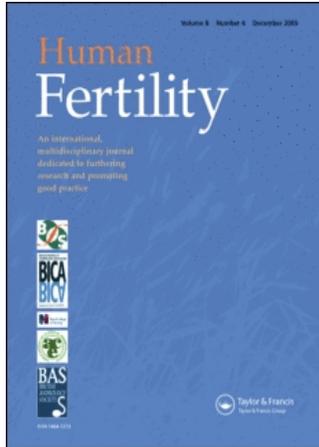


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Application of traditional Chinese medicine in the treatment of infertility

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Application of traditional Chinese medicine in the treatment of infertility

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The philosophy and practice of traditional Chinese medicine (TCM) have been evolving for thousands of years in China, Japan and other Asian countries. TCM is now generating popular interest worldwide for reproductive health care and disease prevention, including applications for treating infertility and improving sexual function. This review focuses on the application of TCM for infertility patients, and provides a critical reflection on the efficacy and safety of selected Chinese herbal formulas. It has been claimed that some formulas produce high clinical pregnancy rates with few or no side effects, as well as improving the general well-being of patients. The need for randomized control trials and research into possible mechanisms of action, effective doses, contraindications and toxicity is self-evident. However, the task is enormous in view of the number of herbal products currently available on the market; yet among these products are undoubtedly some that will prove to be safe and beneficial.

General principles of traditional Chinese medicine

Traditional Chinese medicine (TCM) is a sophisticated medical philosophy that has been practised in China for more than 5000 years and long before the evolution of Western medicine began. It developed continuously and was and is guided by Oriental clinical experience. TCM is still a primary therapy in a number of Asian countries, although Western medicine is usually practised in parallel. The *Yin–Yang* theory provides the rationale for practice. Two opposite and complementary kinds of homeostatic energy are thought to be present in the universe and within the human body, namely, *Yin* and *Yang*. Although these terms are well-known to Western readers, the principles on which they rest and the language used in TCM theory and symptomatology are less familiar (Maciocia, 1997). The *Yin–Yang* axis is a balance between anabolic and catabolic processes, and healthy physiology and metabolism depend on the 'vital energy', or *Qi*, that flows throughout the body. This energy serves to 'warm' the body, protecting it from external pathogens, generating and distributing body fluids (*Jinye*) and blood. Each organ has its own pattern of *Qi* for carrying out its special function.

The *kidney* and *liver* are the two fundamental organs for understanding reproductive function, but they represent more

than just anatomical entities according to Oriental philosophy. The *kidney* includes the functions of the urinary and reproductive systems, as well as parts of the endocrine and nervous systems. The *liver*, on the other hand, represents the same physiological functions as in Western biology and medicine, but also includes part of the central nervous system, the autonomic nervous system, blood and eyes. The *kidney* stores the essence, *Qi*, which includes the female and male gametes. The *liver* stores blood, which is regarded as the 'reproductive essence'. These twin essences, *Qi* and blood, are the *Yang* and *Yin* energies, respectively. A related concept, *spleen*, is concerned with most of the Western concepts of digestive function, but it is also involved with blood coagulation and body fluid metabolism. Some Chinese TCM researchers still include pancreatic function with the *spleen*. Dysfunction in one organ is often closely associated with imbalance in another. A blockage in the pathways along which *Qi* flows, or any imbalance in the two components of *Qi–Yang* and blood–*Yin*, can cause physiological disharmony or disease. Apart from congenital defects, infertility problems are generally thought to be induced by the following: (a) *kidney–Qi* deficiency; (b) weakness of *Qi* and blood or *spleen*; (c) stagnation of *liver–Qi*; and (d) obstruction by 'damp phlegm'. Chinese herbal therapy aims to reinforce *kidney–Yang*, benefit *Qi* and blood, regulate the flow of *liver–Qi*, remove damp phlegm, normalize menstruation and mobilize blood. Moreover, TCM facilitates the patency of *Chong* and *Ren* meridians, which are the channels along which *Qi* flows connecting organs and regions of the body. Thus, Westerners find few parallels in their own philosophy to help them to understand the diagnosis of diseases according to TCM.

Diagnostics

Just as the formulation of TCM treatment using herbal decoctions and acupuncture differs from Western medicine, so does the diagnosis of infertility, which involves various physical manifestations. During a TCM diagnosis and the emergence of a treatment strategem, the involvement and balance of relationships between organs in the pathology are assessed. In addition, the habitus of the patient, pulse, diet, appearance of the tongue, external environment and lifestyle are usually taken into consideration before reaching a conclusion. The differences between TCM and Western diagnoses of female and male infertility are compared in Tables 1 and 2. Clearly, there is no simple correspondence between a Chinese diagnosis and a Western diagnosis, and a single TCM pattern can correspond to several Western diagnoses. These tables serve to illustrate the range of

*Correspondence.

Table 1. Equivalents of traditional Chinese medicine (TCM) patterns and Western diagnosis of female infertility

TCM patterns	Western diagnosis	Manifestations	Tongue	Pulse
Deficient <i>kidney–Yin</i>	Anovulation Immunological infertility Luteal phase defect	Malar flush, night sweats, insomnia, dry throat, low grade fever	Red, peeled cracked	Floating, empty, rapid
Deficient <i>kidney–Yang</i>	Amenorrhoea	Cold knees, weak legs, apathy, poor appetite	Pale, swollen	Deep, weak, wet
Deficiency of the <i>liver–blood</i>	Polycystic ovary syndrome	Dizziness, blurred vision, pale lips, muscle spasm, brittle nails	Pale body, dry	Choppy, fine
<i>Liver–blood</i> stagnation	Endometriosis	Painful periods, dark and clotted blood, abdominal pain and mass	Purple body, spots	Wiry
Damp-heat in the <i>liver</i>	Genital infection Tubal factor infertility	Fever, jaundice, bitter taste, nausea, vomiting, abdominal distension, vaginal discharge	Red body, sticky yellow coat	Slippery, wiry, rapid
<i>Liver–Qi</i> stagnation	Premenstrual syndrome	Depression, sighing, mood swings, painful periods, distension of the breasts	Normal	Wiry
Cold stagnating in the <i>liver</i> channel	Sexual arousal disorder	Fullness and distension of bladder	Pale, wet, white coat	Wiry, deep, slow
Deficient <i>spleen–Qi</i>	Dysfunctional uterine bleeding Uterine fibroids	No appetite, tiredness, lassitude, blood in the urine, excessive menstrual flow	Pale or transverse cracks on sides	Fine

Table 2. Equivalents of traditional Chinese medicine (TCM) patterns and Western diagnosis of male infertility

TCM patterns	Western diagnosis	Manifestations	Tongue	Pulse
Deficient <i>kidney–essence</i>	Impotence Seminal plasma abnormalities	Poor memory, loose teeth, hair loss, weakness of knees and legs, sexual dysfunction	Red, peeled	Floating, empty, leathery
Deficient <i>kidney–Qi</i>	Azoospermia Oligozoospermia Asthenozoospermia Teratozoospermia	Soreness and weakness of lumbar region, urinary incontinence, enuresis, nocturnal urination	Pale, white coat	Weak or thready
<i>Liver–blood</i> stagnation	Varicocele	Painful or irregular abdominal pain, 'mass' in the abdomen	Purple body, spots	Wiry
Damp-heat pouring downward	Male accessory gland infection Immunological infertility	Swelling and cramps in the perineum and lower-abdomen, thirst, bitter taste in mouth	Red with yellow greasy coating	String-like and slippery

Chinese diagnoses recognized by a Western understanding of female and male infertility.

Clinical treatment

Most Chinese herbal treatments use formulas containing at least a dozen herbs. Each herb is thought to have a primary effect on one or more organ. The selection of herbs for a given formula is guided by the clinical diagnosis and according to the particular organ and channel of the body involved in

the disease process. Few herbs are used alone, and they are normally prepared as a slow infusion (decoction). A representative, but incomplete, list of Chinese herbs and their common applications for female and male infertility are provided in Tables 3 and 4.

Ovulatory dysfunction

Ovulatory dysfunction is a common cause of female infertility, and herbal medicine has a role in its treatment. Lu *et al.*

Table 3. Chinese herbs commonly used for female infertility

Latin name	English name	Chinese name	Normal dosage (g per day)	Application in traditional Chinese medicine
<i>Caulis sargentodoxae</i>	Sargent glory vine	Hong teng	25	Dissipating the heat and toxic materials
<i>Cortex phellodendri</i>	Phellodendrom bark	Huang bo	12	Discharging the fire, consolidating the <i>Yin</i>
<i>Flos carthami</i>	Carthamus flower	Hong hua	9	Regulating the flow of <i>Qi</i> to alleviate pain
<i>Fructus ligustri lucidi</i>	Glossy privet fruit	Nu zhen zi	12	Nourishing the <i>kidney</i> and <i>liver</i>
<i>Herba leonuri</i>	Motherwort	Yi mu cao	15	Adjusting menstruation by invigorating <i>Qi</i>
<i>Herba partriniae</i>	Partrinia	Bai jiang cao	30	Clearing away the heat and toxic materials
<i>Radix aconiti praeparata</i>	Lateral root of aconite	Fu zi	9	Warming and tonifying the <i>kidney–Yang</i>
<i>Radix angelicae sinensis</i>	Angelica root	Dang gui	9	Nourishing the blood and alleviating pain
<i>Radix astragali seu hedysari</i>	Astragalus	Huang qi	12	Regulating the <i>spleen</i> and enriching the <i>Qi</i>
<i>Radix ginseng</i>	Ginseng	Ren shen	6	Tonifying the <i>spleen</i> and enriching the <i>Qi</i> and blood
<i>Radix glycyrrhizae</i>	Licorice root	Gan cao	6	Reinforcing the <i>spleen</i> and <i>Qi</i> , removing the heat and toxic materials
<i>Radix paeoniae rubra</i>	Red peony root	Chi shao	12	Resolving the blood stagnation and tissue masses
<i>Radix salviae miltiorrhizae</i>	Codonopsis root	Dan shen	15	Promoting the blood circulation, removing the blood stasis
<i>Rhizoma cyperi</i>	Cyperus root	Xiang fu	15	Rectifying the <i>Qi</i> and moving the stagnation
<i>Rhizoma ligustici chuanxiong</i>	Chuanxiong rhizome	Chuan xiong	9	Promoting the <i>Qi</i> and alleviating the pain
<i>Sargassum</i>	Seaweed	Hai zao	12	Eliminating the phlegm, softening hard lumps
<i>Semen persicae</i>	Peach kernel	Tao ren	9	Promoting the blood circulation and relieving carbuncle
<i>Semen vaccariae</i>	Vaccaria seed	Wang bu liu xing	9	Activating the channels and collaterals
<i>Squama manitis</i>	Pangolin scales	Chuan shan jia	9	Resolving the disperse lumps and soothing the <i>liver</i>

(1998) used *Yangjing* decoction (a Chinese prescription of replenishing *kidney* essence) to treat 22 women with secondary amenorrhoea and four women in whom infertility with oligomenorrhoea was attributed to an ovarian cause. They reported in this series 69 menstrual cycles (60%), 37 follicular maturation cycles (32%) and 21 ovulatory cycles (18%). Overall, the follicular maturation rate was 85% in 26 women after 116 therapeutic cycles with the herbal formula. The authors presumed that after herbal treatment, blood flow disturbances to the ovary and uterus improved and benefited the early embryonic development. However, this study was not placebo-controlled for the treatment outcome, nor did it address the question of pregnancy success. The researchers administered another Chinese herbal medicine, *Hachimijiogan* (5–10 g per day), to another 27 infertile women diagnosed with hyperprolactinaemia (Usuki and Usuki, 1989). This formula decreased serum prolactin concentrations to normal in 15 of 18 patients, and four of six patients with amenorrhoea ovulated. Eleven patients conceived and delivered healthy babies, and hormonal profiles were normalized during and after pregnancy. In three patients with 100–300 ng serum prolactin ml⁻¹, the concentrations were not altered, nor was there any change in an even smaller group of patients (*n* = 3) with or without a pituitary microadenoma who were resistant

to bromocriptine. Nevertheless, the ovulation rate of these patients appeared to improve and they established normal pregnancy and delivered healthy babies (Usuki *et al.*, 1989; Otani *et al.*, 1991). These preliminary findings indicated that *Hachimijiogan* may be useful for treating hyperprolactinaemia and, even if administered throughout pregnancy, *Hachimijiogan* was claimed to carry no obvious side effects.

There have been a number of other claims that herbal medicine is beneficial for improving ovarian function and promoting ovulation (Wang, 1994; Veal, 1998; Wang and Huang, 2002; Edmonds and Montgomery, 2003). Tian *et al.* (1998) reported that the coadministration for 1–3 months of replenishing *kidney* essence herbal formula (KRCH) and acupuncture produced an 89% ovulation rate and a 71% pregnancy rate in 29 anovulatory infertile women who were positive for the endometrial progesterone receptor. On the other hand, only a 30% ovulation rate and 22% pregnancy rate (two of nine) was obtained in a group who were moderately positive for the progesterone receptor. A similar study with 60 patients revealed that endometrial oestrogen receptor expression measured semi-quantitatively was raised from 47% to 65% after treatment in the follicular phase. Furthermore, in experimental rats, KRCH significantly increased the number of antral follicles,

Table 4. Chinese herbs commonly used for male infertility

Latin name	English name	Chinese name	Normal dosage (g per day)	Application in traditional Chinese medicine
<i>Cornu cervi pantotrichum</i>	Velvet deer horn	Lu rong	10	Strengthening the <i>kidney–Yang</i> and replenishing the essence
<i>Cortex cinnamomi</i>	Cinnamon bark	Rou gui	9	Warming the channels and nourishing the <i>kidney–Yang</i>
<i>Cortex eucommiae</i>	Eucommia bark	Du zhong	12	Enriching the <i>kidney</i> and <i>liver</i>
<i>Fructus corni</i>	Cornus fruit	Shan zhu yu	9	Moistening the <i>liver</i> , enriching the <i>kidney</i> and essence
<i>Fructus lycii</i>	Lycium berry	Gou qi zi	15	Nourishing blood and moistening <i>Yin</i>
<i>Fructus psoraleae</i>	Psoralea fruit	Bu gu zhi	6	Warming the <i>spleen</i> and strengthening the <i>kidney–Yang</i>
<i>Fructus rubi</i>	Raspberry fruit	Fu pen zi	9	Replenishing the essence and <i>liver</i>
<i>Fructus schisandrae</i>	Schisandra	Wu wei zi	6	Moistening the <i>kidney</i> to preserve the essence and <i>Qi</i>
<i>Herba cistanches</i>	Cistanche stem	Rou cong rong	12	Strengthening the <i>Yang</i> and essence
<i>Herba epimedii</i>	Epimedium	Yin yang hou	12	Warming the <i>kidney</i> and <i>Yang</i>
<i>Poria</i>	Poria	Fu ling	12	Eliminating the water and damp
<i>Radix morindae officinalis</i>	Morindo root	Ba ji	10	Strengthening the <i>kidney–Yang</i>
<i>Radix rehmanniae Praeparata</i>	Rehmannia root	Shu di	15	Nourishing the <i>Yin</i> and blood, invigorating the <i>kidney</i> and <i>liver</i>
<i>Rhizoma curculiginis</i>	Curculigo root	Xian mao	9	Strengthening the <i>kidney–Yang</i> to expel the cold and dampness
<i>Rhizoma dioscoreae</i>	Dioscorea root	Shan yao	15	Fortifying the <i>spleen</i> and invigorating the <i>kidney</i> essence
<i>Semen cuscutae</i>	Cuscuta seed	Tu shi zi	12	Tonifying and enriching the <i>liver</i> and <i>kidney</i>
<i>Semen plantaginis</i>	Plantago seed	Che qian zi	9	Reinforcing the <i>spleen</i> to remove the dampness and heat

uterine mass, serum oestradiol concentration and endometrial oestrogen receptor status compared with controls (Qian *et al.*, 1998). These results indicated that herbs can improve oestrogen status, promote uterine development and have pro-fertility effects.

In addition, studies on the effects of KRCH in androgen-sterilized rats showed that KRCH reduced weight, restored regular oestrous cycles and induced ovulation, possibly by regulating hypothalamic neuropeptide Y and leptin receptor mRNA expression (Sun and Yu, 1999; Sun *et al.*, 2000). It was suggested that ovulation induction by KRCH in anovulatory rats was promoted by modulation of insulin-like growth factor I or its receptor (Li and Gui, 2000), as well as by reducing androgen concentration. Thus, multiple effects on the pituitary–ovarian axis and adrenal gland were suspected (Wei and Yu, 1994; Gui *et al.*, 1997). However, another study did not find an effect of KRCH on insulin receptor binding, although there was a relatively high rate of ovulation induction in the androgen-sterilized rat model (Li *et al.*, 1998). The relevance of this animal model for polycystic ovaries in women has sometimes been discounted, but the metabolic effects in animals were nonetheless impressive. Polycystic ovaries may benefit from treatment with KRCH for improving fertility, weight loss, and androgen and lipid profiles. It has been reported that another herbal preparation containing five components (bark of *Cinnamomum cassia*, root of *Paeonia lactiflora*, seed of *Prunus persica*, carpophores of

Poria cocos and root bark of *Paeonia suffruticosa*) increased uterine mass and thymidine kinase activity in rats by 29% and 39%, respectively, compared with controls. This herbal preparation also enhanced the gonadotrophin-releasing hormone (GnRH)-induced increase in plasma luteinizing hormone (LH) and follicle-stimulating hormone (FSH) concentrations by up to 2.5-fold compared with those of untreated animals (Sakamoto *et al.*, 1988). These results indicate that this preparation may act on GnRH containing neurones, on gonadotroph cells or as a weak anti-oestrogen. Limited data also indicate an increase in serum leptin and a decrease in gonadotrophins after treatment with KRCH, but further clinical trials are needed before firm conclusions can be drawn about the actions and efficacy in anovulatory women.

Endometriosis

According to TCM convention for symptom differentiation, endometriosis is a disease of blood stasis and abnormal tissue mass in the lower abdomen. Clinical evidence has shown that herbal medicine has a significant regulatory effect on the blood circulatory, immune and endocrine systems. Wang *et al.* (1991) performed a study of 76 patients with endometriosis using a herbal prescription containing rhubarb as the main ingredient to remove blood stasis and to disintegrate and purge the pathological tissue. The authors reported an overall success rate of

80%, with reductions in dysmenorrhoea (89%), pelvic pain (67%), dyspareunia (72%), and diminished nodule sizes (22%). Three out of 22 women who were diagnosed as infertile became pregnant after treatment. In addition, significant changes occurred in serum immunoglobulins, T lymphocyte subsets and prostaglandins, all of which were considered by the authors to be positive for women's health. Liu (1994) reported effective clinical results using similar methods for 46 patients with endometriosis, including reductions in dysmenorrhoea, anal tenesmus, dyspareunia, nodule sizes, and six pregnancies in ten cases. However, the two studies did not prove an association between the herbal formula and clinical outcome because they lacked a suitable control group.

When mice were fed chow containing relatively high doses of another Chinese herbal remedy, *keishibukuryogan* (0.5% and 1%), a significantly lower incidence of adenomyosis and uterine thymidylate synthetase activity was found compared with controls (Mori *et al.*, 1993). During 25–120 days of herbal therapy, there was no significant change in duration of oestrous cycle, food intake or body weight. A lower dose (0.1%) did not diminish the improvement in adenomyosis. The inhibitory effect of the high doses of the remedy was abolished by pituitary iso-grafting, which has been shown to enhance the development of adenomyosis (Mori *et al.*, 1993). Wu *et al.* (2000) reported a large study of clinical efficacy and side effects of Chinese herbal medicine, which they compared with treatment with Danazol in patients with endometriosis. In a randomized prospective trial of 152 patients with either a herbal formula or Danazol, there was no statistically significant difference in the rate of regression of the cysts or in pregnancy, although there was a significant reduction in both plasma prostaglandin $F_{1\alpha}$ and serum CA125 with TCM compared with Danazol. Although the investigators pointed out that minimal adverse effects are one of the potential advantages of herbal medicine, safety studies (especially for pregnancy), optimal doses and tolerance have, in fact, rarely been studied systematically. In view of the limited studies available, rigorously designed investigations of the therapeutic effects and pharmacological actions of herbal remedies are imperative, and this is also true for the following reproductive disorders.

Luteal phase defect (LPD)

In TCM, LPD belongs to the *kidney–Yin* deficiency category (Table 1). Lian (1991) treated 60 cases of infertility associated with LPD using herbs to tone the *kidney–Yin* and regulate *Qi*. Basal body temperature was markedly increased, indicating a functional corpus luteum, and a pregnancy rate of 56% (32 of 60) was obtained. In a similar way, Zhang *et al.* (1992) conducted a randomized clinical trial of 53 patients with LPD by administering various Chinese medicinal herbs at different phases of the menstrual cycle for three cycles with the rationale expressed in a traditional way: 'nourishing the *kidney Yin*, invigorating the *spleen*, replenishing the *Qi*, enriching the blood' (in other words, promoting follicular development) and 'invigorating the *kidney* and strengthening the *Yang*' (that is, maintaining corpus luteum function after the postovulatory phase). The authors reported significant improvements in endometrial histology, basal body temperature and serum progesterone. Forty-two per cent of patients became pregnant,

although serum LH and FSH were reduced significantly in the luteal phase compared with pre-treatment concentrations. These studies indicate that medicinal herbs can replenish the *kidney–yin*, and might directly influence the hypothalamic–pituitary–ovarian axis to improve luteal function. However, few trials have been performed.

Immunological infertility

Immunological infertility is categorized as a *kidney–Yin* deficiency (Table 1). A randomized control trial of 60 women with presumptive immunological infertility was performed using a *guyin* decoction. A significantly higher pregnancy rate was obtained compared with controls (85% versus 56%), as well as supposedly favourable changes in immunological status (Chen *et al.*, 1995; Lian *et al.*, 2002). Li *et al.* (1995) used *Zhibai Dihuang* pills composed of Chinese medicinal herbs to treat infertile couples with serum anti-sperm antibodies (AsAb) or to zona pellucida antigens. The results showed that in 81% of cases antibody titres became negative after treatment. In all of the eight successful pregnancies, negative test results were obtained for AsAb and antibodies to the zona pellucida and these were maintained throughout pregnancy. Unfortunately, the concentration of AsAb in the cervical mucus was not tested. In a large controlled clinical trial, 103 women were randomized to three groups for treatment with *Zhenqi Zhuanyin* decoction or intrauterine insemination (IUI), or both methods. The use of both methods produced the best therapeutic outcome with a 41% pregnancy rate and three-quarters of the patients becoming AsAb negative (Lian *et al.*, 2002). These findings indicated that combination therapy with medicinal herbs and IUI for immunological infertility resulted in a higher pregnancy rate than therapy with IUI alone. Although these accounts certainly appear impressive, the pathological significance of autoantibodies in infertility is still unclear (Tian *et al.*, 1999; Rogoza *et al.*, 2002), and this research raises as many questions as it answers.

Tubal factor infertility

From the TCM perspective, partly or completely blocked Fallopian tubes are due to *Qi* stagnation and blood stasis of the lower abdomen. Therapeutic strategies aim to harmonize the blood, resolve the stagnation and tissue mass, regulate the *Qi* flow and purge the heat and toxic materials. Xu *et al.* (1999) studied 39 infertile women with unilateral or bilateral occluded Fallopian tubes identified by hysterosalpingography. There was a 95% improvement rate and a pregnancy rate of 82% (32 of 39) after completing a 3-month herbal formula course with a follow-up at 9 months. The formula consisted of 17 herbal species, including *Sprina gleditsiae*, *Spica prunellae*, *Myrrha praeparata*, *Resian olibani praeparata* and *Rhizoma zedoariae*, and 12 of the herbs listed in Table 3. The investigators used the first administration as an enema and delivered the second orally. Except for one case of spontaneous miscarriage, all pregnancies progressed to term, but neither antibodies nor hormone parameters were recorded in this study (Wan, 1990). Lin *et al.* (1999) reported a statistically significant improvement of 82% with similar methods of administration over a period of one year in 112 infertile women with chronic salpingitis compared

with 50% using Western drugs. The explanation offered for the improvement was that herbs acting as an enema may directly promote pelvic blood circulation, remove damp heat and toxic materials and restore patency to occluded tubes. Moreover, two randomized controlled studies also showed a statistically significant increase in success in 40 tubal factor patients treated with an oral herbal formula with antibiotics compared with antibiotics alone (Sheng and Hui, 1996; Zhu, 2000). These findings indicate a synergistic effect between herbal formulas and antibiotics, which promotes pregnancy potential and reduces the duration of treatment in tubal factor patients.

Male infertility

Numerous studies have reported that Chinese herbs can significantly improve the quality and quantity of sperm. Table 4 summarizes 17 leading Chinese herbs used for tonifying the kidney to improve spermatogenesis and motility. Peng *et al.* (1997) incubated human spermatozoa with decoctions of *Semen cuscutae*, *Rhizoma curculiginis* and *Radix morindae officinalis* at various concentrations for 30 min, before performing tests for sperm capillary penetration, sperm motility and hypo-osmotic swelling. Sperm motility improved markedly and sperm membranes were stabilized, indicating that herbal decoctions may be beneficial in promoting sperm function for IUI and IVF (Takahashi *et al.*, 1992). Moreover, a few controlled clinical trials have produced satisfactory therapeutic outcomes using herbal formulas (Liu, 1990; Zhai *et al.*, 1990). A larger, non-randomized study of 202 infertile men with abnormal semen profiles was conducted for 2 months using the *Shengjing* pill, a Chinese herbal formula (Table 4). Sperm density, motility and viability were significantly improved. The concentrations of serum FSH, LH and testosterone were normalized by treatment, and 78% of the 116 spouses conceived (Chen and Wen, 1995). The sperm count in men with severe oligospermia rose from $2.1 \times 10^6 \text{ ml}^{-1}$ to $17.9 \times 10^6 \text{ ml}^{-1}$ (Usuki, 1986; Ishikawa *et al.*, 1992). The authors suggested that improvement in sperm concentrations after herbal treatment may be due to a correction in Leydig cell dysfunction, although this explanation now seems implausible. Moreover, the beneficial effect could not be repeated in a small study (Yang *et al.*, 1995), perhaps because different criteria were used to classify severe oligospermia and variations in study design. In addition, two observational studies confirmed the improvement in serum FSH, LH, testosterone, corticosterone and pregnancy rate after herbal treatment, indicating that the herbs had multiple actions on the pituitary axes (Yue *et al.*, 1996; Yang *et al.*, 2001).

Using an animal model of kidney–Yang deficiency in which Wistar male rats received adenine for 30 days at $30 \text{ mg (100 g)}^{-1}$ body weight per day, Yue *et al.* (1997) coadministered *bushen shenjing* decoction (6 g (100 g)^{-1} body weight per day) and obtained an improvement in spermatogenesis. The serum LH and total and free testosterone concentrations increased significantly compared with the controls. Hong *et al.* (1992) screened aqueous extracts of 18 Chinese medicinal herbs for effects on the motility of spermatozoa *in vitro* using a trans-membrane migration method. Only one herb was effective, *Astragalus membranaceus*, and it stimulated a 1.4-fold increase in forward

progression compared with sperm from controls. Maximum effects were obtained at 10 mg ml^{-1} , and partition studies indicated that the active ingredient was soluble. Herbal formulas were also used to treat infertile men with moderate or severe varicocele presenting with abnormal semen. These results indicated that herbal preparations of *guizhi-fuling-wan* (7.5 g per day) for at least 3 months not only improved the semen profile, including sperm density and motility in 71% and 62% of patients, respectively, but also modulated the circulatory disorder in 40 of 50 men with varicocele (Yang *et al.*, 1995; Ishikawa *et al.*, 1996). No adverse effects were observed, which led the authors to conclude that the treatment is superior to surgical ligation of the spermatic vein or inferior epigastric venous bypass (Qi *et al.*, 2001). Thus, the tentative evidence available so far should encourage further study to verify these benefits in infertile men with oligospermia and varicocele.

TCM and Western reproductive medicine

In TCM, herbs have been used singly or, more typically, in combination to preserve reproductive health and treat infertility and endocrine deficiencies. The underlying philosophy has always been to restore the *Yin–Yang* balance in the body, which bears a vague resemblance to Western concepts of physiology and pathology. The attraction of TCM lies in its time-honoured tradition as well as convenience of self-administration and assumptions (rarely tested) that natural products are relatively safe and have minimal, or at least acceptable, side-effects. In practice, the chief disadvantages of unlicensed herbal medicines lie in their lack of regulation and standardization, and these problems were addressed in 2000 by the Ethnic Medicines' Forum established by the Chinese Medicine Control Agency. However, much of the research to date is derived from non-randomized or poorly controlled studies and, therefore, fails to meet criteria for evidence-based Western medicine. On the other hand, TCM is used today by millions of Asians, and is attracting widespread interest in the West where it is available over-the-counter without a prescription. In a recent study, 40% of patients receiving treatment in a private setting in the UK were reported to be using some form of complementary medicine (Coulson and Jenkins, 2003). Consequently, there is a need to test marketed TCM products for therapeutic efficacy, dosage and safety by prospective randomized control trials. Identifying plausible mechanisms of action could also greatly enhance the reputation of herbal remedies and provide a firmer therapeutic basis for practice. As over 300 Chinese herbs are currently in use for restoring female and male fertility and sexual function, the task is enormous. In setting priorities for research a balance will have to be struck between herbal products which have the highest therapeutic promise and those which raise the greatest safety concerns. The concerns are greatest for products claimed to improve pregnancy outcome and where there is a risk of teratogenicity. The benefits of a better scientific understanding of TCM could be considerable, even if only a few products prove to be both efficacious and safe. Although the large claims which are sometimes made for herbal products may never be verified, we predict there will be some confirmations, whether the remedies are used on their own to improve natural fertility or as adjuvants in assisted conception protocols. Most likely,

desperate patients will continue to experiment with unproven products after failing with conventional Western medicine, or as a cheaper alternative.

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