



L-CARNITINE

RESEARCH & REVIEW

A publication from Lonza – The world's leading raw material supplier of L-Carnitine

Issue 5

L-Carnitine – natural support for male fertility

INTRODUCTION

Infertility is more common than most people would imagine. Defined as the inability of a couple to achieve pregnancy after one year of unprotected intercourse, infertility affects about 15% of couples who are attempting their first pregnancy. In the U.S., this amounts to around 5 million couples yearly¹. Apart from the heavy financial burden, infertility interferes with one of the most highly valued of human activities – building a family. **Figure 1** shows the contribution of male- and female-related factors to overall infertility levels.

L-Carnitine provides valuable support for the male reproductive system. Clinical research over the last few decades has reported that L-Carnitine and its metabolite, Acetyl-L-Carnitine, are found in high concentrations in sperm. Furthermore, they play a part in sperm energy metabolism and most importantly, may support sperm quality. L-Carnitine is a naturally occurring vitamin-like substance which plays a vital role in energy metabolism in the human body. In this newsletter, we will look at

MALE INFERTILITY PROBLEMS

- Varicocele (varicose veins located around the testicle)
- Idiopathic causes (unexplained causes)
- Obstructions/mechanical
- Hormonal problems
- Testicular failure
- Sperm problems

FEMALE INFERTILITY PROBLEMS

- Obstructions/mechanical
- Hormonal problems
- Idiopathic causes (unexplained causes)

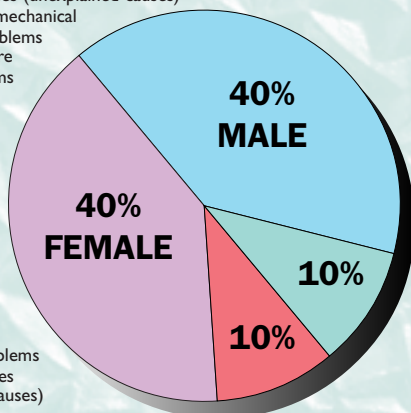


Figure 1: Contribution of Male- and Female-Related Factors to Overall Infertility Levels (adapted from *Resolving Infertility*, HarperCollins Publishers, New York).

how Acetyl-L-Carnitine and particularly, L-Carnitine, may help support male fertility. Although L-Carnitine is typically marketed as a dietary supplement, and the Food and Drug Administration therefore restricts claims to those associated with supporting the reproductive system, studies conducted on L-Carnitine's ability to support healthy sperm provide substantiation in support of dietary supplement claims. Discussions of these studies are solely intended to describe the substantiation underlying dietary supplement claims and are not intended to influence or affect the intended use of L-Carnitine dietary supplement products.

Male Reproductive System

To help in understanding the role of L-Carnitine, here is a very simplified look at how the male reproductive system operates. The organs of the male reproductive system include:

- the testicles which are responsible for producing sperm, a process that takes 65 – 75 days in humans
- a system of ducts or tubes (epididymis, vas deferens, ejaculatory ducts and urethra) which transport and store sperm, assist in their maturation and convey them to the exterior
- accessory sex glands (seminal vesicles, prostate and bulbourethral gland). The prostate gland and seminal vesicles secrete fluids which make up about 85% of the volume of semen
- several supporting structures, including the scrotum and the penis

Semen is a mixture of sperm and seminal fluid, a liquid that consists of the secretions of the testicles and the accessory sex glands. Seminal fluid provides sperm with a transportation medium and nutrients².

Semen Analysis And Sperm Quality

Men frequently have a problem with the number, motility or shape of their sperm and it is estimated that 40% of human infertility is entirely or partly related to deficiencies in sperm quality³. Semen analysis gives an indication as to the type and severity of the issue⁴ and is considered an indirect assessment of fertility potential¹. A number of measurements are made during semen analysis and contribute to semen and sperm quality. These include:

- **Sperm concentration** – the number of sperm that is found in each milliliter of semen⁴
- **Total sperm count** – the total number of sperm present in the semen (semen volume multiplied by sperm concentration); this value accurately describes sperm production by the testicles⁵
- **Sperm motility** – the percentage of sperm that are moving; this is vitally important as the sperm must be motile to “swim” up the vagina⁴
- **Rapid linear progression** – an indication of the percentage of sperm that display rapid, forward movement; these sperm are thought to be most likely to “swim” ahead, reach the egg and cause fertilization³
- **Morphology** – the % of sperm with a normal shape⁴



Values for the various parameters can be seen in **Table 1**.

Table 1: Semen analysis: normal values for men¹

Parameter	Normal Values
Ejaculate (semen) volume	≥ 1.5 ml
Sperm concentration	≥ 20 million/ml
Total sperm count	≥ 40 million
Sperm motility	≥ 50% with forward progression
Sperm with rapid progression	≥ 25%
Morphology (shape)	> 30% normal form

High Levels Of L-Carnitine In Sperm

In males, the highest concentrations of L-Carnitine are found in the epididymal tissue, sperm and seminal fluid⁶.

The L-Carnitine present in the human body comes from food intake and endogenous biosynthesis (i.e. the body can actually manufacture a small quantity itself). In the blood and tissues, L-Carnitine exists as free L-Carnitine and acylcarnitine esters e.g. Acetyl-L-Carnitine. The majority of the free L-Carnitine in sperm and seminal fluid comes from the epididymis⁶, a very long coiled tube where sperm from the testicles mature and increase in motility². Free L-Carnitine is actively transported from the circulating blood into the fluid in the interior of the epididymis^{6,7}. The subsequent passive diffusion of free L-Carnitine from the epididymal fluid into sperm, as they travel along the epididymis, results in a very high concentration of free L-Carnitine in the sperm, some of which is converted to Acetyl-L-Carnitine (in mature sperm only). Worth noting is that the initiation of sperm motility occurs in parallel to the increase of free L-Carnitine inside the epididymis⁶. As sperm mature, the ability to take up L-Carnitine decreases and ejaculated sperm have a limited capacity to take up either L-Carnitine or Acetyl-L-Carnitine^{6,7}. Scientists believe that this new property protects the sperm as they journey through the female reproductive tract and that the storage of free L-Carnitine and Acetyl-L-Carnitine within mature and ejaculated sperm may be a guarantee of sperm viability⁶.

Take Note...

The initiation of sperm motility occurs in parallel to the increase of free L-Carnitine inside the epididymis⁶.



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What's Wrong With Our Sperm?

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L-Carnitine: Important For Sperm Energy Metabolism

Free L-Carnitine and Acetyl-L-Carnitine have an important role to play in sperm energy metabolism.

1. In the human body, L-Carnitine's primary function is to carry fatty acids into the mitochondria ("furnace of the cell") where they can be broken down with the ultimate production of energy. Sperm in the epididymis utilize fatty acids as their source of metabolic energy³ and scientists believe that one of the functions of L-Carnitine in sperm is to carry fatty acids into the sperm mitochondria thereby assisting with the production of energy⁷.
2. Secondly, free L-Carnitine reacts with excess acetyl CoA groups, generated by mature sperm during energy producing processes, thereby forming Acetyl-L-Carnitine. This buffering reaction lowers acetyl CoA levels and restores free CoA levels, thereby facilitating the continuation of energy production within the sperm. At the same time, the Acetyl-L-Carnitine, thus formed, serves as a readily available source of acetyl groups, i.e. energy, for the sperm⁶.

L-Carnitine: Relationship With Sperm Motility And Count

L-Carnitine is reported to be related to sperm motility and count – two important factors in determining sperm quality.

Clinical research has found that the concentration of free L-Carnitine in semen is positively related to sperm count, sperm motility and the number of motile sperm/ml semen in infertile men with varying degrees of sperm count and motility⁹. In a similar population, the concentration of total L-Carnitine in sperm was reported as being directly related to sperm motility, while the concentration of total L-Carnitine in seminal plasma was related to sperm count¹⁰.



February 1, 1995

Study...Sperm Sinking, Not Swimming

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Effects Of L-Carnitine Supplementation On Sperm

Numerous clinical studies have analyzed the effect of oral L-Carnitine supplementation in males (Table 2). Acetyl-L-Carnitine supplementation is also found to be of benefit, although in comparison to L-Carnitine, the clinical data is rather limited.

Although these studies have been conducted in infertile men, L-Carnitine and Acetyl-L-Carnitine are not recommended to treat infertility which is a disease that requires intervention by a health professional. However, since it is well accepted that reproductive efficiency is highest for individuals with good nutritional status and health¹¹, and since these supplements have a role in supporting sperm health, supplementation may be recommended to males interested in supporting their reproductive health.

L-Carnitine Supplementation

The following studies evidence the emerging body of scientific documentation in support of L-Carnitine's ability to help support male reproductive health. Further research, however, must be conducted to confirm the exciting results of these studies.

- In a multicenter study involving 100 males with reduced sperm motility (cause unknown), L-Carnitine supplementation (3g/day for 4 months) was associated with significant increases in sperm concentration and count, % motile sperm and the % sperm with rapid linear progression (Figure 2). The greatest improvement in motility was seen in men who initially had the lowest sperm motility. The researchers

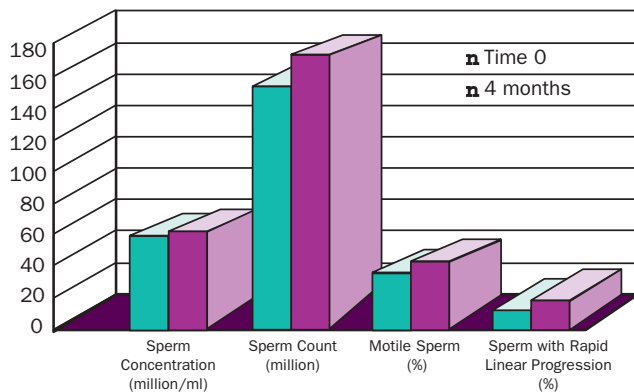


Figure 2: Semen analysis in infertile men before and after L-Carnitine supplementation (3g/day for 4 months)¹².

concluded that L-Carnitine may have the potential to improve sperm quality in men that have reduced sperm motility due to unexplained causes¹².

- In another study, it was found that in 37 out of 47 men with reduced sperm motility (unexplained causes), L-Carnitine

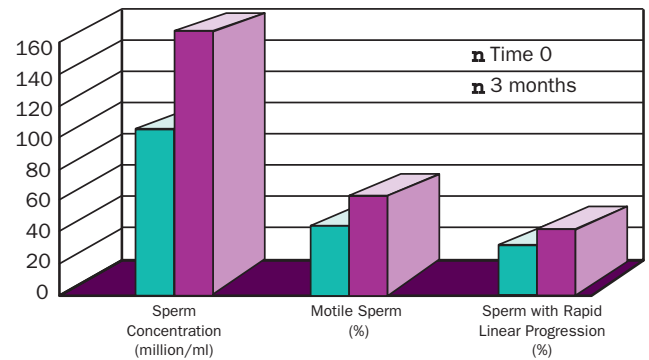


Figure 3: Semen analysis in infertile men before and after L-Carnitine supplementation (3g/day for 3 months)¹³.

supplementation (3g/day for 3 months) increased sperm number, % motile sperms and % sperm with rapid motility (Figure 3)¹³.

- While some studies have used relatively high doses of L-Carnitine and found an increase in sperm motility¹⁴, it appears that lower doses of L-Carnitine also have beneficial effects. For example, 1g L-Carnitine/day for 6 months almost caused a doubling of sperm motility in 20 men with reduced sperm motility due to unknown causes¹⁵.
- L-Carnitine appears to be helpful for infertile men who not only have reduced sperm motility, but also reduced sperm count. In these men, L-Carnitine supplementation (3g/day for 3 months) has been shown to result in a significant increase in seminal L-Carnitine concentration, sperm count and % sperm with progressive motility^{16,17}.

Acetyl-L-Carnitine Supplementation

- The effect of Acetyl-L-Carnitine (4g/day for 2 months) was investigated in 20 men with reduced sperm count and motility of unknown cause. A significant increase in % sperm with rapid progressive motility was reported. Furthermore, the female partners of 7 of the 20 men became pregnant¹⁸.

Table 2: Summary of the beneficial effects of L-Carnitine and Acetyl-L-Carnitine supplementation in infertile men with reduced sperm motility and/or sperm count

L-Carnitine Supplementation (dose: 1-4g/day) (duration: 3-6 months)	Increased: <ul style="list-style-type: none"> • sperm concentration • sperm count • % sperm motility • % sperm with rapid progression
Acetyl-L-Carnitine Supplementation (4g/day for 2 months)	Increased: <ul style="list-style-type: none"> • % sperm with rapid progression

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and so to conclude...

L-Carnitine and its metabolite, Acetyl-L-Carnitine, play an important role in male reproductive health. A number of clinical studies have reported the benefits of L-Carnitine in terms of its effect on sperm. In addition, extensive clinical research has clearly documented the safety of L-Carnitine and its metabolite, Acetyl-L-Carnitine. L-Carnitine supplementation should be considered by all men interested in supporting their reproductive system.

References

1. McClure, R. (1997). In: Hellstrom, W. (ed.) Male Infertility and Sexual Dysfunction. New York, Springer-Verlag, 22.
2. Tortora, G. & Grabowski, S. (2000). Principles of Anatomy and Physiology. New York, Wiley.
3. ADIS International (1999). HNR. 6:189.
4. Schover, L. & Thomas, A. (2000). Overcoming Male Infertility. New York, Wiley.
5. Overstreet, J. (1997). In: Hellstrom, W. (ed.) Male Infertility and Sexual Dysfunction. New York, Springer-Verlag, 39.
6. Jeulin, C. & Lewin, L. (1996). Human Reproduction Update. 2:87.
7. Brooks, D. (1980). In: Frenkel, R. & McGarry, J. (eds.) Carnitine Biosynthesis, Metabolism and Functions. New York, Academic Press, 219.
8. Lenzi, A. et al (1992). Arch. It. Urol. 64:187.
9. Menchini-Fabris, G. et al (1984). Fert. Ster. 42:263.
10. Johansen, L. & Bohmer, T. (1979). Intl. J. Andrology. 2:202.
11. Drobnis, E. (1997). In: Hellstrom, W. (ed.) Male Infertility and Sexual Dysfunction. New York, Springer-Verlag, 54.
12. Costa, M. et al (1994). Andrologia. 26:155.
13. Vitali, G. et al (1995). Drugs Exptl. Clin. Res. 21:157.
14. Campaniello, E. et al (1989). Fourth Intl. Congress of Andrology, Firenze.
15. Loumbakis, P. et al (1996). Eur. Urol. 30(S2): 255.
16. Micic, S. et al (1998). 16th World Congress on Fertility and Sterility and 54th Annual Meeting of the Amer. Soc. Rep. Med. San Francisco.
17. Micic, S. et al (2000). Amer. Soc. Andrology, 25th Annual Meeting, Boston.
18. Moncada, M. et al (1992). Acta Eur. Fert. 23:221.

L-Carnitine can be found in your local health food store, pharmacy, fitness center, or by visiting www.carnitine.com and clicking on the www.drugstore.com hyperlink.

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