

An integrative Approach to diagnosing and treating unexplained Infertility

(Katherine Alexander Anderson, JCM 118 October 2018)

Up to 30% of couples trying to conceive are diagnosed with unexplained infertility, this breaks down into 1/3 male, 1/3 female, 1/3 combination factors.

What does unexplained and idiopathic mean? > unclear in females / normal semen analysis in males

- 1) Sperm ruled normal if tested at least twice
- 2) Regular ovulation
- 3) Fallopian tubes are open

Unexplained = testing has not revealed a known disease

Idiopathic = known pathology but unknown aetiology (e.g. abnormal/slow sperm or low AMH in young women)

Low AMH in young women <36 years old (1.0ng/ml) indicates dwindling egg supply, decreased fertility

Male semen analysis is inaccurate: - 40% of infertile men have normal semen analysis parameters
- Normal or abnormal sperm has no impact on 1 year pregnancy rates

Men with a 'normal' sperm analysis can still be infertile and men with an 'abnormal' sperm analysis can be fertile. (An egg is able to 'correct' male genetic imperfections).

Semen characteristics (WHO)	2010	1999
Volume (ml)	1.5	≥2
Sperm Count (10 ⁶ /ml)	15	≥20
Total Sperm count (10 ⁶)	39	≥40
Total Motility (%motile)	40	≥50
Progressive motility (%)	32	≥25
Morphology (% normal forms)	4	14

14% normal (normal; fertilising capability excellent);
4-14% normal (abnormal; possibly decreased or impaired fertilising capacity);
0-3% normal (abnormal; severe impairment or probably inability to fertilise).

Common reasons for **unexplained male fertility = genetic/epigenetic and immunological cases**

80% of couples diagnosed with unexplained or idiopathic infertility have high DNA damage (DNA fragmentation index ≥ 30%); causes are: smoking, alcohol, heat, radiation, pesticides, herbicides, industrial chemicals => oxidative stress affects spermatogenesis/ sperm function.

Recommended test: Karyotype testing = simple blood test

Immunological causes of male infertility > blood testis barrier compromised by e.g. trauma, varicocele, vasectomy or epididymitis +. Allows anti-sperm antibodies (ASAs) to develop which is associated with low sperm motility.

Age: Orthodox medical thinking >35 y o = advanced maternal age linked to shortening of Telomeres => oocyte aging – associated deterioration in quality/ also impact on sperm (but not associated with abnormal sperm morphology)

Telomeres can be damaged by free radicals from environmental toxins, poor lifestyle

- ⇒ Yangsheng = nourishing life => avoiding harm/promoting health/nourishing life = no excess/ good food, emotions, sleep, rest, friends/ good mind, breathing, food limitations, supplements

Possible TCM patterns to consider: KD Yin/Yang Xu, Liv Qi/ Blood stasis/ Damp heat in LJ

Orthodox treatments for male infertility (limited)

- LH + FSH => increase sperm production and steroidogenesis
- Clomiphene inhibits negative feedback of oestrogen => increase of FSH and LH
- Aromatase inhibitors prevent testosterone to oestrogen conversion
- ICSI (intracytoplasmic sperm injection) or IMSI (intracytoplasmic morphologically selected sperm injection)

Unexplained female infertility = diagnosis of exclusion:

- Fallopian tubes open (HSG = hysterosalpinogram)
- Ovulation normal
- Sperm analysis normal

Should also include:

- Quality of cervical mucus
- Frequency and timing of intercourse (6 days before and including ovulation day)
- Mild endometriosis (via laparoscopy) associated with lower progesterone production because of inefficiency of steroidogenesis in granulosa cells surrounding oocyte affects quality of oocyte and maturation due to greater oxidative stress.
- Longer follicular phases with smaller dominant follicles also associated with endometriosis
- Oxidative stress: follicles grow in hypoxic conditions. To ovulate a certain amount of oxidative stress is needed. (too much from environmental stressors: Bisphenol A (BPA) in plastics, dioxins in chlorinated products, polychlorinated biphenyls (PCBs) in animal fats/ some seafood.

Orthodox treatments for female infertility

- >35 years old try for 6 months / <35 years old try for 1 year => tests: basic hormone profile, HSG, sperm analysis, if all normal ovulation triggers are used (Clomid or Femara [letrozole]) +/- IUI
- Clomiphene = low success rate; thins uterine lining, decreases cervical mucus
- Success rate of Clomid + IUI = 7.6% vs 6% without treatment, however if sperm count + motility are normal there is no pregnancy increase with Clomid + IUI.

Clinical Checklist

Integrative treatment: Confirm:

- Male \geq normal semen analysis
- No female factor issues
- Coital frequency / timing appropriate
- Thorough history (all past and present medical conditions, surgeries, developmental delays, occupational hazards, medication use, previous infections, social habits)
- Double check medical tests (normal may not be normal)

Six aspects to check for proper infertility:

- Ovulatory function
- Insulin resistance
- Thyroid function (TSH, free T3 and T4, thyroid antibodies)
- Androgens (Dihydrotestosterone - DHT, Dehydroepiandrosterone-sulfate - DHEA-sulfate)
- Semen
- Tubal patency
- Endometrial lining ≥ 9 mm
- Cervical mucus reflects oestrogen levels (postcoital test PCT)

Other basic questions for patient

- Seen medical doctor
- Use of lubricants (hostile sperm environment)
- Use of supplements, medication (hormones)
- Use of marijuana => may lower sperm concentration/counts

The unexplained Infertility Checklist

General	Labwork	Female	Male
Seen gynaecologist?	FSH	Over/under weight	Fathered a child?
Seen fertility specialist?	LH	Egg white cervical mucus	Sperm analysis high or low?
Cigarettes?	Estradiol	Make up? Hair dye?	Ejaculation frequency
Marijuana?	AMH	Lotions? Sin products?	Work exposure?
Sauna, hot tub?	AFC	Cleans own house?	Testosterone use?
Car seat heater?	Progesterone	EWG.org	Handyman?
	Prolactin	Acne/hair growth?	Get/sustain erection?
Medication	TSH	Celiac? Leaky gut?	Electronics near testicles?
HBP?	Inhibin B	Nipple discharge	Kidney disease?
Statins?	Sperm analysis x 2?	Lubricants or saliva for intercourse?	
Clomid?	Ultrasound?	Sexual frequency?	
Letrozole?	Sonohystogram?	Type of supplements	
SSRIs?	Laparoscopy?	Alcoholic drinks/week	
Pesticides?	HSG?	How many vegetables?	

The success of IVF according to the Center for Disease Control (2015) in unexplained infertility: 29% live birth

ICSI, IUI, IVF is most successful in cases of

- Anti-sperm antibodies
- DNA damage
- Fertilisation defects
- Oxidative stress

TCM helps to improve DNA fragmentation (Chinese herbs to supplement Kidney Qi), also add:

Carnitine, Selenium, Zinc, Lycopene, Vitamin E and Vitamin C, CoE-Q10 > these improve Sperm DNA damage, semen parameters, pregnancy and life birth rates

In women use acupuncture to increase Blood supply to the ovaries + Chong and Ren Mai + Chinese Herbs to strengthen Kidneys. Calm the Shen.

TCM Diagnosis	Biomedical associations
Kidney deficiency (jing, qi, yin, yang)	PCOS, hypothyroid, genetic, advanced maternal age, diminished ovarian reserve, male factor sperm count/motility, obesity, oral contraceptive use, endometriosis, fibroids
Qi and/or blood stagnation	Hormone imbalance, abnormal menses prolactinemia, erectile dysfunction, endometriosis, fibroids
Cold uterus yang deficiency)	Oral contraceptive use, luteal phase defect, recurrent miscarriage, delayed ovulation
Damp phlegm	Obesity, PCOS tubal obstruction
Qi and blood deficiency	Hypothyroidism, scanty menses, hypothalamic anovulation secondary to excessive weight loss especially in athletes, vegetarianism
Damp-heat	Yeast infections, sexually transmitted diseases, prostatitis
Shen disturbance	Trauma, depression, anti-depressant usage

Compiled and summarised by Pia Huber, 18 September 2019