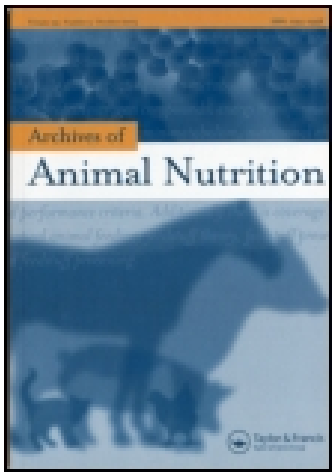


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# Metabolic functions of L-Carnitine and its effects as feed additive in horses. A review

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# METABOLIC FUNCTIONS OF L-CARNITINE AND ITS EFFECTS AS FEED ADDITIVE IN HORSES. A REVIEW

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L-carnitine, a betaine derivative of β-hydroxybutyrate, is found in virtually all cells of higher animals and also in some microorganisms and plants. In animals it is synthesized almost exclusively in the liver. Two essential amino acids, *i.e.*, lysine and methionine serve as primary substrates for its biosynthesis. Also required for its synthesis are sufficient amounts of vitamin $B_6$, nicotinic acids, vitamin C and folate. The first discovered ergogenic function of L-carnitine is the transfer of activated long-chain fatty acids across the inner mitochondrial membrane into the mitochondrial matrix. For this transfer acyl-CoA esters are transesterified to form acylcarnitine esters. Thus, in carnitine deficiency fat oxidation and energy production from fatty acids are markedly impaired. Skeletal muscles constitute the main reservoir of carnitine in the body and have a carnitine concentration at least 200 times higher than blood plasma. Uptake of carnitine by skeletal muscles takes place by an active transport mechanism which transports L-carnitine into muscles probably in the form of an exchange process with γ-butyrobetain.

In young animals including foals, the capacity for biosynthesis of carnitine is not yet fully developed and apparently cannot meet the requirements of sucking animals. Sucking animals depend therefore on an extra supply of carnitine which is usually provided with milk. Additionally, young animals including foals possess a lower concentration of carnitine in blood plasma than adult animals. Besides its role as carrier of activated acyl groups, L-carnitine functions as a buffer for acetyl groups which may be present in excess in different tissues during ketosis and hypoxic muscular activity.

Other functions of L-carnitine are protection of membrane structures, stabilizing of a physiologic CoA-SH/acetyl-CoA ratio and reduction of lactate production. Animal's derived feeds are rich in L-carnitine whereas plants contain usually very little or no carnitine. Carnitine is absorbed from the small intestine by active and passive transport mechanisms. From the increase in renal excretion of L-carnitine after oral supplementations of 10 g/d to horses it has been concluded that the efficiency of absorption of L-carnitine is rather low (about 5 to 10% of the supplied dose). A further decrease in fractional carnitine absorption was observed when the oral dose of carnitine was increased. L-carnitine is virtually not degraded in the body and renal excretion of carnitine is comparatively small under normal conditions. The concentration of L-carnitine in blood plasma of horses varies markedly between animals and between different days. In addition, circadian changes in carnitine concentration in plasma have been reported. Peak concentrations were found during late afternoon, being up to 30% higher than those in the morning.

In breeding mares the carnitine concentration in blood plasma declines with onset of lactation. In resting skeletal muscles about 90% of the total carnitine content is present as free carnitine with the remaining part being available as carnitine esters. With increasing exercise intensity a continuing greater proportion of free carnitine (up to 80%) is converted into carnitine esters, mainly into acetylcarnitine. This shift from free to acetylcarnitine is readily reversed within about 30 min after termination of exercise. It appears that acute exercise does not have a marked effect on the content of total carnitine in skeletal

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muscle whereas training seems to elevate its total concentration in the middle gluteal muscle of 3 to 6 year old horses and to reduce variation of its concentration compared to age-matched untrained horses.

Oral supplementations of 5 to 50 g of L-carnitine per day to horses elevated the carnitine concentration in blood plasma to about twice its basal concentration. No clear relationship existed, however, between the orally administered dose of carnitine and the increase of L-carnitine concentration in blood plasma. Oral supplementations of carnitine also tended to elevate the carnitine concentration in milk of mares and in blood plasma of sucking foals. Long-term oral administration of L-carnitine (*e.g.*, for months) also appeared to increase the carnitine concentration in skeletal muscles. But information is lacking as to whether such administrations also affect physical performance of the exercising muscle.

Oral supplementation of carnitine to horses reduced the resting values of lactate in plasma and appeared to reduce the concentration of non-esterified fatty acids in plasma during exercise. These effects of carnitine appeared also to be influenced by the amount and type of fat which is contained in the feed. Oral supplementations of carnitine to stallions may improve impaired motility of sperm. Improvements of feed conversion and weight gain in growing horses due to oral supplementations of carnitine have been reported. But these preliminary findings probably require further confirmation.

Further studies are also required to better evaluate possible effects of oral supplementations of carnitine on energy metabolism, cardiac functions and physical performance in horses at rest and during exercise, and to perhaps better characterize the conditions under which carnitine may be beneficial to horses.

KEY WORDS: L-Carnitine: Horses: Review: Feed: Additive



## CONTENTS



## 1. INTRODUCTION

The amino acid derivative L-carnitine has gained interest in recent years as a potential feed additive for improving domestic animal production and also as a substance with possibly ergogenic properties for increasing physical performance. In this context experiments have been carried out with various domestic animals including horses in order to study the effects of carnitine on energy metabolism and

on physical performance. Despite a considerable body of information it appears that a number of questions concerning the metabolic effects of carnitine supplementations, particularly in horses, are still unanswered. In this paper an attempt is made to discuss from the published literature the effects of carnitine on horses.

## 2. CHEMISTRY, BIOSYNTHESIS AND OCCURRENCE

The amino acid derivative L-carnitine [L-(-)-3-hydroxy-4N-trimethylaminobutyrate], (Fig. 1) is widely distributed throughout the animal kingdom and may also be found in microorganisms (Emaus and Bieber, 1983; Jung *et al.*, 1993) and in some higher plants (Panter and Mudd, 1969).

Due to its asymmetric structure at carbon 2 the molecule possesses optical activity and exists in two enantiomeric forms. The D-form does not occur in nature but may be obtained by chemical synthesis. Carnitine is a highly polar substance, readily soluble in water and capable of forming an internal salt. Due to its betaine-like structure it is very hygroscopic. The molecule is also of zwitterionic nature and the molecular distance between the acidic and basic groups is about the same than that of lecithin. This chemical property, in addition with some other structural similarities between lecithin and L-carnitine, possibly explains why acylated carnitines can readily traverse through lipid membranes rendering L-carnitine also a suitable carrier for the enzyme mediated transport of long-chain fatty acids across the inner mitochondrial membrane.

In horses as in other mammalian species, carnitine concentrations differ markedly between extra- and intracellular fluids. Apart from epididymal tissues (Brooks, 1980; Carter *et al.*, 1980), carnitine concentrations are highest in skeletal and cardiac muscles and lowest in the extracellular fluid including blood (Harmeyer and Schlumbohm, 1997; Wagenmakers, 1991). In muscles of adult healthy subjects L-carnitine concentrations are at least hundred to two hundred times higher than in blood serum or plasma (Harmeyer and Schlumbohm, 1997). Carnitine concentrations have also been found to be significantly higher in liver ($\sim$3.0 mmol/kg wet weight) and kidney ($\sim$1.0 mmol/kg wet weight) than in blood plasma (Alhomida, 1996; Bell and DeLucia, 1983; Böhles, 1983). In humans and animals skeletal and cardiac muscles constitute the main carnitine reservoir of the body accounting for 80 to 90% of the total carnitine pool (Engel and Rebouche, 1984; Scholte and De Jonge, 1987).

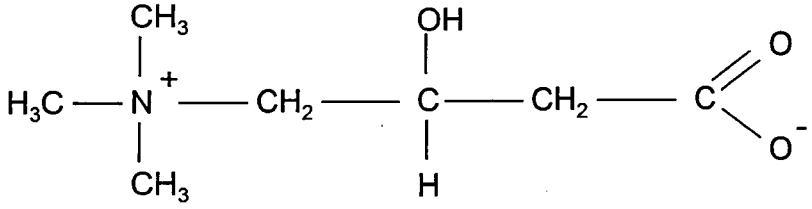


**Fig. 1** L-Carnitine (L-3-hydroxy-4-N-trimethylaminobutyrate)

In early growth the body gradually acquires its full ability to meet the carnitine requirements by endogenous synthesis. This period, depending on species, may last for months or years. Sucking animals usually depend on the provision of carnitine with milk. Despite secretion of substantial amounts of carnitine with milk, carnitine concentrations in blood plasma of sucking animals including foals (Benamou and Harris, 1993) are usually lower than those found in adult animals. Protein bound lysine serves as primary substrate for the biosynthesis of carnitine (Tanphaichitr *et al.*, 1971). In a first series of reactions three methyl groups are transferred from methionine to the $\varepsilon$-N of lysine. These reactions are mediated by S-adenosylmethionine (Bremer, 1961; Paik *et al.*, 1977) which makes L-methionine the second important precursor for carnitine biosynthesis. In addition, biosynthesis of carnitine in animals depends on the presence of a sufficient amount of some vitamins, *i.e.*, vitamin $B_6$, ascorbic acid, nicotinic acid and folate which all function as coenzymes in the course of the biosynthetic pathway. The two $\beta$-C-hydroxylases which are involved in the biosynthetic pathway of carnitine also require the presence of divalent iron ($Fe^{2+}$) (Hulse *et al.*, 1978). The function of L-carnitine may also be impaired by lack of vitamin $B_{12}$ which is necessary for biosynthesis of methionine. This latter compound is an important inhibitor of the ergogenic function of L-carnitine in fat oxidation (Brass and Stabler, 1988).

The immediate precursor of L-carnitine is $\gamma$-butyrobetaine (deoxycarnitine). Whereas this compound can be synthesized by many tissues including muscles its conversion into L-carnitine by the action of $\gamma$-butyrobetaine hydroxylase takes place almost exclusively in the liver, at least in domestic animals (Rebouche and Engel, 1980). Some species specific differences appear to exist in the distribution of $\gamma$-butyrobetaine hydroxylase activity in different tissues. But except in humans, the liver appears to be the main carnitine synthesizing organ of the body. Some biosynthesis of carnitine has, also been reported to occur in testes of rats (Cox and Hoppel, 1974). When judged from the presence of the $\gamma$-butyrobetaine hydroxylase activity, human kidneys also appear to contribute to a certain extent to carnitine synthesis (Rebouche and Engel, 1980). Some carnitine biosynthesis has also been reported to occur in human brain (Rebouche and Engel, 1980), in kidneys of rabbits, cats and Rhesus monkeys (Englard and Carnicero, 1978). In any case, cardiac and skeletal muscles are totally dependent on the provision of L-carnitine from the liver which provides the carnitine *via* the blood stream. Uptake from blood into muscles and into other tissues is mediated by a specific energy requiring sodium dependent and probably secondary active exchange mechanism (Brass, 1992) which at least in part functions as an antiporter with $\gamma$-butyrobetaine (Sartorelli *et al.*, 1985).

## 3. HISTORICAL OVERVIEW

Research about carnitine started comparatively recently (Fraenkel and Friedman, 1957). In 1905 L-carnitine was first isolated from meat extracts almost at the same time by Gulewitsch and Krimberg (1905) in Moscow and Kutscher (1905) in Marburg. The chemical structure of carnitine and its physiological function

remained unclear, however, for some time. In 1927 Tomita and Sendju contributed knowledge to carnitine chemistry by showing that the hydroxy function of $\gamma$-amino-hydroxy-butyrate was located at the $\beta$-carbon. A first indication of the biological function of carnitine was provided by Fraenkel *et al.* (1948) who were studying the vitamin requirements of mealworm (larvae). The authors discovered that growth and metamorphosis of these larvae to adult insects were greatly impaired when the insects were held in a salt mixture in the presence of nine B-vitamins. Insect growth could, however, markedly be improved by addition of liver preparations to the growth medium. The authors named the active principle present in liver extracts vitamin $B_T$, which they presumed to be another vitamin. The letter "T" stands for the abbreviation of *Tenebrio molitor*, the Latin name of the insect under study. And the letter "B" indicates that the authors expected the active principle to be a further B-vitamin (Fraenkel *et al.*, 1948; Fraenkel *et al.*, 1950). In 1952, Carter *et al.*, reported the biological active substance which was required in growth media of mealworms as being identical with L-carnitine. And not before 1962, Kaneko and Yoshida demonstrated that from the two enantiomeres of carnitine, the naturally occurring form was L-carnitine. Metabolic functions of L-carnitine and its involvement in fatty acid oxidation were subsequently identified by a number of investigators, *e.g.*, Bremer (1963); Friedman and Fraenkel (1955); Fritz (1955); Gandour *et al.* (1985); Pande (1975); Ramsay and Tubbs (1975).

## 4. METABOLIC FUNCTIONS

Although L-carnitine participates in several metabolic reactions, its most widely known function is probably its ergogenic effect which results from its involvement in fat metabolism. In this context, L-carnitine acts as a carrier for the bidirectional transport of activated fatty acids through inner mitochondrial membranes (Fig. 2).

Long-chain free fatty acids are activated in the cytosol to form acyl-CoA esters of different chain length. Because the inner mitochondrial membrane is impermeable for these thioesters of coenzyme A the acyl moieties are shifted from the CoA bond to L-carnitine to form acylcarnitine esters. The carnitine esters are then transported into the mitochondrial matrix by an enzyme mediated process, thereby being made available for the $\beta$-oxidation and inclusion of the acetyl moieties into the citric acid cycle. Thus, energy production from long-chain fatty acid oxidation strongly depends on the carrier function of L-carnitine (Fig. 2). Transport of acylcarnitines across the inner mitochondrial membrane takes place as a 1:1 exchange mechanism. With each carnitine ester which passes the inner mitochondrial membrane from the cytosol into the mitochondrial matrix one molecule of free carnitine is transported into the opposite direction. The exchange process may operate in both directions depending on the thermodynamic equilibrium and the concentrations of the substrates, *e.g.*, acetylcarnitine may be transported from the mitochondrial matrix into the cytosol when it is present there in large excess compared to its concentration in the cytosol and *vice versa*.

During energy production acetyl-CoA may be generated through $\beta$-oxidation of long-chain fatty acids, through oxidative decarboxylation of pyruvate, catalyzed by

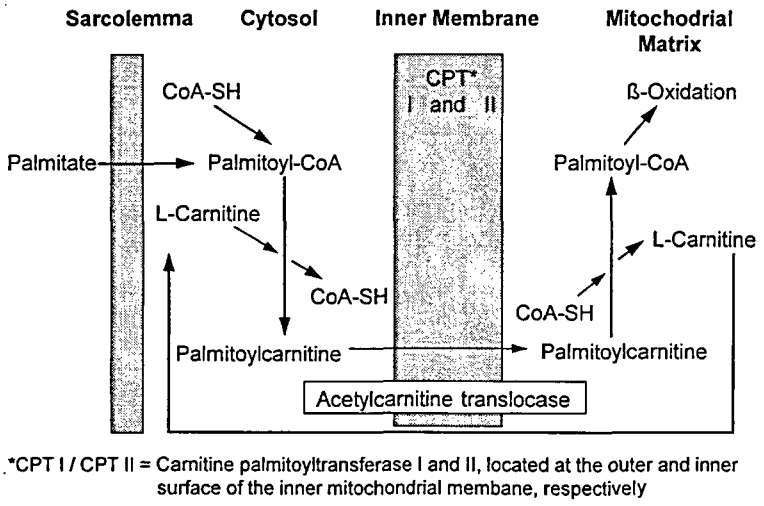


**Fig. 2** Function of L-carnitine for transport of activated long-chain fatty acids (*e.g.*, palmitate) through the inner mitochondrial membrane (Modified after Gürtler and Löster, 1996)

the pyruvate dehydrogenase complex, and by degradation of amino acids. Under certain metabolic conditions, such as ketosis, diabetes, starvation or during high intensity exercise with hypoxia, acetyl-CoA may accumulate in mitochondria (Carter *et al.*, 1981). In such situations L-carnitine may function as an acetyl-buffer. The accumulating acetyl moieties are transferred from coenzyme A to carnitine and stored as acetylcarnitine. Acetylcarnitine may then be transported out of the mitochondria into the cytosol (Hoppel, 1992). The function of L-carnitine as an acetyl buffer exerts beneficial effects to the cell, *e.g.*, by elevating the mitochondrial acetyl-CoA/CoA ratio (Fig. 3). Sufficiently high concentrations of free CoA are required to keep the substrate flux of the citric acid cycle at a high level (Brass and Hoppel, 1980; Bremer, 1995; Hoppel, 1992).

Sequestration of acetyl groups as acetylcarnitine may also facilitate ATP production through the glycolytic pathway which probably predominates during hypoxic muscular exercise. The storage of acetyl moieties as acetylcarnitine retains the activation energy of the CoA-bond for later use. It is possibly this metabolic function of carnitine which explains the remarkably high concentration of L-carnitine in skeletal muscles being in the mieeimolar range. The storage of the acetyl groups as acetylcarnitine has been denoted the "second form" of activated acetic acid. By functioning as an acetyl-buffer, L-carnitine may further facilitate the transport of ATP from the mitochondria into the cytosol. An increased concentration of acetyl-CoA in mitochondria is known to inhibit directly or indirectly the activity of the ATP-synthase ($F_1$, $F_0$-proton ATPase) (Piper and Das, 1987).

Besides the important functions of L-carnitine for the production and control of energy in muscles and other tissues, carnitine probably exerts other effects in the body. There is, for example, evidence that L-carnitine participates in the transport of

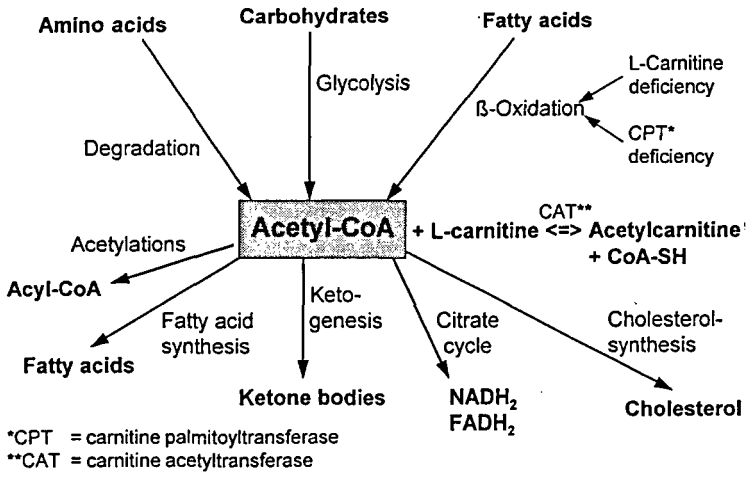


**Fig. 3** Pathways of acetyl-CoA formation and utilization and the function of L-carnitine as acetylbuffer (Modified after Gürtler and Löster, 1996)

activated fatty acids from peroxisomes to mitochondria (Scholte *et al.*, 1996), that it functions as cofactor in the generation of energy from medium-chain fatty acids, pyruvate and ketone bodies (Schonekess and Lopaschuk, 1995), that it has a protective effect on cell membranes through sequestration of excessive amounts of membranetoxic long-chain acyl groups, mainly in the heart (Lamers, 1995) and that it is effective in regulatory control on gluconeogenesis and ketogenesis (Di Lisa *et al.*, 1995; Schonekess and Lopaschuk, 1995). In addition, there is provisional evidence that L-carnitine affects immuno responses by enhancing *e.g.*, phythemagglutinine, bacterial endotoxine and bacteria mediated T-cell and B-cell activation and cytotoxic activities of NK-cells (Uhlenbruck, 1992, 1996).

## 5. L-CARNITINE IN ANIMAL FEEDS

In Table 1 the content of L-carnitine in some feeds of plant and animal origin are compiled. The data show that a significant dietary contribution to body carnitine can only be expected from ingestion of animal derived feeds. Such feeds are, apart from the uptake of limited quantities of skimmed milk powder during rearing periods, of less relevance to horses. Typical horse feeds can be expected to be low in L-carnitine. Vegetable oils also contain, if any, only little amounts of carnitine (Tab. 1).

## 6. INTESTINAL ABSORPTION OF CARNITINE

From the increase in carnitine concentration in blood plasma of horses after its oral administration it can be deduced that carnitine is absorbed in the small intestine (Harris *et al.*, 1995a, b). More careful examination of this problem in other animal species revealed that carnitine is mainly absorbed in the proximal jejunum by both,

**Table 1** Content of L-carnitine in selected feeds [1]

| *Feed* | *[mg/kg or l]* |
|---|---|
| *Feed of plant origin* | |
| Roughages | < 10 |
| Wheat, barley, maize, oats | < 10 |
| Milo corn | – |
| Wheat bran | 10–15 |
| Wheat meal | < 10 |
| Cotton seed | 20–25 |
| Groundnut meal | 5–15 |
| Oil cake (rape, sunflower) | < 10 |
| Extracted oilseed meal (soya, rape, sunflower) | < 10 |
| Roots, tubers | < 10 |
| *Feed of animal origin* | |
| Fish meal | 80–160 |
| Fish and bone meal | 80–100 |
| Blood meal | 155 |
| Plasma protein | 15–25 |
| Feather meal | 125 |
| Meat and bone meal | 150 |
| Cow's milk | 6–50 |
| Goat's milk | 15–20 |
| Sheep's milk | 130–320 |
| Sow's milk | 25–60 |
| Mare's milk | 10–50 |
| Skimmed milk powder | 12–150 |
| Whey powder | 300–1000 |

[1] From Kerner *et al.* (1984); Lonza (1996) and Snoswell and Linzell (1975)



saturable active sodium dependent mechanisms and by non-saturable passive diffusion. A sodium-dependent active transport mechanism was identified in isolated segments of the small intestine from rabbits and rats (Gross and Henderson, 1984; Li *et al.*, 1983; Shaw *et al.*, 1983). At higher carnitine concentrations in the diet, active absorption of carnitine in the upper jejunum is probably paralleled by passive diffusion (Li *et al.*, 1992). Absorption of carnitine from the ileum seems to take place solely by passive diffusion (Shaw *et al.*, 1983). Absorption of L-carnitine is competitively inhibited in the presence of high concentrations of D-carnitine, acetyl-L-carnitine or in the presence of $\gamma$-butyrobetaine (Li *et al.*, 1983; Shaw *et al.*, 1983).

No quantitative measurements have as yet been made to more carefully assess the site of intestinal absorption of carnitine in the horse intestine. Foster *et al.* (1988) offered increasing amounts of carnitine to horses (0, 10, 20, 40 and 60 g/d) and reported that even administration of 60 g carnitine per day resulted in no significant increase in carnitine content of the middle gluteal muscle and that 3.5 to 7.5% of the supplemented dose of carnitine was eliminated with the 24 h urine. From this, they concluded that the absorbability of orally administered carnitine in horses was comparatively low.

In another experiment of Harris and coworkers (1995a) administration of 10 g of carnitine either with feed or *via* esophageal tube resulted in no measurable increase in

renal excretion of carnitine during the subsequent 24 hours. On the other hand, 80 to 90% of an intravenously administered dose of 10 g of carnitine was eliminated with the 24 h urine. The very slight increase in renal excretion of carnitine after an oral dose of 10 g of carnitine indicated that the plasma concentration failed to reach the renal threshold. From this, the authors again concluded that intestinal absorption of orally administered carnitine was comparatively low. Similar findings have been reported for humans. From the study with humans it was estimated that depending on the oral dose (2 and 6 g) 16% and 5%, respectively, were absorbed by the intestine (Harper *et al.*, 1988). But this estimate is probably not entirely conclusive, since the release of absorbed carnitine into the circulation may be delayed by transient storage of carnitine in the intestinal wall (Flores *et al.*, 1996) or in the liver. Erythrocytes have also been shown to possess the ability of sequestering L-carnitine (Rizza *et al.*, 1992). Intestinal absorption of carnitine may also be higher in growing animals for which the carnitine requirement is much higher than for adult animals.

## 7. CARNITINE IN BLOOD AND TISSUES OF HORSES

Information about the concentration of L-carnitine in blood and tissues of horses at rest and its dependence on factors such as age, training and exercise are of interest for the assessment of the physiological role of L-carnitine in this species. Examination of possible effects of oral supplementations of carnitine on its concentration in plasma and tissues, particularly in muscles, is also of interest for evaluating the effectiveness of carnitine supplementations on physical performance. Information related to these problems will be addressed in the following paragraphs.

### *7.1. Carnitine Concentrations in Plasma and the Influence of Age*

The concentration of total carnitine in blood of horses may vary between 15 and 55 μmol/l (Foster *et al.*, 1988; Foster and Harris, 1989a; Foster *et al.*, 1989; Foster and Harris, 1992) with great variation between animals and times of sampling. Seventy to 80% of the total carnitine content in blood plasma is free carnitine (Foster *et al.*, 1988, 1989; Harris *et al.*, 1995a) and about two thirds of the remaining carnitine esters is acetylcarnitine. This leaves about 7% of the total carnitine content in plasma as carnitine esters with fatty acids of long- and medium-chain length. When not measured directly, assessment of this fraction is usually associated with some methodological uncertainty, in particular when it is obtained by subtracting free carnitine and acetylcarnitine from the total amount of carnitine (Foster *et al.*, 1988; Foster and Harris, 1992). In many horses (Foster *et al.*, 1988), but not in all animals (Harmeyer *et al.*, 1998) and also not in yearlings (Foster *et al.*, 1989), the total carnitine concentration increases in the course of the day. Morning values of carnitine are usually lower than those present during the afternoon. Peak concentrations are reached during late afternoon (Foster *et al.*, 1988). The circadian fluctuation may sometimes amount to 30% but is superimposed by large variation present in individual animals (Tab. 2).

**Table 2** Basal concentration of L-carnitine in plasma [μmol/l] of six horses during the day (Means ± SD) (from Harris *et al.*, 1995)

| | *Hours* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 08.00 | 09.00 | 10.00 | 11.00 | 12.00 | 14.00 | 16.00 | 20.00 | 22.00 | *Signi-ficance* |
| FC[1)] | 22 | 22 | 22 | 25 | 25 | 29 | 32 | 34 | 34 | *** |
| | ±5.6 | ±5.1 | ±5.3 | ±4.5 | ±6.3 | ±5.5 | ±6.8 | ±8.3 | ±7.4 | |
| AC[2] | 4.1 | 4.3 | 5.7 | 3.7 | 4.2 | 4.4 | 3.9 | 4.8 | 4.8 | n.s. |
| | ±2.0 | ±2.6 | ±1.6 | ±1.6 | ±2.1 | ±2.3 | ±0.6 | ±2.4 | ±1.5 | |
| TC[3] | 29 | 29 | 32 | 30 | 34 | 38 | 40 | 44 | 41 | *** |
| | ±6.9 | ±5.7 | ±8.6 | ±4.3 | ±5.7 | ±7.4 | ±7.2 | ±10 | ±11 | |
| AcyC[4] | 2.1 | 2.4 | 4.2 | 2.0 | 5.2 | 5.2 | 3.3 | 4.7 | 2.0 | |

[1] FC = free carnitine
[2] AC = acetylcarnitine
[3] TC = total carnitine
[4] AcyC = acylcarnitine
*** = $P < 0.01$

Mean concentrations of free carnitine in horses and thereby also the concentration of total carnitine in plasma increase significantly with age from about 15 to 25 and eventually to more than 30 μmol/l ($P < 0.001$) (Foster and Harris, 1989a). Most of this increase takes place during the first three years of age. After this age the concentration remains fairly stable. The total carnitine concentration in plasma of foals and yearlings is usually less than half of that present in adult animals (Tab. 3) (Foster *et al.*, 1989).

These findings indicate that in foals and yearlings endogenous production of carnitine is either still limited or that their requirement for L-carnitine is less than that of adult animals. Relatively low concentrations of carnitine in plasma can also be observed in young individuals of other animal species (Deufel, 1990). The concentration of free carnitine in plasma of horses is independent from breed and sex (Foster and Harris 1989b, Szilágyi *et al.*, 1992). It appears to be a little bit lower than that found in humans (~ 30 to 40 μmol/l) (Rebouche *et al.*, 1993) and in other animal species (Szilágyi *et al.*, 1992).

In breeding mares the carnitine concentration in plasma drops immediately after birth by about 25% and remains low during the lactation period (Benamou and Harris, 1993). The sudden drop of plasma carnitine during the first days *post partum*

**Table 3** Mean concentration of free carnitine in the plasma of Thoroughbred horses (from Foster and Harris, 1989)

| *Age and status of the horse* | *Free carnitine in plasma [μmol/l]* |
|---|---|
| Foals | 8.0 |
| Yearlings | 7.8 |
| 2-years old | 15.0 |
| 3-years old | 26.3 |
| 4–6 years old | 27.0 |
| > 7 years old (grazing mares) | 21.0 |
| > 7 years old (mares with foals) | 24.6 |

is even greater in the sucking foals than in blood of their mothers (from 21 to 12 μmol/l) (Benamou and Harris, 1993). The higher carnitine concentration in plasma of foals shortly after foaling compared to the subsequent sucking period suggests that the drop in carnitine results mainly from a limited supply of dietary carnitine.

### *7.2. Carnitine Concentration in Muscle*

In the middle gluteal muscle the concentration of total carnitine is about 200 times greater than in blood plasma (Harris *et al.*, 1995). At rest almost 90% of the total carnitine is present as free carnitine. The larger portion of the remaining carnitine esters is acetylcarnitine (Foster and Harris, 1987a, b). Though less clear than for blood plasma, the total carnitine content of the middle gluteal also increases with age (Tab. 4) (Foster and Harris, 1992).

The age related increase does, however, not follow a common pattern in different muscles since it was most apparent in the *M. triceps* and diaphragm and less marked in the *M. semitendinosus* and the superficial portion of the middle gluteal (Foster *et al.*, 1987). In adult horses the total carnitine concentration in the *M. triceps* and middle gluteal reached values of 28 to 30 mmol/kg DM (Foster and Harris, 1987b). At rest the largest portion of this carnitine (about 80 to 88%) was present as free carnitine and 5 to 15% as acetylcarnitine. Only a small fraction of the total carnitine content in muscles was present as carnitine esters with chain length > 2.

### *7.3. Influence of Training and Exercise on Carnitine Concentration in Plasma and Muscles*

It appears improbable that training markedly affects plasma carnitine concentration. Foster and Harris (1989a) found, however, a significantly higher (+30%) concentration of free carnitine in plasma of trained 3 to 6 year old horses than in plasma of untrained age-matched animals. In humans the concentration of carnitine in blood plasma appears also to be about the same in trained and untrained subjects (Arenas *et al.*, 1991; Bordin *et al.*, 1992). The same is true for the total carnitine concentration in human muscle (Huertas *et al.*, 1992; Janssen *et al.*, 1989). From experiments with rats it is known that the capacity of the muscle to oxidize fatty acids almost doubles in the course of training (Molé *et al.*, 1971).

This increase in metabolic capacity is paralleled by an increase in the activities of various enzymes participating in energy metabolism, including carnitine palmitoyl transferase. It is possible that such increases in enzyme activity alone may already

**Table 4** Total carnitine concentration in middle gluteal muscle of Thoroughbred horses (from Foster and Harris, 1992)

| *Age of horses* | *Total carnitine in the middle gluteal muscle [mmol/kg DM]* |
|---|---|
| Yearlings | 10.5–18.8 |
| 2-years old | 14.1–34.7 |
| > 3 years old | 21.3–35.5 |

account for the increased capacity of trained muscles to oxidize fatty acids. In horses, the activities of various muscle enzymes also show an about twofold rise as a result of training (Guy and Snow, 1977). There is no clear evidence that training markedly affects the carnitine concentration in equine muscles. Foster and Harris (1992) measured the carnitine concentration in the middle gluteal in a number of trained and untrained horses. They did not find much of an increase of total carnitine as result of training. The total carnitine concentration in the middle gluteal showed, however, much less variation in trained than in untrained horses (Tab. 5).

A positive correlation was found in the study of Foster and Harris (1992) between total carnitine in muscle and the activity of the mitochondrial marker enzyme, citrate synthase. The authors interpreted this as an indication for coupling between the carnitine content of the muscle and a training-induced increase in mitochondrial density in the myocytes. But this interpretation may not yet be the final answer, since about 90% of the intracellular carnitine appears to be located in the cytosol rather than in the mitochondrial matrix (Idell-Wenger *et al.*, 1978).

Besides examination of basal concentrations of carnitine in plasma and muscles of trained and untrained horses, it appears also of interest to study the effect of exercise on the partition of carnitine into free carnitine and into carnitine esters. In most investigations dealing with this problem short episodes of high intensity exercise were used. Although, no significant changes in the concentrations of total carnitine occurred in both, plasma and middle gluteal muscle (Foster and Harris, 1987b, 1992; Harris and Foster, 1990) a dramatic shift was found to take place from free carnitine to acetylcarnitine (Fig. 4).

This implies that the concentration of acetylcarnitine increased while the concentration of free carnitine decreased (Carlin *et al.*, 1990). In fact, already at low and moderate intensities of exercise, such as a two minutes canter at a speed of 6 m/s, the acetylcarnitine concentration increased to about twice of its resting value. The increase was associated with an equivalent reduction in the concentration of free carnitine (Fig. 5) (Harris and Foster, 1990).

In this study the authors used a comparatively low level of exercise which kept the concentrations of lactate and glycerol-3-phosphate still at their resting values. Nevertheless the ratio of free carnitine/acetylcarnitine had already declined. The finding, therefore, demonstrated that this ratio is probably a quite sensitive indicator for the degree of energy production in exercising muscles. With increasing exercise intensity the concentration of free carnitine in the middle gluteal further decreased, altogether by about 60% (from 24.3 to 9.6 mmol/kg DM). Again, this large decrease was accompanied by a corresponding increase in acetylcarnitine concentration (from

**Table 5** Concentration of total carnitine in the middle gluteal muscle of two-year old Thoroughbred horses with differed training levels (from Foster and Harris, 1992)

| *Training status* | *Total carnitine in the middle gluteal muscle [mmol/kg DM]* |
|---|---|
| Untrained | 18.5 – 34.7 |
| Slightly trained | 14.1 – 24.2 |
| Fully trained | 22.9 – 26.9 |

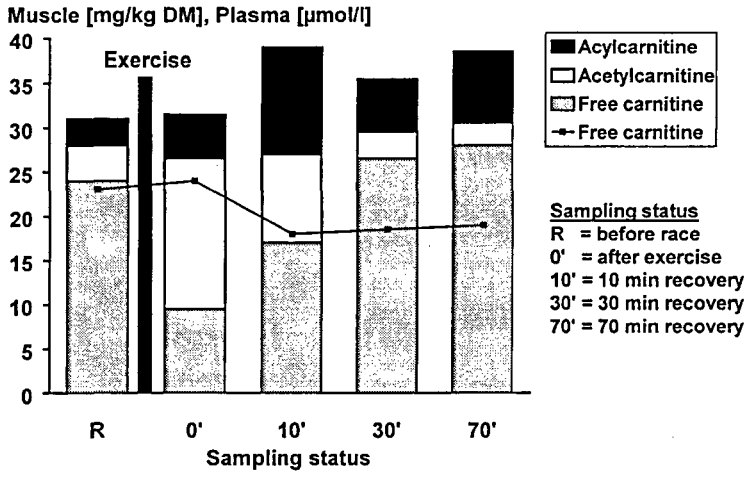


**Fig. 4** Effect of exercise on the concentration of carnitine in the middle gluteal muscle (bars) and plasma (line) of horses (Data from Foster and Harris, 1987b)

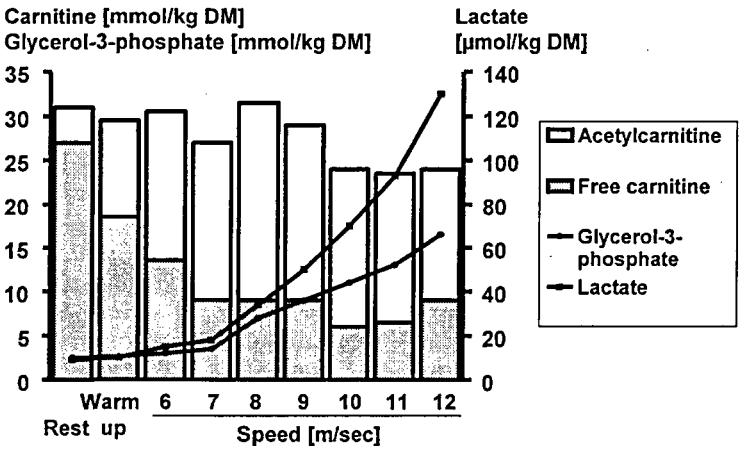


**Fig. 5** Concentration of carnitine, lactate and glycerol-3-phosphate in the middle gluteal muscle of horses during exercise of increasing intensity (Data from Harris and Foster, 1990)

3 to 20 mmol/kg DM) (Fig. 5). Interestingly, the acetylcarnitine concentration did not increase further when the running speed of the horses was further elevated up to 12 m/s. And there was also no further drop in free carnitine concentration. Peak concentrations of acetylcarnitine in the middle gluteal was measurable shortly before the exercise intensity reached the lactate threshold (Fig. 5). Even during high intensity exercise the free carnitine in muscle was at no time completely converted into acetylcarnitine. About 30 min post-exercise, the concentrations of free carnitine and carnitine esters had almost returned to their resting values (Fig. 4) (Harris and Foster, 1990).

The short episodes of intensive exercise did not cause significant changes in the concentration of total carnitine in the middle gluteal (Foster and Harris, 1992). It appeared that the increase in acetylcarnitine always fully accounted for the drop in free carnitine (Harris and Foster, 1990). The shift from free carnitine to acetylcarnitine in the working muscle tallies with the role of carnitine in keeping the intramitochondrial acetyl-CoA/CoA ratio low and in serving as a temporary reservoir for activated acetyl moieties (Foster and Harris, 1987b). The drop in concentration of free carnitine in muscle during episodes of intensive exercise may also limit the transport of long chain fatty acids into the mitochondria. This effect might be beneficial to muscle cells in a situation of hypoxia where long-chain fatty acids cannot contribute much to mitochondrial energy production.



### *7.4. Effects of Carnitine Supplementations*

*Blood Plasma* It has been speculated that the shift from free carnitine to acetylcarnitine in muscles during acute intense exercise might be facilitated by provision of extra carnitine. In humans, for example, an exercise induced decline of free carnitine in muscles was offset by an oral supplementation of L-carnitine (Arenas *et al.*, 1991). With horses as with many other animal species it has been shown that oral administration of L-carnitine elevates the carnitine concentration in blood plasma (Foster and Harris 1989b; Foster *et al.*, 1989). In an experiment with trotting horses where the animals consumed daily 300 g of soya oil in a mixed feed the ration was supplemented with either 0, 1 or 6 g of L-carnitine per day (Falaschini and Trombetta, 1994). The authors reported that addition of soya oil alone did already elevate the concentration of carnitine in plasma. This effect was further enhanced by supplemental carnitine. Surprisingly, the concentration of carnitine in plasma in the two carnitine supplemented groups was highest in those animals which received 1 g of carnitine per day rather than 6 g. Lack of a relationship between oral doses of L-carnitine (5 and 15 g) and the increase in carnitine concentration in plasma was also observed in own experiments (Harmeyer *et al.*, 1998). In another experiment with adult horses 10 g of L-carnitine per day were either administered with feed or applied *via* esophageal tube. Both types of carnitine administration almost doubled the blood carnitine concentration within about 4 h after dosing. The rise in concentration was followed by a gradual return to normal values which, however, were not yet fully attained before 12 h post administration (Tab. 6) (Harris *et al.*, 1995a, b).

From the relatively small increase in carnitine concentration in plasma with respect to the administered dose of 10 g it was concluded that the availability of orally administered carnitine was low. Intravenous injection of an equal amount of carnitine elevated the carnitine concentration in plasma from 25 to about 1000 µmol/l (Harris *et al.*, 1995a). In another 58 days lasting test with Thoroughbred horses increasing L-carnitine supplements from zero to 60 g/d were administered with feed. The carnitine supplements were given in two to three portions and resulted in an increase in the plasma concentration of both, free and acetylcarnitine (Foster *et al.*, 1988). The concentration of free carnitine in this experiment rose from 21 to 32 µmol/l 5 hours after administration of 10 g . When, however, two portions

**Table 6** Concentration of carnitine in plasma[μmol/l] of six horses after oral supplementation of 10 g of L-carnitine. The carnitine was administered either *via* naso-gastric tube (top) or with feed (bottom) (Means ± SD) (from Harris *et al.*, 1995)

| | *Hours* | | | | | | | | | *Signi-* |
|---|---|---|---|---|---|---|---|---|---|---|
| | 08.00 | 09.00 | 10.00 | 11.00 | 12.00 | 14.00 | 16.00 | 20.00 | 22.00 | *ficance* |
| | | | | | *L-carnitine via naso-gastric tube* | | | | | |
| FC* | 26 | 30 | 35 | 37 | 37 | 36 | 33 | 35 | 30 | *** |
| | ±6.8 | ±6.5 | ±5.5 | ±8.2 | ±6.2 | ±6.6 | ±7.7 | ±6.1 | ±9.1 | |
| AC | 2.1 | 2.4 | 5.1 | 3.6 | 4.7 | 4.2 | 4.2 | 3.3 | 3.0 | n.s. |
| | ±1.8 | ±2.4 | ±0.9 | ±1.6 | ±1.8 | ±2.6 | ±1.3 | ±1.1 | ±2.0 | |
| TC | 33 | 39 | 45 | 50 | 47 | 43 | 41 | 43 | 41 | *** |
| | ±7.2 | ±9.0 | ±7.6 | ±7.8 | ±7.5 | ±7.9 | ±7.9 | ±8.3 | ±8.4 | |
| AcyC | 4.2 | 7.1 | 5.1 | 9.3 | 5.1 | 3.1 | 4.0 | 5.5 | 8.5 | |
| | | | | | *L-carnitine with feed* | | | | | |
| FC | 23 | 32 | 38 | 41 | 39 | 42 | 37 | 38 | 37 | *** |
| | ±2.5 | ±3.2 | ±4.9 | ±6.5 | ±5.5 | ±6.6 | ±4.9 | ±4.8 | ±6.8 | |
| AC | 4.2 | 6.1 | 6.4 | 6.2 | 6.1 | 6.2 | 4.9 | 6.0 | 4.5 | n.s. |
| | ±1.6 | ±2.4 | ±0.9 | ±0.9 | ±2.0 | ±1.8 | ±1.0 | ±1.6 | ±1.4 | |
| TC | 29 | 38 | 50 | 51 | 49 | 50 | 51 | 50 | 45 | |
| | ±2.6 | ±5.3 | ±7.3 | ±8.1 | ±7.0 | ±5.9 | ±9.2 | ±11.3 | ±6.3 | |
| AcyC | 1.8 | 0.1 | 5.9 | 3.2 | 3.8 | 2.1 | 8.6 | 6.3 | 3.9 | |

* see foot note of Table 2

of 30 g of L-carnitine were offered, one with the morning and one with the evening feed, the increase in plasma was only slightly greater (*i.e.*, up to 37 μmol/l). The higher dose of L-carnitine, however, also elevated the concentration of acetylcarnitine in plasma from 1 to 5.5 μmol/l with peak concentration 7 h after feeding. Single oral doses of 10 to 30 g of carnitine per day caused the plasma carnitine concentration to peak between the 2nd and the 4th postprandial hour. When carnitine supplementations were offered in two portions, *e.g.*, with morning and evening feed, the plasma free carnitine concentration remained more stable during the day attaining about 2.3 times the basal concentration.

In another experiment the effect of triple doses of oral carnitine was examined on total carnitine concentration in plasma (Foster and Harris, 1989b). Amounts of 5, 10 and 20 g, when offered three times a day, transiently doubled the plasma carnitine concentration but showed no clear relationship between the peak concentration in plasma and the dose level. Increasing the carnitine dose from 5 to 20 g per meal caused the plateau concentration of carnitine to be reached sooner. The authors concluded from these experiments that elevation of the plasma carnitine concentration by oral supplementations might be limited by the intestinal transport capacity for L-carnitine. Possible effects of a supplementation of carnitine on hepatic storage or biosynthesis of carnitine and, thereby also on carnitine turnover in plasma were not examined in this study. With newborn and adult rats it has been demonstrated that the intestine and liver are capable of retaining significant amounts of carnitine after feeding (Flores *et al.*, 1996; Gudjonsson *et al.*, 1985). In situations under which oral supplementations of carnitine to horses are regarded to be necessary for practical purposes and for minimizing fluctuations of plasma carnitine concentration, Foster and Harris (1989b) recommended more frequent administrations of

small amounts of L-carnitine rather than the administration of one large single dose. Elevation of the plasma carnitine concentration by oral supplementations could also be brought about in yearlings (Foster *et al.*, 1989). In this study a dose of 10 g elevated the plasma free carnitine concentration from 12 to 21 μmol/l and the total concentration of carnitine from 18 to 29 μmol/l. In this experiment the concentration of acetylcarnitine remained virtually unaffected. The peak concentration in plasma was reached between the 2nd and the 4th postprandial hour. It should be born in mind that effects of oral supplementations of carnitine on plasma carnitine may be confounded by its circadian changes.

Positive effects of oral supplementations of L-carnitine on its concentration in plasma were also observed in lactating mares and sucking foals. In an experiment from Benamou and Harris (1993) 5 g of L-carnitine was offered to a group of 14 mares two times a day from the 2nd week *ante partum* until the 3rd month of lactation. The carnitine supplementation caused a rise in total carnitine concentration in plasma of mares from 26 to 46 μmol/l. The supplementation of carnitine, however, could not prevent a fall in plasma carnitine in both, mares and foals during the first few days *post partum*. This fall occurred in similar form in the supplemented and the non-supplemented group of animals. However, whereas in the non-supplemented group of mares the plasma carnitine concentration remained at a reduced level it was readily reversed in the supplemented group of mares and foals. In eventers the concentration of plasma free carnitine was significantly increased from 23 to 34 μmol/l by long term administration of 5 g of L-carnitine per day (Iben *et al.*, 1992).

*Kinetic Parameters of Carnitine in Plasma* The rate of disappearance of carnitine from plasma during the first 12 h after an intravenous injection of 10 g of carnitine has also been examined. The decay in plasma carnitine could best be described by a two exponential equation (Harris *et al.*, 1995a). Applying a compartmental analysis mean half times of 20 and 146 min were calculated for the first and the second compartment, respectively. These estimates, however, appear not to be applicable to basal conditions of the animals during which the carnitine pool in plasma is undoubtedly considerably smaller than in these experiments after the intravenous load. From this, it may be expected that the half-times are longer under basal conditions than after an intravenous load of carnitine. The increase of the carnitine pool in plasma due to the intravenous injection of 10 g of L-carnitine also resulted in a marked increase in the renal clearance of carnitine. This effect probably further elevated the carnitine turnover in the experiment of Harris *et al.* (1995a) compared to that present under basal conditions.

*Skeletal Muscles* Information is scarce about possible effects of oral doses of carnitine on its concentration in skeletal muscles. In any case, if such effects exist they appear to be less marked than those observed on its concentration in plasma. Increases in the middle gluteal muscle of exercising horses were barely significant and seldom exceeded 3 to 5% even after 8 weeks of oral supplementation of 10 to 60 g of carnitine per day (Foster *et al.*, 1988). Positive effects of oral supplementations on carnitine content in muscle may be difficult to measure since the carnitine pool of skeletal muscles is more than 200 times greater than that of blood plasma. No significant effect on carnitine content in the middle gluteal was also found in another

study of Harris *et al.* (1995a) with non-exercising horses. In this experiment the horses received either oral supplementations of 10 g/d or intravenous injections of 10 g of L-carnitine for 26 days. Between 80 and 90% of the intravenously injected carnitine was recovered with urine within the following 24 h. Both forms of carnitine administration did not affect the carnitine concentration in muscle. In contrast to these observations, significant increases in muscle carnitine were reported after oral administrations in other species, *e.g.*, in piglets (Coffey *et al.*, 1991), rats (Cerretelli and Marconi, 1990) or chicken (Iben and Meinart, 1997). It might be of interest to further examine whether long-term oral supplementations of carnitine in combination with training affects the content of carnitine in equine muscles.

## 8. DEVELOPMENTAL AND CLINICAL ASPECTS OF L-CARNITINE IN HORSES

Information is very circumstantial about the effect of carnitine supplementations on other biochemical parameters, and in particular, on physical performance in horses.

### *8.1. Broodmares and Stallions*

It has been suggested that a supplementation of carnitine might positively influence breeding animals. The primary energy source of the equine foetus is maternal glucose. Immediately after birth, the energy metabolism of the neonate changes by shifting from glucose oxidation to an increased utilization of fat. This is either released from adipose tissues or is derived from mothers' milk (Novak and Monkus, 1972). In horses about 25% of the total energy provided with milk is derived from fat (calculated from GfE, 1994). In humans depletion of the glycogen stores of muscle and liver takes place probably during the first 24 h after birth (Borum, 1981). Availability of adequate amounts of carnitine during this transition period for enabling fatty acid oxidation appears desirable. In foals the carnitine concentration in plasma decreases markedly during the first week after birth to about 1/3 the concentration found in mature horses (Benamou and Harris, 1993; Foster *et al.*, 1989). This contrasts, for example, with human infants and rat pubs in which plasma carnitine increases concomitantly with first intake of milk. In foals the lowered level of L-carnitine in plasma persists during the whole period of sucking. When the dam is offered oral carnitine its concentration in plasma begins to rise after birth (Benamou and Harris, 1993). In young horses, carnitine levels comparable to those found in adult horses, are not reached until the second or third year of life (Foster *et al.*, 1989). In view of the relatively low concentrations of L-carnitine in foals' plasma (Foster *et al.*, 1989) and in some fetal tissues (Foster *et al.*, 1987) it might appear advantageous to offer some extra carnitine with feed to the dam during late pregnancy and during lactation. This will by virtue increase the carnitine content in milk and improve the carnitine status of the foal. But information is still lacking as to whether this is really necessary. No significant differences in birth weight, weight gain and other growth parameters have been observed so far in foals which could be

related to the supplemental carnitine (Benamou and Harris, 1993). A clear relationship between an elevation of the total carnitine concentration in milk of dams and the carnitine concentration in plasma of the foals which received this milk could not be demonstrated. Other studies (Harmeyer *et al.*, unpublished) have, however, indicated that various clinical problems in mares and/or foals which may occur at birth or shortly thereafter negatively affect the carnitine status of the mares. In such clinical situations the carnitine concentration in plasma further declines and may sometimes reach critically low values. Supplementation of the mares' feed with carnitine may be advantageous in these situations.

*Stallions* Investigations with other species have shown that oral supplementations of L-carnitine may positively affect fertility parameters of semen such as percentage of forward motility of sperm cells. This is particularly true for semen which shows impaired fertility (Brooks, 1980). In a study from Herfen *et al.* (1997) two doses of 6 g of L-carnitine per day were offered with feed over a period of six months to five stallions with unsatisfactory sperm quality before the supplementation. Three other stallions served as non-supplemented controls. Carnitine administration improved sperm motility of the supplemented animals. Allowing for seasonal variations, ejaculate quality of the control stallions remained unchanged.

### *8.2. Growing Horses*

In one experiment 8 cold-blooded yearlings with 400 to 450 kg of body weight were supplemented with 10 g L-carnitine/d for $2\frac{1}{2}$ months. The carnitine supplement was applied in two portions per day. Seven age-matched other horses served as un-supplemented controls (Hausenblasz *et al.*, 1996). The daily gain of the supplemented horses was significantly higher than that of the control animals (641 *vs.* 551 g/d). The efficiencies of utilization of digestible energy (DE) and digestible protein (DP) were in the supplemented group 186 MJ DE and 1413 g DP per kg gain and in the control group 217 MJ and 1643 g DP per kg. The supplemented horses consumed 15.6 g L-carnitine per kg of body weight gain. It should be noted that no comparably high responses of carnitine supplements on weight gain have been observed in similar experiments for example with pigs (Van Kempen and Odle, 1995) or broilers (Rabie *et al.*, 1997) or bulls (Roos *et al.*, 1992). Therefore, the findings of Hausenblasz *et al.* (1996) should await confirmation from other experiments. The concentrations of glucose and urea in plasma were significantly increased in the horses which received carnitine and the concentration of triglycerides was reduced (Tab. 7).

The authors suggested that the carnitine supplementation might have modified the energy metabolism of the horses by inducing a change from a predominant use of glucose towards an increased utilization of fat. The authors had no explanation for the observed increase in blood urea in the carnitine supplemented group of horses.

### *8.3. Exercising Horses*

In an investigation of Falaschini and Trombetta (1994) daily supplementations of 6 g of L-carnitine to trotters resulted in a more rapid recovery of the blood glucose concentration after submaximal exercise compared to a group of horses which

**Table 7** Effects of an oral supplementation of 2 × 5 g of L-carnitine per day on biochemical parameters in blood plasma of growing horses (Means ± SD) (from Hausenblasz *et al.*, 1996)

| *Parameters* | *With carnitine supplementation* | | *Without carnitine supplementation* | |
|---|---|---|---|---|
| | *Day* 1 | *Day* 78 | *Day* 1 | *Day* 78 |
| Blood glucose [mmol/l] | 4.1[a] ±0.50 | 5.3[b] ±0.79 | 3.9 ±0.47 | 4.3 ±0.47 |
| Free fatty acids [μmol/l] | 64 ±12 | 81 ±11 | 79 ±10 | 76 ±10 |
| Triglycerides [μmol/l] | 150[a] ±60 | 90[b] ±30 | 100 ±50 | 120 ±60 |
| Albumin [g/l] | 29 ±1.1 | 30 ±2.2 | 31 ±1.6 | 30 ±1.5 |
| Urea [mmol/l] | 3.8[a] ±0.31 | 4.2[b] ±0.39 | 4.6 ±0.53 | 4.6 ±0.52 |

Data with different superscripts within rows differ by $P < 0.005$

received 1 g of L-carnitine. In another study with five galloping race horses the resting level of lactate in plasma was significantly reduced by feeding 5 g of L-carnitine per day (Zeyner and Lengwenat, 1997). Reduction of the plasma lactate concentration by supplementation of L-carnitine was also observed by Iben *et al.* (1992) after daily administration of 5 g of L-carnitine when compared to horses which received a diet not supplemented with carnitine. Other reported effects of L-carnitine supplementations, for example, on the concentration of non-esterified fatty acids (NEFA) and triglycerides in plasma during exercise are inconsistent. Falaschini and Trombetta (1994) observed with trotting horses receiving a carnitine supplemented diet a reduced increase in triglycerides and an increased rise in NEFA in plasma compared to control animals after 2600 m of trotting. Zeyner and Lengwenat (1997) observed the opposite effect after carnitine supplementation, *i.e.*, a reduced rise of NEFA and an increased rise in triglyceride concentration in plasma after 1280 m of galloping at submaximal speed. The effects of carnitine on some metabolic parameters in relation to exercise are compiled in Table 8.

Quantitative studies on possible effects of carnitine supplementations on physical performance are not available from the literature. When such experiments are going to be carried out various aspects have probably to be taken into account, such as type and duration of exercise, type of diet and, in particular, the amount of added fat, the duration of L-carnitine supplementation and the effect on muscular properties during training and on performance during acute exercise.

## 9. CONCLUSIONS

Similar to other domestic animals L-carnitine plays also in horses an essential role for the provision of energy to the exercising muscles. Oral supplementations of carnitine to horses have brought about marked and sustained increases in the concentration of carnitine in plasma. The effect of such supplementations on carnitine content in muscles, however, is less clear and is possibly less than that

**Table 8** Compilation of effects of oral supplementation of L-carnitine to horses on blood parameters at rest and during exercise

| *Reference* | *Number of animals per group and type of excercise* | *Fat [g/d]* | *L-carnitine [g/d]* | *Effect of carnitine supplementation on plasmaparameters* |
|---|---|---|---|---|
| Iben *et al.* (1992) | ($n = 8$) Uphill 2200 m, trotting in 7 min | – | 0 and 5 | **At rest:** increase of creatinine **Immediately after exercise:** less increase of lactate; increase of the activities of LDH[1], $\alpha$-HBDH[2], ASAT[3] and CK[4] |
| Falaschini and Trombetta (1994) | ($n = 5$) 2600 m trotting, at submaximal intensity | 300 soya oil | 0, 1 and 6 | **At rest:** decrease of $\beta$-hydroxybutyrate **Immediately after exercise:** less increase of lactate; greater increase in free fatty acids; faster recovery of glucose (only with 6 g of L-carnitine) |
| Hausenblasz *et al.* (1995) | ($n = 10$) Modern pentathlon | – | 0 and $2 \times 5$ | **At rest:** increased glucose concentration; decreased CK-activity |
| Zeyner and Lengwenat (1997) | ($n = 5$) Galloping horses, approximately 1280 m galloping, at submaximal intensity | 300 soya oil | 0 and 5 | **At rest:** decreased lactate concentration **After exercise:** greater increase of triglycerides and total cholesterol; less increase in free fatty acids |

[1] LDH = Lactate dehydrogenase
[2] ASAT = Aspartate aminotransferase
[3] $\alpha$-HBDH = $\alpha$-Hydroxybutyrate dehydrogenase
[4] CK = Creatine kinase

observed in blood. Distinct improvements of the carnitine status have been documented in mares and foals by oral supplementations of carnitine during the perinatal period. But no clear evidence was presented by these studies as to whether the improvements in carnitine status had led to similar improvements in general performance of the mares or to improvements in weight gain of the foals. It appears that further studies are required to examine possible beneficial effects of carnitine on parameters of equine physical performance including cardiac and muscular functions during acute and/or prolonged exercise.

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