

Natural Treatment of Female Functional Infertility

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Functional infertility

Infertility is clinically defined as the inability to conceive a child within one year of unprotected intercourse¹. 15%-20% of couples have difficulty conceiving, and in up to 30% of these cases the cause of infertility remains unexplained².

Functional infertility is due to incorrect functioning of the reproductive system, which is not due to an underlying medical condition. It includes both improper functioning of the reproductive hormones for which no cause has been identified, as well as other unexplained causes of infertility³.

Diagnosis of functional infertility

Scientific diagnostic techniques such as blood tests can be useful for choosing the correct treatment protocol. However, scientific diagnostic techniques cannot always provide an explanation for the problems being encountered by the patient.

Although careful case taking frequently reveals symptoms such as menstrual irregularities and abnormal menstrual flow, and there may be a slight hormonal imbalance in some instances, these symptoms are difficult to classify conventionally since they do not fall into any specific disease category⁴. However, the significance of these symptoms may be better understood using a more holistic perspective; and by incorporating traditional or 'energetic' approaches to diagnosis, one may find possible causal factors for the infertility where orthodox medicine has failed to do so.

¹ Abma, J.C., Chandra, A., Mosher, W.D., Peterson, L.S., Piccinino, L.J. (1997). Fertility, family planning and women's health: estimates from the National Survey of family growth. *Vital Health Stat* 23:1-14.

² Beers, M.H., & Berkow, R. (1999). *The Merck Manual of Diagnosis and Therapy*. Merck & Co. Inc. New Jersey.

³ Indhorn, M. & vanBalen, F. (2002). *Infertility around the Globe: New Thinking on Childlessness, Gender, and Reproductive Technologies*. University of California Press.

⁴ Gascoigne, S. (2001). *The Clinical Medicine Guide: A holistic perspective*. Jigme Press, Co. Cork, Ireland.

Figure 1. General themes which may be associated with infertility

Abnormal blood flow	Includes poor peripheral circulation, brownish menstrual flow, and diagnosis Blood stasis using TCM.
Premenstrual syndrome	Includes premenstrual mood swings, mastalgia, abdominal pain, bloating, fatigue, and constipation.
Stress	Includes feelings of being stressed or overworked.
Hyperalgesia	Includes dysmenorrhoea and headaches.
TCM patterns of disharmony	Includes diagnosis of Qi stagnation, Kidney Qi Deficiency, Dampness, and Deep pulse using TCM diagnosis.
Ayurvedic Vata disturbance	Includes cracking joints and diagnosis of 'Vata disturbance' using Ayurvedic diagnostic techniques

Abnormal blood flow

In Traditional Chinese Medicine (TCM), Blood stasis is one of a number of different patterns of disharmony which may contribute to infertility. Blood stasis is indicated by a blue or purple tongue-body colour, and various symptoms such as poor peripheral circulation and dysmenorrhoea with clotty menstrual flow⁵.

Poor peripheral circulation is a common complaint among women with a history of reproductive problems⁶. It is possible, therefore, that women with poor peripheral circulation may also be suffering from poor pelvic circulation, which impairs nourishment of uterus and ovaries⁷.

⁵ Xiufen, W. (Ed.) 2003. *Traditional Chinese Diagnostics*. People's Medical Publishing House, China

⁶ Ward, N. (1994). How successful is the environmental approach to infertility? *Foesight Figures. Journal of Nutritional and Environmental Medicine* 5:205.

⁷ Zhao, L.Q. (2011). TCM Treatment of Premature Ovarian Failure and Infertility. *Journal of the Association of Traditional Chinese Medicine (UK)*. 18(1):22-26.

Dysmenorrhoea may also suggest reduced uterine circulatory capacity⁸. Spasmodic dysmenorrhoea (with cramping pains during menstruation) is caused by a hypertonic uterus which restricts blood flow, while congestive dysmenorrhoea (with a dull, dragging sensation before menstruation) is due to pelvic blood congestion⁹.

Adequate endometrial blood supply is required for implantation to occur, and women with unexplained subfertility demonstrate a significant reduction in endometrial and subendometrial perfusion during the mid-late follicular phase¹⁰. Furthermore, poor ovarian blood flow is associated with luteal phase defect, which results in low progesterone levels during the mid-luteal phase. Improving ovarian blood flow improves both luteal function and endometrial growth¹¹.

Improving Blood Flow

Circulatory stimulants

Warming herbs such as *Rosemarinus officinalis*, *Cinnamomum zeylonicum* and *Zingiber officinale* may be used to stimulate the peripheral circulation, and may also help to promote healthy circulation to the reproductive organs.

Uterine spasmolytics

In cases of spasmodic dysmenorrhoea, uterine spasmolytics such as *Paeonia lactiflora*, *Viburnum opulus*, and *Viburnum prunifolium*, and measures to decrease prostaglandins (see below) may be useful to improve uterine blood flow. Magnesium may also help to decrease uterine cramping⁹. It is found in foods such as soya products, whole-grain cereals, seeds, and green leafy vegetables¹².

⁸ Timonen, S. & Procopé, B.J. (1971). Premenstrual Syndrome and Physical Exercise. *Acta Obstetrica et Gynecologica Scandinavica* 50(4): 331-337.

⁹ Trickey, R. (2003). *Women, Hormones & the Menstrual Cycle*. Allen & Unwin, Australia.

¹⁰ Raine-Fenning, N.J., Campbell, B.K., Kendall, N.R., Clewes, J.S. & Johnson, I.R. (2004). Endometrial and subendometrial perfusion are impaired in women with unexplained infertility. *Human Reproduction* 19(11):2605-2614.

¹¹ Takasaki, T., Tamura, H., Taniguchi, K., Asada, H., Taketani, T., Matsuoka, A., Yamagata, Y., Shimamura, K., Morioka, H. & Sugino, N. (2009). Luteal blood flow and luteal function. *Journal of Ovarian Research* [online]. Available from : <http://www.ovarianresearch.com/content/2/1/1>. (Accessed 24/1/09).

¹² Pitchford, P. (2002). *Healing With Whole Foods (3rd Edition)*. North Atlantic Books, California.

Uterine tonics

In cases of pelvic blood congestion, uterine tonics such as *Chamaelirium luteum* and *Rubus idaeus* may be more useful, as they are thought to encourage more effective uterine contractions⁹. *Achillia millefolium* also reduces pelvic congestion, possibly due to an anti-thrombotic effect¹³, as well as relaxation of the veins, which allows congestion to move out of the capillaries¹⁴.

Amphoterics herbs

There are numerous herbs, including *Leonorus cardiaca*, which seem to possess the apparently contradictory effects of both stimulating uterine activity and relieving spasm. This combination of actions helps to regulate uterine function by encouraging more orderly and effective contractions, which are then followed by an adequate rest period so that blood can circulate through the uterine muscle again⁹.

Angelica sinensis is a uterine tonic and antispasmodic herb, which is widely used to treat dysmenorrhoea¹⁵, and is traditionally used to treat blood stasis in TCM¹⁶. It is also thought to regulate prostaglandin synthesis⁹, and to act as a circulatory stimulant¹⁶.

Other measures

Nutrients which help to reduce blood stagnation include: Niacin (vitamin B3), found in wholegrains and sprouted legumes; Vitamin C, found in fresh fruit and vegetables, Vitamin E, found in whole grains, nuts and seeds and leafy green vegetables; and omega-3 fatty acids, found in seeds such as chia and flax¹³. Increasing exercise may help to improve pelvic circulatory capacity⁸, and other approaches such as sitz baths may also be used to increase the pelvic circulation and reduce congestion¹⁷.

¹³ Weiss, R. (1988). *Herbal Medicine*. Arcanum, Sweden

¹⁴ Wood, M. (2004). *The Practice of Traditional Western Herbalism: Basic Doctrine, Energetics and Classification*. North Atlantic Books, California.

¹⁵ Bartram, T. (1995). *Encyclopedia of Herbal Medicine*. Grace Publishers, Dorset.

¹⁶ Liu, W. & Gong, C. (2009). Opening the Blockage to Reproduction: Infertility. *Traditional Chinese Medicine Information Page* [online]. Available from: <http://www.tcmpage.com/hpinfertility.html> (Accessed 4/7/11).

¹⁷ Hassan, I. (2010). Abzan (Sitz bath) A Regime in Unani System of Medicine. *Articlesbase* [online]. Available from: <http://www.articlesbase.com/alternative-medicine-articles/abzan-sitz-bath-a-regime-in-unani-system-of-medicine-2749047.html>. (Accessed 27/3/12).

Premenstrual Syndrome (PMS)

Although there is no hard evidence of a specific aetiological factor for PMS, many authors have suggested involvement of various reproductive hormones^{2,18}. It is possible that some of the hormonal changes responsible for premenstrual symptoms might also be contributing factors in some women's inability to conceive.

Oestrogen

The oestrogen/progesterone ratio imbalance theory proposes that oestrogen levels are too high in relation to the level of progesterone in women with PMS¹⁹. Relative oestrogen excess may increase feelings of irritability, aggressiveness and anxiety by increasing the availability of Noradrenaline in the brain²⁰. Monoamine Oxidase (MAO) activity is also positively correlated with the progesterone : oestradiol ratio²¹. Oestrogens are also known to increase the renin-angiotensin-aldosterone system and thereby cause fluid retention²².

High levels of oestrogen inhibit secretion of hypothalamic gonadotropin-releasing hormone (GnRH) and other important reproductive hormones such as Follicle Stimulating Hormone (FSH) and Lutenising Hormone (LH)²³, thereby contributing to infertility. The anti-oestrogenic drug clomiphene citrate (Clomid) is used in orthodox medicine to increase the release of FSH²⁴. This suggests that therapeutic measures which reduce relative oestrogen excess may be beneficial in the treatment of infertility in women with symptoms of oestrogen dominance.

¹⁸ Benedek-Jaszmann L. J. & Hearn-Sturtevant M. D. (1976). Premenstrual Tension And Functional Infertility: Aetiology And Treatment. *The Lancet* 307(7969):1095-1098.

¹⁹ Bäckström, T., Carstensen, H. (1974). Estrogen and progesterone in plasma in relation to premenstrual tension. *Journal of Steroid Biochemistry* 5(3): 257-260.

²⁰ Munday, M.R., Brush, M.G. & Taylor, R.W. (1981) Correlations between progesterone, oestradiol and aldosterone levels in the premenstrual syndrome. *Clinical Endocrinology* 14(1):1-9.

²¹ Briggs, M. & Briggs, M (1972). Relationship Between Monoamine Oxidase Activity And Sex Hormone Concentration In Human Blood Plasma. *Journal of Reproduction and Fertility* 29:447-450.

²² Davidson BJ, Rea CD, Valenzuela GJ.(1988). Atrial natriuretic peptide, plasma renin activity, and aldosterone in women on estrogen therapy and with premenstrual syndrome *Fertil Steril.* Nov;50(5):743-6.

²³ Greenstein, B. & Wood, D.F. (2006). *The Endocrine System at a Glance (2nd Edition)*. Blackwell Publishing, Oxford.

²⁴ Hughes, E., Brown, J., Collins, J. & Vanderkerckhove, P. (2000). Clomiphene Citrate for Unexplained Subfertility in Women. *Cochrane Database of Systematic Reviews* [online]. Available from: <http://www.cochrane.org/reviews/en/ab000057.html> (Accessed: 27/1/09).

Reducing relative oestrogen excess

Environmental oestrogen-like chemicals (xeno-oestrogens), which are found in food contaminants (such as pesticides and plastic residues), may have an oestrogenic effect, and are increasingly implicated in cases of infertility²⁵. Non-organic meat and dairy products can also contain high levels of xeno-oestrogens²⁶.

Patients are advised to avoid eating food that has been stored or heated in plastic packaging, to avoid using pesticides in the garden, to buy organic produce where possible, and to peel or scrub any non-organic fruit and vegetables. It is also advisable to take a vitamin B complex supplement, since vitamin B deficiency seems to increase susceptibility to the effects of excess oestrogen²⁷.

Excess oestrogens are conjugated in the liver and excreted in the bile. Therefore, bitter herbs, such as *Taraxacum officinale* and *Iris versicolour*, which increase liver function and reduce constipation, may help to reduce oestrogen excess⁹. Foods high in methionine (such as beans, pulses, onions and garlic) assist with methylation of oestrogen in the liver, the process by which oestradiol is converted into the less potent oestriol. Vitamin B1 is also necessary for the hepatic metabolism of oestrogens⁹. In addition, Cruciferous vegetables (such as cabbage, broccoli, and kale) contain indole-3-carbinol (I3C), which has been shown to increase metabolism and elimination of oestrogen²⁸.

Once oestrogen has been excreted in the bile into the intestine, it may be excreted from the body. However, beta-glucuronidase enzymes, which are produced by intestinal bacteria, may deconjugate oestrogen, allowing it to be re-absorbed into the blood stream. This is known as entero-hepatic circulation.

²⁵ Hudson, T. (2008). *Women's Encyclopedia of Natural Medicine*. McGraw Hill, New York.

²⁶ Wetherbee, K., (2004). Infertility: improving the odds. *Herbs for Health*. [Online]. Available: from <http://cms.herbalgram.org/herbclip/278/review44159.html> (Accessed 28/1/09).

²⁷ Bell, E. (1980). The excretion of a vitamin B6 metabolite and the probability of recurrence of early breast cancer. *European Journal of Cancer* 16(2):297-8.

²⁸ Michnolicz, J.J. & Bradlow, H.L. (1991). Altered estrogen metabolism and excretion in humans following consumption of indole-3-carbinol. *Nutrition and Cancer* 16(1):59-66.

Consumption of saturated animal fats encourages the growth of Beta-glucuronidase-producing bacteria, while probiotic bacteria such as *Lactobacillus acidophilus* reduce it⁹. *Lactobacillus acidophilus* is found in foods such as sauerkraut, or it may be taken as a supplement¹².

Constipation also contributes to entero-hepatic recirculation of oestrogen. Adequate fluid intake and fibre contained in wholegrains, fruit and vegetables reduces excess oestrogen levels by reducing constipation and preventing oestrogens that have been excreted in the bile from being reabsorbed⁹. Women who eat more fibre consequently have a lower risk of infertility²⁹.

Phytoestrogens

Phytoestrogens, found in soybean products, whole-grain cereals, and seeds, are plant compounds such as isoflavones and lignans, which are structurally and functionally similar to human estrogens. They bind weakly to oestrogen receptors, competing with endogenous oestrogens and preventing them from exerting stronger oestrogenic effects³⁰. Phyto-estrogens may also reduce aromatisation of androstenedione to oestrone in fat cells, and stimulate liver production of sex hormone binding globulin (SHBG), which binds to excess oestrogen, reducing its ability to bind to hormone-sensitive tissues⁹.

In order to be absorbed from the digestive system, isoflavones must first undergo hydrolysis of the sugar moiety by β -glucosidase enzymes³¹ which are produced by bifidobacteria in the intestine. Therefore, consuming fermented soya products, or taking a probiotic supplement may help to enhance the bioavailability of isoflavones³².

²⁹ Chavarro, J.E., Rich-Edwards, J.W., Rosner, B.A. & Willett, W.C. (2007). Diet and Lifestyle in the Prevention of Ovulatory Disorder Infertility. *Obstetrics & Gynecology* 110(5):1050-1058.

³⁰ Verheus, M., van Gils, C.H., Keinan-Boker, L., Grace, P.B. Bingham, S.A. & Peeters, P.H.M. (2007). Plasma Phytoestrogens and Subsequent Breast Cancer Risk. *Journal of Clinical Oncology* 25(6): 648-655

³¹ Setchell KDR, Brown NM, Zimmer-Nechemias L, Brashears WT, Wolfe BE, Krischner AS & Heubi JE (2002). Evidence for the lack of absorption of soy isoflavone glycosides in humans, supporting the crucial role of intestinal metabolism for bioavailability. *American Journal of Clinical Nutrition* (76):447 - 453.

³² Tsangalis, D., Wilcox, G., Shah, N.P. & Stojanovska, L. (2005). Bioavailability of isoflavone phytoestrogens in postmenopausal women consuming soya milk fermented with probiotic bifidobacteria. *British Journal of Nutrition*, 93: 867-877

In summary, excess oestrogen levels may be reduced by using herbs which assist its metabolism and excretion, by increasing consumption of organic vegetables, beans, pulses, seeds and wholegrain cereals, and avoiding consumption of meat and dairy products. Indeed, women who eat a vegetarian diet excrete more oestrogen than women who eat meat and have a lower risk of infertility²⁹.

Abnormal progesterone metabolism

Some studies have found higher levels of progesterone or both oestradiol and progesterone in women with PMS^{33 34}. However, it is possible that symptoms may be due to altered progesterone metabolism rather than total progesterone levels². For example, progesterone is a precursor of aldosterone which causes retention of sodium and water²⁰. Increased conversion of progesterone to aldosterone may therefore result in fluid retention.

Allopregnanolone is another important metabolite of progesterone, which is responsible for GABA(A)-mediated anxiolytic responses in stressful conditions. Several studies have demonstrated reduced levels of allopregnanolone in the luteal phase in PMS patients^{35 36}. Conversely, women with PMS may have increased levels of pregnenolone (a precursor of progesterone), which acts as a GABA receptor antagonist and leads to agitation, anxiety and insomnia³⁷. Pregnenolone is also a precursor of DHEA, testosterone and oestradiol²³.

Since decreased progesterone levels may in turn lead to retarded endometrial development, therapeutic measures which improve progesterone function and metabolism may be beneficial in the treatment of infertility.

³³ O'Brien, P.M.S., Selby, C. & Symonds, E.M. (1980) Progesterone, fluid, and electrolytes in premenstrual syndrome. *BMJ*:1161-1163.

³⁴ Redei, E. & Freeman, E.W. (1995). Daily plasma estradiol and progesterone levels over the menstrual cycle and their relation to premenstrual symptoms. *Psychoneuroendocrinology* 20(3): 259-267.

³⁵ Lombardi I, Luisi S, Quirici B, Monteleone P, Bernardi F, Liut M, Casarosa E, Palumbo M, Petraglia F, Genazzani AR. Adrenal response to adrenocorticotrophic hormone stimulation in patients with premenstrual syndrome. *Gynecol Endocrinol.* 2004 Feb;18(2):79-87.

³⁶ Monteleone P, Luisi S, Tonetti A, Bernardi F, Genazzani AD, Luisi M, Petraglia F, Genazzani AR. Allopregnanolone concentrations and premenstrual syndrome. *Eur J Endocrinol.* 2000 Mar;142(3):269-73.

³⁷ Meleran, S.E., Reus, V.I., Webster, R. Shafton, R. & Wolkowitz, O.M. (2003). Chronic pregnenolone effects in normal humans: attenuation of benzodiazepine-induced sedation. *Psychoneuroendocrinology* 29(4):486-500.

Improving progesterone function

Vitex agnus castus addresses a wide range of problems such as premenstrual mood disturbance, fluid retention, and mastalgia due to poor progesterone function and hyperprolactinaemia^{38 39 40}. It is thought to inhibit prolactin release from the anterior pituitary, which leads to an increase in luteinizing hormone (LH), promoting corpus luteum development in the luteal phase, and thereby increasing levels of progesterone⁴¹. Other herbs that are thought to improve progesterone function include *Achillea millefolium*, *Alchemilla vulgaris*⁴², and *Paeonia lactiflora*. In fact, *Paeonia lactiflora* is thought to have a regulating effect on a variety of hormones including oestrogen, androgens progesterone, and prolactin⁹.

Vitamin E supplements may correct an abnormal progesterone/oestradiol ratio⁴³. Vitamin E is also found in whole grains, green leafy vegetables, nuts and seeds¹². Magnesium helps to decrease conversion of progesterone to aldosterone⁹. It is found in soya products, whole-grain cereals, seeds and leafy green vegetables¹².

Adaptogens and adrenal tonics improve adrenal function⁴⁴ and may thereby help to increase adrenal production of progesterone and its metabolites. They include herbs such as *Eleutherococcus senticosus*, *Withania somnifera*, and *Glycyrrhiza glabra*.

Cortisol

Cortisol levels are thought to be low in women with PMS which is associated with depression and fatigue⁴⁵.

³⁸ Berger, D., Schaffner, W., Schrader, E., Meier, B. & Brattstron, A. (2000). Efficacy of *Vitex agnus castus* L. extract Ze 440 in patients with pre-menstrual syndrome (PMS). *Archives of Gynecology and Obstetrics* 264(3):150-3.

³⁹ Gardiner, P. (2000). Chasteberry (*Vitex agnus castus*). *The Longwood Herbal Taskforce* [online]. Available from: <http://longwoodherbal.org/vitex/vitex.pdf> (Accessed 28/2/12).

⁴⁰ Schellenberg, R. (2001). Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study. *BMJ*. 322(7279): 134-137.

⁴¹ Milowicz, A., & Jedrzejuk, D. (2006). Premenstrual syndrome: From etiology to treatment. *Maturitas* 55(1):s47-s54.

⁴² Lapraz, J.C. (2008). *Clinical Phytotherapy and Osteoporosis*. British Endobiogenic Medicine Society, London.

⁴³ London, R.S., Sundaram, G.S., Schultz, M., Nair, P.P. & Goldstein, P.J. (1981). Endocrine parameters and alpha-tocopherol therapy of patients with mammary dysplasia. *Cancer Research* 41(9, Pt 2):3811-3.

⁴⁴ Tillotson, A.K. (2009). *Female Infertility*. [Online] Available from: <http://oneearthherbs.squarespace.com/diseases/female-infertility.html> (Accessed on 28/1/09).

⁴⁵ Odber, J., Cawood, E.H. & Bancroft, J. (1998). Salivary cortisol in women with and without perimenstrual mood changes. *Journal of Psychosomatic Research* 45(6): 557-568.

In stressful situations, the hypothalamus secretes corticotropin-releasing hormone (CRH). CRH then triggers release of adrenocorticotropic hormone (ACTH) from the pituitary, which in turn stimulates release of cortisol from the adrenal glands. However, chronic persistent stress may lead to adrenal exhaustion and low cortisol levels. This results in an increase in CRH as a result of reduced negative feedback²³, which in turn inhibits hypothalamic gonadotropin-releasing hormone secretion⁴⁶, and may therefore contribute to infertility.

Treating Adrenal Exhaustion

Herbal treatment for adrenal exhaustion includes nervine tonics⁹ such as *Hypericum perforatum*, and relaxing nerviness such *Anemone pulsatilla*, *Matricaria recutita* and *Melissa officinalis*. Adrenal adaptogens include *Eleutherococcus senticosus* and *Withania somnifera*⁹. They increase the individual's ability to adapt to various environmental factors, and to avoid the damage they may cause⁴⁷. *Glycyrrhiza glabra* is an adrenal tonic, which is thought to increase production of steroid hormones by the adrenal gland, mimic the activity of cortisol, and prolong its activity by reducing its breakdown⁴⁸.

Cortisol is required for the conversion of glycogen to glucose. When cortisol levels are low, insufficient glucose may be released, leading to hypoglycaemia⁴⁹. It is therefore important to eat small frequent meals in order to maintain stable blood sugar levels and avoid further stress on the adrenal glands. It is also important to avoid consumption of coffee, which increases the rate at which energy is consumed, leading to increased demands on the adrenal glands⁵⁰.

⁴⁶ Chrousos, G.P., Torpy, D.J., & Gold, P.W. (1998). Interactions between the Hypothalamic-Pituitary-Adrenal Axis and the Female Reproductive System: Clinical Implications. *Annals of Internal Medicine* 129(3):229-240.

⁴⁷ Panossian, A. & Wagner, H. (2005). Stimulating effect of adaptogens: an overview with particular reference to their efficacy following single dose administration. *Phytotherapy Resources* 19(10):819-38.

⁴⁸ Mills, S. (1991). *The Essential Book of Herbal Medicine*. Penguim Arkana, London.

⁴⁹ Dalvi, S. (2003). *Adrenal Fatigue, A Desk Reference*. Authors Online Ltd, Bedfordshire.

⁵⁰ Barker, J. & Meletis, C. (2005). The Naturopathic Approach to Adrenal Dysfunction. *Townsend Letter for Doctors & Patients* [online]. Available from: <http://www.encognitive.com> (Accessed 24/3/12).

Prolactin

Prolactin has been suggested as a key factor in premenstrual syndrome. It is thought to contribute to some of the symptoms of PMS, particularly mastalgia and fluid retention^{18 51}. In women with normal prolactin levels, it is thought that symptoms are due to an excessive sensitivity to normal prolactin levels, or 'latent hyperprolactinaemia'⁹.

Prolactin levels are also frequently higher in women with functional infertility¹⁸. Higher concentrations of prolactin inhibit progesterone secretion, and several studies have shown relief from both premenstrual symptoms and infertility using prolactin antagonists such as bromocriptine^{18 51}. However, other therapeutic measures which reduce prolactin may also help to improve fertility. For example, *Vitex agnus castus* has been shown to increase conception in infertile women with hyperprolactinaemia and luteal phase dysfunction^{39 52}.

Stress

Stress may be defined as:

*"Any event or series of events, physical or emotional in a person's life that leads to physiological and biochemical changes"*⁹.

Stress causes the body to increase production of adrenaline, which causes blood to be drawn away from the uterus⁵³ and prevents the uptake of progesterone by progesterone receptors⁵⁴, which, as previously stated, may contribute to infertility. There is also considerable evidence that stress alters prolactin levels⁵⁵.

⁵¹ Sharma, P., Kulshreshtha, S., Mohan, G., Singh, S., & Bhagoliwal, A. (2007). Role Of Bromocriptine And Pyridoxine In Premenstrual Tension Syndrome. *Indian Journal of Physiology & Pharmacology* 5(4): 368-374

⁵² Webster, D.E., Dentali, S.J., Farnsworth, N.R., Wang, Z.J. (2008) Chaste Tree Fruit and Premenstrual Syndrome (Chapter 12). In: Mischoulon, D. & Rosenbaum, J.F. (2008). *Natural Medications for Psychiatric Disorders: Considering the Alternatives*. Wolters Kluwer Health, Illinois.

⁵³ Boyle, M. (2002). *Emergencies around childbirth: a handbook for midwives*. Radcliff Publishing, Milton Keynes.

⁵⁴ Dalton, K. (1990). The aetiology of premenstrual syndrome is with the progesterone receptors. *Med Hypotheses* 31(4): 323-7.

⁵⁵ Harper, R & Lenton, E.A. (1985). Prolactin and subjective reports of stress in women attending an infertility clinic. *Journal of Reproductive and Infant Psychology* 3(1):3-8

According to TCM theory, stress due to overwork may be indicated by swelling along centre crack of the tongue⁵⁶.

Reducing the effects of stress

In conjunction with stress management techniques, the herbal and dietary management of stress involves reducing the adverse effects of stress with nervine tonics and sedatives, as well as improving the body's capacity to adapt to stress with herbal adaptogens⁹.

Hypericum perforatum is a nervine tonic, which is thought to inhibit monoamine oxidase (MAO)⁵⁷. In addition to reducing the effects of stress it may also help to reduce oestrogen excess, since monoamine oxidase activity is positively correlated with the progesterone to oestradiol ratio⁵⁸. Nervine sedatives include *Anemone pulsatilla*, *Leonurus cardiaca*, *Matricaria recutita* and *Melissa officinalis*, while herbal adaptogens include *Eleutherococcus senticosus* and *Withania somnifera*. B vitamins and magnesium also help to reduce tension and to improve sleep patterns⁹.

Hyperalgesia

Prostaglandin E2 (PGE2) causes inflammation⁵⁹, increased uterine muscle spasm and uterine ischaemia⁶⁰; and significantly higher concentrations of Prostaglandin E2 (PGE2) are found in the endometrium and menstrual fluid of women with dysmenorrhoea⁶¹. Abnormal response to prostaglandins may also lead to premenstrual aches and pains (hyperalgesia) and menstrual migraine⁶⁰. High oestrogen levels can also increase Series 2 prostaglandins such as PGE2, while low progesterone levels decrease resistance to prostaglandin-induced uterine spasm⁹.

⁵⁶ Maciocia, G. (2004). *Diagnosis in Chinese Medicine: A Comprehensive Guide*. Elsevier, London.

⁵⁷ Linde, K., Ramirez, G., Mulrow, C.D., Pauls, A., Weidenhammer, W. & Melchart, D. (1996). St John's wort for depression: an overview and meta-analysis of randomised clinical trials. *BMJ* 313(7052):253-258.

⁵⁸ Briggs, M. & Briggs, M (1972). Relationship Between Monoamine Oxidase Activity And Sex Hormone Concentration In Human Blood Plasma. *Journal of Reproduction and Fertility* 29:447-450.

⁵⁹ Curtis-Prior, P.B. (2004). *The Eicosanoids*. John Wiley & Sons, New Jersey

⁶⁰ Benedetto, C. (1989). Eicosanoids in primary dysmenorrhea, endometriosis and menstrual migraine. *Gynecological Endocrinology* 3(1):71-94.

⁶¹ Lumsden, M.A., Kelly, R.W. & Baird, D.T. (2005). Primary dysmenorrhoea: the importance of both prostaglandins E₂ and F_{2α}. *BJOG* 90(12):1135-1140.

Toppozada *et al* (1977)⁶² found an aberrant uterine response to PGE₂ in functionally infertile women. In the normal fertile group there was a definite inhibition of uterine motility, compared to marked uterine stimulation in the functionally infertile group. It is possible that the aberrant response to PGE₂ may be responsible for failure of implantation due to uterine stimulation, and that therapeutic measures to reduce PGE₂ synthesis and uterine stimulation may improve the chance of conception in women with symptoms of hyperalgesia.

Nutrition and supplements to reduce PGE₂

Prostaglandin E₂ is synthesised from arachidonic acid found in animal fats⁵⁹. Therefore, reducing consumption of animal fats and increasing intake of raw vegetable and seed oils selectively decreases dietary precursors of series 2 prostaglandins, and increases series 1 prostaglandins, which have anti-inflammatory, anti-thrombotic and anti-spasmodic effects⁹.

Essential Fatty Acid supplements such as evening primrose or starflower oil contain linolenic and gamma linolenic acid, which increase Prostaglandin E₁ (PGE₁)⁶³. Vitamin E can also positively influence prostaglandin ratios; and Vitamin B₆ and zinc are necessary co-factors in the production of series 1 prostaglandins. Reducing oestrogen excess (as discussed above) can also reduce series 2 prostaglandins⁹.

Herbs that regulate prostaglandin synthesis and reduce uterine stimulation

Zingiber officinale has been shown to reduce the production of prostaglandin E, which reduces excessive uterine contractions and also prevents nausea⁶⁴. *Angelica sinensis* is also thought to regulate prostaglandin synthesis⁹.

⁶² Toppozada, M., Khowessah, S., Osman, M., & Rahman, H.A. (1977). Aberrant uterine response to prostaglandin E₂ as a possible etiologic factor in functional infertility. *Fertility & Sterility* 28(4):434-439.

⁶³ Puolakka, J., Makarainen, L., Viinikka, L. & Ylikorkala, O. (1985). Biochemical and clinical effects of treating the premenstrual syndrome with prostaglandin synthesis precursors. *Journal of Reproductive Medicine* 30(3):149-53.

⁶⁴ Gonlachanvit, S., Chen, Y.H., Hasler, W.L., Sun, W.M. & Owyang, C. (2003). Ginger Reduces Hyperglycemia-Evoked Gastric Dysrhythmias in Healthy Humans: Possible Role of Endogenous Prostaglandins, *JPET* 307(3):1098-1103.

Uterine spasmolytics such as *Anemone pulsatilla*, *Paeonia lactiflora*, *Viburnum prunifolium* and *Viburnum opulus* may be useful for dysmenorrhoea with intermittent cramping pains⁹. Magnesium may also help to decrease uterine cramping⁹. It is found in foods such as soya products, whole-grain cereals, seeds, and green leafy vegetables¹².

Herbs which are Warming, such as *Zingiber officinale* and *Cinnamomum zeylanicum* improve the action of the antispasmodic herbs, especially when the period pain is aggravated by cold, relieved by warmth, or the woman has a tendency to 'feel the cold' easily. The uterine tonics, such as *Chamaelirium luteum*, *Angelica sinensis* and *Rubus idaeus* are also used to treat dysmenorrhoea because they are believed to regulate the activity of the uterus and help initiate contractions which are regular, rhythmic and more orderly as previously discussed in the section on blood flow.

Energetic patterns of disharmony

Traditional Chinese Medicine patterns of disharmony which may contribute to infertility include Blood stasis, Qi stagnation, Kidney Qi Deficiency, Dampness, Cold in the Uterus, and Blood deficiency^{16 56}. The pattern of Blood stasis has been covered previously, and the remaining patterns are discussed below:

Qi Stagnation

Qi Stagnation (particularly Liver Qi Stagnation) is indicated by dysmenorrhoea and P.M.S. with mastalgia⁶⁵ and aches and pains⁶⁶.

Reducing Qi Stagnation

Herbs that are used to treat Qi stagnation in Traditional Chinese Medicine include *Angelica sinensis*, *Paeonia lactiflora* and *Zingiber officinale*¹⁶. Western herbs which may help to reduce Qi stagnation include *Achillia millefolium*, *Anemone pulsatilla*, *Iris versicolour*, and *Leonorus cardiaca*⁶⁷.

⁶⁵ Flaws, B. (1989). *Endometriosis and Infertility and Traditional Chinese Medicine: A Laywoman's Guide*. Blue Poppy Press, Colorado.

⁶⁶ Kaptchuk, T.J. (1983). *Chinese Medicine: The Web that has no Weaver*. Rider Press, London.

⁶⁷ Holmes, P. (2007a) *The Energetics of Western Herbs: A Materia Medica Integrating Western & Chinese Herbal Therapeutics, Volume 2 (Fourth Edition)*. Snow Lotus Press, California.

A primarily vegetarian diet, with an emphasis on fresh raw vegetables and sprouts also helps to reduce Liver Qi Stagnation¹².

The TCM pattern of Liver Qi Stagnation shows some similarity to Pitta aggravation in Ayurveda, which is characterized by symptoms such as inflammation and irritability^{68 69}. Bitter herbs such as *Achillia millefolium* and *Iris versicolour* are useful for reducing Pitta⁷⁰. It is also important to avoid too many pungent, sour and oily foods, red meat, caffeine, and alcohol^{12 68}.

Kidney Qi deficiency

According to Traditional Chinese Medicine theory, the Kidney is responsible for reproduction⁷¹, and more than half of all cases of infertility are associated with a Kidney deficiency^{56 72}. Kidney Yang deficiency is indicated by symptoms such as delayed menstruation, dizziness, tiredness, constipation, cold extremities, a tendency to excess mucous or dampness, a wet tongue, and a deep pulse at the third position on the right hand.

Kidney energy may be depleted by lifestyle factors such as poor diet and overwork⁷¹. Since Kidney Yang is responsible for all transformations within the body, Kidney Yang deficiency may result in insufficient production of Blood, which is required to nourish a developing embryo. Since Kidney Yang is also a source of warmth, there may be insufficient warmth to maintain the embryo. Finally Kidney Yang is responsible for pelvic blood flow, and deficiency may therefore lead to blood stasis in the uterus⁶⁵, which as previously discussed, may also contribute to infertility.

⁶⁸ Lad, V.D. (2006). *Textbook of Ayurveda: A Complete Guide to Clinical Assessment. Volume 2*. The Ayurvedic Press, Albuquerque, New Mexico.

⁶⁹ Stinnett, J.D. (1988). Pitta: The Dosha of Transformation. *Ayurveda Today* 1(1):9-10.

⁷⁰ Frawley, D. & Lad, V. (2001). *The Yoga of Herbs: An Ayurvedic Guide to Herbal Medicine*. Lotus Press, Wisconsin.

⁷¹ Liu, W. & Gong, C. (2009). Opening the Blockage to Reproduction: Infertility. *Traditional Chinese Medicine Information Page* [online]. Available from: <http://www.tcmpage.com/hpinfertility.html> (Accessed 4/7/11).

⁷² Coyle, M. & Smith, C. (2005). A survey comparing TCM diagnosis, health status and medical diagnosis in women undergoing assisted reproduction. *Acupuncture in Medicine* 23:62-69.

Tonifying the Kidney Qi

Warming herbs nourish the Yang and tonify the Kidneys^{12 65}. Warming herbs that may be used to treat infertility due to Kidney Yang deficiency include *Cinnamomum zeylonicum*, *Rosemarinus officinalis*, and *Zingiber officinalis*. It is also important to eat plenty of warm foods, and to get adequate rest.

Dampness

Signs of Dampness include a slippery pulse, a swollen, toothmarked tongue with sticky coating, mid-cycle bleeding, and vaginal *Candida* infection. Dampness in the body may be caused by excessive consumption of greasy foods and dairy products⁷³. It may impede the flow of Qi to the Uterus and thereby contribute to infertility in some women.

Resolving Dampness

Warming herbs such as *Zingiber officinale* and astringent herbs such as *Alchemilla vulgaris* may be used to treat dampness in the reproductive organs. Herbs that stimulate Qi (as discussed in the section on Qi stagnation above) are also used to remove Dampness⁷⁴

The TCM pattern of Dampness shows some similarity to excess Kapha in Ayurveda, which is also characterized by excess mucous and a swollen tongue with white coating⁶⁸. Pungent, astringent and bitter foods reduce Kapha. It is also important to avoid sweet, sour salty and oily and damp foods such as dairy products as they increase Kapha⁷⁴.

⁷³ Schillemans-Eliyah, H. (2011). Stress-induced unexplained infertility - the role of acupuncture. European Academy of Traditional Medical Science TCM Newsletter March 2011 [online]. Available from: <http://www.eatms.nl> (Accessed 20/2/12).

⁷⁴ Tillotson, A.K. (2001). *The One Earth Herbal Sourcebook*. Kensington Books, New York.

Cold in the Uterus.

Excessive exposure to cold, or consumption of cold foods and drinks may lead to Cold in the Uterus⁷³. It is indicated by symptoms such as clotty menstrual flow, feeling of cold, dysmenorrhoea, a pale tongue, and a wiry or tight pulse⁷⁵. Coldness causes contraction, and therefore Cold in the Uterus may impede the flow of Qi and Blood, thereby contributing to infertility. It may also dampen the Kidney Yang, which is needed for conception⁷³.

Warming the Uterus

Warming herbs are recommended to treat uterus cold, such as *Cinnamomum zeylonicum*, *Rosemarinus officinalis* and *Zingiber officinalis*. It is also important to avoid consumption of cold foods and drinks, raw food and exposure to cold¹².

Blood Deficiency

Blood deficiency is very common in women, and may be caused by loss of Blood during menstruation, poor diet, overwork, or emotional stress. It is indicated by a pale, thin, moving tongue and scanty menses. Blood deficiency results in insufficient nourishment of the reproductive organs and reduced receptivity for implantation⁷⁶.

Nourishing the blood

Angelica sinensis is considered to be a Blood Tonic, which is used to treat Blood Deficiency in TCM⁷¹. *Withania somnifera* is an Ayurvedic herb that is used to treat anaemia⁷⁷. The nutrients required to generate healthy blood include iron, vitamin B12, Folic acid and vitamin C. These are found in chlorophyll-rich foods such as micro-algae and dark green leafy vegetables¹².

⁷⁵ Liu, W. & Gong, C. (2009a). A Natural Option for Endometriosis. *Traditional Chinese Medicine Information Page* [online]. Available from: <http://www.tcmpage.com/hpinfertility.html> (Accessed 20/2/12).

⁷⁶ Maciocia G. (1998). *Obstetrics and Gynecology in Chinese Medicine*. Elsevier, London.

⁷⁷ Pole, S. (2006). *Ayurvedic medicine: The Principles of Traditional Practice*. Churchill Livingstone, An imprint of Elsevier, Philadelphia.

Vata disturbance

Vata disturbance may be caused by problems such as stress, anxiety, tiredness and overwork, and eating too many dry or cold foods⁷⁷. Vata disturbance is suggested by symptoms such as: fatigue, feeling stressed, feeling cold, poor peripheral circulation, palpitations, abdominal bloating, constipation, dry skin and hair, cracking joints, muscle spasm, pins and needles, scanty menstruation, and infertility⁶⁸.

Reducing Vata aggravation:

Sweet, sour, salty and moist foods and herbs help to reduce Vata aggravation⁷⁸. Herbs such as *Withania somnifera*, *Glycyrrhiza glabra*, *Cinnamomum zeylonicum* and *Rosemarinus officinalis* also reduce Vata aggravation⁷⁰.

Figures 2 a, b, and c, provide a summary of the various orthodox, TCM and Ayurvedic diagnoses discussed above, examples of symptoms that are suggestive of each diagnosis, and the recommended treatments.

⁷⁸ Lad, V.D. (2002). *Textbook of Ayurveda: Fundamental Principles. Volume 1*. The Ayurvedic Press, Albuquerque, New Mexico

Figure 2a. Orthodox diagnoses

Diagnosis	Symptoms	Examples of herbs used	Other recommendations
Poor circulation	Poor peripheral circulation and dysmenorrhoea	<i>Zingiber officinale</i> , <i>Cinnamomum zeylonicum</i> , <i>Rosmarinus officinalis</i> , <i>Achillea millefolium</i> .	Increase consumption of wholegrains, nuts, seeds, and leafy green vegetables. Increase exercise.
Oestrogen dominance and progesterone insufficiency	PMS	<i>Taraxacum officinale</i> , <i>Iris versicolour</i> , <i>Vitex agnus-castus</i> , <i>Alchemilla vulgaris</i> , <i>Achillea millefolium</i> , <i>Paeonia lactiflora</i> . <i>Eleutherococcus senticosus</i> , <i>Withania somnifera</i> , <i>Glycyrrhiza glabra</i> .	Take probiotics and B vitamins. Eat green leafy vegetables, soya products, seeds, pulses and wholegrain cereals. Avoid meat & dairy products.
Low cortisol levels	Depression and fatigue	<i>Hypericum perforatum</i> , <i>Anemone pulsatilla</i> , <i>Melissa officinalis</i> , <i>Eleutherococcus senticosus</i> , <i>Withania somnifera</i> , <i>Glycyrrhiza glabra</i> .	Avoid coffee and refined sugar. Eat small regular meals to balance blood sugar levels.
Latent hyperprolactinaemia	Mastalgia and fluid retention	<i>Vitex agnus-castus</i>	Reduce stress levels.
Stress	Overwork, feeling stressed, swelling along centre crack of the tongue.	<i>Anemone pulsatilla</i> , <i>Leonorus cardiaca</i> , <i>Matricaria recutita</i> , <i>Melissa officinalis</i> , <i>Hypericum perforatum</i> , <i>Eleutherococcus senticosus</i> , <i>Withania somnifera</i> .	Magnesium and B vitamins. Take measures to reduce stress levels such as meditation, yoga, or enjoyable social activities.
Abnormal response to prostaglandins	Aches and pains; dysmenorrhoea; headaches and migraines.	<i>Zingiber officinalis</i> , <i>Angelica sinensis</i> , <i>Viburnum spp.</i> <i>Anemone pulsatilla</i> , <i>Paeonia lactiflora</i> .	Avoid animal fats and increase consumption of omega 3 oils from nuts and seeds.

Figure 2b. TCM diagnoses

Diagnosis	Symptoms	Examples of herbs used	Other recommendations
Blood Stasis	Dysmenorrhoea, clotty menstruation, and blue/purple tongue. (See also poor circulation in figure 23a above)	<i>Chamaelirium luteum, Angelica sinensis, Leonorus cardiaca, Rubus idaeus.</i>	Increase consumption of wholegrains, nuts, seeds and leafy green vegetables. Increase exercise.
Qi stagnation / Liver Qi stagnation	Dysmenorrhoea, P.M.S. aches and pains.	<i>Angelica sinensis, Paeonia lactiflora, Zingiber officinale, Achillea millefolium, Iris versicolour, Anemone pulsatilla.</i>	Vegetarian diet.
Kidney Qi Deficiency	Delayed menstruation, constipation, tiredness, dizziness, and deep pulse at third position.	<i>Cinnamomum zeylonicum, Rosmarinus officinalis, Zingiber officinale, Paeonia lactiflora</i>	Eat plenty of warm foods and get adequate rest.
Dampness	Swollen, toothmarked tongue, slippery pulse, sticky tongue coating, mid-cycle bleeding and <i>Candida</i> infection.	<i>Zingiber officinale, Alchemilla vulgaris, Anemone pulsatilla, Iris versicolour.</i>	Avoid greasy foods and dairy products.
Uterus cold	Clotty menses and feeling of cold.	<i>Cinnamomum zeylonicum, Rosmarinus officinalis, Zingiber officinale</i>	Avoid exposure to cold, and cold foods and drinks.

Figure 2c. Ayurvedic Diagnoses

Diagnosis	Symptoms	Examples of herbs used	Other recommendations
Vata disturbance/ excess	Feeling of cold, poor peripheral circulation, palpitations, pins & needles, muscle spasm, cracking joints, constipation, feeling stressed and insomnia between 2am and 6am.	<i>Withania somnifera</i> , <i>Glycyrrhiza glabra</i> , <i>Cinnamomum zeylonicum</i> , <i>Rosmarinus officinalis</i> .	Increase consumption of moist, warm, sweet, sour and salty foods. Avoid dry, and bitter foods, and getting tired or stressed.
Pitta excess	Inflammation and irritability.	<i>Achillia millefolium</i> and <i>Iris versicolour</i>	Increase fresh fruit and vegetables, avoid pungent, sour and oily foods, caffeine, alcohol and red meat.
Kapha excess	Sweet cravings, constipation, excess mucous and fatigue	<i>Achillea millefolium</i> <i>Alchemilla vulgaris</i> , <i>Iris versicolour</i> , <i>Taraxacum officinale</i> , <i>Zingiber officinale</i>	Avoid sweet, sour and salty, cold damp and oily foods. Avoid overeating and take regular exercise.

Other Factors Affecting Fertility

Nutrition

The nutritional factors that may affect fertility have been discussed in the previous section. The main foods that may help to increase fertility, and those which are best avoided are summarised in Figure 3 below.

Figure 3. General nutritional advice for increasing fertility

Foods to include in the diet	Foods to avoid
<ul style="list-style-type: none"> ● Omega-3 fatty acids from non hydrogenated seed oils. ● Wholegrains, nuts and seeds. ● Beans and pulses (especially soya products). ● Fresh fruit and vegetables, especially leafy green, cruciferous vegetables. ● High fibre, low glycaemic index foods. ● Organic foods. 	<ul style="list-style-type: none"> ● Animal fats ● Meat and dairy products ● High glycaemic index carbohydrates. ● Non-organic foods

Fertility increases with diets which include a lower intake of animal protein with greater vegetable protein intake; a lower intake of trans-fat with a greater intake of monounsaturated fat; and a lower intake of high glycaemic index foods with a higher intake of high-fibre, low-glycaemic index carbohydrates⁷⁹. The latter is thought to be due to the effect of carbohydrate consumption on insulin sensitivity, which effects ovulatory function and fertility. Improved insulin sensitivity is associated with improved ovulatory function and fertility in both healthy women and women with polycystic ovary syndrome (PCOS)⁸⁰.

Nutritional deficiencies

Infertility is also associated with deficiencies of various nutrients including vitamins A, C, E, B6, B12, folic acid, zinc⁸¹, iron, and essential fatty acids such as EPA and DHA⁸².

⁷⁹ Chavarro, J.E., Rich-Edwards, J.W., Rosner, B.A. & Willett, W.C. (2007). Diet and Lifestyle in the Prevention of Ovulatory Disorder Infertility. *Obstetrics & Gynecology* 110(5):1050-1058.

⁸⁰ Chavarro, J.E., Rich-Edwards, J.W., Rosner, B.A. & Willett, W.C. (2009). A prospective study of dietary carbohydrate quantity and quality in relation to risk of ovulatory infertility. *European Journal of Clinical Nutrition* 63:78-86.

⁸¹ Mortimore, D. (2001). *The Complete Illustrated Guide to Vitamins and Minerals*. Element, London.

⁸² Mehendale, S.S., Kilari Bams, A.S., Deshmukh, C.S., Dhorepatil, B.S., Nimbargi, V.N. & Joshi, S.R. (2009). Oxidative stress-mediated essential polyunsaturated fatty acid alterations in female infertility. *Human Fertility* 12(1):28-33.

Women who take multivitamins have a lower risk of infertility^{79 83}. 400mcg folic acid per day is also recommended for women who are trying to conceive in order to prevent spina bifida⁸⁴.

Gluten Intolerance

Consumption of foods containing gluten (wheat, rye, barley, spelt and oats) may contribute to infertility in patients with gluten intolerance^{85 86}. It has been suggested that this may be due to resulting malabsorption of folic acid and other nutrients⁸⁷.

Caffeine

Wilcox *et al* (1988) found that the fertility of healthy women attempting to conceive may be halved by consumption of the equivalent of one cup of coffee or more per day⁸⁸. The mechanism of action of caffeine on fertility is unknown, however, it may be due to a combination of reduced circulatory capacity and depletion of the adrenal glands. Therefore, women who are trying to conceive are advised to avoid consumption of coffee and other caffeine-containing substances.

Alcohol

Several studies have demonstrated that the likelihood of conception decreases with increasing alcohol intake even among women with an alcohol intake corresponding to five or less drinks per week⁸⁹. Therefore women who are trying to conceive should be advised to avoid alcohol consumption.

⁸³ Czeizel A, Metneki J, Dudas I. (1996). The effect of preconceptional multivitamin supplementation on fertility." *International Journal for Vitamin and Nutrition Research* 66:55-58

⁸⁴ NICE (2004). *Fertility: assessment and treatment for people with fertility problems*. National Institute for Clinical Excellence [online] available from: www.nice.org.uk. (Accessed 28/1/09).

⁸⁵ Collin, P., Vilska, S., Heinonen, P.K., Hallstrom, O. & Pikkarainen, P. (1996). Infertility and Coeliac Disease. *Gut* 39:382-384.

⁸⁶ Sher. K.S., & Mayberry, J.F. (1996) Female fertility, obstetric and gynaecological history in coeliac disease: a case control study. *Acta Paediatrica* 85(412):76-77.

⁸⁷ Pellicano, R., Astegiano, M., Bruno, M., Fagoonee, S. & Rizzetto, M. (2007). Women and celiac disease: association with unexplained infertility. *Minerva Med.* 98(3):217-9.

⁸⁸ Wilcox, A., Weinburg, C. & Baird, D., Caffeinated beverages and decreased fertility. *Lancet* 2(8626-8627):1453-6.

⁸⁹ Jensen, T.K., Henrik, N. Hjollund, I., Henriksen, T.B., Scheike, T., Kolstad, H., Giwercman, A Ernst, E., Bonde, J.P., Skakkebaek, N.E. & Olsen, J. (1998). Does moderate alcohol consumption affect fertility? Follow up study among couples planning first pregnancy. *BMJ* 317(7157): 505-510.

Smoking

Cigarette smoking has also been linked with reduced fertility in women^{90 91}. This may be due to increased levels of adrenalin and noradrenalin, with resulting vascular resistance⁹², leading to impaired blood flow.

Exercise

Women who exercise tend to have lighter and less frequent periods⁹³. This may be as a result of increased oestrogen clearance. Women who exercise regularly have a reduced risk of infertility due to ovulatory disorders⁷⁹. However it is also important to avoid over-exercising, since vigorous exercise for more than one hour per day is associated with infertility⁹⁴.

⁹⁰ Augood, C., Duckitt, K. & Templeton, A.A. (1998). Smoking and female infertility: a systematic review and meta-analysis. *Human Reproduction* 13:1532-1539.

⁹¹ Laurent, S.L., Thompson, S.J., Addy, C. Garrison, C.Z. & Moore, E.E. (1992). An Epidemiologic study of smoking and primary infertility in women. *Fertil steril* 57(3):565-72

⁹² Grassi, G., Seravalle, G., Calhoun, D.A., Bolla, G.B., Giannattasio, C., Marabini, M., Del Bo A. & Mancia G. (1994). Mechanisms responsible for sympathetic activation by cigarette smoking in humans. *Circulation* 90:248-253.

⁹³ Harlow, S.D. & Campbell, B.C. (1994). Host Factors That Influence the Duration of Menstrual Bleeding. *Epidemiology* 5(3):352-355.

⁹⁴ Green, B.B., Daling, J.R., Weiss, N.S., Liff, J.M. & Koepsell, T. (1986). Exercise as a Risk Factor for Infertility with Ovulatory Dysfunction. *American Journal of Public Health* 76:1432-1436.