



The Medicine is on the Table: How your Food Choice Can Affect Pain and Fertility

Scandic Oslo City
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12:00 – 15:00
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Cert Ed. BA. BSc.Dip ION. MA.

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Need to Know



- How to reduce the pain and inflammation
- Sub-fertility and how to improve endometrium and egg quality
- How crucial the microbiome is in its role of breaking down circulating oestrogen and excreting it from the body
- What to eat, what to avoid/reduce, plus which supplements may be helpful

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Food as Medicine



- To encourage both men and women to eat healthy food to improve their preconception health status, to avoid transgenerational changes in coming decades.
- 50 A.D. the Susrata Samitha named 500 remedies
- 400 B.C. Chinese Huangoi Neijin named 3,000 healing foods
- 25% of all prescriptive drugs used in the world are derived from natural plant sources and have excellent correlation with folk remedies
- 74% of drugs using the purified active chemicals are used to treat the same disease as the plant was reputed to cure in folk medicine
- Only 5-10% of the quarter of a million plant species on the face of the earth have ever been examined

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Common Symptoms of Endometriosis



Women with endometriosis often display a range of pelvic–abdominal-pain symptoms, e.g.

- painful periods (dysmenorrhoea),
- painful intercourse (dyspareunia),
- heavy menstrual bleeding,
- non-menstrual pelvic pain,
- pain at ovulation,
- pain with defecation (dyschezia) and urination (dysuria),
- chronic fatigue,

noted in research conducted by Kennedy and Bergqvist (2005) and Nnoaham and Hummelshoj (2011).

More research is required to ascertain how endometriosis implants affect digestion, immune, nervous and endocrine systems.

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Types of Diagnosed Endometriosis Symptoms Reproductive 96%, Urinary 49%, Digestive 55%, Thoracic 14%



- 52% Disrupted menstrual cycle, too long, too heavy, too painful, too short, 63% stale brown blood clots
- 93% Extremes of pain at periods, 84% pain at ovulation, 84% pain with bowel movements, 48% bladder involvement, 79% dyspareunia, 81% low back pain, 65% pain into legs
- 67% Nausea and vomiting, 83% diarrhoea and constipation, with bloating and distention
- 39% infertility, 52% food intolerances, 50% seasonal allergies, 95% fatigue, 76% PMS
- www.endostats.com.
- 15/2/2017 to 51/5/2017 on-line survey

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Endometrial Invasion



- Fragments of endometrial tissues must have the capacity to attach and invade into the surface of the peritoneal wall or organs, rapidly developing a vascular supply, proliferating under the influence of oestrogen
- Cell membrane integrity depends upon nutrients. Skin and epithelial layers are a defense system, a barrier against infection. Growth factors, remodeling enzymes and integrins are the main substances involved in attachment and invasion of endometriosis.
- When cell membranes are damaged Vitamins A, C and zinc are found at the site. The membranes are also dependent upon cis essential fatty acids and magnesium for their integrity.

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Peritoneal fluid inflammatory cells



- Research shows that certain chemicals (cytokines, which are produced by macrophages) are implicated in cell proliferation and inflammatory reactions:
- "The volume of peritoneal fluid and its content of the inflammatory cells called macrophages have been shown to be significantly increased in patients with endometriosis, particularly in the mild forms of the disease"
- Macrophages produce cytokines, interferon and prostaglandins PGE2, inducing inflammation and affecting the energy output of cells
- Vitamin B6 and choline are essential for the phagocytic cells to clean up effectively

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Food Nutrients and Health



- Nutrients are crucial to life and health
- We all eat every day
- Our choice of food essentially is our choice of health or illness
- The fresher the food the more nutrient dense
- The older the food the less nutrients it contains
- Processed foods have some nutrients removed and some added back
- Nutrients are essential for body system function
- Reproductive organs require a variety of vitamins and minerals, not just folic acid

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Nutrients regulate the genes that encode the various proteins that act as enzymes, carriers, receptors, and structural elements of the living system



- Nutrients do not only serve as substrates for metabolic processes or as coenzymes or cofactors for these processes.
- The diversity in cell type and function depends on the appropriate intake of nutrients
- These nutrients sustain your metabolism and dictate the phenotypic expression of each individual's genotype.
- Manipulation of the nutrient intake (specific nutrients and total nutrient supply) can manipulate this expression.

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What Constitutes a Balanced Diet



- No single food contains all of the nutrients that the body needs, so eating a balanced diet means eating a wide variety of foods in proportions needed for good health
- "A well balanced diet should contain plenty of starchy foods such as wholegrain bread, pasta and rice, fruit and vegetables and some protein foods such as lean meat, fish, eggs and lentils. "

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» **What is a balanced diet?**
Cardiff University 2010



- Women have trouble interpreting and applying such guidelines to their daily lifestyles
- Women's descriptions of balanced diets were not in line with official definitions
- 46 mothers with children aged 16 years or younger were questioned about balanced diets and the main reasons for ill health
- TV programmes and adverts were their only sources of dietary advice, slogans being easily recited

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What are women eating?



- 110 published research studies reviewed the diets of UK women in childbearing years,
- 1:5 low iron (42% less than 8mg/day)
- 11% inadequate Vitamin B2
- 9% low magnesium
- 25% had low 2.1ug intake Vitamin D (norm 7- 41ug/day)
- Many fall below recommended levels of iodine
- 83% ate 6g+ salt daily
- 19-24 year olds ate 1 1/2 portions Fruit/Veg only per day
- 11g dietary fibre per day
- Excesses of total fat intake, alcohol and sodium were exceeded

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Teenage girls' junk food diet leaves them starved of nutrients. What hope is there for future generations?



- Typical teenagers eat pizza, pasta, crisps, chips, chocolate, ice cream, coffee and soda.
- Research at Manchester Metropolitan University combined results from 38 studies of teenage diets.
- Millions teens - dangerously low on key vitamins and minerals e.g., calcium, iodine, iron, magnesium, selenium, zinc
- 1 in 10 girls is dangerously low on calcium
- 1 in 6 girls is low on iodine
- 1 in 10 boys lacks zinc
- They were found to skip meals, shun fruits and vegetables and oily fish.
- They eat high levels of salt, sugar and alcohol

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Major Diseases



- "There is only one major disease in the world today and that is malnutrition
- All ailments and afflictions to which we may fall heir to are directly traceable to this major disease"
- Dr. D.W. Cavanaugh
- Cornell University

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Nutrition and Heart Disease



- 50 years ago Ancel Keys demonstrated the tremendous impact of nutrition on heart disease and brought the 'Mediterranean Diet' to popular attention
- The European Prospective Investigation into Cancer and Nutrition (EPIC) Study.
- Documented a dramatic reduction of diabetes (-93%), myocardial infarction (-81%), strokes (-50%), and overall reduction in cancer development (-36%) by using a 'healthy diet' – low meat consumption, high plant food.

• **Why not endometriosis?**



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Endometriosis and Diet



A hospital-based Italian case-controlled study on 504 patients observed a statistically significant protective effect of current green vegetable (OR=0.3; CI=0.2–0.5) and fruit (OR=2.0; CI=1.4–2.8) consumption and a significant risk of endometriosis with greater red meat consumption (OR=2.0; CI=1.4–2.8) (Parazzini et al. 2004).

The research also showed that women who eat meat once a day are up to twice as likely to have endometriosis compared with those who eat less red meat and more fruit and vegetables.

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Randomised Controlled Trials following endometriosis surgery



Randomised controlled trials (RCTs) show that dietary intervention (vitamins, minerals, salts, lactic ferments and fish oils) following endometriosis surgery appears to be an effective alternative to hormone treatment that is associated with similar pelvic pain reduction and quality of life improvement

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How to Reduce the Pain & Inflammation



Quality of Life

Quality of life studies undertaken by Huntingdon and Gilmour (2005), show that symptoms of endometriosis impact on many aspects of a woman's life, including work and education, relationships and social functioning.

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Oestrogen dependent pain syndrome



- Endometriosis has elements of a pain syndrome with central neurological sensitization (and has some hallmarks of a neurological disorder) 1
- It is a proliferative, estrogen-dependent disorder (with growing evidence of progesterone resistance) 2
- It appears to be similar to other conditions characterized by pelvic-abdominal pain and infertility

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Loss of endometrial sensitivity to progesterone



- Progesterone has potent anti-inflammatory effects
- Reduced sensitivity to progesterone may contribute to the auto-immune-like nature of endometriosis
- The loss of endometrial sensitivity to progesterone has been recognized as a potential immunologic component of the pathophysiology of endometriosis (Progesterone resistance)
- As progesterone levels fall, pro-inflammatory cytokines play a role in menstruation, leading to high levels of MMP expression and rapid endometrial breakdown.

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Nutrients & Endometriosis Pain



A small trial on patients with dysmenorrhoea by Proctor and Murphy in 2001 showed that fish oils (omega-3 fatty acids) were more effective than placebo for pain relief.

Cellular immunity is reduced in women with endometriosis.

The presence of endometriosis increased oxidative stress, and depletion of anti-oxidants may contribute to excessive growth of endometrial cells.

Research also suggests that vitamins B1 and B6 are beneficial while the use of magnesium also shows some benefit in pain reduction.

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Nutrients known to relieve pain



- Vitamin C
- Vitamin E
- Vitamin K
- Zinc and selenium
- Essential Fatty Acids
- B1 + B6 + B12
- Magnesium
- DL Phenylalanine
- Turmeric
- Pine Bark

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Turmeric



- Turmeric helps to turn off NF-Kappa B
- This is a protein which regulates the immune system and triggers the inflammation process
- Turmeric depletes the neurotransmitter responsible for pain, neuropeptide substance P, and has an analgesic effect that gives pain relief
- Turmeric is a powerful antioxidant which aids the body in fighting free radical damage, it also aids liver function. Regenerating liver cells and stimulates enzymes which flush toxins from the body

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Pine Bark Extract / Pycnogenol



- Pine bark extract is an antioxidant from the bark of the French maritime pine tree
- Research in the Journal of Reproductive Medicine it was seen to significantly reduce the symptoms of endometriosis by 33 percent.
- Pycnogenol 30mg capsules were taken orally twice daily for 48 weeks after breakfast and dinner.
- Pycnogenol slowly but steadily reduced all symptoms from severe to moderate.
- Research showed a reduction of abdominal pain due to endometriosis in 73% of the women in the trial.

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Resveratrol



- Resveratrol is a member of a group of plant compounds called polyphenols
- It may help with insulin resistance
- Animal based studies suggest it may improve the number and quality of oocytes
- It has anti-inflammatory properties that are critical for treating pelvic inflammation as seen with endometriosis
- It has anti-angiogenic properties that inhibit the development of endometriotic lesions
- Resveratrol is found in red wine, berries, fungi, peanuts and legumes

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Nutrients known to relieve pain



- For dysmenorrhoea in the absence of proven endometriosis, one small trial showed fish oil (omega 3 fatty acids) to be more effective than placebo for pain relief
- Limited evidence suggests that vitamins B1 and B6 are beneficial
- The use of magnesium shows some evidence
- Dietary advice to women to eat a healthy balance of nutrient-dense anti-inflammatory foods

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Vitamin E



- It acts slowly to limit inflammation, so needs to be taken regularly 1
- Vitamin E has an analgesic effect because it is able to inhibit pro-inflammatory prostaglandin PGE2 production
- Research has shown that 300 IU per day reduced muscle cramps and pains in the lower back
- Seeds, EV olive oil, green leafy vegetables, whole grain cereals, avocado, salmon, eggs

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Thiamine and pain transmission



- High doses of thiamine (B1) can suppress pain transmission.
- There appears to be some relationship between thiamine and morphine ⁽¹⁾
- Morphine significantly increased the amount of thiamine in the cortical hemisphere by 21%, in the cerebellum by 44% and in the brain stem by 29%
- High doses of vitamin B1 have been reported to produce ganglionic blockade and to suppress the transmission of neural stimuli to skeletal muscles ^(2, 3)
- This effect has been demonstrated in humans using 10-30 mg vitamin B1 intravenously 4 5 6

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Omega 3 and Omega 6 Reduced menstrual pain



- In a group of Danish women, a higher intake of omega 3 fatty acids or a higher ratio of omega 3/omega 6 fatty acids was associated with reduced menstrual pain
- Omega-3 fatty acids encourage the production of helpful prostaglandins that inhibit inflammation
- Omega-3 fatty acids are in green leafy vegetables, legumes, fish, walnut, linseed and hemp oils

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Magnesium and pain reduction



- 1991 British study found that magnesium was useful in chronic fatigue syndrome, improving energy levels and reducing pain in 80% of subjects
- The study used an injection form of magnesium weekly for six weeks, but magnesium may also be taken orally
- Nuts and seeds, buckwheat, millet, garlic, raisins, green peas, green leafy veg, jacket potato, crab, banana, sweet potato, blackberry, broccoli, cauliflower, carrot

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Extra Virgin Olive Oil



- Olives contain oleocanthal, chemically related to ibuprofen.
- University of Philadelphia found that it is a potent anti-inflammatory painkiller ⁽¹⁾
- Pain and inflammation can be triggered in the body when levels of TNF-alpha and interleukin-6, increase
- Studies on olive oil extract shows it reduces both TNF-alpha and interleukin-6 ⁽²⁾

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*Anti-inflammatory foods Eat 3 portions each day



- | | |
|---------------------|-----------------|
| • Berries | • Mackerel |
| • Flax seeds | • Pumpkin seeds |
| • Omega-3-rich eggs | • Salmon |
| • Garlic | • Sardines |
| • Herrings/kippers | • Turmeric |
| • Olives | • Boswellia |
| • Red onions | • Ashwaghandha |

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Sub-fertility and how to improve endometrium and egg quality



- Environmental Reproductive Health
- “This focuses on exposures to environmental contaminants, particularly during critical periods in development (such as prior to conception and during pregnancy), and their potential effects on all aspects of future reproductive life course, including conception, fertility, pregnancy, child and adolescent development”

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Ina May Hobbler
Nutrition and Maternal Health, Proceedings of the First
Conference on Human Nutrition, Ohio State Department of
Health, Columbia, Ohio 1952



- “I would like to emphasize maternity as the frontier of human welfare and that the defence of mothers is the defence of nations.
- There is no place in the public health field that offers greater opportunity for service to mankind and the welfare of the human race than the application of newer and ever increasing knowledge of nutrition at the human frontier “

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Endocrine Disrupting Chemicals



- They also alter the regulation of gene expression (e.g. DNA methylation, RNA stability, protein degradation)
- They target the neuroendocrine system which plays a regulatory and homeostatic roles in the control of human physiology
- Key development stages:
 - 1) conception (gamete and blastocyst),
 - 2) prenatal development (embryo and foetal stages),
 - 3) infancy and childhood.

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Epigenetics



- All kinds of labels get attached to the DNA in our cells as we go through life
- Think of DNA as a recipe book
- Methyl groups are like yellow note stickers
- “Don’t make this”
- “Do make this”
- No stickers or many stickers
- Many are added in the mothers womb
- Cells take on special roles according to the note received

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Epigenetic change: The physiologic response(s) to the continuous interaction between DNA and the environment

Kind permission Kevin Ossten



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The Barker Hypothesis



- Malnutrition and other adverse environmental exposures during development alter gene expression and program the body structures and functions for life
- Embryo plasticity changes during development with indications from nutrient cofactors & coenzymes
- **Physiology develops according to prevailing environment**
- Adverse exposures also result in slow growth and small body size
- Epigenetic changes in ova, sperm, fetus, blastocyst

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Nutrient Support for Methylation and Trans-sulphuration



- Adequate methylation is important in sex hormone balance
- Low levels of methylation results in high levels of gene expression, predisposing towards disease
- High levels of methylation silence gene expression and reduce disease risk
- Vitamins B12, folate, B6 and B2 are used to convert choline to betaine
- Choline - Eggs, lambs liver, oatgerm, soy-beans
- B12 – animal produce
- B6 – meat, lambs liver, oats, corn
- B2 – milk and lambs liver
- Folate – green leafy vegetables and lambs liver
- Iron – lambs liver, red meat, eggs, green leafy vegetables, beans, lentils, nuts, seeds, beetroot, dried apricots
- Betaine – seafood, spinach, oatgerm
- Sulphur – eggs, Brazil nuts, onions, garlic, leeks, cabbage, kale, broccoli

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Rand Jirtle's Experiment



- Simply by slightly altering the diet of a certain type of pregnant mouse (Agouti mice) you can change their offspring from chubby blondes to skinny brunettes; and moreover that this effect of grandma mouse's diet can be passed on for three or more generations until it fades.
- The Agouti gene normally produces a yellow fur pigment, but if it is switched off by methylation-inducing chemicals in food, it produces a brown pigment.
- This reversible inherited change, which does not alter the DNA structure, is the essence of epigenetics.

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Dioxins and endometriosis subfertility



- Reducing toxic exposures is crucial to reduce onset of endometriosis.
- Toxic effects of dioxins and PCBs, phthalates and bisphenol A (BPA) are well known endocrine-disruptors, (xeno-oestrogens), damaging the embryo, foetus and newborns, and women with endometriosis.
- Endocrine-disrupting chemicals (phthalates, BPA, dioxins, PCBs) settle into body fat cells, causing inflammation in endometriosis.

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PCB and Dioxin increase endometriosis severity



- There may be a link between the incidence of endometriosis with exposure to PCB or dioxin.
- Studies on monkeys showed that both chemicals may increase the severity of endometriosis due to the impact they have upon the immune system
- Avoidance of fatty foods (e.g. red meat, dairy), which may contain high levels of PCB and dioxins, may help to reduce the exposure to these chemicals

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Macaque Monkeys



- Fed on dietary dioxin for 5 years
- Developed spontaneous endometriosis
- 71% and 86% monkeys treated with 5ppt and 25ppt dioxin respectively
- 33% of the animals, not exposed to dioxins, also developed minimal disease

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Two dietary mechanisms that help counteract pesticide exposure



- Exposure to TCDD (dioxin) and xeno-oestrogens from contaminated fatty foods such as meat and dairy and treated plants, probably reduces fertility.
- Two dietary mechanisms that may help to counteract these effects are supplementation of:
 - - **cleaned omega-3 fatty acids**
 - - **vitamin B3 (nicotinamide)**
- M K Johnson of the Medical Research Council reported in 1975 that nicotinamide (vitamin B3) was the only nutrient that would take the organophosphate-pesticides out through the liver.

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Mediterranean Diet "reduces birth defects"



- France, Italy and Spain fare significantly better than other nations in avoiding defects such as congenital heart problems and spina bifida
- French 39.7 babies born with birth defects per 1,000 live births (1/2 that of the Sudan, highest in the world)
- 250,000 babies are born with inherited birth defects each year in Europe
- "The Mediterranean Diet" doesn't just prevent heart disease - it seems to have an effect on birth defects too
- It is probably the effect of folic acid, but it is quite possible there are multiple vitamin effects"

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Anti – Inflammatory Diet Mediterranean Diet



- 'Eat food, not too much, mostly plants'
- Avoid highly processed foods high in chemical additives
- Avoid trans-fats – hydrogenated oils
- Eat a Mediterranean anti-inflammatory diet, a variety of fresh fruits and vegetable, white and oily fish, poultry, lamb or game (pasture-fed meats), type 2 dairy foods, organic eggs, nuts and seeds, legumes in moderation, extra virgin olive oil, organic butter and coconut oil, herbs and spices. Fresh nutrient-dense foods.
- Prof. Michael Pollan, University of Berkeley suggests a sound rule is that 'if your grandmother couldn't pronounce and didn't use chemical additives as ingredients in her food, then neither should we'

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Organic food to cleanse the body?



- Research in Australia suggests that organic foods cleanse the body, and whilst it is only a small-scale study, results look promising.
- After eating organic food for one week, pesticide levels were cut by 90 per cent (Oates et al. 2014).
- Thirteen people were given a diet of 80 per cent organic food for seven days, then the diet was changed to seven days on 80 per cent 'conventional' food.
- Urine samples were taken each week on day seven.
- The researchers tested for six chemicals, including organophosphates, and dialkyl phosphates (DAPs).
- The body produces DAPs as it attempts to break down pesticides. In the organic food group, DAP levels were 89 per cent lower than in those eating foods containing pesticides (Oates et al. 2014).

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Avoiding Exposure to Environmental Toxins



- **Dirty Dozen TM**
Highest Pesticide List 2016
Foods testing positive for numbers of different pesticides at high concentrations:
Strawberries, apples, nectarines, peaches, celery, grapes, cherries, spinach, tomatoes, bell-peppers, cherry tomatoes, cucumbers
98% strawberries, peaches, nectarines and apples were positive for one pesticide residue
Potatoes had more pesticides than any other produce
1 grape and 1 bell-pepper contained 15 pesticides
www.ewg.org/foodnews/summary.php

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Avoiding Exposure to Environmental Toxins



Clean Fifteen: TM Lowest Pesticide Exposure

- Foods testing nearly negative for pesticides at low concentrations:
- Avocado, sweet corn, pineapples, cabbage, frozen sweet peas, onions, asparagus, mango, papaya, kiwi, aubergine, honeydew melon, grapefruit, cantaloupe, cauliflower
- Avocado was the cleanest, only 1% showed any pesticides
- 89% pineapples, 81% papaya, 78% mango, 73% kiwi, 62% cantaloupe had no pesticide residues

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12 Steps to Reducing Environmental Exposures



1. **Pesticides:** Avoid use in home and garden. 1st trimester the baby's neural tube and nervous system are forming. CA birth defects monitoring program reports that 3:4 women are exposed to pesticides within the home. J. Environmental Health Perspective Vol.10 says that exposure leads to childhood leukaemia.
2. **Paint:** Avoid exposure to oil based paints, lead and mercury. Latex paints contain ethylene glycol esters and biocides (used to retard mould growth). Children sleeping in rooms with fumes from water-based paints and solvents are 2 to 4 times more likely to suffer allergies and asthma.
3. **Solvents, paint thinners, paint strippers, polyurethane, etc.:** J Am Medical Assoc., reports more malformations in foetus of mothers exposed to solvents. Turps, paint removers, polyurethane flooring should be avoided.

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12 Steps to Reducing Environmental Exposures



4. **Toxic cleaning products:** Avoid oven and tile cleaners, anything with a powerful smell. Good ventilation and protective clothing should be worn. Never mix chemicals together as it creates poisonous fumes. e.g. ammonia and bleach.
5. **Fragrances:** Selected scented consumer products emitted more than 100 volatile organic compounds (VOCs), classified as toxic or hazardous chemicals according to Federal Laws. 10:100 qualify petroleum based fumes dangerous to pregnant women, children and pets.
6. **Plastics:** Phthalates and Bisphenol A: BPA is oestrogenic, causing heart disease, obesity, diabetes, reproductive problems in lab animals. BPA is in the lining of tin cans, hard and clear plastics that are say 7 or PC on the base. Phthalates are endocrine disruptors, used to soften plastics, shower curtains, toys, flooring, and enhance fragrances and scents. They mimic testosterone. Seen to cause reproductive abnormalities in rats.

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12 Steps to Reducing Environmental Exposures



7. **Teflon-coated cooking utensils:** A 2005 study found PFOA (perfluorooctanic acid), in the umbilical cords of newborns. In 2006 John Hopkins Centre found PFOA in umbilical blood of 99% of 300 tested infants. It is a carcinogen in teflon-coated pans and **fabrics like children's school clothing**.
8. **Cell phones:** Pregnant women should not keep cell phones turned on close to their bodies. Use a wired earpiece.
9. **Cat litter:** Cats carry parasitic toxoplasmosis, living in their intestines. Pregnant women should wear gloves and masks. Depression, hearing loss and developmental delays are reported.

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12 Steps to Reducing Environmental Exposures



10. **Fish containing mercury:** Avoid swordfish, tuna (bigeye, ahi). Eat no more than three 6oz servings per month of bluefish, grouper, canned white albacore tuna. Eat no more than six 6oz servings per month of bass, cod, halibut, lobster, mahi-mahi, snapper.
11. **Artificial sweeteners:** Use in moderation. Saccharin crosses the placenta and may remain in foetal tissue. Aspartame avoid.
12. **Clean air and adequate ventilation:** Well ventilate homes.

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Alcohol



- Alcohol may result in a rise in oestrogen, which reduces FSH secretion suppressing folliculogenesis and ovulation
- It has an effect upon ovum maturation, ovulation, blastocyst development and implantation
- An 18 year study involving 7,393 individuals found that high alcohol consumption was associated with increased risk of infertility and endometriosis
- A meta analysis found an association between the consumption of alcohol with the development of endometriosis – 1gm fat= 7 calories, creates fat

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Multi-Vitamin-Mineral use



- In Hungary 8,000 women planning a pregnancy took a multi-vitamin-mineral.
- 50% took 12 vitamins and 7 minerals
- 800mcg folate, 60mg iron
- 50% took Cu, Mn, Zn, Vit C only
- Half as many congenital defects were seen in the Multi-Vit-Min group as in the trace element group
- 71.3% were pregnant over the year, with more twins born in the Multi-Vit-Min group

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Diet and IVF outcome?

UNIVERSITY OF Southampton School of Medicine

ARTICLE IN PRESS

The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/ intracytoplasmic sperm injection treatment increases the chance of pregnancy

Marijana Vujkovic, B.Sc., Jeanne H. de Vries, Ph.D., Jan Lindemann, Ph.D., Nick S. Makin, Ph.D., Peter J. van der Spiek, Ph.D., Eric A. P. Steegers, Ph.D., and Regine P. M. Steegers-Theunissen, Ph.D.

Fertil Steril 2010

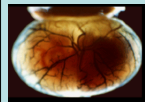
- 161 women undergoing IVF/ICSI
- Validated dietary questionnaire

DIET: 'Health conscious' 'Mediterranean'		
Blood Folate	+	+
Blood Vit B6	+	+
Follicle Vit B6	+	+
Chance of pregnancy	+	OR 1.4 (1.0-1.9)

Kind permission Nick Macklon, University Southampton

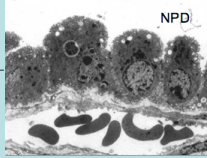
Maternal LPD induces responses in the visceral yolk sac

LPD = low-protein diet; NPD = normal protein diet



LPD increases numbers of endocytic vesicles

Endocytic vesicles per area (µm²)	NPD	LPD
~10	~25	~45



LPD increases rate of endocytosis

ci	LPD	NPD
~10	~25	~15

Day 17 P<0.05 Mother

Kind permission Tom Fleming, Southampton University

Does changing a patient's dietary consumption of proteins and carbohydrates impact blastocyst development and clinical pregnancy rates from one cycle to the next?

- Seemingly young healthy patients with poor embryo development can possibly increase the percentage of blastocyst formation by increasing their daily intake of protein and lowering their daily carbohydrate intake 3 months prior to their IVF cycle.
- 12 women average 35 years of age BMI 26.5
- Blastocyst formation increased significantly from 18.9% to 45.3%
- Clinical pregnancy rates increased from 16.6% to 83%

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Protein Rich Foods

Animal and Plant sources

- Lean meat
- Poultry
- Game
- White fish
- Oily fish
- Shell fish
- Eggs
- Dairy foods
- Legumes/Pulses
 - Peas
 - Beans
 - Lentils
- Nuts/Seeds
- Variety of red/green Vegetables
- Spirulina
- Chlorella
- Cereals

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The Responsibility of Motherhood

MOTHER

EMBRYO (~5 days)

Maternal-embryonic communication regulates:

- Features of blastocyst morphogenesis
- Coordination of implantation
- Maternal immunotolerance
- Developmental plasticity – 'selecting' the right phenotype to fit the anticipated future environment

Implications: DOHaD; ART, maternal health at conception

Kind permission Tom Fleming, Univ Southampton, UK www.fertilityclinic.com

Critical window of foetal development.

Weeks of gestation												
← Embryonic period (weeks) →						← Foetal period (weeks) →					Term	
1	2	3	4	5	6	7	8	12	16	20-36	38	
Implantation												
Central nervous system												
Heart												
Arms												
Eyes												
Legs												
Teeth												
Palate												
Germ Cells												
External genitalia												
Ears												

Critical window of foetal development. (Adapted from Selevan et al. (2000). Derbyshire.E. Nutrition in childbearing years. 2011.Wiley-Blackwell. P172.Critical window of foetal development. ©The Endometriosis and Fertility Clinic

1926
Derbyshire

How the Mid-Victorian Ate

- High level physical activity (>4000 calories/day)
- High intake: Omega-3, pre-biotic fibre, whole grain
- Fruits and vegetables: 10 or more portions/day
- Low intake: salt/alcohol
- Very low intake: tobacco, spirits, processed foods
- A super-Mediterranean diet

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Mid-Victorian diet rich in...



- Phase-2 upregulators (watercress, brassica)
- Innate immuno-primers (e.g., 1-3, 1-6 b-g)
- Anti-inflammatory compounds (various)
- Prebiotics (Jerusalem artichokes, chicory)
- Re-differentiators - inhibit cancer cell lines (beta-glycans)
- Mid-cell cycle arresters (onions)
- Apoptosis-inducers (fruit/vegetables, bitter varieties)
- Matrix stabilizers/angiostats-prevent cancers (low meat, butyric acid)
- 1919-1939: processed foods start to be used by the middle class
- World War II: Dig for Victory, rationing
- 1950: processed foods increase

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Rainbow Meals for Phytochemicals



- Flavonoids & Indoles: Dark green leafy vegetables
- Carotenoids: Red vegetables
- Proanthocyanidins: Blue-black-red berries/fruits
- Eicosapentanoic acid: Oily and white fish
- Lean meat free-from hormones ie. organic pasture-fed
- Ellagic acid: Nuts, seeds, pulses/legumes, raspberries
- Unhydrogenated oils: linseed, olive, hemp, evening primrose
- Lycopene - carotenoid antioxidant - does not produce Vit A in the body, but is protective against cancer
- Canthaxanthin - carotenoid family, protects against cancer
- Lutein - antioxidant carotenoid in tomato, red pepper, pink grapefruit

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Surprising origin of the gut flora in newborns



- Until recently it was thought that babies were born with a sterile gut, picking up microbes via their mother's vagina during birth
- Bacteria were found in the meconium - the babies first stool passed within hours of birth
- The DNA of the bacteria in the placenta was sequenced from 320 women after the birth. A broad range of bacteria were found, including those necessary for metabolising nutrients needed by the foetus
- **Surprisingly the bacterial species were most similar to those normally found in the adult mouth, as opposed to the vagina or gut.** They must travel via the bloodstream crossing the blood placental barrier or by passing into the amniotic fluid and being swallowed by the foetus

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*Surprising origin of the gut flora in newborns



- Women who had given birth prematurely before 37 weeks had different amounts of some bacterial species.
- Previous studies found that gum disease raises the risk of premature birth. Harmful bacteria may therefore colonise the placenta triggering an early birth. A high fat diet also changed the bacterial makeup
- [ScienceTranslationalMedicine.doi.org.sv5](https://doi.org/10.1186/s12916-015-0355-5)

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How crucial the microbiome is in its role of breaking down oestrogen and excreting it from the body



- Endometriosis implants produce their own oestrogen, implants 'feed' on oestrogen and proliferate
- Every fat cell produces oestrogen
- The ovaries and adrenals produce oestrogen
- Plants contain phyto-oestrogens
- Pesticides, plastics (bisphenol A & phthalates) contain oestrogen mimics - xeno-oestrogens
- Oestrogen dominance is common with endometriosis, along with progesterone resistance, causing hormone imbalance

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OESTROGEN METABOLISM IN THE GUT



- Healthy gut flora and liver enzymes break down the used oestrogen into a safe form ready to be bound to soluble fibre such as oats, vegetables, (wheat is insoluble fibre) within the gut.
- Safe forms of oestrogen can be excreted from the body in stools.
- Blood-levels of oestrogen are affected by activity of bacterial enzymes in the intestine and drop significantly when their activity is reduced (Gorbach and Goldin 1992).
- If oestrogen remains in the body it can cause havoc.
- Eating green leafy vegetables containing indoles and soluble fibres reduces oestrogen levels.
- Oestrogen excess acutely inhibits the rate of thyroxine release from the thyroid in adults, but any effect appears to be transient (Gambert 1991).

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Anti-Thyroid Foods – Goiters: Contain High Oxalates – these interfere with calcium absorption and can affect nerve conduction



Eat only vegetables and fruits that have been cooked, this prevent the goiters worsening hypothyroid problems.

Cook all before eating

- | | |
|-------------------|----------|
| • Soya | Wheat, |
| • Cabbage | Broccoli |
| • Brussel sprouts | Turnips |
| • Kale | Spinach |
| • Peaches | Pears |

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Effects of Gut Flora on Immunity and CNS



There are 300 billion bacteria living inside our small intestinal gut flora and they collectively express 100-fold more genes than the human genome (Rabizadeh and Sears 2008).

80% of immunoglobulins are produced at the gut membrane, immune cells,

The Human Genome Project showed that **man has 23,000 genes** which we inherit from our parents

The healthy gut flora passengers (good bacteria), in our **microbiome contains at least four million genes** (Nicolle 2007).

Damage to the gut membrane by gluten/gliadin alters the way gut flora behave.

Research suggests that gut bacteria may even alter our brain chemistry, affecting moods and behaviour (Blaser and Falkow 2009).

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Dietary Fibre & Oestrogen Excretion



- Dietary fibre increases excretion of excess oestrogen from the body; fibres such as lignins in nuts and seeds are changed by gut flora to form anti-oestrogen compounds, which protect against cancers (Stock 1995) ...and probably endometriosis?
- Safe forms of oestrogen can be excreted from the body in stools. But if oestrogen remains in the body it can cause havoc.
- Blood-levels of oestrogen are affected by activity of bacterial enzymes in the intestine and drop significantly when their activity is reduced (Gorbach and Goldin 1992).
- Eating green leafy vegetables containing indoles and soluble fibres reduces levels.

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Fibre-Rich Foods Eat 50mg fibre rich foods daily



- | | |
|----------------|--------------------|
| • Blueberries | • Almonds |
| • Bilberries | • Pumpkin seeds |
| • Pears | • Flaxseeds |
| • Carrots | • Oats |
| • Blackberries | • Coconut |
| • Strawberries | • Vegetables |
| • Raspberries | • Pulses |
| • Walnuts | • Corn |
| • Millet | • Brown rice |
| • Buckwheat | • Green vegetables |

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Sex-hormone-binding globulin & oestrogen



- Eating moderate saturated fats and cold pressed cis-oils is vital for steroid hormone production and fat-soluble vitamin storage.
- Soluble fibre binds to oestrogen and inhibits its reabsorption.
- 'Good quality fibre encourages a hormone known as SHBG...
- Whilst oestrogen is bound to the SHBG, it cannot exert any biological effect within the body' (Cowan 1981).
- If fibre intake is low then the oestrogen has a biological effect, triggering endometrial implant growth.
- Vegetarian, low-fat diets reduced period pain and increased SHBG (Barnards et al. 2000).

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Beta Glucuronidase and Oestrogen



- Bifidobacteria encourage oestrogen clearance by inhibiting an enzyme known as beta glucuronidase. It uncouples the bond between the excreted toxin and glucuronic acid - which can increase cancer risk
- When beta glucuronidase is too high it encourages the deactivated safe oestrogen to become reactivated so that it can be sent back into circulation (not a good idea for endometriosis).
- The activity of this enzyme can be reduced by establishing proper bacterial flora using a probiotic of 4 billion viable L acidophilus and B bifidum
- Eat foods such as onions, chicory, J artichokes, asparagus, bananas, maple syrup to encourage good gut flora
- (Shepperson-Mills and Vernon 2002).

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Enzyme Rich Foods To aid digestion & absorption



- Pineapple – Bromelain
- Papaya – Papain
- Sauerkraut - made from fresh
- Wild Salmon – Proteases
- Yoghurt - from grass-fed animals
- Avocado - lipase-like
- Alfalfa –lipase
- Amylase
- Pectinase-like enzymes
- Coconut - kefir contains enzymes
- Banana - when fresh

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Naringenin flavonoid in citrus fruits Optimising liver detoxification of oestrogen



- Naringenin is a flavonoid in citrus fruits (orange, grapefruit)
- - biological and pharmacological effects - Phytoestrogenic & antioxidant
- - oestrogen activities at low concentrations,
- - anti-oestrogenic activities at high concentrations.
- - ligand-dependent activation of oestrogen receptors in osteoblastic cells
- -has an inhibitory effect on human cytochrome P450 - CYP1A2, slowing down phase 1 enzyme activity (in liver)
- -inhibits aromatase and interacts with oestrogen receptors
- Citrus fruits are high in naringenin - it prevents liver enzymes breaking down oestrogen ready for excretion
- Eat small amounts only of lime and lemon, tart cherries, cocoa, Greek oregano, tomatoes, bergamot.

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Vegetarian Diets



Vegetarian women excrete 2–3 times more oestrogen in their stools and have 50 per cent lower free oestrogen in their blood compared with meat eaters.

High-fibre diets may help explain lower pre-menstrual-syndrome symptoms, as excess oestrogen binds to soluble fibre and can then be excreted from the body (Goldin *et al.* 1982).

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Saturated Fats and Hormone Balance Cis and Trans Fatty Acids



Diets high in saturated animal fat are seen to increase concentrations of serum oestrogen, so eating in moderation is important (Nagata *et al.* 2000).

Studies by Goldin *et al.* in 1982 have shown - that women with the highest intake of red meat increase their risk of endometriosis by between 80 and 100 per cent, while those with the highest intake of fresh fruit and vegetables lowered their risk of endometriosis by 40 per cent.

Reducing consumption of foods high in saturated fats and replacing them with fruit and vegetables such as broccoli, cauliflower and cabbage, which contain indoles (compounds that break oestrogen down), improves oestrogen metabolism (Goldin *et al.* 1982; Gorbach and Goldin 1987).

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Do foods cause endometriosis?



- Harvard School of Public Health have shown that women who have 2 or more cups of caffeinated coffee (4 cans of cola) per day were found to be twice as likely to develop endometriosis as other women
- 1992 German research found that women with high blood levels of PCBs (polychlorinated biphenyls) had a higher prevalence of endometriosis
- Pesticide chemicals weaken the immune system. The natural killer cells and other white blood cells that are meant to watch for abnormal cells have been shown to be less effective in women with endometriosis
- PCBs show up in fish, chicken, cattle, pigs - animals that are fed grains contaminated with organochlorines that concentrate in their organs and tissues; these may also be on non-organic fruits and vegetables. GM soya & GM wheat pellets are associated with development of enlarged uterus in animals

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Cruciferous Vegetables - Indoles Oestrogen metabolism



Eating vegetables from the cruciferous family, rich in B complex vitamins and magnesium, such as cabbage, sprouts, broccoli, cauliflower, kale, turnip, swede, radish, horseradish, mustard and cress, is protective.

Brassica vegetables contain three compounds – indoles, dithiolethiones and isothiocyanates. These influence liver enzymes that rev up the body's degradation system, so that oestrogen is 'metabolised' and ultimately excreted from the body.

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Sources of Indoles (for deactivating oestrogens):



Eat more of these foods with endometriosis, breast cancer.

- Cabbage
- Turnip
- Kale
- Cauliflower
- Rapeseed
- Sprouts
- Broccoli
- Peel – avocado – banana
- Mustard
- Garlic & Onion
- Olive oil
- Horseradish, chamomile, passiflora

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Foods to Cleanse Liver enzyme support



- Avocado
- Raw coconut cream
- Flaxseeds
- Sauerkraut
- Chicory
- Jerusalem artichokes
- Fresh vegetable juice
- Blueberries
- Cucumber
- Tomatoes
- Live Kefir and Yoghurt
- Coconut Kefir and yoghurt

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Fatty acids & Plant Fibre to Reduce Oestrogen Levels



Women should reduce their saturated and trans- fatty-acid intake by half, then oestrogen levels would be 20 per cent lower.

This research advised the use of oily fish, nuts, seeds, dark leafy vegetables, cold-pressed extra virgin olive and walnut oils.

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What to eat, what to avoid/reduce plus which supplements may be helpful



- The judicious use of nutritional supplements whilst the diet is being corrected may improve reproductive health.
- Harvard University and the American Dietetics Association both advise that a multivitamin- mineral should be taken each day
- Basic supplements were used for one month, then changes made were reviewed monthly.
- Studies have suggested that users of micronutrient supplements achieve a higher pregnancy rate

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Endometriosis and Hypothyroidism



- Hypothyroidism is a significant risk factor for infertility, especially in women with endometriosis
- High oestrogen invites cancer (and endometriosis), whereas normal oestrogen lessens its development.
- Oestrogen and thyroxine (built from iodine) have to be in balance in the body. Oestrogen excess acutely inhibits the rate of thyroxine release from the thyroid in adults, but any effect appears to be transient (Gambert 1991).
- Eating iodine contained in fish or seaweed in a healthy diet is important as it is a precursor to thyroxine production and so is vital for thyroid function.

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Healthy Gut Flora & Crohn's Disease



- Healthy gut flora are crucial for oestrogen metabolism in the intestine and liver.
- Changes in women's sex hormone profile can make the gut lining more permeable and reduce levels of 'friendly' bacteria in the intestines, thus disrupting immune system function.
- Research by Khalili et al 2013, a Harvard gastroenterologist, suggests that in susceptible women with high-risk genes, taking the contraceptive pill triples the risk of Crohn's disease, in one in every 650 people. Cohort 1500 women.
- The OCP is taken by 3.5 million women at present in Britain.
- Research is needed in women with endometriosis to look at this area.

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Prevalence of nutrient deficiencies in patients hospitalised for irritable bowel diseases



Deficiency	Prevalence %
Iron deficiency	40
Low serum B12	48
Low serum folate	54-64
Low serum magnesium	14-33
Low serum potassium	6-20
Low serum retinol	21
Low serum ascorbate	12
Low serum 25-OH D (Vit D)	25-65
Low serum zinc	40-50

• Low levels of vitamin K, copper, niacin and vitamin E have also been reported

• Why not test for nutrient deficiencies in endometriosis patients? Look for commonalities

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Gluten links to Endometriosis and infertility



- Gluten intolerance refers to a category of gluten issues:
- Non-coeliac gluten sensitivity - causes the body to mount a stress response
- Wheat allergy - causes an immune reaction to wheat gluten
- Coeliac disease is an inherited genetic auto-immune disorder which causes an immunological response to trigger intestinal tissue damage
- Studies show that infertility could indicate early autoimmune changes, (gluten intolerance, maybe clinically silent coeliac disease. In Iran positive results were detected in 13 infertile couples (6.5%).

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Coeliac Disease and Endometriosis



- Two studies by researchers in Sweden have shown that compared with controls, after a review of 11,000 women with coeliac disease, CD women were found to have a much higher risk of endometriosis, especially in the first year after diagnosis with coeliac disease (overall hazard ratio 1.39).
- They postulate that the shared inflammatory process was seen in both disorders.

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Coeliac Disease and Endometriosis



- Brazilian researchers, found that 2.5% of women diagnosed with endometriosis also had coeliac disease.
- Research by Shepperson Mills (2011a) showed that 85 per cent of women whilst off wheat/gluten for three months reported that their endometriosis pain was reduced by fifty per cent. On a coeliac GF diet periods become much lighter, the blood is a healthy red rather than a sludgy brown, and clots lessen and pain becomes more like a normal mild cramp rather than a severe tearing pain.

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Endometriosis and Coeliac Disease



- Endometriosis is associated with having the HLA-DQ2 and HLA-DQ8 genes (which are also present in approximately 96% of patients with coeliac disease), as well as the DQ7 gene, which has been associated with Coeliac Disease in some Southern Italians, Sicilians and Sardinians.
- CD is triggered by gliadin protein antigen, zonulin is then expressed.
- Zonulin regulates the permeability and integrity of epithelial tissue in the body
- Gliadin affects zonulin expression even in people without the gene for CD

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Endometriosis and Coeliac Disease



- A gluten-free diet has recently been recommended as a strategy to manage the pain of endometriosis. A study by Marziali (2012) in Italy shows that painful symptoms of endometriosis decrease after 12 months on a gluten-free diet. Two hundred and seven patients entered the study, diagnosed with endometriosis and chronic pelvic pain.
- After 12 months, 75 per cent of the patients reported a statistically significant change in painful symptoms. Twenty-five per cent reported improvement of symptoms, and no patients reported worsening of pain. This strongly suggests that gluten sensitivity and/or Coeliac Disease play a role in endometriosis.

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Food Rules



1. **Eat food, Not too much, Mostly plants**
1. Pollan M, Food Rules: an eaters manual. Penguin Books 2009.
2. **Balance gut flora – balance oestrogen**
3. **The fresher the more nutrient dense**
4. **Variety means more nutrients ingested**
5. **Eat in moderation, eat freshly prepared**
6. **Avoid or reduce sugar, trans-fats, alcohol, caffeine, excess packet foods**

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Healthy Eating Guidelines



- Reduce saturated fat by using Extra Virgin olive oil, nuts, seeds and avocados
- Eat oily fish two to three times each week for EPA and DHA
- Eat a handful of mixed nuts and seeds daily for ALA and LA
- Avoid trans and hydrogenated oils and refined sugars
- Eat green leafy vegetables to support oestrogen detoxification in the liver; plus red, legume and root
- Eat two portions of fruit daily, especially berries

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Healthy Eating Guidelines



- Eat non-gluten grains, rice, corn, millet, buckwheat, WFGF oats
- Eat high sulphur foods (eggs, lean meat, onions, garlic, brassicas) in moderation.
- Eat foods to support healthy gut flora
- Low glycaemic, fresh nutrient-dense foods, 30 gm protein daily
- Eat rainbow meals: red, orange, yellow, green, blue, black foods daily

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Foods to Eat Raw Eat a plate of raw salads daily



- | | |
|--------------------------------|--------------------------------|
| • Green leafy salad vegetables | • Watermelon |
| • Fresh berries | • Cantaloupe melon |
| • Seeds – sunflower – pumpkin | • Live natural yoghurt & kefir |
| • Carrots | • Avocado |
| • Coconut | • Nuts – almonds – walnut |
| • Celery | – pecan |

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Drug Induced Nutrient Depletion



- **NSAIDS** (ibuprofen, mefenamic acid, naproxen) deplete - folic acid and iron. Pregnancy risk factor B (D month 6-9)
- Take with food to decrease gastrointestinal (GI) irritation, heartburn, vomiting, abdominal cramps and pains, peptic ulcer, GI bleeding, GI perforation, fluid retention and indigestion
- **OCP** deplete the body of folic acid, vitamin B2, vitamin B6, vitamin B12, vitamin C, magnesium and zinc.
- OCP - take alongside a basic multi-vitamin-mineral
- Omega-3 fatty acids, bioactive food-derived substances, impart a unique safety and efficacy profile in reducing inflammation compared to NSAIDS

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Nutritional Supplements



- **Multivitamin-mineral**, 1 per day at Breakfast
- (low-dose Vitamin A, 25mg B complex, no iron)
- ***Omega 3 Fish oil** (1,200mg 5:1 DHA/EPA) 1 Breakfast, 1 Dinner (or an omega 3 Linseed oil if vegetarian)
- Magnesium malate or citrate (116mg), 1 at dinner (supports energy in Krebs cycle)
- Acidophilus (1 billion acidophilus, 300mg glutamine), 1-2 a day
- Slippery elm (600mg), 1-2 a day
- The choice has to be the best quality supplements, made free from wheat, gluten, lactose, sugar, yeasts. Capsules not tablets, free from excipients (which may trigger immune system reactions and inflammation).

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Conclusion



- The role of nutrition in women at risk of endometriosis should be included in published guidelines.
- This could be helpful not only for the patient's themselves but also for their daughters.
- Nutritional counseling should be an important component of multimodal therapy in patient's with endometriosis. Especially in women who desire pregnancy or have other contraindications to oral contraceptive use, nutritional counseling, offers patient's a self-determined alternative tool.

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Michael Murray Bastyr University



“It's crazy not to care about how you treat your body, it's the only one you are going to get”

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Integrative Healthcare & Applied Nutrition

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The image displays three book covers. The first is 'endometriosis: A KEY TO HEALING AND FERTILITY THROUGH NUTRITION' by Dian Shepperson Mills MA & Michael Vernon PhD FRCO. The second is 'MAKING BABIES THE NUTRITION RECIPE' by Dian Shepperson Mills. The third is 'INTEGRATED APPROACHES TO INFERTILITY, IVF AND RECURRENT MISCARRIAGE A HANDBOOK' edited by JUSTINE BOLD and SUSAN BEFFORD.

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