Endometriosis &Infertility Treatment

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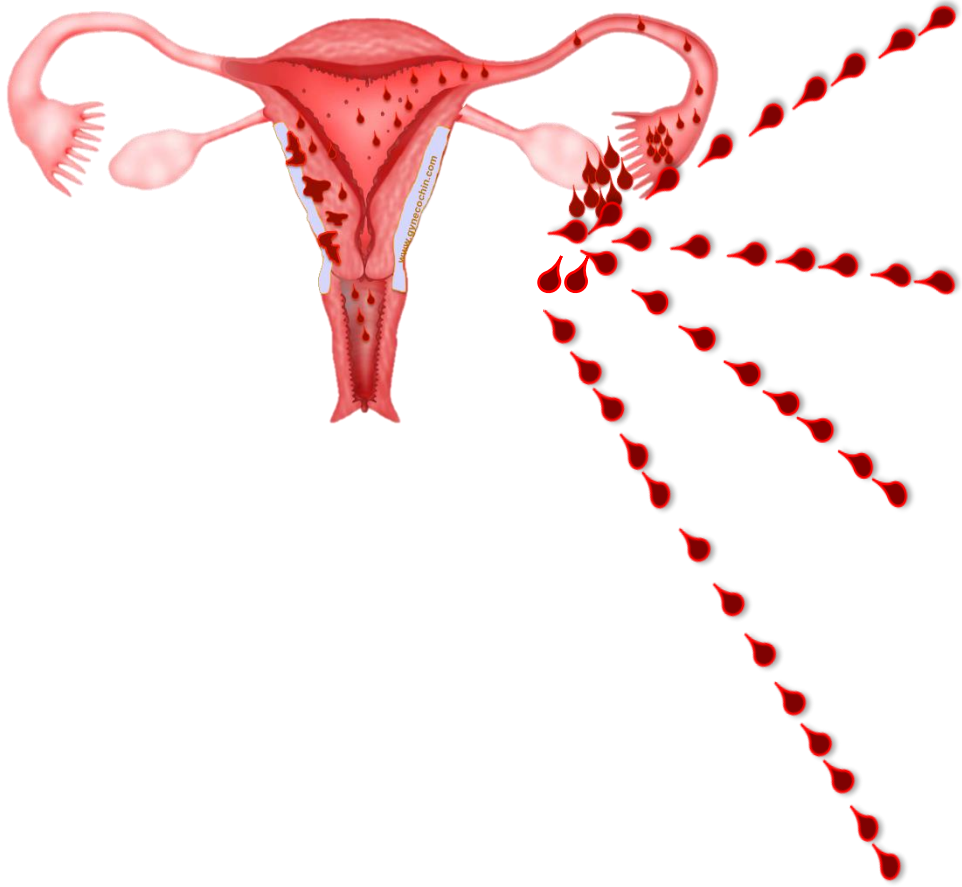
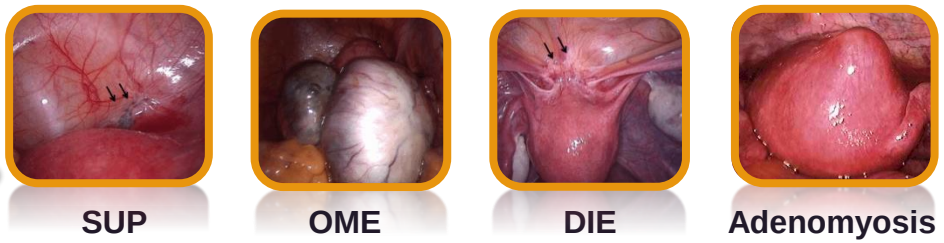
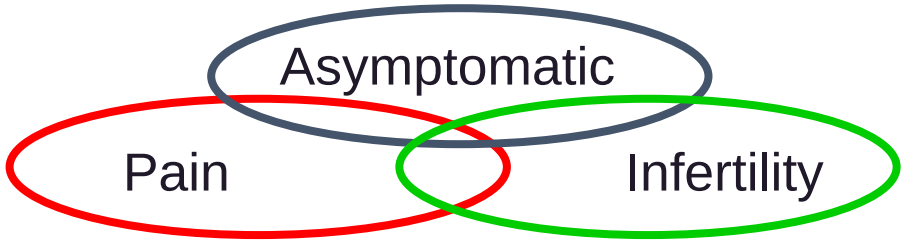
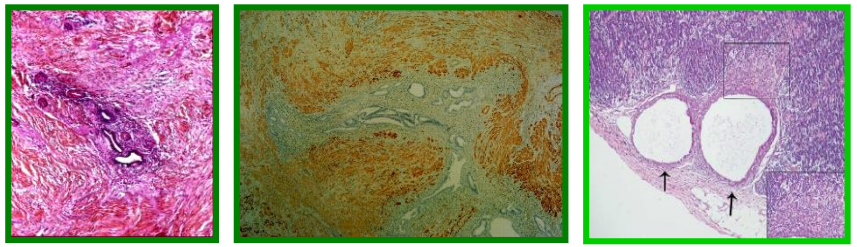
Endometriosis

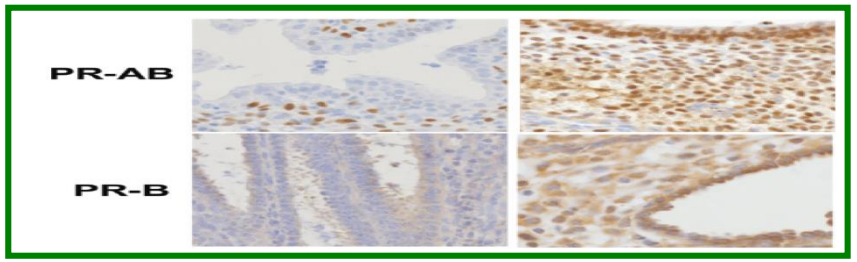
Heterogeneous disease



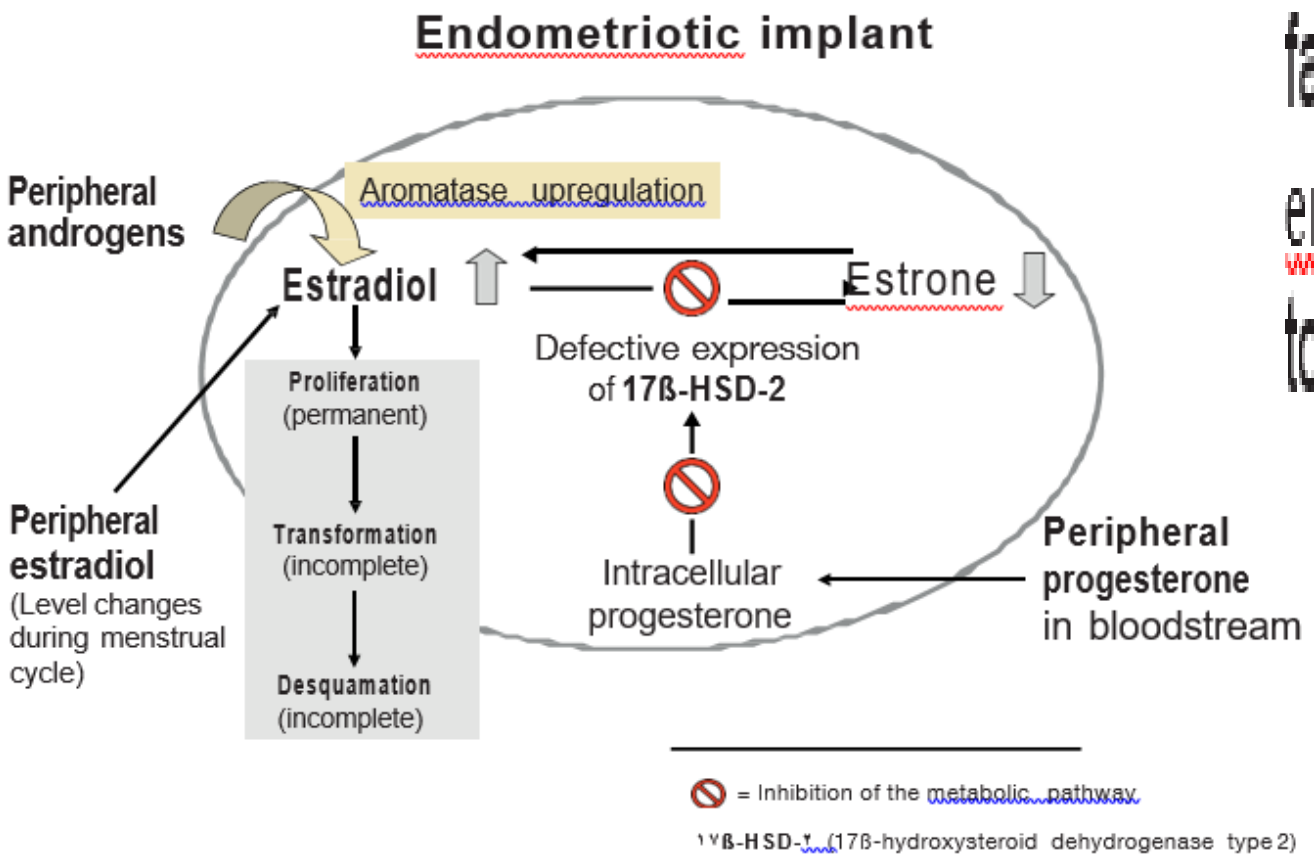




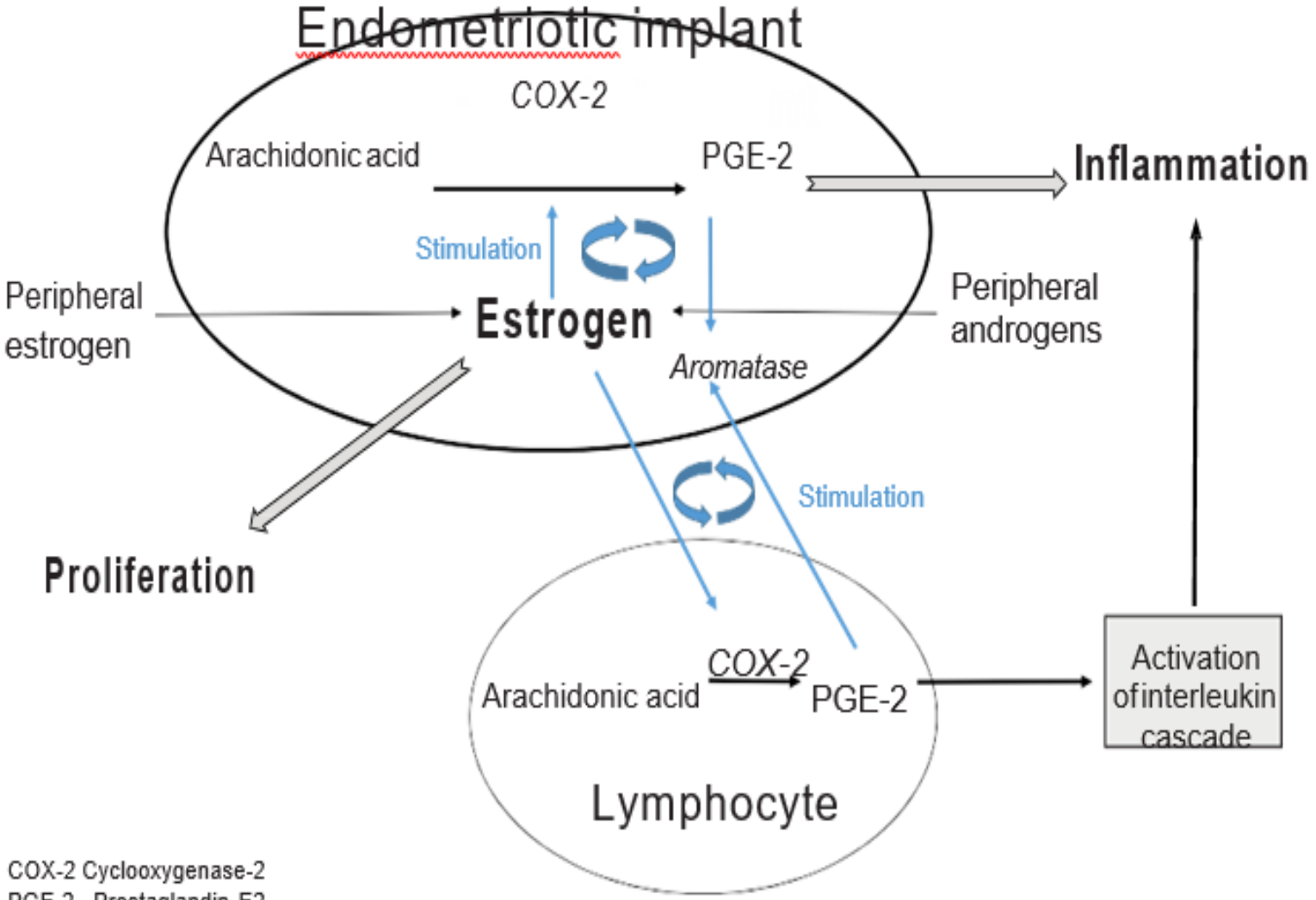




Dr. Kh. Shadjoo



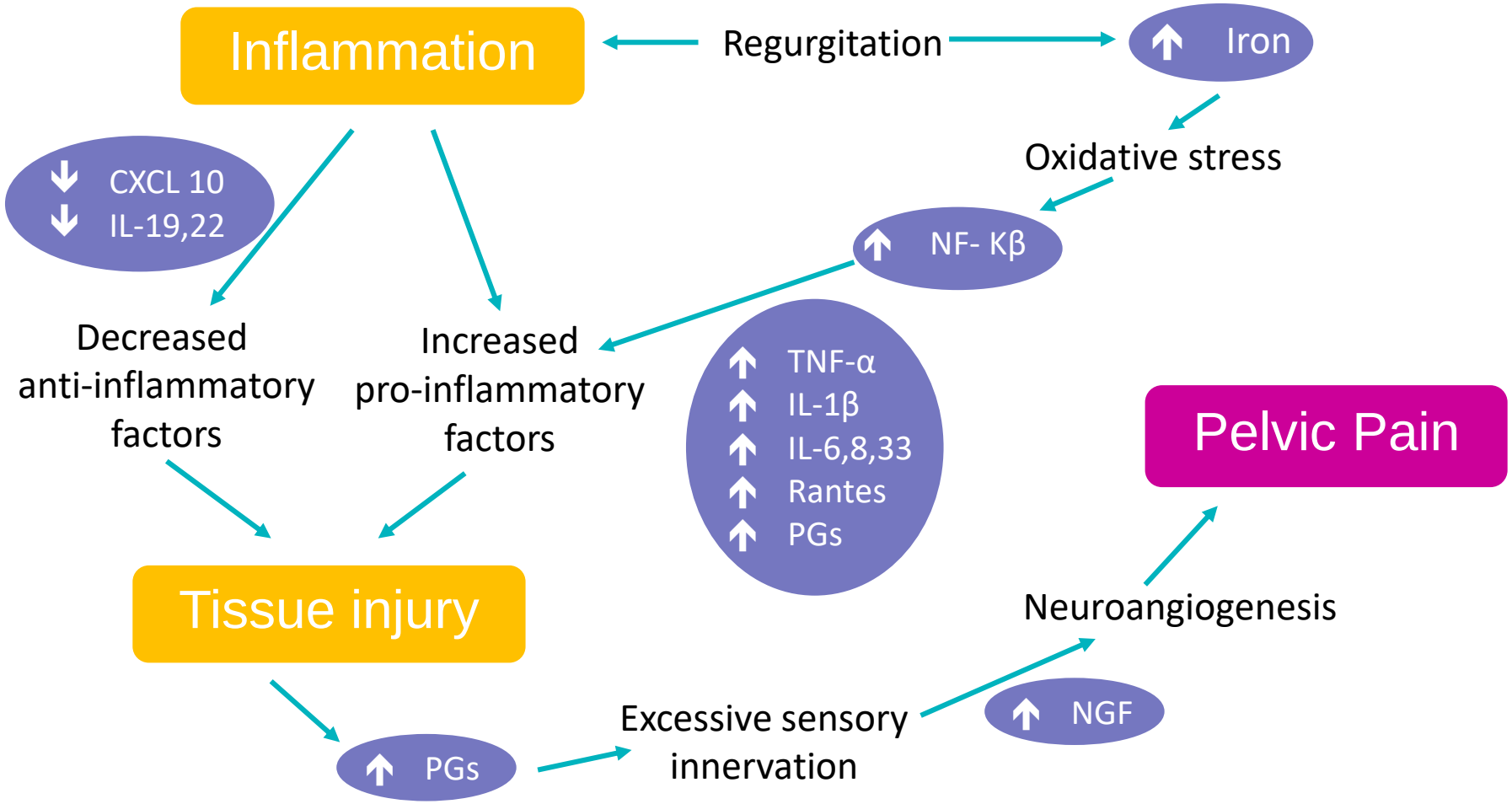
factors involved in the pathogenesis of endometriotic lesions (modified according to Noble LS, et al. (1996).[22]



the impact of prostaglandins and oestrogen on the inflammatory reaction in endometriosis tissue.

Inflammatory response pathway

Tissue injury and chronic pain



IL, interleukin; TNF, tumor necrosis factor; PG, prostaglandin; CXCL, chemokine; NGF, nerve growth factor; NF-Kβ, nuclear factor kappa beta.

- 25-40% of endometriosis cases experience inability in becoming pregnant
-

30-50% of them have difficulty in conceiving

The link between endometriosis and infertility is not fully understand

- the most probable involving mechanisms:
- endocrine malfunctions
- immune disorders
- inflammatory responses caused by the endometriotic tissue

Causes of endometriosis-related infertility

- distorted tubo-ovarian relationship
- impaired folliculogenesis
- hormonal dysfunction
- disturbed local milieu
- fertilization failure
- impaired endometrial receptivity

How minimal or mild endometriosis can lead to infertility

- the molecular alterations in endometriosis:
- ovarian, tubal, or endometrial dysfunction
- which leads to infertility

chronic inflammation

- The progesterone resistance
- hyper estrogenic state
- chronic inflammation:
- endometrium non-receptive for normal embryo implantation

peritoneal fluid

- In women with endometriosis
- inflammatory markers present in peritoneal fluid :
- hamper oocyte competence
- impair sperm motility, function, and oocyte-sperm interaction
- sperm DNA fragmentation
- Abnormal acrosome reaction

oocyte quality

- oocyte quality is impaired (even in minimalto mild endometriosis)
- because the mitochondrial structure and function are hampered

abnormal LH production

- In endometriosis, the granulosa cells are resistant
- to luteinizing hormone (LH) to some extent; there
- is hypothalamic-pituitary-ovarian axis dysfunction with
- abnormal LH production which affects ovulation

Hyperprolactinemia

- Hyperprolactinemia may be associated with endometriosis
- and its progression
- with a significant association
- between the severity of endometriosis and prolactin levels

endometriosis-related infertility

- distorted tubo-ovarian relationship
- impaired folliculogenesis
- hormonal dysfunction
- disturbed local milieu
- fertilization failure
- impaired endometrial receptivity

- It is not clear
- whether the products of endometriosis are a cause of
- infertility or a para-phenomenon
- To operate or not to operate on women with deep infiltrating
- endometriosis (DIE) before *in vitro* fertilization (IVF)
- Márcia Mendonça Carneiro2017

- Present treatment options of endometriosis-associated infertility：

❖ surgery

❖superovulation with intrauterineinsemination

❖*in vitro* fertilization (IVF))

- many questions remain unanswered

- (de Ziegler*et al.*, 2010; American Society for Reproductive Medicine
- (ASRM), 2012; Johnson *&* Hummelshoj, 2013

laparoscopic surgery

- there is evidence to support

- the use of laparoscopic surgery to improve fertility.
- (Vercellini *et al.*, 2009; Berlanda *et al.*, 2013)

- The role of surgical treatment in infertile women with
- endometriosis remains elusive
- (Vercellini *et al.*, 2009;
- Douay-Hauser *et al.*, 2011; Berlanda *et al.*, 2013)
- . With the exception of peritoneal disease, randomized trials have
- not looked into the effects of surgery in subfertile women
- with endometriosis (Dufy *et al.*, 2014)

first-line IVF treatment or surgery

- dilemma remains:
- when we are faced with an infertile woman suffering from DIE:
- should they be offered first-line IVF treatment or surgery

How should DIE be diagnosed in infertile women

- Clinical history and symptom
- Ultrasound
- diagnosis of DIE
- transvaginal ultrasound (TVUS) is not only useful, but a strategic tool in the preoperative mapping of
- lesions and in surgery planning
- (Ferreira & Carneiro, 2010;
- Dunselman *et al.*, 2014; Exacoustos *et al.*, 2016).

The decision to perform surgery for deep endometriosis mainly clinical

- TVUS
- other imaging techniques such as MRI
- the preoperative estimation of lesion size
- lateral extension
- play a vital role in surgical planning and choice of approach

How might DIE affect fertility and pregnancy

- Although DIE has been frequently associated with
- infertility, there is little evidence connecting the disease
- and infertility
- Studies suggest that infertility in women with DIE :
- the strong link between DIE and adhesions
- superficial endometriotic implants
- ovarian endometriomas, and adenomyosis
- (Somigliana & Garcia-Velasco, 2015)

superficial peritoneal lesions

- produce inflammatory cytokines and chemokines, and thus
- produce, in an altered hormonal milieu, increased oxidative
- stress and impaired sperm and tubal function
- (Gupta *et al.*,2008; de Ziegler *et al.*, 2010).

Medidal therapy before IVF

- GnRH agonists should be given for 3–6
- months prior to IVF as per ESHRE recommendations to
- increase the clinical pregnancy rates

- extensive studies are required to see whether dienogest
- therapy before IVF can help improve the clinical outcome
- of patients.

Surgical management
The decision for surgery in endometriosis-associated infertility

- Age
- previous ovarian surgery
- ovarian reserve
- duration of infertility
- grade of endometriosis
- tubal status
- cost of treatment, expected outcome of the procedure
- and priorities of the patient

Surgical management

- The reconstruction of the normal pelvic anatomy
- to achieve an excellent tubo-ovarian relationship
- remove all macroscopically visible disease is the main aim of the surgery.
- Minimally invasive surgery is preferred over laparotomy
- for obvious reasons

Surgery for moderate to severe endometriosis

- surgery restores the distorted

  pelvic anatomy

- restores the tubo-ovarian relationship
- prevention of adhesion by:
  - Oxidized regenerated cellulose during operative laparoscopy for endometriosis
  - ovaries are temporarily suspended post laparoscopic resection

Ovarian endometrioma

- Clinical data has suggested that ovarian endometrioma:
- damages surrounding healthy ovarian tissue
- presence of proteolytic enzyme
- inflammatory mediators
- reactive oxygen species,
- iron in concentrations many times higher than
- those present in serum or other types of cysts; all of these
- lead to cell damage

SURGERY vs ART

Table 1 Surgery vs ART in endometriosis [37]

Factor	In favour of surgery	In favour of ART
• Age	Young	Old
• Associated infertility factors (tubal or male factor) [5]	No	Yes
• Infertility duration	Short	Long
• Ovarian reserve	Satisfactory	Decreased
• Patients choice	Patient choice	Patient choice
• Pelvic pain intensity	Severe	Mild
• Ovarian endometrioma especially bilateral	No	Yes
• Previous surgery	No	Yes
• Associated adenomyosis	No	Yes

Endometriosis and assisted reproductive technology (ART)

- ESHRE recommends using ART in endometriosis if there
- is tubal or male factor infertility, and/or other treatments
- have failed
- effect of endometriosis on IVF outcome have shown mixed results

- Women with endometriosis who undergo IVF have half the pregnancy
- rate compared to those who get IVF done for other

Fertility Preservation in Endometriosis

- oocyte and embryo cryopreservation can be good options for fertility
- preservation in young endometriosis patients at risk of premature
- ovarian failure increased
- chances of ovarian abscess formation following oocyte
- Pickup; although overall risk is low, antibiotic prophylaxis
- has been suggested

RIF (recurrent implantation failure)

- the failure in achieving clinical pregnancy after transferring of at least
- Four good quality embryos during at least three fresh or frozen
- embryo transfer (FET) cycles in women under 40 years old

Pathogenesis for RIF cases with concomitant endometriosis

- Disruption of endometrial receptivity is proposed as the core pathogenesis for RIF in different conditions

- endometrial dysfunction

- alterations in molecular mechanisms

- **Conclusions**

- laparoscopic surgery (laparoscopic removal of endometriotic tissues 4-6 months prior to FET cycles) can serve as a useful approach for improving the

- pregnancy outcome in RIF endometriosis patients prior to ET during

- ICSI/FET cycles