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CARNITINE STATUS IN ADULT PROTEIN-CALORIE MALNUTRITION

BY

NUSIRI LERDVUTHISOPON

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CHAPTER I

INTRODUCTION

1.1 Historical landmarks

Carnitine (3-hydroxy-4-trimethylamino butyric acid) was independently discovered by Gulwitch and Krimberg (1) as well as Kutscher (2) in 1905 as a constituent of meat extract. In 1907, Krimberg (3) proposed the correct structural formula of carnitine. Twenty years later, Tomita and Sendju (4) separated the two isomers of carnitine and identify the levorotatory isomer as being the natural form of carnitine.

The history of carnitine, is diffent from that of almost all other vitamins in that its discovery and identification precede recognition of its vitamin function by almost 50 years. In 1948, Fraenkel (5) discovered that a new food factor present in the charcoal filtrate of aqueaus liver or yeast extract was a growth factor for the yellow meal worm, Tenebrio molitor. The factor was coined vitamin B_T to indicate its place in the vitamin B group and the "T" designating Tenebrio. Subsequently, Carter et al (6) demonstrated that carnitine was identical with vitamin B_T.

One of the significant achievement in carnitine research was made by Fritz (7) during the year 1955-1961. He demonstrated the carnitine property of increasing oxygen consumption and catalytically stimulating long chain fatty acid oxidation by a variety of suitable tissue preparations, of which heart responds to the greatest degree.

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The aforesaid findings have stimulated a number of investigators around the world to study the functions and metabolism of carnitine. Much of these knowledges have been summarized in a number of reviews (7-11).

1.2 Food sources of carnitine

Carnitine in the body is derived from two sources, i.e., exogenous and endogenous sources. The exogenous sources come from the availability of carnitine in the diet whereas the endogenous sources stem from the carnitine synthesis in vivo.

Fraenkel (12, 13) has made an extensive survey of the occurrence of carnitine in nature using Tenebrio molitor as a bioassay procedure. Table 1-1 shows examples of biological materials containing carnitine derived from his studies. Two general conclusions can be drawn from the table ; (a) animal tissues contain very much higher levels of carnitine than do microorganisms or plants ; (b) the richest sources of carnitine is muscle both vertebrate and invertebrate. However, the figures in the table are based on the assumption that carnitine or its esters is the only compound with vitamin B_T activity present in natural materials and the supposition that a diet on which Tenebrio larvae show a maximum survival up to a weight of about 60 mg contains 0.35 ug carnitine per g of the dry diet. It is self-evident that the accuracy of such a method cannot be very high (8).

Other methods for assaying carnitine have been developed which include a bioassay dependent upon the response of frog rectus to

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Table 1-1 The carnitine content of a number of materials of biological origin, determined by the Tenebrio assay[a]

Organism	Description of materials	Carnitine ug/g dry matter
Microorganisms		
E. coli	Grown on synthetic medium	None
Strep. hemolyticus	Not entirely synthetic medium	28
Torula yeast, Brewers'yeast		17.5-35
Plants		
Wheat	Seeds	7-14
Corn	Seeds	None
Invertebrates		
Horseshoe crab	Hepatopancreas	2100
	Muscle	8,800-35,000
Sea urchin	Whole	35
Vertebrates		
Mustalus canis (dog fish)	Liver	420
	Muscle	700
Chick	Egg	None
	Liver	22.4
	Muscle	175-350
Dog	Liver	140-280
	Muscle of leg	1120
Rabbit	Liver	370
	Muscle of leg	700

[a]Reported by Fraenkel (12, 13).

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carnitine derivatives (14), chemical determination based upon the complexing of quaternary compounds with bromphenol blue (15, 16) and chromatographic separation, with subsequent conversion of the compound to its periodide derivative (17). However, the high degree of specificity demanded in determining the carnitine content in tissue extracts has been achieved by Marquis and Fritz (18), in 1964, using the enzyme carnitine acetyltransferase method. The sensitivity of the latter has been improved and simplified by several investigators, using radioisotopic assay (19-21).

Tanphaichitr, Prombun and Lerdvuthisopon (22) have recently investigated the total carnitine content of some Thai food, including meat and poultry (Table 1-2) as well as fish, shellfish and rice (Table 1-3). Carnitine was extracted by the method of Tanphaichitr and Broquist (23) and assayed by the method of Cederblad and Lindsted (19). It is clear from these data (Table 1-2, 1-3) that milled rice is the poor sources of carnitine and 35 % of carnitine present in rice is lost during cooking whereas rich sources of carnitine are beef, pork, and beef heart.

1.3 Carnitine biosynthesis

During the year 1953-1954, Fraenkel (12, 13) showed that (i) the tissue carnitine content of beetle, Dermestes vulpinus, rat and chick was not noticeably affected by the dietary supply of carnitine; and (ii) the carnitine content of chick embryo increased during the development. These findings indicate that carnitine can be synthesized in vivo.

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Table 1-2 Carnitine content of meat and poultry

Food and description	Carnitine content umole per 100 g edible portion[a]
Beef : thigh, lean	548
Chicken : whitemeat	36
Gizzard, chicken : raw	52
Heart, raw :	
beef	771
chicken	28
duck	34
hog	71
Kidney, raw :	
hog	53
Liver, raw :	
beef	55
chicken	26
duck	21
hog	22
Pork : thigh, lean[b]	166 ± 0.1

[a] 1 umole of carnitine equals to 161.2 ug of carnitine

[b] Mean ± SEM, 10 determinations.

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Table 1-3 Carnitine content of fish, shellfish and rice

Food and description	Carnitine content umole per 100 g edible portion
Fish	
Striped mackerel (Rastrelliger chrysozonus) : raw	27
White pomfret (Pampus chineusis) : raw	10
Black pomfret (Parastromateus niger) : raw	36
Malabar redsnapper (Lutjanus malabaricus) : raw	26
Fusilier (Caesio pinjalo) : raw	35
Feather back (Notopterus chitala) : raw	87
Serpent-headed fish (Chana striatus) : raw	34
Climbing perch (Anabas testudineus) : raw	19
Cat-fish (Pangasius sutchi) : raw	15
Shellfish	
Swimming crab (Portunus pelagicus) : raw	154
Shrimp (Penaeus mergulensis) : raw	9
Squid (Loligo sp.) : raw	76
Rice (Oryza sativa) milled, uncooked	40
milled cooked	26

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Studies in the rat by Lindstedt and Lindstedt (24), in 1961, and Bremer (25), in 1962 and mouse by Lindstedt and Lindstedt (26), in 1965, have been shown that (carboxy-^{14}C)γ-butyrobetaine is readily converted to carnitine. These findings confirm the previous report of Linneweh (27), in 1929, that there was an increase in urinary carnitine excretion of dogs given γ-butyrobetaine. Meanwhile, Bremer (28) in 1961, Wolf and Berger (29) in the same year. Strenght and Yu, in 1962, (30) have independently established that the N-methyl groups of carnitine are derived from methyl groups of methionine. Corredor et al, (31), in 1967, have shown that there is incorporation of S-adenosyl-(methyl-^{14}C)methionine into carnitine of rat liver homogenates. However, the biosynthetic origin of the butyrobetaine is obscure prior to 1971.

In 1970, Kakimoto and Akazawa (32) reported the significant amount of ε-N-dimethyllysine and ε-N-trimethyllysine in human urine whereas Nakajima and Volcani (33) demonstrated the present of ε-N-trimethyllysine and ε-N-trimethyl-S-hydroxylysine in the cell walls of diatoms. The close structural relationship between these lysine metabolites and carnitine suggested the possibility that the biosynthesis of carnitine might be derived from lysine metabolism. A series of experiments have been carried out in Neurospora crassa and the rat at Dr. Broquist's laboratory, Vanderbilt University, to test this hypothesis.

In 1971, Horn, Tanphaichitr and Broquist (34) as well as Tanphaichitr, Horn and Broquist (35) are the first group who have shown that lysine is the precursor of carnitine on Neurospora crassa

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lysine auxotrophs and the rat respectively. It is now clear, from their studies that carbon atoms 3, 4, 5 and 6-N atom of lysine form the carbon and nitrogen skeletons of carnitine (36, 37). Similar findings have been reported by Cox and Hoppel (38).

The details of the biosynthetic pathway of carnitine derived from lysine in the rat have been reported by Tanphaichitr and Broquist (37). The investigation was made by administratering appropriate levels of L-(6-^{14}C)lysine, DL-(2-^{14}C)lysine, L-(6-^{3}H)lysine, L-(methyl-^{3}H) methionine, ϵ-N-(methyl-^{3}H)trimethyl-L-lysine or (carboxy-^{14}C) - γ butyrobetaine intraperitoneally into rat fed 20 % wheat gluten diets. Carnitine was subsequently isolated by ion exchange chromatography from a number of tissues and examined for radioactivity. In most trials about 0.1 % of administered DL-(6-^{14}C)lysine or L-(methyl-^{3}H)methionine was incorporated into tissue carnitine. Dietary lysine significantly decreased the utilization of DL-(6-^{14}C)lysine for carnitine synthesis. ϵ-N-(Methyl-^{3}H)trimethyl-L-lysine and (carboxy-^{14}C)γ-butyrobetaine were converted in high yield to carnitine, e.g., 23 % and 45 % of administered dose per 100 grams of skeletal muscle. Radioactive carnitine was also detected in the urine in these latter instances. It was shown that ϵ-N-trimethyllysine is converted to γ-butyrobetaine in the rat. The inability of DL-(2-^{14}C)lysine to label biosynthesized carnitine is interpreted to mean that ϵ-N-trimethyllysine is cleaved losing carbon atoms 1 and 2 , and that the remainder of the molecule then serves as the source of γ-butyrobetaine. This postulation is supported by the recent studies of Hochalter and Henderson (39). In their studies, ϵ-N-trimethyl-L-(1-^{14}C)lysine was administered into the

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rats together with a dose of sodium benzoate. It was found that 21 to 30 % of the isotope from metabolized substrate was incorperated into hippuric acid. These findings indicate that there is a rather direct conversion of carbons 1 and 2 of ε-N-trimethyl-L-lysine to glycine.

Figure 1-1 summarizes the current knowledges on carnitine biosynthetic pathway which is based on the aforesaid findings in the rat and the related studies of the lysine : carnitine precursor : product relationship in Neurospora crassa (34, 35). The cofactor requirements of γ-butyrobetaine hydroxylase have been established by Lindstedt and Lindstedt (40).

The lysine : carnitine precursor : product relationship is also supported by the nutritional studies of Tanphaichitr and Broquist (23) and Tanphaichitr, Zaklama and Broquist (41). Lysine-deficient rats induced by 20 % wheat gluten diets (23) or 6 % rice-protein (41)diet had decreased carnitine level in muscle tissue. It should be noted that the methionine : carnitine : precursor : product relationship has been established by Khairallah and Wolf (42).

1.4 Site of carnitine biosynthesis

Recently, Tanphaichitr and Broquist (43) have elucidated that liver is the active site of carnitine biosynthesis. The cleavage of ε-N-trimethyllysine to γ-butyrobetaine occurs readily in a number of rat tissues. Labelled γ-butyrobetaine was detected in the tissues at 2 hours following intraperitoneal injection or 6 hours following intratesticular injection of ε-N-(methyl-^{3}H)trimethyl-L-lysine. However, the process of hydroxylation of γ-butyrobetaine to yield carnitine is

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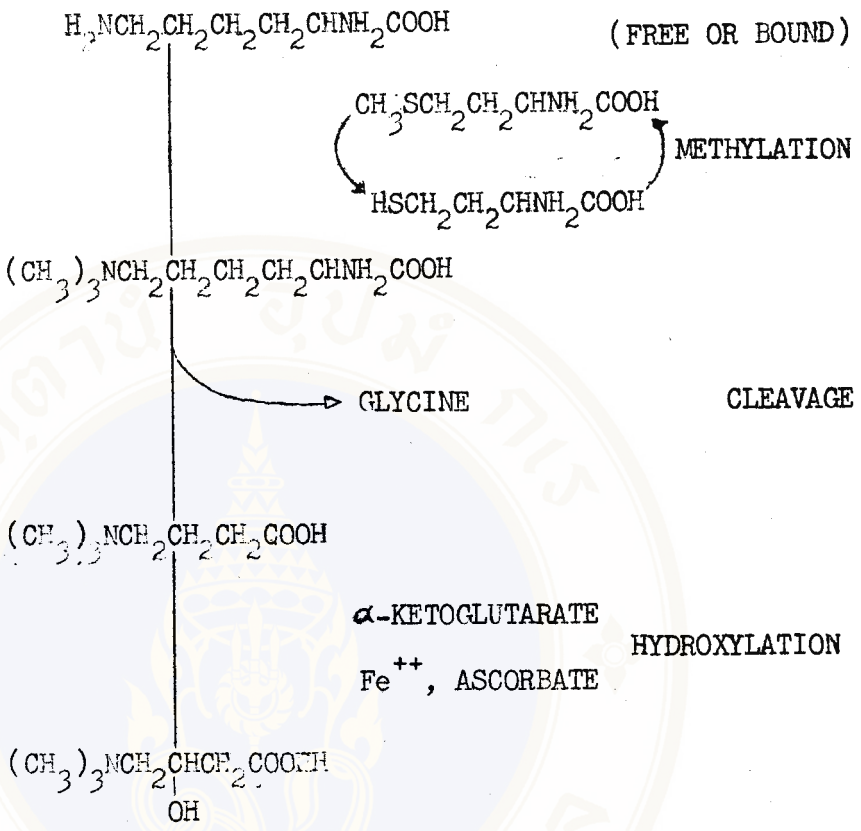

Figure 1-1 Carnitine biosynthetic pathway.

active only in the liver. This is based on the findings that (a) there was more labelled carnitine in the liver than extrahepatic tissues ... following intraperitoneal or intratesticular injection of ε-N-(methyl-^{3}H)trimethyl-L-lysine at 2 or 6 hours, respectively ; and (b) at 1.5 hours following intratesticular injection of (carboxy-^{14}C) γ-butyrobetaine, liver contained more labelled carnitine than testes, epididymis, skeletal muscle and plasma though γ-butyrobetaine remained adequately in the testes. The data are consistent with the existing knowledge that γ-butyrobetaine hydroxylase is active in the liver (44, 40).

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1.5 Various forms of carnitine

It is now known that carnitine in animal tissues can exist in two forms, namely free carnitine and bound carnitine or acylcarnitines. Recently, Bieber and Choi (45) isolated aliphatic acylcarnitines from a water-soluble fraction of beef heart and characterized them by gas chromatography and mass spectrometry. The following residues derived from the acylcarnitine fraction were unequivocally identified : acetyl, propionyl, isobutyryl, butyryl, α-methylbutyryl, valeryl, isovaleryl, tiglyl and caproyl. β-Methylcrotonyl and methacrylyl were tentatively identified.

1.6 Carnitine functions

It is now well established that carnitine participates in shuttling long-chain acyl residues across the inner membrane of mitochondria (11). This process is requisite for the fatty acid oxidation providing energy to the cell. The aforesaid findings of considerable quantities of branched-chain acylcarnitines suggest a role of carnitine in branched-chain amino acid metabolism (45) other than its role in shuttling of acetyl residues at the level of acetyl-CoA (11).

There are also reports, which deal with other physiologic functions of carnitine, including the effect on nerve function, isolated muscle and growth of organism. Details of these have been reviewed by Friedman and Fraenkel (8).

The other important function of carnitine is its role in reproductive system. Some recent findings carried out by Dr. Nongnuj

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Tanphaichitr's group can be summarized as following (a) acetylcarnitine and carnitine can stimulate human sperm motility in vitro (46) ; (b) in ejaculated human semen, carnitine and acetylcarnitine are found in seminal plasma whereas little is found in sperm. About 50 % of total carnitine in normal human seminal plasma exists in the form of acetylcarnitine ; (c) the level of acetylcarnitine in oligospermic human seminal plasma is significantly lower than that in normal samples (47). Such findings imply that the level of acetylcarnitine may be related to sperm fertility and for viability.

1.7 Statment of problem and objectives

It is well known that Thailand is distinctly a "rice economy" country and rice is the staple food of Thais (48, 49). Besides, limiting in lysine and threonine, we have shown that rice is also limiting in carnitine (Table 1-3). If the major energy intake is derived from rice coupled with the long-term consumption of such diet it will lead not only to serious protein-calorie malnutrition (PCM) but also a concomitant carnitine deficiency. Infact Tanphaichitr et al (50) have recently demonstrated that the plasma and urinary carnitine levels in Bangkok adults are higher than those in Ubol villagers. The serum albumin level and hematocrit in the former group are also higher than those in the latter group. The inadequate carnitine status in Ubol villagers could be due to low carnitine intake and impaired carnitine biosynthesis stemming from lysine.

Recently, Tanphaichitr, Komindr and Chotibut (51) reported that the prevalence of adult PCM in the medical wards at Ramathibodi

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Hospital was 59.3 % according to weight-height and 52.9 % according to upper arm muscle circumference. Tube feeding and/or parenteral nutrition are indicated for the proper management of adult PCM. This provides a unique opportunity to study the lysine-methionine : carnitine precursors a : product relationship in these patients.

Carnitine status of the subjects in the present study is assessed by the determination of the total carnitine, free carnitine and acylcarnitine in serum and urine. The specific aims of the study are as follows :

(a) to assess carnitine status in normal Thai adults ;

(b) to assess carnitine status in underweight adults ;

(c) to assess carnitine status in adult patients before and during receiving total parenteral nutrition (TPN) ;

(d) to assess carnitine status in adult patients before and during receiving tube feedings ;

(e) to determine the relationship between carnitine status and indices of PCM ;

(f) to determine the relationship between carnitine and lipid statuses.

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CHAPTER II

MATERIALS AND METHODS

2.1 Subjects

Four groups of subjects were included in this study. These were : control Thai adults, underweight adults, adult patients on tube feedings and adult patients on TPN.

2.1.1 Control Thai adults

They were healthy subjects without any known diseases and consisted of 22 men and 22 women. All of them resided in Bangkok. The mean ± SEM of their age was 27.0 ± 1.1 years. Serum and urinary carnitine levels as well as other parameters were determined in these subjects.

2.1.2 Underweight adults

They were subjects who attended the Nutrition Clinic, Department of Medicine, Ramathibodi Hospital, because of feeling thin. They consisted of 6 men and 13 women. The mean ± SEM of their age was 25.2 ± 1.0 years. Throughout the study period, they could perform their daily work. Two subjects were in the recovery period after receiving complete treatment for amebic liver abscess in subject S.CV and typhoid fever in subject P.TP whereas S.TR was a case of chronic arsenic poisoning.

The study was divided into two treatment periods. At first, pizotifen (one tablet of Mosegor, Sandoz, Ltd, Basle, Switzerland) was given by oral route before bedtime to each subject for 56 days. In the

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second period, 10 mg of pyridoxine hydrochloride (one vitamin B-6 tablet, the Government Phamaceutical Organization, Bangkok, Thailand) was given daily by oral route before bedtime to each subject for 28 days.

Carnitine status and other parameters were assessed at the beginning of study and at the end of each treatment period.

2.1.3 Adult patients on tube feedings

2.1.3.1 Tube feeding formulae

Two types of tube feeding formulae, Ramathibodi and Sobel formulae were used in this study.

Ramathibodi blenderized formula. This tube feeding formula was regulary prepared by the staffs of Division of Dietetics, Ramathibodi Hospital for feeding the hospitalized patients who required tube feeding. Its ingr dients are shown in Table 2-1. Table 2-2 shows the nutrient composition of Ramathibodi blenderized formula analysed by Tanphaichitr et al (52).

Sobel formula. This is a commercial formula manufactured by Mead Johnson and company, Evansville, Indiana, USA. Its nutrient composition is shown in Table 2-3. The amino acid content of Sobel is shown in Table 2-4.

2.1.3.2 Experimental design

Twenty four hospitalized patients on tube feedings were included in this study. 17 of them received Ramathibodi blenderized formula whereas the remaining received Sobel formula. Their clinical conditions are summarized in Tables 2-5 and 2-6, respectively.

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Table 2-1 Food composition of Ramathibodi blenderized formula[a].

Food items	Amount g/liter
Hog liver	100
Banana	100
Egg	200
Sucrose	100
Vegetable oil[b]	32[c]
Water added to	1000 ml

[a]Each liter provided 50 g of protein , 56 g of fat, 127 g of carbohydrate and 1212 kcal, obtained by computing from Thai Food Composition Table.

[b]Tip made from soy bean oil 50 % and kapok seed oil 50 % or cotton seed oil 25 %, kapok seed oil 25 %, soy bean oil 25 % and rice bran oil 25 %.

[c]Amount adjusted according to the desired energy content per liter.

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Table 2-2 Nutritive properties of Ramathibodi blenderized formula[a]

Nutritive property	No of analysis	Amount per liter Mean ± SEM	Amount per 1000 kcal
Protein, g	47	45.6 ± 0.9	35.05
Fat[b], g	46	60.4 ± 0.8	46.48
Carbohydrate, g	45	146.4 ± 1.6	112.47
Minerals (ash), g	46	0.4 ± 0.01	0.33
Calcium, mg	29	144.7 ± 7.2	111.16
Phosphorus, mg	30	737.2 ±16.8	566.34
Sodium, mg	12	450.8 ±17.4	346.32
Potassium, mg	13	1289.4 ±64.4	990.55
Magnesium[c], mg		90	69.14
Carnitine[d], umole		166.0	127.5
Energy content, kcal/l	47	1301.7 ±15.5	
Caloric distribution, %			
Protein	45	13.9 ± 0.9	
Fat	45	41.6 ± 0.8	
Carbohydrate	45	44.6 ± 1.6	
Average non protein caloric : nitrogen ratio			154.7 : 1

[a] Obtained from Tanphaichitr et al (52).
[b] The estimated amount of linoleic acid was 14 g per liter or 10.76 g per 1000 kcal.
[c,d] Derived from computation, using Food Composition Table for Use in East Asia and Tanphaichitr et al (54,22), respectively.

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Table 2-3 Nutritive properties of Sobel formula per 1000 kcal[a]

Nutritive property	Amount per 1000 kcal[b]
Protein, g	40.2
Fat, g	32.8
Carbohydrate	136.0
Minerals (ash),	
calcium, mg	1248
phosphorus, mg	590
magnesium, mg	57.5
iron, mg	10
iodine, mg	81
copper, mg	0.5
Carnitine, umole[c]	0.48 ± 0.12 (3 determinations)
Caloric distribution, %	
protein	16.1
fat	29.5
carbohydrate	54.4
Non protein calorie : nitrogen ratio	130 : 1

[a]Obtained from Mead Johnson & Company, Evansville, Indiana, USA. Sobel powder was made from soy flour, sucrose, corn syrup solids, soybean oil, coconut oil, soy lecithin, vitamins and minerals ; artificial flavor in Sobel Strawberry and coloring added.

[b]Each 1000 kcal provided the following amount of vitamin A, 3,750 IU ; D, 500 IU ; E, 6.3 IU ; B-1, 0.06 mg ; B-2, 1.3 mg ; B-6, 0.5 mg ; niacin, 8.8 mg ; calcium panthothenate 3.1 mg ; B-12, 2.5 ug ; ascorbic acid 125 mg ; choline 85 mg.

[c]Determined by the present study.

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Table 2-4 Amino acid pattern and content of Sobel[a]

Amino acid	g per 1000 kcal Sobel
Isoleucine	1.74
Leucine	2.80
Lysine	2.45
Methionine	0.49
Cysteine	0.51
Phenylalanine	1.89
Tyrosine	1.20
Threonine	1.48
Tryptophan	0.49
Valine	1.84
Arginine	2.78
Histidine	0.96
Alanine	1.63
Aspartic acid	4.48
Glutamic acid	7.16
Glycine	1.60
Proline	2.10
Serine	1.96

[a]Otained from Mead Johnson & Company, Evansville, Indiana, USA.

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Table 2-5 Clinical data in 17 patients on Ramathibodi blenderized formula

Patient	Age yr	Sex	Clinical condition
S.MS	15	M	1. Tetanus. 2. Tracheostomy and under Bird respirator. 3. P.C.M.
S.SM	17	M	1. Meningoencephalitis (?viral). 2. Aspirated pneumonia right lower lobe. 3. Tracheostomy. 4. P.C.M.
L.YM	17	F	1. Tetanus grade I. 2. P.C.M.
F.SB	29	M	1. Tetanus grade III. 2. Tracheostomy. 3. Carbuncle of scalp. 4. P.C.M.
B.BN	29	M	1. Drug intoxication (methaqualone). 2. Coma. 3. Aspirated pneumonia. 4. P.C.M.
V.TN	30	M	1. Tetanus grade III. 2. Aspirated pneumonia. 3. Tracheostomy. 4. P.C.M.
A.TS	33	M	1. Tetanus. 2. Tracheostomy and under Bird respirator. 3. P.C.M.
C.SP	45	M	1. Hypoglycemic coma caused by alcohol. 2. Aspirated pneumonia. 3. Tracheostomy. 4. Decubitus ulcers. 5. P.C.M.
K.ST	56	F	1. Status post surgical removal of meningoma (meningothelial type) at posterior fossa. 2. Left hemiplegia caused by cerebral embolism (post angiogram). 3. Tracheostomy. 4. Dicubitus ulcers. 5. Urinary tract infection. 6. P.C.M.
J.MG	57	M	1. Tetanus grade I. 2. Infected compound fracture of left forearm. 3. P.C.M.
L.HS	58	M	1. Status post-amebic liver abscess. 2. P.C.M.
N.KP	59	M	1. Hyperthyroidism. 2. Dysphagia. 3. P.C.M. 4. Gastrostomy.
S.KR	60	M	1. Leptospiracis. 2. Acute renal failure. 3. Adult respiratory distress syndrome. 4. Tracheostomy and under Bird respirator. 5. Explore laporatomy. 6. P.C.M. 7. Gastrostomy.

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Table 2-5 -continued

Patient	Age yr	Sex	Clinical condition
Y.JD	62	M	1. Pellagra. 2. P.C.M.
J.SP	62	F	1. Total thyroidectomy with right radical neck dissection caused by papillary carcinoma of thyroid gland. 2. Accidental injury to right internal carotid artery during operation. 3. Aspirated pneumonia at right lower lobe. 4. Tracheostomy with under Bird respirator. 5. P.C.M.
P.SH	63	M	1. Left hemiplegia due to right middle cerebral artery thrombosis. 2. Hypertension. 3. Upper gastrointestinal hemorrhage. 4. Aspirated pneumonia. 5. Gastrostomy. 6. P.C.M.
T.SU	72	M	1. Chronic obstructive pulmonary disease. 2. Pulmonary tuberculosis (minimal pulmonary infiltration left upper lobe). 3. P.C.M.

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Table 2-6 Clinical data in 7 patients on Sobel formula

Patient	Age yr	Sex	Clinical condition
B.IN	20	M	1. Klebseilla meningitis post compound fracture of skull. 2. P.C.M.
P.VS	28	F	1. Status post surgical removal of meningioma (meningothelial type) at left cerebellopontine angle. 2. Dysphagia caused by injury of left craneal nerves IV and V during operation. 3. Obesity.
K.CK	40	M	1. Guillain-Barre' syndrome. 2. Pulmonary atelectasis at right lower lobe. 3. Pneumonia at left lower lobe. 4. Tracheostomy and under Bird respirator.
T.CP	56	M	1. Tetanus grade III. 2. Pneumonia. 3. Tracheostomy and under Bird respirator. 4. P.C.M.
P.HP	56	M	1. Diabetes mellitus. 2. Melloidosis. 3. P.C.M.
J.SS	68	M	1. Diabetes mellitus. 2. Pakinsonism. 3. P.C.M. 4. Gastrostomy.
H.SS	82	F	1. Diabetes mellitus. 2. Dementia and cerebral thrombosis. 3. Polyneuropathy of both lower extremities. 4. Tracheostomy. 5. P.C.M.

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The tube feeding formula was given through nasogastric, gastrostomy or jejunostomy route depending upon the condition of the patients. The were aimed to receive 2000-2500 kcal per day. Usually six feedings were provided at 8 am, 11 am, 2 pm, 5 pm, 8 pm, and 12 pm. Most cases received extra vitamins and minerals supplementation before and during receiving tube feeding. Tube feeding was discontinued when the oral route was capable of meeting nutrient needs.

Serum levels of carnitine and other parameters were determined in these patients before and during receiving tube feedings weekly whereas their urinary carnitine and creatinine levels were analysed daily.

2.1.4 Adult patients on TPN

Fourteen hospitalized patients on TPN were included in this study. Their clinical conditions are summarized in Table 2-7. Percutaneous subclavian vein catheterisation was employed to deliver the nutrients. Polyethylene catheter with three outlets (Cat.No. 12 SY-2717, Sorenson Research, Salt Lake City, Utah, USA) was used and connected with the respective intravenous lines of amino acid solution, 50 % dextrose solution and 0.9 % saline solution or 5-10 % dextrose solution. They were administered simultaneously throughout the day. Appropriate amounts of vitamins and minerals mixed with dextrose solution were given through the TPN lines. Since the TPN regiment was fat-free, phosphate-free and trace minerals-free, 200-300 ml of plasma was given through the peripheral veins twice weekly.

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Table 2 - 7 Clinical data in 14 patients on TPN

Patient	Age yr	Sex	Clinical conditions
N.MN	15	F	1. Ileostomy done due to rupture of appendicitis and pyoperitoneum. 2. Urinary tract infection. 3. PCM.
V.NL	19	M	1. Multiple fistulae connecting between intestinal tract and abdominal wall post-operation due to rupture appendicitis. 2. Colostomy. 3. PCM.
T.CP	21	M	1. Blunt traumatic duodenal rupture, peritonitis. 2. Surgical operation : first operation : duodenal rupture; second operation : gastrojejunostomy and gastrostomy; third operation : ileostomy. 3. PCM.
S.JR	22	M	1. Stricture of esophagus caused by unintentional drinking of acetic acid. 2. PCM.
S.SN	22	M	1. Malabsorption caused by Capillaria phillipinensis. 2. PCM.

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Table 2 - 7 -continued

Patient	Age yr	Sex	Clinical conditions
S.MC	35	M	1. Peritonitis caused by rupture of empyema of gall bladder. 2. First explore laporatomy : cholecystectomy, operative cholangiogram, T-tube drain at common bile duct. 3. Second explore laporatomy : gastrojejunostomy and jejunostomy due to leakage of duodenostomy. 4. PCM.
J.CP	44	M	1. Tuberculosis of small intestine. 2. PCM.
Y.NK	46	F	1. Poorly differentiated lymphocytic lymphoma of small intestine. 2. Severe post-pandrial abdominal pain. 3. PCM.
B.PG	50	M	1. Status post right ureterostomy from pyelo-duodenal fistula. 2. Pseudomonas septicemia. 3. PCM.
T.SL	56	M	1. Carcinoma of stomach with gastrojejunostomy. 2. PCM.

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Table 2- 7 -continued

Patient	Age yr	Sex	Clinical conditions
A.SJ	62	M	1. Progressive dysphagia due to carcinoma of oesophagus, status post irradiation. 2. Pulmunary tuberculosis with pleural effusion. 3. PCM.
C.PP	70	M	1. Lymphoma step IV. 2. Gut obstruction. 3. Gastrojejunostomy. .
T.SK	72	M	1. Status post choleoystectomy due to gall stones. 2. Massive bleeding of gastrointestinal tract due to stress ulcers. 3. E. coli septicemia. 4. PCM.
T.VS	81	F	1. Status post lower lip and jaw resection due to well differentiated squamous cell carcinoma of lower lip. 2. Decubitus ulcers. 3. Aspirated pneumonia. 4. PCM.

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Parenteral nutrition was discontinued when the oral route was capable of of meeting nutrient needs.

Serum carnitine levels and other parameters were determined in these patients before and during receiving TPN weekly, whereas their urinary carnitine and creatinine levels were analysed daily.

2.2 Dietary assessment

Twenty-four hour dietary recall and dietary habits of control Thai and underweight adults were recorded. The data were then calculated for carnitine, total calorie intake per capita as well as its percentage distribution derived from fat, carbohydrate and protein. The computation was made by using Booklet of Meal Planning with Exchange Lists of the American Association (53), Food Composition Table for Ude in East Asia (54), and carnitine content in foods reported by Panter and Mudd (55) and Tanphaichitr et al (22).

Nutrient intakes in patients on tube feedings of TPN were also calculated before and during receiving the aforesaid nutritional therapy.

2.3 Anthropometry

The following anthropometric measurement were carried out in the subjects involed in this study : height, body weight, triceps skin fold thickness and mid upper arm circumference. The mid upper arm muscle circumference was calculated from the following formula : $c_2 = c_1 - \pi S$ where c_2 is muscle circumference and S is triceps skin fold thickness (56). Standard of weight-height was taken from Medio-Actuarial

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Mortality Investigation (57). Standards of triceps skin fold thickness, mid upper arm circumference and upper arm muscle circumference were taken from the standard source (56).

2.4 Blood collection

Venous blood was obtained from control Thai and underweight adults after a 12 - 14 hours fast, using disposable syrings and needles.

For patients on tube feedings or TPN, venous blood was obtained between 7 - 8 am.

2.5 Urine collection

Twenty four hour urine samples were collected from control and underweight adults one day prior to the venipuncture whereas daily collection of urine was made for patients on tube feeding or TPN. Toluene was used as the preservative.

2.6 Determination of hematocrit

Venous blood anticoagulated with ethylene diamine tetraacetate was used for the determination of hematocrit by micromethod (58).

2.7 Determination of serum total protein and albumin

Serum total protein and albumin were measured by biuret assay (59) and bromocresol green dye-binding technique (60) respectively.

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2.8 Determination of cholesterol and triglycerides

Serum cholesterol was determined by the method of Searcy and Berquist (61) whereas the assay procedure for serum triglycerides was based on the method of Leveille et al. and van Handel and Zilversmit (62, 63).

2.9 Determination of carnitine in serum and urine

Carnitine was determined by the modified enzymatic-radioisotopic method of McGarry and Foster (64). Basically, the initial step was incubation of serum or neutralized urine with (1-^{14}C) acetylCoA of known specific activity and carnitine acetyltransferase (EC 2.3.1.7.)(CAT). The labelled acetylcarnitine formed according to the reaction was separated from the unreacted (1-^{14}C) acetyl-CoA by mixing the solution with an anion exchange resin.

$$\text{L-carnitine} + \text{acetyl-CoA} \underset{\longleftarrow}{\overset{\text{CAT}}{\longrightarrow}} \text{Acetyl-L-carnitine} + \text{CoASH}$$

The supernatant fluid after centrifugation was then counted for radioactivity.

2.9.1 Reagents and chemicals

A batch of solution was prepared and divided into portions suitable for 30 determinations.

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The solution was prepared as follows :

(a) stock standard L- carnitine, 500 μM was prepared by dissolving 9.88 mg L-carnitine (General Biochemicals, Chagrin Falls, Ohio) in cold distilled water and the volume was adjusted to 100 ml;

(b) acetylCoA, 500 uM was prepared by the methods modified from Simon and Shemin (65) and Ochoa (66). Detail of the method was described by Tanphaichitr (67).

(c) (1-^{14}C) acetylCoA, 9.26 μM (0.5 μCi/ml) was prepared by diluting 2.5 ml of (1-^{14}C) acetylCoA (specific activity = 52.4 mCi/mmole) (New England Nuclear Corp. Boston Mass.) to 100 ml with cold distilled water;

(d) tris-HCl buffer, pH 7.3, 0.24 M, was prepared by dissolving 29.0736 g of tris (hydroxymethyl)-aminomethane (E. Merck. Darmstadt) in aproximately 900 ml of distilled water and the pH was adjusted to 1 liter with distilled water;

(e) sodium tetrathionate, 0.04 M, was prepared by disolving 0.5405 g of sodium tetrathionate (I.C.N. Pharmaceuticals, Inc. Life Science Group, Plainview, N.Y.) in 50 ml of distilled water. The filtration was necessary if the solution was not clear and this solution must be prepared monthly;

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(f) carnitine acetyltransferase, 200 units/ml, was prepared by diluting 1 ml of the enzyme acetyl-CoA : carnitine-O-acetyltransferase, EC 2.3.1.7. specific activity = 110 units/mg protein (Sigma Chemical Co., St. Louis, Mo.) with 1.75 ml of cold distilled water;

(g) tris base, 1M, was prepared by dissolving 12.11 g of tris (hydroxymethyl)-aminomethane (E. Merck, Darmstadt) in 100 ml distilled water.

The solutions (a) - (c) were kept at - 20°C whereas the solutions (d) - (g) were kept at 4°C

2.9.2 Procedure

2.9.2.1 Assay for free carnitine

Assay were carried out in a 75 X 125 mm test tubes. The reagents were added in the following order :

(a) 50 µl of serum or urine or standard L-carnitine containing 2, 4, 6, 8, 10 nmole, or distilled water serving as the blank in separated tubes.

(b) 350 µl of distilled water to every tube;

(c) 500 µl of tris buffer pH 7.3;

(d) 50 µl of sodium tetrathionate;

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(e) 100 µl of the mixture of acetylCoA and (1-^{14}C) acetylCoA (1 : 1); and

(f) 5 µl of the enzyme to initiate the reaction.

(g) A continuously stirred slurry of Dowex AG 2 X 8, 200-400 mesh, anion exchange resin (chloride form) (Bio-Rad Laboratories, Calif.) was prepared by mixing 2 parts of resin with 1 part of distilled water :

(h) liquid scintillation fluid was prepared by dissolving 0.9 g of 1.4-bis-2(5-phenyloxazolyl) benzene (POPOP) and 30 g of 2,5- diphenyloxazol (PPO) in 1800 ml of methoxyethanol and 3000 ml of toluene (19).

The solution was mixed and allowed to stand at room temperature for 30 minutes. Then 300 µl of a continuously stirred slurry of Dowex AG 2 X 8 was added to each tube. The mixture was then agitated with Vortex mixer and placed in ice. This step was repeated twice at 10 minute intervals, after which the tubes were centifuged and 0.3 ml of the supernatant fluid was mixed with 10 ml of scintillation fluid and assayed for radioactivity in a liquid scintillation counter (TriCarb model 3 Packard Instrument Co., Downers Grove, III.).

2.9.2.2 Assay for total carnitine (free plus acylcarnitines)

The procedure was identical with that described above except that the sample, usually 50 µl in volume, was added to 100 µl of 1 M Tris base

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and 50 µl of 0.4 N KOH (pH of mixture approx. 13) and allowed to stand for 1 hour at 37°C in order to hydrolyze any acylcarnitines present. Thereafter, 200 µl of 0.575 N HCl was added to return the pH to 7.3, followed by the steps (c) - (h) listed in the assay for free carnitine.

2.9.3 Calculation

Carnitine content in specimens was obtained from the standard curve run in each assay. Figure 2 - 1 shows the typical standard curve determined by the aforesaid method.

Acylcarnitine content was calculated from the difference between the total and free carnitine content in each specimen. The percentage of acylcarnitine was calculated as follows :

$$\frac{(\text{total carnitine} - \text{free carnitine})}{\text{total carnitine}} \times 100$$

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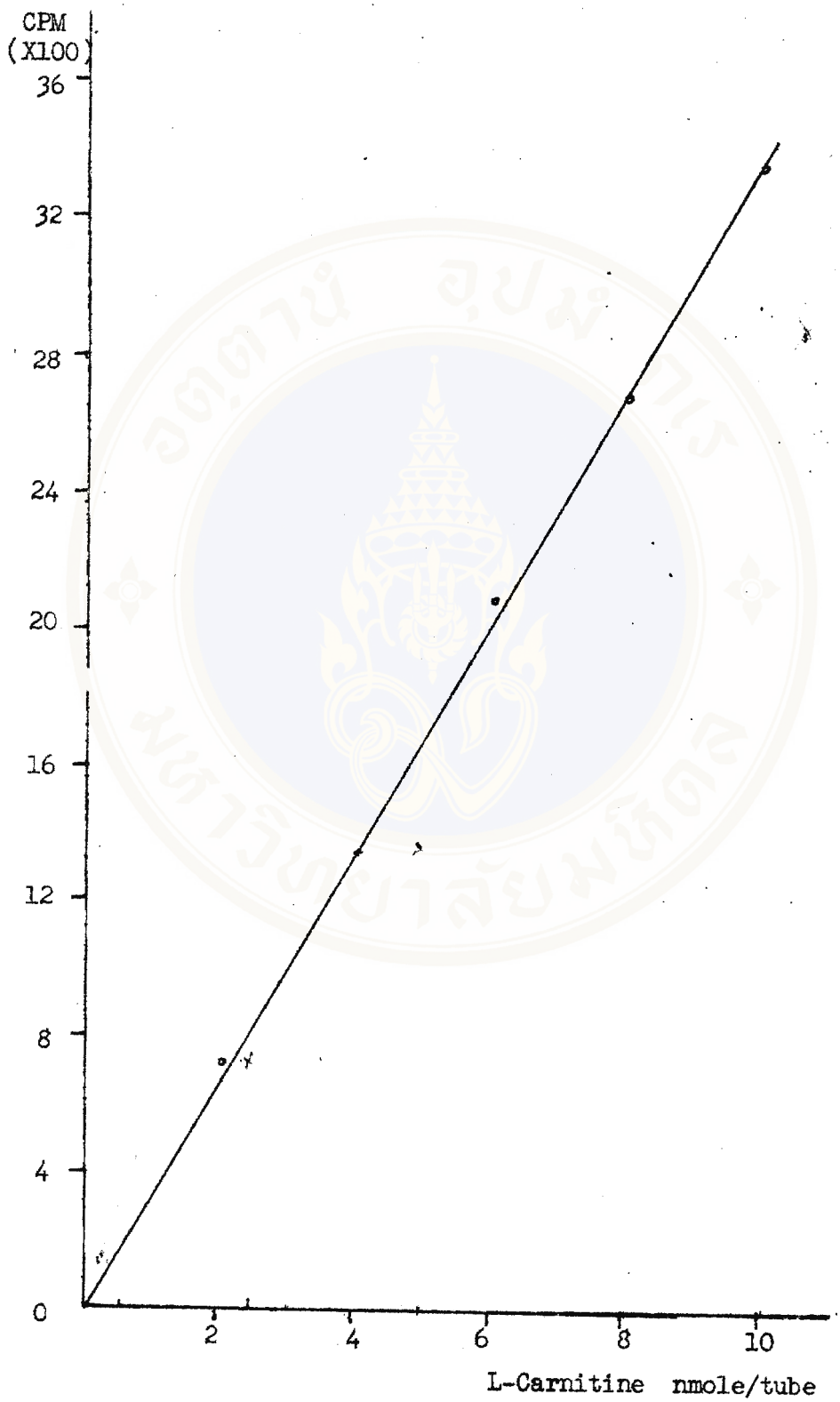

Fig 2-1 A typical standard curve for carnitine assay

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CHAPTER III

RESULTS

3.1 Age and anthropometric measures in control and underweight adults

Table 3 - 1 shows the means ± SEM of age, height, body weight and body mass index in control and underweight adults. No significant difference was found in mean ages when comparisons were made between men and women within the same group of subjects as well as between underweight adults and the corresponding sex of control adults.

With respect to height, there was no significant difference in this parameter when comparisons were made between corresponding sex of the two groups. However, the mean heights in control and underweight men were significantly taller than that in control and underweight women respectively ($P < 0.001$; $P < 0.001$).

The mean body weights in underweight men and women were significantly lower than those in control men and women respectively ($P < 0.001$; $P < 0.001$). The mean body weights in control and underweight men were significantly higher than those in control and underweight women respectively ($P < 0.001$, $P < 0.001$).

Significantly lower percent standard weight-height and body mass index were observed when comparisons were made between underweight adults

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Table 3 - 1 Means ± SEM of age, height, body weight and body mass index in control and underweight adults.

Subject Group		No	Age yr	Height cm	Body weight kg	Body weight %Std[a]	BMI[b] kg/m^2
I.	Control men	22	25.5±1.4	167.6±1.4	58.6±1.7	89.5±1.7	20.9±0.5
II.	Control women	22	28.4±1.6	155.6±0.8	47.0±1.0	82.9±2.4	19.3±0.3
III.	Underweight men	6	28.5±2.3	169.0±2.7	48.5±1.5	71.9±3.4	17.0±0.8
IV.	Underweight women	13	23.9±0.9	158.0±1.0	39.5±0.9	67.9±1.5	16.0±1.3
P value by t test (2 tailed)							
II	vs I		ns	<0.001	<0.001	<0.05	<0.02
IV	vs III		ns	<0.001	<0.001	ns	ns
III	vs I		ns	ns	<0.01	<0.001	<0.001
IV	vs II		ns	ns	<0.001	<0.001	<0.001

[a]Std = standard weight-height Medio Actural Mortulity Investigation (57).

[b]BMI = body mass index.

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and the corresponding sex of control adults ($P<0.001$ $P<0.001$; $P<0.001$; $P<0.001$). These two parameters in control women were significantly lower than those in control men ($P<0.05$; $P<0.02$).

Table 3 - 2 shows the means ± SEM of triceps skin fold thickness, mid upper arm circumference and upper arm musele circumference in control and underweight adults. These three parameters in underweight men and women were significantly lower than those in control men ($P<0.05$; $P<0.01$; $P<0.025$) and women ($P<0.005$; $P<0.001$; $P<0.001$) respectively.

When comparisons were made between men and women within the same group of subjects it was found that triceps skin fold thickness in control and underweight men were significantly lower than those in control women and underweight women respectively ($P<0.001$; $P<0.005$), whereas the other two parameters were significantly higher ($P<0.001$; $P<0.001$; $P<0.001$; $P<0.001$).

3.2 Hematocrit, serum total protein, albumin, cholesterol and triglycerides in control and underweight adults

Table 3 - 3 shows means ± SEM of hematocrit, serum total protein, albumin, cholesterol and triglycerides in control and underweight men were significantly higher than those in the corresponding groups of women ($P<0.001$; $P<0.001$) whereas their serum total protein, albumin, cholesterol, and triglycerides levels were not significantly different.

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Table 3 - 2 Means±SEM of triceps skin fold thickness, mid upper arm circumference and muscle circumference in control and underweight adults

Subject			TST[b]		MUC[c]		UMC[d]	
	Group	No	mm	%Std[a]	cm	%Std	cm	%Std
I.	Control men	21	9.2±0.8	73.5±6.3	27.2±0.5	93.2±1.8	24.3±0.4	96.6±1.4
II.	Control women	21	16.3±0.9	98.9±5.6	24.4±0.4	85.6±1.4	19.3±0.2	81.2±1.0
III.	Underweight men	5	5.4±0.6	42.9±4.8	23.9±0.9	81.5±3.0	22.2±0.7	88.0±2.9
IV.	Underweight women	10	10.8±1.0	65.3±6.4	20.4±0.3	71.8±1.1	17.1±0.3	74.9±1.8
P value by t test (2 tailed)								
II	vs I		<0.001	<0.005	<0.001	<0.005	<0.001	<0.001
IV	vs III		<0.005	<0.05	<0.001	<0.005	<0.001	<0.005
III	vs I		<0.05	<0.005	<0.01	<0.01	<0.025	<0.025
IV	vs II		<0.005	<0.05	<0.001	<0.001	<0.001	<0.005

[a]Std = standard; [b]TST = triceps skinfold thickness; [c]MUC = mid upper arm circumference; [d]UMC = upper arm muscle circumference.

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Table 3 - 3 Means ± SEM of hematocrit, serum total protein, albumin, cholesterol and triglycerides in control and underweight adults

	Subject	Hematocrit	Serum constituents			
			TP, g/dl	Alb, g/dl	Cho, mg/dl	TG, mg/dl
I.	Control men	44.8±0.8 (21)[a]	7.1±0.2 (20)	5.0±0.2 (20)	207±9 (21)	76±11 (21)
II.	Control women	39.4±0.7 (21)	7.3±0.2 (21)	4.9±0.1 (21)	217±13 (22)	60±5 (22)
III.	Total controls	-	-	-	211±8 (43)	68±6 (43)
IV.	Underweight men	44.0±1.8 (6)	7.6±0.2 (6)	4.9±0.2 (6)	184±16 (6)	69±13 (6)
V.	Underweight women	39.7±0.9 (13)	7.6±0.2 (9)	5.2±0.1 (9)	190±8 (13)	70±10 (13)
VI.	Total underweights	-	-	-	188±7 (19)	70±8 (19)
P value by t test (2 tailed)						
II.	vs I.	<0.001	ns	ns	ns	ns
V.	vs IV.	<0.001	ns	ns	ns	ns
IV.	vs I.	ns	ns	ns	ns	ns
V.	vs II.	ns	ns	<0.05	ns	ns
VI.	vs III.				ns	ns

TP = total protein; Alb = albumin; Cho = cholesterol; TG = triglycerides.

[a] Figures in parenthesis is the number of subjects.

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When comparisons were made between underweight adults and the corresponding sex of control adults it was found that only serum albumin level in underweight women was significantly higher than that in control women ($P<0.05$).

3.3 Serum carnitine levels in control and underweight adults

Table 3 - 4 shows the means $\pm$ SEM of various forms of serum carnitine levels in control and underweight adults. No significant differences in serum free carnitine, acylcarnitine and total carnitine levels as well as percent acylcarnitine were found between men and women within the same group of subjects.

When comparisons were made between underweight adults and the corresponding sex of control adults it was found that only underweight men had significantly lower serum acylcarnitine and tolat carnitine levels than those in control men ($P<0.02$; $P<0.02$). It should be noted that these two parameters in total underweights were also significantly lower than those in total controls ($P<0.01$; $P<0.05$).

3.4 Urinary carnitine excretion in control and underweight adults

Table 3 - 5 shows the means $\pm$ SEM of various forms of urinary carnitine excretion in umole per liter of urine and umole per day in control and underweight adults. It was observed that the various forms of urinary carnitine concentrations in control and underweight men were greater than those in control and underweight women, respectively. However,

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Table 3 - 4 Means ± SEM of various forms of serum carnitine levels in control and underweight adults

	Subject		Carnitine forms in serum, umole/L			%acyl carnitine
	Group	No	free-	acyl-	total-	
I.	Control men	22	69.2±2.4	71.3±6.3	140.6±6.5	49.1±2.4
II.	Control women	22	66.2±4.3	70.4±7.7	136.6±10.3	48.9±2.8
III.	Total controls	44	67.7±2.4	70.8±4.9	138.6±6.0	49.0±1.8
IV.	Underweight men	6	69.1±1.4	51.5±3.7	122.3±1.6	42.0±2.5
V.	Underweight women	13	63.6±3.7	52.4±6.4	116.0±8.3	43.6±3.0
VI.	Total underweights	19	65.3±2.6	52.1±4.5	118.0±5.6	43.1±2.1
P value by t test (2 tailed)						
II. vs I.			ns	ns	ns	ns
V. vs IV.			ns	ns	ns	ns
IV. vs I.			ns	<0.02	<0.02	ns
V. vs II.			ns	ns	ns	ns
VI. vs III.			ns	<0.01	<0.05	ns

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Table 3 - 5 Means ± SEM of various forms of urinary carnitine excretion in umole per liter of urine and umole per day in control and underweight adults

	Subject		Carnitine forms in urine, umole/L			Carnitine forms in urine, umole/day			% acyl carnitine
	Group	No	free-	acyl-	total	free-	acyl-	total	
I	Control men	22	195±31	186±25	380±45	185±27	186±21	371±41	52.2±3.9
II	Control women	22	136±28	166±26	302±51	142±18	172±18	341±36	58.4±2.8
III	Total controls	44	165±21	176±18	341±34	163±17	179±14	342±27	55.3±2.4
IV	Underweight men	6	196±31	237±53	433±80	240±40	275±38	516±76	52.1±3.4
V	Underweight women	11	104±25[b]	149±43	253±67	105±23[a]	148±46	253±68[b]	55.9±3.2
VI	Total underweights	17	137±22	180±34	316±54	153±26	193±35	346±59	54.6±2.4

Comparisons were made between men and women within the same group of subjects using the t test (2 tailed) : a = $P < 0.01$, b = $P < 0.05$.

No significant differences were observed between underweight men, underweight women or total underweights and the corresponding groups of control adults.

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significant differences in the following parameters were observed only between underweight men and women:free urinary carnitine concentration in umole per liter of urine ($P<0.05$) and free and total urinary carnitine concentration in umole per day ($P<0.01$; $P<0.05$). The urinary percent acylcarnitine in men and women of both groups was not significantly different.

When comparisons were made between underweight adults and the corresponding sex of control adults. There were no significant differences in various forms of carnitine excretion which were expressed as umole per liter of urine or umole per day. Their urinary percent acylcarnitine was not significantly different.

Table 3 - 6 shows the means $\pm$ SEM of various forms of urinary carnitine excretion in umole per g creatinine and umole per kg body weight per day in control and underweight adults. When comparisons were made between men and women within the same group of subjects it was found that only urinary free carnitine excretion in umole per kg per day in underweight men was significantly higher than that in control men ($P<0.05$).

When comparisons were made between underweight men, underweight women or total underweights and the corresponding group of controls. Significant differences in the following parameters were observed only between underweight and control men:urinary acylcarnitine excretion in umole per g creatinine ($P<0.01$), urinary free, acyl and total carnitine concentrations in umole per kg per day ($P<0.05$; $P<0.005$; $P<0.01$).

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Table 3 - 6 Means ± SEM of urinary carnitine excretion umole per g creatinine and umole per kg body weight per day in control and underweight adults

Subject			Carnitine forms in urine, umole/g creatinine				Carnitine forms in urine, umole/kg/day		
	Group	No	free-	acyl-	total	No	free-	acyl-	total
I	Control men	16	138±16	144±17	282±26	22	3.1±0.4	3.2±0.4	6.2±0.6
II	Control women	22	157±24	185±17	342±37	22	3.1±0.5	3.6±0.4	6.7±0.8
III	Total controls	38	149±15	168±12	316±25	44	3.1±0.3	3.4±0.3	6.5±0.5
IV	Underweight men	6	236±60	261±50[c]	496±109	6	4.9±0.7[a,d]	5.6±0.6[b]	10.5±1.2[c]
V	Underweight women	10	137±26	199±63	336±86	10	2.6±0.6	3.8±1.3	6.3±1.9
VI	Total underweights	16	174±29	222±43	396±68	16	3.4±0.5	4.4±0.8	7.9±1.3

Comparisons were made between men and women within the same group of subjects using the t test (2 tailed) : a = $P<0.05$

Comparisons were made between underweight men, underweight women or total underweights and the corresponding groups of control adults using the t test (2 tailed) : b = $P<0.005$; c = $P<0.01$; d = $P<0.05$.

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3.5 urine free, acyl and total carnitine clearance in control and underweight adults.

Table 3 - 7 shows the means ± SEM of urinary creatinine excretion per day, carnitine clearance and carnitine excretion per 100 glomerular filtration rate (GFR) in control and underweight adults. The levels of urinary creatinine excretion per day in control and underweight men were significantly higher than those in control and underweight women whereas the creatinine clearances were not significantly different. For carnitine excretion per 100 GFR, free and total carnitine excretion in underweight men was significantly higher than those in underweight women ($P<0.05$; $P<0.05$).

When comparisons were made between underweight adults and the corresponding sex of control adults significant differences were observed as follows:lower creatining clearance in underweight women than that in control women ($P<0.0005$), higher acyl-and total carnitine excretion per 100 GFR in underweight men than those in control men ($P<0.02$; $P<0.05$).

Table 3 - 8 shows the means ± SEM of carnitine clearance in ml/min and ml/min/1.73m^2 body surface area. When comparisons were made between men and women within control or underweight adults it was found that only underweight men had free carnitine clearance in ml/min and ml/min/1.73m^2 significantly higher than those in underweight women ($P<0.01$; $P<0.025$).

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Table 3 - 7 Means + SEM of urinary creatinine excretion per day, creatinine clearance and carnitine excretion per 100 glomerular filtration rate in control and underweight adults

Subject			Creatinine	Creatinine clearance	Carnitine excretion/d/100GFR		
	Group	No	mg/d	ml/min	free-	acyl-	total
I	Control men	16	1508±90	109±7	201±30	201±30	402±53
II	Control women	21	928±39	98±4	152±23	182±19	335±38
III	Underweight men	6	1170±196	84±15	350±102	382±87	732±189
IV	Underweight women	10	754±95	70±8	142± 25	206±62	333±85
P value by t test (2 tailed)							
II	vs I		<0.001	ns	ns	ns	ns
IV	vs III		<0.05	ns	<0.05	ns	<0.05
III	vs I		ns	ns	ns	<0.02	<0.05
IV	vs II		ns	<0.0005	ns	ns	ns

Urinary creatinine clearance as glomerular filtration rate (GFR).

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Table 3 - 8 Means ± SEM of carnitine clearance in ml per minute and ml per minute per $1.73m^2$ of body surface area in control and underweight adults

	Subject		Carnitine clearance, ml/min			Carnitine clearance, ml/min/$1.73m^2$		
	Control	No	free-	acyl-	total	free-	acyl-	total
I	Control men	22	1.8±0.2	2.2±0.4	1.9±0.2	1.8±0.2	2.3±0.4	1.9±0.2
II	Control women	22	1.4±0.2	2.1±0.3	1.6±0.2	1.7±0.2	2.5±0.3	2.0±0.2
III	Underweight men	6	2.4±0.4	3.9±0.3	2.9±0.4	2.7±0.3	4.4±0.3	3.2±0.4
IV	Underweight women	10	1.1±0.2	2.3±0.9	1.5±0.4	1.4±0.3	3.0±1.3	1.9±0.6
P value by t test (2 tailed)								
II	vs I		ns	ns	ns	ns	ns	ns
IV	vs III		<0.01	ns	ns	<0.025	ns	ns
III	vs II		ns	<0.05	ns	ns	<0.02	<0.02
IV	vs II		ns	ns	ns	ns	ns	ns

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When comparisons were made between underweight adults and the corresponding sex of control adults there were significantly higher acylcarnitine clearance in both units and total carnitine clearance in ml/min/1.73m^2 in underweight men than those in control men ($P<0.05$; $P<0.02$; $P<0.02$).

3.6 Effect of pizotifen treatment on serum cholesterol, triglyceridex levels and carnitine status in underweight adults.

There was no significant difference in serum cholesterol level before and after pizotofen treatment while the lower serum triglycerides level was found after pizotifen treatment in male underweight ($P<0.0025$) (Table 3 - 9).

Table 3 - 10 shows the means $\pm$ SEM of various forms of serum carnitine levels before and after pizotifen treatment. In both unpaired and paired groups, there were no significant differences in the serum free, acyl and total carnitine levels as well as per cent acylcarnitine. In unpaired group after pizotifen treatment, the serum free carnitine level in women was significantly lower than that in men ($P<0.05$).

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Table 3 - 9 Effect of pizotifen treatment on serum cholesterol and triglycerides levels in underweight adults

Subject[1]	Serum lipid	Means ± SEM of serum lipid levels, mg/dl[2]	
		Before treatment	After treatment
Men	Cholesterol	177±30	161±13
Women		206±14	186±13
Total		196±14	178±10
Men	Triglycerides	45±8	83±8[a]
Women		70±18	64±11
Total		62±13	70±8

[1] Three men and six women.

[2] Values were obtained from the same subject before and after treatments.

[3] Comparisons were made between before and after pizotifen treatment using the paired t test (1 tailed); a = $P < 0.005$.

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Table 3 - 10 Effect of pizotifen treatment on mean ± SEM of serum carnitine levels in underweight adults

Subject		Carnitine forms in serum umole/l			% Acyl
Group	No	free-	acyl-	total	carnitine
Unpaired					
Before treatment;					
Men	6	69.1±1.4	51.5±3.7	122.3±1.6	42.0±2.5
Women	13	63.6±3.7	52.4±6.4	116.0±8.3	43.6±3.0
Total	19	65.3±2.6	52.1±4.5	118.0±5.6	43.1±2.1
After treatment;					
Men	4	74.9±2.7	49.0±13.3	123.9±13.9	37.4±6.7
Women	9	60.0±1.6[a]	52.4±6.7	112.4±6.6	45.4±3.0
Total	13	64.6±2.4	51.3±5.9	115.9±6.1	43.0±3.0
Paired[b]					
Before treatment		65.5±3.7	52.9±4.8	119.2±6.7	43.8±2.4
After treatment		64.6±2.4	51.3±5.9	115.9±6.1	43.0±3.0

[a]There was only significant difference when comparison was made between men and women ($P < 0.05$) after pizotifen treatment.

[b]Thirteen underweight adults were compaired between before and after pizotifen treatment using the paired t test.

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Table 3 - 11 shows the various forms of urinary carnitine excretion in umole per day, and umole per kg body weight per day as well as percent acylcarnitine in underweight adults before and after pizotifen treatment. It was observed that there were no significant differences in various forms of urinary carnitine excretion in both unit expressions before and after pizotifen treatment.

The effect of pizotifen on urine creatinine excretion and carnitine clearance was shown in Table 3 - 12. In underweight men, after pizotifen treatments there was significant decrease in free and total carnitine clearance expressed as ml/min ($P<0.01$; $P<0.005$) and ml/min/1.73m^2 ($P<0.0125$; $P<0.005$). In underweight women, after treatment there was significant increase in creatinine excretion ($P<0.05$).

3.7 Effect of pizotifen and pyridoxine treatment on serum carnitine levels in underweight adults

Seven underweight adults received pizotifen treatment for 56 days which was then followed by pyridoxine treatment for 28 days. The effect of these treatments on serum carnitine levels was shown in table 3 - 13. No significant difference was observed between after pizotifen treatment and before treatment, after pyridoxine treatment and before treatment, and after pyridoxine treatment and pizotifen treatment.

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Table 3 - 11 Effect of pizotifen treatment on urinary carnitine excretion in underweight adults[1]

Treatment	Means ± SEM of carnitine forms in urine, umole/day			umole/kg/day			% Acyl carnitine
	free-	acyl-	total	free-	acyl-	total	
Before treatment	117±19	155±24	272±42	2.82±0.46	3.70±0.46	6.52±0.80	57.1±2.7
After treatment	152±37	142±24	294±58	3.61±1.00	3.30±0.57	6.91±1.47	53.5±5.4

[1]Three men and six women.

[2]No significant difference was observed before and after pizotifen treatment.

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Table 3 - 12 Effect of pizotifen on urinary creatinine excretion and carnitine clearance in underweight adults[1]

	Creatinine mg/d	Carnitine clearance ml/min			Carnitine clearance ml/min/1.73m^2		
		free-	acyl-	total	free-	acyl-	total
Before treatment							
I Men	1065±246	1.8±0.2	3.6±0.4	2.3±0.2	2.0±0.3	4.2±0.5	2.7±0.3
II Women	606±110	0.9±0.1	1.4±0.2	1.1±0.1	1.2±0.2	1.8±0.3	1.5±0.1
After treatment							
III Men	994±180	0.9±0.3[c]	3.5±1.8	1.2±0.2[a]	1.0±0.4[b]	4.5±2.8	1.3±0.3[a]
IV Women	786± 49[d]	1.7±0.6	1.6±0.4	1.6±0.4	2.2±0.7	2.0±0.5	2.3±0.5

[1]Four men and six women.

[2]Comparisons were made between before and after pizotifen treatment in men or women using the t test : (2 tailed) a = $P<0.005$; b = $P<0.0125$; c = $P<0.01$; d = $P<0.05$.

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Table 3 - 13 Effect of pizotifen and pyridoxine treatment on serum carnitine levels in underweight adults[1]

	Treatment	Means ± SEM of carnitine forms in serum, umole/l			% Acyl carnitine
		free-	acyl-	total	
I	Before treatment	66.6±2.1	46.3±2.1	114.3±3.0	40.5±1.6
II	After pizotifen treatment	66.8±4.2	50.3±7.3	117.1±8.2	42.0±4.2
III	After pyridoxine treatment	66.1±6.3	62.7±11.9	128.7±16.2	47.1±3.2

[1]Four men and three women.

[2]No significant difference was observed between II and I, III and I, and III and II.

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3.8 Dietary assessment in control and underweight adults

Table 3 - 14 shows the means $\pm$ SEM of energy, protein, fat, carbohydrate and carnitine intake as well as percentage of caloric distribution in control and underweight adults. Energy, fat and carbohydrate intake in control women is significantly lower than those in control men ($P<0.005$; $P<0.05$; $P<0.005$) whereas no significant differences were observed between underweight men and underweight women. When comparisons were made between underweight adults and the corresponding sex of control adults there were significantly lower energy and carbohydrate intake but higher percent protein calorie intake than those in control men ($P<0.02$; $P<0.05$; $P<0.005$). No significant differences in these parameters were found between control and underweight women.

3.9 Relationship between dietary intake and levels of various forms of carnitine in serum or urine

3.9.1 Relationship between carnitine intake and levels of various forms of carnitine in serum or urine.

There were significant positive correlations between carnitine intake and free or total carnitine in urine expressed as umole per liter ($r = 0.37$, $P<0.01$; $r = 0.25$, $P<0.05$) or umole per day ($r = 0.33$, $P<0.025$; $r = 0.30$, $P<0.05$) whereas there was significant negative

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Table 3 - 14 Means ± SEM of energy, protein, fat, carbohydrate and carnitine intake and percentage of caloric distribution in control and underweight adults

	Subject		Consumption per capita per day					% Caloric distribution		
	Group	No	Energy kcal	Pro g	Fat g	CHO g	Carn umole	Pro	Fat	CHO
I	Control men	15	2013±100	63±3	66±4	292±21	176±25	13±0	30±2	57±2
II	Control women	15	1547± 83	56±3	52±4	212±14	319±73	15±1	30±2	55±2
III	Underweight men	5	1537±101	63±3	60±3	200±26	159±18	17±1	36±4	51±4
IV	Underweight women	10	1642±186	59±8	56±6	234±28	271±52	14±1	31±1	56±3
P value by t test (2 tailed)										
II	vs I		<0.005	ns	<0.05	<0.005	ns	ns	ns	ns
IV	vs III		ns	ns	ns	ns	ns	ns	ns	ns
III	vs I		<0.02	ns	ns	<0.05	ns	<0.005	ns	ns
IV	vs II		ns	ns	ns	ns	ns	ns	ns	ns

Pro = protein; Fat = fat; CHO = carbohydrate; Carn = carnitine

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correlation between carnitine intake and % acylcarnitine in urine ($r = -0.28$, $P<0.05$). However no significant correlation between carnitine intake and carnitine forms in serum (Table 3 - 15).

3.9.2 Relationship between protein intake and various forms of carnitine in serum or urine.

There were significant positive correlations between protein intake and free or total carnitine in urine expressed as umole/l ($r = 0.28$, $P<0.05$; $r = 0.25$, $P<0.05$). However no significant correlation between protein intake and levels of various forms of carnitine in serum or urine expressed as umole/day or their percent acylcarnitine were observed (Table 3 - 16).

3.9.3 Relationship between fat intake and levels of various forms of carnitine in serum or urine.

There were significant negative correlation between fat intake and percent acylcarnitine in serum ($r = -0.29$, $P<0.05$), and significant positive correlations between fat intake and free, acyl- or total carnitine in urine in umole per day ($r = 0.34$, $P<0.0125$; $r = 0.29$, $P<0.05$; $r = 0.36$, $P<0.01$) (Table 3 - 17).

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Table 3 - 15 Relationship between carnitine intake in umole per capita per day and levels of various forms of carnitine in serum or urine

Variable (Y)	$Y = a_o + a_1 x$	r	DF	t	p
Carnitine forms in serum, umole/l					
Free carnitine	65.79 + 0.01x	0.1197	43	0.7908	ns
Acylcarnitine	61.20 + 0.01x	0.0594	43	0.3903	ns
Total carnitine	127.44 + 0.02x	0.1000	43	0.6589	ns
% Serum acylcarnitine	46.95 - 0.001x	-0.0238	43	-0.1564	ns
Carnitine forms in urine, umole/l					
Free carnitine	85.78 + 0.27x	0.3724	42	2.6009	<0.01
Acylcarnitine	167.77 + 0.06x	0.0938	42	0.6104	ns
Total carnitine	271.09 + 0.29x	0.2543	42	1.7044	<0.05
Carnitine forms in urine, umole/day					
Free carnitine	26.40 + 0.19x	0.3312	42	2.2750	<0.025
Acylcarnitine	172.24 + 0.09x	0.1240	42	0.8099	ns
Total carnitine	306.07 + 0.26x	0.2591	42	1.7387	<0.05
% Acylcarnitine in urine	59.02 - 0.02x	-0.2804	42	-1.8932	<0.05

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Table 3 - 16 Relationship between protein intake in gram per capita per day and levels of various forms of carnitine in serum or urine

Variable (Y)	$Y = a_o + a_1 x$	r	DF	t	P
Carnitine forms in serum, umole l					
Free carnitine	63.75 + 0.07x	0.0704	43	0.4631	ns
Acylcarnitine	81.20 - 0.30x	-0.1707	43	-1.1358	ns
Total carnitine	145.48 - 0.23x	-0.1044	43	-0.6884	ns
% Acylcarnitine in serum	56.63 - 0.17x	-0.2292	43	-1.5443	ns
Carnitine forms in urine, umole/l					
Free carnitine	20.64 + 2.31x	0.2839	42	1.9187	<0.05
Acylcarnitine	89.32 + 1.56x	0.1768	42	1.1640	ns
Total carnitine	109.79 + 3.85x	0.2530	42	1.6945	<0.05
Carnitine forms in urine, umole/day					
Free carnitine	58.85 + 1.90x	0.2503	42	1.6758	ns
Acylcarnitine	141.22 + 0.92x	0.1258	42	0.8221	ns
Total carnitine	200.07 + 2.82x	0.2136	42	1.4171	ns
% Acylcarnitine in urine,	67.18 - 9.22x	-0.2342	42	-1.5611	ns

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Table 3 - 17 Relationship between fat intake in gram per capita per day and levels of various forms of carnitine in serum or urine

Variable (Y)	$Y = a_o + a_1 x$	r	DF	t	P
Carnitine forms in serum, umole/l					
Free carnitine	56.68 + 0.20x	0.2075	43	1.3908	ns
Acylcarnitine	82.28 - 0.33x	-0.2053	43	-1.3754	ns
Total carnitine	139.36 - 0.13x	-0.0662	43	-0.4352	ns
% Acylcarnitine in serum	57.92 - 0.19x	-0.2936	43	-2.0144	<0.05
Carnitine forms in urine, umole/l					
Free carnitine	87.22 + 1.24x	0.1727	42	1.1360	ns
Acylcarnitine	122.31 + 1.03x	0.1335	42	0.8728	ns
Total carnitine	209.43 + 2.27x	0.1703	42	1.1199	ns
Carnitine forms in urine, umole/day					
Free carnitine	37.36 + 2.31x	0.3464	42	2.3933	<0.0125
Acylcarnitine	86.76 + 1.87x	0.2909	42	1.9704	<0.05
Total carnitine	124.12 + 4.18x	0.3602	42	2.5024	<0.01
% Acylcarnitine in urine	61.07 - 0.12x	-0.1441	42	-0.9437	ns

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3.10 Relationship between levels of various forms of serum carnitine and their corresponding forms in urine.

There were significant possitive correlation between serum free carnitine level and urinary free carnitine level expressed as umole per day ($r = 0.44$, $P<0.0005$) or umole per kg per day ($r = 0.48$, $P<0.0005$) (Table 3 - 18).

3.11 Relationship between various forms of serum carnitine level and the variables of serum : albumin, cholesterol and triglycerides leve's

There were significant positive correlation between serum acyl- or total carnitine level and serum albumin level ($r = 0.297$, $P<0.01$; $r = 0.32$, $P<0.005$) and between every form of serum carnitine and serum cholesterol ($r = 0.247$, $P<0.025$; $r = 0.239$, $P<0.025$; $r= 0.300$, $P<0.005$) whereas no significant correlation between various forms of serum carnitine and serum triglycerides (Table 3 - 19).

3.12 Relationship between various forms of carnitine in serum and anthropometric measures

There were significant negative correlation between serum free carnitine and percent upper arm muscle circumference ($r = -0.366$, $P<0.0025$) and between serum acylcarnitine and percent upper arm circumference ($r = 0.212$, $P<0.05$) (Table 3 - 20).

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Table 3 - 18 Relationship between levels of various forms of serum carnitine in umole per liter and the corresponding forms in urine

Variable (Y)	$Y = a_o + a_1x$	r	DF	t	P
Carnitine forms in urine, umole/d					
Free carnitine	-68.95 + 3.40x	0.4440	69	4.1158	<0.0005
Acylcarnitine	202.86 - 0.40x	-0.1129	69	-0.9436	ns
Total carnitine	238.95 + 0.73x	0.1325	69	1.1106	ns
Carnitine forms in urine, umole/kg/d					
Free carnitine	-1.52 + 0.07x	0.4800	67	4.4791	<0.0005
Acylcarnitine	4.30 - 0.01x	-0.1362	67	-1.1253	ns
Total carnitine	5.12 + 0.01x	0.1180	67	0.9730	ns
% Acylcarnitine in urine	59.04 - 0.09x	-0.0667	69	-0.5556	ns

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Table 3 - 19 Relationship between various forms of serum carnitine level and the variables of serum albumin, cholesterol and triglycerides levels

Variable (Y)	$Y = a_o + a_1x$	r	DF	t	P
When x = serum free carnitine					
Albumin	3.59 + 0.02x	0.1863	70	1.5880	ns
Cholesterol	146.79 + 0.80x	0.2470	74	2.1925	<0.025
Triglycerides	53.04 + 0.24x	0.0951	74	0.8217	ns
When x = serum acylcarnitine					
Albumin	4.54 + 0.004x	0.2970	70	2.6021	<0.01
Cholesterol	176.32 + 0.38x	0.2389	74	2.1160	<0.025
Triglycerides	63.51 - 0.07x	-0.0283	74	-0.2434	ns
When x = serum total carnitine					
Albumin	4.31 + 0.004x	0.3202	70	2.8278	<0.005
Cholesterol	149.28 + 0.39x	0.2997	74	2.7020	<0.005
Triglycerides	67.62 + 0.01x	0.0108	74	0.0931	ns

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Table 3 - 20 Relationship between various forms of serum carnitine levels and variables of anthropometric measures

Variable (Y)	$Y = a_o + a_1 x$	r	DF	t	P
When x = serum free carnitine					
% Std weight-height	80.07 - 0.02x	-0.0249	81	-0.2241	ns
% Std TST	89.05 - 0.23x	-0.1153	72	-0.9849	ns
% Std MUC	83.18 + 0.01x	0.0116	72	0.0984	ns
% Std UMC	94.34 - 0.09x	-0.3656	72	-3.3325	<0.0025
When x = serum acylcarnitine					
% Std weight-height	74.78 + 0.06x	0.1568	81	1.4291	ns
% Std TST	64.36 + 0.13x	0.1394	72	1.1944	ns
% Std MUC	79.13 + 0.07x	0.2124	72	1.8444	<0.05
% Std UMC	82.48 + 0.05x	0.1665	72	1.4332	ns
When x = serum total carnitine					
% Std weight-height	73.72 + 0.04x	0.1181	81	1.0707	ns
% Std TST	65.89 + 0.06x	0.0696	72	0.5917	ns
% Std MUC	77.21 + 0.05x	0.1814	72	1.5650	ns
% Std UMC	79.74 + 0.05x	0.1798	72	1.5514	ns

TST = triceps skin fold thickness; MUC = mid upper arm circumference; UMC = upper arm muscle circumference.

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3.13 Nutritional status in patients on tube feeding

The dietary assessment, fever and treatment in individual patients on Ramathibodi blenderized formula are shown in Table 3 - 21 to 3 - 37. Their free and total carnitine levels in serum and urine are shown in Figures 3 - 1A, 3 - 1B, 3 - 1C and 3 - 1D.

The same tabulation were made in patients on Sobel formula (Table 3 - 38 to 3 - 44) and their free and total carnitine levels in serum and urine are shown in Figure 3 - 2

It should be noted that the urinary carnitine excretion levels in each patient were measured daily throughout the study period. However, only the means of urinary carnitine excretion in each 7 - day study period are shown in those Figures.

3.14 Nutritional status in patients on TPN

The dietary assessment, fever and treatment in individual patients on TPN are shown in Table 3 - 45 to 3 - 58 and their free and total carnitine levels in serum and urine are shown in Figures 3 - 3A, 3 - 3B, 3 - 3C and 3 - 3D. The notify as in the previous figures (Figures 3 - 1A....1D and 3 - 2) should be reminded as well.

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Table 3 - 21 Dietary assessment, fever and treatment in patient S.MS

Parameter	Before study	During study, week	
		1st	2nd
Intake/day[a]			
Energy, kcal	1308 ± 246	2080 ± 60	1542 ± 499
Protein, g	19.9 ± 11.7	71.8 ± 6.2	27.5 ± 9.9
Fat, g	11.9 ± 7.0	49.0 ± 2.9	47.3 ± 17.0
Carbohydrate, g	280 ± 43	338 ± 10	247 ± 77
Carnitine, umole	72 ± 43	261 ± 23	100 ± 36
Fever, ^{o}C	No fever throughout the study		

[a]Derived from Ramathibodi blenderized formula plus IV glucose.

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Table 3 - 22 Dietary assessment, fever and treatment in patient L.YM

Parameter	Before study	During study, week	
		1st	2nd
Intake/day			
Energy, kcal	1561[1]	1497 ± 177[2]	-[3]
Protein, g	68.4	68.9 ± 7.6	-
Fat, g	41.0	44.0 ± 3.5	-
Carbohydrate, g	229.6	198 ± 38	-
Carnitine, umole	249	208 ± 54	-
Fever, °C	No fever throughout the study		

[1]Derived from IV glucose plus Ramathibodi blenderized formula.

[2]Derived from Ramathibodi blenderized formula plus soft diet.

[3]Prescription of regular diet plus soy bean milk. Actual intake was unavailable.

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Table 3 - 23 Dietary assessment, fever and treatment in patient F.S.

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1	2384 ± 97[2]	2440 ± 119[2]	2631 ± 53[3]	2008 ± 436[3]
Protein, g		73.9 ± 5.0	84.7 ± 3.6	92.2 ± 3.4	69.4 ± 16.0
Fat, g		98.9 ± 4.3	110.0 ± 5.7	122.1 ± 2.5	91.9 ± 21.2
Carbohydrate, g		300	278	291	226
Carnitine, umole		269 ± 15.3	308 ± 13	336 ± 7	253 ± 58
Fever, °C					
Range		37.5 - 40	37.4 - 40	37.5 - 39	37.5 - 38.2
Days of fever > 37.5°C		7	5	7	7
Antibiotics :					
Penicillin G		+	+		
Kanamycin		+	+		
Dicloxacillin				+	

[1]Preseription of IV glucose.

[2]Derived from Ramathibodi blenderized formuls plus IV glucose.

[3]Derived from Ramathibodi blenderized formula.

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Table 3 - 24 Dietary assessment, fever and treatment in patient V.TN

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	1014 ± 131[1]	2403 ± 123[2]	2581 ± 108[2]
Protein, g	0	66.8 ± 8.1	82.9 ± 3.9
Fat, g	0	81.5 ± 14.0	109.7 ± 5.2
Carbohydrate, g	254 ± 33	351	316
Carnitine, umole	0	243 ± 30	302 ± 14
Fever, °C			
Range	37 - 39	38 - 38.8	37 - 38.4
Days of fever>37.5°C	6	7	6
Antibiotics :			
Penicillin G	+	+	+
Gentamicin	+	+	+

[1]Derived from IV glucose.

[2]Derived from Ramathibodi blenderized formula plus IV glucose.

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Table 3 - 25 Dietary assessment, fever and treatment in patient A.TS

Parameter	Before study	During study
Intake/day		
Energy, kcal	[1]	2425 ± 76[2]
Protein, g		92.4 ± 2.2
Fat, g		103.8 ± 4.7
Carbohydrate, g		280 ± 22
Carnitine, umole		336 ± 8
Fever, °C		
Range	36 - 39	35.2 - 39.3
Days of fever > 37.5°C	5	3
Antibiotics :		
PGS	+	+
Kanamycin		+
Robaxin		+

[1] Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.

[2] Derived from Ramathibodi blenderized formula.

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Table 3 - 26 Dietary assessment, fever and treatment in patient J.MG

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day[1]			
Energy, kcal	1483 ± 218	1699 ± 127	1517 ± 279
Protein, g	59.4 ± 8.5	76.2 ± 4.1	58.2 ± 10.8
Fat, g	41.9 ± 9.0	53.5 ± 4.2	43.5 ± 9.2
Carbohydrate, g	224.3	228.5	222.6
Carnitine, umole	216 ± 31	277 ± 15	212 ± 39
Fever, °C			
Range	36.8 - 38	36.4 - 37.6	36.3 - 37.3
Days of fever >37.5°C	3	1	
Antibiotics :			
Penicillin G	+	+	+
Gentamicin	+	+	+

[1]Derived from Ramathibodi blenderized formula and IV glucose.

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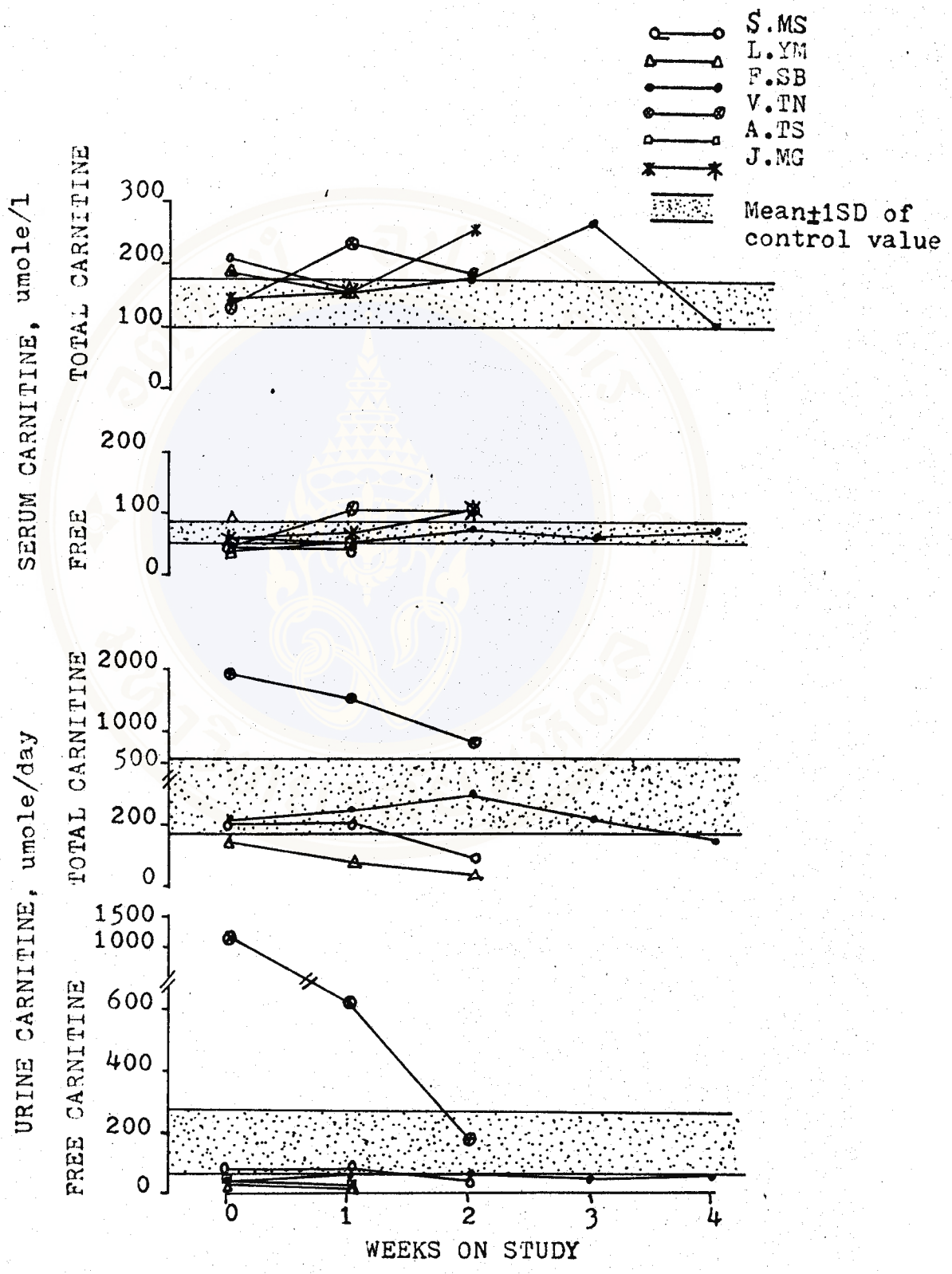

FIGURE 3-1A CARNITINE STATUS IN TETANUS PATIENTS ON RAMATHIBODI BLENDERIZED FORMULA

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Table 3 - 27 Dietary assessment, fever and treatment in patient B.BN

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	1	3102 ± 199[2]	2982 ± 74[2]
Protein, g		154 ± 7	143 ± 4
Fat, g		159 ± 19	129 ± 6
Carbohydrate, g		284 ± 10	312 ± 3
Carnitine, umole		488 ± 27	520 ± 16
Fever, °C			
Range	36.5 - 38.8	36.3 - 39	36.5 - 39.3
Days of fever >37.5°C	7	6	7
Antibiotics :			
PGS	+	+	
Gentamicin	+	+	
Hormones :			
Dexamethasone	+		

[1]Preseription of Ramathibodi blenderized formula. Actual intake was unavailable.

[2]Derived from Ramathibodi blenderized formula.

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Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1	2443 ± 217[2]	3115 ± 30[3]	2674 ± 394[3]	4
Protein, g		86 ± 8	109 ± 1	100 ± 8	
Fat, g		114 ± 10	144 ± 1	122 ± 18	
Carbohydrate, g		268.7	344.9	292.8	
Carnitine, umole		360 ± 112	398 ± 0.4	364 ± 8	
Fever, °C					
Range	37.5 - 37.8	37.0 - 38.5	37.0 - 38.5	37 - 38	
Days of fever > 37.5°C	7	2	2	2	
Antibiotics :					
Amikycin	+				
Hormones :					
Deca-dulabolin		+			

[1]Prescription of Ramathibodi blenderized formula or Sobel fromula or soft diet. Actual intake was unavailable.

[2]Derived from Ramathibodi blenderized formula or Sobel formula.

[3]Derived from Ramathibodi blenderized formula.

[4]Prescription of Ramathibodi blenderized formula, Actual intake was unavailable.

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Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	[1]	2343 ± 85[2]	2734 ± 0[2]	2734 ± 0[2]
Protein, g		81 ± 4	96	96
Fat, g		109 ± 4	127	127
Carbohydrate, g		295	349	349
Carnitine, umole		295 ± 10	302	302
Fever, °C				
Range	37 - 38.5	37 - 38.5		37 - 38.8
Days of fever ⩾ 37.5°C	1	5		3
Antibiotics :				
Chloramphenicol		+		
Gentamicin		+		
Ampicillin		+	+	
Nitrofurantonin		+	+	+
Hormones :				
Thyroid extract	+	+	+	+
Vitamin D_2	+	+	+	+

[1]Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.
[2]Derived from Ramathibodi blenderized formula.

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Table 3 - 30 Dietary assessment, fever and treatment in patient T.SU

Parameter	Before study	During study, wk				
		1st	2nd	3rd	4th	5th
Intake/day						
Energy, kcal	[1]	1556 ± 164[2]	1397 ± 320[3]	1	1814 ± 299[2]	4
Protein, g		114 ± 10	125 ± 16		87 ± 14	
Fat, g		48 ± 5	38 ± 12		39 ± 2	
Carbohydrate, g		167	142		265	
Carnitine, umole		416 ± 2	446 ± 46		317 ± 51	
Fever, °C						
Range		37 - 38	-		-	
Days of fever > 37.5°C		3				
Antibiotics :						
Isoniazid		+	+	+	+	
Ethambutol HCl		+	+	+	+	
Streptomycin		+	+	-	-	
Phenoxymethyl penicillin		+	+	-	-	

[1] Prescription of soft diet. Actual value was unavailable.

[2] Derived from Ramathibodi blenderized formula plus IV glucose.

[3] Derived from Ramathibodi blenderized formula plus IV glucose and soy bean milk.

[4] Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.

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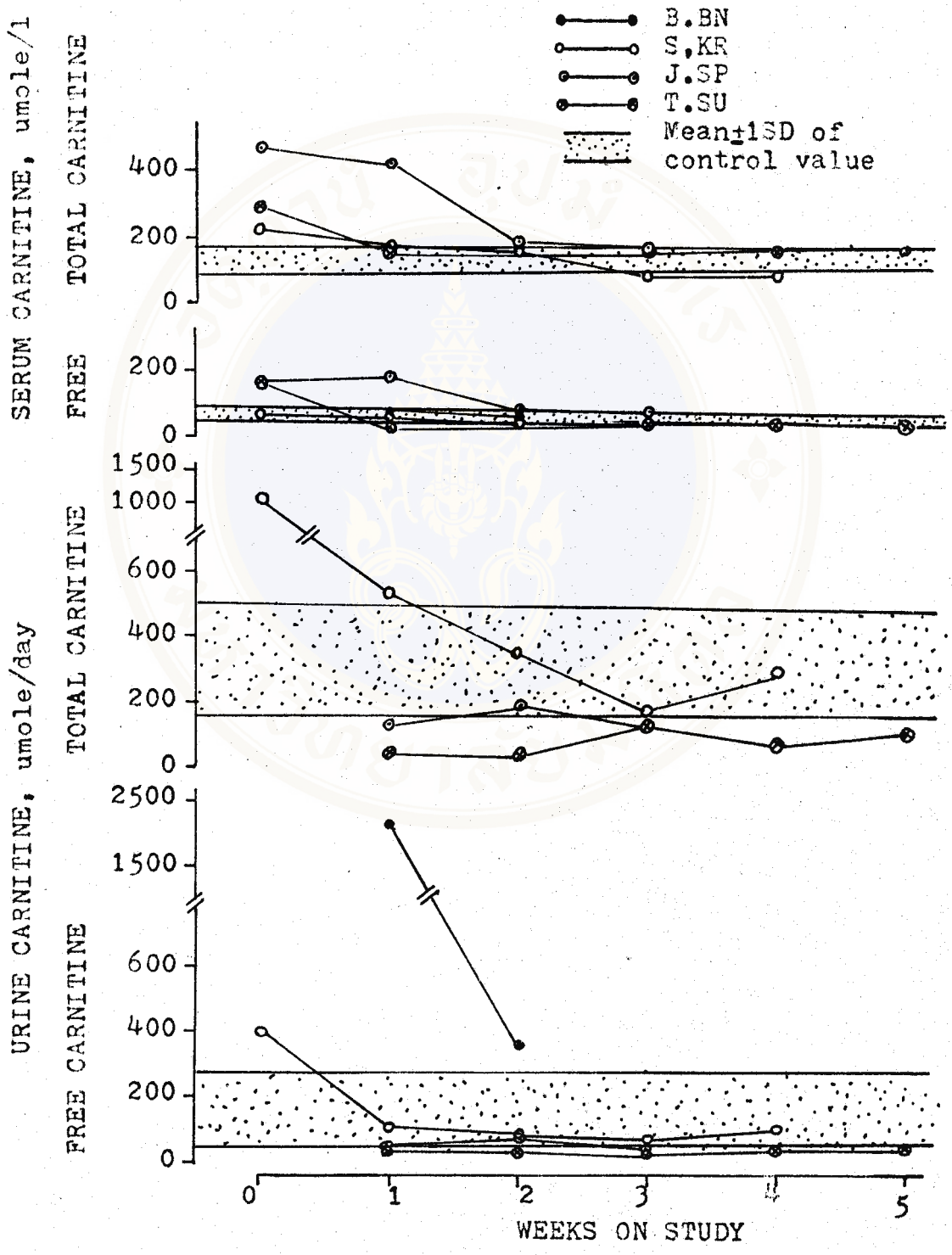

FIGURE 3-1B CARNITINE STATUS IN PATIENTS ON RAMATHIBODI BLENDERIZED FORMULA

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Table 3 - 31 Dietary assessment, fever and treatment in patient S.SM

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	1794 ± 177[1]	2650 ± 119[2]	2650 ± 119[2]	3
Protein, g	72 ± 4	93 ± 4	88 ± 5	
Fat, g	53 ± 12	122 ± 5	115 ± 6	
Carbohydrate, g	257 ± 22	298 ± 13	282 ± 16	
Carnitine, umole	263 ± 14	324 ± 20	320 ± 18	
Fever, °C				
Range	37.8 - 39	37.7 - 39.6	37.6 - 39	37.4 - 40
Days of fever > 37.5°C	7	7	7	3/4
Blood transfusion	+			
Hormone :				
Dexamethasone	+			
Antibiotics :				
Penicillin	+	+		
Gentamicin	+	+		

[1]Derived from IV glucose plus Ramathibodi blenderized formula.

[2]Derived from Ramathibodi blenderized formula.

[3]Prescription of RBF. Actual intake was unavailable.

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Table 3 - 32 Dietary assessment, fever and treatment in patient C.P

Parameter	Before study	During study, wk			
		1st	2nd	3nd	4th
Intake/Day					
Energy intake, kcal	[1]	1683 ± 300[2]	2278 ± 147[2]	1532 ± 164[2]	1219[2]
Protein, g		60 ± 11	82 ± 5	59 ± 7	50
Fat, g		77 ± 14	104 ± 7	68 ± 5	56
Carbohydrate, g		186	236	169	129
Carnitine, umole		220 ± 39	300 ± 20	214 ± 24	180
Fever, °C					
Range	37.5 - 38.5	37.5 - 39	38.4 - 39.1	37.7 - 37.5	37.7 - 39.7
Days of fever > 37.5°C	6	7	7	7	7

[1] Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.

[2] Derived from Ramathibodi blenderized formula.

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Table 3 - 33 Dietary assessment, fever and treatment in patient K.ST

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1114[1]	2708 ± 99[1]	2705 ± 53[1]	2759 ± 105[1]	2724 ± 41[1]
Protien, g	46	89 ± 4	92 ± 4	90 ± 4	92 ± 2
Fat, g	26	126 ± 5	126 ± 2	132 ± 6	128 ± 3
Carbohydrate, g	148	305 ± 11	299 ± 6	304 ± 12	297 ± 7
Carnitine, umole	168	324 ± 14	334 ± 14	326 ± 14	336 ± 8
Fever, ^{o}C					
Range	36.5 - 39.5	37.2 - 38.4	37.2 - 38	-	37 - 37.8
Days of fever > 37.5^{o}C	5	5	2	-	3
Blood transfusion	+				
Antibiotics :					
Chloramphenical	+	+	-	-	-
Ampicillin	-	+	-	-	-
PGS	+	+	-	-	-
Bactrim	-	+	+	-	-

[1]Derived from Ramathibodi blederized formula.

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Table 3 - 34 Dietary assessment, fever and treatment in patient P.SH

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1	2351 ± 186[2]	2793 ± 42[2]	2724 ± 126[2]	2810[2]
Protein, g		82 ± 2	91 ± 1	90 ± 6	92
Fat, g		102 ± 18	128 ± 2	131 ± 4	134
Carbohydrate, g		275 ± 8	318 ± 7	296 ± 18	309
Carnitine, umole		300 ± 8	331 ± 3	329 ± 20	336
Fever, °C					
Range				37.5 - 38.5	
Days of fever >37.5°C				7	
Hormones :					
Dexamethasone	+	+			

[1] Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.

[2] Derived from Ramathibodi blenderized formula.

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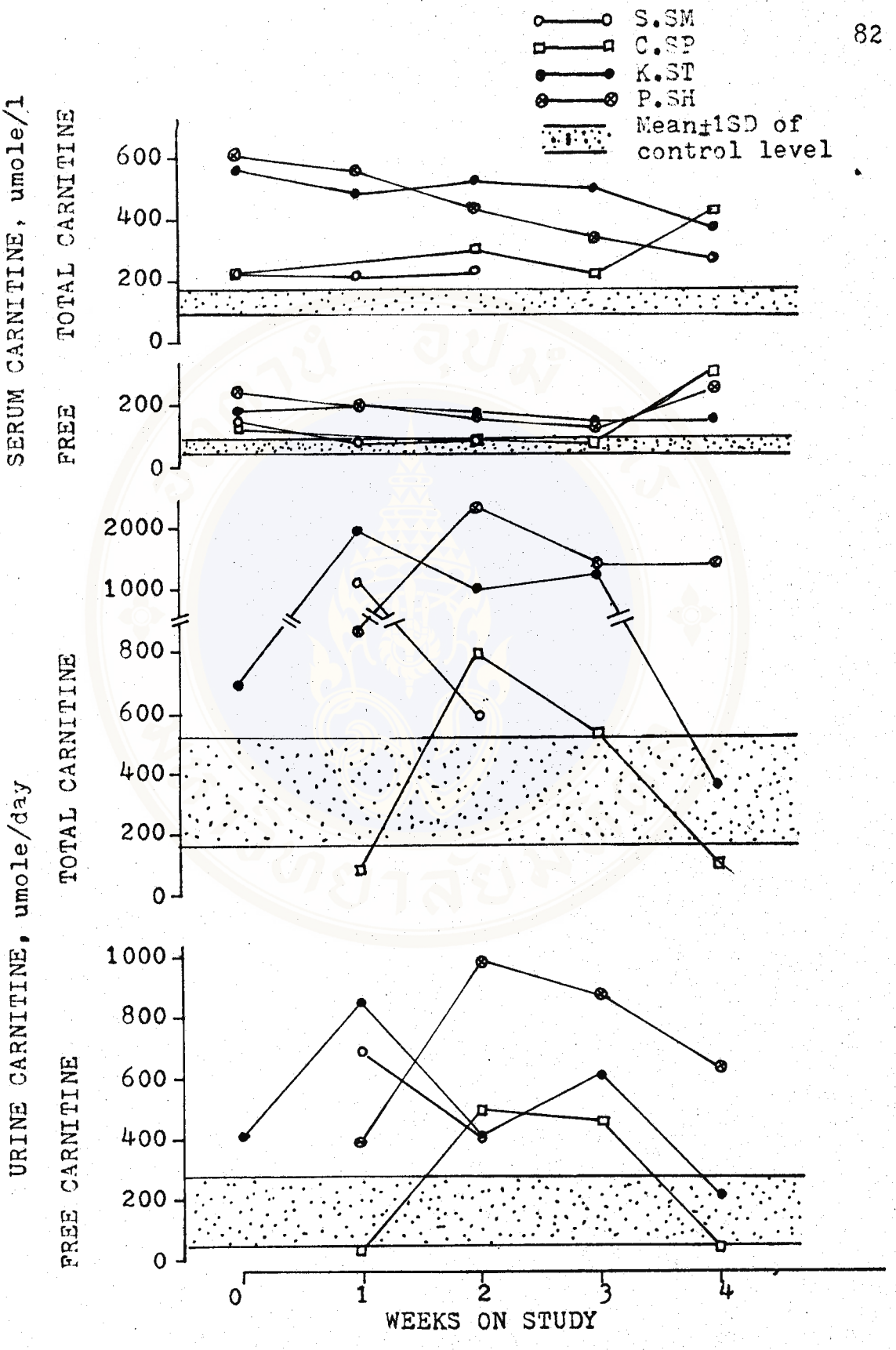

FIGURE 3-1C CARNITINE STATUS IN PATIENTS ON RAMATHIBODI BLENDERIZED FORMULA

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Table 3 - 35 Dietary assessment, fever and treatment in patient L.HS

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	[1]	1651 ± 47[2]	[3]
Protein, g		72 ± 2	
Fat, g		76 ± 2	
Carbohydrate, g		170 ± 5	
Carnitine, umole		263 ± 8	
Fever, °C	No fever throughout the study		
Hormone :			
Prednisolone	+	+	-

[1] Prescription of Ramathibodi blenderized formula.
Actual intake was unavailable.

[2] Derived from Ramathibodi blenderized formula.

[3] Prescription of Ramathibodi blenderized formula or soft diet.
Actual intake was unavailable.

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Table 3 - 36 Dietary assessment, fever and treatment in patient Y.JD

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	[1]	1328 ± 199[2]	1725 ± 93[2]	[3]
Protein, g		66 ± 4	60 ± 3	
Fat, g		52 ± 12	79 ± 4	
Carbohydrate, g		150 ± 22	194 ± 10	
Carnitine, umole		240 ± 16	220 ± 12	
Fever, °C				
Range		37.2 - 38	37 - 37.6	36.6 - 37.7
Days of fever > 37.5°C		4	1	2
Antibiotic :				
Biotrim	-	+	+	-

[1] Prescription of Ramathibodi blenderized formula. Actual intake was unavailable.

[2] Derived from Ramathibodi blenderized formula.

[3] Prescription of regular diet plus soy bean milk.

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Table 3 - 37 Dietary assessment, fever and treatment in patiens N.KP

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1	2300[2]	1902 ± 376[2]	2653 ± 68[2]	3720[2]
Protein, g		106	66 ± 11	91 ± 5	96
Fat, g		83	91 ± 20	125 ± 0.4	125
Carbohydrte, g		283	207 ± 38	290 ± 11	551
Carnitine, umole		387	234 ± 40	332 ± 17	349
Fever, °C	No fever throughout the study				
Drugs :					
Inderal	+	+	+	+	+
Tapazol	-	-	-	+	+

[1]Prescription of Ramathibodi blenderized formula or full liquid diet plus IV glucose.

[2]Derived from Ramathibodi blenderized formula.

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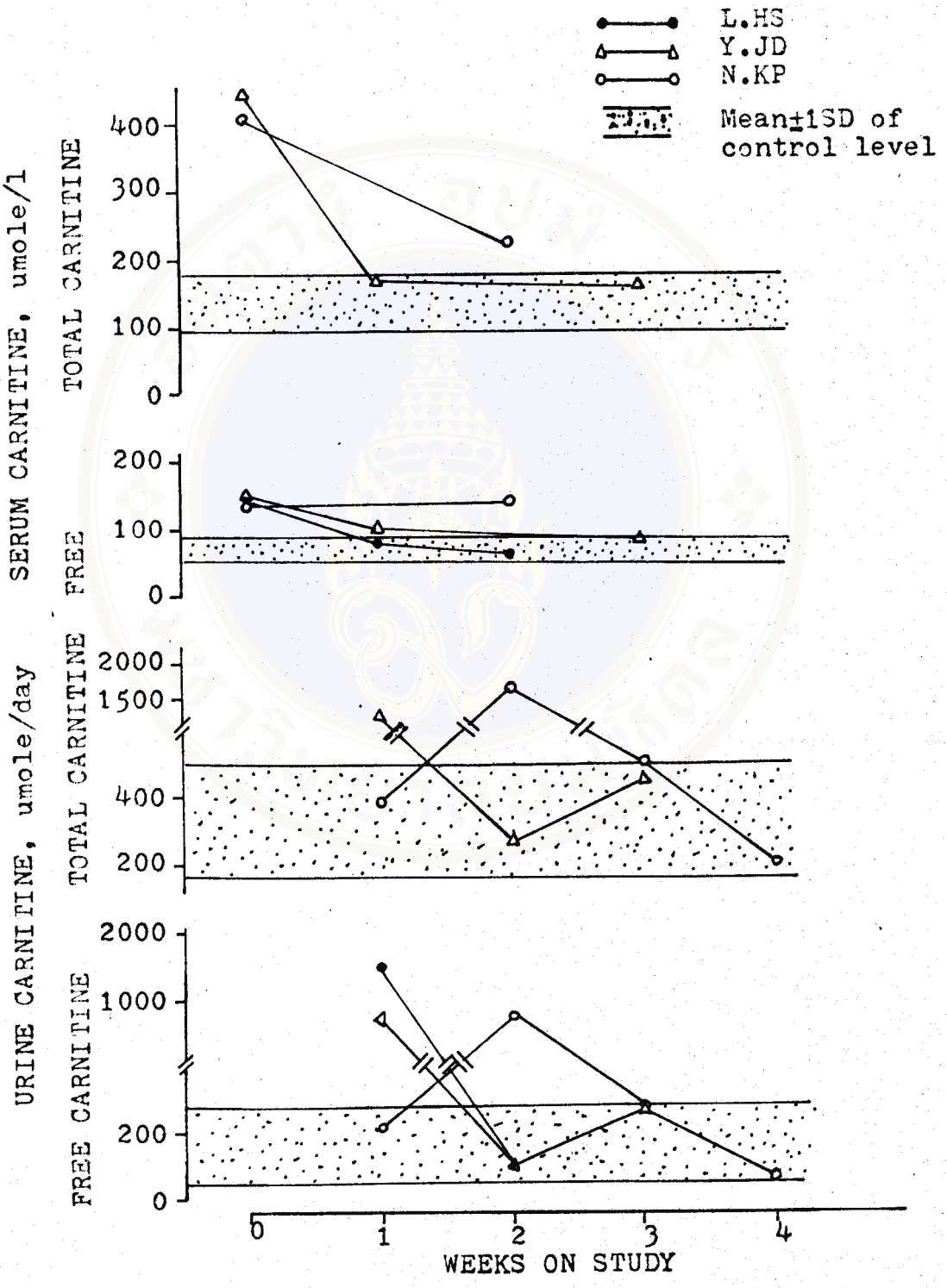

FIGURE 3-1D CARNITINE STATUS IN PATIENTS ON RAMATHIBODI BLENDERIZED FORMULA

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Table 3 - 38 Dietary assessment, fever and treatment in patient N.H

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	2340[1]	2320 ± 129[2]	2537 ± 17[2]	2460 ± 65[2]	2520[2]
Protein, g	88	93 ± 5	102 ± 0.7	99 ± 2	101
Fat, g	109	72 ± 4	79 ± 1	76 ± 2	78
Carbohydrate, g	256	324	355	344	352
Carnitine, umole	320	1.11 ± 0.06	1.22 ± 0.01	1.18 ± 0.03	1.21
Lysine, g	UA	5.95 ± 0.33	6.54 ± 0.04	6.32 ± 0.15	6.47
Methionine, g	UA	1.18 ± 0.06	1.30 ± 0.01	1.25 ± 0.03	1.28
Fever, °C					
Range	37 - 39.4	37 - 38.5		37 - 38	38 - 40
Days of fever >37.5°C	4	4		3	7
Antibiotics :					
Gentamicin	+	-	-	-	-
Chloramphenical	+	-	-	-	-
Penicillin G	+	-	-	-	-
Colistin	+	+	+	-	-

[1]Derived from Ramathibodi blenderized formula.

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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Table 3 - 39 Dietary assessment, fever and treatment in patient P.VS

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	1622[1]	1857 ± 166[2]	2500[2]
Protein, g	73	75 ± 7	101
Fat, g	97	58 ± 5	78
Carbohydrate, g	234	260	349
Carnitine, umole	266	0.89 ± 0.08	1.20
Lysine, g	UA	4.77 ± 0.43	6.42
Methionine, g	UA	0.94 ± 0.08	1.27
Fever, °C			
Range	37 - 38	37 - 37.9	37 - 37.4
Days of fever > 37.5°C	2	3	
Whole blood transfusion	+	-	-
Antibiotic :			
Chloramphenical	+	+	-
Hormones :			
Dexamethasone	+	-	-
Prednisolone	+	-	-

[1]Derived from Ramothibodi blenderized formula.

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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Table 3 - 40 Dietary assessment, fever and treatment in patient K.CK

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	2048 ± 386[1]	2830 ± 144[2]	2592 ± 38[2]	2691 ± 29[2]
Protein, g	70 ± 15	101	101	101
Fat, g	75 ± 2	80	80	80
Carbohydrate, g	273 ± 76	427 ± 14	367 ± 10	392 ± 7
Carnitine, umole	18 ± 8	12.1	12.1	12.1
Lysine, g	UA	6.42	6.42	6.42
Methionine, g	UA	1.27	1.27	1.27
Fever, ^{o}C				
Range	38 - 36.9	38.9 - 37.4	37.4 - 37.8	37.3 - 37.8
Days of fever $> 37.5^{o}C$	2	4	4	3
Hormones :				
Dexamethasone	+	-	-	-
Predrisolone	+	+	+	-
Antibiotic :				
PGS	+	+	+	-

[1]Derived from Ramathibodi blenderized formula or Sobel formula.

[2]Derived from Sobel formula plus IV glucose,

UA = Actual intake was unavailable.

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Table 3 - 41 Dietary assessment, fever and treatment in patient T.CPK

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	683 ± 197[1]	2468 ± 159[2]	2678 ± 31[2]	2837 ± 94[2]	3
Protein, g	25 ± 11	94 ± 6	102 ± 1	111 ± 2	
Fat, g	20 ± 12	78 ± 1	79 ± 0.5	86 ± 2	
Carbohydrate, g	102	348	390	406	
Carnitine, umole	79	1.12 ± 0.07	1.21 ± 0.01	1.32 ± 0.03	
Lysine, g	UA	5.99 ± 0.39	6.52 ± 0.04	7.07 ± 0.15	
Methionine, g	UA	1.18 ± 0.08	1.29 ± 0.01	1.40 ± 0.03	
Fever, °C					
Range	38 - 39.5	38 - 39.8	37.3 - 38.2	37 - 38	37 - 37.8
Days of fever > 37.5°C	7	7	5	2	2
Plasma transfusion	+	+			
Antibiotics :					
PGS	+	-	-	-	-
Gentamicin	-	+	-	-	-
Chloramphenical	-	+	+	+	-
Cefacidal	-	+	+	+	-

[1]Derived from Ramathibodi blenderized formula

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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Table 3 - 42 Dietary assessment, fever and treatment in patient P.HP

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	1128 ± 173[1]	2355 ± 244[1]	2573 ± 682[2]
Protein, g	51 ± 8	94 ± 9	98 ± 20
Fat, g	30 ± 5	76 ± 8	80 ± 16
Carbohydrate, g	163 ± 12	325	365
Carnitine, umole	185 ± 14	20 ± 9	2.3 ± 0.6
Lysine, g	UA	UA	9.9 ± 4.2
Methionine, g	UA	UA	2.0 ± 0.8
Fever, °C			
Range		36.4 - 37.6	
Days of fever > 37.5°C		1	
Blood transfusion		+	
Hormones :			
Stenozolol	+	+	+
NPH	+	+	+

[1]Derived from Ramathibodi blenderized or Sobel formula.

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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Table 3 - 43 Dietary assessment, fever and treatment in patient J.SS

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	1082 ± 22[1]	1333 ± 47[2]	1193 ± 40[2]	1254 ± 86[2]
Protein, g	42	53 ± 4	48 ± 2	50 ± 3
Fat, g	33	42 ± 2	37 ± 1	39 ± 3
Carbohydrate, g	155	186	167	175
Carnitine, umole	52	0.63 ± 0.04	0.57 ± 0.02	0.6 ± 0.04
Lysine, g	UA	3.4 ± 0.24	3.06 ± 0.10	3.22 ± 0.2
Methionine, g	UA	0.67 ± 0.05	0.6 ± 0.02	0.64 ± 0.04
Fever, °C				
Range		37 - 37.8		
Days of fever > 37.5°C		2		
Antibiotics :				
Penicillin G	+	-	-	-
Gentamicin	+	-	-	-
Bactrim	-	-	+	+
Hormones :				
DOPA	+	+	+	+
NPH	+	+	+	+

[1]Derived from Ramathibodi blenderized formula.

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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Table 3 - 44 Dietary assessment, fever and treatment in patient H.SS

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1100 ± 100[1]	1586 ± 108[2]	1800[2]	1800[2]	1800[2]
Protein, g	44 ± 5	61 ± 5	72	72	72
Fat, g	24 ± 2	48 ± 4	56	56	56
Carbohyarate, g	176	228	252	252	252
Carnitine, umole	161 ± 20	0.73 ± 0.66	0.86	0.86	0.86
Lysine, g	UA	3.91 ± 0.34	4.02	4.02	4.02
Methionine, g	UA	0.77 ± 0.07	0.92	0.92	0.92
Fever, °C					
Range	37.2 - 37.7	37.4 - 38.7			
Days of fever > 37.5°C	1	6			
Antibiotics :					
Gentamicin	+	+	+	+	+
Carbenicillin	-	+	+		

[1]Derived from Ramathibodi blenderized formula.

[2]Derived from Sobel formula.

UA = Actual intake was unavailable.

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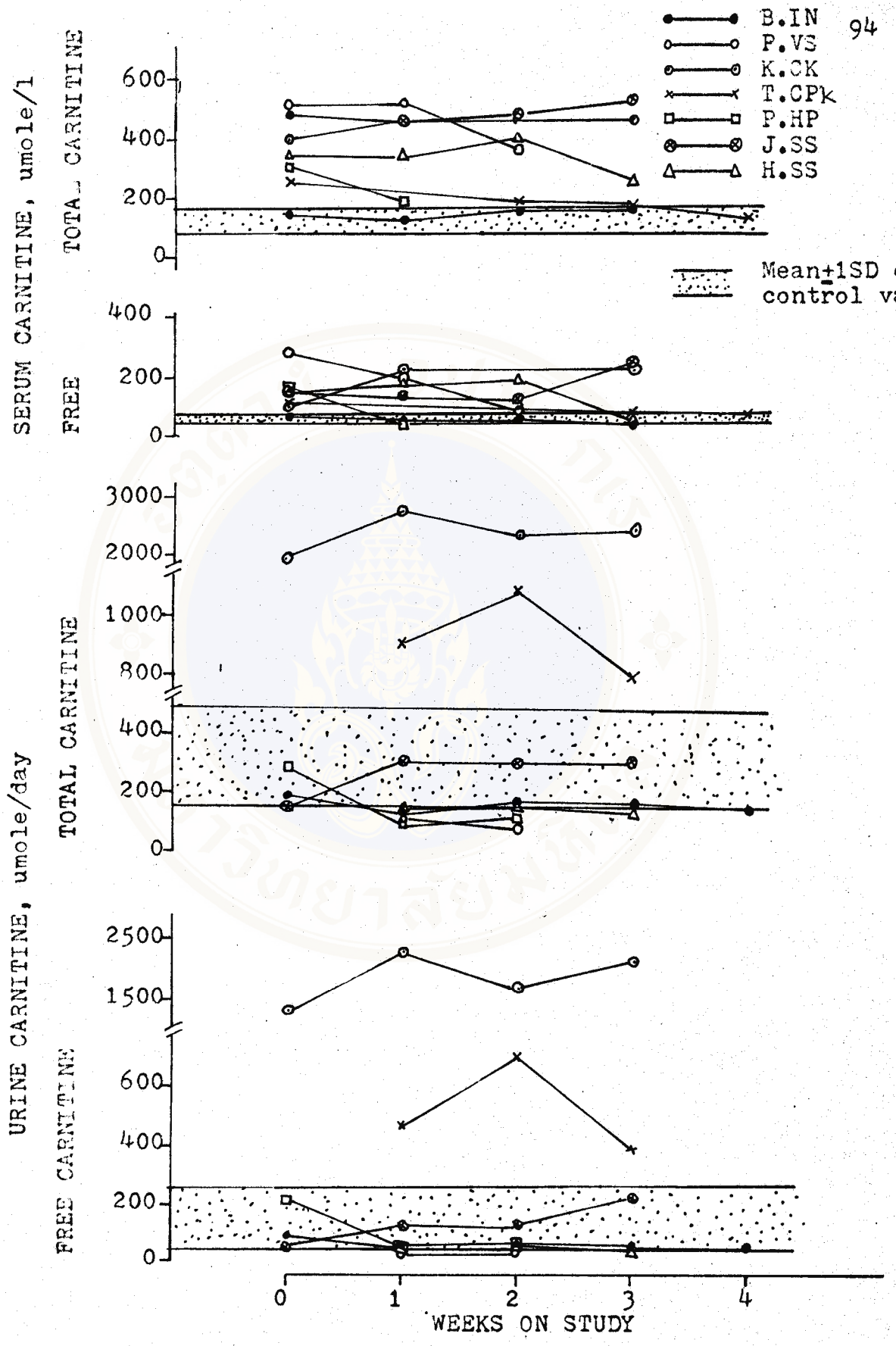

FIGURE 3-2 CARNITINE STATUS IN PATIENTS ON SOBEL FORMULA

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Table 3 - 45 Dietary assessment, fever and treatment in patient N.MN

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	[1]	2027 ± 378[2]	1631 ± 719[2]	1841 ± 814[3]
Protein, g		42 ± 0	36	43
Fat, g		0	0	0
Carbohydrate, g		507 ± 94	408 ± 180	460 ± 204
Carnitine, umole		0	0	UA
Lysine, g		0.6 ± 0	0.5 ± 0.1	UA
Methionine, g		0.4 ± 0	0.4 ± 0.2	UA
Fever, ^{o}C				
Range		37.3 - 37.9	37 - 39.8	37.3 - 39.5
Days of fever > 37.5^{o}C		4	4	4
Blood transfusion		-	-	+
Plasma transfusion		+	-	-
Antibiotic :				
Bactrim		-	+	+

[1] Prescription of regular diet. Actual intake was unavailable.

[2] Total parenteral nutrition

[3] Total parenteral nutrition plus soft diet.

UA = Actual intake was unavailable.

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Parameter	Before study	During study, wk				
		1st	2nd	3rd	4th	5th
Intake/day						
Energy, kcal	300[1]	1800 ± 251	1554 ± 151	2097 ± 428	3011 ± 458	3055 ± 357
Protein, g	0	43 ± 8	36 ± 8	52 ± 7	88 ± 5	106 ± 4
Fat, g	0	0	0	10 ± 7	45 ± 2	85 ± 6
Carbohydrate, g	75	450 ± 63	389 ± 38	506 ± 101	643 ± 111	658 ± 85
Carnitine, umole	0	0	0	28 ± 18	171 ± 18	242 ± 7
Lysine, g	0	4.3 ± 0.9	3.0 ± 0.7	UA	UA	UA
Methionine, g	0	2.6 ± 0.5	2.0 ± 0.4	UA	UA	UA
Fever, °C						
Range		36.8 - 37.6	37.4 - 39.5	37.6 - 39.7	37.5 - 39	36.8 - 37.6
Days of fever > 37.5°C		2	6	7	6	1
Plasma transfusion	+		+			
Antibiotics :						
PGS	+	+	+	+	+	+
Kanamycin	+	+	+	+	-	-
Chloramphenical	-	-	-	+	+	+
Colimycin	-	-	-	+	+	+

[1] Partial parenteral nutrition

[2] TPN

[3] TPN plus Ramathibodi blenderized formula.

UA = Actual intake was unavailable.

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Table 3 - 47 Dietary assessment, fever and treatment in patient S.MS

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	557 ± 61[1]	1881 ± 327[2]	1431 ± 330[3]
Protein, g	0	39 ± 8	15 ± 9
Fat, g	0	0	0
Carbohydrate, g	139 ± 15	470 ± 82	398 ± 82
Carnitine, umole	0	0	0
Lysine, g	0	6.7 ± 1.29	2.6 ± 1.5
Methionine, g	0	3.0 ± 0.6	1.1 ± 0.7
Fever, °C			
Range	38 - 39	37.5 - 38	37.5 - 38.5
Days of fever > 37.5°C	7	6	6
Antibiotics :			
PGS	+	-	-
Chloramphenical	+	+	+
Gentamicin	+	+	+
Plasma transfusion	-	+	+
Blood transfusion	-	-	+

[1]Derived from IV glucose.

[2]Derived from TPN.

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Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1150 ± 447[1]	1642 ± 86[2]	2110 ± 76[2]	2200[2]	1168 ± 354[3]
Protein, g	0	29 ± 5	42 ± 6	67 ± 10	32 ± 12
Fat, g	0	0	0	0	1.94
Carbohydrate, g	288	382	486	483	260
Carnitine, umole	0	0	0	0	9.48
Lysine, g	0	6.16 ± 0.96	6.16 ± 0.97	7.66 ± 0.94	UA
Methionine, g	0	2.71 ± 0.42	2.71 ± 0.43	3.37 ± 0.41	UA
Fever, °C					
Range	37.8 - 38.9	37 - 38.5	37.1 - 40	37.1 - 40.4	38.2 - 40.2
Days of fever> 37.5°C	7	5	5	6	7
Blood transfusion	+	-	-	+	+
Plasma transfusion	-	+	-	-	-
Antibiotics :					
Gentamicin	+	+	+	-	-
Chloramphenical	+	+	+	+	+
Kanamycin	-	-	+	+	-
Bactrim	-	-	-	-	+

[1]Derived from IV glucose.

[2]Derived from TPN.

[3]Derived from TPN plus Ramathibodi blenderized formula.

UA = Actual intake was unavailable.

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Table 3 - 49 Dietary assessment, fever and treatment in patient T.SK

Parameter	Before study	During study, wk				
		1st	2nd	3rd	4th	5th
Intake/day						
Energy, kcal	620 ± 40[1]	2274 ± 142[2]	2220 ± 82[2]	1900 ± 160[2]	2561 ± 117[3]	1283 ± 44[3]
Protein, g	3.6 ± 0	36 ± 3	43 ± 7	54 ± 0	65 ± 2	43 ± 10
Fat, g	0	0	0	0	21 ± 4	39 ± 2
Carbohydrate, g	151	533	512	421	572	278
Carnitine, umole	0	0	0	0	0.3	0.6
Lysine, g	0.6	6.2 ± 0.5	7.7 ± 0.8	9.2	8.6 ± 0.5	7.7 ± 1.7
Methionine, g	0.3	2.7 ± 0.2	3.4 ± 0.4	4.1	3.4 ± 0.3	2.6 ± 0.7
Fever, °C						
Range	36.5 - 39	36 - 38.5				
Days of fever > 37.5°C	2	2				
Antibiotics :						
Ampicillin	-	+	+	+	+	+
Kanamycin	-	+	+	+	+	+
PGS	+	+	+	+	-	-
Gentamicin	-	+	+	+	-	-
Bactrim	-	+	+	+	-	-
Plasma transfusion	-	+	+	+	-	-
Blood transfusion	-	+	-	-	-	-

[1]Partial parenteral nutrition; [2]TPN; [3]TPN plus cow's milk or Sobel or Pregestimil.

Table 3 - 50 Dietary assessment, fever and treatment in patient V.NL

Parameter	Before study	During study, wk					
		1st	2nd	3rd	4th	5th	6th
Intake/day							
Energy, kcal	1838±183[1]	3641±114[1]	3337±100[2]	3130±114[2]	2896±211[2]	3286±26[2]	2886± 360[2]
Protein, g	34± 6	68± 3	56± 2	53± 1	52± 2	54± 1	47± 7
Fat, g	1.1± 0	11± 0	0	0	0	0	0
Carbohydrate, g	423	818	778	730	672	768	675
Carnitine, umole	0	0.1	0	0	0	0	0
Lysine, g	5.7±1.0	9.8±0.6	9.3±0.4	9.0±0.2	8.9±0.4	9.2±0.2	8.0±1.2
Methionine, g	2.6±0.4	4.2±0.2	4.1±0.2	4.0±0.1	4.0±0.2	4.1±0.1	3.5±0.5
Fever, °C							
Range	36.3-37.9	37 - 37.6	37 - 37.8	37.3 - 38			
Days of fever > 37.5°C	1	1	2	3			
Plasma transfusion	-	+	+	-	-	-	-

[1]Derived from TPN plus Sobel formula.

[2]TPN.

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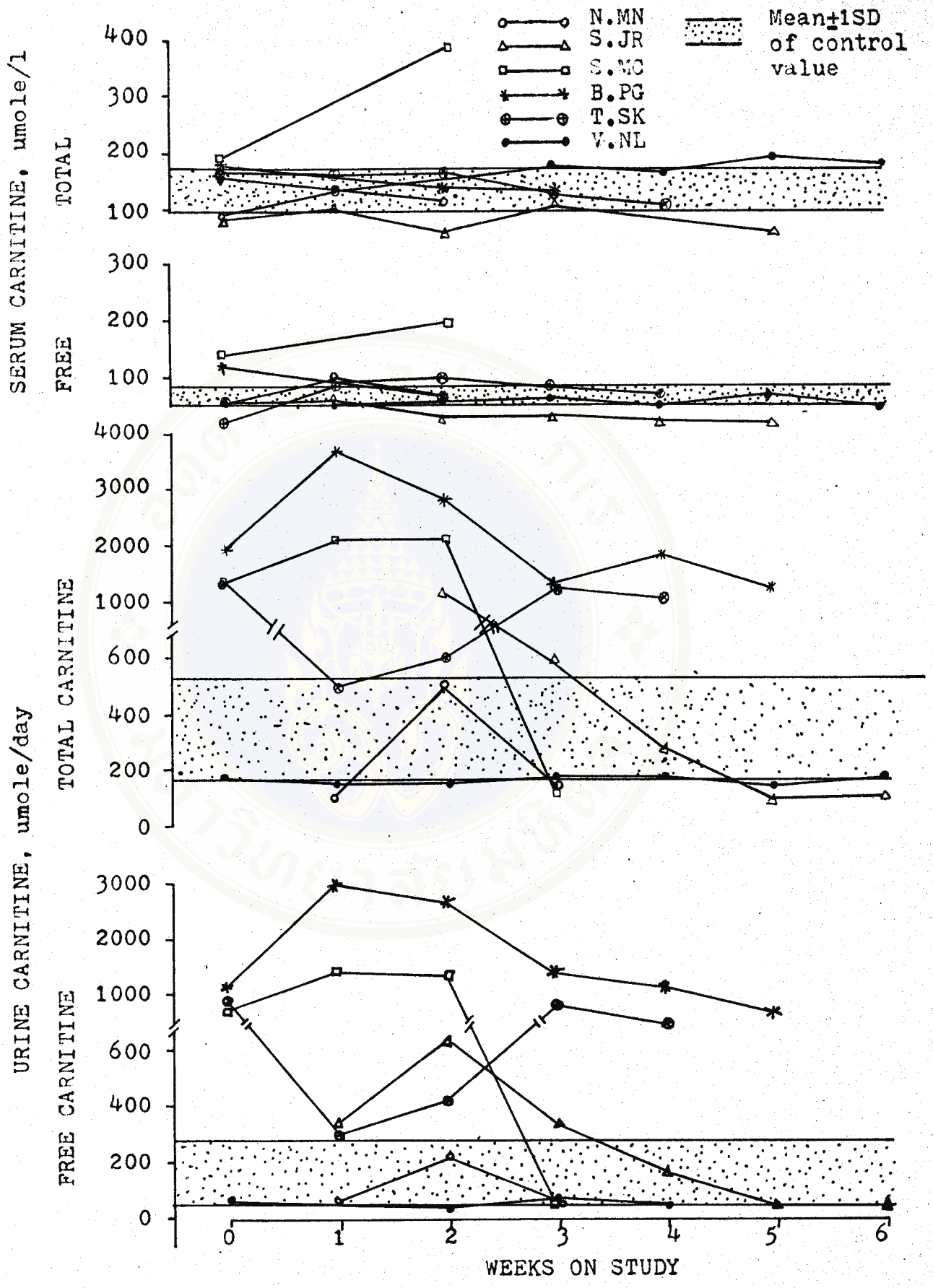

FIGURE 3-3A CARNITINE STATUS IN SURGICAL PATIENTS ON TOTAL PARENTERAL NUTRITION

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Table 3 - 51 Dietary assessment, fever and treatment in patient T.CP

Parameter	Before study	During study, wk					
		1st	2nd	3rd	4th	5th	6th
Intake/day[1]							
Energy, kcal	790±154	2335±84	2396±112	3283±157	3469±88	3457±91	2972±236
Protein, g	21± 2	34± 2	50± 2	49± 2	62± 5	54	43± 3
Fat, g	0	0	0	0	0	0	0
Carbohydrate, g	176	549	548	772	805	810	700
Carnitine, umole	0	0	0	0	0	0	0
Lysine, g	3.6±0.4	5.9±0.3	8.6±0.4	8.4±0.4	10.6±0.8	9.2	7.3±0.6
Methionine, g	1.6±0.2	2.6±0.2	3.8±0.2	3.7±0.2	4.6±0.4	4.1	3.2±0.2
Blood transfusion	+	+	+	-	+	+	+
Plasma transfusion	+	+	-	+	-	+	+
Fever, °C							
Range	37.8-39.5	37.8-38.8	38.3-39.5	38 -38.6	37.5-39.5	37.5-38	37.5-38.1
Days of fever > 37.5°C	7	7	7	7	5	3	6
Antibiotics :							
PGS	+	+	-	-	-	-	-
Gentamicin	+	+	+	+	-	-	-
Chloramphenical	+	+	+	+	+	+	+
Ampicillin	-	-	-	-	+	+	+

[1]Derived from TPN.

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Parameter	During study, wk					
	7th	8th	9th	10th	11th	12th
Intake/day						
Energy, kcal	2387±131[1]	2273±67[2]	2211±285[3]	3301±134[3]	3173±62[3]	2837±246[3]
Protein, g	49± 3	53± 1	57± 2	93± 3	88± 1	81± 6
Fat, g	0	0	4.1	30± 2	26± 1	28± 1
Carbohydrate, g	548	515	486	664	646	566
Carnitine, umole	0	0	11.5±5.7	0.5	0.5	0.5
Lysine, g	8.4±0.6	9.1±0.1	UA	12.0±0.4	11.8±0.2	10.6±2.5
Methionine, g	3.7±0.3	4.0±0	UA	4.6±0	4.6±0	4.0±0.4
Plasma transfusion	-	+	-	-	-	-
Fever, °C						
Range	37.3-37.8	37 -38.5	37 -37.6	36.7-38.5	37.1-37.9	
Days of fever > 37.5°C	2	5	1	1	1	

[1] TPN.

[2] TPN plus Ramathibodi blenderized formula.

[3] TPN plus Soble formula.

UA = Actual intake was unavailable.

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Table 3 - 51----continued

Parameter	During study, wk					
	13th	14th	15th	16th	17th	18th
Intake/day						
Energy, kcal	3166±69[3]	3156±45[3]	2644±48[3]	2638±22[3]	2468±63[1]	3146±97[1]
Protein, g	89± 1	88± 1	89± 1	72± 2	53± 1	71± 5
Fat, g	27± 1	27± 1	28	27± 1	0	17
Carbohydrate, g	642	640	509	526	564	677
Carnitine, umole	0.5	0.5	0.5	0.5	0	0.2±0.1
Lysine, g	11.9±0.1	12.0	12.0	8.9±0.2	9.1±0.1	10.6±0.4
Methionine, g	4.6	4.6	4.6	3.2±0.3	4.0±0.1	4.3±0.1
Fever, °C						
Range	37-37.8			36-38.2	37-39	37.5-38
Days of fever > 37.5°C	1			1	5	6

[1] TPN.

[3] TPN plus Sobel formula.

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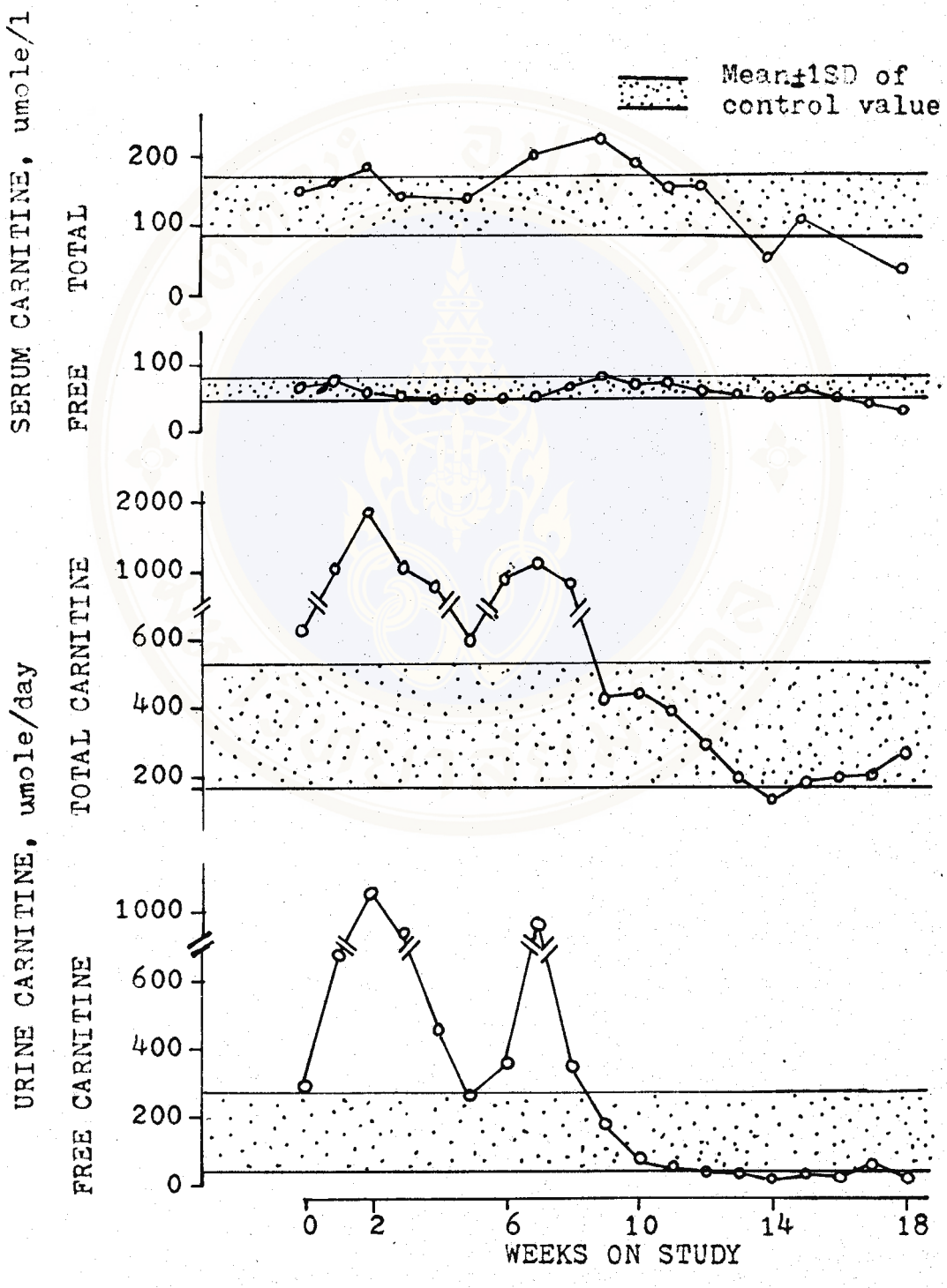

FIGURE 3-3B CARNITINE STATUS IN PATIENT T.CP

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Table 3 -- 52 Dietary assessment, feve and treatment in patient T.VS

Parameter	Before study	During study, wk		
		1st	2nd	3rd
Intake/day				
Energy, kcal	1972±42[1]	811±44[2]	1429±116[2]	1485±103[2]
Protein, g	60± 6	33± 2	39± 5	46± 1
Fat, g	73±11	0	0	0
Carbohydrate, g	409	170	318	326
Carnitine, umole	83	0	0	0
Lysine, g	UA	5.58±0.43	5.13±0.34	2.03±0.06
Methionine, g	UA	2.47±0.19	2.50±0.27	2.53±0.07
Blood transfusion	-	-	-	+
Fever, °C				
Range		37.3-38.5	37.8-39.3	37.7-38.2
Days of fever > 37.5°C		5	7	7
Antibiotics :				
Chloramphenical	-	+	+	+
Cefazolin	-	+	+	+
Amikycin	-	-	+	+

[1]Derived from IV glucose plus Ramathibodi blenderized formula or Sobel formula.

[2]Derived from TPN. UA = Actual intake was unavailable.

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Table 3 - 53 Dietary assessment, fever and treatment in patient S.SN

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day[1]					
Energy, kcal	1150 ± 447	1643 ± 240	2110 ± 0	2200 ± 0	1168 ± 354
Protein, g	0	29 ± 5	42 ± 6	67 ± 10	32 ± 12
Fat, g	0	0	0	0	0
Carbohydrate, g	288	382	488	483	260
Carnitine, umole	0	0	0	0	0
Lysine, g	0	3.18 ± 0.67	1.87 ± 0.25	2.30 ± 0.26	UA
Methionine, g	0	1.83 ± 0.24	2.32 ± 0.31	2.85 ± 0.32	UA
Fever, °C					
Range			36.5 - 37.8	37.2 - 38.5	
Days of fever >37.5°C			1	5	
Antibiotics :					
Gentamicin	-	+	+	-	-
Penicillin	-	+	+	-	-
Plasma transfusion	+	+	+	+	-

[1]Derived from TPN. UA = Actual intake was unavailable.

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Table 3 - 54 Dietary assessment, fever and treatment in patient C.CP

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	1	1343 ± 247[2]	2000 ± 0[2]
Protein , g		42 ± 0	42 ± 0
Fat, g		0	0
Carbohydrate		336 ± 163	500
Carnitine, umole		0	0
Lysine, g		0.6 ± 0	0.6 ± 0
Methionine, g		0.4	0.4
Fever, ^{o}C			
Range	38 - 39.2	37.7 - 39.1	37.3 - 39.5
Days of fever $\geq 37.5^{o}C$	7	7	5
Antibiotics :			
$StrepSO_4$	+	-	+
Sulfadiazine	+	+	+

[1]Prescription of regular diet. Actual intake was unavailable.

[2]Derived from TPN.

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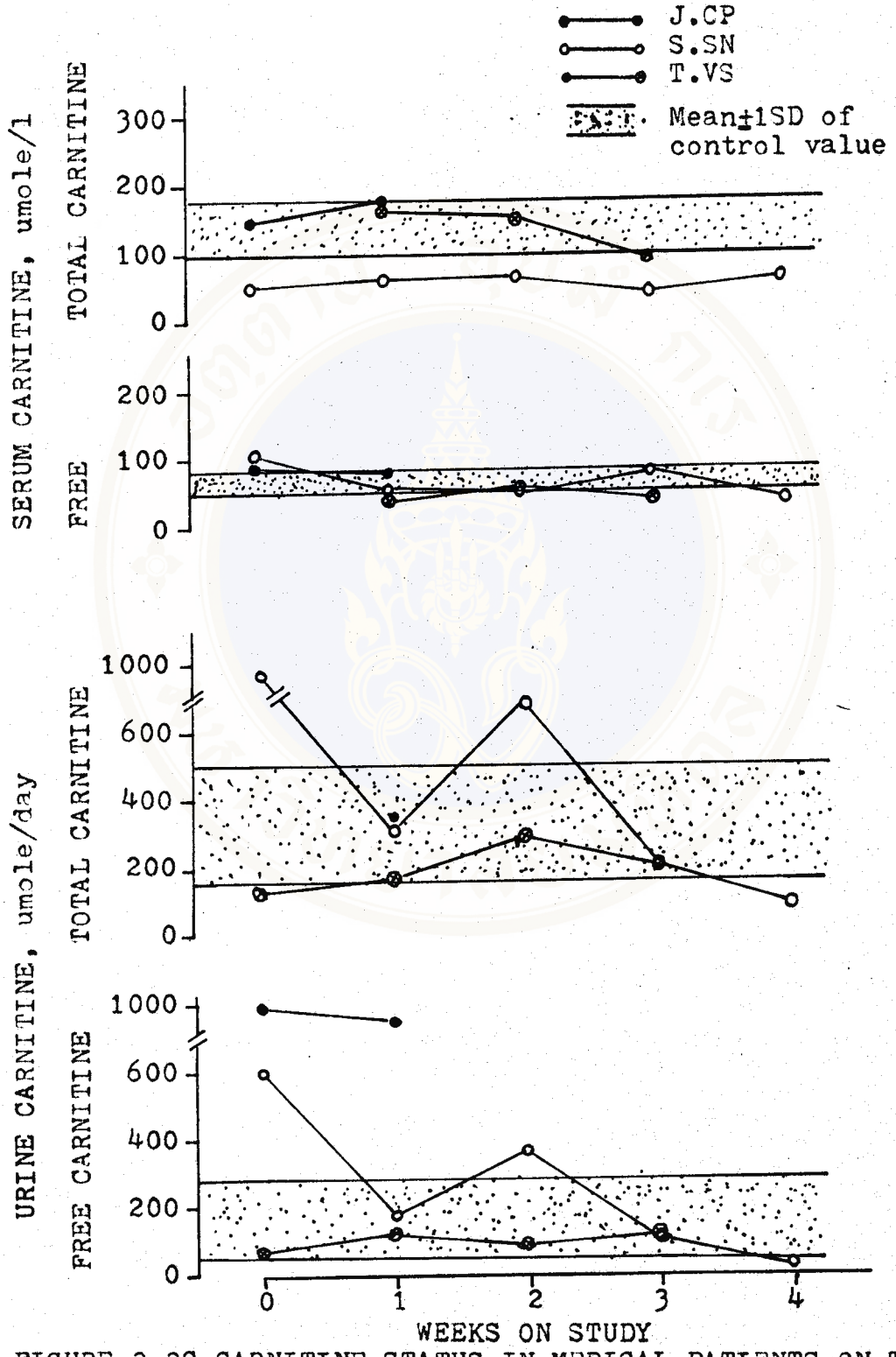

FIGURE 3-3C CARNITINE STATUS IN MEDICAL PATIENTS ON TPN

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Table 3 - 55 Dietary assessment, fever and treatment in patient T.SL

Parameter	Before study	During study, wk	
		1st	2nd
Intake/day			
Energy, kcal	913 ± 114[1]	2369 ± 179[2]	1823 ± 251[2]
Protein, g	10.3	38 ± 5	40 ± 4
Fat, g	0	1.8	9.7
Carbohydrate, g	218	550	394
Carnitine, umole	0	0	0
Lysine, g	1.75	6.44 ± 0.84	6.78 ± 0.6
Methionine, g	0.78	2.86 ± 0.37	3.0 ± 0.26
Fever, ^{o}C			
Range	37 - 37.6	37.3 - 38	37 - 38.5
Days of fever > 37.5^{o}C	2	5	3
Antibiotics :			
Kanamycin	+	+	-
Penicillin G	+	+	-

[1]Derived from TPN.

[2]Derived from TPN plus cow's milk or soy bean milk.

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Table 3 - 56 Dietary assessment, fever and treatment in patient A.SJ

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	634 ± 101[1]	2116 ± 95[2]	2386 ± 139[2]	2540 ± 287[3]	1388 ± 0[3]
Protein, g	18 ± 7	30 ± 5	35 ± 1	43 ± 3	40
Fat, g	12 ± 3	0	0	9 ± 4	33
Carbohydrate, g	120 ± 15	529 ± 24	596 ± 35	602 ± 84	232
Carnitine, umole	0	0	0	12 ± 8	0.5
Lysine, g	UA	5.1 ± 0.8	6.0 ± 0.2	5.8 ± 0.5	2.5
Methionine, g	UA	2.2 ± 0.4	2.6 ± 0.1	2.2 ± 0.5	0.5
Plasma transfusion	+	-	-	--	-
Fever, °C					
Range				37 - 37.8	
Days of fever > 37.5°C				1	

[1]Derived from partial parenteral nutrition plus cow's milk and or soy bean milk.

[2]Derived from TPN.

[3]Derived from TPN plus Ramathibodi or Sobel formula.

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Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	720 ± 70[1]	2093 ± 99[2]	2352 ± 127[2]	2555 ± 143[3]	2779 ± 70[3]
Protein, g	18 ± 5	29 ± 5	40 ± 4	43 ± 3	60 ± 6
Fat, g	0	0	0	5.0	11.6
Carbohydrate, g	162	494	548	585	609
Carnitine, umole	0	0	0	19 ± 8	34 ± 6
Lysine, g	2.9 ± 0.9	5.0 ± 0.8	6.9 ± 0.6	UA	UA
Methionine, g	1.3 ± 0.4	2.2 ± 0.4	3.0 ± 0.3	UA	UA
Blood transfusion	-	-	+	-	-
Plasma transfusion	-	-	-	-	+
Fever, °C					
Range		37 - 37.7	38 - 39.1	37 - 38.5	37.2 - 39.5
Days of fever >37.5°C		1	7	2	6
Antibiotics :					
Kanamycin	-	+	-	-	-
Penicillin G	-	-	+	+	+
Chloramphenical	-	+	+	-	-
Gentamicin	-	-	+	+	+

[1]Derived from partial parenteral untrition. [2]Derived from TPN.

[3]Derived from TPN plus Ramathibodi blenderized formula.

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Table 3 - 58 Dietary assessment, fever and treatment in patient Y.NK

Parameter	Before study	During study, wk			
		1st	2nd	3rd	4th
Intake/day					
Energy, kcal	1634 ± 236[1]	2024 ± 86[2]	2120[2]	2319 ± 80[2]	3
Protein, g	58 ± 7	49 ± 4	55 ± 1	54 ± 1	
Fat, g	54 ± 14	0	0	0	
Carbohydrate, g	337 ± 33	505 ± 22	530 ± 0.1	580 ± 18	
Carnitine, umole	0	0	0	0	
Lysine, g	UA	8.4 ± 0.8	9.3 ± 0.1	9.1 ± 0.2	
Methionine, g	UA	3.5 ± 0.3	4.1 ± 0.1	4.0 ± 0.1	
Blood transfusion	+		+	+	
Plasma transfusion	-		+	+	
Fever, °C					
Range	37.1 - 38.2	37.4 - 38.8	37.5 - 38.8	36.4 - 38.7	37.2 - 38
Days of fever > 37.5°C	3	6	5	2	4
Antibiotic :					
Gentamicin	+	-	-	-	-
Hormone :					
Decadson	-	-	-	+	-

[1]Derived from Pregestimil plus IV glucose. [2]Derived from TPN.

UA = Actual intake was unavailable.

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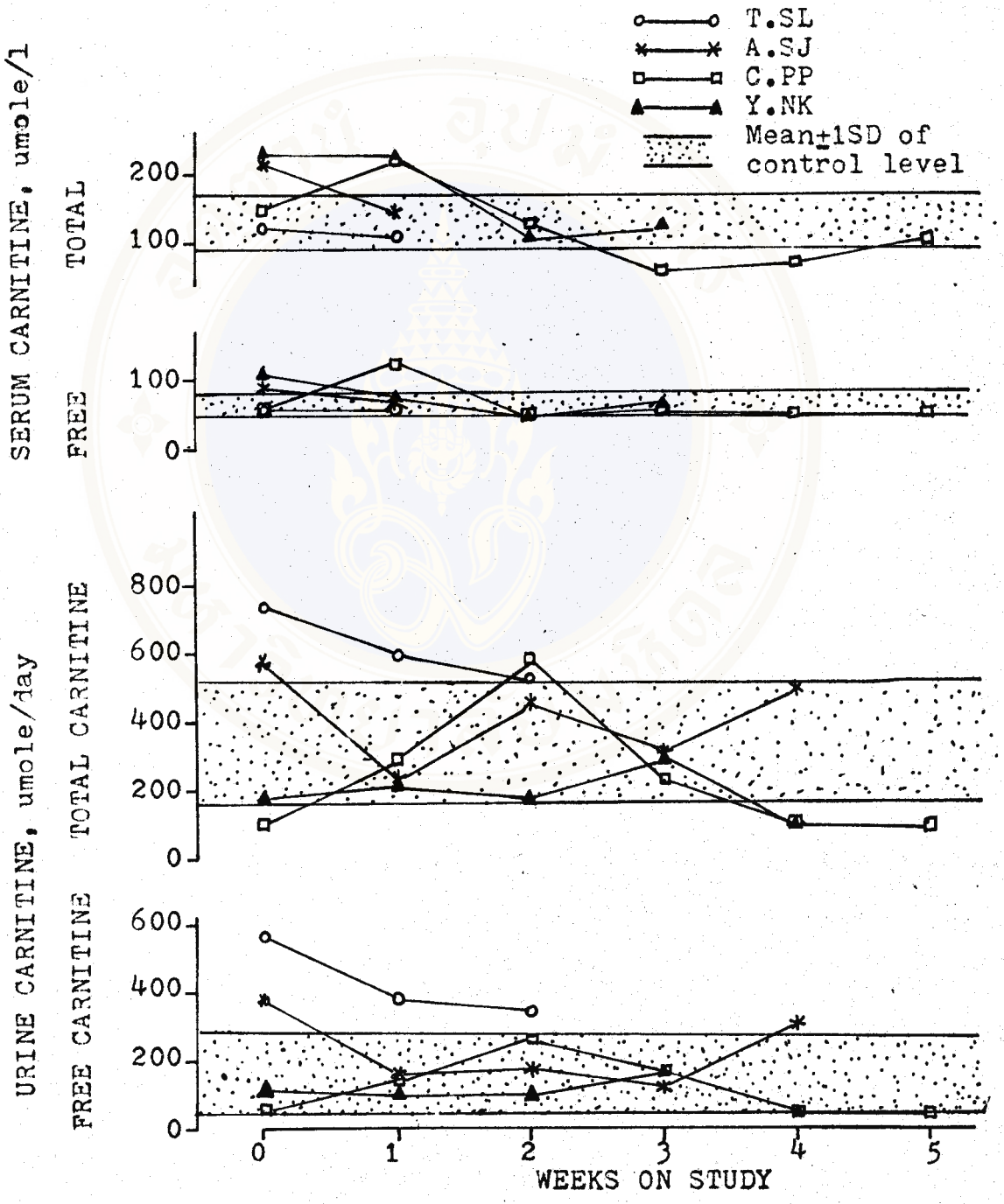

FIGURE 3-3D CARNITINE STATUS IN PATIENTS WITH MALIGNANCY ON TPN

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CHAPTER IV

DISCUSSION

4.1 Studies in control and underweight adults.

4.1.1 General nutritional status

It is well established that triceps skin fold thickness represents fat store, upper arm muscle circumference represents the skeletal muscle mass, and mid upper arm circumference is the composite measure of the two parameters whereas the body weight reflects the whole body tissue (56). Data from diverse populations have indicated the superiority of body mass index (weight/height^2) as the index of relative weight which is best correlated with other measures of obesity, such as skin fold thickness and which is least correlated with height independent of weight (64). Thus body mass index is included in this study.

The findings of significantly higher body weight, mid upper arm circumference, upper arm muscle circumference and body mass index but significantly lower triceps skin fold thickness in control men than those in control women agree with the previous report (56.64). Similar findings were observed in underweight adults.

Despite no significant differences in hematocrit, serum total protein, cholesterol and triglycerides levels between

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control and underweight adults (Table 3 - 3). The anthropometric data indicated inadequate protein-caloric status in the latter group (Table 3- 1, 3 - 2). The Significantly higher serum albumin levels in underweight women than that in control women needs further investigation before any conclusion can be drawn (Table 3 - 3).

It was also observed that the energy and carbohydrate intake in underweight men were significantly lower than those in control men. Though the control men had significantly higher energy, fat and carbohydrate intake than those in control women, This finding could not demonstrated in underweight adults (Table 3 - 14).

4.1.2 Carnitine status

It has been established from the animal studies that liver is the major site for carnitine synthesis and most of the body carnitine resides in skeletal muscle (23, 41, 43). However, one must consider the feasible tissues for the determination of carnitine content in men. Thus serum and urine specimen were used for the analysis of carnitine level in this study and we intend to evaluate the possibility of using serum and urinary carnitine levels as the indices for human carnitine status.

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Though serum carnitine levels have been measured in 'control or normal subjects' and patient with various diagnosis by several investigators (19, 50, 65 - 79). There is difficulty in interpreting the results. At least, the following problems are encounted. These are : (a) different assay method are used among various laboratories; (b) most of the reports did not provide the information, age and sex of the subjects; (c) nutritional status of the subject was not specified; (d) the information on fasting or non-fasting state at the time of venepuncture was not available and; (e) some studies included hospitalized patients other than the disease under the study as control subjects.

In surveying the existing reports on serum or plasma carnitine level in man analyzed by enzymatic-radioisotopic method. It is found that the mean free serum carnitine level in our control subjects is higher than other reports (Table 4 - 1) (19, 20, 66, 67, 72, 74). This difference could be due to several aforementioned factors.

In 1975, Maebashi et al (80) report no carnitine esters were presented in human serum. However, their method of analysis was base on the colorimetric assay of Friedman (15) and the hydrolysis of carnitine esters to obtained total carnitine in the free form was done by heating the sample with 6N methanolic HCl. In 1976,

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Table 4 - 1 Mean ± SD of serum or plasma carnitine levels analyzed by the enzymattic-radioisotopic method reported by various investigators

Author	Subject						Specimen	Carnitine, umole/l	
	Nationality	Sex	Age yr	No	Description	Fasting		free	total
Cederblad & Lindstedt (19)	Swedish	M	17-60	33	Healthy	yes[1]	Plasma	51± 10.5	-
Cederblad et al (67)	Swedish	NA	21-30	8	Healthy	yes[1]	Plasma	43± 58	-
Cederblad (66)	Swedish	M	21-64	16	Obese	NA	Plasma	57± 13	-
		F	19-67	45	Obese	NA	Plasma	46± 12	-
Böhmer et al (72)	Norvegian	NA	NA	30	Healthy	NA	Serum	43± 9	-
Karpati et al (74)	NA	NA	NA	20	NA	NA	Plasma	52± 12	-
McGarry & Foster (20)	NA	NA	NA	10	NA	NA	Plasma	56± 2	66± 3
This study	Thai	M	19-43	22	Healthy	yes[2]	Serum	69± 11	141±30
		F	20-48	22	Healthy	yes[2]	Serum	66± 20	137±48

NA = Not available,

[1] Number of the fasting hour was not available.

[2] 12 hr.

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McGarry and Foster (20) assayed the plasma free and total carnitine levels by the enzymatic-radioisotopic method. They reported the mean ± SD of plasma free and total carnitine levels were 55.7 ± 1.99 and 65.7 ± 2.55 umole/l, respectively (Table 4 - 1). The hydrolysis of acylcarnitine was done by adding 0.4N KOH in the present of 1M Tris base to the sample and allowing it to stand for 1 hour at 37°C. In our analysis of serum free and total carnitine levels, we have used the same method as described by McGarry and Foster(20). The mean ± SD of serum free and total carnitine levels were 69.2 ± 11.2 and 140.6 ± 30.5 umole/l for men and 66.2 ± 20.2 and 136.6 ± 48.3 umole/l for women (Table 4 - 1). Since there was no information on the description of subjects in the study of McGarry and Foster (20) the difference in this result could not be interpreted.

In 1973, Dimauro et al (69) mentioned in their report that the serum carnitine levels in men and women were not different. Hence the combined value was presented. However, Cederblad (66) found that the mean plasma carnitine level in obese men was significantly higher than that in obese women (Table 4 - 1) and a significantly positive relationship between plasma carnitine level and age in obese women. Though our control and underweight men had higher serum free carnitine, acylcarnitine and total carnitine levels than control and underweight women, respectively the values were not significant different (Table 3 - 4). It should

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be noted that there was no significant difference in the age between control men and control women as well as between underweight men and underweight women (Table 3 - 1).

In the fasting state the major energy source for the body is derived from mobilised fatty acids originating from the store triglycerides droplets in adipose tissue (87). It is known that these fatty acids are bound to albumin and transported in plasma to tissue such as skeletal and heart muscle that predominantly oxidized fatty acids as their energy source in the fasting state. Free fatty acids also go to the liver where they may be oxidized to carbondioxide and ketone bodies, which are subsequently transported to and metabolized by other tissues. The triceps skin fold thickness in underweight men was significantly lower than that in control men (Table 3 - 2) which indicated the decrease in adipose tissue. This would lead to decrease free fatty acid release during their fasting. The significantly lower serum total carnitine level in underweight men than control men was due to the decrease in serum acylcarnitine level. Though the types of acylcarnitine were not identified in this study the decrease in serum acylcarnitine level in underweight adults could be related to the amount of fatty acid release from their adipose tissue.

Table 4 - 2 summarized the urinary carnitine excretion reported by various investigators. The Swedish (81) and American

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Table 4 - 2 Mean ± SD of urinary free carnitine excretion per day reported by various investigators

Author	Subject					Carnitine umole	Method of analyzed (ref)
	Nationality	Sex	Age yr	No	Description		
Cederblad & Lindstedt (81)	Swedish	M	20-47	28	Laboratory staff	170± 80.7	Enzymatic (81)
		F	38-60	42	Healthy	86± 72.6	Enzymatic (81)
Maebashi et al (82)	Japanese	M	8-15	15	Healthy	356± 60	Colorimetric (15)
			16-50	106	Healthy	368± 20.5	Colorimetric (15)
			51-85	22	Healthy	310± 42.8	Colorimetric (15)
		F	8-15	16	Healthy	246± 62.6	Colorimetric (15)
			16-50	84	Healthy	274± 18	Colorimetric (15)
			51-85	35	Healthy	240± 24.8	Colorimetric (15)
Suzuki et al (83)	Japanese	NA	21-23	4	Physical education student	540± 74	Colorimetric (15)
DiMauro & Rowland (84)	USA	Boys	4-12	21	Normal	97± 95	Enzymatic (86)
Maebashi et al (85)	Japanese	M	8-45	121	Normal	358± 60	Colorimetric (15)
		F	8-45	101	Normal	274± 18	Colorimetric (15)
This study	Thai	M	19-43	22	Healthy	185±127.6[1]	Enzymatic-radioisotopic (20)
		F	20-48	22	Healthy	142± 98.9[2]	

NA = Not available, [1]total carnitine = 371 ± 192, [2]total carnitine = 341 ± 169.

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investigators (84) used the enzymatic method in the analysis of urinary carnitine whereas the Japanese workers (82, 83, 85) used the colorimetric assay. It should be noted that the values reported were, free carnitine. However, our studies have demonstrated the presence of acylcarnitine in urine and serum was in the same order, ie, 49% and 55.3% acylcarnitine in serum and urine respectively, of total controls : 43.1% and 54.6% acylcarnitine in serum and urine, respectively, of total underweights (Table 3 - 5, 3 - 6).

Regarding to urinary free carnitine excretion per day the value of our control subjects was higher than those reported by the Swedish and American groups but lower than those reported by the Japanese workers (Table 4 - 2). Like the serum carnitine case, it is difficult to evaluate this difference since there may by several factors affecting the level of urinary carnitine excretion too.

Data from Cederblad and Lindstedt (81) and the Japanese workers (82, 85) showed that urinary carnitine excretion per day in men was higher than women. Maebashi et al (82) also reported that urinary carnitine excretion in the aged group ($>$ 51 yr) was lower than that in adult (16 - 50 yr) and the young ($<$ 15 years) (Table 4 - 2). Though our control and underweight men had higher free, acyl- and total carnitine excretion than control and underweight

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women, respectively, significant difference was observed in underweight adults only (Table 3 - 5). It should be noted that the mean ages among these four groups of subjects were not different.

Carnitine occurs in the body mainly in muscle tissue and the total muscle carnitine may therefore be taken as an estimate of the body store of carnitine (23, 66). Since the body weight, body mass index and upper arm muscle circumference in underweight men and women were lower than those in the control men and women, respectively, this led us to study the effect of muscle mass on urinary carnitine excretion. The results were expressed in umole per day and umole per kg body weight per day. When the former unit was used there was no difference between control and underweight men as well as control and underweight women (Table 3 - 5). However, underweight men excreted free, acyl- and total carnitine per unit body weight per day higher than those in control men (Table 3 - 6). This could be related to the significantly lower energy intake in the underweight men than the control men (Table 3 - 14) without the difference in carnitine intake. The results agree with the other reports that fasting or starvation lead to an increase in urinary carnitine excretion (82, 83). It should be noted that there was no significant difference in urinary free, acyl- and total carnitine excretion (Table 3 - 6) as well as the energy intake between underweight men and women.

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Maebashi et al (82) reported that in 4 women with menstrual cycle, carnitine excretion did not vary during the follicular phase but increased toward ovulation. An excretion peak was observed in the day of ovulation. Following the peak, the excretion decreased and remained relatively constant during the luteal phase and during the menstrual period. However, we had not recorded the relationship between the uriney collection and menstrual period in our female subjects cirtain circumstances 24 hour urine collection may not be practical and the nutrient analysis must be made from the casual specimens. Therefore two other units in umole per liter of urine and umole of carnitine per gram creatinine are evaluated for the potential are if carnitine analysis has to be made from the casual urine samples. When the former unit was used it was agreeable with the unit of umole per day (Table 3 - 5). On the contrary, control women had higher urinary carnitine level than control men when it was expressed in umole per gram creatinine. Since findings were related to the significant lower creatinine excretion in control women than control men (Table 3 - 7). However, underweight men still had higher urinary carnitine level than control women when it was expressed in umole per gram creatinine. This was visualized by the significant decrease in creatinine excretion in both underweight men and women from the corresponing sex of control adults without significant difference in this parameter between themselves (Table 3 - 7).

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The data presented to this point indicated that urinary carnitine determination should be made from the 24 hour urine collection and expressed in umole per day and umole per kg body weight per day. However, if casual urine specimens have to be used for the analysis of carnitine concentration umole of carnitine per liter of urine is better than the unit of umole per gram creatinine.

The significant higher urinary total and free carnitine excretion with concomitant lower serum total and acylcarnitine levels in the underweight men than the control men. Suggested that during a 12 hour fast in the former group, there might be more carnitine release from skeletal muscle and/or increased hepatic synthesis of carnitine. However, due to the low amount of free fatty acid oxidation. The excess carnitine was then excreted by the kidney.

An analysis of the dynamics of urinary carnitine excretion must take into account the large interindividual variation in glomerular filtration rate. It has been shown that changes in glomerular filtration rate can also be induced by varying protein intake (88). By relating the carnitine excretion to a fixed volume of glomerular filtrate, it is possible to eliminate the difference in glomerular filtration rate, free, acyl- and total carnitine excretion per day per 100 GFR in control and underweight adults

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were shown in Table 3 - 7. Control and underweight men had higher creatinine clearance and free, acyl- and total carnitine excretion per day per 100 GFR than control and underweight women. However, the values were significant only for carnitine excretion per day per 100 GFR between underweight men and women. The findings were similar to carnitine excretion expressed in umole per day (Table 3 - 5). Underweight men had lower creatinine clearance than control men. When the carnitine excretion was equated to 100 GFR it was found that underweight men had significantly higher carnitine excretion than control men. This finding was similar to the carnitine excretion expressed in umole per kg body weight per day (Table 3 - 6).

Like creatinine, the urinary carnitine concentration is higher than its concentration in serum. This emphasizes the important role of kidney in hemostasis of carnitine in the body. To our knowledge, carnitine clearance in man has not been reported. Since we have demonstrated the appearance of free and acylcarnitine both in serum and urine the free, acyl- and total carnitine clearance expressed in ml/min and m./min/1.73m^2 are presented in Table 3 - 8. The values of free, acyl- and total carnitine clearance in a given group of subjects were in the same order. Underweight men had significantly higher free carnitine clearance than underweight women and significantly higher acyl- and total carnitine clearance in underweight men than control men was observed. Such findings

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support the aforesaid thesis that during a 12 hour fast in underweight men more carnitine was released from skeletal muscle but less carnitine was utilized for fatty acid oxidation due to lower amount of free fatty acid release.

In 1954, Ansell et al (89) reported that a protein free diet gave urinary carnitine excretion of 490 umole per day. A diet with 190 gram protein increase urinary carnitine to 1241 umole per day but was lowered to 930 umole per day when the protein was released to 153 gram per day. Colorimetric method was used to determine the carnitine content in their studies. Except this report, little attention on the effect of diet on serum or urinary carnitine excretion levels was paid by the subsequent reports. Thus for there are 3 additional reports which pronded some dietary information when carnitine was measured in urine. These are :

(1) Cederblad's study (66). Urinary carnitine excretion was measured by the enzymatic method in a 34 years old healthy Swedish woman. The study was divided into two periods of a consecutive days. Ordinary food (details were not given) was eaten during one period and during the other period the diet consisted of gruel 263 g, bread 122 g and orange juice 0.5 liter with whe total carnitine intake of 190 umoles. The means $\pm$ SD of free urinary carnitine excretion during these two periods were 239 $\pm$ 55.7 and

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243 ± 40.8 umole per day, respectively. The values did not differ. Again, it is difficult to evaluate the effect of diet on the urinary carnitine excretion since there was limitted dietary information in this report.

(2) Study of Suzuki et al (83). Urinary carnitine excretion was measured by the colorimetric method on 4 physical education students with the age of 21 to 23 years. Their body weight ranged from 57 to 75 kg. Their energy intake was 2,866 kcal derived from protein 69.8 g, fat 106.8 g and carbohydrate 392.9 g. In another experiment, 4 physical education students with the ages of 21 to 23 years and weighing 56 - 65 kg were fed the diet pronding 2,688 kcal derived from protein 93.3 g fat 72.5 g and carbohydrate 401 g. The means ± SD of urinary carnitine excretion in the first and second group of subjects were 540 ± 74 and 470 ± 10 umole per day, respectively.

(3) Mitchell's study (90). Urinary carnitine was measured by the enzymatic method in a 37 years old Oriental weighing 48 kg and 161 cm tall. Two types of diets, meat and vegetable diets, were fed for 3 days each. The meat diet provided 1,106 kcal derived from protein 74.2 g, carbohydrate 124 g and fat 34 g whereas the vegetable diet provided 913 kcal derived from protein 37.8 g, carbohydrate 130 g and fat 32 g. On the third day of consuming

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each diet, urine was collected for 24 hours. The urinary carnitine excretion was 202 umole per day during the meat diet and 15 umole per day during vegetable diet.

From the aforementioned reports, it can be visualized that the nutritional conditions should be more well defined to evaluate the influence of dietary intake in serum and urinary carnitine levels. The mean carnitine intake per capita per day varied from 159 umole in underweight men to 319 umole per day in control women (Table 3 - 14). Though the carnitine intake was not significantly different between men and women in control and underweight adults, there was significant positive correlation between carnitine intake and free or total carnitine excretion expressed in umole per day or umole per liter (Table 3 - 15). Similar findings were observed between the protein intake and free or total carnitine excretion expressed in umole per liter. (Table 3 - 16). Our findings may explain the wide variation in urinary carnitine excretion reported by other workers.

Fat intake in the control and underweight adults possitively correlated with the free, acyl- and total carnitine excretion (Table 3 - 17). This may reflect that more carnitine is needed for fatty acid oxidation during an increase in fat intake and the excess carnitine from the fatty acid oxidation was excreted in urine.

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Though there was no direct relationship between the carnitine, protein or fat intake and serum free, acyl- and total carnitine levels (Table 3 - 15, 3 - 16 and 3 - 17). Significant positive correlation was observed between serum and urinary free carnitine levels (Table 3 - 18). The significant negative correlation between fat intake and percent acylcarnitine in serum could be due to more carnitine being utilized intracellular for fatty acid oxidation.

Our study had demonstrated a significant positive correlation between serum free carnitine, acylcarnitine or total carnitine level and serum cholesterol level (Table 3 - 19). The results agreed with Cederblad's study (66). A significant positive correlation between serum acylcarnitine or total carnitine level and serum albumin level was also observed (Table 3 - 19). The mechanism for these relationships need further investigation.

It should be noted that the negative correlation between serum free carnitine level and upper arm muscle circumference (Table 3 - 20) might reflect during catabolic state carnitine was released from the muscle, the site of carnitine store, into the circulation. The possitive correlation between serum acylcarnitine and upper arm circumference might reflect the influence of fatty acid release and muscle mass on the level of acylcarnitine.

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After treatment with pizotifen, an appetite stimulant (90) for 8 weeks, the mean ± SEM of net weight gain in 9 underweight adults was 2.5 ± 0.1 kg. There was significant increase in urinary creatinine excretion in women from their initial value (Table 3 - 12). This could reflect and increase in lean body mass (91). In underweight men, there was a significant increase in serum triglycerides level after pizotifen treatment which could reflect an increase in adiposity (92).

We have demonstrated that pizotifen or pyridoxine treatment did not affect serum, free, acyl- and total carnitine levels (Table 3 - 10, 3 - 13). Though there was an increase in urinary acylcarnitine excretion. After pizotifen treatment these changes were not significantly different from the corresponding initial value (Table 3 - 11. However, there was a significant decrease in free and total carnitine clearance in underweight men after pizotifen treatment.

4.2 Studies in patients on Ramathibodi blenderized formula

Studies on carnitine status in control and underweight adults have shed some light on the influence of nutritional factors on serum and urinary carnitine levels. Thus it is interesting to know the carnitine status in patients with protein-calorie malnutrition and under proper nutritional management.

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The carnitine status in patients in tube feedings depend not only on the amount of carnitine intake but also the quantity and quality of protein intake. Since it is now established that lysine and methionine are the precursors of carnitine in the body (37) as shown in Table 2 - 2. The amount of protein and carnitine present in Ramathibodi blenderized formula was 35 g and 127 umole per 1000 kcal, respectively.

Though the nutritional status of 17 patients on Ramathibodi blenderized formula was protein-calorie malnutrition at the beginning of the study. Their other medical problems should be examined for interpreting the serum and urinary carnitine levels. Particular attention was paid to the following factors before and during study in each patient. There were energy, protein, carbohydrate, fat and carnitine intake, fever, blood or plasma transfusion, antibiotics and hormonal treatment. These informations of the individual patient are shown in Table 3 - 21 to 3 - 37.

For simplicity, the carnitine status in 17 patients on Ramathibodi blenderized formula is presented in 4 figures. These are : Figure 3 - 1A, 3 - 1B, 3 - 1C and 3 - 1D representing the carnitine status in 6 patients with tetanus (S.MS, L.YM, F.SB, V.TN, A.TS, J.MG), 4 patients with pulmunary problem (P.BN, S.KR, J.SP, T.SU), 4 patients with neurologic problem (S.SM, C.SP, K.ST, P.SH) and 3 patients with primary malnutrition or endocrine problems

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(L.HS, Y.JD, N.KP), respectively. Serum or urinary total carnitine level was not determined in 4 patients (J.MG, L.HS, A.TS, B.BN).

In general, urinary total carnitine excretion and serum free carnitine level paralleled with free urinary carnitine excretion. It has been shown that carnitine, protein and fat intake correlated positively with free and total urinary carnitine excretion in control and underweight adults. This mean $\pm$ 1SD of urinary free carnitine excretion in control adults was then considered to be the normal limit as a guide to compare the carnitine status between the patient and the control adults.

Before and during the first week of the study, the 16 patients (urinary carnitine excretion was not determinad in J.MG) could be divided into 2 groups. Group A having urinary free carnitine excretion within or below the normal limit consisted of 8 patients (S.MS, L.YM, F.SB, A.TS, J.SP, T.SU, C.SP, N.KP). Group B having urinary free carnitine excretion above the upper normal limit consisted of 8 patients (V.TN, B.BN, S.KR, S.SM, K.ST, P.SH, L.HS, Y.JD) (Figures 3 - 1A, 3 - 1B, 3 - 1C, 3 - 1D).

In group A, six patients (S.MS, L.YM, F.SB, A.TS, J.SP, T.SU) had the urinary free carnitine excretion below or being close to the lower normal limit (49 umoles/day) before and throughout the study. Their urinary total carnitine excretion

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also lied within or below the normal limit. Before study, their carnitine intake ranged from 0 to 249 umole per day, their energy intake ranged from 1014 to 1561 kcal per day, their protien intake ranged from 0 to 68.4 g per day and their fat intake ranged from 0 to 41.9 g per day. The aforesaid parameters during the study were 100 to 336 umole, 1497 to 2631 kcal, 27.5 to 92.4 g and 43.5 - 122.1 g per day, respectively (Table 3 - 21 to 3 - 37). Though carnitine and protein intake increased during the study the exogenous source of carnitine derived from the diet and the de novo synthesis of carnitine stemming from lysine and methionine did not raise the urinary total and free carnitine excretion. This indicated that carnitine was captured by the avid tissues for the utilization in energy metabolism whenever fat was supplied in the diet. This was supported by their serum free carnitine level being within or close to the normal limit in S. MS, L.YM, F.SB and A.TS (Figure 3 - 1A) before and during the study, J.SP and T.SU during the study (Figure 3 - 1 B).

The other two patients, C.SP and N.KP the urinary free and total carnitine excretion was not stable within or below the normal limit. In C.SP, the increase in urinary free and total carnitine excretion was related to fever caused by infection (Figure 3 - 1C, Table 3 - 32). This same phenomenon was found in Group B patients. In N.KP, the diagnosis of hyperthyroidism was not made

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when the patient was first admitted, However, he received propanolol, a betablocker before and throughout the study. His serum free and total carnitine levels before and at the second week of the study were higher than the normal limit. His urinary free and total carnitine excretion before the study was closed to the normal upper limit. The values went up at second week and returned to the normal limit after prescription of methimazole at third week. He did not have any fever thoughout the study. In 1966, DeFellice and Gilgore (93) reported that after treatment with DL-carnitine in 3 patients with hyperthyroidism for 2 weeks the patients became euthyroid though there were no consistent effects on the laboratory parameters of thyroid function. Their result suggested the peripheral antagonism of thyroid hormone. Recently, Vick et al (94) reported the protective effect of carnitine against propanolol induced cardiac depression in isolated canine hearts without preventing the betablockade effect of propanolol. It was possible that an increase in carnitine release from skeletal muscle and/or increase in hepatic carnitine biosynthesis occured in N.KP during hyperthyroxinemia and receiving propanolol treatment to protect the adverse effects of excess thyroxine and propanolol.

In group B, the 8 patients before and during the first week of the study and the urinary free carnitine excretion higher than the normal upper limit (277 umole per day) with the value

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ranging from 394 to 2136 umole per day. Their total carnitine excretion was also higher than the normal upper limit (522 umole per day). Six out of these patients (SKR, S.SM, K.ST, P.SH, L.HS AND Y.JD) also had serum free and/or total carnitine level greater than the normal upper linit. In reviewing their clinical condition and treatment, it was found that 7 out of 8 patients (except Y.JD) had fever greater than 37.5°C due to infection. Two patients, P.SH who also had fever and L.HS received corticosteroid treatment. Subsequently urinary or serum carnitine levels varied according to the aforesaid factors. It is now established that severe trauma and sepsis are followed by a catabolic state which has been characterized chiefly by its negative nitrogen balance (95). Border et al (96) reported that a combination of sepsis and starvation in man was associated with essentially unchanged skeletal muscle carnitine levels whereas pure sepsis without starvation was associated with decreased skeletal muscle carnitine levels. Sequential skeletal muscle biopsies showed a progressive fall in the tissue carnitine levels with a subsequent rise in those animals which survived and cleared their peritonitis. Serum and urinary carnitine were not measured in their study. It was interpreted that their changes were in the direction expected for a limitation of fat catabolism and in the presence of limited exogenous source of glucose, that this would result secondarily in a protein catabolic state to

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supply for the body's energy needs. Our seven patients in group B had the problem of infection with fever while still received nutrient supply, This condition was more or less similar to sepsis without starvation in the study of Border et al (96). It is known that during infection or tissue injury there are several metabolic responses including endocrine changes (95). Infection stimuli via the nervous system suddently increase pituitary production of ACTH which, in turn, stimulates the adrenocortical production of cotisol. Catecholamine stimulation inhibits pancreatic secretion and peripheral activity of insulin as well as stimulates glucagon secretion. In addition, catecholamines synergize with corticosteroids and glucagon to fasten gluconeogenesis from protein. Recent report in an abstract cy Pace et al (97) demonstrated that free and total carnitine increased to the same extent in fasted and S. pneumoniae infected rats. However, carnitine derivatives were significantly altered in S. pneumoniae infected rats; short-chain fatty acylcarnitine decreased in liver and plasma, long-chain fatty acylcarnitine decreased in liver and muscle. Liver short-chain fatty acylcarnitine was inversely proportional to plasma ketone body in fed, fasted and infected rats. Despite elevated free and total carnitine, an infected rats has a low ketotic capacity. It appeared that hepatic ketone body production during infection might well be altered, at least in part, by the relative proportions of short- and long-chain

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acylcarnitine which differed from those measured in fasted controls.

Gathering from these reports, it was possible that the increase in urinary carnitine excretion during infection in our patients could be due to the adrenocortical response affecting skeletal muscle catabolism which would lead to the release of carnitine from muscle store. This is supported by (a) tube feeding that prednisolone treatment in L.HS without any fever also increased his urinary carnitine excretion, and (b) the report of Maebashi et al (85) who demonstrated that ACTH-Z injection stimulated carnitine excretion in controls.

4.3 Carnitine status in patients on Sobel formula

One striking features in Sobel formula is that it is limiting in carnitine. Every 1000 kcal of Sobel provides carnitine 0.4 umole whereas every 1000 kcal of Ramathibodi blenderized formula provides 127.5 umole (Table 2 - 2 and 2 - 1). Sobel is made from soy bean thus it is limiting in methionine. However, if energy supply is from Sobel for a given individual is inadequate the total amount of methionine intake can meet the requirement (98, 99).

Based on the urinary free and total carnitine excretion, two patients, K.CK and T.CPk had the values above the normal upper

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limit (Figure 3 -2). This was related to infection and corticosteroid treatment (Tables 2 - 6, 3 - 40, 3 - 41) as already discussed (Chapter IV : 4.2). However, five out of seven patients (B.IN, P.VS, P.HP, J.SS, H.SS) had urinary free and total carnitine excretion within or below the normal limit but higher serum free and total carnitine level than the normal upper limit both before and during the study. This suggested that under this stringent carnitine economy with adequate fat intake the following events could occur : (a) an increase in carnitine biosynthesis in the liver and/or (b) an increase in mobilization of carnitine from the skeletal muscle store to meet the requirement for fatty acid oxidation, (c) reduction of urinary carnitine excretion to conserve the body store and (d) infection stimulating skeletal muscle catabolism as already discussed and disrupting the conversation of body carnitine.

4.4 Carnitine status in patients on TPN

It should be noted that the prescription of TPN in our patients was a fat-free formula. The energy supply was derived from carbohydrate (mainly glucose) and amino acids. This was also carnitine-free. The results presented in Finure 3 - 3A, 3 - 3B, 3 - 3C and 3 - 3D and the data in each patient shown in Table 3 - 45 to 3 - 58 clearly demonstrated that under carnitine-free and fat-free intake there was decrease in urinary and serum

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free and total carnitine levels. Whenever there was an infection or surgical operation, there was an increase in urinary free and total carnitine excretion. This was best illustrated in patient T.CP (Figure 3 - 3B) who was on TPN for 18 weeks. It should also be noted that under high caloric supply derived from glucose given continuously and intravenously throughout 24 hours will lead to high circulating insulin level with concomitant decrease in glucagon level (100). Recent report by McGarry and Foster (101) has shown that all ketogenic status are accompanied by an increase in hepatic carnitine content. The increase can be produced rapidly by glucagon or antiinsulin serum and is likewise seen in starvation and experimental diabetes mellitus. However, their experiments could not tell whether the increased carnitine content represents de novo synthesis in the liver or whether it or its precursors is transported from peripheral tissues to the liver in the same way that amino acids are mobilized for gluconeogenesis and ketogenesis. However, we believe that the latter mechanism should be the priority in our patients on TPN since it is known that the anabolic action on protein synthesis and antilipolytic action of insulin will prevent the muscle catabolism and free fatty acid release from adipose tissue (102). This, in turn, would affect the release of carnitine from the skeletal muscle store.

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CHAPTER V

SUMMARY

Four groups of Thai adults were included in this study (a) control adults consist of 22 healthy men and 22 healthy women (b) 6 underweight men and 13 underweight women attending on Nutrition Clinic because of feeling thin; the means ± SEM of the age in control and underweight adults were 27.0 ± 1.1 and 25.2 ± 1.0 years, respectively; all of them resided in Bangkok; (c) 24 adult hospitalized patients on tube feedings; 17 of them received Ramathibodi blenderized formula whereas the remaining received Sobel formula, and (d) 14 adult hospitalized patients on total parenteral nutrition (TPN).

The dietary intake, anthropometry, hematocrit, serum total protein and albumin, cholesterol and triglycerides levels and carnitine concentration in serum and urine were assessed in these subjects. The results are summarized below.

1, Study in control and underweight adults.

1.1 Acoording to anthropometric data, inadequate protein-caloric status was observed in underweight adults, whereas no significant difference in other serum constituents and hematocrit was seen.

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1.2 The presence of acylcarnitine was identified in this study, both in serum and urine. The means ± SEM of percentage oe acylcarnitine in serum of control and underweight adults were 49.0 ± 1.8 and 43.1 ± 2.1 whereas the values in urine were 55.3 ± 2.4 and 54.6 ± 2.4 respectively.

1.3 The mean ± SEM of serum free, acyl- and total carnitine levels in total controls were 67.7 ± 2.4, 70.8 ± 4.9 and 138.6 ± 6.0 umole/l, respectively. Whereas the coresponding values in underweight adults were 65.3 ± 2.6, 52.1 ± 4.5 and 118.0 ± 5.6 umole/l. These values were obtained after a 12 hr fast. Sex did not affect the serum carnitine levels in these two groups of subjects.

1.4 The means ± SEM of serum free, acyl- and total carnitine levels in control men were 69.2 ± 2.4, 71.3 ± 6.3 and 140.6 ± 6.5 umole/l, respectively whereas the coresponding values in underweight men were 69.1 ± 1.4, 51.5 ± 3.7 and 122.3 ± 1.6 umole/l, respectively, The significantly lower serum total carnitine level in underweight men than control men was due to the decrease in serum acylcarnitine level which could be related to the amount of fatty acid release from their adipose tissue.

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1.5 Twenty four hour urine samples were used for carnitine determination. The values were expressed in 4 units, umole/day, umole/kg/day, umole/l of urine and umole/g creatinine. The data indicated that the latter unit should not be used due to the influence of lean body mass on creatinine excretion.

1.6 The means ± SEM of urinary free, acyl- and total carnitine excretion in control men were 185 ± 27, 186 ± 21 and 371 ± 41 umole/day, respectively, in control women were 142 ± 21, 172 ± 18 and 341 ± 36 umole/day, respectively, in underweight men were 240 ± 30, 275 ± 38 and 516 ± 76 umole/day, respectively, in underweight women were 105 ± 23, 148 ± 46 and 253 ±68 umole/day, respectively, Significant difference in these parameters were observed between underweight men and women.

1.7 Underweight men excreted free, acyl- and total carnitine per unit body weight per day higher than those in control men. This finding with concomitant lower serum total and acylcarnitine levels in the underweight men than the control men suggest that during a 12 hour fast there might be more carnitine release from skeletal muscle and/or increased hepatic synthesis of carnitine. However, due to the low amount of free fatty acid oxidation. The excess carnitine was excreted by the kidney.

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1.8 To eliminate the influence of protein intake on GFR carnitine excretion was expressed as umole per day per 100 GFR. Significant differences were observed between underweight men and women only. This was similar to the unit umole/day.

1.9 Underweight men had significantly higher free carnitine clearance than underweight women. Significantly higher acyl- and total carnitine clearance in underweight men than control men was observed. Such finding support the discussion in 1.7.

1.10 The means $\pm$ SEM of carnitine intake in control men and women and underweight men and women were 176 $\pm$ 25, 319 $\pm$ 73, 159 $\pm$ 18 and 271 $\pm$ 52, respectively. These values were not significantly different.

1.11 Correlation studies revealed the following findings (a) positive correlation between carnitine intake and free or total carnitine excretion, (b) positive correlation between protein intake and free or total carnitine excretion, (c) positive correlation between fat intake and free, acyl- or total carnitine excretion (d) positive correlation between serum and urinary free carnitine levels, (e) negative correlation between fat intake and percent acylcarnitine in serum, (f) positive correlation between serum free, acyl- or total carnitine and serum cholesterol level; (g) positive correlation between serum acyl- or total

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carnitine and serum albumin level, (h) negative correlation between serum free carnitine and AMC and (i) positive correlation between serum acylcarnitine and UAC.

1.12 After pizotifen (an appetite stimulant) treatment for 8 wks, underweight women had significant in urine creatinine excretion whereas underweight men had significant increase in serum triglycerides level. However, pizotifen or pyridoxine treatmont did not affect the levels of various froms of carnitine in urine or serum. Significantly decrease in free and total clearance in underweight men was observed after pizotifen treatment.

2. Studies in patients on Ramathibodi blenderized formula

2.1 Ramathibodi blenderized formula provides 35 g of protein, 112 g of carbohydrate, 46 g of fat and 127.5 umoles of carnitine per 1000 kcal. The formula was given though tube feeding. Usually 6 feedings were provided at 8 am, 11 am, 2 pm, 5 pm, 8 pm and 12 pm. Though they were aimed to receive 2000-2500 kcal per day which gave 255 to 319 umole of carnitine. Some patients could not accept this amount of energy supply. This would decrease the carnitine intake.

2.2 Though the nutritional status of 17 patients before the study were PCM. The values of serum or urinary carnitine concentration could not be grouped together due to several

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variables existing in each patient. There were energy, protein, carbohydrate, fat and carnitine intake, fever, blood or plasma transfusion and drug treatment. Thus, mean $\pm$ 1 SD of serum or urinary carnitine level in control adults were considered to be the normal limit as a guide to compare the carnitine status between the patients and the control adults, among the patient themselves, and between before and during the study in each patient.

2.3 'Before study' in patients on tube feeding or total parenteral nutrition (TPN) meant the patients were not under the care of our nutrition team. They might be any kind of diet according to the prescription of the physicians taking care the patients. Some of them were already on partial parenteral nutrition and/or tube feeding.

2.3 Twenty four hour urine was available for carnitine analysis in 16 patients. Based on their urinary free carnitine excretion, before and during the first week of study the patients could be divided into two groups.

Group A consisting of 8 patients who had urinary free carnitine excretion within or below the normal limit. Six of them had the level below or being close to the lower normal limit (49 umoles/day) before and throughout the study. Their urinary total carnitine excretion was also within or below the normal

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limit. Though carnitine and protein intake increased during the study the exogenous source of carnitine derived from the diet and the de novo synthesis of carnitine stemming from lysine and methionine did not raise the urinary total and free carnitine excretion. This indicated that carnitine was captured by the avid tissues for the utilization in energy metabolism whenever fat was supplied in the diet. This was supported by their serum free carnitine level being within or close to normal limit. The other two patients in group A had increased in urinary free and total carnitine excretion during the study. One was related to fever caused by infection and the other was related to the state of hyperthyroidism and oral administration of propanolol, a betablocker.

Group B consisting of 8 patients who had urinary free carnitine excretion above the upper normal limit (277 umoles/day) with the value varying from 394 to 2136 umoles per day. Their total carnitine excretion was also higher than the upper normal limit (522 umoles/day). Six of them also had serum free or total carnitine level greater than the upper normal limit. This was related to fever caused by infection in 6 patients, infection and corticosteroid treatment in one patient and only corticosteroid treatment in one patient.

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3. Studies in patients on Sobel formula

3.1 Sobel formula provides 40.3 g of protein, 136 g of carbohydrate, 32.8 g of fat and 0.48 umoles of carnitine. This indicates that Sobel is limiting in carnitine.

3.2 At the time of the study, protein caloric malnutrition, normal nutritional status and obesity were found in 5, 1 and 1 patients, respectively.

3.3 Two out of 7 patients had urinary free and total carnitine excretion greater than the upper normal limit. This was related to infection and corticosteroid treatment. The remaining 5 patients had urinary free and total carnitine excretion within or below the normal limit but higher serum free and total carnitine level than the upper normal limit both before and during study. The findings in the latter group indicate this under stringent carnitine economy with adequate fat intake. There might be an increase in hepatic carnitine biosynthesis and/or carnitine mobilization from skeletal muscle to meet the requirement for fatty acid oxidation.

4. Studies in patients on TPN

4.1 TPN formula used in this study was a fat-free and carnitine-free regiment. The energy supply was derived from carbohydrate (mainly glucose) and amino acids.

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4.2 The nutritional status of all 14 patients before the study was PCM.

4.3 All patients exhibited the same findings. There were decrease in urinary and serum free and total carnitine levels. Whenever there was an infection or operation an increase in urinary free and total carnitine excretion was observed.

Our studies have demonstrated the significant low of carnitine in energy metabolism in man. If carnitine is limiting in the diet and fat is still one of the energy source catabolism in skeletal muscle may be inivitable to release carnitine from this tissue store for the process of fatty acid oxidation. Our data indicated that both urinary and serum free and total carnitine levels should be measured simultaneously for the better evaluation of carnitine status which may be influenced by untritional and non-nutritional factors. It can be concluded that urinary carnitine excretion is a good index for body catabolism, too. However, further investigation is needed to evaluate carnitine requirement and the relationship between carnitine status and health in man.

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