Introduction

Defenition:

- **Fecundability** is the probability of achieving a live birth in 1 menstrual cycle. It is estimated to be approximately 20-25%/ cycle. Approximately 90% of couples with unprotected intercourse will conceive within 1 year.

- **Infertility** is defined as the inability of a couple to conceive within 1 year, who have taken no contraceptive methods.

- **Sterility** implies an intrinsic inability to achieve pregnancy. It is synonymous with subfertility.

- **Primary infertility** applies to those who have never conceived.

- **Secondary infertility** designates those who have conceived at some time in the past.
Introduction

- Epidemiology:
  - Prevalence: 10-13%, with range from 7-28%, depending on the age of women during childbearing time.
  - It should be changed with different race, region, ethnicity, nationality, etc.
  - It seems has increased over the past decades. During the past 40yrs, the incidence of primary infertility has increased, with a concurrent decrease in secondary infertility, most likely as a result of social changes such as delayed childbearing.
Etiology

Female factor (40%)

Male factor (30-40%)

Both of couple’s factor (10-20%)

Cause of infertility

Unexplained infertility: etiology cannot be found after standard infertility work-up, 15-20%
Etiology

- Female’s factors (40%)
  - Ovulatory factors
    - Central defects
      1. chronic hyperandrogenemic anovulation
      2. hyperprolactinemia (drug, tumor, empty selia)
      3. hypothalamic insufficiency
      4. pituitary insufficiency (trauma, tumor, congenital)
    - Peripheral defects
      1. gonadal dysgenesis
      2. premature ovarian failure (POF)
      3. ovarian tumor
      4. ovarian resistance
Etiology

❖ Female’s factors (40%)
  • Ovulatory factor

Other metabolic disease
  1 thyroid disease
  2 liver disease
  3 renal disease
  4 obesity
  5 androgen excess, adrenal or neoplastic
Etiology

- Female’s factors (40%)
  - Oviduct factor (1/2, obstruction or adhesion)
Etiology

- **Female’s factors (40%)**
  - Oviduct factor (1/2, obstruction or adhesion)
Etiology

 Female’s factors (40%)

- Oviduct factor (1/2, obstruction or adhesion)

Reason:
1. Pelvic inflammatory disease, causing pathological changes in oviductal cilia, mucous layer, obstruction etc.
2. Endometriosis
3. Congenital abnormalities of oviducts
4. Pelvic tuberculosis, oviducts involved

Results: Ovum cannot be fertilized by sperms in oviduct, or the developing embryo cannot be transferred into endometrial cavity
Female’s factors (40%)

- Uterine factor—-influencing embryo implantation
  1 uterine neoplasia: polyps, Submucous myoma
  2 uterine adhesion: Asherman’s syndrome
  3 uterine inflammation: infection, tuberculosis, endomeitritis
  4 cervical factor: congenital, surgical treatment, Mullerian duct abnormality (structural abnormalities), immune factors
Etiology

- **Male factors (30-40%)**
  - Anatomic disorders: congenital absence of vas deferens, obstruction of vas deferens, congenital abnormalities of ejaculatory system
  - Abnormal spermatogenesis: chromosomal abnormalities, mumps orchitis, cryptorchidism, chemical or radiation exposure
  - Abnormal sperm motility: absent cilia (Kartagener’s syndrome), varicocele, antibody formation
  - Sexual dysfunction: retrograde ejaculation, impotence, decreased libido
  - Self antisperm antibodies formation
Etiology

- Both of couple’s factor (10-20%)
  - Sexual dysfunction
  - Immune factor: antisperm antibody, antiendometrial antibody, antiphosphate antibody into serum
  - Unexplained infertility: no positive found after regular examination for infertility
Examination and diagnosis

Examination method

Male

Female
Examination and diagnosis

The armamentarium of diagnostic tests available for the evaluation of an infertile couple is large. Therefore, a clinician should be judicious in his/her use of tests. The history and physical exam shape the endocrinologic and radiologic testing algorithm specific to each patient.

Other factors to consider include patient age, risks associated with the test, invasiveness, expense, and probabilities of significant findings. The patients should be included in the decision-making process.
Examination and diagnosis

For female

1 History, esp. related infertility

2 Physical exam: general condition, secondary sexual characteristics, development of external and internal genitalia, etc

3 Specific tests
Specific test for female

Test for Ovarian function

Exam for Oviduct

Exam for Uterine

Serum tests For immune problem

Ovulatory monitoring:
1. Ultrasound
2. Basal body temperature (BBT)
3. Endocrine serum test
4. Biopsy of endometrium
5. Cervical mucous characters

1. Hysterosalpingogram
2. Sonohysterogram
3. Laparoscopy with chromotubation

Hysteroscopy. We can see submucous polyps, myoma, adherence etc.

Postcoital tests (PCT) controversial

Serum test for antibodies
Examination and diagnosis

For male

1. History, esp. related infertility, history of mumps, etc.

2. Physical exam: general condition, secondary sexual characteristics, development of external and internal genitalia, etc.

3. Specific tests: semen test 🌟
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>volume</td>
<td>≥1.0 ml</td>
</tr>
<tr>
<td>pH</td>
<td>7.0 ~ 7.8</td>
</tr>
<tr>
<td>Time for liquification</td>
<td>Within 30min (room temp)</td>
</tr>
<tr>
<td>concentration</td>
<td>≥15 ~ 200 × 10^6 / ml</td>
</tr>
<tr>
<td>Total sperm count</td>
<td>≥40 × 10^6 / ejaculate</td>
</tr>
<tr>
<td>vitality</td>
<td>Rapid forward ≥18% or rapid forward + slow forward ≥32%</td>
</tr>
<tr>
<td>morphology</td>
<td>normal &gt; 4%</td>
</tr>
<tr>
<td>motility</td>
<td>≥48%</td>
</tr>
<tr>
<td>WBC count</td>
<td>≤1 × 10^6 / ml</td>
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</tbody>
</table>
Treatments: for female

❖ For fallopine tubes:
  • Physical treatment, traditional chinese drugs
  • Surgical treatment: laparoscopy or transabdominal salpingostomy, tubal anastomosis, tubal plastic surgery, tubal ligation, salpingectomy
  • Injection of drugs into fallopine tubes to eliminate local inflammation

❖ For uterus problems:
  • Hysteroscopy or laparoscopy to deal with myoma, polyps, adhesion, etc
Treatments: for female

❖ For ovarian problems
  • Operation for ovarian tumors, esp functional tumor
  • Ovarian reserve evaluation

❖ For vaginal problems
  • Treatment for vaginitis based on the pathogens
  • Corrective surgery for abnormalities
Treatments: for female

- For ovulatory factor: ovulation induction

Usually used drugs:

- Clomiphene citrate: 50-150mg/d *5d
- Gonadotrophin: Human menopausal hormone (HMG), follicular stimulating hormone (rFSH/ uFSH), luteinizing hormone (LH), human chorionic gonadotropin (HCG)
- Luteinizing hormone releasing hormone (LHRH) for hypothalamic amenorrhea
- Aromatase inhibitors for PCOS
Treatments: for male

For mild to moderate oligozoospermia:
- drug treatment, artificial insemination, in vitro fertilization & embryo transfer

For azoospermia:
- live sperm in testic tissue: TESA 、 MESE
- no sperm found: artificial insemination from donor sperm bank
Assisted Reproductive Technology (ART)
**Definition & Classification**

- **Assisted Reproductive Technologies (ART)** are defined as all techniques that allow gamete or embryo manipulation outside the body so as to help couple making pregnancy.

- **ARTs are classified 2 main techniques:**
  - Artificial Insemination (AI)
  - In vitro Fertilization & Embryo Transfer (IVF-ET) and its related techniques
IVF–ET

- IVF–ET involves the removal of eggs from ovary, fertilizing them with sperm in laboratory, and replacing them in the patient’s uterus.

- Classification (main)
  - Conventional IVF
  - Intracytoplasmic sperm injection (ICSI)
  - Preimplantation genetic diagnosis (PGD)/ Preimplantation genetic screening (PGS)
  - In vitro maturation of immature oocytes (IVM)
  - Cryopreservation / thawing of embryos and gamates
  - Ovum donation

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**IVF-ET**

- Convitional IVF
  - Indication:
    1. Tubal disease
    2. Endometriosis
    3. Mild male oligozoospermia, asthenozoospermia
    4. Unexplained infertility, esp not obtained pregnancy after artificial insemination treatment for 2–3cycles
    5. Immune infertility
    6. Decreased ovarian reserve/ POF who need egg donor
First IVF baby: Louis Brown, born in Bonne Hall Clinic, London, 1978

Father of IVF: Prof. Robert G. Edwards
The first IVF baby in China: 1988
Zheng mengzhu and the Mother of IVF in China—Prof. Zhang
Procedure of IVF

- GnRHa
- Ultrasound monitoring
- Retrieval of egg
- ET
- Pregnancy test
- GnRHa
- FSH
- LH
- HCG
- Luteal support
Retrieval of eggs (transvaginal aspiration by ultrasound)
Mature oocyte
3-day embryo
Embryo transfer
Complications

- Multiple gestations — due to transfer ≥1 embryo
- Ovarian hyperstimulation syndrome (OHSS) — characterized by ovarian enlargement, ascites, and hemoconcentration. Risk factors include polycystic ovary syndrome, multiple follicles, and high estradiol levels. The prognosis is usually worse in patients who get pregnant and have this syndrome. Patients with this syndrome may be at risk for blood clots.
- Heterotopic pregnancies — patients who undergo ART procedure are at twice the risk for having an ectopic pregnancy as the general population due to tubal reason.
- Congenital abnormalities — controversial, In patients who have ICSI performed, the risk of imprinting disorders may be increased
Indication:

- Severe male oligozoospermia, Asthenozoospermia
- Azoospermia (obstructed vas deferens)
- Fertilization rate ≤30% in past conventional IVF cycle(s)
- Single gene disorders with need for genetic testing of embryos by polymerase chain reaction (PCR) method for avoiding the genetic pollution from sperm DNA
Complications:

- Same to conventional IVF
- Special possibility: risk of vertical inheritance to male offspring when infertile men’s problem is due to Y chromosome microdeletion
Preimplantation genetic diagnosis (PGD)

- PGD allows many genetically heritable diseases to be identified using a variety of molecular biologic techniques. These techniques usually include polymerase chain reaction (PCR) and fluorescent in situ hybridization (FISH). Today, geneticists have invented many advanced molecular biology techniques, so more and more genetic disease can be avoided at embryo stage.

- In patients at risk of passing along a heritable genetic disease, PGD has made possible the identification of normal embryos (those with no risk of passing the heritable disease).

- Biopsy materials can be from: 1st or 2nd polar body, 1 or 2 blastomeres from a developing 4- to 8-cell embryo, trophoblast cells from blastocyst.
(preimplantation genetic diagnosis)
PGD

Normal morphologic embryo

biopsy

PCR

biopsy

fixed

Healthy embryo transfer

FISH
Factors that influencing the pregnancy rate during IVF

**Age of Female partner:**
- The most important prognostic indicator
- Pregnancy rate: 35~60% when age ≤38yr, 2.4~12% when >40yr

**Factors**
- Sperm quality
- Endometrial receptivity
- Some barrier, such as hydrosalpinx
Artificial insemination (AI)

- AI is the method that sperm is put directly into female genital tract during periovulatory period.
- Classification:
  - Based on inseminated place
    - Intravaginal insemination
    - Intrauterine insemination (IUI)
    - Intrafallopian insemination
  - Based on source of sperm
    - Artificial insemination by husband’s sperm (AIH)
    - Artificial insemination by donor (AID)
Artificial Insemination

- **Indication**

- **AIH**
  1. mild or moderate male oligozoospermia, Asthenozoospermia or poor morphology
  2. male erectile dysfunction (ED)
  3. female infertility is due to cervical factor
  4. immune infertility
  5. unexplained infertility
Intraruterine insemination (IUI)
Artificial Insemination

- Indication
- AID

1. azoospermia due to spermatogenic dysfunction of testis (nonobstructive azoospermia)
2. genetic diseases of male
Thanks!