

ACUPUNCTURE AND PCOS

About PCOS

Polycystic ovarian syndrome (PCOS) is the most common female endocrine disorder. Up to one-third of women in the UK have polycystic ovaries (i.e. 10 or more follicles per ovary detected on ultrasound), and around a third of these are thought to have the syndrome.(DTB 2001) PCOS is strongly associated with hyperandrogenism, ovulatory dysfunction and obesity.(Stener-Victorin 2008) The syndrome also increases the risk for metabolic disturbances such as hyperinsulinaemia and insulin resistance, which can lead to type 2 diabetes, hypertension and an increased likelihood of developing cardiovascular risk factors and impaired mental health later in life.(Stener-Victorin 2008)

Despite extensive research, little is known about the aetiology of PCOS, but the syndrome is associated with peripheral and central factors that influence sympathetic nerve activity.(Stener-Victorin 2008) Thus, the sympathetic nervous system may be an important factor in the development and maintenance of PCOS.

Many women with PCOS require prolonged treatment. Polycystic ovarian syndrome (PCOS) is characterised by the clinical signs of oligo-amenorrhoea (infrequent or very light menstruation), infertility (failure to conceive), acne, male patterned baldness and hirsutism (excessive hair growth). The current conventional medical treatments for women with PCOS are prescription medications, surgery, and lifestyle changes aimed at controlling symptoms.

References

Stener-Victorin E et al. Acupuncture in polycystic ovary syndrome: Current experimental and clinical evidence. *Journal of Neuroendocrinology* 2008; 20: 290-8.

Tackling polycystic ovary syndrome. *DTB* 2001; 39: 1-3

How acupuncture can help

This Factsheet focuses on the evidence for acupuncture in the treatment of PCOS. There are also Factsheets on Anxiety, Depression, Female Fertility, Infertility ART, Obesity, Stress and Type 2 Diabetes, which may have relevant information related to symptoms and conditions associated with PCOS.

Two systematic reviews by the same author (Lim 2010, 2011) of acupuncture for PCOS have drawn conflicting conclusions. One found no truly randomised controlled trials of acupuncture for PCOS and, while it found non-randomised studies that suggested acupuncture was associated with a low adverse events rate and no increased risk of multiple pregnancies, the reviewers concluded that properly designed RCTs are needed before a conclusive statement can be drawn to support the use of acupuncture in the management of PCOS.(Lim 2011) The other review concluded that acupuncture is a safe and effective treatment for PCOS, and may have a role: increasing blood flow to the ovaries, reducing ovarian volume and the number of ovarian cysts, controlling hyperglycaemia by increasing insulin sensitivity and decreasing blood glucose and insulin levels, reducing cortisol levels and assisting in weight loss and anorexia.(Lim 2010) Several randomised controlled trials have been published since the systematic reviews. One trial found that acupuncture can improve the clinical pregnancy rate in patients with PCOS undergoing IVF-ET.(Cui 2011) Another found that abdominal acupuncture treatment can improve the endocrine and metabolic function of patients with obesity-type PCOS.(Lai 2010) A third found low-frequency electroacupuncture and physical exercise improved hyperandrogenism and menstrual frequency more effectively than no intervention in women with PCOS, and that it was superior to physical exercise.(Jedel 2011) Another recent study did not find a difference between 'real' and sham acupuncture protocols for women with PCOS.(Pastore 2011), but this may be due to sham acupuncture being an active treatment rather than a placebo (Lundeberg 2009).

In general, acupuncture is believed to stimulate the nervous system and cause the release of neurochemical messenger molecules. The resulting biochemical changes influence the body's homeostatic mechanisms, thus promoting physical and emotional well-being.

Research has shown that acupuncture treatment may specifically help with symptoms of PCOS by:

- impacting on beta-endorphin production, which may affect gonadotropin-releasing hormone (GnRH) secretion (Lim 2010; Stener-Victorin 2009; Feng 2009; Manneras 2009);
- a regulatory effect on follicle stimulation hormone (FSH), luteinising hormone (LH) and androgens (Lim 2010; Feng 2009);
- modulating the activity of the sympathetic nervous system and improving blood flow to the ovaries (Stener-Victorin 2006, 2009);
- regulating steroid hormone/peptide receptors (Feng 2012);

- downregulating the expressions of serum levels of testosterone and oestradiol (Zang 2009);
- controlling hyperglycaemia by increasing insulin sensitivity and decreasing blood glucose and insulin levels (Lim 2010);
- acting on areas of the brain known to reduce sensitivity to pain and stress, as well as promoting relaxation and deactivating the 'analytical' brain, which is responsible for anxiety and worry (Hui 2010; Hui 2009);
- increasing the release of adenosine, which has antinociceptive properties (Goldman 2010), and;
- reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007).

About traditional acupuncture

Acupuncture is a tried and tested system of traditional medicine, which has been used in China and other eastern cultures for thousands of years to restore, promote and maintain good health. Its benefits are now widely acknowledged all over the world and in the past decade traditional acupuncture has begun to feature more prominently in mainstream healthcare in the UK. In conjunction with needling, the practitioner may use techniques such as moxibustion, cupping, massage or electro-acupuncture. They may also suggest dietary or lifestyle changes.

Traditional acupuncture takes a holistic approach to health and regards illness as a sign that the body is out of balance. The exact pattern and degree of imbalance is unique to each individual. The traditional acupuncturist's skill lies in identifying the precise nature of the underlying disharmony and selecting the most effective treatment. The choice of acupuncture points will be specific to each patient's needs. Traditional acupuncture can also be used as a preventive measure to strengthen the constitution and promote general well-being.

An increasing weight of evidence from Western scientific research (see overleaf) is demonstrating the effectiveness of acupuncture for treating a wide variety of conditions. From a biomedical viewpoint, acupuncture is believed to stimulate the nervous system, influencing the production of the body's communication substances - hormones and neurotransmitters. The resulting biochemical changes activate the body's self-regulating homeostatic systems, stimulating its natural healing abilities and promoting physical and emotional well-being.

About the British Acupuncture Council

With over 3000 members, the British Acupuncture Council (BAcC) is the UK's largest professional body for traditional acupuncturists. Membership of the BAcC guarantees excellence in training, safe practice and professional conduct. To find a qualified traditional acupuncturist, contact the BAcC on 020 8735 0400 or visit www.acupuncture.org.uk

ACUPUNCTURE AND PCOS

The evidence

Research

Conclusion

Systematic reviews

Lim DC et al. Acupuncture for polycystic ovarian syndrome. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD007689.

A systematic review that assessed the efficacy and safety of acupuncture treatment for women with polycystic ovarian syndrome (PCOS). No truly randomised controlled trials of acupuncture for PCOS were found. Non-randomised acupuncture studies in PCOS have suggested a low associated adverse events rate, no increased risk of multiple pregnancies, and that it is inexpensive. However, properly designed RCTs are required before a conclusive statement can be drawn to support the use of acupuncture in the management of PCOS.

Lim DC et al. Current evidence of acupuncture on polycystic ovarian syndrome. Gynecol Endocrinol. 2010 Mar 16. [Epub ahead of print]

A literature review evaluating the efficacy of acupuncture therapy in the treatment of polycystic ovarian syndrome (PCOS) by reviewing randomised and non-randomised and observational studies. It also looked at the possible mechanism of acupuncture treatment in PCOS. Four studies were included. Several showed that acupuncture significantly increases beta-endorphin levels for up to 24 hours and may have a regulatory effect on follicle stimulation hormone (FSH), luteinising hormone (LH) and androgens. Beta-endorphin levels increased secondary to acupuncture promoting the release of adrenocorticotrophic hormone (ACTH). The reviewers concluded that acupuncture is a safe and effective treatment for PCOS, and may have a role: increasing blood flow to the ovaries, reducing ovarian volume and the number of ovarian cysts, controlling hyperglycaemia by increasing insulin sensitivity and decreasing blood glucose and insulin levels, reducing cortisol levels and assisting in weight loss and anorexia.

Randomised controlled trials

Cui W et al. Effect of electroacupuncture on oocyte quality and pregnancy for patients with PCOS undergoing in vitro fertilization and embryo transfer. Zhongguo Zhen Jiu. 2011; 31:687-91.

A randomised controlled trial that assessed the impacts and mechanisms of electroacupuncture (EA) on oocyte quality and pregnancy outcome in 66 women with PCOS who were undergoing in vitro fertilization and embryo transfer (IVF-ET). The women were allocated to an observation group and a control group. Ethinylestradiol and cyproterone acetate tablets and gonadotropin-releasing hormone agonist were administered for long-program superovulation in both groups. With EA, the fertilization rate (76.2% vs. 66.3 %, cleavage rate (98.7% vs. 94.5%) and the rate of high-quality embryos (60.2% vs. 50.5%) were all superior to those in control group (all $p < 0.05$). Clinical pregnancy rate was also higher with EA (46.7% vs. 37.9%) but this was not statistically different. In addition, stem cell factor levels in the serum and follicular fluid on the day of ovary

collection were higher with EA (all $p < 0.05$). The researchers concluded that electroacupuncture can play an active role in the pregnancy outcomes of patients with PCOS undergoing IVF-ET and it can improve clinical pregnant rate.

Pastore LM et al. True and sham acupuncture produced similar frequency of ovulation and improved LH to FSH ratios in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2011; 96: 3143-50.

A randomised controlled trial that compared sham and 'real' acupuncture on pituitary gonadotropin hormones and ovulatory frequency in 84 women with PCOS. Serum luteinising hormone (LH) and follicle stimulating hormone (FSH) were measured at baseline, after intervention, and 3 months later. Ovulation was measured with weekly urine or blood samples. Both groups demonstrated a similar mean ovulation rate over the 5 months (0.37/month with 'real' acupuncture and 0.40/month sham participants; $p = 0.6$), similar LH to FSH ratio improvement (-0.5 and -0.8 with 'real' and sham acupuncture, respectively; $p < 0.04$ after intervention vs. baseline) and a similar decline in LH over the 5-month protocol ($p < 0.05$). Neither group experienced a change in FSH. There were seven pregnancies (no difference by intervention, $p = 0.7$). Lower fasting insulin and free testosterone were highly correlated with a higher ovulation rate within the true acupuncture group only ($p = 0.03$), controlling for prestudy menstrual frequency and body mass index. The researchers concluded that they were unable to discern a difference between the 'real' and sham acupuncture protocols for these women with PCOS, and both groups had a similar improvement in their LH/FSH ratio.

Jedel E et al. Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: a randomized controlled trial. *Am J Physiol Endocrinol Metab.* 2011; 300: E37-45.

A randomised controlled trial that assessed whether low-frequency electro-acupuncture (EA) would decrease hyperandrogenism and improve oligo/amenorrhea more effectively than physical exercise or no intervention in 84 women with PCOS. After 16 weeks of intervention, circulating testosterone decreased by 25%, androsterone glucuronide by 30% and androstane-3 β ,17 β -diol-3-glucuronide by 28% in the EA group ($p = 0.038$, 0.030 , and 0.047 , respectively vs. exercise); menstrual frequency increased to 0.69/month from 0.28 at baseline in the EA group ($p = 0.018$ vs. exercise). After 16 weeks of follow-up, the acne score decreased by 32% in the EA group ($p = 0.006$ vs. exercise). Both EA and exercise improved menstrual frequency and decreased the levels of several sex steroids at week 16 and after follow-up compared with no intervention. The researchers concluded that low-frequency EA and physical exercise improved hyperandrogenism and menstrual frequency more effectively than no intervention in women with PCOS, and EA was superior to physical exercise and may be useful for treating hyperandrogenism and oligo/amenorrhea.

Lai MH et al. Effect of abdominal acupuncture therapy on the endocrine and metabolism in obesity-type polycystic ovarian syndrome patients. *Zhen Ci Yan Jiu.* 2010; 35: 298-302.

A randomised controlled trial that compared the effects of abdominal acupuncture with metformin (250mg three times daily for one week then 500mg three times a day thereafter) in 86 women with obesity-type polycystic ovarian syndrome (PCOS) patients. After treatment, body mass index (BMI), waist-hip ratio (WHR), Ferriman-Galleey score (FGS) and ovarian volume (OV) were reduced significantly in both groups ($p < 0.05$), while

menstrual frequency (MF) increased significantly in both groups ($p < 0.05$). However, the effects of abdominal acupuncture were significantly superior to those of medication in down-regulating BMI and WHR, and upregulating MF ($p < 0.05$). Serum luteinising hormone (LH) and follicle stimulating hormone (FSH) decreased significantly ($p < 0.05$), but abdominal acupuncture reduced them more ($p < 0.05$). Following the treatment, fasting blood glucose (FBG), fasting insulin (FIN) and the Homa insulin resistance index (IRI) in both groups all decreased considerably ($p < 0.05$), but without significant differences between them ($p > 0.05$). Serum total cholesterol, triglycerides, and low density lipoprotein-cholesterol levels decreased significantly ($p < 0.05$), while serum high density lipoprotein-cholesterol levels increased significantly ($p < 0.05$) in both groups without significant differences between them. The researchers concluded that abdominal acupuncture treatment can improve the endocrine and metabolic function of patients with obesity-type PCOS.

Stener-Victorin E et al. Low-frequency electroacupuncture and physical exercise decrease high muscle sympathetic nerve activity in polycystic ovary syndrome. *Am J Physiol Regul Integr Comp Physiol* 2009; 297: R387-95.

A randomised controlled trial that compared the effects of low-frequency electroacupuncture (EA) with exercise or no treatment on sympathetic nerve activity in 20 women with PCOS. Direct recordings of multiunit efferent postganglionic muscle sympathetic nerve activity (MSNA) in a muscle fascicle of the peroneal nerve were taken before and following 16 weeks of treatment. Biometric, hemodynamic, endocrine, and metabolic parameters were measured. Low-frequency EA and physical exercise decreased MSNA burst frequency compared with the untreated control group. The low-frequency EA group reduced sagittal diameter ($p = 0.001$), while the physical exercise group reduced body weight ($p = 0.004$) and body mass index ($p = 0.004$) compared with the untreated control group. Sagittal diameter was related to MSNA burst frequency ($p < 0.005$) in the EA group. No correlation was found for body mass index and MSNA in the exercise group. There were no differences between the groups in hemodynamic, endocrine, and metabolic variables. The researchers concluded that the results demonstrate that low-frequency EA and physical exercise lower high sympathetic nerve activity in women with PCOS.

Possible mechanisms of acupuncture

Feng Y et al., Electrical and manual acupuncture stimulation affects estrous cyclicity and neuroendocrine function in a DHT-induced rat polycystic ovary syndrome model. *Exp Physiol*. 2012 Feb 24. [Epub ahead of print]

An animal study that assessed the effects of electroacupuncture (EA) and manual acupuncture in rats. It found that the effects of low-frequency EA may be mediated by central opioid receptors, while manual stimulation may involve regulation of steroid hormone/peptide receptors.

Goldman N et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. *Nat Neurosci* 2010; May 30.

A study showing that the neuromodulator adenosine, which has anti-nociceptive properties, was released during acupuncture in mice, and that its anti-nociceptive actions required adenosine A1 receptor expression. Direct injection of an adenosine A1 receptor agonist replicated the analgesic effect of acupuncture. Inhibition of enzymes involved in adenosine degradation potentiated the acupuncture-elicited

	<p>increase in adenosine, as well as its anti-nociceptive effect. The researchers concluded that their observations indicate that adenosine mediates the effects of acupuncture and that interfering with adenosine metabolism may prolong the clinical benefit of acupuncture.</p>
<p>Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. <i>Auton Neurosci</i> 2010; 157: 81-90.</p>	<p>Studies have shown that acupuncture stimulation, when associated with sensations comprising deqi, evokes deactivation of a limbic-paralimbic-neocortical network, as well as activation of somatosensory brain regions. These networks closely match the default mode network and the anti-correlated task-positive network. The effect of acupuncture on the brain is integrated at multiple levels, down to the brainstem and cerebellum and appears to go beyond either simple placebo or somatosensory needling effects. Needling needs to be done carefully, as very strong or painful sensations can attenuate or even reverse the desired effects. Their results suggest that acupuncture mobilises the functionally anti-correlated networks of the brain to mediate its actions, and that the effect is dependent on the psychophysical response. They discuss potential clinical application to disease states including chronic pain, major depression, schizophrenia, autism, and Alzheimer's disease.</p>
<p>Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. <i>Human Brain Mapping</i> 2009; 30: 1196-206.</p>	<p>This study assessed the results of fMRI on 10 healthy adults during manual acupuncture at 3 acupuncture points and a sham point on the dorsum of the foot. Although certain differences were seen between real and sham points, the hemodynamic and psychophysical responses were generally similar for all 4 points. Acupuncture produced extensive deactivation of the limbic-paralimbic-neocortical system. Clusters of deactivated regions were seen in the medial prefrontal cortex, the temporal lobe and the posterior medial cortex. The sensorimotor cortices, thalamus and occasional paralimbic structures such as the insula and anterior middle cingulate cortex showed activation. The researchers concluded that their results provided additional evidence that acupuncture modulates the limbic-paralimbic-neocortical network. They hypothesised that acupuncture may mediate its analgesic, anti-anxiety, and other therapeutic effects via this intrinsic neural circuit that plays a central role in the affective and cognitive dimensions of pain.</p>
<p>Zang WY et al. Influences of acupuncture on infertility of rats with polycystic ovarian syndrome. [In Chinese]. <i>Zhongguo Zhong Xi Yi Jie He Za Zhi</i>. 2009; 29: 997-1000.</p>	<p>An animal study that researched the effects and mechanism of acupuncture on infertility in rats with polycystic ovarian syndrome. It found that acupuncture can significantly downregulate the expressions of serum levels of testosterone and oestradiol, improve the development of ovaries and uterus, promote ovulation, enhance endometrial receptivity, and advance blastocyte implantation.</p>
<p>Feng Y et al. Hypothalamic neuroendocrine functions in rats with dihydrotestosterone-induced polycystic ovary syndrome: effects of low-frequency</p>	<p>An animal study that assessed the effects of low-frequency electroacupuncture (EA) in adult rats with dihydrotestosterone-induced polycystic ovary syndrome. Repeated low-frequency EA was found to normalise oestrous cyclicity and restored</p>

electro-acupuncture. PLoS One. 2009; 4: e6638. gonadotropin-releasing hormone and androgen receptor protein expression. The researchers suggested their results may help explain the beneficial neuroendocrine effects of low-frequency EA in women with PCOS.

Manneras L et al. Acupuncture and exercise restore adipose tissue expression of sympathetic markers and improve ovarian morphology in rats with dihydrotestosterone-induced PCOS. American Journal of Physiology - Regulatory Integrative and Comparative Physiology. 2009; 296: R1124-R1131. An animal study that investigated the effects of low-frequency EA and physical exercise on mRNA expression of sympathetic markers in adipose tissue and on ovarian morphology in female rats with dihydrotestosterone (DHT)-induced PCOS. Low-frequency EA and exercise was found to downregulate mRNA expression of nerve growth factor and neuropeptide Y, and EA also downregulated expression of beta3-adrenergic receptor, compared with untreated rats with DHT-induced PCOS. EA and exercise improved ovarian morphology, as reflected in a higher proportion of healthy antral follicles and a thinner theca interna cell layer than in the untreated rats. The researchers concluded that their findings support the theory that increased sympathetic activity contributes to the development and maintenance of PCOS, and that the effects of EA and exercise may be mediated by modulation of sympathetic outflow to the adipose tissue and ovaries.

Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. Integr Cancer Ther 2007; 6: 251-7. Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.

Methodological considerations concerning acupuncture trials

Lundeberg T et al. Is Placebo Acupuncture What It is Intended to Be? Evid Based Complement Alternat Med. 2009 Jun 12. [Epub ahead of print] Discusses the concerns with sham acupuncture and recommends instead that the therapy be evaluated by comparisons with standard treatments.
