions in the degree of ascites present, more heroic measures should be considered. Suchmeasures include intermittent paracentesis, surgical implantation of some type orperitoneovenous shunt, or creating a surgical portocaval shunt. Paracentesis for removal ofascites should generally be avoided except as a temporary measure to provide immediate relieffor a dyspneic or painful patient, or for patients in which aggressive medical therapy has beenunsuccessful. Small quantities may be removed for diagnostic purposes. Complicationsassociated with paracentesis of patients in hepatic failure include albumin depletion, peritonitis,hypovolemia, hepatic coma, and oliguria. Two surgical procedures have been used clinically in man and experimentally in dogs, tocontrol chronic, diuretic resistant ascites. The first is the LaVeen shunt, initially developed in1972. The LaVeen shunt is a one-way pressure actuated valve. The valve is inserted into theperitoneal cavity and connected by subcutaneous tubing to the jugular vein. Ascitic fluid ispropelled into the venous system by the pumping action of the diaphragm. Such surgicaldrainage systems have been well tolerated by experimental dogs. These shunts are oftensuccessful in controlling ascites in humans; however, their use is associated with many majorcomplications. Shunt failure due to clogging of the valve occurs in 10 per cent of cases. Analternative surgical procedure for ascites management is the creation of a portal-systemic venousshunt. Such shunts decompress the portal system and relieve portal hypertension. If portalhypertension can be alleviated, ascites may disappear. Unfortunately, this procedure isassociated with high surgical mortality and patients are prone to develop hepatic coma. Thetrade-off lies in whether the ascites is a worse problem than managing the encephalopathy.

Intercurrent Infections

Intercurrent infections are one of the most frequent complications of hepatic cirrhosis. Gram-negative septicemias often develop in humans, with the bowel being the presumed sourceof the infection. Because many cases of chronic active liver disease are associated with a nonspecificfever, an infection tends to be overlooked and must be guarded against. The normal dogliver harbors anaerobic gram-positive organisms that may proliferate if hypoxic conditionsdevelop within the liver. The addition of prophylactic antibiotics to the therapeutic regime ofanimals with acute hepatic failure is justified in such cases.

Malabsorption

Clinically significant malabsorption associated with chronic hepatic and biliary tractdiseases is uncommon in animals. Steatorrhea due to reduced bile salt excretion probably occursin many cholestatic liver diseases but its magnitude has not been assessed. Several products mayhelp alleviate or reduce the severity of the problem. Oral bile salts may increase theemulsification of triglycerides and aid in the digestion and absorption of intestinal fats(Decholin). These products contain unconjugated fractions that are irritating to the bowel andmay cause diarrhea. Neutral fats may be added to the diet in the form of water soluble mediumchain triglycerides (Portagen), which do not require the action of lipase or bile salts forabsorption. This preparation may increase caloric intake and promote weight gains, but it has therisk of aggravating hepatic encephalopathy because it contains significant quantities of shortchain fatty acids. Lastly, occasional cases of biliary tract disease with steatorrhea may benefitfrom the addition of pancreatic enzymes to the diet.

Hemorrhage and Anemia

Coagulopathies associated with hepatic disease are common, but clinical bleedingassociated with the coagulopathy is rare, except in acute fulminant hepatic failure or chronic endstage liver disease. Abnormalities associated with prothrombin deficiencies are frequent. Prothrombin synthesis is impaired in any hepatic disease that compromises the ability of the liverto synthesize prothrombin from dietary precursors. Chronic cholestatic diseases or prolongedbile duct obstruction can induce vitamin-K deficiencies due to impaired absorption of fat solublevitamins. If overt hemorrhage occurs secondary to a coagulopathy, fresh whole blood isnecessary to provide clotting factors and red blood cells. Injections of parenteral vitamin-K1 0.5mg/lb/day (1.1 mg/kg, Menadione) will reverse hypoprothrombinemia associated with bile ductobstruction, but is of no benefit when hemorrhage is secondary to hepatic functional failure. Disseminated intravascular coagulation (DIC) can occur in severe hepatic failure and is verydifficult to manage successfully. If evidence for DIC exists, the patient should be transfused andheparin therapy instituted, 50 units/lb/SQ, three times daily (110 mg/kg). Frequent monitoring ofcoagulation parameters must be done when heparin is given. Bleeding into the gastrointestinaltract is particularly devastating to patients in hepatic failure. Blood is a highly effective proteinsource for inducing hepatic coma. If bleeding is secondary to gastric or duodenal ulcers patientshould be given cimetidine (Tagamet) at 2.5 mg/lb (5 mg;kg) every 8 hours, or ranitidine(Zantac) at 0.25 mg/lb (5 mg/kg) every 12 hours. In addition, ulcer protective agents such assucralfate (Carafate) can be given at 1 gm/27 kg every 6 hours. Anemia of liver failure ismultifactorial. Blood loss, lack of production secondary to malnutrition, and sequestration and15destruction of red blood cells all may play a role. If bleeding tendencies can be controlled andthe liver disease stabilized or reversed, these anemias will resolve. In most animals the degree ofanemia is not severe and the patient will not need transfusions.

Fulminant Hepatic Failure

Fulminant hepatic failure (FHF), is a syndrome associated with acute, massive necrosis ofparenchymal cells and with sudden severe impairment of hepatic function. This syndrome isuncommon in small animals. The causes are variable, but most cases are associated with viralinfections (rare), or exposure to drugs or toxins. The author has observed a number of cases inBedlington terriers with copper toxicosis. Occasional cases occur following severe abdominaltrauma or prolonged hypotension. Before beginning intensive therapy, it is important to be surethe situation is acute and that the patient is not in end stage chronic liver failure . This is becauseacute severe failure is potentially completely reversible, while the outcome of animals withchronic failure is invariably death. The primary goals of therapy are supportive andsymptomatic. The animal is supported long enough for sufficient repair and regeneration tooccur to allow for survival. Fulminant hepatic failure is associated with multiple organ system abnormalities that mayneed to be aggressively managed (Table 1). The majority of humans that die in fulminant failuredo not succumb from the loss of hepatic parenchyma, rather, they most often die from cerebraledema, hemorrhage, or sepsis. Central nervous signs in FHF are due to both hepaticencephalopathy and cerebral edema. Cerebral edema is not seen in chronic hepatic failure. Cerebral edema of FHF is thought to be primarily of vasogenic origin. Permeability of the bloodbrainbarrier is altered, allowing circulating toxins and plasma proteins to egress fromintracerebral capillaries into the extracellular space. The permeability of the blood-brain barrieris increased by ammonia, short chain fatty acids, and mercaptans, which are known to beincreased in the circulation in FHF. If patients are hypoproteinemic, fluid transudation out ofcapillaries is also promoted. Determining whether cerebral edema is present and causing some ofthe CNS signs in these patients is difficult. If the neurological status of the patient continues todeteriorate in spite of aggressive management of hepatic encephalopathy, it is best to treat forcerebral edema for 12 to 24 hours rather than do nothing. Steroids are ineffective in controllingcerebral edema in FHF. Mannitol (20 per cent solution) is given at 0.45 gm/lbIV (1 gm/kg/IV)over 30 minutes and is repeated every 4 hours if the patient does not improve neurologically. Furosemide is also given at 0.5mg/lb/IV (1 to 2 mg/kg/IV) every 8 hours for two or three doses. If patients are hypoproteinemic, plasma transfusions should be given, if available. Hypoglycemiacan be severe in FHF and contribute to the CNS signs. Anorexia, depleted glycogen reserves andreduced hepatic insulin degradation all contribute to this effect. Intravenous glucose may have tobe given as 10 or 20 percent solutions in order to maintain blood glucose concentrations in thenormal range. Frequent blood glucose monitoring is essential. Sepsis is responsible for the death of 10 to 15 per cent of humans with FHF. It isextremely important that great care be taken to maintain asepsis in catheter placement and torapidly control any infections that develop. Broad spectrum antibiotics should be routinelyadministered. Hemorrhage occurs early and often in FHF. Bleeding may be evident from any locationin the body. Hemorrhage is usually secondary to decreases in prothrombin dependent clottingfactors. Increasing gastric pH to greater than 4.0 with intravenous cimetidine or ranitidinesignificantly reduces gastrointestinal bleeding. Hemorrhagic tendencies are managed as16indicated previously. The use of injectable vitamin-K1 is indicated because it may be rapidlyincorporated into prothrombin by newly regenerating hepatocytes. Renal failure occurs in up to 40 percent of patients with FHF and is termed hepato-renalsyndrome. When present, the prognosis is usually very poor. This appears to be a result ofintense renal vasoconstriction, which may cause acute tubular nephrosis. Therapeutic measuresare often ineffective in reversing this problem. Prerenal components must be reversed rapidly. Hemodialysis is often necessary in humans to support patients with hepato-renal syndrome. Glucocorticoids have been used for years in patients with FHF. Recent clinical trials inhumans with viral induced FHF indicate they have no benefit and may be harmful. However,when methylprednisolone was given to rabbits with galactosamine induced FHF, significantlyimproved survival was noted when compared to control animals. Most cases of FHF in humansare viral induced and it was suggested that steroids may have benefit in non-viral FHF.

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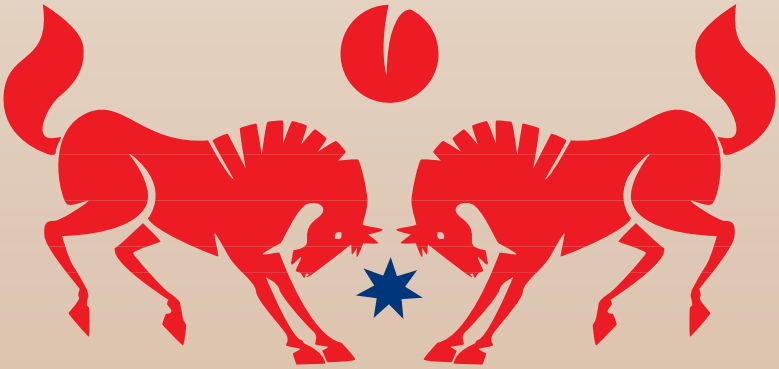
DRUG INDEX

Drug	Dose/Route/Frequency	Indications
Allopurinol	*9.9 mg/kg/os/q8h*	*Uric acid calculi*
Ampicillin	*10-20 mg/kg/os/q6-8h*	*Hepatic coma, sepsis*
Cimetidine	*5 mg/kg/os/q8h*	*GIulcers*
Colchicine	*0.03 mg/kg/os/q24h*	*Antifibrotic agent*
Dehydrocholic acic	*10-15 mg/kg/os/q8h*	*Bile stasis ?*
Diazepam	*0.3 mg/kg/os/q8h*	*Anorexia in cats*
Ensure-HN	*1-kcal/ml*	*Liquid enteral dietsImpactIsocal*
Flumazenil	*0.03-0.075 mg/kg*	*V I Hepatic coma*
Furosemide	*1-2 mg/kg/q8-12h*	*Ascites management*
Heparin	*23 units/kg SQ q8h*	*DIC in liver failure*
Lactulose	*2.5-5 ml/os/q8h (cats)*	*Hepatic coma*
	2.5-25 ml/os/q8h (dogs)	*Hepatic coma*
Metronidazole	*10-15 mg/kg/os/q8h*	*Hepatic coma*
Neomycin sulfate	*22 mg/kg/os/q6-8h*	*Hepatic coma*
Oxazepam	*0.3-0.1 mg/kg/os/q 12h*	*Appetite stimulant,cat*
Prednisone	*1-2 /mkg/q12h*	*Chronic hepatitis dogs,cholangitis-cats*
Ranitidine	*5 mg/kg/q 12h*	*GIulcers*
Spironolactone	*1 mg/kg/q12h*	*Diuretic, ascites*
Ursodeoxycholic acid	*10-15 mg/kg q24h*	*Chronic cholestasis*
Vitamin K1	*1 mg/kg/day/os/IM*	*Bleeding, liver failure*
Zinc sulfate	*0.7-1 mg/kg/q 8h*	*Hepatic coma*

System Abnormalities Seen in Fulminant Hepatic Failure

Major Organ Failure	Metabolic Derangements
Hepatic coma	*Jaundice*
Cerebral edema	*Hypoalbuminemia*
Circulatory failu re	*Coagulopathies*
Respiratory failure	*GI bleeding (ulcers)*
Renal failure	*Hypoglycemia*
Pancreatitis	*Hypothermia*
Electrolyte	*abnormalities*
Acid-base disorders (alkalosis)	*Sepsis*

BULL POWER



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