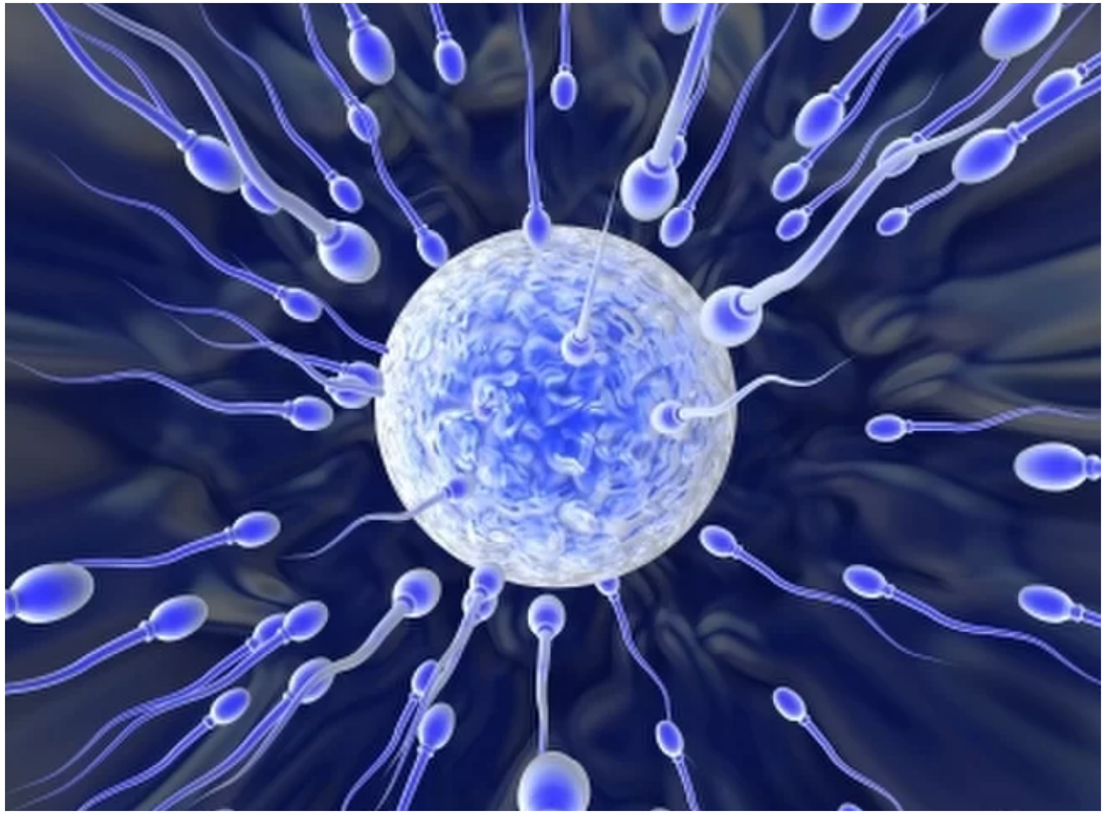
Male Infertility

It is only in the past few decades that male factor has been recognised as a significant cause of infertility.

Session overview

- Male infertility and definitions
- Specific pathology testing
- Nutritional interventions for sperm quality, motility and morphology
- Dietary considerations
- Lifestyle support



Male infertility crisis

Sperm counts among men have more than halved in the last 40 years, research suggests, although the drivers behind the decline remain unclear.

The latest findings reveal that between 1973 and 2011, the concentration of sperm in the ejaculate of men in western countries has fallen by an average of 1.4% a year, leading to an overall drop of just over 52%.

A 2017 published comprehensive meta-regression analysis reports a significant decline in sperm counts (as measured by SC and TSC) between 1973 and 2011, driven by a 50–60% decline among men unselected by fertility from North America, Europe, Australia and New Zealand.

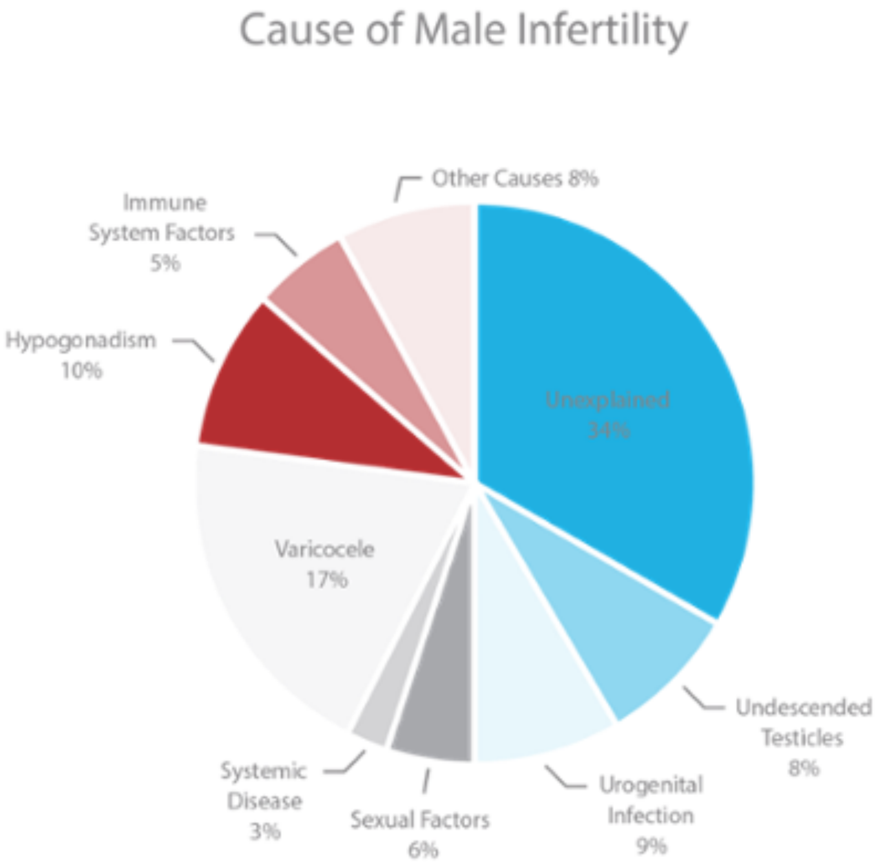
Because of the significant public health implications of these results, research on the causes of this continuing decline is urgently needed.

Levine, Hagai, et al. "Temporal trends in sperm count: a systematic review and meta-regression analysis." *Human reproduction update* 23.6 (2017): 646-659.

Factors affecting fertility

<u>Factors affecting fertility</u>

- Endocrine disorders
- Anatomical disorders (varicocele, ductal obstructions, or ejaculatory disorders)
- Sperm abnormalities
- Abnormal spermatogenesis from; chromosomal, infection, radiation
- Abnormal motility
- Sexual dysfunction
- Environmental exposures
- Nutritional deficiency
- Psychological stressors

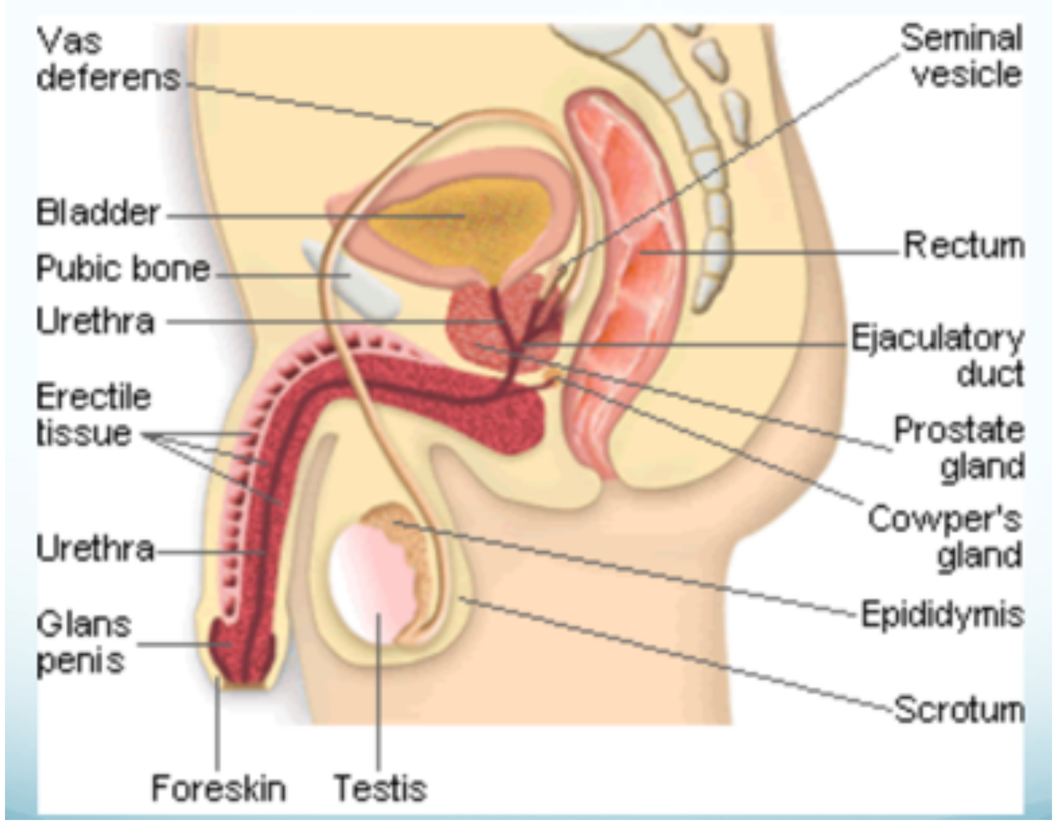


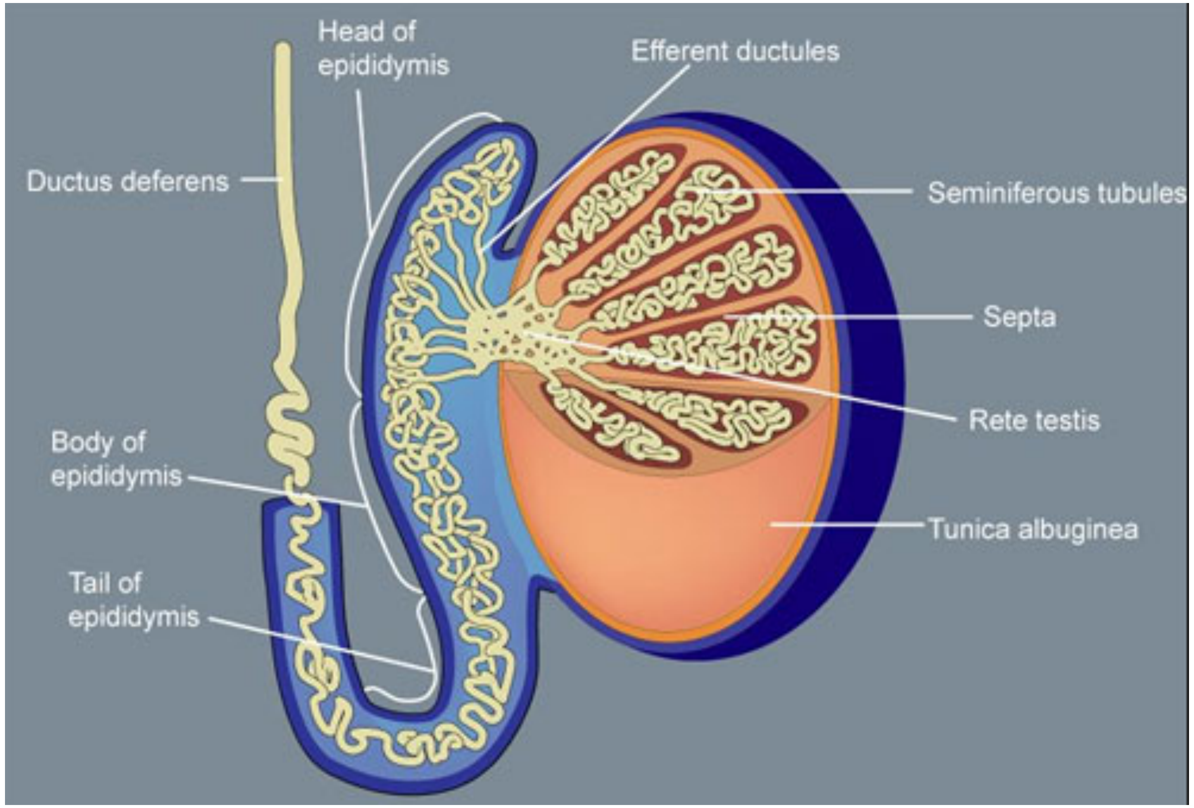
Data source: G. R. Dohle et al. 2010. European Association of Urology Guidelines on Male Infertility.

Definitions of male infertility

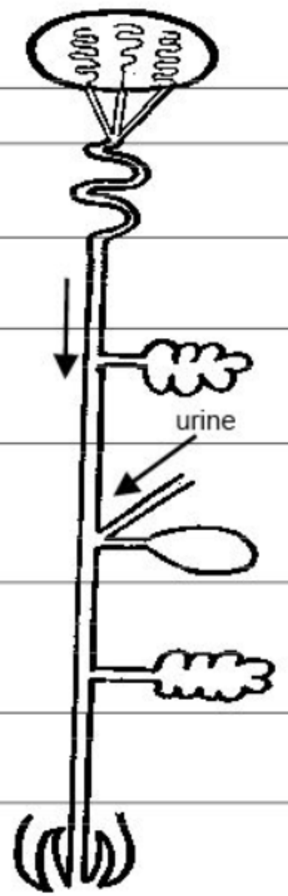
- **Idiopathic Oligospermia or Oligozoospermia** – a decreased number of spermatozoa in semen
- **Oligoasthenoteratozoospermia (OAT)** – abnormally low number of sperm and an abnormally low number of sperm with good motility
- **Azoospermia** – absence of sperm cells in the semen
- **Leukocytospermia** – high levels of white blood cells in the semen
- **Teratospermia** – an increase in sperm with abnormal morphology
- **Asthenozoosoermia or Asthenozoospermia** – reduced sperm motility, complete asthenozoospermia is 100% immotile spermatozoa in the ejaculate.

Anatomical structure





The journey for sperm



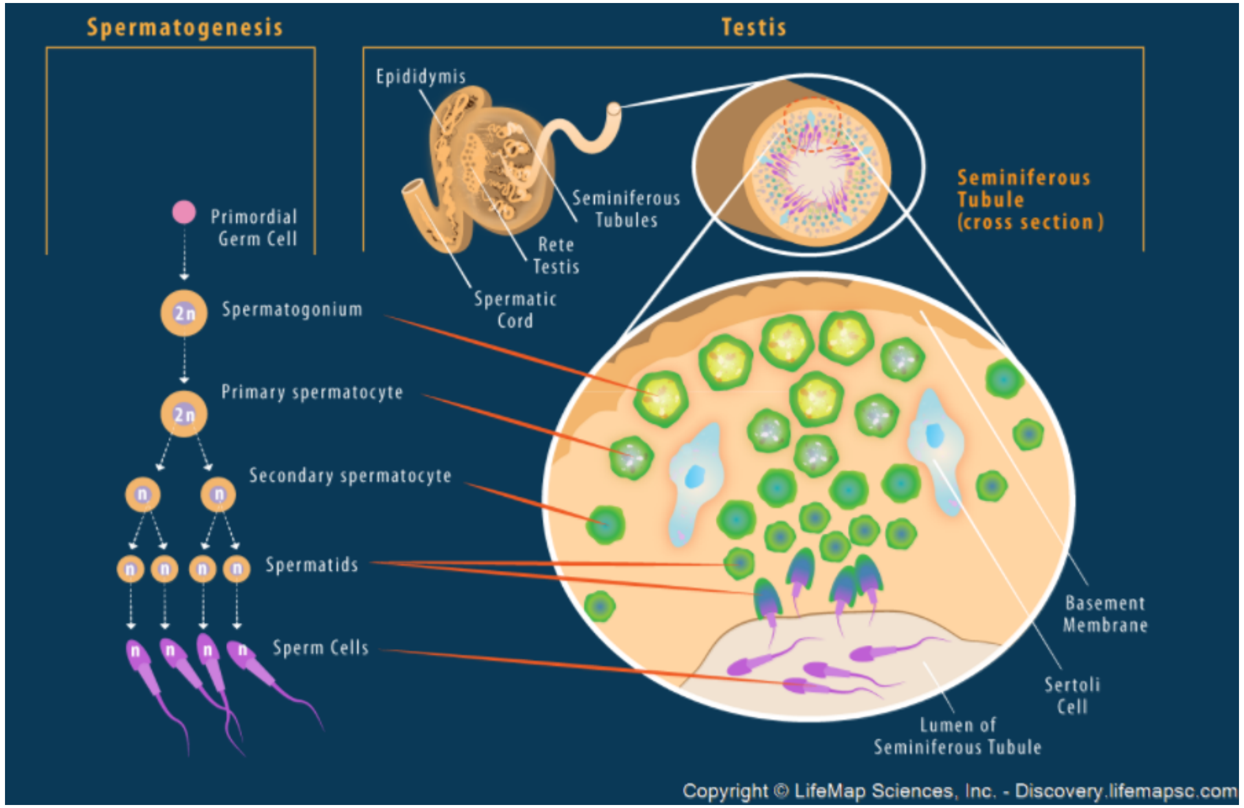
organ	function
testis with seminiferous tubules	sperm production
collecting ducts	transport and storage
epididymis	transport, maturation and ejaculation
vas deferens (sperm duct)	transport and ejaculation
seminal vesicles	secrete thick liquid to transport sperm
prostate gland	secretes thin alkaline solution to neutralise urine and female system
cowper's gland	secretions may lubricate, flush out urine or form a gelatinous plug
urethra	passage for urine and sperm
penis	copulation

Spermatogenesis

For humans, the entire process of spermatogenesis is variously estimated as taking 74 days (according to tritium-labelled biopsies) and approximately 120 days (according to DNA clock measurements).

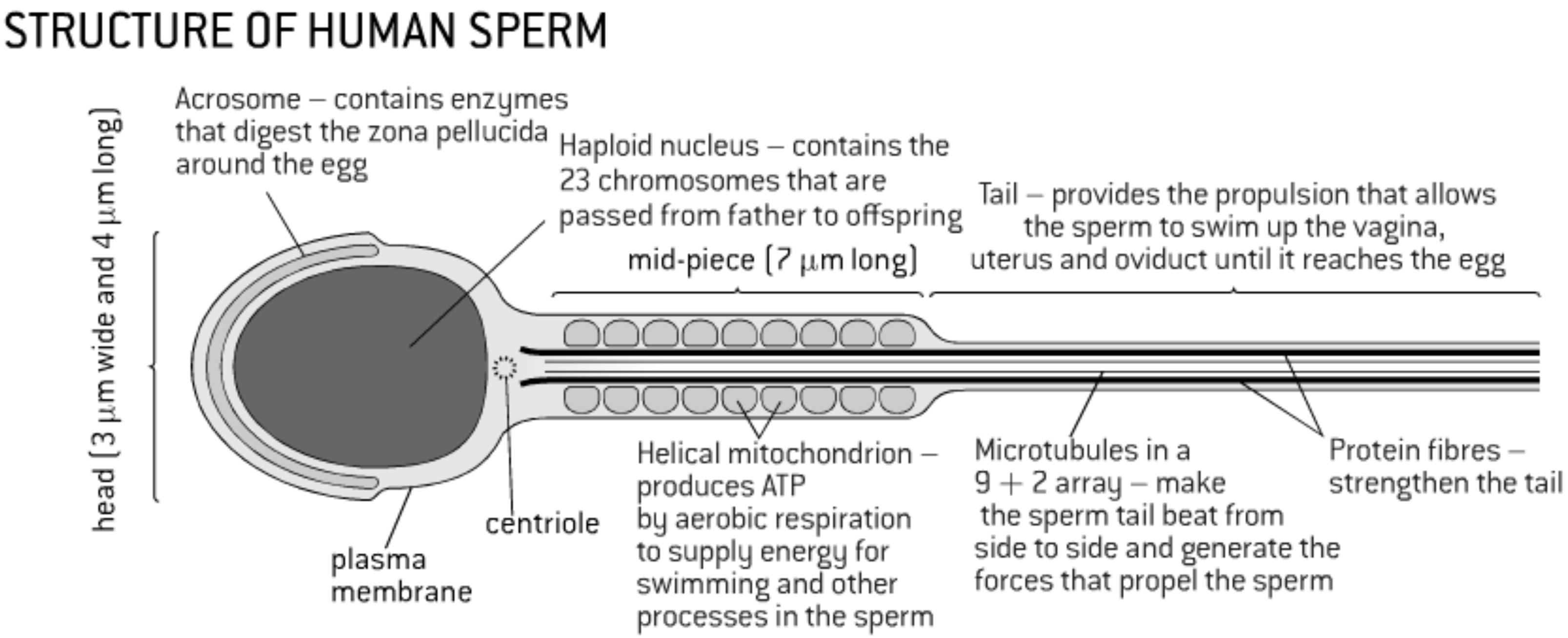
Including the transport on ductal system, it takes 3 months.

Testes produce 200 to 300 million spermatozoa daily. However, only about half or 100 million of these become viable sperm.



Mitochondrial Function

Spermatozoa are cells sentenced to death, and it seems reasonable that reduced sperm motility represents the initial hallmark of depressed mitochondrial function, eventually leading to sperm death.



Sperm testing

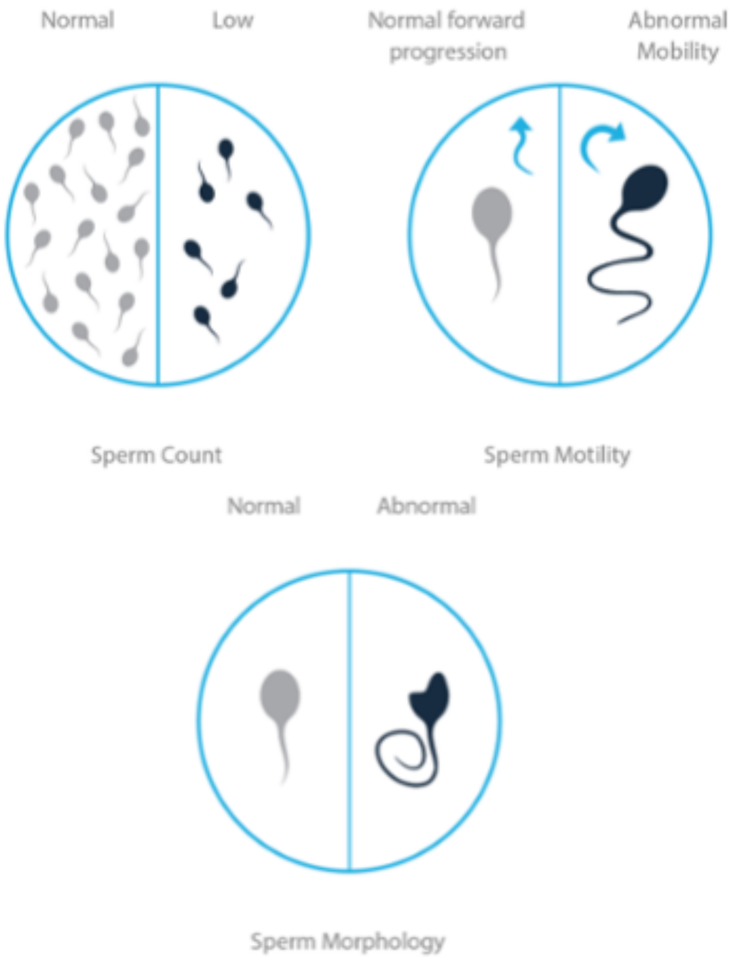
The semen analysis is a fundamental lab test for testing infertility that investigates:

- the number of sperm in a given sample
- the motility of those sperm (can they move properly?)
- the morphology (do they look normal?)

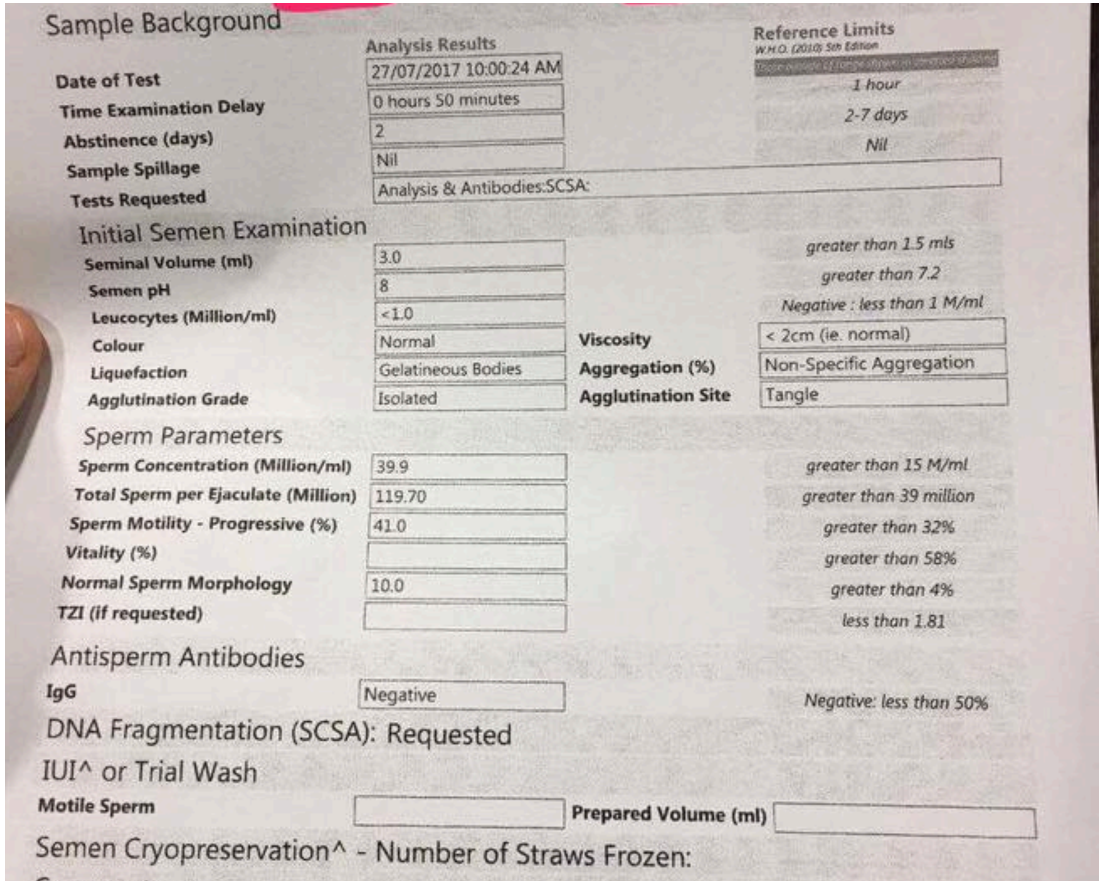
This test also typically looks for signs of infection (i.e., so-called "round cells" in the semen sample).

Although the semen analysis is a reasonable first test for assessing the male, it does not provide a very accurate read on the fertility of the man 100% of the time.

Just because a semen test looks normal doesn't necessarily mean the patient is fertile. Remember, a large proportion of infertile men are diagnosed with unexplained infertility.



Sample tests



Sample Background

	Analysis Results		Reference Limits W.H.O. (2010) 5th Edition
Date of Test	27/07/2017 10:00:24 AM		
Time Examination Delay	0 hours 50 minutes		1 hour
Abstinence (days)	2		2-7 days
Sample Spillage	Nil		Nil
Tests Requested	Analysis & Antibodies:SCSA:		

Initial Semen Examination

Seminal Volume (ml)	3.0		greater than 1.5 mls
Semen pH	8		greater than 7.2
Leucocytes (Million/ml)	<1.0		Negative : less than 1 M/ml
Colour	Normal	Viscosity	< 2cm (ie. normal)
Liquefaction	Gelatineous Bodies	Aggregation (%)	Non-Specific Aggregation
Agglutination Grade	Isolated	Agglutination Site	Tangle

Sperm Parameters

Sperm Concentration (Million/ml)	39.9	greater than 15 M/ml
Total Sperm per Ejaculate (Million)	119.70	greater than 39 million
Sperm Motility - Progressive (%)	41.0	greater than 32%
Vitality (%)		greater than 58%
Normal Sperm Morphology	10.0	greater than 4%
TZI (if requested)		less than 1.81

Antisperm Antibodies

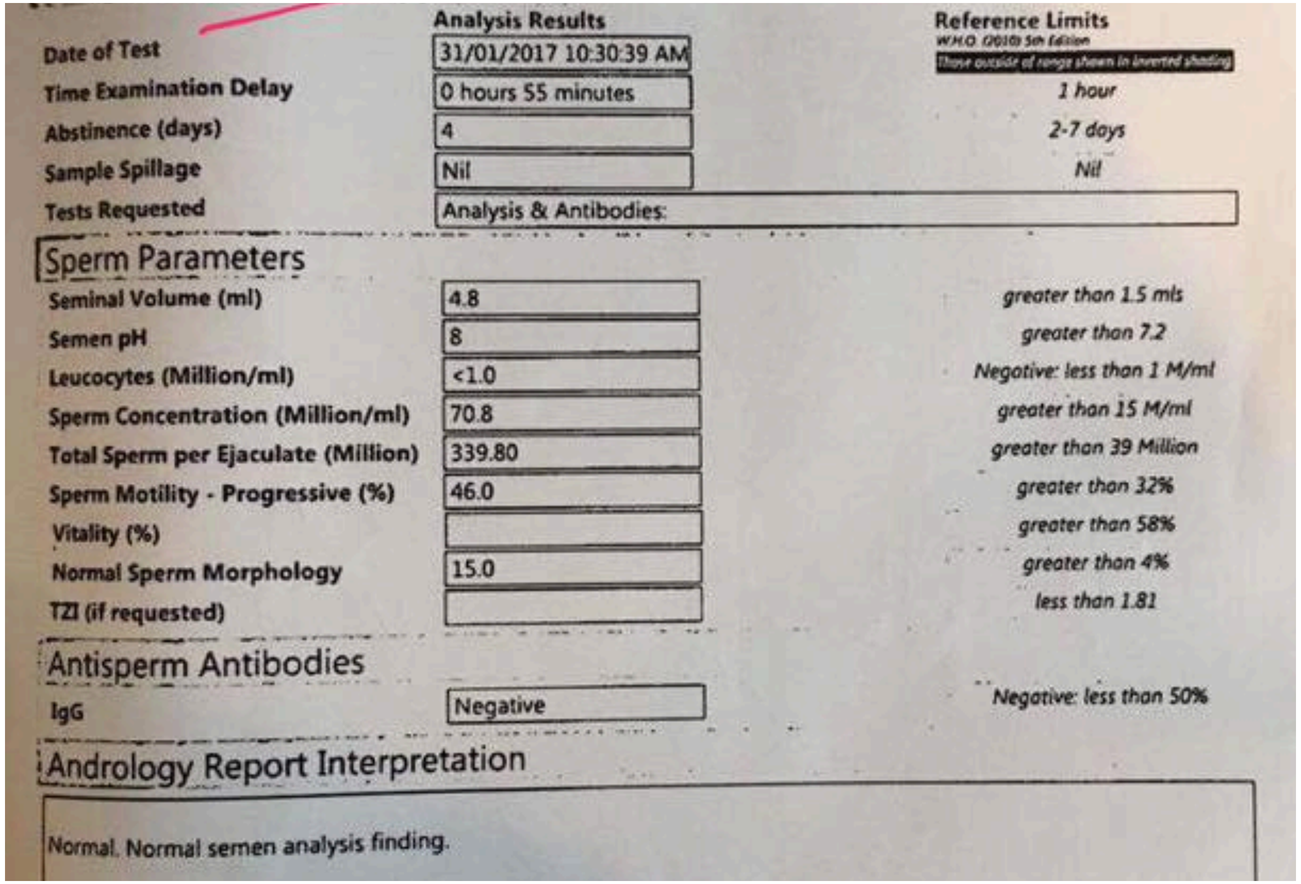
IgG	Negative	Negative: less than 50%

DNA Fragmentation (SCSA): Requested

IUI^ or Trial Wash

Motile Sperm		Prepared Volume (ml)	

Semen Cryopreservation^ - Number of Straws Frozen:



	Analysis Results	Reference Limits W.H.O. (2010) 5th Edition Those outside of range shown in inverted shading
Date of Test	31/01/2017 10:30:39 AM	
Time Examination Delay	0 hours 55 minutes	1 hour
Abstinence (days)	4	2-7 days
Sample Spillage	Nil	Nil
Tests Requested	Analysis & Antibodies:	

Sperm Parameters

Seminal Volume (ml)	4.8	greater than 1.5 mls
Semen pH	8	greater than 7.2
Leucocytes (Million/ml)	<1.0	Negative: less than 1 M/ml
Sperm Concentration (Million/ml)	70.8	greater than 15 M/ml
Total Sperm per Ejaculate (Million)	339.80	greater than 39 Million
Sperm Motility - Progressive (%)	46.0	greater than 32%
Vitality (%)		greater than 58%
Normal Sperm Morphology	15.0	greater than 4%
TZI (if requested)		less than 1.81

Antisperm Antibodies

IgG	Negative	Negative: less than 50%

Andrology Report Interpretation

Normal. Normal semen analysis finding.

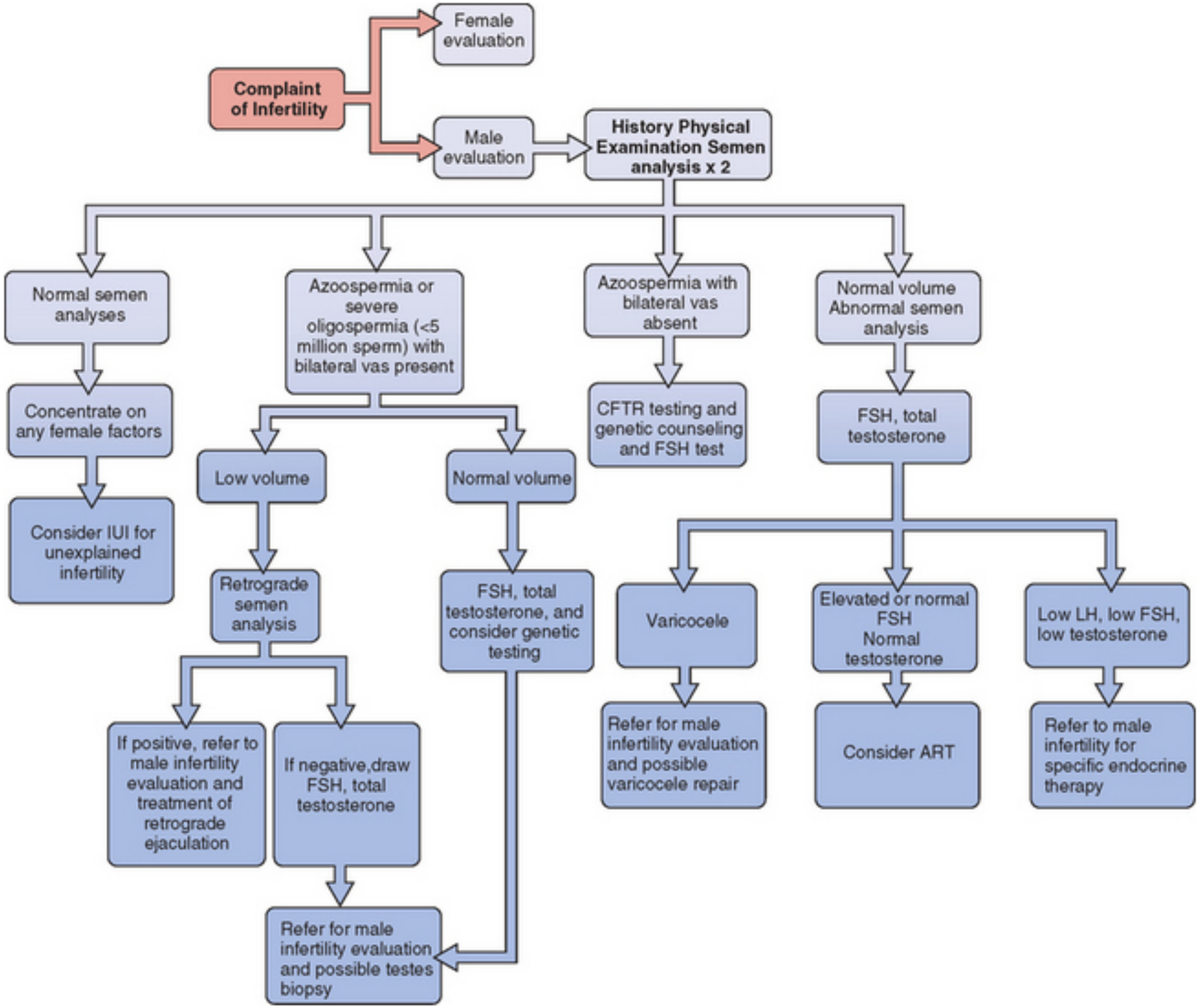
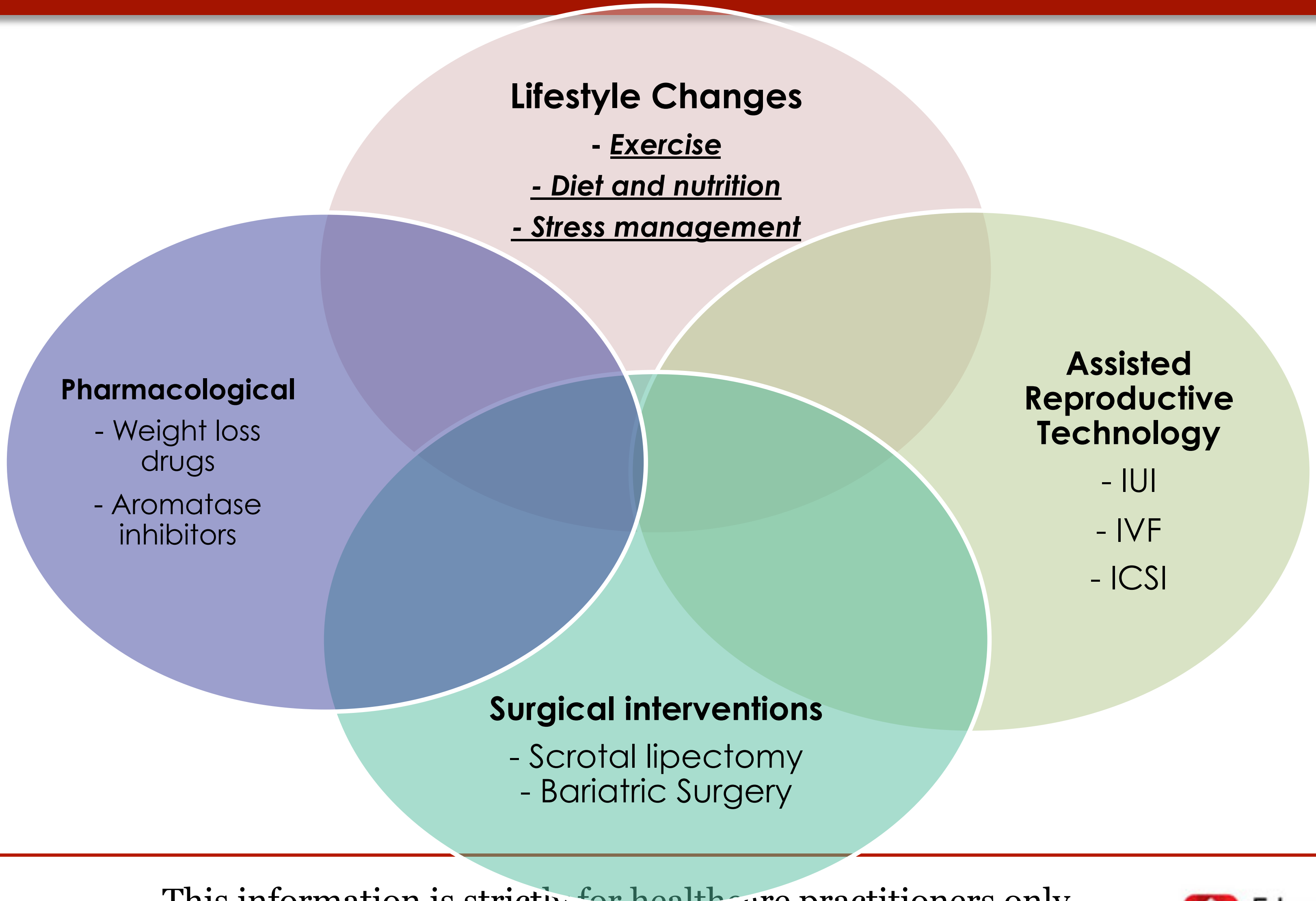


Figure 35-1 Suggested algorithm for the evaluation of male infertility.

Interventions



Acetyl-L-Carnitine

Effect of L-carnitine and/or L-acetyl-carnitine in nutrition treatment for male infertility: a systematic review

Xin Zhou MD[1,2], Fang Liu MD[2] and Suodi Zhai MD[2]

Approximately 60% of male infertility cases are idiopathic and related to sperm dysfunctions such as oligo-astheno-teratozoospermia (OAT)

A key role in sperm metabolism is strongly suggested by the **high levels of L-carnitine (LC) found in epididymal fluid** due to an active secretary mechanism, and there is also evidence that **the initiation of sperm motility is related to an increase of L-carnitine** in the **epididymal lumen and L-acetyl-carnitine (LAC) in sperm cells.**

Free L-carnitine is much more concentrated at the **epididymal level than in blood**.

In the epididymis, free **L-carnitine is transported from blood plasma** into the **epididymal fluid** and **spermatozoa** and **accumulates as both free and acetylated L-carnitine.**

Carnitines may be also responsible for **removing excess intracellular toxic acetyl-CoA**, which **protects spermatozoa from oxidative damage**.

It could be concluded that LAC is a bioactive production from LC and they both participate in the energy metabolism, which **positively affects sperm motility especially forward moving sperm, maturation and the spermatogenic process**.

L-Carnitine

Original Article

Role of L-carnitine in male infertility

Syed Danish Haseen Ahmed,[1] Khemomal Asudo Karira,[2] Jagdesh,[3] Shahid Ahsan[4]
Department of Biocemistry, Hamdard College of Medicine & Dentistry, Karachi ,[1] Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi,[2]
Department of Biochemistry, Muhammad Medical College, Mirpurkhas,[3] Baqai Institute of Diabetes & Endoccrinology, Karachi.[4]

Approximately **75% of the body stores of L-carnitine are derived from the diet**, where as only **25%** are **synthesized** de novo from **lysine and methionine.**

L-carnitine is concentrated in high energy demanding tissues such as skeletal and cardiac muscles and in a specialised reproductive tract organ, the epididymis.

It plays an **important role in transferring long-chain fatty acids into the mitochondria for oxidation & producing energy.**

In addition, **modulation of acyl-CoA / CoA ratio, storage of energy as acetyl-carnitine**, and the modulation of toxic effects of poorly metabolised acyl groups by **excreting them as carnitine esters** are the **functions of L-carnitine**.

L-Carnitine

The **concentration of L-carnitine in epididymal plasma and spermatozoa varies from 2 to 100 mmole**, which is **nearly 2000 fold greater than circulating levels** (10-50 mole).

The initiation of sperm motility occurs in parallel with the increase in concentration of free L-carnitine in the epididymal lumen.

Another potential use of seminal free L-carnitine is in the diagnosis of the etiology of azoospermia. Men with **obstructive azoospermia** whose level of obstruction is post epididymal, such as those with agenesis of **vas deferense**, have extremely low concentrations of carnitine.

Original Article

Role of L-carnitine in male infertility

Syed Danish Haseen Ahmed,[1] Khemomal Asudo Karira,[2] Jagdesh,[3] Shahid Ahsan[4]
Department of Biocemistry, Hamdard College of Medicine & Dentistry, Karachi ,[1] Department of Biochemistry,
Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi,[2]
Department of Biochemistry, Muhammad Medical College, Mirpurkhas,[3] Baqai Institute of Diabetes & Endocrinology, Karachi.[4]

L-Carnitine

- The total of sixty one subjects were selected and were distributed into two main groups, fertile (control) and infertile.

Table-3: Comparison of seminal free l-carnitine among fertile (control) Azoospermic, Asthenospermic and Oligoasthenoteratospermic subjects.

Parameters	**Group A Fertile n=19**	**Group B Azoospermic n=10**	**Group C Asthenospermic n=13**	**Group D OligoAstheno Teratospermic n=19**
Seminal Free L-Carnitine mole/L	447.6±23.86	46.5±7.93*ϕ§	233.3±21.25^£	157.6±7.09†

A fertile (control), group B azoospermic, group C asthenospermic and group D oligoasthenoteratospermic groups. In all **azoospermic, asthenospermic, and oligoasthenoteratospermic the seminal free L-carnitine was found significantly low** when compared independently with fertile (control) group. The mean value of azoospermic was also found significantly decreased ($p<0.05$) when compared with asthenospermic and oligoasthenoteratospermic, whereas the value of asthenospermic was significantly increased ($p<0.05$) when compared with oligoasthenoteratospermic. The lowest value of seminal free L-carnitine was found in azoospermic group.

L-Carnitine

Use of carnitine therapy in selected cases of male factor infertility: a double-blind crossover trial

Andrea Lenzi, M.D., Francesco Lombardo, Ph.D., Paolo Sgrò, M.D., Pietro Salacone, M.D., Luisa Caponecchia, B.Sc., Franco Dondero, M.D., and Loredana Gandini, B.Sc.

Patient(s): One hundred infertile patients (ages 20–40 years) with the following baseline sperm selection criteria: concentration, 10–20 x 106 mL; total motility, 10%–30%; forward motility, <15%; atypical forms, <70%; Eighty-six patients completed the study.

Intervention(s): Patients underwent **L-carnitine therapy 2 g/day or placebo**; the study design was **2 months of washout, 2 months of therapy/placebo**, **2 months of washout, and 2 months placebo/ therapy.**

Excess weight/obesity?

MOLECULAR MEDICINE REPORTS 14: 4659-4665, 2016

Protective effect of resveratrol on spermatozoa function in male infertility induced by excess weight and obesity

XIANGRONG CUI[1], XUAN JING[2], XUEQING WU[1] and MEIQIN YAN[1]

[1]Reproductive Medicine Center, Children's Hospital of Shanxi and Women Health Center of Shanxi, Taiyuan, Shanxi 030000; [2]Clinical Laboratory, Shanxi Province People's Hospital, Taiyuan, Shanxi 030000, P.R. China

Received October 7, 2015; Accepted September 1, 2016

Several studies have investigated the association between BMI and different sperm parameters. In the present study, the **semen quality and serum sex hormone** levels were evaluated in **324 men.**

In addition, previous studies have demon- strated that low (<18.5 kg/m2) and high (≥25 kg/m2) BMIs are associated with reduced testicular volume and reduced semen quality, which suggests an impairment of spermatogenesis.

When compared with the normal weight group, the sperm concentration, normal sperm morphology and testosterone levels in the abnormal weight groups demonstrated a significant decrease, whereas the E2 levels were significantly increased. No

The seminal plasma zinc concentration was significantly reduced in the obese group compared with normal weight group.

Sperm perameters across BMI

Table II. Comparison of routine semen parameters and serum sex hormone levels among BMI groups.

Parameter	Normal weight (18.8≤BMI<23)	Underweight (BMI<18.5)	Overweight (23≤BMI<25)	Obese (BMI≥25)
Semen volume (ml)	3.56±1.74	3.54±1.68	3.10±0.88[a]	3.02±0.73[a]
Sperm concentration ($x10^6$/ml)	68.39±8.54	59.42±8.16[b]	65.39±8.22[a]	64.39±8.19[b]
Progressive motility (%)	40.28±12.98	33.62±11.31[b]	39.56±11.74	36.39±10.39[a]
Morphology (% normal)	12.11±3.59	7.63±1.33[b]	11.08±3.32[a]	10.21±2.9[b]
Follicle stimulating hormone (mIU/ml)	6.98±2.55	4.71±1.83	5.11±2.24	5.49±1.79
Luteinizing hormone (mIU/ml)	9.35±2.35	9.1±1.32	8.74±1.66	8.63±1.29
Estradiol (pg/ml)	29.32±7.90	34.11±8.27[b]	36.63±7.53[b]	37.21±8.94[b]
Testosterone (ng/dl)	386.58±21.32	398.24±22.19[b]	369.76±19.38[b]	354.71±19.23[b]
Prolactin (mIU/ml)	12.28±4.87	12.26±3.48	12.38±4.25	12.45±4.71

[a]P<0.05 and [b]P<0.01 vs. the normal weight group. BMI, body mass index.

Anioxidants

Vitamin C and sperm quality

Original Article J. Clin. Biochem. Nutr., **45**, 144–149, September 2009

Ascorbic Acid in Human Seminal Plasma: Determination and Its Relationship to Sperm Quality

The **higher concentrations of ascorbic acid in the epididymal fluid and seminal plasma compared with blood plasma** have been reported previously for several species.

High concentrations of ascorbic acid in seminal plasma may protect sperm from ROS and maintain the genetic integrity of sperm cells by preventing oxidative damage to DNA.

This study focused primarily on **ascorbic acid levels in the seminal plasma of fertile and infertile subjects (smokers and nonsmokers)**. The association of ascorbic acid with sperm quality in the seminal plasma of all groups was evaluated.

One hundred and-one semen samples were collected from fertile nonsmokers (n = 21), fertile smokers (n =25), infertile nonsmokers (n = 32) and infertile smokers (n = 23)

Ascorbic acid and semen parameters

Table 1. Comparison of sperm parameters quality and ascorbic acid in the fertile and infertile smoker-nonsmoker men

Variable	Nonsmoker men ($n = 53$)		Smoker men ($n = 48$)	
	Fertile ($n = 21$)	Infertile ($n = 32$)	Fertile ($n = 25$)	Infertile ($n = 23$)
Age (years)	31.38 ± 4.36	29.55 ± 4.46	29.7 ± 5.14	31.37 ± 7.4
Volume (ml)	4.14 ± 1.36	3.85 ± 1.53	4.35 ± 1.47	3 ± 1.53
Sperm count ($\times 10^6$ ml)	80 ± 29.63	36.90 ± 29.91*	71 ± 28.81	31.81 ± 21***
Total sperm ($\times 10^6$)	330.71 ± 145.60	137.11 ± 124.33*	310.5 ± 150.63	60.63 ± 47.04***
Motility (%)	73.1 ± 16.3	50.06 ± 29.69†	72 ± 16.73	43.75 ± 32.99***
Normal morphology (%) (by Kruger criteria)	14.93 ± 3.63	5.96 ± 4.36*	12.9 ± 4.78	3.75 ± 2.11***
Ascorbic acid (μmol/l)	448.71 ± 98.13	412.81 ± 114.51**	440.04 ± 103.31	383.13 ± 94.89††

bioconcepts

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Education Centre
Founded by Henry Osiecki

Ascorbic acid and ROS

Fertile groups (smokers or nonsmokers) demonstrated significantly higher ascorbic acid levels in their seminal plasma than any infertile groups ($p<0.01$).

Fertile nonsmokers had significantly high levels of ascorbic acid in their seminal than infertile nonsmokers ($p<0.05$), moreover, fertile smokers had significantly high levels of ascorbic acid in their seminal plasma compared with infertile smokers ($p<0.01$).

Conclusion findings suggested that idiopathic infertile men have significantly low levels of ascorbic acid in their seminal plasma than fertile men.

Evidence suggests that one consequence of ascorbic acid deficiency can be an increase in oxidative damage induced by ROS.

Recent studies have indicated that high levels of ROS are detected in the semen of 25 to 45% of infertile men.

A small amount of ROS is necessary for sperm to acquire fertilizing capabilities, but it appears that high levels of seminal ROS may decrease the effective concentration of seminal ascorbic acid.

Vitamin C – varicocele

ORIGINAL ARTICLE

Vol. 41 (2): 230-238, March - April, 2015
doi: 10.1590/S1677-5538.IBJU.2015.02.07

The effect of adjuvant vitamin C after varicocele surgery on sperm quality and quantity in infertile men: a double blind placebo controlled clinical trial

Varicocele is one of the most common causes of male infertility and although its surgical repair results in improved spermatogenesis in 70% of patients, spontaneous pregnancy rate is only about 30% after varicocele repair without other treatments.

Recently, **oxidative stress** has been proposed to be an **important factor in the pathophysiology** of **varicocele induced infertility**.

The most important seminal antioxidant is ascorbic acid (vitamin C) which comprises **65% of antioxidant capacity of semen and is currently used in-vitro to improve sperm quality in infertility clinics.**

Vitamin C – varicocele

ORIGINAL ARTICLE

Vol. 41 (2): 230-238, March - April, 2015
doi: 10.1590/S1677-5538.IBJU.2015.02.07

The effect of adjuvant vitamin C after varicocele surgery on sperm quality and quantity in infertile men: a double blind placebo controlled clinical trial

115 eligible patients that had surgery supplemented **250 mg of vitamin C in two daily doses**, one in the morning and one in the evening or placebo for **three months after surgery**.

Vitamin C was not effective within this study on sperm count; but **effective on sperm motility and morphology.**

Zinc

Journal of Bangladesh College of Physicians and Surgeons
Vol. 35, No. 1, January 2017

Impact of Seminal Plasma Zinc and Serum Zinc Level on Semen Parameter of Fertile and Infertile Males

P FATIMA[a], MM HOSSAIN[b], D RAHMAN[c], CR MUGNI[d], HB HOSSAIN[e], HN HOSSAIN[f], GM SUMON[g]

The **Zinc concentration of semen is 87 times than that in the blood** and has been reported to **protect sperm from bacteria and chromosomes damage.**

Male fertility is influenced by zinc and plays an important role in normal testicular development, spermatogenesis, and sperm motility

Low zinc levels have a **negative effect on serum testosterone concentration and seminal volume.**

Zinc in seminal plasma stabilizes the cell membrane and nuclear chromatin of spermatozoa.

It may also have an antibacterial function and protect the testes against the degenerative changes.

The study was done to find the impact of seminal plasma zinc and serum zinc levels on semen parameters in fertile and infertile males.

Journal of Bangladesh College of Physicians and Surgeons
Vol. 35, No. 1, January 2017

Impact of Seminal Plasma Zinc and Serum Zinc Level on Semen Parameter of Fertile and Infertile Males

P FATIMA[a], MM HOSSAIN[b], D RAHMAN[c], CR MUGNI[d], HB HOSSAIN[e], HN HOSSAIN[f], GM SUMON[g]

<u>Sixteen fertile males</u> whose wives were pregnant at the time of the assessment were taken as control **<u>and sixty nine infertile males</u>** whose wives were facing difficulty in conceiving due to poor semen parameters, were taken as cases.

Semen parameters and Zinc levels in fertile and infertile males

Parameters (μg/dl) Mean±SD	Control (n=16) Mean±SD	Case (n=69)	P value
Semen volume (ml)	2.46±1.27	2.47±1.07	0.978^{ns}
Total sperm count (million/ml)	85.00±32.04	47.87±46.45	0.003^{**}
Sperm motility (%)	81.88±7.50	52.39±23.68	0.0001^{***}
Rapid linearity (%)	69.06±8.98	31.45±20.55	0.0001^{***}
Morphology (%)	52.50±4.47	25.00±11.97	0.0001^{***}
Serum zinc (ìg/dl)	68.39±14.37	75.83±17.41	0.116^{ns}
Seminal P zinc (μg/dl)6175.44±2569.52	5851.46±2076.11	0.593^{ns}	

Unpaired Student's 't' test, ns = Not significant, ** = Significant (P<0.01), *** = Significant (P<0.001)

Zinc with seminal fluid

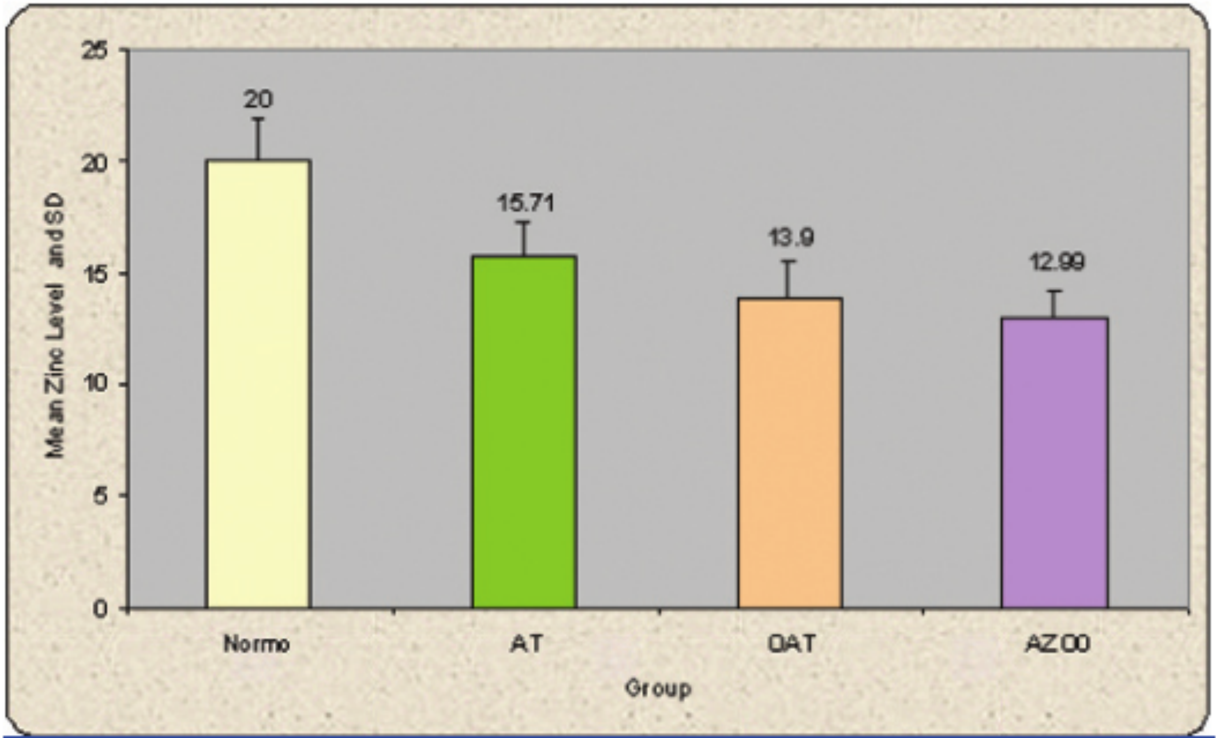
Original Article

Zinc Levels in Seminal Fluid in Infertile Males and its Relation with Serum Free Testosterone

Zinc is one of the most important compound of seminal fluid **contributed by prostate gland.**

Semen samples were obtained from **150 male partners of infertile couples aged between 21-50 years.**

Cases of both primary as well as secondary infertility were included in the study.



[Table/Fig-2]: Zinc levels (mg/dl) of seminal plasma in normal ejaculate and abnormal ejaculate group.
Normo- Normozoospermics, AT- Asthenoteratozoospermics
OAT-Oligoasthenoteratozoospermics, AZOO- Azoospermics

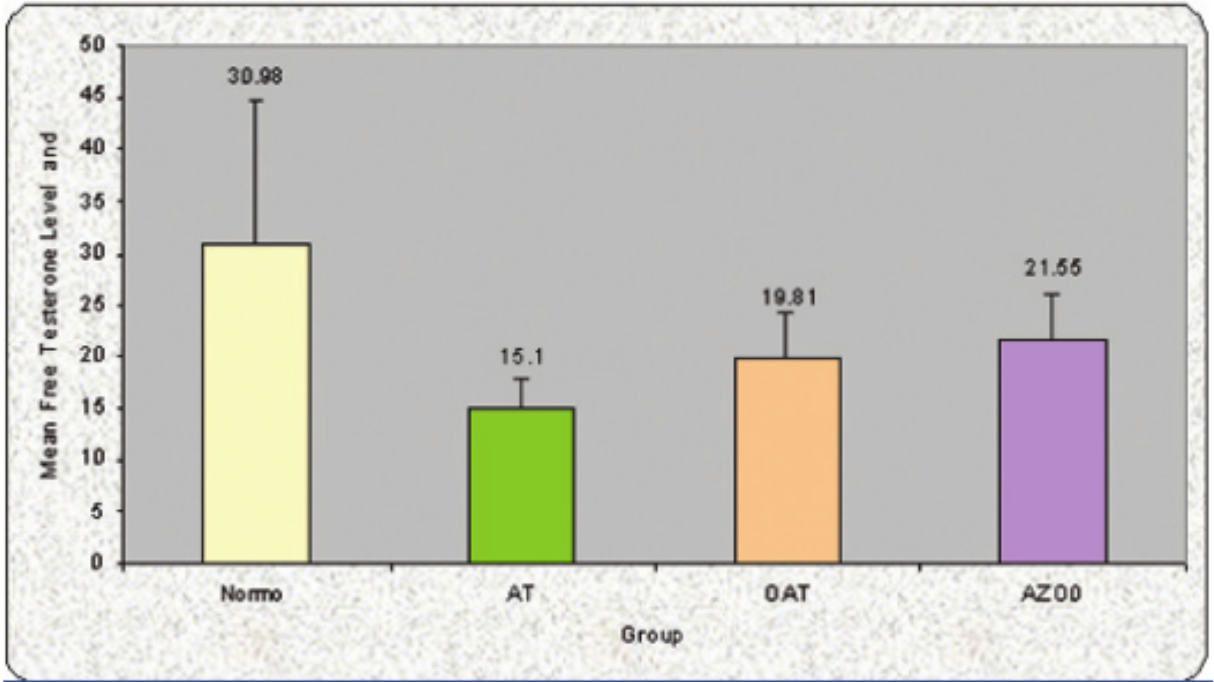
Zinc – plasma seminal levels

Original Article

Zinc Levels in Seminal Fluid in Infertile Males and its Relation with Serum Free Testosterone

In present study the **seminal plasma zinc levels** (in mg/dl) were found to be **highest in Normozoospermics** (Mean 20.00±1.93), followed by **Asthenoteratozoospermics** (Mean 15.71±1.63), **Oligoasthenoteratozoospermics** (Mean 13.90±1.62) and **Azoospermics** (Mean 12.99±1.25).

The mean **serum free testosterone** level (pg/ml) was found to be **highest in Normozoospermics.**



[Table/Fig-7]: Serum free Testosterone levels (pg/dl) in normal ejaculate and abnormal ejaculate group.

Review Article

Role of Zinc in Male Infertility: Review of Literature

Naina Kumar[1,*], Amit Kant Singh[2]

[1]Associate Professor, Dept. of Obstetrics & Gynecology, Maharishi Markandeshwar Institute of Medical Sciences & Research, Haryana, [2]Professor, Dept. of Physiology, Rural Institute of Medical Sciences, Uttar Pradesh

In a trial of **37 males with idiopathic infertility**, **24 mg of elemental zinc** was supplemented for **45 to 50 days.**

Resulted in a **substantial increase in testosterone level and sperm count from eight million to 20 million/ ml**, leading to nine successful conceptions.

Table 1: Global male and female infertility rates based on various studies

Country	Infertile Males	Infertile Couples	Couples in which male factor is one of multiple factors involved
North America	4.5-6%a	15%	50%
Middle East	Unknown	Unknown	60%-70%b[20]
Sub-Saharan Africa	2.5%-4.8%a	12.5%-16%[21]	20-40%[21]
Europe	7.5%a[22]	15%[22]	50% of all infertile couples
Australia	8%; 9%b[23]	15%	40%[24]
Central/Eastern, Europe	8%-12%[25,26]	20%[26]	56%[25]
Asia	Unknown	Unknown	37%[27]
Latin America	Unknown	Unknown	52%[27]
Africa	Unknown	Unknown	43%[27]

Selenium- sperm motility

The effect of oral selenium supplementation on human sperm motility

R. SCOTT, A. MACPHERSON*, R.W.S YATES†, B. HUSSAIN and J. DIXON*
*Departments of Urology and †Obstetrics and Gynaecology, Glasgow Royal Infirmary, Glasgow and *Biochemistry and Nutrition, SAC, Auchincruive, Ayr, UK*

Sixty-nine patients were recruited and received **either placebo, selenium alone or selenium plus vitamins A, C and E daily for 3 months.**

Selenomethionine 100 mcg per day or selenium combined with **vitamins A 1mg, Vitamin C 10 mg and Vitamin E 15 mg supplements against a placebo**. One tablet taken at night for **3 months.**

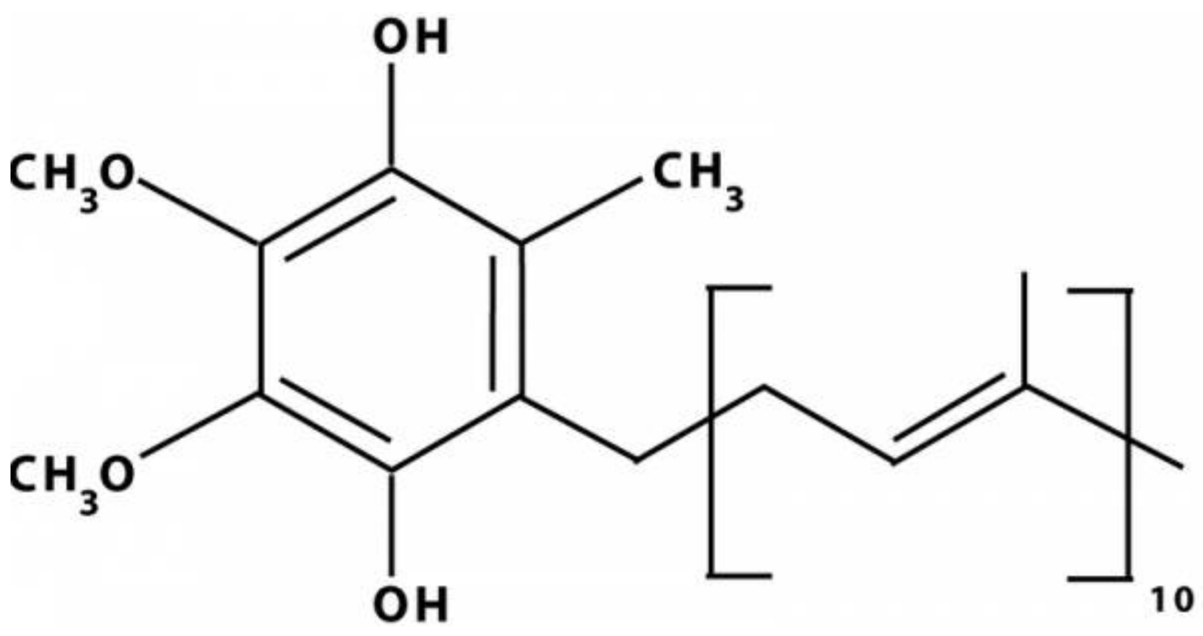
After treatment the **plasma selenium concentration in the two groups was significantly higher in comparison to the placebo group.**

22% increase in sperm count in treatment group one

40% and 34% increase in sperm motility in the two treatment groups and no change in the placebo group

Five of those receiving the supplement have now produced a successful pregnancy.

Coenzyme Q10



CoQ10's benefits are possibly related not only to its **antioxidant role**, but also its function in **mitochondrial respiration** (**enhancing sperm endurance**).

Low seminal plasma concentrations of CoQ10 have been correlated with impaired sperm parameters (e.g. **count/density, morphology, motility**) and it has been shown that CoQ10 supplementation in men with idiopathic OAT results in improved semen parameters.

Coenzyme Q10 and fertility

Sexual Function/Infertility

Efficacy of Coenzyme Q10 on Semen Parameters, Sperm Function and Reproductive Hormones in Infertile Men

Mohammad Reza Safarinejad*

From the Urology and Nephrology Research Center, Shahid Beheshti University (MC), Tehran, Iran

A total of **212 infertile men** with **idiopathic oligoasthenoteratospermia** were randomly assigned to receive **300 mg coenzyme Q10 orally daily**, or a similar placebo during a **26 week period**, followed by a 30 week treatment free period.

Significant improvement in sperm density was evident with coenzyme Q10 therapy ($p = 0.01$). Also shown was

The **coenzyme Q10 group had a significant decrease in serum follicle- stimulating hormone and luteinizing hormone at the 26-week treatment phase** ($p = 0.03$).

A **positive correlation** was found between treatment duration with **coenzyme Q10 and sperm count** ($p = 0.03$), **sperm motility and sperm morphology**.

Coenzyme Q10 and fertility

J Assist Reprod Genet (2013) 30:1147–1156
DOI 10.1007/s10815-013-0047-5

GONADAL PHYSIOLOGY AND DISEASE

Coenzyme Q10 and male infertility: a meta-analysis

Rafael Lafuente · Mireia González-Comadrán · Ivan Solà · Gemma López · Mario Brassesco · Ramón Carreras · Miguel A. Checa

Both the bioenergetic and the antioxidant role of CoQ_{10} suggest a possible involvement in sperm biochemistry and male infertility.

It can function in the mitochondrial respiratory chain but also to its antioxidant properties.

The analysis showed, among patients receiving CoQ10 treatment, a statistically significant increase in:

- **CoQ10 seminal concentration** (RR 49.55, 95 % CI 46.44 to 52.66, I2=17 %)
- **Sperm concentration** (RR 5.33, 95 % CI 4.18 to 6.47, I2=58 %)
- **Sperm motility** (RR 4.50, 95 % CI 3.92 to 5.08, I2=0 %)

This study found a global improvement in sperm parameters.

Antioxidant capacity

Int J Reprod BioMed Vol. 14. No. 12. pp: 729-736, December 2016

Evidence based review

Antioxidant supplements and semen parameters: An evidence based review

Sedigheh Ahmadi[1] M.Sc., Reihane Bashiri[1] M.Sc., Akram Ghadiri-Anari[2] M.D. Azadeh Nadjarzadeh[1]

Approximately, **30-80% of infertility cases are caused by oxidative stress and decreased level of seminal total antioxidant capacity.**

Ordinary antioxidants in semen include vitamin E, vitamin C, superoxide dismutase, glutathione and thioredoxin. These antioxidants neutralize free radical activity and protect sperm from ROS that are already produced.

690 infertile men with **idiopathic asthenoteratospermia** who received **daily supplement of selenium (200 μg) in combination with vitamin E (400 IU) for at least 100 days.**

They reported **52.6% (362 cases) total improvement in sperm motility, morphology, or both, and 10.8% (75 cases) spontaneous pregnancy in comparison with no treatment.**

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CoQ10 also known as ubiquinone dosage varied between 100-200mg daily

228 unexplained infertile men with abnormal sperm concentration, motility and morphology, showed that 28 wk treatment with ubiquinone led to improvement in **sperm density, sperm motility and sperm morphology in the intervention group compared to the control group**

Balercia and colleagues examined the effect of CoQ10 on sperm motility in infertile men, which **60 men with idiopathic asthenoteratospermia received CoQ10 therapy in a double-blind controlled trial.**

After 6 months therapy, CoQ10 **increased in the semen of patients who received CoQ10**, and the **sperm motility was improved** in these individuals.

Twelve spontaneous pregnancies were occurred.

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<u>Selenium 200mcg and N-acetyl-cysteine 600mg daily on 468 infertile men with idiopathic oligo-asthenoteratospermia.</u>

They were followed by a **<u>30 weeks treatment period</u>**.

In response to treatment, **<u>serum follicle-stimulating hormone decreased but serum testosterone and Inhibin B increased.</u>**

In addition, **<u>all semen parameters significantly improved with selenium and N-acetyl-cysteine treatment</u>**.

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Table I. Characteristics of clinical trials reviewed in the study

Author Year	Number of participants/ Abnormality	Antioxidant type and dose	Intervention period	Controlled/ Blinded	Results
Lenzi 2004 (33)	60/ Oligoasthenoteratozoospermia	2 g/d LC plus 1 g/d LAC	6 months	Yes/ Yes	Increase in sperm motility
Balercia 2005 (34)	60/ Asthenozoospermia	a) 3 g/d LC b) 3 g/d of LAC c) 2 g/d of LC and 1 g/d LAC d) Placebo	6 months treatment and 1 month follow up	Yes/ Yes	LCand LAC increased sperm motility and TOSC. Nine pregnancies occurred in carnitine-treated patients during therapy and five of them were achieved after combined supplement
Greco 2005 (26, 27)	64/ Unexplained infertility with high DNA fragmentation	a) 1g/d vitamin E and 1g/d vitamin C b) Placebo	2 months	Yes/ Yes	No significant relationship was found between vitamin E and C intake and sperm motility or concentration but improved ICSI in patients with sperm DNA damage and reduced the level of DNA damage.
Ebisch 2006 (50)	47/ Fertile 40/ Subfertile	a) 5 mg folic acid and 66 mg zinc b) Placebo	26 weeks	Yes/ Yes	Improvement of sperm concentration with no effect on other parameters
Sigman 2006 (35)	21/ Asthenozoospermia	2 g/d LCplus 1 g/d LAC	24 weeks	Yes/Yes	No significant effect of LC / LAC and sperm motility / concentrations
Galatioto 2008 (56)	42/ Oligospermia	a) 600 mg NAC plus vitamins-minerals b) no treatment	3 months	Yes/ No	Increase in number of sperms in intervention group with no differences in other semen parameters
Balercia 2009 (39)	60/ Asthenozoospermia	a) 200 mg Co Q10 b) Placebo	6 months	Yes/ Yes	Improvement in sperm motility and twelve spontaneous pregnancies
Safarinejad 2009 (55)	468/ Oligoasthenoteratozoospermia	a) 200 µg selenium, b) 600 mg N-acetyl-cysteine, c) 200 µg selenium+ 600 mg N-acetyl-cysteined) Placebo	30 weeks	Yes/ Yes	All semen parameters significantly improved with selenium and N-acetyl-cysteine

bioconcepts

Education Centre
Founded by Henry Osiecki

Int J Reprod BioMed Vol. 14. No. 12. pp: 729-736, December 2016

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Safarinejad 2009 (55)	468/ Oligoasthenoteratozoospermia	a) 200 µg selenium, b) 600 mg N-acetyl-cysteine, c) 200 µg selenium+ 600 mg N-acetyl-cysteined) Placebo	30 weeks	Yes/ Yes	All semen parameters significantly improved with selenium and N-acetyl-cysteine
Nadjarzadeh 2014 (41)	47/ Oligoasthenoteratozoospermia	a) 200 mg Co Q10 b) Placebo	3 months	Yes/ Yes	Increase in seminal catalase and SOD with a significant positive correlation between CoQ10 concentration and normal sperm morphology, catalase, and SOD
Safarinejad 2012 (40)	228/ Oligoasthenoteratozoospermia	a) 200 mg Ubiquinone b) Placebo	26 weeks	Yes/ Yes	Improvement in sperm density, motility and morphology
Moslemi 2011	690/ Asthenoteratospermia	200 µg Selenium + 400 IU vitamin E	100 days	No/ No	52.6% total improvement in sperm motility, morphology, or both with 10.8% spontaneous pregnancy
Hadwan 2012 (45)	37/ Fertile 37/ Asthenozoospermia	220 mg zinc sulfate bid	3 months	Yes/ Yes	Increase in semen volume, sperm count and motility
Raigani 2014 (51)	83/ Oligoasthenoteratozoospermia	a) 220 mg folic acid and 5 mg zinc b) placebo	16 weeks	Yes/ Yes	No significant improvements in sperm concentration, motility and morphology
Abad 2013 (57)	20/ Asthenoteratozoospermia	1500 mg of LC, 60 mg vitamin C, 20 mg Co Q10, 10 mg vitamin E, 10 mg zinc, 200 µg folic acid, 50 µg selenium, and 1 µg vitamin B12	3 months	No/ No	Significant increase in concentration, motility, vitality and morphology of sperm. Also a significant improvement of DNA integrity was observed.
Nadjarzadeh 2011 (42)	47/ Oligoasthenoteratozoospermia	a) 200 mg Co Q10 b) Placebo	3 months	Yes/ Yes	Improvement in seminal oxidative defense but does not affect on semen parameters in idiopathic oligoasthenoteratozoospermia
Hadwan 2014 (46)	60/ Fertile 60/ Asthenozoospermia	220 mg zinc sulfate bid	3 months		Increase in semen volume, forward motility and sperm count

Mediterranean Diet

Human Reproduction, Vol.32, No.1 pp. 215–222, 2017
Advanced Access publication on November 14, 2016 doi:10.1093/humrep/dew288

human reproduction | ORIGINAL ARTICLE *Reproductive epidemiology*

Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility

Dimitrios Karayiannis[1], Meropi D. Kontogianni[1], Christina Mendorou[2], Lygeri Douka[2], Minas Mastrominas[2], and Nikos Yiannakouris[1,*]

2017 study on the Mediterranean Diet and its impact on semen quality.

Researchers assessed the diets of **225 men, aged 26-55 at a fertility clinic**. More than half of the men were **overweight** and more than 20% smoked cigarettes.

It was already known that diets high in vegetables, fruits, whole grains, and fish and decreasing diet components of meat and processed foods are good for overall health.

They found that the men in the upper range of eating the Mediterranean Diet had the greatest sperm concentration, sperm count, sperm motility (movement), and sperm morphology (size and shape). Normal sperm have an oval head and long tail.

The men in the lowest 1/3 range had the lowest sperm concentration, sperm count, sperm motility, and abnormal sperm shape and size.

Hinderances in Diet

< Previous Abstract | Next Abstract >

Intake of Sugar-sweetened Beverages and Fecundability in a North American Preconception Cohort

Hatch, EE[1]; Wesselink, AK[1]; Hahn, KA[1]; Michiel, JJ[1]; Mikkelsen, EM[2]; Sorensen, HT[2]; Rothman, KJ[1]; Wise, LA[1]

Epidemiology: January 30, 2018 - Volume Publish Ahead of Print - Issue - p
doi: 10.1097/EDE.0000000000000812
Original Article: PDF Only

2018 study on the link between drinking soft drink and reduced fertility in men and women.

Evaluating their data, the researchers revealed that drinking soda was linked with a 20 percent reduction in the average monthly probability of conception for both men and women.

Men who drank at least one soda per day had a 33 percent lower probability of successfully conceiving with their partner.

Urine bisphenol-A (BPA) level in relation to semen quality

De-Kun Li, M.D., Ph.D.,[a] ZhiJun Zhou, M.D., Ph.D.,[b] Maohua Miao, Ph.D.,[c] Yonghua He, Ph.D.,[b] JinTao Wang, Ph.D.,[d] Jeannette Ferber, M.P.H.,[a] Lisa J. Herrinton, Ph.D.,[a] ErSheng Gao, M.D., M.P.H.,[c,e] and Wei Yuan, M.D., Ph.D.[c,e]

For their study of 218 workers in factories in China, researchers at Kaiser Permanente, a California-based research centre, found that men with higher urine BPA levels were two to four times more at risk of having poor semen quality, including low sperm concentration, low sperm vitality and mobility.

What is more the amount of the BPA in the blood seemed to be inversely proportional to sperm quality.

Even those with less than the national average BPA levels in America were effected, it was claimed.

Stress and Mental Health

Men can to feel isolated and alone with a diagnosis of infertility. This can be due to:

- Lack of information from doctors or specialists due to the, often, unexplained nature of male infertility
- Reduced male-only support services
- A feeling of failure, grief or hopelessness

We know that depression and mood can negatively impact areas of health. What's a way to look at this?

Infertility counselling

J Assist Reprod Genet (2012) 29:243–248
DOI 10.1007/s10815-011-9701-y

ASSISTED REPRODUCTION TECHNOLOGIES

An introduction to infertility counseling: a guide for mental health and medical professionals

Brennan Peterson · Jacky Boivin · Jan Norré · Cassandra Smith · Petra Thorn · Tewes Wischmann

The practice of infertility counselling delivered by mental health and medical professionals has become more sophisticated and widespread over the past decade.

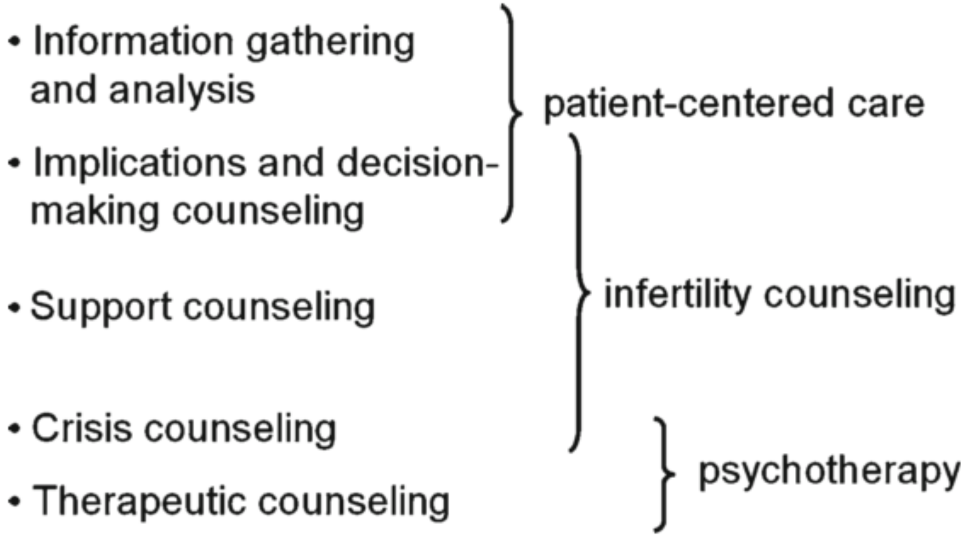
Highlights issues that infertility counsellors must consider in their work with couples experiencing infertility, and outlines psychosocial interventions and treatments to support couples during the infertility experience.

Infertility counselling

Typically, providing psychosocial care and psychological help for infertile couples or individuals is seen as a stepwise process.

Medical doctors and the staff of the fertility centre should deliver patient-centred care. They should offer sufficient information about the pros and cons of medical treatments so that the patient knows enough about treatment implications to make informed decisions.

Infertility counselling and psychotherapy should be offered by independent providers rather than by the medical team so that issues about ART success rates, ART with third-party reproduction, and issues related to stopping treatment can be sufficiently addressed.



Thank you for participating