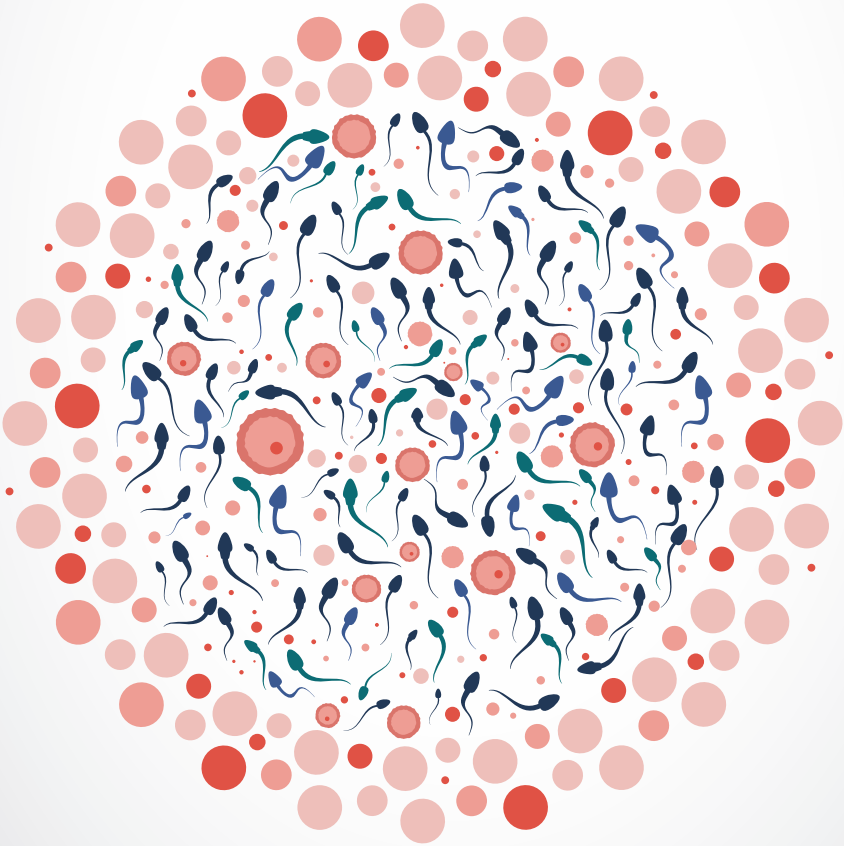
NUMBER 12

CYTOPLAN

THE HEALTH INFORMATION SERIES



FERTILITY & CONCEPTION

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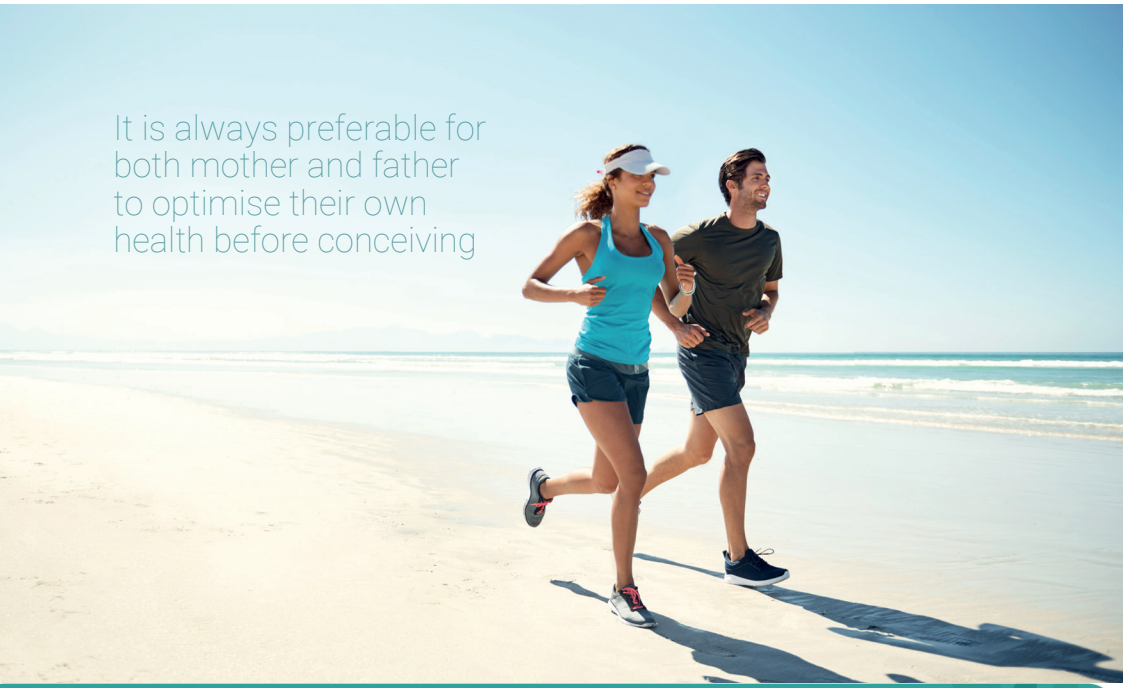
Fertility and conception

Planning a pregnancy is both an exciting and important time. It is always preferable for both mother and father to assess their health before conceiving a child; which will optimise the chances of conception, wellbeing in pregnancy and the health of the baby.

Unfortunately, conceiving and giving birth to a healthy baby can sometimes be a challenge. Infertility can be heart-breaking for those involved and have a significant detrimental effect on mental health and wellbeing. Often there is no clear causative factor leading to infertility or subfertility. Although this can be frustrating, it does mean that if wellbeing is optimised, the chances of conception and a healthy pregnancy may improve.

In couples who do not suspect or have not been diagnosed with infertility, it is still advisable for both the mother and father to optimise their own health before conceiving in order to support a healthy conception and pregnancy.



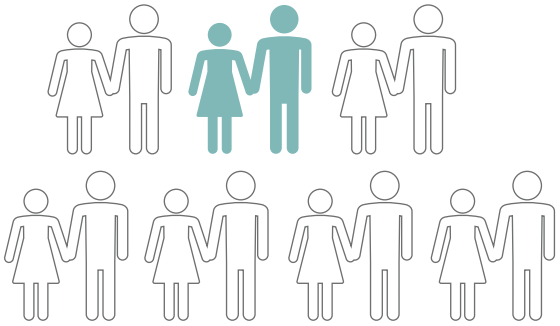
What is infertility or subfertility and how is it diagnosed?

The World Health Organisation defines infertility as failure to achieve a clinical pregnancy after twelve months or more of regular unprotected sexual intercourse with the same partner (specified as on average twice a week)[1]. Approximately 80% of couples will conceive within the first year; half of the remaining 20% will conceive within the second year. Infertility occurs in 5-10% of couples and it is accepted that one third is due to female causes, one third male causes and one third combined causes.[2] Male infertility may additionally be diagnosed by sperm abnormalities confirmed by two analyses of sperm count, morphology, motility or other aspects. Other conditions which may lead to infertility are discussed below.[3]

Subfertility is similar to infertility, however, with subfertility there is no specific reason why a pregnancy cannot occur and therefore optimising health has the potential to allow a successful pregnancy.

Incidence

Around one in seven couples may have difficulty conceiving. This is approximately 3.5 million people in the UK.[3]



1 IN 7

couples may have difficulty conceiving

What causes infertility or subfertility?

Low fertility can be due to many factors, however it is often considered by health professionals to be idiopathic, meaning there is no known cause.

Female reproductive conditions such as blocked fallopian tubes, polycystic ovary syndrome (PCOS), endometriosis, fibroids, hyperprolactinemia, anovulation and other hormone imbalances can contribute to, or cause, infertility; these should be investigated and treated as appropriate.

Male infertility can be due to poor sperm count or quality e.g. low motility or abnormal morphology. There are many factors which can directly affect sperm quality or interfere with hormone signalling which controls sperm production.

Interruption to hormonal control, which affects the ability to produce adequate sperm, ovulate or maintain pregnancy, can be influenced by a number of factors, including:

- **Stress and adrenal dysfunction** – cortisol inhibits the release of gonadotrophin releasing hormone (GnRH) and therefore can supress ovulation or spermatogenesis (sperm production) as well as sexual activity. Adrenaline can also inhibit the utilisation of progesterone, therefore disrupting hormonal control of the female reproductive system. Cortisol and the sex hormones are synthesised from pregnenolone therefore excess production of cortisol has the ability to deplete production of other steroid hormones – sometimes referred to as 'the pregnenolone steal'.[6] Some studies have now also identified that stress increases the newly discovered gonadotrophin inhibiting hormone (GnIH)[5] which will prevent the production of hormones responsible for ovulation and spermatogenesis (luteinising hormone, LH and follicle stimulating hormone, FSH). So if excess stress or adrenal dysfunction is suspected, stress management techniques and adrenal support should be put in place[4,5]

- **Low thyroid function** – hypothyroidism is associated with low fertility, particularly in females, therefore thyroid conditions or sub-clinical hypothyroidism should be investigated and supported if fertility is reduced[7]

- **Poor gut and liver function** – the liver and gut are responsible for the metabolism and elimination of oestrogen. If the gut is not working efficiently, oestrogen, which should be excreted, can be reabsorbed into the body (particularly in cases of constipation). The liver is responsible for detoxifying waste oestrogen to allow it to be excreted. Therefore inadequate liver and/or digestive function can lead to a higher ratio of oestrogen to progesterone, known as oestrogen dominance, which has been shown to have a negative effect on fertility and also increase the risk of conditions such as endometriosis and PMS. Therefore the health of the gut and liver should be considered when supporting fertility[8]

- **Weight** – a low BMI (under 19) or less than 17% body fat, can result in anovulation (absence of ovulation). A BMI of over 30 can also interfere with ovulation and spermatogenesis (obese men have up to 50% fewer sperm), increase risk of miscarriage and reduce IVF success. Optimum fat percentage for fertility is 20-25% (this is also a healthy BMI)[2,9]

- **Age** – after the age of 35 female fertility begins to reduce, although this is not a modifiable factor it is advisable that women over 35, who have been attempting to conceive for over a year, should seek potential investigations or interventions to optimise chances of conception[2]

Other factors which affect fertility in both men and women are:

- **Mitochondrial function** – energy production by the mitochondria is essential for normal sperm production, morphology and motility. It is also essential for the normal production of an oocyte (egg) by the mother[10-13]
- **Oxidative stress** – affects sperm quantity and quality as it can damage:

  i) the mitochondria of the spermatogonium (sperm producing cells) which will directly affect adequate sperm production

  ii) the sperm, particularly the cell membranes which are so important for the function of each sperm

In women, if the cell membrane of the oocyte is exposed to oxidative stress, it can be more difficult for the spermatozoa to penetrate it.[3, 14]

Other factors associated with poor fertility which should be addressed, if relevant:[2]

- Irregular sleep patterns
- Smoking
- Alcohol
- Environmental toxins
- Marijuana
- Caffeine

NHS treatment approach

Fertility treatments include:

Medical treatment – for lack of regular ovulation i.e. use of fertility drugs to stimulate ovulation, these include:

- Clomid (serophene, clomiphene citrate)
- Femara or letrozole and other aromatase inhibitors
- Injectable gonadotropins, injectable FSH hormone products
- The GnRH pump
- Bromocriptine

Surgical procedures – such as treatment for endometriosis, repair of the fallopian tubes, or removal of scarring (adhesions) within the womb or abdominal cavity.

Assisted conception – this may be intrauterine insemination (IUI), directly inserting sperm into the woman's uterus or *in-vitro* fertilisation (IVF), an egg is removed from the woman's ovaries and fertilised with sperm in a laboratory. An embryo is then returned to the woman's uterus to grow and develop.

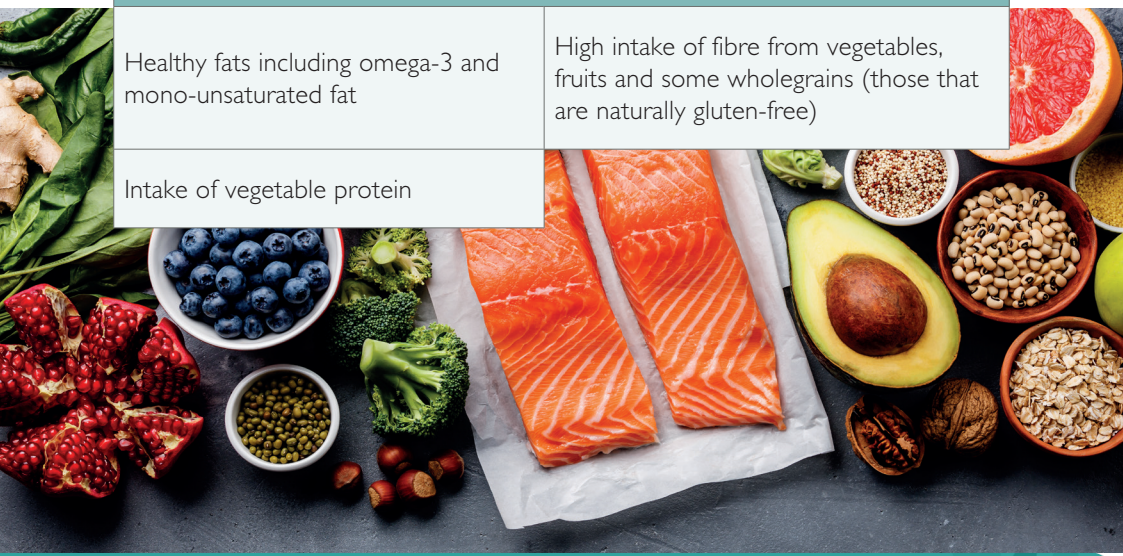
The treatment offered will depend on the cause of fertility problems and what is available from the specific Primary Care Trust (PCT).[3]

Dietary recommendations

Preconception is an important time, during which both prospective parents can prepare their bodies by ensuring good nutrition to assist fertility and conception. Once conception has occurred, then continuing with a high quality, nutrient dense diet and balanced lifestyle can support the health of both mother and baby.

Dietary recommendations for fertility are aimed at supporting healthy hormone, oocyte and sperm production as well as mitochondrial function which is required for DNA replication and cell (oocyte or sperm) formation. Dietary characteristics associated with optimal fertility include:[2]

Avoid/Reduce	
Trans fatty acids (found in heavily processed and baked goods)	Excessive intake of animal protein
Gluten – this should be considered as subfertility is seen in individuals with coeliac disease and non-coeliac gluten sensitivity	High glycaemic load carbohydrates (e.g. white bread, pasta and rice) and sugar
Increase	
Healthy fats including omega-3 and mono-unsaturated fat	High intake of fibre from vegetables, fruits and some wholegrains (those that are naturally gluten-free)
Intake of vegetable protein	



Preconception, detoxification and gut support programme

As mentioned earlier, the liver and the digestive system are very important for supporting fertility and also the heath of the pregnancy and baby. The gut and the liver are responsible for biotransformation and excretion of toxins and hormones, excess levels of which can be a barrier to conception. The balance of oestrogen and progesterone is extremely important. A high ratio of oestrogen to progesterone can affect fertility and is also associated with conditions such as PMS and endometriosis.

A 5R programme (Remove, Replace, Reinoculate, Repair, Rebalance) aims to support and repair digestive and liver function by reducing toxin exposure and ensuring intake of appropriate nutrients. It can be really useful to carry out the programme with couples who are struggling to conceive and also as a wellness plan for couples who are planning a pregnancy in order to optimise their chances of conception. See our Candida booklet for more information on the 5R programme.

Once a detoxification programme is started, stored toxins are liberated into the circulation, therefore it is important not to conceive at this time; pregnancy should be prevented until the programme is complete.[8]

Note: It takes three months for egg and sperm to form so prenatal preparations should begin three months prior to conception. A 5R programme will take between two and three months, this means a 5R programme should begin six months before conception (and be completed three months before conception is attempted).

It can be useful to perform a hair mineral analysis or red blood cell analysis to identify heavy metal load. A heavy metal detox programme can then be included if necessary.

Even if your client does not carry out a full 5R programme or is already pregnant it is still helpful to minimise exposure to toxins and gently support detoxification. You can do this by:

Avoid/Reduce	Choose
Alcohol and smoking	Organic personal hygiene products, free from parabens, sodium lauryl sulphate and aluminium
Plastic food and drink containers, particularly soft plastics and also avoid microwaving them	Organic food
Household sprays and cleaning chemicals (including air fresheners)	Cruciferous and brassica vegetables as well as onion, garlic and leek to support Phase 2 liver detoxification; they provide sulphur for sulphation pathways and di-indole methane (DIM) to support healthy oestrogen clearance[8]
	Antioxidant rich foods - zinc, selenium, vitamin C, beta-carotene, vitamin E, flavonoids and polyphenols – these will help quench any free radicals created during detoxification
	Ensuring healthy bowel movements to prevent reabsorption of toxins and hormones in the digestive tract

Many studies have identified a link between a balanced gut flora in the mother and the health of the baby. A healthy maternal gut flora has been linked to reduced risk of inflammation, asthma, eczema and coeliac disease as well as improved immune function. The main reason for this is that during a natural birth the child will pass through the birth canal and pick up microbes from the mother which will inoculate the child's sterile gut. This flora is also passed onto the child through colostrum during breastfeeding. The mother's gut flora is thus reflected in the child. Research now suggests that this transfer of gut flora may even begin *in utero*.[15,16,17]

Gut flora can be supported throughout pregnancy by taking probiotics, however, again it is also beneficial to ensure that the gut is supported prenatally. This will also improve natural hormone excretion so supporting fertility as well.[18, 19]

If timescales are short and a full 5R programme cannot be carried out, some support can still be provided by:

- Ensuring adequate zinc levels – in relation to the gut, zinc is important for the production of stomach acid as well as for maintenance of the epithelial tissue lining the digestive system
- Consuming prebiotic foods such as baked apples, onions, leeks, dark green leafy vegetables, chicory and artichoke
- Consuming fermented foods such as kefir, sauerkraut and kimchi to support gut flora
- Taking a multi-strain probiotic
- Considering a digestive enzyme to improve nutrient digestion (and therefore absorption), if it is suspected this is impaired

Lifestyle

Stress can have a negative impact on fertility and therefore adopting lifestyle techniques that support a healthy response to stress is useful. Stress relieving techniques include:

- Meditation and mindfulness
- Yoga
- Reading
- Massage
- Neuro Linguistic Programming (NLP) or Cognitive Behavioural Therapy (CBT)

Exercise – the benefits of exercise for physical and psychological health are well understood. Obtaining 150 minutes of moderate exercise each week is advisable.

Specific nutrients to support female fertility and pregnancy

The aim here is to optimise cell membrane and mitochondrial function, hormone balance, methylation and reduction of oxidative stress as appropriate.

Nutrient	Function
Essential Fatty Acids (EFAs)	The cell membrane surrounding the oocyte is important for overall oocyte development and also for allowing the sperm to penetrate it. Therefore cell membrane health should be supported[2,20,21] Omega-3 fats can be incorporated into the cell membrane aiding membrane fluidity and assisting oocyte penetration. EFAs are also associated with supporting normal hormone production, mitochondrial and adrenal function. DHA (an omega-3 fatty acid found in fish/krill oil and some algal supplements) is particularly important for cognitive and visual development of the growing foetus[22]
L-carnitine	Involved in fatty acid metabolism within the mitochondria, it therefore supports energy production required for oocyte development, acceptance of spermatozoa and subsequent formation and development of the embryo (embryogenesis)[23]
Alpha lipoic acid	Powerful antioxidant which also regenerates vitamin C, vitamin E, CoQ10 and glutathione.[24] Safety has not been established in pregnancy, therefore do not take during pregnancy
Vitamin A	Antioxidant that also has an important role in cellular growth and differentiation and is required for embryonic development.[25, 26] Caution is needed with supplementation in pregnancy as high vitamin A intakes have been associated with congenital abnormalities

Nutrient	Function
Vitamin C	Antioxidant that has the ability to regenerate glutathione. It has further effects on reproductive health as it has a positive effect on growth and repair of the ovarian follicle and the development of the corpus luteum (essential for maintaining pregnancy).[27] Vitamin C is also associated with a reduced risk of pre-eclampsia
Vitamin E	A fat soluble antioxidant which is important for maintaining ovarian health[28]
Selenium	Supports thyroid hormone production (as mentioned earlier, suboptimal thyroid function is associated with low fertility). It is also a powerful antioxidant involved in glutathione regeneration[29]
Zinc	A cofactor for enzymes which are involved in the production of DNA and RNA as well as protecting against oxidative damage. Zinc also plays an essential role in the production and transport of reproductive hormones and enables ovulation, fertilisation and oocyte development[29,30,31]
Flavonoids and carotenoids	Possess antioxidant as well as anti-inflammatory capabilities. Some additionally act as polyphenols which can be considered prebiotics, supporting the microbiota[32,33]

Other nutrients important for fertility include:

B Vitamins: many of the B vitamins are involved in cellular replication and normal DNA as well as hormone production. Specific roles in fertility and pregnancy include:	
Thiamine (B1)	Shown to stabilise membranes of newly generated neural cells[34]
Riboflavin (B2)	Important for mitochondrial energy production as well as antioxidant defence[35]
Niacin (B3)	Research suggests that the supplementation of vitamin B3 in pregnant women could prevent miscarriages and birth defects[36]
P5P (B6)	Required for normal production and metabolism of reproductive hormones and neurotransmitters. A lack of B6 may be associated with pregnancy related nausea[35,37,38]
Folate (B9)	Required for DNA and RNA synthesis and associated with a reduced risk of spina bifida[39] (ideally women should supplement 400µg for at least three months prior to conception)
Methylcobalamin (B12)	Works with folate for DNA and RNA synthesis and also protects against neural tube defects. As well as affecting cell replication, sub-optimal levels can lead to high homocysteine levels which can have a negative effect on fertility[2,40]

Additional nutrients:

Vitamin D	Important for healthy bone function of developing foetus, modulates immunity (autoimmunity has been linked to poor fertility and miscarriage) and is also involved in cell proliferation and differentiation[2]
Iodine	Major constituent of thyroid hormone, maturing oocytes are heavily dependent on thyroid hormone levels, for optimal reproductive function[2,28]
Iron	Formation of red blood cells in mother and developing foetus and is also involved in energy production within the mitochondria[2]

Supporting Gut Health

Live bacteria supplements – the mother's gut flora play a role in fertility, pregnancy and the health of the baby. A balanced gut microbiota has been shown to protect against atopic conditions such as allergy, eczema and asthma in the baby. It is also essential for the development of the baby's immune system. Therefore using a live bacteria supplement to support the balance of the microflora within the mother's gut is recommended.[19]

Specific nutrients for male fertility

One of the most important factors for supporting fertility in males is supporting mitochondrial function. Mitochondria, the energy production powerhouses in our cells, are fundamental to the ability for adequate sperm production and function i.e. motility and morphology. It has been shown that mitochondrial function plays a pivotal role in fertility and it is interesting to note that all of the factors linked to low fertility have the ability to affect mitochondrial function. Studies have found a direct relationship between the activity of sperm mitochondrial enzymes and sperm parameters, including concentration, vitality and motility. Therefore, the higher the activity of the mitochondria, the more energy is produced resulting in improved sperm count and motility.[2,8,13]

Nutrients that support chemical energy production by mitochondria[28]	
Thiamin (B1)	Cofactor in the essential step which converts pyruvate to acetyl CoA
Riboflavin (B2)	Also known as FAD, accepts and donates electrons to the electron transport chain (ETC) in order to produce ATP (energy)
Niacin (B3)	Also known as NAD (similar to FAD) accepts and donates electrons to ETC in order to produce ATP
Pantothenic acid (B5)	Carrier of coenzyme A, essential for acetyl CoA and therefore energy production
Iron	An essential cofactor in the ETC (specifically complex I and III)
Copper	Important cofactor in complex IV of ETC
CoQ10 (Ubiqinol)	Utilised as a carrier in complex II of ETC. CoQ10 also has antioxidant properties and is found in high concentrations in the head and mid-piece of the sperm. It is considered to promote motility, foster sperm survival and provide optimal energy[2]

Nutrients that support chemical energy production by mitochondria[28]	
Alpha lipoic acid	A coenzyme of pyruvate dehydrogenase and α-ketoglutarate; enzymes responsible for reactions involved in the breakdown of fat and carbohydrate within the mitochondria. It also has antioxidant function
Magnesium	Binds to ATP and affects its structure making energy more easily available

Insufficiencies in any of the above nutrients can affect the rate of energy production and will have a direct impact on the ability to produce sperm effectively.

Other nutrients important for energy production and maintaining mitochondrial function include:

L-carnitine plays a vital role in fatty acid metabolism, transporting fatty acids into the mitochondria for conversion into energy and again a deficiency can lead to reduced energy production. Carnitine concentrations have been found to be very high in the epididymis and testes. Studies which have compared fertile and infertile men have found that fertile men have statistically significantly more carnitine in their seminal sample than infertile men. Also low levels of plasma carnitine are associated with infertility.[41]

Omega-3 fatty acids are incorporated into the mitochondrial membrane helping to maintain membrane fluidity and therefore signalling. Omega-3 fatty acids are also important for the cell membrane of the sperm; adequate membrane fluidity supports sperm motility and the ability to penetrate the oocyte.[20,42]

Other nutrients important for male fertility:

Zinc	Involved in almost every aspect of male fertility (hormone metabolism, spermatogenesis and sperm motility).[43] Also a major antioxidant
Vitamin D	VDR (vitamin D receptor) expression in human spermatozoa serves as a positive predictive marker of semen quality, and VDR mediates an increase in intracellular calcium concentration that induces sperm motility. Therefore vitamin D signalling has a positive effect on semen quality[44]
Folate and B12	Essential for adequate DNA and RNA synthesis.[28] Low folate in seminal plasma is associated with increased sperm DNA damage[2]
L-arginine	A precursor to nitric oxide which has been shown to be required for hormone secretion and fertility in general. It is also required for cellular replication[45]
Selenium	Development of male reproductive tissue requires an optimal level of selenium in the testes with a small deviation leading to abnormal development[46]
Vitamin A and beta-carotene	Vitamin A is necessary for the health of the testes and sperm production, low concentrations are associated with abnormal semen parameters. Intake of beta-carotene is positively associated with higher sperm concentration and increased motility[2]
Lycopene	Found in high concentrations in testes and seminal plasma and reduced levels are seen in men with infertility[2]
Vitamin E	Vitamin E significantly decreases oxidative stress in spermatozoa and improves sperm motility[47]


CYTOPLAN
PRODUCTS

Cytoplan products: Female

Pregna-Plan

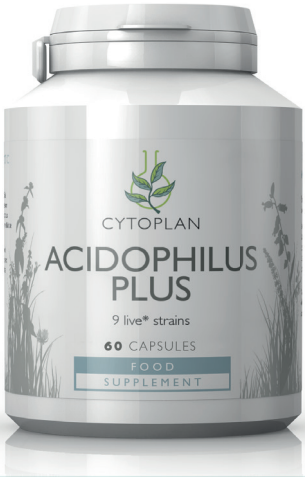
A comprehensive multivitamin and mineral suitable for preconception, pregnancy and breastfeeding. Two tablets contain the full range of B vitamins including 400µg of methylfolate, (folic acid) essential for nerve and cognitive development and for the prevention of spina bifida. Also contains vitamin D3, iodine, zinc, calcium and magnesium, as well as beta-carotene.

Omega 3 Vegan

An omega-3 supplement isolated from algae providing a higher ratio of DHA to EPA than that of fish oils. DHA is an important fatty acid for cognitive and visual development.
Alternative products: R-Omega, Krill Oil, Lem-O-3 fish oil

Acidophilus Plus

A live bacteria supplement containing nine strains of bacteria as well as 35mg of fructo-oligosaccharides (FOS), in capsule form.
Alternative product: Cytobiotic Active (powder)



Cytoplan products: Female

Vitamin D3

62.5µg (2500IU) of vitamin D3. Also available as drops which can be added to water,
2 drops = 5µg (200IU)
Alternative product: Vitamin D3 & K2

Methylfolate (400µg)

Folate in the active form as methylfolate. In specific cases where there is a high risk of neural tube defects the G.P. may recommend additional methylfolate

Thyroid Support

Complex containing L-tyrosine, iodine, selenium and manganese to support the production of thyroid hormones. This is relevant for preconception if there are thyroid issues but should not be used during pregnancy

Adrenal Support

Complex containing adaptogenic herbs ginseng (Siberian and Chinese) and liquorice as well as pantothenic acid (B5), selenium, chromium and iodine from kelp. This is relevant for preconception if there are adrenal issues but should only be used under supervision of a G.P. during pregnancy

Cytoplan products: Female

Phytoshield

Phytonutrient and antioxidant supplement containing a variety of flavonoids and carotenoids. Can be used in the preconception period

Cell-Active Curcumin Plus

Contains 95% curcuminoids with gingerols to support anti-inflammatory pathways, appropriate for preconception. Includes Longvida® optimised curcumin, an innovative, more bioavailable form of curcumin. Longvida® is scientifically proven to be up to 285 times more bioavailable than standard curcumin. Can be used in the preconception period

Cell-Active Glutathione

For preconception; provides antioxidant and mitochondrial support as it contains liposomal glutathione, L-carnitine, alpha lipoic acid, *Gingko biloba*, rosemary and resveratrol. Can be used in the preconception period

Choline Bitartrate

Supports normal liver function and is a precursor to phosphatidylcholine found in cell membranes. Choline has been found to help with nausea during pregnancy

Cytoplan products: Male

CoQ10 Multi

Comprehensive multivitamin and mineral containing a full spectrum of B vitamins including methylfolate and B12 as methyl- and adenosylcobalamin. Vitamin D3, zinc, selenium, vitamin C, vitamin E and beta-carotene are included. Also provides 80mg of CoQ10 which is involved in mitochondrial function, acts as an antioxidant and has been associated with improved fertility.

Alternative product: Foundation Formula 2 (does not contain CoQ10)

Cyto-Renew

Contains antioxidants CoQ10, alpha lipoic acid and N-acetyl cysteine. Also contains L-carnitine which supports fatty acid oxidation within the mitochondria and is indicated for supporting fertility.

Alternative product Cell-Active Glutathione

Phytoshield

Phytonutrient and antioxidant supplement containing a variety of flavonoids and carotenoids. These possess many qualities but include antioxidant properties and therefore support mitochondrial function and protect sperm

Cytoplan products: Male

Krill Oil

Omega-3 supplement containing DHA and EPA as well as phospholipids which aid fat absorption and support cell membrane health. Also contains astaxanthin, an antioxidant.

Alternative products: Lem-O-3 fish oil, R-Omega or Omega 3 Vegan

L-Arginine Plus

Contains 500mg of L-arginine and 250mg of L-ornithine, which are associated with improved lean muscle mass and fat reduction. L-arginine is also indicated for male fertility due to its involvement in cellular replication

Cell-Active Curcumin Plus

Contains 95% curcuminoids with gingerols to support anti-inflammatory pathways. Includes Longvida® optimised curcumin, an innovative, more bioavailable form of curcumin. Longvida® is scientifically proven to be up to 285 times more bioavailable than standard curcumin

Cytoplan products: Male

Cell-Active Glutathione

Provides antioxidant and mitochondrial support as it contains liposomal glutathione, L-carnitine, alpha lipoic acid, *Gingko biloba*, rosemary and resveratrol

Vitamin A (Retinol Palmitate)

Vegan source of vitamin A containing 5000IU per capsule.

Caution is needed with supplementation in pregnancy (in females) as high vitamin A intakes have been associated with congenital abnormalities

Mixed Tocopherols and Tocotrienols

Full spectrum of vitamin E which includes all eight tocopherols and tocotrienols

Zinc Citrate

Provides 30mg of zinc per capsule

Alternative product: Wholefood Zinc

Cytoplan products: Male

Selenium

Provides 100µg of selenium per tablet

Vitamin D3

Available in high strength, 62.5µg (2500IU) and also as drops which can be added to water, 2 drops = 5µg (200IU).

Alternative product: Vitamin D3 & K2

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