Learning Outcomes

On successful completion you will be able to:

• Explain the structure and function of the female reproductive system.

• Identify symptoms of imbalance in female reproductive system.

• Identify the causes of imbalance in the female reproductive system.

• Evaluate orthodox medical and nutritional therapy approaches to modulating pathologies within the female reproduction system.

• Show awareness of the importance of referral with ‘Red Flag’ symptoms.
Revision of the Menstrual Cycle

http://embryology.med.unsw.edu.au/wwwhuman/MCycle/images/Mcycle.GIF
Female Reproductive Organs

www.kensbiorefs.com/NewHumPhy.html
Female Reproductive Organs

- Fimbriae
- Ovary
- Fallopian tube
- Urinary bladder
- Pubic bone
- Clitoris
- Labium minorus
- Labium majorus
- Urethra
- Perineum
- Vagina
- Suspensory ligament
- Uterus
- Rectum
- Buttock
- Cervix - the entrance to the womb
- Anus
Oestrogen Revision

- Produced by the ovary and the adrenal glands.

- 3 main oestrogens:
  - Oestradiol: Active form
  - Oestrone: Acyclic
  - Oestriol: Weak form for excretion- present in high amounts during pregnancy

- Oestrogen’s main role is to increase the growth of cells in places where there are oestrogen receptors (proliferation)

The Story of Oestrogen
Sex Hormone Binding Globulin

- Oestradiol is transported by SHBG in the blood stream.
- This is also responsible for binding testosterone.
- Made in the liver- it is upregulated when there is a high amount of free oestrogens and a low amount of testosterone.

The ovaries secrete oestradiol after the period as FSH starts to develop the follicles.

Some oestradiol is converted to oestrone which is weaker in action.

Both stimulate growth via binding to oestrogen receptors.

Ovarian oestrogens reach a peak just before ovulation then stay stable until a drop just prior to menstruation.

Aromatase

- Oestrogen also comes from a peripheral conversion of androgens to oestrone via aromatase (aromatisation).

- Aromatase is a CYP450 enzyme that is mainly found in the gonads, brain, adipose tissue, placenta, blood vessels, skin, bone, and endometrium, as well as in tissue of endometriosis, uterine fibroids, breast cancer, and endometrial cancer.

Aromatase

• Oestradiol is then converted in to one of three metabolites by enzymatic conversion
  – 2-hydroxyestrone
  – 4-hydroxyestrone
  – 16-hydroxyestrone

• An elevated amount of the 4 and 16-OH oestrone has been associated with a higher risk of breast cancer due to its toxicity and reactivity, but there is contention about this theory.

Jones D (2006) Textbook of Functional Medicine, The Institute of Functional Medicine, WA,USA, Chapter 19; Bethany Hays
Conversion of Oestrogen

- Occurs in the CYP450 pathway via CYP1A1 (2-OH), CYP1B1 (4-OH), CYP2C and 3A4 (16-OH)

- Then phase two pathways mop up the molecule to a water soluble molecule that is excreted via urine or bile.

- Phase 2 conjugation can either be sulfation, methylation or glucoronidation

Jones D (2006) Textbook of Functional Medicine, The Institute of Functional Medicine, WA,USA, Chapter 19; Bethany Hays
Conversion of Oestrogen

- Sulfation: Adds to the circulating oestrogen pool as it can be de-sulfated by sulfotransferase to then be used again.

- Methylation: Produces 2-methoxyoestrogen which appears to have a protective quality. Methylation is modulated by the B-Vitamins (5MTHF).

- Testing for homocystiene levels can check for the methylation activity, or checking for polymorphisms of folate metabolism (MTHFR).
Conversion of Oestrogen

- Glucoronidation- via UDP-glucuronyltransferase (UGT). Once glucuronidated it is excreted via the bile to the small intestine. In the presence of imbalanced bowel flora (excess beta-glucuronidase production) the metabolites become de-conjugated and re-absorbed in to the entero-hepatic circulation.

- Symbiotic bacteria, d-glucurate and adequate fibre will improve excretion of oestrogens.

- All remaining circulating oestrogen eventually passes through the kidney where it is changed into a weak form called oestriol, which is excreted in the urine.

Jones D (2006) Textbook of Functional Medicine, The Institute of Functional Medicine, WA,USA, Chapter 19; Bethany Hays
Progesterone

• 21-carbon steroid manufactured by the adrenals in small amounts, the corpus luteum of the ovaries in large amounts and by the placenta by massive amounts.

• Progesterone mainly as a role in maintaining a healthy pregnancy but it also has been shown to:
  – Down regulate oestrogen receptors
  – Inhibit oestrogen transcription
  – Effect cellular adhesion
  – Effects local oestrogen conversion
  – Effects sulfation
• Hans Selye in the 1940’s discovered that progesterone and some of its metabolites have anaesthetic qualities- via the GABA receptor in the brain.

• This is thought to be the link between the effect of progesterone and CNS activity.

• Different metabolites can effect the brain adversely, while others can induce a feeling of wellbeing.

• Progesterone is a highly potent antagonist of the mineralocorticoid receptor.

• It prevents MR activation by binding to this receptor with an affinity exceeding even those of aldosterone and other corticosteroids such as cortisol and corticosterone.
• An ELISA method for measuring 2- and 16-alpha-hydroxylated oestrogen (OHE) metabolites in urine is available and the ratio of urinary 2-OHE/16-alpha-OHE (2/16-alpha ratio) may be a useful biomarker for oestrogen-related cancer risk.

• Genova diagnostics offers urinary excretion tests.

• Recent reviews have disputed the clinical value of the 2/16 ratio, and whether or not it is worth doing. For the other side of the argument, see here: http://www.townsendletter.com/Jan2013/estrogen0113.html?goback=%2Egde_4633986_member_245033129

Reducing Oestrogen Metabolites

• Adequate fibre (soluble and insoluble) will bind to conjugated oestrogens to remove them from the diet
  – Pectin
  – Rice bran
  – Slippery elm
  – Pysillum husks

Jones D (2006) Textbook of Functional Medicine, The Institute of Functional Medicine, WA, USA, Chapter 19; Bethany Hays
Reducing Oestrogen Metabolites

• Normal bowel flora is important for preventing the de-conjugation of excreted oestrogens.

• Using the 4 R/5 R program (weed, seed, feed) may be prudent.

• Species can include but not be limited to:
  – Lactobacillus Acidophilus
  – Lactobacillus rhamnosus
  – Lactobacillus bifidobacterium
  – Streptococcus thermophilus
Reducing Oestrogen Metabolites

- Ensuring liver detoxification pathways are working correctly:
  - CYP1A1 can be upregulated by the glucosinolates (such as indole-3 carbinol) which will then produce more of the 2-OH oestrogen.
  - Methylation can be increased by supplementing the B vitamins- 5-MTHF (folic acid), B12 and B6.
  - Glucuronidation can be increased by supplementing calcium d-glucurate.
Hormone Disruptors

- ‘An exogenous agent that interferes with the production, release, transport, metabolism, binding, action or elimination of natural hormones in the body responsible for the maintenance of homeostasis and the regulation of developmental processes’ (Kavlock et al. 1996)

Sources:
- DDT
- Chlordane
- Endosulphane
- Phtlalate plastacisers from plastic food packaging
- Poly-chlorinated biphenyls (PCB’s)
- Nonyl-phenol
- Food colour red no.3

Jones D (2006) Textbook of Functional Medicine, The Institute of Functional Medicine, WA, USA, chapter 19; Bethany Hays
Endocrine Disruptors in Soft Plastics

- This provides first evidence that substances leaching from plastic food packaging materials act as functional oestrogens in vivo.

- Our results demonstrate a widespread contamination of mineral water with xenoestrogens that partly originates from compounds leaching from the plastic packaging material.

- These substances possess potent oestrogenic activity in vivo in a molluscan sentinel.

- Overall, the results indicate that a broader range of foodstuff may be contaminated with endocrine disruptors when packed in plastics.
## Endocrine Disruptors in Soft Plastics

<table>
<thead>
<tr>
<th>Group</th>
<th>Chemical</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elements</td>
<td></td>
<td>Cadmium, Lead, Mercury, Arsenic</td>
</tr>
<tr>
<td>Detergents</td>
<td>Alkyphenols</td>
<td>Spermicide, Wool washing detergent, Car washing detergents</td>
</tr>
<tr>
<td>Pesticides</td>
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<td>Lindane, Metiram, Mirex, Aldrin, Dieldrin, Endrin, Endosulfan, Captan, Aldicarb, Toxaphene</td>
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<tr>
<td>Insecticides</td>
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<td>Chlorpyrifos, DDT, Deltamethrin, Dimethoate, Carbofuran, Amitraz, Trichlorfon, Chlordane</td>
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<tr>
<td>Drugs</td>
<td>Estradiol</td>
<td>Hormone replacement pills, Contraceptive pills</td>
</tr>
<tr>
<td></td>
<td>Estropipate</td>
<td>Hormone replacement pills</td>
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</tbody>
</table>
## Endocrine Disruptors in Soft Plastics

<table>
<thead>
<tr>
<th>Group</th>
<th>Chemical</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plastics</td>
<td>BPA</td>
<td>Lightweight plastics—reusable food and drink containers, CDs, DVDs, Electronic equipment, Automobiles, Sport safety equipment, Carpets</td>
</tr>
<tr>
<td></td>
<td>Epoxy Resins</td>
<td>Circuit boards, Paints, Adhesives, Coatings on inside of metal cans, Coatings on water pipes</td>
</tr>
<tr>
<td></td>
<td>Phthlates</td>
<td>PVCs, I.V. Bags, Antibacterial toothpaste, Dummys</td>
</tr>
<tr>
<td></td>
<td>Nematocides</td>
<td>Flame retardants</td>
</tr>
<tr>
<td></td>
<td>Parabens</td>
<td>Cosmetics, Antibacterial agents, Jams and Jellies, Soft drinks, Frozen dairy desserts</td>
</tr>
</tbody>
</table>
### Endocrine Disruptors in Soft Plastics

<table>
<thead>
<tr>
<th>Group</th>
<th>Chemical</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Styrenes-</td>
<td>Cigarette smoke, Auto exhaust, Picnic utensils, Envelope windows, Egg cartons, Insulation</td>
</tr>
<tr>
<td></td>
<td>PCBs</td>
<td>Transformer fluid, Capacitors, Lubricants</td>
</tr>
<tr>
<td></td>
<td>Dioxins</td>
<td>Paper manufacturers, Incinerators, Water treatment</td>
</tr>
<tr>
<td>Fungicides</td>
<td>Carbendazim, Benomyl, Vinclozolin, Penconazole, Prochloraz, Tridemorph, Epoxyconazole</td>
<td></td>
</tr>
<tr>
<td>Herbicides</td>
<td>Atrazine, Linuron, alachor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alkylphenols</td>
<td>Paints</td>
</tr>
</tbody>
</table>
Further Reading

• There are various websites on hormone disruptors and their effects.
• Numerous studies have shown links with the increase of fertility issues in men (poor sperm production) and possible involvement with oestrogen dominant cancers.
• Avoidance is prudent- especially in women that have high risk of breast cancer.
• http://www.breastcancerfund.org/clear-science/environmental-breast-cancer-links/food/
Phthalates and Sperm Count

• ‘We decided to study the effect of endocrine disruptors on human fetal testis and, more particularly, the effect of phthalates, by using an organ culture system developed for human. In contrast to the data obtained in rat, mono (ethylhexyl)-phthalate (MEHP), an active metabolite of the most widespread phthalate in the environment, does not disturb the steroidogenic function. On the other hand, it has a negative effect on the male germ cells number. This study is the first experimental demonstration of a negative effect of phthalates directly on human fetal testis.’

Parabens, Breast Cancer and Male Reproductive Function

• This toxicology update reviews research over the past four years since publication in 2004 of the first measurement of intact esters of p-hydroxybenzoic acid (parabens) in human breast cancer tissues, and the suggestion that their presence in the human body might originate from topical application of bodycare cosmetics.

• With the continued use of parabens in the majority of bodycare cosmetics, there is a need to carry out detailed evaluation of the potential for parabens, together with other oestrogenic and genotoxic co-formulants of bodycare cosmetics, to increase female breast cancer incidence, to interfere with male reproductive functions and to influence development of malignant melanoma which has also recently been shown to be influenced by oestrogenic stimulation.
Oestrogen and Dairy

- The occurrence of the steroid hormones estrone (E1), 17alpha-estradiol (alphaE2), 17beta-estradiol (betaE2), and estriol (E3) in processed bovine milk with different fat contents and in raw milk from (non)gestated cows was investigated.

- The oestrogen concentration in processed milk coincides with that of raw milk between first and second trimesters, reflecting the contribution of lactating pregnant cows to the final consumable product. The daily intake of total investigated oestrogens through milk is 372 ng, which is dramatically more than currently recognised.

Dairy as a Source of Hormones

- Dairy products contain amounts of hormones (esp. oestrogens) and insulin like growth factors (ILGF).
- Even though the amount is deemed safe for human consumption, it is not advisable to add the free circulating oestrogen load.
- Organic and raw milk is no different.
- Avoidance of dairy products is prudent in any hormonal imbalance condition.
Diindolylmethane (DIM)

• Diindolylmethane is a type of cruciferous indole that consists of two molecules of Indole-3-Carbinol bound together.
  – Diindolylmethane inhibits the conversion of oestrone to 16-Hydroxyestrone.

• Diindolylmethane Compared to Indole-3-Carbinol:
  – Diindolylmethane is believed to more potent (therapeutically) per mg than Indole-3-Carbinol, and recent research has shown that DIM may be safer to use.
  – The usual recommended therapeutic dosage for supplemental Diindolylmethane is 100 - 400 mg per day.

Indole-3 Carbinol

• The therapeutic dosage of Indole-3-Carbinol is 200 - 800 mg per day.

• A more precise optimal therapeutic dosage of Indole-3-Carbinol is 5 - 7 mg per kg of body weight.

• Osiecki recommends 400- 800mg as a SR.

• It has been estimated that the mean daily intake of Glucobrassicin, the precursor for Indole-3-Carbinol) in the UK is approximately 19.5 mg per day from fresh and cooked sources.

• Possible interaction with the OCP and oestrogen containing drugs.

• Potentiates the effects of tamoxifen.
# Cruciferous Indoles

## Vegetables (mmol per 100 Grams):

<table>
<thead>
<tr>
<th>Vegetable</th>
<th>Indoles (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brussels Sprouts</td>
<td>327.8-469</td>
</tr>
<tr>
<td>Broccoli</td>
<td>42.2-71.7</td>
</tr>
<tr>
<td>Cauliflower</td>
<td>18.8-104.7</td>
</tr>
<tr>
<td>Kale</td>
<td>44.2-102.3</td>
</tr>
<tr>
<td>Collards</td>
<td>67.2-165.3</td>
</tr>
<tr>
<td>Mustard Greens</td>
<td>4.2-12.2</td>
</tr>
</tbody>
</table>

- Vegetables do not actually contain Indole-3-Carbinol itself. Vegetables do contain mg/g levels of Glucobrassicin, an Indolylmethyl Glucosinolate. When the plant cells are damaged by cutting or chewing, a thioglucosidase-mediated autolytic process takes place generating Indole-3-Carbinol, Glucose, and thiocyanate.
I3C and Genistein

• Studies increasingly indicate that dietary indole-3-carbinol (I3C) prevents the development of oestrogen-enhanced cancers including breast, endometrial and cervical cancers.

• Epidemiological, laboratory, animal and translational studies support the efficacy of I3C. Whereas oestrogen increases the growth and survival of tumors, I3C causes growth arrest and increased apoptosis and ameliorates the effects of oestrogen. Our long-range goal is to best use I3C together with other nutrients to achieve maximum benefits for cancer prevention.

• This study examines the possibility that induction of growth arrest in response to DNA damage (GADD) in genes by diindolylmethane (DIM), which is the acid-catalyzed condensation product of I3C, promotes metabolically stressed cancer cells to undergo apoptosis.

I3C and Genistein

- We evaluated whether genistein, which is the major isoflavonoid in soy, would alter the ability of I3C/DIM to cause apoptosis and decrease expression driven by the oestrogen receptor (ER)-alpha. Expression of GADD was evaluated by real-time reverse transcription-polymerase chain reaction. Proliferation and apoptosis were measured by a mitochondrial function assay and by fluorescence-activated cell sorting analysis. The luciferase reporter assay was used to specifically evaluate expression driven by ER-alpha. The oestrogen-sensitive MCF-7 breast cancer cell line was used for these studies.

- We show a synergistic effect of I3C and genistein for induction of GADD expression, thus increasing apoptosis, and for decrease of expression driven by ER-alpha. Because of the synergistic effect of I3C and genistein, the potential exists for prophylactic or therapeutic efficacy of lower concentrations of each phytochemical when used in combination.

Genistein Receptor Binding

- Genistein (phytoestrogen) competes with oestrogens (including estradiol 17-Beta) for occupancy of oestrogen receptors.

- The phytoestrogen properties of genistein and daidzein causes it to be weakly oestrogenic.

- For example, the equilibrium dissociation constant for genistein is 100 to 10,000 times greater than for estradiol or DES, which means that genistein’s ability to stay bound to an oestrogen receptor is less than one-hundredth that of the more potent oestrogens.

- If genistein binds with an oestrogen receptor, it elicits less than one-thousandth the response of endogenous oestrogens.

Genistein Receptor Binding

- Soy beans contain high levels of the isoflavones genistein and daidzein and their glucosides.

- ‘We investigated the relationship between soy milk intake and plasma concentrations of oestradiol, sex hormone-binding globulin, and, in premenopausal women, follicle-stimulating hormone, luteinizing hormone, and progesterone in a cross-sectional study of 636 premenopausal and 456 postmenopausal British women.’

- ‘We conclude that soy milk intake does not change plasma concentrations of sex hormones in pre- or postmenopausal British women who consume soy milk as a part of their regular diet.’

The Shanghai Breast Cancer Survival Study, a large, population-based cohort study of 5042 female breast cancer survivors in China.

Among women with breast cancer, soy food consumption was significantly associated with decreased risk of death and recurrence.

Please note this study occurred in China, where the sources of soy are different than the western population.
• High dietary intakes of plant lignans and high exposure to enterolignans were associated with reduced risks of ER- and PR-positive postmenopausal breast cancer in a Western population that does not consume a diet rich in soy.

• The health impact of GM soy should be considered. Further reading:
Balancing Hormones Naturally

• Increase dietary fibre- this can be through fruit and vegetable intake rather than cereal grains.

• Increase lignans in the diet- as in whole flaxseeds.

• Ensure adequate protein intake:
  – Proteins are needed for metabolism of oestrogen in the liver
  – Protein intake plays a major role in a low GL diet
Phytoestrogens:
- Can modulate oestrogen levels by up-regulating the amount of SHBG in the liver.
- May slow down the conversion of androgens to oestrogen.
- Perform competitive inhibition for oestrogen receptors.

Increase sources of the brassica family:
- Source of cruciferous indoles
- Cancer protective
- Up regulates CYP 1A1
Brassica Family

- Broccoli
- Brussels Sprouts
- Cabbage
- Cauliflower
- Chinese Broccoli
- Choy Sum
- Daikon
- Kale
- Kohlrabi
- Mustard Greens
- Radish
- Rutabaga
- Turnip
• Increase methylation abilities
  – Include foods rich in folic acid, Vitamin B6 and B12 and B2
  – Vitamin B6 has also shown other protective effects on oestrogen modulation

• Increase sources of cultured foods in the diet to obtain probiotic bowel flora
  – Cultured yoghurt
  – Sauerkraut

• Alcohol: Advice on alcohol consumption varies. Moderate consumption of red wine seems to have a protective effect in comparison to being teetotal. However alcohol can interfere with liver detoxification pathways and increase oestrogen levels, daily consumption is associated with increased risks. Genetic screening re: liver pathways is likely to elucidate the varied responses.
Remove Hormone Disruptors and Exogenous Oestrogens

- Clingfilm- especially use on fatty foods
- Plastic water bottles
- Dairy
- OCP
- Soft plastic food containers
- Non-organic chicken, eggs and meat
- Home chemicals and body care products with parabens
Reducing Oestrogen Metabolites

- Calcium d-glucurate may increase glucoronidation pathway
- Indole 3 carbinol or DIM may help increase oestrogen clearance
- Inositol may reduce elevated oestradiol levels
- Vitamin B6 may reduce elevated oestradiol levels
- Zinc and magnesium are essential co-factors in hormonal production
PCOS - Clinical Features

- **Definition:** Characterised by multiple small cysts on the ovaries and excess androgen production in a female

- **Symptoms:**
  - Amennorhea / oligomenorrhea
  - Hirsuitism
  - Acne on face, back and chest
  - Insulin resistance and raised abdominal adiposity
  - Infertility
  - Acanthosis nigricans on the neck

Investigations

• Serum testosterone and other androgens may be raised (DHEA and androstendione)
• LH hypersecretion may be shown
• Estradiol should be normal but oestrone levels will be elevated
• Ovarian ultrasound may show a pearl necklace of the cysts around the ovary
• Serum prolactin may be raised
• Blood glucose and insulin may be raised
• Cholesterol levels (esp. apolipoprotien A) may be raised
• SHBG may be decreased

Possible Causes of PCOS

- **Insulin resistance**: Through complex metabolic pathways, elevated insulin levels lead to increased ovarian androgens, increased adrenal androgens, increased triglycerides and decreased HDL cholesterol.

- **Ovarian dysfunction**: Very low oestradiol and very high ovarian androgens lead to elevated acyclic oestrogen (oestrone) which potentiate the development of numerous immature cystic follicles. This in turn perpetuates elevated LH (luteinising hormone) and lowered FSH (follicle stimulating hormone) levels.

- **Excess weight gain**: an increase in fatty tissue leads to the conversion of androgens to oestrone (aromatisation) which increases the levels of the non-variable oestrogens (it has been suggested that marked weight gain can trigger PCOS in some individuals).
Possible Causes of PCOS

- **Adrenal dysfunction**: Excessive adrenal production of androgens leads to elevated oestrone.

- **Hypothalamic-pituitary axis dysfunction**: Inappropriate GnRH (gonadotropin releasing hormone) release leads to elevated LH and lowered FSH.

- **Genetic predisposition**: It has been shown that PCOS may be inherited. Approximately 40% of the women with a family history of PCOS will have the condition. However not all of these will develop symptoms.

- **Leptin regulation**: This is a hormone secreted by the adipocytes that regulates body weight. Its full role in PCOS is yet to be ascertained.

Modern Phytotherapist Vol 8 No. 2 pp 13-21,
Menstrual irregularity:

- Eight or fewer menstrual cycles per year
- Unpredictable menstrual cycles
- Amenorrhea for longer than 4 months in the absence of pregnancy or menopause
- Infertility of sub fertility
- History of ovarian cysts
- Irregular bleeding
- Excessive or heavy bleeding
Skin complications:

• Adult acne
• Severe adolescent acne
• Cystic acne on face, neck, back shoulders
• Hirsutism with excessive hair on face, body, upper lip, chin, neck, abdomen
• Thinning of the head hair or male pattern balding
• Acanthosis nigricans: discoloration or darkening of skin (may be in patches) around neck, groin, under arms
• Skin folds or skin tags
PCOS Holistic Diagnostic Criteria

**Insulin resistance:**

- Weight gain, especially around trunk (apple body shape)
- Dysglycemia
- Difficulty losing weight
- Family history of diabetes or menstrual irregularity
- Obesity
- A higher waist to hip ratio
- Please note, not all insulin resistance cases will appear as overweight
• Insulin levels of greater than 25 μIU/dL.

The typical PCOS lipoprotein profile includes:

• Elevated total cholesterol
• Elevated triglycerides
• Elevated low density lipoproteins (LDL)
• Low high density lipoproteins (HDL)
• Low apolipoprotein A-12
Recommended naturopathic hormonal evaluation:

- Salivary Adrenal Stress Index
- Salivary or serum expanded female hormonal panel, including testosterone and LH to FSH ratio
- Glucose tolerance test
- Thyroid panel
- Blood lipid profile

Typical hormonal disturbances associated with PCOS

- LH is elevated while FSH is usually low at a ratio of 2:1
- Progesterone can be low
Testing (Orthodox and Naturopathic)

- Sex Hormone Binding Globulin (SHBG) is usually low

- Androgens such as testosterone and DHEA-S are usually elevated
Orthodox Treatment

- **Metformin** (hypoglycaemic): To moderate insulin resistance
- **Cyproterone acetate** (antiandrogenic): To treat acne and hirsutism
- **Oral contraceptive pill** (especially those containing Cyproterone acetate) to treat acne and hirsutism
- **Spironolactone** (diuretic, aldosterone antagonist): To treat acne and hirsutism
- **Progesterone, oral and micronised**: To trigger withdrawal bleeding
- **Clomiphene** (oestrogen agonist or antagonist (depending on the target tissue)): To improve ovulation and fertility for those wishing to conceive
Many research trials have shown a positive correlation between weight loss and improvement of PCOS symptoms, especially depression, anovulation and insulin resistance.

Diets vary, but generally the use of a low GI, monitored calorie or modified Atkins diet is used.

Exercise also plays an important role.
Naturopathic Treatment Aims for PCOS

- Decrease central obesity and improve waist-to-hip ratio
- Increase insulin sensitivity and decrease glucose resistance
- Promote oestrone clearance by supporting phase 1, 2 liver pathways and the phase 3 detoxification pathway (anti porter activity; cruciferous indoles work increase anti porter activity)
- Lower circulating androgens
Decrease Insulin Resistance

- Exercise: At least 1 hour for three times a week (or 20mins daily)
- Increase fibre in the diet
- Reduce trans and saturated fats
- Decrease sugar and refined food intake
- Increase protein intake
- GL diet or a modified Atkins may be needed
  - A loss of just a few kilos can decrease the insulin resistance enough to bring back regular menstruation
Promoting Oestrone Clearance

- Evaluate bowel function and microflora of the intestine
- Increase the brassica family
- Support phase 2 liver clearance through supplemental or herbal support
- Reduce sources of endocrine disruptors
Both myo-inositol and D-*chiro*-inositol have been shown to improve insulin resistance, and inducing ovulation in women with PCOS.


Fruits, beans, grains, and nuts contain myoinositol.
B Vitamins

• A common side effect of metformin therapy is raise to homocystiene levels.

• A randomised controlled trial showed that supplementation with the B group vitamins (plus folic acid) decreased homocystiene in the patients under this therapy.
Vitamin D3

- Recent studies indicate the possible role of vitamin D3 in the pathogenesis of insulin resistance and glucose metabolism.

- Women with PCOS have mostly insufficient vitamin D3 levels.

- Administration of a single dose of 300 000 units of vitamin D3 orally was given.

- The authors concluded that vitamin D3 replacement therapy may have a beneficial effect on IR in obese women with PCOS.
The aim of this study was to evaluate the effects of calcium-vitamin D and metformin on the menstrual cycle and ovulation in patients with polycystic ovary syndrome (PCOS).

The number of dominant follicles during the 2-3 months of follow-up was higher in the calcium-vitamin D plus metformin group than in either of the other two groups (metformin alone or Ca/D alone).

The dosages used in this trial was 1,000 mg of calcium and 400 IU of vitamin D per day, orally.

Spearmint Tea and Androgens

- Anti-androgenic effects of spearmint and peppermint were found previously in rats.

- In this study, subjects took a cup of herbal tea which was steeped with *Mentha spicata* (spearmint) for 5 days twice a day in the follicular phase of their menstrual cycles.

- There was a significant decrease in free testosterone and increase in luteinizing hormone, follicle-stimulating hormone and estradiol, but no significant decreases in total testosterone or dehydroepiandrosterone sulphate levels.
Other Nutrients

• Lipoic acid:
  – Used to reduce insulin resistance and increase glucose metabolism
  – Antioxidant
  – 100-600mg daily

• Magnesium:
  – For insulin resistance, reducing cardiovasicular risk factors
  – 300-1000mg daily
Omega-3 Fatty Acids

• Used to competitively inhibit AA therefor reducing inflammation and to reduce the inflexibility of cell membranes that is shown on the ovaries and cysts.

• One study showed Omega-3 fatty acids particularly decreased hepatic fat in women with PCOS and hepatic steatosis, defined as liver fat percentage greater than 5% dose 4g/d of omega-3 fatty acids), therefore reducing CVD risk factors.

Uterine Fibroids

- Non-cancerous tumours of the uterus which may occur sub-mucosally or intramurally.

- They may be any size or shape and they range in their symptoms dependant on their location, number and size.

Uterine Fibroids - Symptoms

• Heavy bleeding or flooding

• Larger fibroids may result in increased urinary frequency, heaviness and congestion in the lower abdomen

• Abdominal enlargement

• Infertility and miscarriage

• Sometimes pain when they are peduculated

Uterine Fibroids

• Majority are asymptomatic.

• Abnormal bleeding occurs in 30% of women with fibroids.

• Fibroids can undergo degenerative changes with necrosis, resulting in cystic degeneration.

• Calcification can occur.

• The main diagnostic consideration is differentiating a possible fibroid from: ovarian malignant tumor, abscess in the fallopian tube/ovarian region, diverticulum from the colon, pelvic kidney, endometriosis, adenomyosis, congenital anomalies, and uterine sarcoma.
Uterine Fibroids

- The cause of uterine fibroids remains poorly understood.

- Increases in local oestradiol concentration within the fibroid itself may play a role in the cause and growth.

- Concentrations of oestrogen receptors in fibroid tissue are higher than in the surrounding myometrium but lower than in the endometrium.

- Aromatisation is normally higher in fibroid tissue.

Uterine Fibroids - Risk Factors

- Pregnancy: Reduces the risk due to a period of lower exposure to oestrogen and higher exposure to progesterone.
- Coffee: Mice fed the equivalent of three cups of coffee had a higher incidence of fibroids.
- Hypertension: People with hypertension seem to have a higher incidence, probably due to similar aetiology (inflammation, poor phase 2 detox?).
- Obesity: Due to the higher amount of oestrogen in overweight women.
- Use of OCP
- Smoking

Medical Diagnosis and Treatment

- Diagnosis is by ultrasound or laparoscopy
- Observation of growth
- Surgical intervention: Removal, hysterectomy or uterine artery embolisation
- GnRH agonists or Danazol (to decrease aromatisation)

Nutritional Aims for Uterine Fibroids

• Regulate excess bleeding.

• Reduce free circulating oestrogens - especially the 16-OHE form.

• Reduce inflammation and kinase signalling.

• Dietary changes by themselves are not able to reduce fibroids, but can help in the management of symptoms and prevention of further occurring.
Reducing Bleeding

- Check for anaemia and serum ferritin levels and replace Iron if necessary 10-30mg daily.
- Increase amount of Iron will reduce excessive bleeding tendencies.
- Do not replace Iron in menopausal women without checking blood levels.
- Herbs and homeopathic can be used to reduce bleeding also.
- Yarrow tea may be helpful.
Reduce Circulating Oestrogens

• I3C or DIM- cruciferous indoles to improve 2/16 ratio.

• Reduce xenoestrogen sources.

• Address any defective digestion (increase fibre rich foods to improve oestrogen excretion).

• Nutrients to support phase 2 detoxification.

• ‘Hormone friendly’ dietary advise as per earlier slides.
Reducing Inflammation

• Manage any obesity or insulin resistance.

• Reduce any pro-inflammatory foods in diet (trans fats, sources of AA).

• Introduce prostaglandin or kinase modulating substances:
  – Bromelain
  – EPA- 2000mg
  – Digestive enzymes- used on an empty stomach
  – Functional foods such as ultrainflamX
  – Kaprex
  – Turmeric
Menopause

• The time which menstruation ceases.

• A natural part of life for women, the same as when menstruation starts.

• Normally the whole menopause can last for around 7 years.

1. Peri-menopause: Starts around 45-50 when hormonal changes start to occur and cycles and symptoms start to be experienced.


3. Post-menopause: From 55 onwards. When no more periods occur.
Menopausal Symptoms

1. Hot flushes and night sweats – it is suggested this may be from low oestrogen or fluctuations in oestrogen levels.

2. Lethargy, lack of concentration, irritability, aggressiveness, depression, mood swings or anxiety and memory problems.

3. Decreased libido.

4. Increased urgency and frequency of urination.

5. Decreasing muscular strength and ligament attachment may cause a variety of joint-related aches and pains.

6. Vaginal dryness and pain on intercourse.

7. Atrophy of breasts.
Menopause - Diagnostic Summary

- Last spontaneous menstrual period 12 months prior to consultation.

- Follicle stimulating hormone (FSH) measurement - normally a level of over 30 IU/L is indicative of menopause, but subsequent readings may need to taken to show steady increases.

- Laboratory and imaging findings may be used to assess risks for osteoporosis and cardiovascular disease.

Menopause - Hormonal Changes

• Both oestrogen and progesterone decline gradually.

• Usually start around 2-3 years before ovulation stops.

• Before menstruation stops, there is a transition stage where periods may:
  1. Become further apart
  2. Some have surprise flooding
  3. Or a variation in cycle and/or bleeding patterns occurs

• Small (but biologically significant) quantities of testosterone are manufactured by the ovaries up until menopause.
  – This ovary-manufactured testosterone contributes to female sexual desire - after menopause approximately 35% of females have reduced sexual desire due to the cessation of testosterone production by the ovaries (the other 65% manufacture enough testosterone in their adrenal glands to sustain their sexual desire).
Hormonal Replacement Therapy

• Oestrogen-only preparations include:
  – Oral tablet (daily).
  – Transdermal patch (once weekly or twice weekly) or gel (daily).
  – Creams and pessaries.
  – Implant (every 6 months).

• Combined oestrogen–progestogen preparations include:
  – Oral tablet (daily).
  – Transdermal patch (once weekly or twice weekly):
    • In transdermal combined hormone replacement therapy (cyclical or continuous combined oestrogen plus progestogen), the progestogen is either combined into the patch, or given separately as a tablet.
Menopause is NOT a disease!

It is a natural part of life, a transition that all women will experience.

Sometimes though, the symptoms of menopause can be debilitating, and this means the woman may decide to choose HRT.

Even your client does choose HRT, it is still important for them to adopt a positive lifestyle and attitude, have good eating habits, exercise and listen to their body.
Contraindications to HRT

- Hormone-dependent cancer (e.g. endometrial cancer, current or past breast cancer).
- Active or recent arterial thromboembolic disease (e.g. angina or myocardial infarction).
- Venous thromboembolic disease, pulmonary embolism, or current pregnancy.
- Severe active liver disease.
- Undiagnosed breast mass.
- Un-investigated abnormal vaginal bleeding
Naturopathic Menopause Considerations

- The body has to rely on the adrenal glands to produce the sex hormones once the ovaries stop producing the majority, and conversion happens via aromatisation in the muscle and adipose tissue.

- Support adrenal function if necessary to make for a smoother transition (see stress lecture).

- Other endocrine disturbances will exacerbate weight gain and hot flashes, check thyroid function.
Menopause and CVD

• The lack of oestrogen increases a women’s risk for CVD after the menopause.

• Risk factors for CVD should be evaluated and monitored, and preventative strategies put in place (see CVD lecture).
Antioxidants and Menopause

- Vitamin C reduces elevated CRP (risk factor for CVD).

- Higher antioxidant status has been shown to reduce the risk of breast cancer and CVD after menopause, especially dietary carotenoids.

Menopause and Osteoporosis

- Osteoporosis risk increases after menopause due to the lack of oestrogen.

- Monitor bone density carefully, and levels of Calcium, magnesium, boron, Vitamin K and vitamin D.

- Advise on weight bearing exercise to build bone density.

- Smoking is associated with an increased risk of osteoporosis.
Calcium and Vitamin D

- Calcium supplementation alone did not improve bone density in a five year follow-up in the elderly.

- However, supplementation with vitamin D and Ca has been shown to reduce fracture rates in the institutionalised elderly, but there remains controversy as to whether supplementation is effective in reducing fracture in free-living populations.

- Low vitamin D status is associated with an increased risk of falling and a variety of other health outcomes and is an area that requires urgent attention. The role of other micronutrients on bone remains to be fully defined, although there are promising data in the literature for a clear link between vitamin K nutrition and skeletal integrity, including fracture reduction.
Calcium and Menopause

- Calcium intake is inversely associated with the risk of having metabolic syndrome in postmenopausal women. Prospective or longitudinal studies concerning sex and menopause status are necessary to evaluate an association between calcium intake and metabolic syndrome.
Lignans and Post - Menopausal Women

- The aim of the present study was to compare the metabolic profile of post-menopausal women consuming various amounts of dietary lignans.

- In conclusion, women with the highest lignan concentrations had a better metabolic profile including higher insulin sensitivity and lower adiposity measures.
Vitamin E

- Has small effects on the vasomotor symptoms of hot flushes with menopause.

- May be helpful for use for the reduction of hot flushes.
Soy Isoflavones

• The results of 6 clinical studies on soy (Glycine max L.) isoflavone extracts are mixed. Moreover, the composition and dose of soy supplements varies widely across studies, making comparisons and definitive conclusions difficult.

• One study challenged the long-term safety of high-dose soy isoflavone extract (150 mg/day for 5 years) on the uterine endometrium.
Red Clover Isoflavones

• Clinical data from 5 controlled trials assessing the efficacy of semipurified isoflavone red clover (Trifolium pratense L.) leaf extracts to reduce hot flash frequency and severity or to relieve symptoms associated with the domains of the Greene Menopausal Symptom Scale are contradictory.

• No significant adverse events have been reported in the literature.
Black Cohosh and Menopause

• The majority of studies indicate that extract of black cohosh (Cimicifuga racemosa L.) improves menopause-related symptoms; however, methodologic shortcomings in the trials were identified.

• To date, 4 case reports of possible hepatotoxicity have been published, although previous safety reviews suggest that black cohosh is well tolerated and that adverse events are rare when it is used appropriately.
Nutritional Therapy Suggestions

1. Adopt sound eating habits such as:
   - Two pieces of fruit and five vegetables (increase antioxidants)
   - Consume whole grains (gamma-oryzanol)
   - Fibre to support healthy hormone metabolism
   - Proteins – more vegetarian than animal to reduce sources of endocrine disruptors
   - Eating organic if possible
   - Low GL dietary pattern to reduce CVD risk
   - Keep caffeine at a minimum e.g. Less than 250mg a day
   - Limit alcohol intake
   - Drink at least 2 litres of water a day
2. Avoid foods which seem to aggravate hot flushes. E.g. coffee, excessively spicy food and alcohol.

3. Dress accordingly. Try light, loose fitting clothes made from natural fibre such as cotton. Its all about layering!

4. If suffering from night sweats, it’s advisable to sleep on a towel or folded sheet. So you can then pick it up and wash it without having to take the entire sheets off. Use natural fibres that breathe better.

5. Eat phytoestrogen rich foods. These include non-genetically modified soy products such as soy milk, tofu, legumes, tempeh and beans. Increase lignan intake via flaxseeds.
Nutritional Therapy Suggestions

6. A simple home remedy for hot flushes is as follows: Chop about 6 fresh sage leaves and soak overnight in fresh lemon juice. In the morning, strain and drink the lemon juice diluted in water to taste. This should be drunk before food as it also aids digestion.

6. EXERCISE! It doesn’t have to be hard but it is advisable to exercise 3-4 times a week for at least 30mins to increase bone density.
Endometriosis

• Triad of symptoms: dysmenorrhea, dyspareunia, and infertility.

• Pelvic ultrasounds: detection and consistency of endometriomas.

• Definitive diagnosis: a laparoscopy or laparotomy visualizing endometrial implants within the pelvic cavity.
Endometriosis

- Endometriosis affects 10% to 15% of menstruating women between the ages of 24 and 40 years old.

- The main risk factor for endometriosis is heredity. Women with a mother or a sister with endometriosis have an increased risk.

- Also, women with shorter menstrual cycles and longer duration of flow have been found to be at higher risk for endometriosis.
Currently, there is no clear-cut understanding as to the cause of endometriosis. Two main theories are:

1. **Retrograde flow**: During menses, blood flows backward and becomes seeds of implants in the pelvic cavity.
   - The problem found with this theory was that more than 90% of menstruating women without endometriosis have retrograde flow.

Causative Theories

2. Altered cell immunity:

- Implants found in odd locations such as the nose and lungs suggest transportation of endometrial tissue through lymphatic channels and blood vessels.

- Some researchers believe the implants to be of embryologic origin, when pieces of the uterus were left behind during development and, when activated, secrete a chemical causing the nearby capillaries to bleed.

- Other research on endometriosis in baboons suggests activation by environmental toxins that mimic oestrogens. Immunologic alterations may exist in women with endometriosis. Women with endometriosis have been found to have suppressed natural killer cell activity in their peritoneal fluid, high levels of immunoglobulins IgG and IgM, and high levels of autoantibodies against ovary and endometrial cells.
Causative Theories

- Lack of exercise from an early age, a high-fat diet, use of intrauterine devices, increased or unbalanced oestrogen levels, and even natural-red hair colour have been suggested as factors in the development of endometriosis.

- A greater number of women with adhesions or endometriosis, or both, have reported abuse in their history.

- Increased immune action within the pelvic cavity and the possibility of antibody reactions to sperm has prompted recognition of an immunologic basis for endometriosis.
Endometriosis and Fertility

- In severe cases, formation of connecting tissues around endometriosis near the Fallopian tubes or ovaries may reduce fertility.

- Fortunately, most women with endometriosis have a mild form of disease and their fertility is not impaired.

- Once pregnant, most women's endometriosis gets better under the influence of the constant high levels of female hormones produced in pregnancy.

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Medical Treatment for Endometriosis

- Some women with endometriosis improve spontaneously, although most find that their symptoms continue or gradually worsen.

- Medical treatments rely on anti-inflammatory pain-killers and hormone treatments designed to shrink endometrial tissues:
  1. Danazol
  2. Gestrinone
  3. GnRH agonist analogs
  4. Progesterone derivatives
  5. Progesterone-oestrogen combinations.

- Surgical treatments include removing cell clumps, severing pain nerves, and even hysterectomy, sometimes with removal of the ovaries.

Hormone Disruptors and Endometriosis

• Polychlorinated biphenyls (PCBs) were commonly used in electrical equipment, hydraulic fluid and carbonless carbon paper, and organochlorine pesticides have been commonly used in agriculture.

• In 1992, German researchers found that women with high blood levels of PCBs had a higher prevalence of endometriosis.¹²

• Further studies have correlated the same risk

Hormone Disruptors and Endometriosis

• In addition, some organochlorines mimic the effects of oestrogens.

• These toxins tend to accumulate in animal fat, and the major route of human exposure is through food, particularly fish.

• They also show up in meats and dairy products.


Fish Intake and Organophosphates

• This study suggests that Japanese women who consume fish frequently in their reproductive period tend to accumulate higher levels of organochlorines in their bodies.

• The downside of this, is a high EPA content has been shown to reduce symptoms of period pain.

• So fish is beneficial if it is not polluted....
Hormone Disruptors and Endometriosis

- To measure the concentration of organochlorines in a woman's body, researchers sometimes check samples of breast milk.

- Breast tissue is a natural target for chemicals that dissolve into fat, and, during breast-feeding, a woman can excrete up to half of all the dioxin she has accumulated in her body tissues.

- By avoiding fish, other meats, and cow's milk, you avoid the foods that harbour most organochlorines.

- Researchers have found that vegetarian women have much lower levels of pollutants in their breast milk, compared to other women.


Caffeine and Endometriosis

- According to researchers at the Harvard School of Public Health, women who have two or more cups of caffeinated coffee (or four cans of cola) per day were found to be twice as likely to develop endometriosis as other women.

- The reason why caffeine has this effect is unknown.

• A recent study investigated the occurrence of coeliac disease in women with endometriosis.

• 2.5% of the women tested has coeliac disease, and it is thought that this may clinically relevant.
Vitamin C and E

- Thirty-four women with endometriosis received a bar containing vitamins C and E (343 mg and 84 mg, respectively) or placebo for 6 months.

- Vitamins C and E supplementation was associated with a decrease in the concentration of oxidative stress markers in women with endometriosis. The pregnancy rate, however, did not improve during or after the intervention.

- In a further study, this combination of antioxidants reduced pelvic pain in endometriosis sufferers, read more: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484190/
• The development of new blood vessels plays an essential role in growth and survival of endometriosis. Epigallocatechin gallate (EGCG) from green tea has powerful anti-angiogenic properties and our aim was to evaluate these properties in experimental endometriosis.

• Results show that EGCG significantly inhibits the development of experimental endometriosis through anti-angiogenic effects.
Exercise

- Regular exercise has been associated with a 40%-80% reduction in risk for endometriosis in several case-control studies.

- However, women experiencing symptoms prior to their diagnosis may be less likely to exercise than healthy controls, thus biasing the observed association.
A comparative RCT showed that use of dietary therapy was effective in regards to pain associated with endometriosis post surgery.

Dietary therapy was a protocol consisting of nutritional intake in addition to vitamins (B6, A, C, E), minerals salts (Ca, Mg, Se, Zn, Fe), VSL3 lactic ferments (Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus bulgaricus, Streptococcus thermophilus), and omega-3 and omega-6 fatty acids (fish oil).
Diet, Surgery and Placebo

• Hormonal suppression therapy and dietary supplementation were equally effective in reducing non-menstrual pelvic pain.

• Postoperative hormonal suppression treatment or dietary therapy are more effective than surgery plus placebo to obtain relief of pain associated with endometriosis stage III-IV and improvement of quality of life.

• Read more: http://www.fertstert.org/article/S0015-0282(07)00202-6/fulltext
Endometriosis and Diet

• Compared to women in the lowest tertile of intake, a significant reduction in risk emerged for higher intake of green and fresh fruit whereas an increase in risk was associated with high intake of beef and other red meat and ham.

• Consumption of milk, liver, carrots, cheese, fish and whole-grain foods, as well as coffee and alcohol consumption, were not significantly related to endometriosis in this study.
High omega-3:omega-6 fatty acid ratios in culture medium reduce endometrial-cell survival in combined endometrial gland and stromal cell cultures from women with and without endometriosis.

Omega-3 PUFA may have a suppressive effect on the in vitro survival of endometrial cells and omega-3 PUFA be useful in the management of endometriosis by reducing the inflammatory response and modulating cytokine function.
• Trial design: Rats induced with endometriosis and fed a rich EPA diet.

• In the EPA group, the n-3:n-6 ratio in each tissue significantly increased and the thickening of the interstitium, an active site for inflammation in endometriosis, was significantly suppressed. The mRNA of metalloproteinases, interleukin-1beta, interleukin-1r, prostaglandin E synthase, and nuclear factor (NF)-kappaB were reduced in the EPA group.

• CONCLUSION(S): EPA supplementation might be a valid strategy for the treatment of endometriosis.
• The Pycnogenol treatment group took 60 mg Pycnogenol orally a day for 48 weeks.

• Measurement was for endometriosis signs and symptoms, including changes in CA-125 and oestrogen levels (E2).

• No influence of treatment on menstrual cycles or E2 was observed in the Pycnogenol group. CA-125 decreased in both treatment groups. Patients with smaller endometriomas responded better to treatment as compared to patients with larger endometriomas. In the Gn-RHa group, the lowering of CA-125 concentrations was far more pronounced; however, a clear rebound effect was observed.

• Pycnogenol is a therapeutic alternative to Gn-RHa in the treatment of endometriosis.
Pycnogenol and Period Pain

- Pycnogenol was given in a multi-centre, RCT to women with dysmenorrhea of a dosage of 60mg daily.

- The analgesic-sparing effect of Pycnogenol increases with duration of supplementation and benefits persist even after discontinuation.
Oxidative stress has been identified in the peritoneal fluid and peripheral blood of women with endometriosis.

The high antioxidant diet (HAD) guaranteed the intake of 150% of the suggested daily intake of vitamin A (1050 microg retinol equivalents), 660% of the recommended daily intake (RDI) of vitamin C (500 mg) and 133% of the RDI of vitamin E (20 mg).

Peripheral oxidative stress markers diminished, and antioxidant markers were enhanced, in Women with endometriosis after the application of the HAD.
Nutritional Therapy Aims for Endometriosis

- Normalise the immune response.
- Optimize liver function to conjugate and metabolize hormones (2/16 ratio) and to detoxify endogenous and exogenous toxins.
- Eliminate metabolic wastes.
- Assist optimal transit time and proper intestinal microflora.
- Reduce exposure to hormone disruptors.
- Reduce inflammatory process and oxidative stress.
- Check thyroid and adrenal function, and support if necessary.
Pre-Menstrual Syndrome - PMS

• Up to 85% of women report some symptoms of PMS.

• Recurrent signs and symptoms that develop during the late luteal phase of the menstrual cycle and disappear by the end of the full flow of menses.

• Typical symptoms are: decreased energy, tension, irritability, depression, headache, altered sex drive, breast pain, backache, abdominal bloating, and oedema of the fingers and ankle.
PMS

• Several other conditions have overlapping symptoms:
  – Diabetes
  – Hypothyroidism
  – Eating disorders
  – Depression
  – CFS
  – IBS
Several theories have been proposed to explain the causes of PMS, and the current strongest is the interaction of the ovarian steroids and the brain neurotransmitters.

Genetic predispositions and sociocultural beliefs about menstruation may also influence what women experience.

At present, the dominant thinking is that cyclic changes in the ovarian steroids oestrogen and progesterone cause changes in many body systems, including brain neurotransmitters, which then have emotional and physical manifestations.
• Of the neurotransmitters studied, serotonin is the principal one implicated in the pathogenesis of PMS and PMDD.

• Other neurotransmitter systems may also be involved in PMS and PMDD. They include the adrenergic, opioid, and gamma-aminobutyric acid (GABA) systems. Research over the last 10 years has shown that serotonin agents can alleviate both the psychological and physical symptoms in most women with PMDD.
• In the early 1940s, Dr. Morton Biskind observed an apparent relationship between B vitamin deficiency and PMS. He postulated that PMS, as well as excessive menstruation and fibrocystic breast disease, was due to an excess in oestrogen levels caused by decreased detoxification and elimination in the liver as a result of B vitamin deficiency. The liver utilizes various B vitamins to detoxify oestrogen and excrete it in the bile.
Vitamin B6 and PMS

• Vitamin B₆ levels are typically quite low in depressed patients, especially women taking oestrogens (birth control pills or conjugated oestrogens).

• Vitamin B₆ supplementation has been shown to have positive effects on all PMS symptoms (particularly depression) in many women (discussed in greater detail later). The improvement is achieved via a combination of a reduction in mid-luteal oestrogen levels and an increase in mid-luteal progesterone levels.
Diet, Lifestyle and PMS

- A lower dietary GI diet was independently associated with decreased premenstrual symptoms in a group of young Japanese women.

- Higher alcohol intake was associated with an increase in symptoms.

- Exposure to cigarette smoke increased severity of PMS symptoms read more: http://aje.oxfordjournals.org/content/168/8/938.full

Vitex Agnus - Castus and PMS

- Hyperprolactinemia seems to be an important factor which is considered to be part of the endocrine disorder.

- Different clinical investigations and double blind trials have shown that preparations containing Vitex agnus castus fruit extract are a useful tool to decrease increased prolactin serum levels and could be an effective treatment for women suffering from premenstrual syndrome.
Calcium and PMS

• A double-blind clinical trial was designed to evaluate the effect of calcium supplement therapy on PMS symptoms.

• 500 mg of calcium carbonate twice daily for 3 months to the test group.

• Early tiredness, appetite changes, and depressive symptoms were significantly improved in the group receiving calcium treatment compared with the placebo group.

• Calcium is an effective treatment for PMS. Read more: http://www.cfp.ca/content/48/4/705.long
Magnesium and PMS

• Magnesium deficiency has been implicated as a possible contributing factor to some symptoms of premenstrual syndrome (PMS) and several studies have reported a lower intracellular magnesium concentration in women with PMS.

• Modified-release magnesium 250 mg tablet was given.

• Concluded that modified-release magnesium was effective in reducing premenstrual symptoms in women with PMS in this preliminary study.
Herbs, Vitamins and Minerals in the Treatment of Premenstrual Syndrome

• Data supports the use of calcium for PMS, and suggests that chasteberry (vitex) and vitamin B6 may be effective.

• Preliminary data shows some benefit with ginkgo, magnesium pyrrolidone, saffron, St. John's Wort, soy and vitamin E.

• No evidence of benefit with evening primrose oil or magnesium oxide was found.
Five Subgroups of PMS - A Woman May Have Some Of or All of These!

- **PMT-P:**
  - **Pain:** Crampy and reduced pain threshold.
  - Responds well to EPO and Mg supplementation.

- **PMT:**
  - **Anxiety:** Anxious, nervous tension, mood swings and irritability.
  - Generally high oestrogen to progesterone ratio
  - Responds well to opioid peptides- 5- HTP, L-theanine, DL- phenylalanine and the 4 R program
  - B6 and methionine
  - I3C
  - High fibre diet
Five Subgroups of PMS - A Woman May Have Some Of or All of These!

• PMT-C:
  – **Craving**: Increased appetite, sweet cravings, fatigue, dizziness
  – Blood sugar control: Lipoic acid, chromium, magnesium, B vitamins and EPA

• PMT-D:
  – **Depression**: Depression, crying, forgetfulness, confusion and insomnia
  – Low oestrogen to progesterone ratio often with elevated adrenal androgens
  – May have high lead levels
  – Tyrosine, 5-HTP or St John’s Wort may be of help
Five Subgroups of PMS - A Woman May Have Some Of or All of These!

- PMT-H:
  - **Hyperhydration**: Fluid retention, weight gain, breast tenderness and abdominal distension.
  - Reduce sodium and increase potassium foods
  - Avoidance of coffee
  - Vitamin B6 to help regulate aldosterone
  - Vitamin E may help breast tenderness
PMS General

• Watch for thyroid inactivity and treat if necessary.

• Prolactin levels are often raised in stress and PMS, which will make breast tenderness worse and possibly make a longer luteal phase.
Major Guidelines

• Reduce high GI foods- especially prior to menses
• Avoid caffeine, alcohol and tobacco
• Reduce salt intake
• Restrict dairy products, choose other high Ca foods
• Normalise sleeping patterns
• Increase green leafy vegetables
• Increase Mg, Zn, B6, tryptophan, iodine and tyrosine containing foods
• Increase oily fish in the diet
• Decrease hormone disruptor exposure