

Infertility: What the general practitioner should know

Ghina Ghazeeri, MD

Reproductive Endocrinology and infertility

American University of Beirut

Outline:

- Infertility: definition
- Causes of infertility: male and female
- Male factors and when to refer
- Female factors and when to refer
- PCOS: metabolic disease
- Ovarian reserve: the clock is ticking
- Where are we now: PGD, IVF, ICSI, AH, SET, Stem cell research
- Draw backs: Cost, Multiples, Safety

Infertility

Ω the failure to achieve a pregnancy within 1 year of regular unprotected intercourse ([Evers, 2002](#); [Zegers-Hochschild et al., 2006](#)).

Ω one in four women are affected at sometime ([Gunnell and Ewings, 1994](#)).

Ω ~20% of couples consult their general physician because of difficulty conceiving, and half of those couples (10%) require specialist care ([Hull et al., 1985](#); [Beurskens et al., 1995](#)).



Workup done by general practitioner:

Clinical evaluation of the infertile couple may be grouped into five categories:

semen analysis, the post-coital test (PCT), assessment of ovulation, uterine and tubal evaluation, and laparoscopy ([Balasch, 2000](#))

Semen analysis

Ωnormal' as a sperm concentration of $>20 \times 10^6/\text{ml}$ with $>50\%$ of progressively motile sperm and the presence of sperm with standard (no parameters provided) morphology ([World Health Organization, 1999](#))

Ωthe choice of expectant management, intrauterine insemination (IUI), *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI).

ΩSperm function tests

Post Coital test:

routine use of this test in clinical practice is not recommended (National Institute for Clinical Excellence, 2004; Male Infertility Best Practice Policy Committee of the American Urological Association and Practice Committee of the American Society for Reproductive Medicine, 2006)

Uterotubal evaluation:

- hysteroscopy, hysterosalpingography (HSG), transvaginal ultrasonography (TVS), saline infusion sonohysterography (SIS), magnetic resonance imaging (MRI) or laparoscopy. ([Crosignani and Rubin, 2000](#))
- 14% of infertility causes
- no consensus of opinion ([National Institute for Clinical Excellence, 2004](#); [den Hartog et al., 2008](#)).

- Laparoscopy with dye testing was considered useful for patients with positive *Chlamydia* serology or evidence of bilateral tubal occlusion on HSG ([den Hartog et al., 2008](#)).
- hydrosalpinx has a negative effect on clinical pregnancy and live birth rates following IVF ([Strandell, 2007](#)).
- Compared with hysteroscopy, HSG has high sensitivity (81–98%) but low specificity (23–35%), and high false-negative (10–90%) and false-positive (22–44%) rates.

- Late follicular phase TVS has proved to be a useful tool for the detection of intrauterine abnormalities such as polyps, synechiae, fibroids and Müllerian anomalies ([Van Voorhis, 2008](#)).
- SIS offers enhanced visualization of the endometrium and better detection of intrauterine pathology than does standard TVS, and may be as effective as hysteroscopy in detecting intracavitary abnormalities ([Ragni et al., 2005](#); [Valenzano et al., 2006](#)).
- MRI may be used for patients with suspected complex Müllerian anomalies ([Deutch and Abuhamad, 2008](#)).

Uterine Fibroids

- 20–50% of women aged over 30 years and are the most common benign tumour of the female genital tract ([Eldar-Geva *et al.*, 1998](#); [Okolo, 2008](#)).
- Size and location
- Removal of submucosal fibroids improves clinical pregnancy rates (RR 2.03, 95% CI 1.08–3.83), but the limited available data suggest no improvement in treatment outcomes after removal of intramural fibroids ([Pritts, 2001](#)).

Evaluation of ovarian reserve

- the remaining population of primordial and resting follicles ([Gougeon, 1996](#)).
- The quantity and quality of the follicles present in the ovary ([Broekmans *et al.*, 2006](#))
- FSH, Estradiol, AMH, Inhibin B
- Antral follicle count



ASSESSMENT OF OVULATION

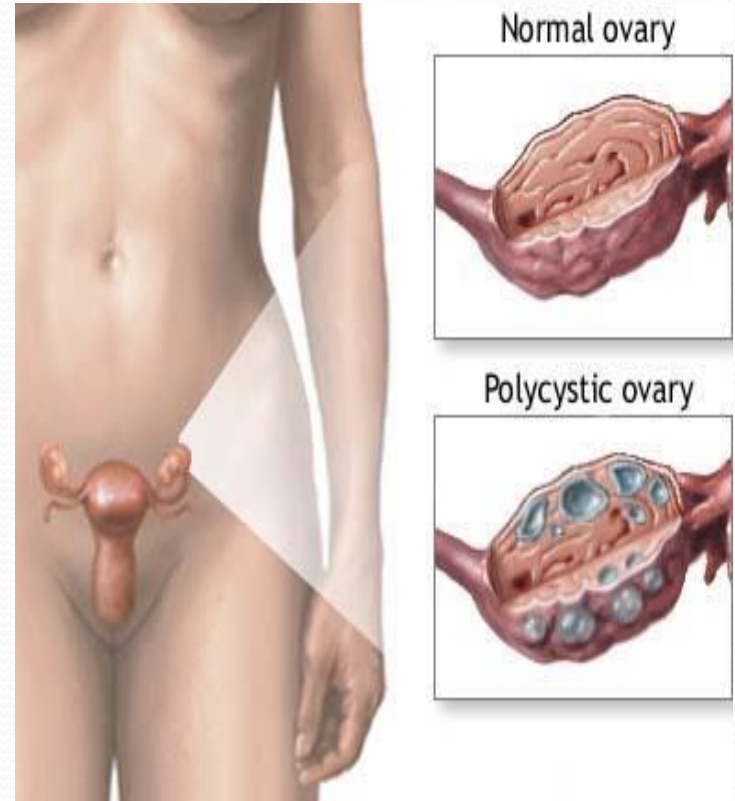
- Day 21 progesterone
- LH surge
- Endometrial biopsy
- U/S
- Cervical mucus testing

Ovulatory defects

- *Polycystic ovary syndrome :*

Definition

- 1935 Stein-Leventhal Syndrome
- 1990 NIH conference on PCOD
- 2003 Joint ESHRE-ASRM Conference- Rotterdam



Definition

Rotterdam 2003. Joint meeting of the ESHRE and ASRM reached a consensus on the definition

Two of the following

1. Oligo and/or anovulation
2. Hyperandrogenism (clinical and /or biochemical)
3. Polycystic ovaries, with the exclusion of other etiologies

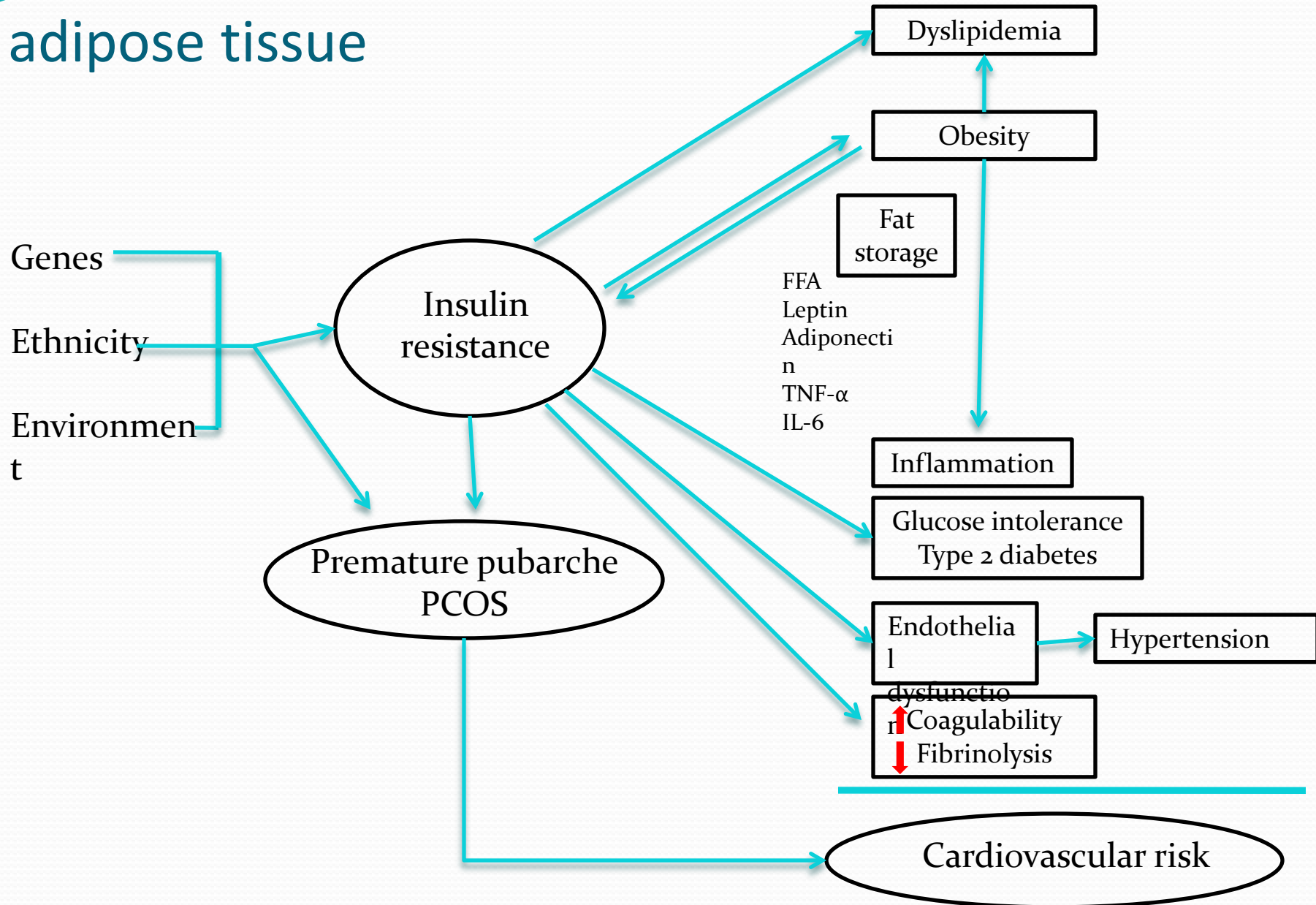
Acanthosis Nigricans



Treatment:

- Ovulation induction: insulin sensitizers, clomid , gonadotropins
- older women may benefit from earlier use of IVF ([Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2008](#))

Insulin resistance and the adipose tissue



Metformin

- Biguanide
- Acts at the receptor and post receptor level
- Superior surgical treatment (Plaomba Fertil Steril 2004)
- Lactic acidosis, Hepatic dysfunction, Heart failure
- Improves cardiovascular risk factors
- Significant improvement in androgen and hirsutism score.

The following recommendations are based on good and consistent scientific evidence (Level A):

-All women with PCOS should be screened for glucose intolerance with a 2-hour glucose level after a 75-g fasting glucose challenge.

All women with PCOS should be screened for dyslipidemia with a fasting lipoprotein profile, including total cholesterol, LDL, HDL, and triglyceride determinations.

Interventions that improve insulin sensitivity, including weight loss, use of metformin, and use of thiazolidinediones, are useful in improving ovulatory frequency in women with PCOS.

Use of clomiphene citrate is appropriate because it effectively results in pregnancy in women with PCOS.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Improvements in insulin sensitivity, by weight loss or by the use of insulin-sensitizing agents, may favorably improve many risk factors for diabetes and cardiovascular disease in women with PCOS.
- When using gonadotropins to induce ovulation, low-dose therapy is recommended because it offers a high rate of monofollicular development and a significantly lower risk of ovarian hyperstimulation in women with PCOS.
- The benefit and role of surgical therapy in ovulation induction in women with PCOS is uncertain.

When to refer:

- Male infertility:

Obstructive or non obstructive azospermia ([National Institute for Clinical Excellence, 2004](#)).

Mild male factor: 1 million TMC

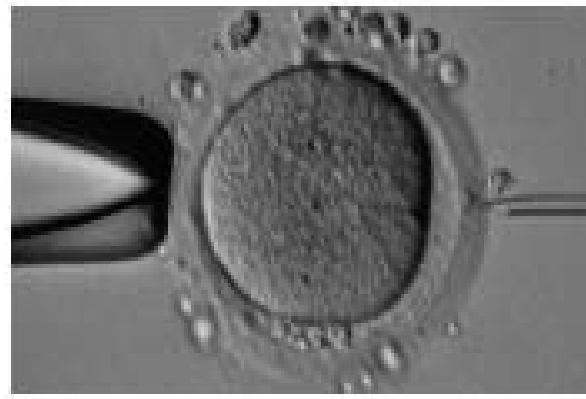
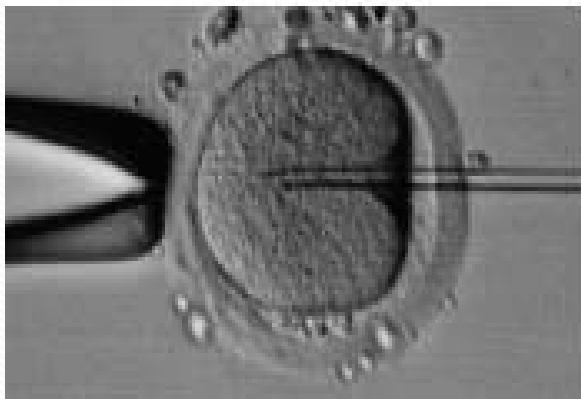
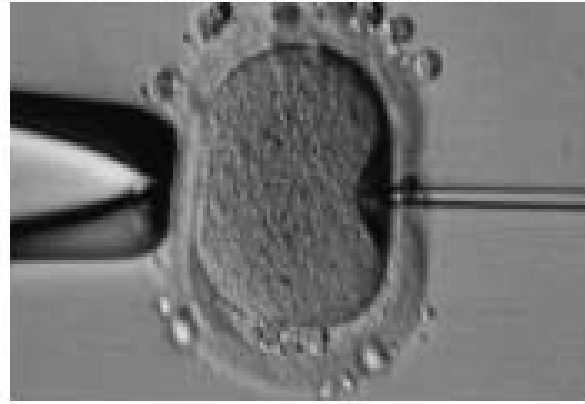
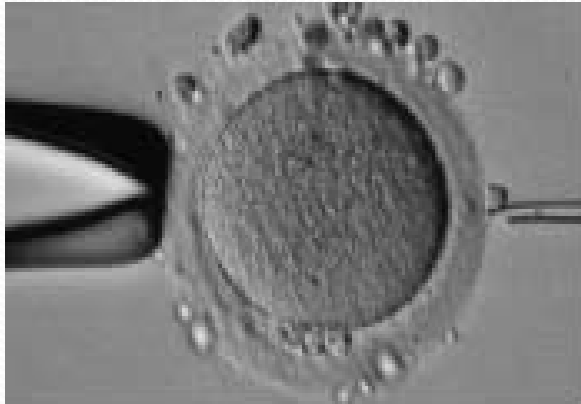
Expectant management:cochrane review ([Bensdorp et al., 2007](#)).

- *Bilateral tubal occlusion*

Difficult and old cases of PCOS : candidates for ART

Where are we now

- ICSI
- PGD
- IVM
- Cryopreservation
- SET

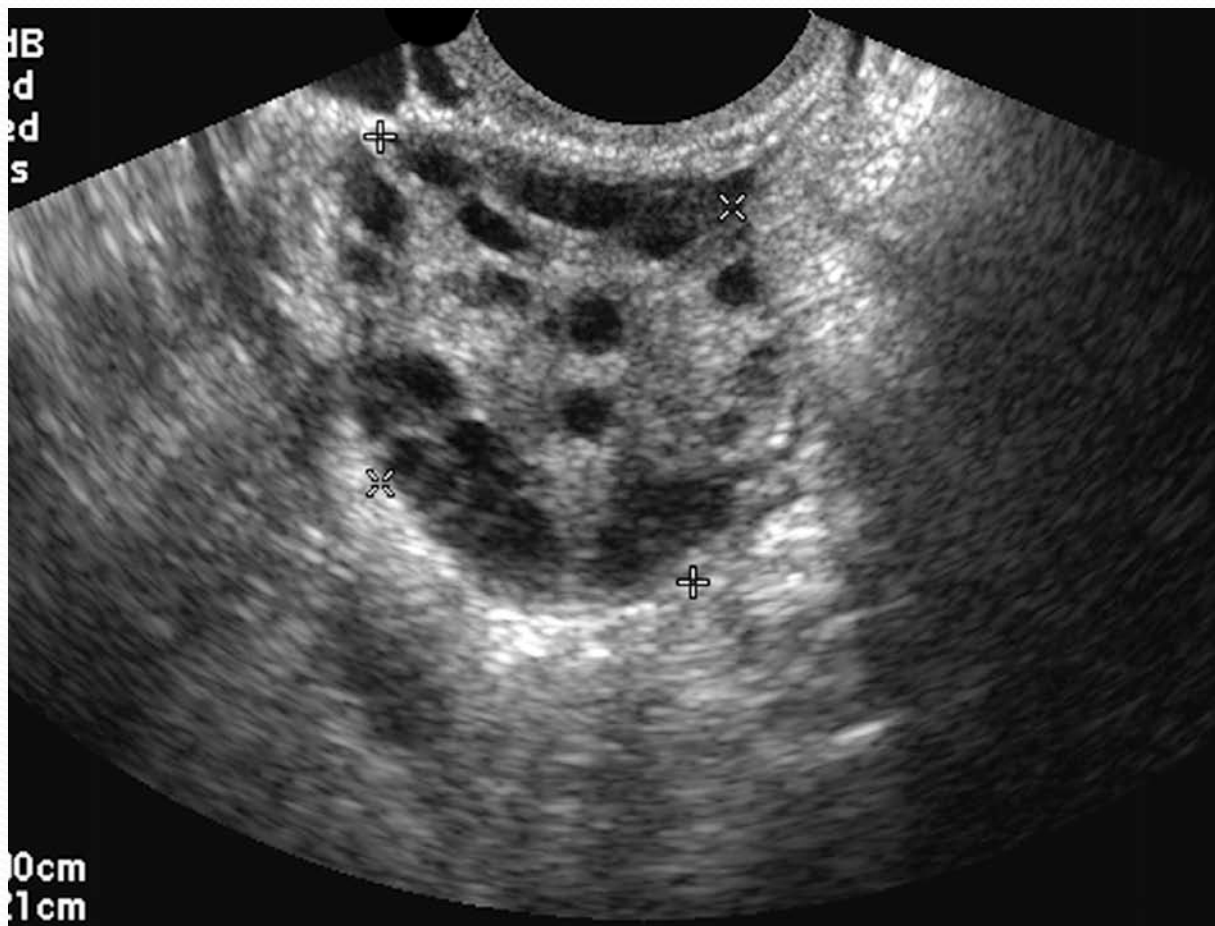




candidates

- Preimplantation genetic screening
- Single gene defects: Thalassemia, sickle cell anemia
- Sex-linked chromosomal defects: hemophilia, Muscular dystrophies.


IVM



Cryopreservation

- Sperm
- Embryo
- Egg and ovarian tissue: medical and non medical



- 
- cryopreservation maximizes cumulative pregnancy rates per oocyte retrieval by storing unused embryos for future use ([Youssry et al., 2008](#))
 - Slow freezing and vitrification

ART: assisted reproductive technology: not always happy ending

- OHSS
- Cost
- Risk of malignancy
- Risk of multiples

Single embryo transfer

half of all babies born from IVF globally are from multiple pregnancies ([Adamson *et al.*, 2006](#)), 20-30% are twins or higher.

considerable fetal morbidity and costs ([ESHRE Campus Course Report, 2001](#); [Land and Evers, 2003](#))

recommendations to limit the number of embryos transferred ([The ESHRE Capri Workshop Group, 2000](#); [Land and Evers, 2003](#); [Wright *et al.*, 2003](#); [Practice Committee of Society for Assisted Reproductive Technology and Practice Committee of American Society for Reproductive Medicine, 2008a](#)).