

Case Report

Integrative techniques using acupuncture, Chinese herbal medicine, diet, and supplements for polycystic ovary syndrome: a case report

Dagmar Ehling

Oriental Health Solutions, LLC., Durham, North Carolina 27705, USA

KEYWORDS: polycystic ovary syndrome; infertility; Hashimoto disease; acupuncture therapy; medicine, Chinese traditional; medicine, herbal; diet; dietary supplements; case reports

DOI: 10.3736/jintegrmed2013055

Ehling D. Integrative techniques using acupuncture, Chinese herbal medicine, diet, and supplements for polycystic ovary syndrome: a case report. *J Integr Med*. 2013; 11(6): 422-427.

Received June 24, 2013; accepted September 11, 2013.

Open-access article copyright © 2013 Dagmar Ehling.

Dagmar Ehling, MAc, LAc, DOM(NM), Dipl OM, FABORM;

1 Introduction

Patients with a diagnosis of polycystic ovary syndrome (PCOS) are on the rise. About 4%-12% of women are currently estimated to have this condition^[1]. It is hypothesized that PCOS appears in women who have long-standing insulin resistance (IR), which leads to high androgen and testosterone levels; this ultimately disrupts their menstrual cycles^[1,2]. Some researchers attribute IR to genetic factors^[3], although there have been only minute changes in the human genome in the past 20 000 years^[4]. However, even with a stable gene pool, genes can be turned on and off by the environment, food and air quality and toxin exposure^[4,5].

Human diets have changed dramatically over the past sixty to seventy years. Farm fresh food has been replaced with factory farming, and home-cooking has been replaced with microwaved TV-dinners, soda pops, donuts, and processed foods — all of which have reduced overall nutrient density^[6]. Average grain consumption has increased 45% from the 1970s to year 2000^[7]. The United States Department of Agriculture food pyramid and food plate recommends 6-11 servings of carbohydrates per day^[8,9]. Carbohydrates act like a sugar in the body. The average sugar consumptions in the US was 2 pounds annually in the 1800s^[10]. By 1970 it rose to 123 pounds, and today that number lies at an enormous 152 pounds per year^[10]. These numbers only include refined sugars, so if we also include the sugars from other carbohydrates or alcohol,

total sugar consumption would be even more staggering! The number of patients with type 2 diabetes between 1983 and 2008 increased sevenfold^[4]. In 2011 those numbers have increased to 347 million worldwide^[11].

The incidence of PCOS is high in women who have IR. IR can develop when blood glucose rises steeply after consumption of a high carbohydrate or sugary meal several times per day for many years. Each time, the pancreas secretes insulin in order to counteract the high glucose levels and push glucose into cells^[12]. Over time, the insulin receptors become resistant to insulin's effects. Males with IR aromatize testosterone into estrogen^[13], which can manifest as gynecomastia and excess adipose tissue (apple shape). Women who have IR can develop high testosterone, which results in masculine features such as hirsutism[14-16] and male pattern baldness. Typically, women with PCOS show additional traits such as obesity (though not all women with PCOS are obese), acanthosis nigricans, unripe ovarian follicles that look like cysts, acne, amenorrhea, anovulation, and/or irregular ovulation and menstruation^[1,2]. Many patients with PCOS should be evaluated for hypothyroidism and/or Hashimoto's disease^[17,18], which are common conditions in this patient population. Diet-induced inflammation is a common factor in patients with PCOS^[19].

Common laboratory findings include the following indices: elevated androstenedione, free testosterone, dehydroepiandrosterone sulfate, triglycerides, and an abnormal ratio between luteinizing hormone to follicle-stimulating hormone



(FSH). Ultrasound may show the "string of pearls", or follicles that have undergone atresia^[1,2].

Western medical treatments for patients with PCOS include birth control pills to help regulate the menstrual cycle^[1,2]. Anti-androgens are also used to suppress the androgenic features. Another treatment for PCOS is the use of metformin (glucophage), which treats IR to some degree^[1,2]. Many women who suffer from infertility choose assisted reproductive technologies to stimulate ovulation. However, none of the above treatments address the cause of IR^[1,2].

2 Case report

The following case report illustrates integrated therapies of acupuncture, Chinese herbal medicine, nutrition, and functional medicine. A 31-year-old white female patient was first seen in our clinic in the fall of 2010. She presented with infertility (the couple had tried to conceive for five years prior), hair loss, hirsutism, acanthosis nigricans, a small number of unripe follicles visualized on ultrasound, obesity, decreased libido, night sweats, and vaginal dryness. The patient stated that she was menstruating irregularly every 34-50 days; she suffered from irritability and breast distention prior to the onset of her menstrual cycle, which was characterized by a scanty, dark red menstrual flow lasting about 6 d. She had been diagnosed with PCOS in 2006 by her doctor who confirmed polycystic ovaries imaged via ultrasound. This patient met two of three criteria for a diagnosis for polycystic ovarian disease^[1]: positive finding of multiple cysts via ultrasound and signs of hyperandrogenism (hirsutism, hair loss, and acanthosis nigricans). She was put on metformin by her doctor in 2007. Unfortunately, she had significant side effects which stopped when she discontinued the medication. Her doctor diagnosed her hypothyroidism in early 2010 and placed her on thyroid medication. Other complaints included obesity, dizziness, cold hands and feet that were exacerbated at night, rapid heartbeat, allergies, bloating, and decreased appetite. She also suffered from fullness and fatigue after eating, sugar cravings, increased memory loss, poor concentration, mood swings, over-thinking, and anxiety.

Her diet consisted of the following: breakfast: none; lunch: leftovers such as chicken breast, vegetables, bread and cookies; afternoon snack: chocolate, chips or pie; dinner: rice 6× per week, pasta 1× per week, with chicken, turkey, or fish. She used olive and canola oil for cooking oils. She did not consume much red meat.

Her laboratory results from May 2010 show the functional medical [20] not standard Western medical laboratory ranges: hemoglobin A1c 5.6% (<5.7%), thyroid stimulating hormone (TSH) 3.67 mIU/L (1.8-3.0 mIU/L), total thyroxine (TT4) 7.9 µg/dL (6-12 µg/dL), neutrophils 71% (40%60%), lymphocytes 21% (25%-40%), neutrophils (absolute)

 $8.4\times10^3/\mu L~((1.8-7.8)\times10^3/\mu L),~$ white blood cell (WBC) $11.9\times10^3/\mu L~((5.0-8.0)\times10^3/\mu L),~$ triglycerides 115 mg/dL (<100 mg/dL), cholesterol 203 mg/dL (150-200 mg/dL), low-density lipoprotein 130 mg/dL (<99 mg/dL), high-density lipoprotein 50 mg/dL (>55 mg/dL), vitamin D3 14.7 ng/mL (optimal range ~40 ng/mL) $^{[21]},~$ gamma-glutamyl transpeptidase 46 IU/L (10-26 IU/L).

Her tongue was pale and slightly swollen; her pulse was slightly thin, and weak.

Her medication/supplement list included levothyroxine, vitamin D3, black cohosh, and prenatal vitamins.

3 Diagnosis and treatment

Her traditional Chinese medicine diagnosis included kidney yang deficiency which was characterized by her cold hands/feet, thyroid disorder, infertility, and weak pulse; kidney yin deficiency which was seen in the night sweats, lowered libido, memory loss, and thin pulse; spleen qi deficiency which was seen in the fatigue, poor appetite, over-thinking, and slightly swollen tongue; blood deficiency which was seen in the dizziness, blurry vision, delayed menses, leg cramps, pale tongue, and thin pulse; liver qi stagnation which was seen in her mood swings and premenstrual syndrome (PMS); and finally, phlegm stagnation which was seen on ultrasound showing several unripe follicles and in her obesity.

Her functional medical diagnosis consisted of IR (triglycerides > 100 mg/dL, sugary, carbohydrate-rich diet, fatigue after meals, sugar cravings) coupled with mild reactive hypoglycemia (RHG) (no breakfast) contributing to PCOS. IR and PCOS can lead to systemic inflammation[19,22,23] and stress the adrenals. In addition, she had hypothyroidism, poor acetylcholine firing in the brain and poor peripheral circulation. This may result possibly from sympathetic upregulation from inflammatory processes. It may also result from nutrient deficiency. Dietary sources of L-tyrosine are found in highprotein foods such as eggs, dairy, nuts, avocados, and meat^[24]. L-tyrosine is one of several components needed to make T4 in the thyroid gland^[25]. A key nutrient needed to form acetylcholine is choline which is primarily found in organ meats and other meats^[26,27]. Given her immune marker elevations it was requested that her doctor run thyroid antibodies (thyroid peroxidase and antithyroglobulin antibodies) to rule out Hashimoto's disease.

She was counseled on her diet, particularly on the importance of eating breakfast. Not eating breakfast contributes to starving the brain of much-needed glucose. We discussed the importance of reducing carbohydrates (rice and pasta), removing sugar, soft-drinks, chips, cookies, chocolate, and pie, and increasing whole fat dairy, meats, fish, and poultry, and lots of vegetables and vegetable juices. She was advised to include home-made bone marrow broth and have it

available to mix in with vegetables or any whole grains or soups she might prepare.

She received an acupuncture treatment using late twentieth century Japanese Kiiko Matsumoto acupuncture style, which focuses on palpating certain painful reflex zones that are then cleared of the pressure pain with distal acupuncture points during treatment. The theory is that relieving pressure pain in the micro-system provides beneficial and noticeable effects in the macro-system^[28].

Additionally, her vitamin D3 dosage, originally at 1 000 IU, was increased to 8 000 IU with the goal to retest the levels in two months. Research has shown that sufficient vitamin D3 helps with glucose uptake^[29-31]. She was advised to take cod liver oil, 500 mg betaine HCl with pepsin before each meal (for bloating), and a supplement containing chromium, vanadium, alpha lipoic acid, magnesium, and biotin, one cap with each meal to resensitize the insulin receptors. Cod liver oil is an omega-3 fatty acid which helps with brain function and has potent anti-inflammatory effects; cod liver oil was also used in many traditional cultures to increase the health of the offspring^[32]. Betaine HCl with pepsin was used to increase hydrochloric acid so that her digestion would be optimized, bile secretion would be sufficiently enhanced and enzyme secretion in the small intestines would be increased, with the ultimate goal to enhance nutrient uptake. Patients with low hydrochloric acid tend to rot and putrify their food instead of digesting it; therefore they experience gas and bloating^[33]. Her prenatal vitamin contained sufficient folic acid.

She came back for her second visit three weeks later with the following additional labs (again, they were interpreted using functional medicine rather than Western laboratory ranges): thyroid peroxidase (TPO) antibodies 89 IU/mL (0-34 IU/mL), TSH 4.70 mIU/L (1.8-3.0 mIU/L), day 3 FSH 5.5 mIU/mL (< 10 mIU/mL), WBC $12.4\times10^3/\mu$ L ((5.08.0)× $10^3/\mu$ L), neutrophils (absolute) $8.5\times10^3/\mu$ L((1.8-7.8)× $10^3/\mu$ L). It appeared that she had Hashimoto's disease as her TPO antibodies were elevated^[17,18]. Her TSH required a bit more thyroid medication, which was adjusted by her doctor. She still showed the inflammatory pattern.

She reported that she had radically changed her diet as advised, that her energy was much better, the afternoon fatigue was gone, but she still had bloating. Her overall day-time fatigue was gone, her memory improved along with better recall and concentration. She reported a 5 pounds weight loss.

Her Chinese medicine diagnosis still included kidney yang deficiency, kidney yin deficiency, spleen qi deficiency, blood deficiency, liver qi stagnation, and phlegm stagnation.

Her functional medical diagnosis was adjusted to IR coupled with mild RHG contributing to PCOS; Hashimoto's hypothyroidism, systemic inflammation, poor acetylcholine firing in the brain and poor peripheral circulation, and adrenal stress

She was still treated with acupuncture and supplements. She was instructed to remove gluten from her diet. There is considerable research that gluten^[34-39], low vitamin D status^[40] and low levels of glutathione^[41,42], the main amino acid that enhances phases 1 and 2 detoxification in the liver, increase cytokine activity in patients with auto-immune diseases. Western medicine does not address the immune aspect of Hashimoto's disease but functional medicine has the capability to subdue cytokine activity from the presence of auto-antibodies by using natural substances and dietary modifications. Therefore, in addition to a gluten-free diet she was instructed to apply a topical glutathione cream twice daily, by massaging it directly onto the skin around on her thyroid gland.

By her fifth visit six weeks later, she reported that she had lost 18 pounds, her memory was great, and her energy level was excellent. Her last menstrual cycle was 33 d with very little PMS or pain. During this visit she was placed on Six-Ingredient Pill with Rehmannia (Liu Wei Di Huang Wan) plus Minor Bupleurum Decoction (Xiao Chai Hu Tang), with the additions of Gecko (Gejie), Carapax et Plastrum Testudinis (Guijia), Radix Polygoni Multiflori Preparatae (Heshouwu), Fructus Psoraleae (Buguzhi), Pericarpium Citri Reticulatae (Chenpi) in granule form (3 g twice daily) since she also reported that her cervical fluid was still scanty and she had mild right upper quadrant pain. The rationale was that her yin nourishment was not entirely sufficient with diet alone and therefore her herbs needed to provide additional yin nourishment as well as to harmonize liver and gallbladder.

During her sixth visit three weeks later, she reported that her gallbladder pain was much improved. Her body basal temperature chart showed a normal pattern; in fact, it looked triphasic, which according to fertility awareness method can indicate pregnancy^[43].

She was happy to report during her seventh visit that she was eight weeks pregnant. She reported mild nausea. Her acupuncture treatment was now changed toward miscarriage prevention. We changed her supplement regimen as follows: vitamin D3 one day 4 000 IU alternating with 8 000 IU (her D3 level was now 32 ng/mL) the following day; prenatal vitamin, 500 mg betaine HCl + pepsin with larger meals, cod liver oil, and topical glutathione 1× per day. We changed her herbal formula to Ass-Hide Gelatin and Mugwort Decoction (Jiao Ai Tang) plus Radix Aucklandiae (Muxiang), Rhizome Pinelliae (Banxia), Pericarpium Citri Reticulatae (Chenpi), Radix Astragali (Huangqi), and Radix Bupleuri (Chaihu), 2 g twice daily. Rhizome Ligustici Chuanxiong (Chuanxiong) was deleted from Jiao Ai Tang as this herb is contraindicated during pregnancy. Her doctor had changed her medication to 50 μg of synthroid per day.



I then saw her again at 10 weeks and she reported that her TSH had gone to 7.9 mIU/L, which was concerning to her. She was due to see the endocrinologist the following week. Her ultrasound showed the baby's normal growth and heartbeat.

During her next visit at 14 weeks her thyroid levels were much better with increased medication. In addition, she felt really well on the gluten-free diet. I discontinued the Chinese herbal formula at that point. Retesting of her vitamin D3 showed levels of 52 ng/mL; we reduced her supplementation to 4 000 IU/d.

When she was at 28 weeks she sent an email stating that her prenatal visits with her obstetrician were all normal, as were her glucose tests and measurements for the baby. She had lots of energy and felt great!

I then saw her again at 37 weeks. The baby was head down and her cervix was slightly dilated. She was still using the betaine HCl plus pepsin with heavy meals. She continued to come in for acupuncture treatments on a weekly basis to ready her for the birthing process. She went into labor at 40 weeks and 2 d; she was in full labor for 4.5 h, and delivered a healthy baby boy.

4 Discussion

Overall, it took three months (6 visits) for this patient to conceive her child, another four visits during the first fourteen weeks of pregnancy, and five more visits to prepare her for the birthing process at a total cost of \$2 100.00 for the office visits, acupuncture, herbs and supplements. These costs are considerably lower compared to conventional Western treatments^[44] which may range between \$10 000 and \$100 000 depending on the need for *in-vitro*-fertilization (IVF) or IVF with donor-eggs.

The patient did not present with anovulation which is common in patients with PCOS, but she met the diagnostic criteria of PCOS in that her doctor confirmed polycystic ovaries via ultrasound and she presented with signs of hyperandrogenism^[1,2] such as hirsutism^[1,2], acanthosis nigricans^[1,14-16], and hair loss^[1]. Her doctor excluded other causes for her irregular menses.

It is difficult to ascertain which of the four modalities used ultimately resulted in the positive outcome. PCOS is a complex condition requiring complex intervention and the use of integrative therapies might be desirable. There are currently no studies looking at combined therapies of acupuncture, Chinese herbs, diet, supplements, and functional medicine for the treatment of PCOS. Monotherapies have only partially been effective in treating ^{IR[45-47]}. Acupuncture showed better outcomes than metformin in endocrine and metabolic function in patients with obesity-type PCOS^[48,49]. The use of berberine in women with PCOS appears to show promising results^[50].

Health care providers might benefit from becoming versatile in a number of treatment modalities so they may better serve the increasingly complex disease patterns presented by their patients. The most important question is why certain women develop PCOS in the first place, which environmental factors play a role, and what is the patient's terrain that allows for this condition to occur? As mentioned in the introduction, a drastic change in the food supply during the past sixty years has shifted patients' terrain, hence, the propensity toward type 2 diabetes and obesity in the overall population. Lowcarbohydrate diets perform well to reduce IR^[51]. In particular, the hunter-gatherers diet shows marked improvements in glucose, insulin receptor site sensitivity and weight reduction^[52]. Therefore, counseling the patient on her diet was a first logical step. Clinically, this author sees less of a tangible outcome in this patient population when patients do not follow a low-carbohydrate diet. However, most patients are very motivated to lose weight, manage blood sugar, and get pregnant! Acupuncture and Chinese herbal medicine have a long history of treating gynecological and hormonal problems^[53,54]. Both modalities can be used safely during pregnancy by a trained practitioner. In particular, the Japanese acupuncture style used with this patient^[28] deals well with hormonal, blood sugar and auto-immune conditions due to its diagnostic framework. When the patient presented with right upper quadrant pain and lack of cervical fluid the use of Chinese herbs was indicated. The author suspected that the low-carbohydrate diet was insufficient to increase her cervical fluid and that with the increase of pastured meats and eggs there may have been an issue with her biliary function. Hence, a custom-tailored herbal formulation was the best short-term treatment route at that point to assist with both of those concerns. By using principles of functional medicine^[55] and appropriate supplementation, each modality can be applied clinically to achieve the best possible outcome. Clinical experience guides the practitioner as to which modality is used at which point in time.

5 Conclusion

PCOS is a complex condition and therefore, needs comprehensive intervention. This case may serve as an example that when using integrative therapies, significant hormonal and brain effects take place in addition to modulating auto-immune thyroiditis. Combining dietary changes, acupuncture, Chinese herbs and nutritional supplementation resulted in a healthy pregnancy outcome.

6 Competing interests

The author declares she does not have any competing interests.

REFERENCES

- Lucidi RS. Polycystic ovarian syndrome. (2013-03-04) [2013-05-07]. http://emedicine.medscape.com/article/256806-overview.
- Madnani N, Khan K, Chauhan P, Parmar G. Polycystic ovarian syndrome. Indian J Dermatol Venereol Leprol. 2013; 79(3): 310-321.
- 3 Seccombe A. New research finds genetic defect linking PCOS and insulin resistance. (2013-03-20) [2013-0507]. http://www.examiner.com/article/new-research-finds-genetic-defect-linking-pcos-and-insulin-resistance.
- 4 Hyman M. The blood sugar solution. New York: Little, Brown and Company. 2012.
- Nugent BM, Tobet SA, Lara HE, Lucion AB, Wilson ME, Recabarren SE, Paredes AH. Hormonal programming across the lifespan. Horm Metab Res. 2012; 44(8): 577-586.
- 6 Bayol SA, Simbi BH, Bertrand JA, Stickland NC. Offspring from mothers fed a 'junk food' diet in pregnancy and lactation exhibit exacerbated adiposity that is more pronounced in females. J Physiol. 2008; 586(Pt 13): 3219-3230.
- 7 United States Department of Agriculture. Agriculture factbook 2001-2002: profiling food consumption in America. (2002),[2013-05-07].
 - http://www.usda.gov/factbook/chapter2.htm.
- 8 United States Department of Agriculture, Center for Nutrition Policy and Promotion. The food guide pyramid. (2005) [2013-05-07]. http://www.diet.com/g/usda-food-guide-pyramid-mypyramid.
- 9 United States Department of Agriculture. Choose my plant. [2013-05-07]. http://www.choosemyplate.gov/food-groups/.
- 10 New Hampshire Division of Public Health Services (DHHS-DPHS) Health Promotion in Motion. How much sugar do you eat? You may be surprised! [2013-05-07]. http://www.dhhs.nh.gov/DPHS/nhp/adults/documents/sugar.pdf.
- Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, Lin JK, Farzadfar F, Khang YH, Stevens GA, Rao M, Ali MK, Riley LM, Robinson CA, Ezzati M; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet. 2011; 378(9785): 31-40.
- 12 Wikipedia. Insulin resistance. [2013-05-07]. http://en.wikipedia.org/wiki/Insulin_resistance.
- 13 Wikipedia. Aromatase. [2013-05-07]. http://en.wikipedia. org/wiki/Aromatase.
- 14 Kluczynik CE, Mariz LS, Souza LC, Solano GB, Albuquerque FC, Medeiros CC. Acanthosis nigricans and insulin resistance in overweight children and adolescents. An Bras Dermatol. 2012; 87(4): 531-537.
- 15 Barbato MT, Criado PR, Silva AK, Averbeck E, Guerine MB, Sá NB. Association of acanthosis nigricans and skin tags with insulin resistance. An Bras Dermatol. 2012; 87(1): 97-104.

- 16 Abraham C, Rozmus CL. Is acanthosis nigricans a reliable indicator for risk of type 2 diabetes in obese children and adolescents? A systematic review. J Sch Nurs. 2012; 28(3): 195-205.
- 17 Garelli S, Masiero S, Plebani M, Chen S, Furmaniak J, Armanini D, Betterle C. High prevalence of chronic thyroiditis in patients with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2013; 169(2): 248-251.
- 18 Janssen OE, Mehlmauer N, Hahn S, Offner AH, Gärtner R. High prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Eur J Endocrinol. 2004; 150(3): 363-369.
- 19 González F. Inflammation in polycystic ovary syndrome: underpinning of insulin resistance and ovarian dysfunction. Steroids. 2012; 77(4): 300-305.
- 20 http://www.youtube.com/watch?v=j2znWMwNUE0
- 21 Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr. 2006; 84(1): 18-28.
- 22 Duleba AJ, Dokras A. Is PCOS an inflammatory process? Fertil Steril. 2012; 97(1): 7-12.
- 23 Gonzalez F, Thusu K, Abdel-Rahman E, Prabhala A, Tomani M, Dandona P. Elevated serum levels of tumor necrosis factor alpha in normal-weight women with polycystic ovary syndrome. Metabolism. 1999; 48(4): 437-441.
- 24 Wikipedia. Tyrosine. [2013-05-07]. http://en.wikipedia.org/ wiki/Tyrosine.
- 25 Wikipedia. Thyroid hormone. [2013-05-07]. http://en.wikipedia.org/wiki/Thyroid_hormone.
- 26 Wikipedia. Acetylcholine. [2013-05-07]. http://en.wikipedia.org/wiki/Acetylcholine.
- 27 Zeisel SH, Mar MH, Howe JC, Holden JM. Concentrations of choline-containing compounds and betaine in common foods. J Nutr. 2003; 133(5): 1302-1307.
- 28 Matsumoto K, Euler D. Kiiko Matsumoto's clinical strategies. Vol 1 and Vol 2. Natick: Kiiko Matsumoto International. 2004.
- 29 Marcotorchino J, Gouranton E, Romier B, Tourniaire F, Astier J, Malezet C, Amiot MJ, Landrier JF. Vitamin D reduces the inflammatory response and restores glucose uptake in adipocytes. Mol Nutr Food Res. 2012; 56(12): 1771-1782.
- 30 Biesalski HK. Vitamin D recommendations: beyond deficiency. Ann Nutr Metab. 2011; 59(1): 10-16.
- 31 Sainaghi PP, Bellan M, Nerviani A, Sola D, Molinari R, Cerutti C, Pirisi M. Superiority of a high loading dose of cholecalciferol to correct hypovitaminosis d in patients with inflammatory/autoimmune rheumatic diseases. J Rheumatol. 2013; 40(2): 166-172.
- 32 Olafsdottir AS, Magnusardottir AR, Thorgeirsdottir H, Hauksson A, Skuladottir GV, Steingrimsdottir L. Relationship between dietary intake of cod liver oil in early pregnancy and birthweight. BJOG. 2005; 112(4): 424-429.
- 33 Kelly GS. Hydrochloric acid: physiological functions and clinical implications. Altern Med Rev. 1997; 2(2): 116-127.
- 34 Akçay MN, Akçay G. The presence of the antigliadin antibodies in autoimmune thyroid diseases. Hepatogastroenterology. 2003; 50 (Suppl 2): cclxxix-cclxxx.
- 35 Shaoul R, Lerner A. Associated autoantibodies in celiac disease. Autoimmun Rev. 2007; 6(8): 559-565.



- 36 da Silva Kotze LM, Nisihara RM, da Rosa Utiyama SR, Piovezan GC, Kotze LR. Thyroid disorders in Brazilian patients with celiac disease. J Clin Gastroenterol. 2006; 40(1): 3336.
- 37 Ventura A, Magazzù G, Greco L. Duration of exposure to gluten and risk for autoimmune disorders in patients with celiac disease. SIGEP Study Group for Autoimmune Disorders in Celiac Disease. Gastroenterology. 1999; 117(2): 297-303.
- 38 Barton SH, Murray JA. Celiac disease and autoimmunity in the gut and elsewhere. Gastroenterol Clin North Am. 2008; 37(2): 411-428, vii.
- 39 Duggan JM. Coeliac disease: the great imitator. Med J Aust. 2004; 180(10): 524-526.
- 40 Zold E, Szodoray P, Kappelmayer J, Gaal J, Csathy L, Barath S, Gyimesi E, Hajas A, Zeher M, Szegedi G, Bodolay E. Impaired regulatory T-cell homeostasis due to vitamin D deficiency in undifferentiated connective tissue disease. Scand J Rheumatol. 2010; 39(6): 490-497.
- 41 Fraternale A, Paoletti MF, Casabianca A, Oiry J, Clayette P, Vogel JU, Cinatl J Jr, Palamara AT, Sgarbanti R, Garaci E, Millo E, Benatti U, Magnani M. Antiviral and immunomodulatory properties of new pro-glutathione (GSH) molecules. Curr Med Chem. 2006; 13(15): 1749-1755.
- 42 Paolicchi A, Dominici S, Pieri L, Maellaro E, Pompella A. Glutathione catabolism as a signaling mechanism. Biochem Pharmacol. 2002; 64(5-6): 1027-1035.
- 43 Weschler T. Taking charge of your fertility. New York: HarperCollins Publishers Inc. 2002.
- 44 How much will my fertility treatments and drugs cost? (2013-01-04) [2013-05-07]. http://www.pcosjournal.com/ how-much-will-my-fertility-treatments-and-drugs-cost/.
- 45 Rathnayake D, Sinclair R. Innovative use of spironolactone as an antiandrogen in the treatment of female pattern hair loss. Dermatol Clin. 2010; 28(3): 611-618.
- 46 Hwang KR, Choi YM, Kim JJ, Chae SJ, Park KE, Jeon

- HW, Ku SY, Kim SH, Kim JG, Moon SY. Effects of insulinsensitizing agents and insulin resistance in women with polycystic ovary syndrome. Clin Exp Reprod Med. 2013; 40(2): 100-105.
- 47 Rice S, Elia A, Jawad Z, Pellatt L, Mason HD. Metformin inhibits follicle-stimulating hormone (FSH) action in human granulosa cells: relevance to polycystic ovary syndrome. J Clin Endocrinol Metab. 2013; 98(9): E1491-E1500.
- 48 Zheng YH, Wang XH, Lai MH, Yao H, Liu H, Ma HX. Effectiveness of abdominal acupuncture for patients with obesitytype polycystic ovary syndrome: a randomized controlled trial. J Altern Complement Med. 2013; 19(9): 740-745.
- 49 Stener-Victorin E, Jedel E, Janson PO, Sverrisdottir YB. 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(2): R387-R395.
- 50 An Y, Sun Z, Zhang Y, Liu B, Guan Y, Lu M. The use of berberine for women with polycystic ovary syndrome undergoing IVF treatment. Clin Endocrinol (Oxf). 2013 Jul 19. [Epub ahead of print]
- 51 Westman EC, Feinman RD, Mavropoulos JC, Vernon MC, Volek JS, Wortman JA, Yancy WS, Phinney SD. Lowcarbohydrate nutrition and metabolism. Am J Clin Nutr. 2007; 86(2): 276-284.
- 52 O'Dea K. Marked improvement in carbohydrate and lipid metabolism in diabetic Australian aborigines after temporary reversion to traditional lifestyle. Diabetes. 1984; 33(6): 596-603
- 53 Yang SZ, Li DW. Fu Qing-Zhu's gynecology. Boulder: Blue Poppy Press, Inc. 1996.
- 54 Maciocia G. Obstetrics & gynecology in Chinese medicine. New York: Churchill Livingstone. 1998.
- 55 Jones DS. Textbook of functional medicine. Gig Harbor: The Institute of Functional Medicine. 2010.



Submission Guide

Journal of Integrative Medicine (JIM) is a PubMed-indexed, peer-reviewed, open-access journal, publishing papers on all aspects of integrative medicine, such as acupuncture and traditional Chinese medicine, Ayurvedic medicine, herbal medicine, homeopathy, nutrition, chiropractic, mind-body medicine, Taichi, Qigong, meditation, and any other modalities of complementary and alternative medicine (CAM). Article

types include reviews, systematic reviews and meta-analyses, randomized controlled and pragmatic trials, translational and patient-centered effectiveness outcome studies, case series and reports, clinical trial protocols, preclinical and basic science studies, papers on methodology and CAM history or education, editorials, global views, commentaries, short communications, book reviews, conference proceedings, and letters to the editor.

No submission and page charges Quick decision and online first publication

For information on manuscript preparation and submission, please visit JIM website. Send your postal address by e-mail to jcim@163.com, we will send you a complimentary print issue upon receipt.

Editors-in-Chief: Wei-kang Zhao & Lixing Lao. ISSN 2095-4964. Published by Science Press, China.