

Supplement Book

My Best Up-To-Date Recommendations For Supplements



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N-acetylcysteine (NAC)

Not only does N-acetylcysteine have its own antioxidant effects that help increase fertility and egg health but it also helps the body create more glutathione. Glutathione is what is commonly referred to as the "mother of antioxidants" because of how incredibly powerful it works to neutralize free radicals and decrease cellular damage (see Glutathione section for more). While N-acetylcysteine helps the body to produce more glutathione, it also reduces homocysteine levels, inflammation, and aids the body's detoxification.

Most of the clinical studies available are in the settings of PCOS and IVF, but given its far reaching effects the implication is that it helps increase egg health to such a degree that it can be helpful in many situations.

But wait, there's more! There are also some clinical trials that show NAC helps increase sperm count, motility, and morphology especially in combination with other elements like selenium.

You can take N-acetylcysteine if you have:

- premature ovarian failure
- **PCOS**
- **Endometriosis**
- History of miscarriages
- MTHFR
- Low sperm count and/or quality

All of these fertility challenges are associated with high levels of homocysteine and inflammation, and in clinical studies NAC was correlated with an increase in pregnancy outcome and decrease in miscarriage rates through its powerful anti-inflammatory effects.

There has even been data showing a 60% decrease in miscarriage rate in women with PCOS. As for endometriosis, N-acetylcysteine can help to reduce the pain and the occurrence of cysts.

Dosing:

- For cleanse phase: 1800mg per day divided into 3 doses (600mg per dose)
 - Start slow with 1 capsule the first day and work up slowly over a week or two
- For Balance phase: 600 mg per day (the lowest dose is 600 but you can choose to keep the dose at 1800 or 1200)

In women with PCOS, NAC dosed at 1200mg per day was given for 5 days with Clomid and resulted in 21% of the NAC/Clomid women becoming pregnant versus only 9% of the Clomid group

Cautions and Concerns:

Headache, dizziness, nausea, vomiting, diarrhea or abdominal pain has been reported at high doses of 1200mg.

It can worsen symptoms of asthma.

Should not be taken with nitroglycerine.

Recommendations:

- Solgar® NAC 600 mg (600 mg per vegetable capsule)
- Life Extension® N-Acetyl-L-Cysteine (600 per vegetarian capsule)

Vitamins C and E

These are both antioxidants, which you know by now are extremely important in neutralizing free radicals in your body and decreasing inflammation. Though they go about it in slightly different ways they both help with normal age-related decreases in antioxidants and have been found to be helpful in unexplained infertility and IVF.

Vitamin C is a water-soluble antioxidant, is found in large quantities in follicle fluid, and is associated with shorter times to pregnancy. Vitamin E is fat-soluble, is also linked with shorter time to pregnancy, as well as improved IVF outcome. It's also been shown to increase uterine lining.

Both of these safe supplements can be used in women who are experiencing any of the following:

- · unexplained fertility
- · preparing for IVF
- over the age of 35
- · premature ovarian failure

Dosing Vitamin E:

• 200 IU/day

Dosing Vitamin C:

• 1000 mg/day

Cautions and Concerns:

High doses of vitamin C have been shown to cause some GI distress. This can be minimized by taking a slow acting form.

Vitamin E should <u>not</u> be combined with any anticoagulant therapy or in those taking aspirin because of the risk of bleeding.

Recommendations:

Vitamin C:

- 1. <u>Dr. Mercola Liposomal Vitamin C</u>
- 2. Thorne Vitamin C

Vitamin E:

- 1. Swanson Vitamin E 200iu
- 2. Solgar Vitamin E 200iu
- 3 Fertility Mom

Magnesium

Magnesium is the 4th most abundant mineral in our bodies and is used by every single organ and cell. It's important in temperature regulation, protein and nucleic acid synthesis, muscle cell regulation, and so much more. It's also involved in progesterone production as well as melatonin production.

Our biggest source of magnesium comes from our soil, which has been declining rapidly due to our modern farming practices. As the magnesium in the soil lessens, so does the magnesium in our foods. It is estimated that up to 80% or more of women and men have a magnesium deficiency!

It's so commonly found in circumstances of illness that many leading researchers and physicians believe that a magnesium deficiency is the potential root of many diseases. Deficiency in this mineral has been linked to increasing risk of certain cardiovascular diseases, and has also been implicated in contributing to infertility, especially in women.

It's an easily overlooked piece of the puzzle and is further complicated by the fact that a magnesium deficiency doesn't typically show on a regular blood test. This is because only 1% of our magnesium is stored in our blood while the rest of the 99% is off doing work in our cells. It's impossible to measure the 99%, so this deficiency frequently goes unrecognized. Many people don't even exhibit the symptoms of a magnesium deficiency such as headache, insomnia, irritability, anxiety, muscle cramping, and fatigue just to name a few.

Magnesium also has a large role in brain function, neurotransmitter systems, and is critically important in your stress regulation. In the setting of fertility, this becomes something we need to pay attention to. A magnesium deficiency contributes to increased feelings of stress and increased cortisol levels, which then in turn make the magnesium deficiency even worse. Its importance goes well beyond fertility and into pregnancy itself. Studies have shown that women who take a magnesium supplement have healthier pregnancies, decreased occurrences of preeclampsia, preterm birth, and low birth weight.

Type of Magnesium To Take

There are four main forms of magnesium to take. Each is useful for a different situation. You may find you only need one, or you may take more than one.

1) Magnesium Bisglycinate

- This form is highly absorbable and is also least likely to result in any kind of laxative effect. Daily magnesium replenishment of at least 200 mg of Magnesium Bisglycinate should be your absolute minimum. You may also see this form under the names magnesium glycinate, magnesium chelate, or magnesium diglycinate.
- Recommended Dose = 200mg minimum with dinner (you can easily take 400 or 600mg if you determine you need more magnesium).

2) Magnesium Malate

- This type of magnesium is combined with malic acid, and is also highly absorbable. It's good for those who suffer from chronic fatigue, chronic pain (fibromyalgia), migraines, and depression. It can cause an energy surge so this type needs to be taken with breakfast.
- Recommended Dose = 360mg in the morning
- Take in addition to the Magnesium Bisglycinate if you suffer from chronic fatigue, chronic pain (fibromyalgia), migraines, and/or depression

3) Magnesium Chloride

- This can be a topical form of magnesium and is a wonderful way to get magnesium in the body without going through the gut. If you suffer from leaky gut or nutrient absorption problems then this is a good form to take in addition to the bisglycinate (which you should be taking daily). You may also see this as "Magnesium Oil".
- Dose = between 100-200 mg at night. Exact dosage will depend on your specific product's concentration, but 100-200 is the approximate range.

4) Magnesium Citrate

- This form of magnesium pulls water in the intestine and has a laxative effect. This is useful for those with constipation issues.
- Dose = 300mg when needed or at nighttime

Combining Different Types of Magnesium

You can take all 4 types of magnesium daily if necessary, though you may want to rotate for best effect. I personally only take Magnesium Glycinate daily, magnesium Citrate if needed, and I have recently added topical Magnesium Chloride at bedtime to help with sleep. Some days I only take the glycinate, some days I take all 3.

**Magnesium depletes daily, so there is a need to replace it daily. Some women need up to 1200mg of magnesium to adequately replace a sufficient level.

Don't underestimate the importance of magnesium! One of my clients made the simple switch of adding appropriate magnesium type and dose. She not only felt better throughout the day, she got pregnant the very next cycle after trying for over 1 year.

Bisglycinate:

- 1. <u>Naturelo Magnesium Glycinate 200mg per serving (200mg capsules)</u>
- 2. <u>Kal Magnesium Glycinate 400mg per serving</u> (200mg capsules)
- 3. <u>Solar Chelated Magnesium Glycinate 400mg per serving (100mg capsules)</u>
- 4. <u>Wellena Magnesium Replenish 240mg per serving</u>

Malate:

- 1. <u>Designs For Health Chelated Magnesium Malate</u> 360mg per serving
- 2. Wellena Mag Energy 360mg per serving

Citrate:

- 1. NOW Magnesium Citrate 400mg per serving (133mg per capsule)
- 2. <u>Pure Encapsulations Magnesium Citrate 150mg capsules</u>

Protein Powder

This by no means should be your major source of protein, but is a great supplement to help get more protein and amino acids into your diet. With protein supplements, it's best to use a meat-based protein powder so you're getting the amino acid building blocks necessary for a multitude of bodily functions. These building blocks not only help your liver but they also help heal the gut, build cells, and keep inflammation down.

Recommended Products:

- Vital Proteins Beef Gelatin
- Vital Proteins Collagen Peptides
- Rootcology Paleo Protein

Ideally you're looking for a meat-based or beef-based protein powder free of dairy, soy, and gluten. There are many products out there!

Vitamin A

Vitamin A specifically is incredibly important because it helps promote proper development of a baby's face like eyes, nose, lips, and dental arches. It also promotes full term pregnancy and can prevent lengthy labors. It's important in kidney development as well. In terms of sperm health, vitamin A is needed to produce adequate amounts of sperm. Vitamin A is also a potent antioxidant, which protects the body from free radical damage.

There was a study done claiming that women who consumed more than 20,000 IU of vitamin A daily had an increased rate of birth defects, but this study has been widely criticized for its methods. Other studies have also found the exact opposite: that vitamin A is not associated with increased birth defects but rather is associated with decreasing the rate of defects. Vitamin A deficiency has a known association with increased risk for congenital diaphragmatic hernia (CDH), which can be fatal in newborns.

It is important to note that vitamin A has the potential to be toxic but only in the presence of a vitamin D3 deficiency. Adequate Vitamin D3 protects against vitamin A toxicity, and vitamin D3 is kept in check by Vitamin A and K2. This is why we look at fat soluble vitamins together as a group. They all help to check and balance each other.

There are 2 forms of Vitamin A found in the human diet:

- 1) Preformed Vitamin A -> also known as retinol or retinol ester
- Preformed Vitamin A is found in animal sources like dairy products, fish, and meat (especially in beef liver).
- 2) Provitamin A Carotenoids
- the most important provitamin A carotenoid is beta-carotene. Other provitamin A carotenoids include alpha-carotene and beta-cryptoxanthin.

Current recommended daily allowance (RDA) of Vitamin A is 2,600 IU (900 mcg), which is too low considering its critical importance for a variety of bodily processes. According to research, approximately 30% of women of childbearing age don't consume enough vitamin A even when comparing against the inadequate recommendation of 2600 IU.

Some hunter/gatherer tribes like the Inuit have been known to have 35,000+ IU of vitamin A daily with no toxicity issues. Consuming Vitamin A 10,000 IU daily is both safe and helpful for maintaining bodily processes and even decreasing instance of birth defects. There was a study done in Ghana that showed even a supplementation dose of 100,000 IU of Vitamin A didn't show toxicity, and in fact the high vitamin A group had significantly lower all-cause hospitalization risks during the study.

It is best to get your vitamin A from food sources, and mostly animal sources since plants are not adequate. We need to convert plant beta-carotene to active vitamin A (retinol), and only about 3% of beta-carotene gets converted. Add to this that around 45% of people lack the proper enzymes for this conversion and you can begin to see why it could be hard to get your full vitamin A needs from plants only. You would need to consume an insane amount of plants to provide enough vitamin A. For instance, you would have to eat around 10-20 cups of carrots to even get close to enough vitamin A.

Your best food sources of vitamin A are: Beef liver, chicken liver, egg yolks, and dairy like cheeses, yogurts, and milk.

Best supplementation if you're not going to add in liver to your diet in any significant amount is fermented cod liver oil as either a liquid or capsule form.

Recommendations:

 Rosita Fermented Cod Liver oil - liquid form or the capsules if you can't do the liquid

Vitamin D₃

Vitamin D is a fat-soluble vitamin found only in a few food sources. There are two forms of vitamin D: ergocalciferol (vitamin D2) and cholecalciferol (vitamin D3). Vitamin D3 is the naturally occurring and active form of Vitamin D, and is mostly made in the body from sun exposure on the skin.

This vitamin is actually a hormone, and it's important in the calcium/phospherous levels in the blood, bone formation, immune health, thyroid function, and fertility function. In fact, it's been found that low levels of vitamin D3 is related to inadequate ovarian function and decreased sperm count and motility. It's also related to AMH levels, though the relationship is complicated. In essence, lower vitamin D3 levels relate to lower AMH levels. When vitamin D3 rises, there is also a rise in AMH.

One study found that women with higher vitamin D levels had pregnancy outcomes four times higher than the women with lower vitamin D levels. It has also been implicated in pregnancy outcome for women undergoing IVF and women with PCOS. Women undergoing IVF with higher vitamin D levels have increased rates of embryo fertilization and implantation.

Get yourself a vitamin D supplement! While our bodies can make an immense amount of vitamin D from even 10-20 minutes of sun exposure, research shows that the majority of the US population is vitamin D deficient. More current statistics say that this amount is only getting worse with estimations of vitamin D deficiency affecting up to 70% of the population.

In addition to our deficient status, current supplementation guidelines are woefully inadequate. A measly recommendation of 600 IU/d for adults has been shown to do little for increasing serum Vitamin D levels. Multiple studies have shown that supplementation of 4,000 IU/d, and even up to 10,000 IU/d, of vitamin D increased levels to within desired limits with no adverse effects experienced. Some studies even went as high as 20,000 IU/d. It is not recommended to supplement with a high amount of vitamin D3 without knowing your own vitamin D levels.

The blood test for vitamin D level is called Serum 25(OH)D.

For reference, serum 25(OH)D levels are normal between 30 ng/mL and 50ng/mL (75nmol/l - 100nmol/l). Anything less than 30 is considered deficient. Optimally, we'd like to value to be closer to or above 50ng/mL. Levels of 60ng/mL and above have been reported as being beneficial for women with thyroid issues.

Basic research shows that your blood values of serum 25(OH)D rise approximately 1 ng/mL (2.5nmol/l) for every 100IU/d of vitamin D you take in. Robert Heaney, a world renowned vitamin D researcher, claimed that not only was 10,000IU per day a safe upper limit for vitamin D3 supplementation, but that the daily recommendation should be changed from 600IU per day up to 7,000IU per day.

In terms of vitamin D toxicity, there have been studies done where no toxicities were reported where people who consumed 50,000IU/d for a span of up to 5 months. It should be noted that a fair-skinned individual exposed to sunlight without sunblock for approximately 15 minutes can make up to 20,000IU of vitamin D whereas a dark skinned person may need 30 minutes of sun exposure. There have been zero reported cases of vitamin D toxicity due to sunlight.

For fertility purposes, supplementing with approximately 4,000IU/d of vitamin D3 daily is recommended. If you have had your blood drawn and know you are on the low or very low end of vitamin D3, then work with your practitioner on the best amount to take (generally speaking it should be more than 4,000IU/d and closer to maybe 10,000IU/d if you are very low).

How To Take:

Since it is a fat-soluble vitamin you should take this when eating a meal that has a good amount of fat to increase absorption.

Recommendations:

- Nutra BioGenesis Vitamin D3/K2 emulsion
- Pure Therapro Rx Vitamin D3 and K2, Vegan
- Nusava Organic D3/K2 drops

Vitamin K2

There are two different forms of Vitamin K: K1 and K2. Up until just a handful of years ago we didn't know much about vitamin K2, but its vital importance is becoming clearer.

Vitamin K2 is important in a lot of functions throughout your body:



Decreases heart disease risk

Vitamin K2 keeps calcium deposits and calcifications from forming on the inside of blood vessels, and decreases heart disease risk



Decreases kidney stone formation

Vitamin K2 keeps the excess calcium out of your kidneys and prevents stones from forming



Keeps bones healthy and teeth cavity resistant

In addition, Vitamin K2 deficiency results in narrowed dental arches, crooked teeth, sinus malformations, and an underdeveloped jaw.



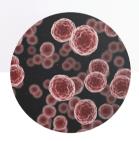
Helps the body make insulin and decreases insulin resistance

This is extremely important in stabilizing blood sugar, protecting against diabetes, and obesity related issues.



Regulates reproductive hormones

Has been found to help increase testosterone in men but also decreases the high male hormones found in women with PCOS



Cancer protective

Many studies have been finding that Vitamin K2 protects against cancer by suppressing genes that make cancerous cells grow Food sources high in Vitamin K2 include cheese, egg yolk, dark chicken meat, and butter. It is important that all of these foods come from high quality sources such as eggs and meat from pasture-raised chickens, and cheese from grass-fed cows.

There is actually no official recommendation for the minimum daily consumption of vitamin K2. Current official recommendations only focus on total Vitamin K (90 mcg/day), which is a mixture of K1 and K2. However, the majority of the information about vitamin K2 has surfaced after that recommendation was made.

The current research suggests that somewhere around 1000 mcg of vitamin K2 daily is optimal combined between food and supplements.

How to Take:

Vitamin K2 is absorbed best when taken with a fat containing meal. Take it at the meal you eat the most fat at. Your fat sources should be from animal sources, butter, avocado oil, olive oil and not from processed vegetable ones like canola or soybean oil. Taking this with Vitamin D3 helps the absorption of D3, which is why I suggest combined Vitamin D3+ K2 supplements as noted in the Vitamin D3 section.

Vitamin K2 is light sensitive. Keep your supplement in a cabinet away from light and other vitamin K2 foods in the fridge.

Cautions and Concerns:

Do not take any kind of vitamin K2 supplement if you are on any kind of blood thinning medication like warfarin (Coumadin). Any kind of dietary or supplementary change needs to be done in strict coordination with a physician if you're on a blood thinning medication used for heart disease or clotting disorders.

There is very little concern over toxicity. There have been long-term studies using high dose vitamin K2 supplementation without any toxicity or adverse side effects established. This high dose regimen used in the study is 20 times higher than the recommended dose of 1000 mcg, so there is a huge margin of safety in this recommendation.

Zinc

ZINC IS NECESSARY FOR THE PRODUCTION OF EVERYTHING IN THE BODY.

It is massively important in the methylation cycle and therefore is directly responsible for every single protein made in the body and indirectly responsible for everything else through those proteins. It has main functions relating to structural, catalytic (enzymes), and regulatory aspects in the body.

It is estimated by the World Health Organization that as much as 50% of the global population has or is at risk of having a zinc deficiency.

A lot has been studied regarding zinc and you will hear everything from "you must take zinc if you want to get pregnant" to "zinc doesn't help at all with increasing pregnancy rates". Yes, there are literally studies that exist that show both sides of this spectrum.

So what is one to do?

Well, we take a big picture viewpoint. We know zinc's importance in the methylation cycle - it's incredibly important to everything in the body including things that have huge impacts on fertility.

Zinc is really important in the regulation of insulin not only in its storage and release but in insulin sensitivity itself. So a deficiency of zinc could compromise glucose tolerance and impact fertility in this area alone. We know that poor glucose control and insulin resistance decrease fertility and can even be the root cause of a fertility challenge.

We also know that zinc is enormously important for immune function and oxidative stress. It not only helps the body control oxidative stress to begin with but it also helps the body respond to oxidative stress when it's occurring. We know oxidative stress and inflammation are largely important in both male and female fertility.

There are studies regarding zinc supplementation in men and women and many conflicting arguments in this area. A recent study released in early 2020 claimed that zinc supplementation in men didn't lead to any increase in pregnancy outcome. Even though it was a well designed study – a randomized placebo-controlled trial – I think there are many more variables to control for when talking about a mineral as intensely complicated as zinc. This study *only* controlled the supplementation and did not look at other extremely important variables that affect outcome.

Zinc is an integral part of every function in our bodies and is absolutely important in fertility, but it is still only a part of the whole. Simply adding in zinc when there are other missing parts won't fix the root cause, and <u>adding in zinc to those who don't have a zinc deficiency to begin with won't yield any benefit</u>.

So yes, having enough zinc is very valuable in overall fertility and health but that doesn't mean you should run out and start taking a zinc supplement. Signs and symptoms relating to a zinc deficiency can include anything from dry patches of skin to diarrhea, increased rate of infection, loss of appetite, severe acne, sore throat, and more.

Zinc Testing:

A zinc deficiency isn't diagnosed based on symptoms alone and is most reliably discovered through a zinc plasma test.

For men, the plasma zinc level should be above 740 $\mu g/L$ (ppb) or 0.74 $\mu g/m$.

For women it should be above 700 μ g/L (ppb) or 0.7 μ g/mL.

A low plasma zinc level in combination with signs and symptoms of a zinc deficiency would mean supplementation may be necessary.

Eat Your Zinc!

As with everything, we should be getting our nutrients from food first and supplementing as needed. So it's best to try increasing your zinc intake through foods before supplementing unless you're unable to eat zinc-rich foods. Supplementation might be necessary even when eating zinc-rich food if you have a condition that inhibits nutrient absorption like Crohn's or celiac disease.

Eating foods high in zinc also ensures you're keeping a good nutritional balance. There are many other nutrients like copper, manganese, and more that can be affected by only supplementing with zinc.

The best foods that are high in zinc include shellfish (oysters, specifically), beef, cheese, chicken, and eggs.

When I say "best" I'm referring to the body's ability to absorb these nutrients.

The biggest factor impacting how much zinc your body absorbs is how much phytate is present in your diet. While plant foods do contain zinc, they also have high amounts of phytate which inhibits the absorption.

Phytate is primarily used by plants for storage of phosphorous and other minerals when it's not ready to germinate its seeds. Seeds can actually sense their environment around them and know when the best time to grow a plant is (germinate). When a plant is ready to germinate it breaks down the phytate and releases the minerals it needs to complete the process. This means that seeds, grains, legumes, and nuts are all very high in phytate, which inhibits zinc absorption. This is the primary reason why a diet low on animal foods and high in grains leads to a zinc deficiency. So even though you can go online right now and find a ton of nuts and seeds that have high levels of zinc in them, your body's ability to <u>absorb</u> that zinc is massively decreased by the phytate also present in those foods. Animal sources are the best foods to eat for highest zinc <u>absorption</u>.

Don't Zinc-Zap Your Copper!

Some of you reading this may not even be aware that we have copper inside our bodies and that it's actually a very important part of our system, but we do! A copper deficiency is exceedingly rare BUT you can *cause* a copper deficiency if you have high levels of zinc from over supplementation. That's why it's SO important to concentrate on zinc-rich foods first because those foods carry the balance of everything your body needs. If you do end up needing supplementation then you should use a supplement that has copper in it to avoid this issue.

Symptoms of a copper deficiency would be the same as a high zinc level. These include low level of white blood cells (neutropenia), anemia, osteoporosis, and hair with less pigment than normal.

Type of Zinc Supplementation:

There are many different forms of zinc including zinc gluconate, acetate, sulfate, or citrate. Any of these forms are great to take. The zinc oxide and zinc picolinate forms should be avoided.

It's important to have a supplement that you swallow because zinc absorption is done in your gut. Zinc supplements that come in lozenge form are really only good for getting zinc in your nose and throat to protect against infection, but this won't raise your plasma zinc levels.

Zinc should ideally be taken on an empty stomach or at a phytate free meal (no nuts, seeds, or legumes). It can cause GI upset like nausea and vomiting so if you're unable to take on an empty stomach then eat it with food.

I personally need to take zinc with a lot of food, so if you're prone to GI upset with taking vitamins then eat this at your largest meal of the day, again avoiding high phytatecontaining foods.

Dose:

Zinc 10-15mg daily is a great dose to take. Some research suggests the body can only absorb 7mg at a time so 10mg at once is plenty.

Cautions and Concerns:

Your main concern would be causing a deficiency of copper with over supplementation of zinc. The most common side effect is nausea, vomiting, and GI upset.

Recommendation:

• Jarrow Formulas Zinc Balance 15mg zinc and 1mg copper per capsule

Folate

Folate is probably the most recognized B vitamin, especially when talking about trying to conceive. You may know it under the name of Folic Acid, which is my first point:

Folate and folic acid are not the same and not interchangeable.

Popular belief, and maybe even your own doctor, would tell you to make sure you're taking folic acid. Folic acid is the synthetic version of folate and while many people use these terms interchangeably they are not the same thing.

Folate is a B vitamin (specifically B9) and is important in the neuronal tube development of a fetus. When it was discovered how important folate was in fetal development, synthetic folic acid was then added to foods like bread, pastas, and cereals in an effort to reduce defects like spina bifida. The problem is that folic acid is not a biologically active form of folate, which means that it needs to go through several processes in the body for it to actually be used.

Not only is the average person not able to turn all of the folic acid they take into a biologically active form but it's important to know that approximately 50% of the population has a genetic variant called MTHFR. This gene doesn't allow folic acid to be broken down to its active form and instead it remains in your bloodstream unmetabolized. There have been multiple studies that link excess folic acid levels in blood to increased rates of colon and prostate cancer in men. MTHFR is also associated with fertility issues and miscarriages.

Ideally you should be getting a good amount of naturally occurring folate from the food you eat. Foods like leafy greens, asparagus, nuts, seeds, eggs, beef liver, brussels sprouts, and broccoli just to name a few. Even in the presence of a healthy diet including all of these mentioned foods, additional supplementation of 800mcg of methyl folate is recommended. Your prenatal vitamin label should say "methyl folate", "5-methyltetrahydrofolate" or "5-MTHF" on the label. If you see that it says "folic acid" then throw it away and get yourself one with folate.

Folate is also crucial to the functioning of our methylation system, which is important in our fertility as well as hundreds of processes throughout the body. If you're unable to tolerate taking methyl-folate, or any methylated vitamins, then concentrate on your diet and food folate first and foremost. This should be done first before trying to supplement, especially if you know you have reactions to supplemental methylfolate.

If you have taken methylfolate supplements in the past and experienced headaches, rash, muscle pain that persists for more than 3 days, or any other symptom then it's best to focus on eating food folate. Once a good dietary foundation is built, a supplement using folinic acid and a non-methylated version of B12 (hydrocobalamin) can be used.

Recommendations for Prenatal with Methylfolate:

- Fullwell Prenatal (Use coupon code FERTILITYMOM)
- · Optimal Prenatal by Seeking Health

If you take the Fullwell or Optimal Prenatal vitamin, additional vitamin D3 supplementation is not necessary unless you test extremely low. Also **please note the serving size of 8 capsules**, which is a lot but necessary to get this type of nutrition. There are thousands of prenatals out there, maybe even more. If yours has methylfolate in it and is a quality brand then it is likely fine to continue taking. If it has folic acid then you need to replace it with something that has 5-methylfolate (5-MTHF or L-5-MTHF) in it.

If you have MTHFR, then an additional <u>B complex with methylfolate</u> and <u>plain methylfolate</u> will be necessary. Dosing should be discussed with your doctor, and a dose should be decided on depending on your specific polymorphism. Doses for this can range into the 3500 mcg range, or even higher, with good outcome. If you're taking a prenatal with 1000 mcg, then you can take the B complex with an additional 400mcg plus the methylfolate at another 1000 mcg for a total of 2,400mcg. You can even take 2 methylfolate tablets for a total of 3,400 mcg.

If you can't take methylated vitamins, you can take a methyl-free prenatal.

Vitamin B6

Vitamin B6 is extremely important in hormonal balance, endometrial lining preparation and thickness, luteal phase length, progesterone production, and much more.

You should be getting enough B6 through your daily diet in foods like chicken, turkey, bananas, fish, sweet potatoes, spinach, pistachios, and avocados. Supplementation should not be necessary for this specific nutrient if your diet is whole, unprocessed, and varied.

If you struggle with gut flora issues or have trouble absorbing nutrients, then consider supplementing with a whole **B** vitamin complex.

Vitamin B₁₂

Vitamin B12 is extremely important to pay attention to, especially if you are vegetarian or vegan (more on this below). Vitamin B12 is vital in how your fertility functions, and is actually one of the most important nutrients you can get from your food.

Vitamin B12 is involved in red blood cell production, nerve cell development, proper nerve impulse function, and DNA synthesis to name a few. A B12 deficiency can cause symptoms ranging from fatigue and weakness to more pronounced problems such as severe anxiety and depression.

A vitamin B12 deficiency can be a contributing factor to infertility for both men and women. Low vitamin B12 levels in women interfere with normal ovulation and can prevent the implantation of a fertilized egg due to cell division abnormalities. In men, a vitamin B12 deficiency can cause low sperm counts, poor motility, and DNA damage.

It's a water-soluble vitamin so it doesn't get stored in any significant amounts in the body and needs to be replaced daily through diet.

Current research has found that approximately 40% of the population is deficient in vitamin B12. This deficiency rate increases to 50% for vegetarians and 80% for vegans because true vitamin B12 is almost exclusively found in animal products with only small amounts found in some plant products.

It was previously believed that there was a high amount of vitamin B12 in plant foods like fermented soy, spirulina, nutritional yeast, algae, and seaweed but these items contain vitamin B12 analogues. These analogues are so similar in chemical structure to true vitamin B12 that they attach to the same receptors. Vitamin B12 analogues have no beneficial vitamin effect on the body and actually contribute to a vitamin B12 deficiency by blocking the uptake of real vitamin B12 to those receptors. A high intake of vitamin B12 analogues can worsen a deficiency, which is why it's extremely important to ensure intake of real vitamin B12.

Getting enough real vitamin B12 through your diet is extremely easy if animal products are consumed. The following gives you enough vitamin B12:

- shellfish, especially oysters and clams you would only need to eat this once a week to get the appropriate amount of vitamin B12
- other types of fish like salmon and tuna
- beef -3 ounces of beef carries the entire recommended daily intake of vitamin B12
- beef liver has an incredibly high amount of vitamin B12 and you would only need to eat it once a week or even less to get the correct amount of vitamin B12
- poultry
- eggs
- dairy

If you consume these foods frequently there should not be a need for supplementation. Should you suspect you might have a vitamin B12 deficiency, please see the testing section for more information regarding accurate testing.

Vegetarians and Vegans - Supplementation of Vitamin B12

For those following a vegetarian or vegan way of living, it is extremely important to properly supplement with real vitamin B12. Since true vitamin B12 is only available in trace amounts in plant sources, and most plant sources contain more B12 analogues, it is highly likely that you are vitamin B12 deficient without proper supplementation.

Methylcobolamin is the most active form of vitamin B12 and is better absorbed by the body than cyanocobalamin, which is the chemical version. Eat with fat for best absorption.

Dose of Supplementation:

The dose of methylcobolamin should be at least 250 mcg/day.

If you test as vitamin B12 deficient then your dose needs to be 500 mcg/day or more.

The only plant source with higher amounts of true vitamin B12 than B12 analogues is a very high quality, naturally sourced, organic chlorella. And even with this source there is conflicting research.

Vitamin B12 Testing:

Testing for a vitamin B12 deficiency can be tricky, mostly because a large majority of doctors test serum B12 as the only measure of B12 status. This is flawed because a serum B12 will show how much is in the blood but won't give an accurate indication of how well the vitamin B12 is being used (like in the methylation cycle).

For instance, someone who has a high amount of B12 in their serum means that their body is unable to <u>use</u> that B12. It's a signal that we need to dig deeper. A low serum B12 level indicates that a B12 deficiency has last for a long time and has been missed - serum B12 level will eventually fall in a deficiency but not until later stages.

Other tests involved are are the MMA (Methylmalonic Acid), homocysteine, MCV (mean corpuscular volume), and HoloTC tests, though these can all become quite expensive.

If your MMA and homocysteine are elevated this indicates deficiency in B12 that impacts important cycles throughout the body (methylation, methionine, etc). If your MCV is high that could also indicate a deficiency of B12. Again, the serum lab test is the least sensitive for a deficiency and frequently leads to misdiagnosis or under-diagnosis of a vitamin B12 deficiency.

Recommendations:

If you are vegan or vegetarian then you absolutely must take a quality B12 supplement preferably of methylcobolamin. It is a water soluble vitamin and therefore doesn't get stored in the body. Replacement needs to occur daily. You will see enormous variations in dosing. Some of these products offer many hundreds or thousands of mcg above my recommended dose. I recommend finding a liquid that has a dropper. The serving size is usually 1 mL, which is one full dropper of liquid. You can simply take just a few drops to get your daily dose without overdoing it. And your bottle will last much longer!

• Global Healing Center Vegansafe B12, 2500mcg per one full dropper (1mL)

If you have MTHFR, then an additional **B complex with additional folate** (separate but in addition to your prenatal) is also recommended - preferably methylcobolamin and 5methyltetrahyfrofolate if you're able to tolerate methylated supplements. This should be something your doctor is on top of, but if they're not it should be something you speak with them about.

If you're unable to tolerate methylated supplements but you want to add in an additional B complex then a methyl-free folinic acid/hydroxycobolamin mix is great (see Folate section).

Omega-3 (DHA)

Omega 3's are a type of fatty acid chain - some omega's have short chains and some have long chains, but your body gets the most benefit out of the long chain fatty acids.

Omega 3 fatty acids decrease inflammation and protect against disease, which is extremely important when protecting and preserving fertility.

The most common ones you may have heard of are the long chain fatty acids and they are:

- 1. EHA (eicosapentanaenoic acid)
- 2. DHA (docosahexaenoic acid) is considered the most beneficial Omega 3 for reasons I will go over below.

The short chain Omega 3 is alpha-linolenic acid (ALA) and while it is still an omega 3, it is not the one that gives you the most benefit. This less desirable ALA is found in flax, pumpkin seeds, walnuts, and hemp.

Nutrition textbooks will say that ALA can provide you enough Omega 3 fatty acid because our bodies convert it to EHA and DHA but this is slightly misleading. Our bodies can convert ALA over to EHA and DHA but in very limited and small amounts. Less than 5% of ALA can be converted to EHA and less than 1% (more like ~ 0.4%) can be converted to DHA! That's not very much at all and while it is technically possible to eat enough flax oil to give you enough DHA it would be extremely difficult (and would probably result in some disaster pants).

In addition to the already low conversion rate, conversion of ALA to EHA/DHA relies on many other nutrients like zinc and iron (and others), which can often be deficient. Based on these facts, it is not realistic to get your DHA requirements from only eating plant sources of ALA.

DHA is the most beneficial and, because of the low rate of ALA conversion, it must come primarily from food sources. DHA aids fertility by increasing egg quality, increasing sperm count and quality, and decreasing overall body inflammation. Multiple studies have shown it also increases chances of live births from IVF.

DHA food sources include marine algae, fatty fish, pasture-raised meats and eggs. There are many studies showing the more seafood and fatty fish a couple consumes the higher their chances of conceiving are.

What's the story with Omega 6 vs Omega 3 Fatty Acids?

While Omega 3's are incredibly healthy and beneficial for your body, Omega 6 fatty acids contribute to increased inflammation and can increase disease risk. Omega 6 fats are those found in processed vegetable oils like soybean, sunflower, safflower, corn, peanut, sesame, canola, and even walnut oil. Too much omega 6 and not enough omega 3 increases inflammation in the body while more omega 3 and less omega 6 decreases inflammation and risk for disease.

To be clear: it's not Omega 6 fatty acids themselves that are bad, it's the <u>ratio</u> of your omega 6 to omega 3. Ideally you want to be taking in more Omega 3 than Omega 6 fatty acids. This can be achieved easily by avoiding vegetable oils and processed foods while also increasing your consumption of fatty fish and omega 3 rich foods.

Dosing:

You can get enough DHA from food and diet alone. Since I always advocate from getting your nutrients from food first and only supplementing when there's a need, this is one of those areas I would encourage getting it from the diet. This would mean eating 3 full 4–5 oz helpings of a fatty fish per week.

The best food sources of DHA include salmon, mussels, cod, and fish eggs (caviar), herring, sardine, trout, and eggs from pasture-raised animals. The amount of DHA in fish sources is the highest with around 1,400 mg DHA coming from 3 oz of salmon versus only 100mg from grass-fed beef or an egg. It's important to note that DHA coming from a fatty fish source carries with it many other necessary nutrients, so it's benefits far outweight only supplementing.

Supplement dosing is one that has a combined EHA/DHA dose of 650mg with at least 215mg of that coming from DHA alone. You may need to take an additional capsule or teaspoon of some supplements to get this amount, while others may over shoot the mark. There are studies done where levels of over 2,000mg were used with no toxic effect or harm so there's a lot of wiggle room here.

If you can't eat fish itself but can still take a fish product then I recommend cod liver oil or krill oil.

If you do not consume fish products, then you should go with a good quality marine algae supplement.

- Rosita Premium Extra Virgin Cod Liver Oil Capsules
- Rosita Premium Extra Virgin Cod Liver Oil Liquid
- Future Kind Vegan Omega 3 (take 2 softgels)
- Good Earth Nutrition Vegan DHA Omega 3

Cautions and Concerns:

Many people are concerned about eating fish because of possible mercury content. While some fish do have higher mercury levels, others do not. There are many reasons not to be terribly concerned with this, especially if you eat the food sources listed above. Wild caught seafood that carry higher levels of mercury in them also naturally have higher levels of selenium in them. The selenium provides a protective effect by binding the mercury and allowing the body to excrete it before being absorbed. This effect makes the mercury risk from seafood much less to nonexistent.

A very important point is that the majority of fish consumed by people has significantly more selenium in them than mercury. Fish to avoid include king mackeral, swordfish, tilefish, shark, and pilot whale. Albacore Tuna is safe to eat since it has more selenium content than mercury, but to be safe it should still be limited to once or twice weekly.

L-Glutamine

This essential amino acid is a potent anti-inflammatory and helps heal the broken and damaged cells within the gut. Ideally you want to get L-Glutamine naturally through your food, primarily bone broth, but if you're having bad leaky gut symptoms or if bone broth is difficult for you then an L-Glutamine supplement will help.

Recommended dose is 2 to 5 grams of a powdered L-Glutamine three times per day with meals or as directed.

Recommended: <u>Jarrow Formulas L-Glutamine</u> 2grams per serving (with 500 servings!)

Digestive Enzymes

When our stomach acid levels are low we can't properly digest our meals and absorb all the nutrients. For some people this can lead to feelings of fatigue and exhaustion no matter how well their diet is.

Betaine (trimethylglycine) and pepsin are naturally occurring components of digestive gastric juices that break the protein bonds in our food to separate the nutrients and amino acids for absorption. These two enzymes taken at a protein-containing meal can help your body digest food and absorb nutrients better, resulting in improved energy and nutrient status.

A symptom of low stomach acid is actually acid reflux, which fequently gets misdiagnosed as "too much" stomach acid and treated with acid-blocking medications like Nexium, Prilosec, or Pepcid. If these medications are taken when you have low stomach acid, it will actually make digestion worse and exacerbate nutrient deficiencies.

Do not take with a history of ulcers, while taking steroid medication or NSAIDS, or acid-blocking medications like PPI's.

Recommended: Pure Encapsulations Betaine HCL with Pepsin

How to find the right dose: Take <u>after</u> meals containing protein. Start with 1 capsule - if you feel a burning sensation then you likely don't need this type of supplement. If you don't feel burning, then continue increasing the dose by 1 capsule after protein containing meals until you start to feel a warmth or slight burning sensation. Your dose is 1 less than when you feel that burning. So if you take 2 capsules and feel no burning, but feel a burning when you take 3, then your dose is 2. If you take 4 with no burning sensation but feel it at 5 capsules, then your dose is 4 capsules.

Probiotics

There are trillions of bacterial cells living within your gut and collectively we call these bacteria your gut flora, or microbiome. In a normal, healthy gut flora the vast majority of bacteria should be "good bacteria" otherwise known as probiotics. The link between the bacteria in the gut and all aspects of health is well established in quality research studies.

Probiotics serve our bodies in many ways. The bacteria found in our gut have an impact on our digestion, brain, metabolism, thyroid, skin health, hormone balance, sleep health, inflammation, and immune system. The gut microbiome is so important that it is one of the absolute foundations of our entire body's health.

If your gut is unhealthy, then your entire body suffers.

An inflamed gut can cause inflammation throughout your entire body and through every system, including your reproductive organs. Widespread inflammation causes symptoms like fatigue, brain fog, depression, anxiety, insomnia, acne, hormone imbalances, and contributes to mitochondrial dysfunction. Inflammation originating in the gut due to imbalanced gut bacteria becomes a problem for every system of your body.

The gut is connected to everything...

DIGESTION

Gut bacteria help us break down and absorb the food we eat. When there is an imbalance of gut bacteria then our digestion suffers. Approximately 30% of the population suffer from what is called irritable bowel syndrome, or IBS. Those suffering with symptoms like bloating, cramping, gas, abdominal pain, loose stools and/or constipation usually get honored with a diagnosis of IBS, but are then given no real pathway for curing this problem. In fact, IBS has largely been considered a catch-all diagnosis wherein you can have many of the symptoms like those listed above but nobody can find anything physically "wrong" to fix.

Luckily, research is now showing that up to 84% of those suffering with IBS have an overgrowth of certain bacteria in their intestines causing these uncomfortable symptoms. When we take care of this overgrowth, these symptoms go away, as I myself have experienced.

It's also important to note that with an imbalanced gut flora, it is possible that nutrient deficiencies can occur from the inability of the body to breakdown or use nutrients from food. You could be eating the healthiest diet in the entire world, but if your gut is unable to take in those nutrients then you will have deficiencies. In fertility, nutrient deficiencies can make all the difference.

BRAIN

Imbalanced gut flora can impact mood, memory, and cognition. There is research now showing anxiety and depression can be improved through probiotic treatment, as well as brain fog and decreased memory function.

WEIGHT AND METABOLISM

Gut flora imbalance has been linked to metabolic problems such as being overweight or obese, high blood sugar, insulin resistance, and high cholesterol.

IMMUNE SYSTEM

The largest amount of immune cells in your body are found in your small intestine! Any damage done in the small intestine from inflammation, oxidation, imbalanced bacteria etc, results in leaky gut and can contribute to food allergies, autoimmune conditions, and overall decreased immune function. Bacterial imbalance in the small intestine contribute and/or cause issues like hypothyroidism, celiac disease, food allergies, IBS, rheumatoid arthritis, Crohn's disease, and ulcerative colitis.

THYROID

Autoimmune thyroid disease is the most common type of organ-specific autoimmune disease and this is important in fertility. The body can't support full fertility or a pregnancy without the thyroid. Hypothyroidism affects 10–12% of the general population and impacts women to a higher degree than men. Not only is there evidence showing that autoimmune hypothyroidism improves with improved gut flora balance but more and more evidence is coming to light to show that inflammation originating in the gut is one of the causes of autoimmune issues, including hypo- and hyper-thyroidism.

SLEEP

Inflammation in the intestines has been found to cause insomnia. A reduction in this inflammation and healing gut flora imbalances dramatically improves sleep, which helps improve overall health.

SKIN

Rashes, lesions, acne, keratosis pilaris, redness, or skin inflammation have been linked to gut health. Removal of inflammatory foods and rebalancing the gut microbiome has been shown to improve these skin conditions. I personally used every cream and medicine available to help with my own keratosis pillars (chicken skin), but was only able to get rid of it completely with removal of the offending foods and a rebalancing of my gut.

HORMONES

This one is wildly important, especially in terms of fertility. The gut microbiome plays a pivotal role in the breakdown and removal of hormones. Without proper gut bacteria balance things like estrogen dominance and high testosterone can become a problem in women, which can seriously affect the function of fertility. For men, a gut imbalance may result in higher estrogen, which can impact libido, sperm quality, and overall health. The bacteria balance in your gut closely resembles that of women's vaginal tracts, so the better your gut, the better your entire body.

Probiotic supplementation has been shown to help increase sperm health in men, and is so overwhelming in evidence that probiotic supplementation is now being presented as a hopeful addition to official medical infertility management guidelines.

Strain Of Probiotic To Take:

You will want to have a probiotic regimen that has many different strains to help balance the gut appropriately.

A Lactobacillus and Bifidobacterium probiotic blend is beneficial for most conditions and there is a large variety of research that show this type of blend is your best bet. It's also extremely safe to take.

A spore-based probiotic (Bacillus) is great because spores cannot be killed in the stomach acid allowing those spores make their way into the intestine to exert really great effect. Stomach acid can kill other strains making the amount that reaches your intestine less, so I like to add in a spore-based probiotic in addition to the lactobacillus/bifidobacterium blend. This can also help replace a lot of what is missing in our overly clean environment because they come from the soil - interestingly enough spore-based probiotics can help a lot with allergies.

RECOMMENDED PROBIOTICS:

Saccharomyces Boulardii is a yeast-based probiotic, which might seem counter-intuitive if you have issues with candida and yeast infections. This specific strain, however, pushes out the other bad types of yeast and can even help with parasitic infections or other harmful bacteria in the gut. It's also been shown to be as powerful as the antibiotic metronidazole (Flagyl) in treating Blastocytis hominis, which can be a contributor to autoimmune hypothyroidism.

Dose

15-100 billion CFU per day combined between different strains. Ideally around the 50-60 billion CFU range unless you feel you need more.

Lactobacillus/Bifidobacterium Blends:

- Dr. Mercola Probiotics 70 billion cfu
- Pro-45 Probiotic Formula
- Physician's Choice 60 Billion Probiotic
- 1 MD Complete Probiotics

Spore-Based Probiotic:

- Megasporebiotic (from website)
- <u>Megasporebiotic (From Amazon)</u>

Saccharomyces Boulardii:

- Pure Therapro Rx 10 billion CFU
- Pure Encapsulations

For a mix of Lacto/Bifido, spore-based, and SB:

• DrFormula's NexaBiotic

Coenzyme Q10

More commonly known simply as CoQ10, this molecule is used specifically by your body's cells to make energy. Cells create and use an energy source called ATP, which is made by mitochondria. Nicknamed the "powerhouse of the cell", mitochondria make all the ATP a cell needs for everything it needs to do. Mitochondria are so important that the majority of a cell's contents can be comprised of these energy-producing powerhouses.

Dysfunctional mitochondria are unable to make enough energy for a cell to maintain its normal activity. This is of particular concern when speaking about egg health. In order for an egg to become a high-quality embryo and viable pregnancy it must go through a complicated series of cell and chromosomal divisions that require an immense amount of energy. If the required energy is not there at specific times during cell division then chromosomal abnormalities can occur, which is a primary reason for early miscarriages.

It is widely accepted within research that mitochondrial health and function is a prime indicator of an egg's health, and has implications for women with recurrent miscarriages, failed IVF cycles, or unexplained infertility.

Many things can affect the quality and function of mitochondria. They naturally decrease in quality and effectiveness with age and studies that tested eggs from women over 40 have shown mitochondria damage to be more common. Things other than aging that especially affect mitochondria are oxidative damage (inflammation), toxins, medications, and most notably nutrient deficiencies.

Since mitochondria use several nutrients and substances to make energy, it makes sense to give the mitochondria what they need. CoQ10 is not only something mitochondria need to create energy for the cell, it also acts as an antioxidant to protect mitochondria from oxidative stress. The positive effects of CoQ10 supplementation on egg health has been well documented in studies. Most recently one such study says that not only is CoQ10 a perfectly effective way to preserve the quality of the egg and decrease oxidative damage, but it also contributes to improved rates of IVF.

I highly recommend adding CoQ10 in your normal fertility supplement regimen as one of the foundation supplements. It's powerful benefits greatly outweigh any risk and helps increase egg health from multiple angles.

Type To Take:

Coenzyme Q10 comes in two forms - ubiquinone and ubiquinol.

When looking to supplement with this powerful nutrient you should make sure you get the ubiquinol form as this is the active form. Dosing can vary depending on your specific needs.

Dosing:

- Ubiquinol 200mg per day if newly trying to conceive, age 30 or above, with no reason to suspect any difficulty
- Ubiquinol 400mg per day if age 35 or above or with history of recurrent miscarriage
- Ubiquinol 600mg per day if undergoing IVF

How To Take CoQ10

Take ubiquinol divided between morning and afternoon doses with food. Do not take your afternoon dose of CoQ10 past 2pm.

Fat helps with the absorption of CoQ10 so you want to make sure you're taking this supplement when you're eating a meal containing fat. Take throughout your cycle and stop when you get a positive pregnancy test if that's what makes you feel comfortable. There is no evidence to say you can't or shouldn't take CoQ10 while pregnant and there are even studies that show taking CoQ10 during early pregnancy may decrease miscarriage rates. It may also decrease pregnancy complications from high blood pressure, or pregnancyinduced hypertension (PIH). Speak with your particular doctor or midwife regarding the research and make the decision whether to continue your supplementation once you get a positive pregnancy test. My recommendation is to slowly wean yourself off this over the course of several weeks rather than stopping cold turkey.

Cautions and Concerns

As far as side effects go, there have been many studies that have supplemented CoQ10 in doses far exceeding 600mg per day. Studies done looking at CoQ10 supplementation of 1800mg-2700mg per day were shown to have great benefits and no side effects to illicit any safety concerns.

Some GI upset symptoms have been reported with taking CoQ10, but this is minimized by splitting the dose between breakfast and lunch.

Do not take CoQ10 before bed as it can interfere with sleep. Insomnia has been reported with a small dose of just 100mg in the evening hours. If you are taking more than 300mg per day and are having trouble sleeping at night then make sure your doses are before 2pm. If this doesn't help then consider reducing the dose.

**If you take beta blockers, cholesterol-lowering drugs, antidepressants, or antipsychotic medications then you may want to consider taking 400-600mg per day as these medications naturally decrease the amount of CoQ10 within the body.

**If you are taking any blood thinners such as warfarin then speak with your doctor as CoQ10 may interfere with this medication.

Recommendations:

- Jarrow Formulas Ubiquinol 200mg
- Healthy Origins Ubiquinol 100mg
- <u>Dr Mercola Ubiquinol 100mg or 200mg</u>
- <u>Life Extension Super ubiquinol</u>

Melatonin

THE SLEEP HORMONE

You probably know melatonin as "the sleep hormone" and its important role in your sleep-wake cycle, otherwise known as your circadian rhythm.

Melatonin is made and released by your pineal gland in response to light. It is highest at night through the very early morning hours, and decreases as the sun rises to remain at its lowest levels throughout the day. This hormone is your body's messenger that it's getting dark, and helps us prepare for sleep. While it's extremely important for your sleep cycles it also plays a pivotal role in our fertility.

Melatonin is a powerful antioxidant that can actually get inside our mitochondria and exert its antioxidant effects there- it works to decrease damage from free radicals and it increases levels of glutathione, the master antioxidant. Studies have found large amounts of melatonin in follicular fluid and within the ovary itself, indicating its importance in egg quality.

Through research it is becoming clearer that melatonin has a very important role in the maturation cycle of eggs, and it enacts its effects through its powerful neutralization of free radicals inside mitochondria.

Studies have found that women with higher melatonin also have higher anti- mullerian hormone, or AMH, and that this also correlated to a higher follicle counts. In the context of IVF, it is being found that high levels of melatonin relate to higher quality eggs and embryos. There have even been some well formulated studies done involving women with PCOS where it was shown that supplementing melatonin for 6 months helped to improve menstrual irregularities and improve hormonal imbalances.

Dosing:

• Melatonin 3mg at night before bed

Best taken if you're preparing for an IVF treatment or have PCOS

Cautions and Concerns:

The most common adverse effects have been reported as headache, dizziness, drowsiness, mild abdominal cramps and nausea. It's also associated with increased depression but at much larger doses of 250mg - 1200mg. Since we're not taking anywhere close to that, it's most likely not of concern.

Alpha Lipoic Acid

ALPHA-LIPOIC ACID IS A POWERFUL ANTIOXIDANT THAT IS BOTH WATER-SOLUBLE AND FAT-SOLUBLE GIVING IT THE ABILITY TO HAVE A WIDE REACH THROUGHOUT THE BODY.

It is a normally occurring compound in our bodies that is used by our mitochondria to make energy, but with age it decreases substantially. Alpha- lipoic acid is particularly unique because it helps the body to regenerate already used antioxidants like vitamins C and E, and CoQ10 back into their active forms. It's also important in glucose control, brain health, and liver detoxification.

Alpha-Lipoic acid has been found to have beneficial impact on men's sperm quantity and overall quality including increased motility. While it's clearly shown to be beneficial in men with previous sperm issues, it may be most beneficial in women with PCOS or endometriosis.

One study showed that more high-quality embryos resulted during IVF cycles where alphalipoic acid was used in combination with myo-inositol rather than myo-inositol alone. This same study also showed better metabolic profiles related to these women's glucose and insulin levels with the use of alpha-lipoic acid.

One of the most recent studies released showed that long-term treatment with alpha-lipoic acid in women with PCOS helped to normalize the menstrual cycle and lessen insulin levels.

Type to Take:

There are 2 forms of alpha-lipoic acid: R- and S-isomer forms.

R-Isomer alpha-lipoic acid is the more biologically active form that resembles what the body naturally produces.

The S-isomer is synthetically made, and alpha-lipoic acid supplements usually come as a mixture of 50:50 R:S-isomer unless specifically indicated on the bottle that it's made of only R-isomer. This matters in terms of dosing - while the price is much lower of a 50:50 mixture, the dose needed is much higher. A lower dose is necessary with R-isomer but the supplement itself will be more expensive.

In the end, either the 50:50 mixture or the R-isomer is fine. You need to know which one you take only because it changes the dose.

Dosing:

- 50:50 Mixture alpha-lipoic acid: notated as "racemic" or "rac" on the label = 400-600 mg per day split between two doses
- R-isomer alpha-lipoic acid: notated as R-isomer-only form on the label = 200-300 mg per day taken once per day

Some studies used doses as high as 1200mg split between 2 doses in women with PCOS. Though this dose may seem high, it was also safely used in studies looking specifically at diabetes type 2. Those studies showed improved levels of insulin sensitivity and glucose control. If you have PCOS, speak with your doctor regarding the studies and validity of using alpha-lipoic acid and myo-inositol (see below for more info on this). If your doctor doesn't know anything about it, find another doctor.

How To Take:

Alpha-lipoic acid should be taken on an empty stomach either 30 minutes before food or two hours after. Though it's absorbed better if taken on an empty stomach, the decrease in absorption rate is only about 20-30% if taken with food. As with CoQ10, take until positive test and then discontinue not because it's dangerous or unsuitable for pregnancy but simply because there is insufficient evidence to say otherwise.

Cautions and Concerns:

Some cases of skin rash or nausea have been reported with use of alpha-lipoic acid, though these have been mild. Take with food if nausea is a problem for you.

Diabetics taking alpha-lipoic acid may need to work with their doctors and adjust diabetes medications as needed. Since this supplements lowers glucose and increases insulin sensitivity, this may decrease medication need.

Very rarely, something called Insulin Autoimmune Syndrome (IAS) occurred in some people taking alpha-lipoic acid. This syndrome causes higher blood insulin levels, which can decrease glucose levels dramatically and result in symptoms like shaking, dizziness, and weakness. People of Japanese descent are potentially more prone to this.

Alpha-lipoic acid may increase thyroid-stimulating hormone (TSH) as it can potentially interfere with the conversion of T4 to T3. Those with thyroid issues or are taking thyroid medications should consult with their doctor.

Recommendations:

- Jarrow Formulas R-Alpha Lipoic Acid, 100mg per capsule
- Pure Encapsulations Alpha-Lipoic Acid 200mg per capsule (mixed isomer)

Myo-inositol

Unofficially dubbed as "vitamin B8", this molecule has been shown to increase ovulation and egg health in the settings of PCOS, insulin resistance, irregular cycles without ovulation, IVF cycles in women who have a history of immature eggs during a precious cycle, and unexplained/recurrent miscarriage.

In the context of IVF, studies show a direct correlation between a higher amount of myo-inositol naturally found in an egg and more mature eggs that were then fertilized. Myo-Inositol improves embryo quality and performance according to multiple IVF studies.

This supplement is especially important in women with PCOS because it has a crucial role in insulin function. Myo-inositol helps reduce insulin resistance, which is a key problem in PCOS. In doing this, it helps to balance blood sugar, balance hormones, and restore ovulatory cycles. It is quickly becoming favored over metformin, a prescription diabetes medication typically used in treatment of PCOS.

D-Chiro Inositol

D-Chiro Inositol is a lesser known supplement and is a chiral epimer of Myo-Inositol. A chiral epimer is essentially a fancy name for mirror image. Myo-inositol and D-chiro Inositol are mirror images of each other and they can be used for PCOS, however they're used for slightly different reasons so determining which one of the two you should take is the tricky part.

Both Myo-Inositol (MI) and D-Chiro Inositol (DCI) are used in important parts of the insulin signaling pathway, as well as in many other signaling pathways throughout the body. In terms of PCOS, we mainly want to focus on the insulin pathway because this is one of the most important pieces in controlling symptoms of PCOS.

MI mainly exerts its function on the ovary and controls glucose uptake as well as FSH (Follicle Stimulating Hormone) signaling. DCI is involved in androgen production induced by insulin and is responsible for symptoms related to higher testosterone found in women with PCOS.

Both MI and DCI can be ingested through food sources but naturally sourcing enough D-Chiro Inositol is extremely hard to do, which means the body needs to create its own supply. The most current research shows that D-Chiro Inositol is made in the body from Myo-Inositol.

However, some people are unable to convert Myo-Inositol to D-Chiro Inositol and therefore have a higher MI:DCI ratio. Since both elements are important for proper insulin signaling, an imbalance of one will throw the entire pathway out of sync. It has been found that the desired ratio of MI:DCI naturally occurring in the body is 40:1.

So how do you decide which to take?

It is highly personalized and dependent on your symptoms, however, the most up-to-date research suggests that taking a Myo-Inositol and D-Chiro Inositol blend is best, especially if you have PCOS. The studies that used an MI/DCI blend at a 40:1 ratio show a significant increase in ovulation. These studies also found that a blend of the two improved insulin sensitivity, reduced circulating insulin, improved FSH sensitivity, and resulted in better egg quality.

A blend of the two inositol isomers hits all the positive marks we want to get when treating PCOS, and it does it while replacing natural compounds found in the body.

Dosing:

- A Myo-Inositol and D-Chiro Inositol blend at a 40:1 ratio: MI of 2000mg and DCI of 50mg or a simple myo-inositol of 2000mg
- Do not go in excess of the 40:1 ratio in favor of more DCI it's better to just take myo-inositol alone rather than get too much DCI

Recommendation

- Fairhaven Health Myo-inositol for couples fertility
- Fairhaven Health Myo + D Chiro Inositol at 40:1 ratio

Calcium D-Glucarate

This nutrient is important in liver detoxification, estrogen metabolism, and is even being studied for its anti-cancer properties. It is not considered an essential nutrient, meaning that the body is able to produce some calcium D-Glucarate on its own. Even though the body can produce some, it's beneficial effects are too important to ignore especially in the context of hormonal regulation and fertility.

Calcium D Glucarate supports phase 2 in our liver's detoxification, helps to eliminate dirty estrogens, and promotes healthy metabolism as well as proper hormonal balance. Not only does it support phase 2 liver detoxification, it also inhibits an enzyme produced by our gut bacteria called beta glucoronidase. This enzyme can unpackage toxins and dirty estrogens that are in our bowel to be eliminated, releasing them back into the body before actually being eliminated. This can contribute to estrogen dominance - calcium D glucarate can be useful in bringing estrogen back into balance. If you struggle with issues of constipation and have estrogen dominance symptoms this might be a beneficial addition for you, or if you have received test results stating you have high beta-glucoronidase then you should absolutely add this in.

Calcium D-Glucarate also boosts the immune system by increasing anti-inflammatory cytokines, which reduces inflammation and promotes healing.

Dosing:

• The dose can range anywhere 150 to 300mg per day, taken with meals

Cautions and Concerns:

Since calcium D-Glucarate helps enhance liver detoxification it can actually speed up metabolism of other medications. Specifically, any medication that is metabolized via glucoronidation in the liver may need to be increased to ensure proper therapeutic dosage is maintained. Consult with your doctor if you are taking any type of heart, seizure, antidepressive, antipsychotic, or any other medications.

Recommendations:

- Wellena Calcium D Glucarate 150mg per 2 capsules
- Life Extension Calcium D Glucarate 200mg per capsule
- Seeking Health Calcium D Glucarate 250mg per capsule

Calcium

This nutrient is actually somewhat controversial, if you can believe that. With a highly nutritious diet, this should not need to be supplemented. There are some important things to note, and potentially some situations where an increased intake of calcium might be beneficial.

It is a common misconception that calcium is only present in dairy when in fact there is an abundance of calcium found in leafy green vegetables and other foods. For instance, one cup of cow's milk has approximately 140 mg of calcium while one cup of spinach has 245 mg.

Current FDA recommendations is to get anywhere from 1000mg to 1300mg of calcium per day, but experts and research disagree on this point. Many experts suggest that eating between 600-800mg of calcium from highly absorbable food sources is plenty to keep optimal health.

This can be easily attained from eating a variety of whole food sources that are high in calcium. The foods below list some of the foods with the highest calcium content:

Food/Serving	Calcium (mg)
Sesame Seeds/0.25 cup	351
Sardines (with bones)/3.75 oz can	351
Yogurt/1 cup	296
Collard Greens/1 cup	268
Spinach/1 cup	245
Cheese/1 oz	204
Turnip Greens/1 cup	197
Mustard Greens/1 cup	165
Beet Greens/1 cup	164
Bok Choy/1 cup	158
Almonds, dry roast/2 oz	150
Cow's milk/4 oz	138
Swiss Chard/1 cup	102
Kale/1 cup	94
Cabbage/1 cup	63
Broccoli/1 cup	62
Brussels Sprouts/1 cup	56
Green Beans/1 cup	55
Oranges/1 medium	52
Cinnamon/2 tsp	52
Summer Squash/1 cup	49
Parsley/0.5 cup	42
Asparagus/1 cup	41
Celery/1 cup	40
Cumin/2 tsp	39
Basil/0.5 cup	38
Garlic/6 cloves	33
Oregano/2 tsp	32
Leeks/1 cup	31
Romaine Lettuce/2 cups	31

You'll notice that most of the foods highest in calcium are actually leafy greens and not dairy. If you are avoiding dairy for any reason then it is extremely easy to get enough calcium in any given day.

In terms of fertility, calcium is very important in sperm production and function. There are many studies showing that a decreased calcium intake in men is associated with irregular sperm motility and inability to carry out functions related to fertilization. It is in the specific instance of male infertility that calcium supplementation may be beneficial. Outside of male infertility, adequate calcium intake of approximately 800mg per day should be achieved through diet.

Dosing:

It's important that if you're experiencing sperm motility problems or infertility that you mostly concentrate on increasing consumption of foods that have a high calcium content. The calcium found in foods is going to be much more bioavailable and easily absorbed into the body than supplements.

There is no definitive human research concluding that a certain type of calcium supplement at a certain dose does, in fact, increase male fertility. The current research points to the fact that lack of calcium in men contributes to mitochondrial dysfunction, sperm production and function problems, and male infertility.

I believe the evidence doesn't clearly suggest calcium supplementation when dietary intake is beneficial enough to warrant adding a specific calcium supplement. It's so easy to "over supplement" while trying to conceive, right? Let's not add things we don't need to.

My best recommendation is to concentrate on increasing dietary intake of calcium primarily through leafy green foods, bone-in fish, almonds, and other foods listed above. Doing this will also increase the amounts of other beneficial nutrients and will only help.

Selenium

Selenium is an essential trace element important in thyroid hormone metabolism, DNA synthesis, and also works as an antioxidant. In male fertility, its antioxidant effects protect the quality of sperm. The exact pathway through which selenium protects sperm is unknown but the theory is that it works in combination with glutathione. These 2 antioxidants maintain the proper structure of the sperm, specifically at the mid-piece, so that it has good motility.

For women, we are just beginning to learn the importance selenium might have especially in terms of egg health and quality. Recent studies show that there are significant amounts of selenium present in larger, healthier follicles and this may have an important antioxidant effect on the growth and development of a healthy egg. Follicles/eggs are extremely vulnerable to inflammatory effects and can be damaged by free radicals. While there are only a handful of studies regarding selenium and female fertility, they generally imply that lower selenium relates to higher infertility rates.

Selenium also has important impact on thyroid function and maintenance of proper thyroid hormone levels. In fact, the tissue in the body with the most selenium found in it is the thyroid. There are many studies showing its usefulness in managing thyroid disease so if you're struggling with Hashimoto's or other autoimmune thyroid problems then selenium supplementation, in addition to adequate dietary intake, may be something to ask your doctor about. Those who have Hashimoto's have reduced their antibodies by 50% over 3 months in some studies.

Testing:

Serum selenium results are <u>normal</u> between 70-150 mcg/L.

The Lancet suggests that those with levels less than 122mcg/L could benefit from supplementation, while those who have serum levels above 122mcg/L could have negative effects from additional selenium.

As with everything, you should concentrate on a good overall diet that contains seleniumrich foods rather than trying to immediately supplement.

Requirement and Dosing:

The recommended daily requirement of selenium is around 60-70µg/day (micrograms/day).

Deficiencies are generally rare but it's important to maintain a good dietary intake and assess if supplementation beyond that is required.

The upper limit used in studies involving selenium (for fertility and thyroid) was 200 mcg/day.

Those with Hashimoto's hypothyroidism are frequently deficient in selenium, and taking selenium at a dose of 200mcg/day has been shown to decrease antiobodies by 50% in 3 months.

Selenium-Rich Foods:

Foods to concentrate on that contain high amounts of selenium are: seafood (salmon, cod, shrimp, tuna, halibut, scallops), chicken, eggs, mushrooms (shiitake and crimini), turkey....and Brazil nuts.

But Brazil Nuts, Right?

Yes...and no.

Just 2-3 Brazil nuts contains approximately 200mcg of selenium, which is the amount used to supplement in the studies. If you are eating a diet made of whole, unprocessed foods then Brazil nuts every once in a while is fine but you shouldn't go wild with them.

If you choose to add Brazil nuts to your diet (or use them as your selenium supplement), do not eat more than 2 Brazil nuts per day. While the upper limit of selenium intake is 400mcg/day, the safe intake limit is about 300mcg/day. Eating only 2 nuts should keep your limit within a good range.

Cautions and Concerns:

Too much selenium can cause a range of symptoms including: nausea and diarrhea, visual disturbances, hair and nail brittleness, nervousness, depression. If you decide to supplement use a dose of 200mcg/day and then abstain from eating Brazil nuts

Glutathione

GLUTATHIONE IS CONSIDERED ONE OF THE MOST POWERFUL ANTIOXIDANTS IN THE BODY AND IS THE CELL'S PRIMARY ANTIOXIDANT.

You may hear it referred to as "the mother of antioxidants". It is the ultimate detoxifier and critical in proper immune functioning of the body. There are about 100,000 medical articles relating to glutathione and its effects in everything from preventing cancer, treating autism and alzheimer's, to - you guessed it - its role in fertility.

Its importance for overall health really can't be understated but you've probably never heard of it or may have heard the name in passing. Why? Well, the modern medical system concentrates so much on symptom management and not on root causes. This causes certain things like a deficiency in glutathione to be completely overlooked and the majority of the time this won't even be on your practitioner's radar unless they concentrate on a more functional medicine approach.

There's good news and bad news when it comes to glutathione!

The good news is that the body is incredible and can produce glutathione on its own! With the right ingredients your body pulls together its own supply of glutathione and can even recycle certain parts to be used again in the next batch. In fact, glutathione helps recycle other antioxidants like vitamin C and vitamin E as well! Pretty impressive, right?

The bad news is that a lot of things will deplete your glutathione and not allow your body to make enough. Things like poor diet, stress, high toxic load, medications, infections, and age all contribute to a low glutathione level.

Our goal is to keep our glutathione levels high so that our bodies can get the full benefit of its detoxification magic and disease prevention.

Fertility and Glutathione:

The main function of glutathione in terms of both male and female fertility is its protection against Reactive Oxygen Species (ROS), or free radicals. Glutathione is found in high levels in seminal fluid and is important in quality and motility of sperm itself. Since the majority of male fertility challenges are due to sperm malformation or malfunction it becomes very important to assess oxidation, free radicals, and toxic load. Glutathione is a critical piece and a deficiency can lead to motility problems and overall poor quality.

For women, glutathione is extremely important in egg quality. Its main function is protecting eggs from damage caused by oxidative stress and inflammation. A glutathione deficiency is related to premature ovarian aging, and some studies have even found it can be related to increased rates of ovarian cancer.

For women undergoing IVF, higher levels of glutathione increased fertilization rates.

Tricky Glutathione:

You're probably thinking, "Great! Tell me where I can get this stuff!" Right?

Ah, well, there's a little trick to glutathione. You can't simply take a supplement of this stuff, even though you can pop online right now and buy yourself a bottle labeled "Glutathione". There's a bit of a tricky situation with this that *isn't* on that bottle's label:

Glutathione is a protein made up of 3 amino acids (protein molecules) and when you put protein into your stomach, your body digests it! If you were to take a pill of glutathione you wouldn't get the full benefit or dose.

Your efforts are better spent in supporting your body in making its own adequate supply! Let's not over supplement, right? Concentrate on taking only what you need to take, and providing your body with the rest.

Building Your Glutathione:

The following are the best ways to boost your body's natural production of glutathione:

- Eat sulfur rich foods like garlic, onions, broccoli, kale, cabbage, cauliflower.
- Exercise also boosts your glutathione levels and is a great overall immune stimulator. Try to get 15-30 minutes of activity in your day that includes cardio like walking/jogging and/or weight training.
- Take glutathione supporting supplements. This will help your body in producing its own Mother Antioxidant. Glutathione production requires various nutrients that you can help your body in getting. These include: N-Acetyl-Cysteine, Alpha Lipoic Acid, Folate, vitamins B6 and B12, Selenium, Vitamins C and E. These all have various effects on the production and recycling of glutathione and are also very important in overall heath as discussed in their respective sections. Milk thistle can also be used since it helps in liver detoxification and also boosts glutathione levels.

DHEA (Dehydroepiandrosterone)

DHEA IS ACTUALLY AN ADRENAL HORMONE!

It is necessary for follicle development, and there is some strong evidence behind it in the setting of low ovarian reserve and IVF. DHEA is also a precursor to some of our steroid hormones and is at its peak in our 20's.

This hormone naturally decreases with age and contributes to the decreasing ovarian reserve and egg quality/quantity available. Studies have found that supplementing this hormone can increase both egg quality and quantity by way of helping early follicle development. Since this supplement is a hormone, it's safest and most prudent to get your DHEA levels checked with your doctor before using this.

Since a pioneering study done in 2005 by Baylor University found a direct and cumulatively positive effect of supplementing with DHEA, more and more studies have been done to verify these results.

Studies have shown DHEA supplementation significantly decreases miscarriage rates, increases pregnancy chances in natural settings as well as IUI and IVF, and is also associated with higher live birth rates.

The following lab results of DHEA-Sulfate (the blood test used) and testosterone are normal:

DHEA-Sulfate Normal Results

 Age 18-29 	44-332 µg/dL (1.19-9.00 µmol/L)
 Age 30-39 	31-228 µg/dL (0.84-6.78 µmol/L)
 Age 40-49 	18-244µg/dL (0.49-6.61 µmol/L)

Normal Testosterone Levels for Age 20-50

 Testosterone (Bioavailable) 	0.8-10.0 ng/dL (0.03-0.35 nmol/L)
 Testosterone (Free) 	0.3-1.9 ng/dL (0.01-0.07 nmol/L)
 Testosterone (Total) 	8-60 ng/dL (0.3-2.1 nmol/L) (female)

Please consult with your provider and get testing to see if supplementation of DHEA would be appropriate for you. Your blood levels should be monitored as well to ensure therapeutic range.

Dosing:

The dose most often used and recommended by fertility clinics is 25mg per day, though many recommend up to 50mg. If your doctor recommends a higher dose than go with that.

Recommendations:

• Life Extension DHEA (many doses available from 15-100 mg per capsule)

Cautions and Concerns:

DHEA may increase testosterone, and is <u>not</u> recommended for women with PCOS.

There is limited data to show that some women with endometriosis may benefit in the setting of IVF.

Women with a history of hormonal cancers (such as estrogen-induced breast cancer) should not use DHEA.

DHEA may increase the blood levels of certain medications that are metabolized through the liver's CYP450 system.

DHEA can affect insulin in either way - either increasing insulin resistance or increasing insulin sensitivity. It's dependent upon the person, and those with diabetes should be closely monitored.

This supplement should be taken when it is agreed upon with you and your healthcare provider

Don't go rogue on this one and randomly start taking it!