

Basics of infertility Student Lecture

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Definitions

- **Infertility**
 - ✓ One year of 'frequent' unprotected intercourse without conception (U.S. ACOG) or → 2 years (WHO)
 - ✓ Primary infertility: no prior pregnancy
 - ✓ Secondary infertility: Prior pregnancy by woman or man
- **Fecundity**
 - ✓ The ability/chance of achieving a live birth during any one menstrual cycle
- **Fecundability**
 - ✓ The ability/chance of achieving a pregnancy during any one menstrual cycle

Time To Conception In Fertile Women

Time	% pregnant
1 month	50%
6 months	72%
12 months	85%
24 months	93%

Prevalence of Infertility in US women age 18-45

	1965	1982	1988	1995
All	13.3	13.9	13.7	11.9
Primary	2.2	5.8	6.0	5.7
Secondary*	11.1	8.1	7.7	6.2

Definition: Inability to conceive >1 year, within past 3 years. NSFG 1965 – 1995

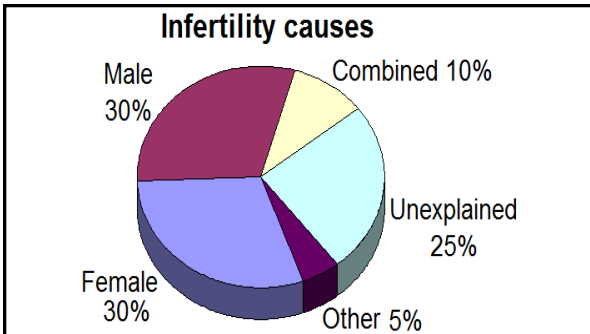
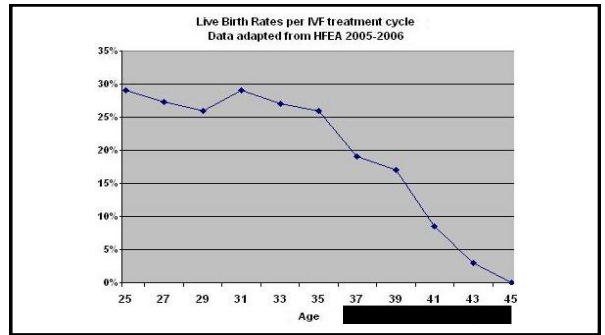
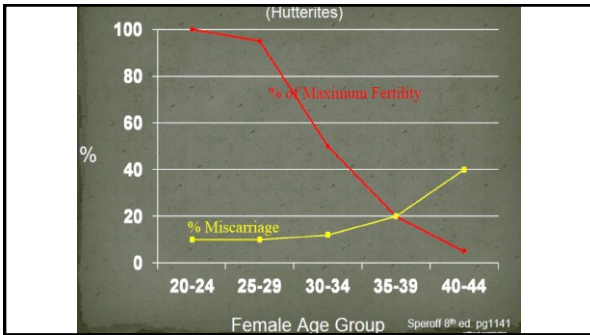
Source: Chandra. Infertile Repro Clin North Amer 1995;5:283.

Trends in primary infertility

- Demographic:
 - Delay in marriage
1968: 24.9 vs 2002: 25.1 yrs
 - **Delay in first birth**
1968: 21.4 vs 2002: 25.1 yrs
– Delayed childbearing
→ shifts first births to later ages when fertility is lower

Age and Fertility

- Peak fertility age 20-24
- Decrease starting age 30-32
- Rapidly declines after age 40
- Due to decline in quantity and quality of oocytes



- Always remember!
- Uterus and tubes
 - Are tubes patent?
 - Is the uterus normal?
 - Egg
 - Are eggs ovulated on a regular basis?
 - Sperm
 - Are the sperm swimming?
 - Are there enough sperm?

Investigations for Infertility

The Basic Infertility Work-up

Uterine/Tubal Factor

30% of all infertile couples

Tools to diagnose Tubal Factor

Basic infertility workup

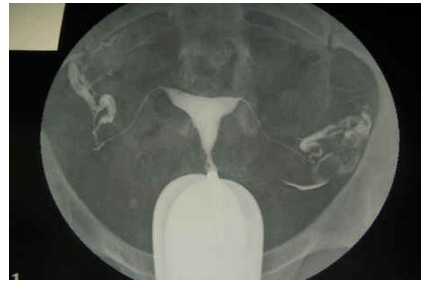
Uterus and tubes

- ✓ Hysterosalpingogram
- ✓ Sonohysterogram
- ✓ Laparoscopy with dye test
- ✓ Hysteroscopy
- ✓ Pelvic ultrasound

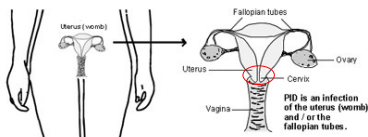


Diagnosing tubal factor

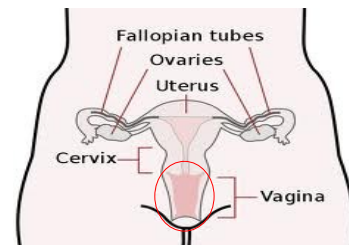
- Hysterosalpingogram:
 - Most utilized method (TFC first step)
 - Not useful for peritubal adhesions/endometriosis
 - Not as useful for intrauterine adhesions/filling defects
 - Sens. 65%, spec. 83% (Worse for proximal tubal factor)
 - Therapeutic benefit: 12 RCT
 - PR with HSG: (OR 3.3)



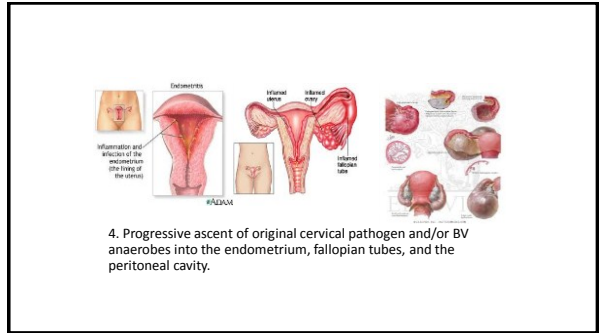
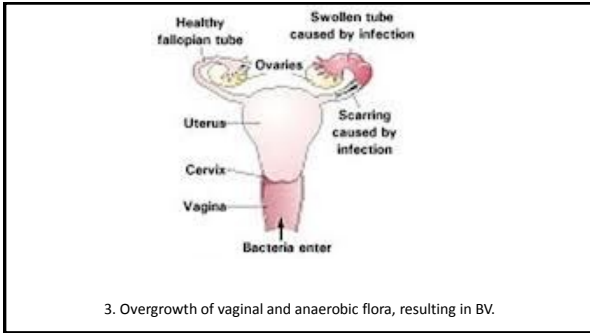
Pelvic Inflammatory Disease and Infertility



1. Cervical infection (C. trachomatis and/or N. gonorrhoeae)



2. Alteration of cervicovaginal microenvironment, increased pH



Clinical signs

- **Endocervicitis:** May be asymptomatic; vaginal discharge, cervical inflammation, or infection; local tenderness
- **Endometritis:** Menstrual irregularity
- **Endosalpingitis:** Constant bilateral lower quadrant abdominal pain aggravated by body motion. Tenderness in one or both adnexal areas. Abscess formation may occur.
- **Peritonitis:** Nausea, emesis, abdominal distention, rigidity, tenderness. Pelvic or abdominal cavity abscess formation may follow.

Salpingitis and PID

Episode of PID	Risk of Tubal disease
1 st	10-12%
2 nd	25-35%
3 rd	75%

The Fertility Clinic
London Health Sciences Centre



Uterine Anatomical Factors

- Polyps
- Fibroids
- Septums
- Adhesions

Sonohysterography

- Advantage of assessing tubes/ovaries/uterine cavity over HSG
- Compared to HSG: Metanalysis Holtz 1997.
 - 83% concordant with HSG for tubal factor
- Compared to hysteroscopy for uterus:
 - Sensitivity 93%, specificity of 89%



Endometriosis & Fecundity

- The monthly fecundity rate in subfertile women with endometriosis vs. Fertile is

2-10% vs. 15-20%

The Practice Committee of the American Society for Reproductive Medicine, 2004

Endometriosis

Prevalence is part of the enigma

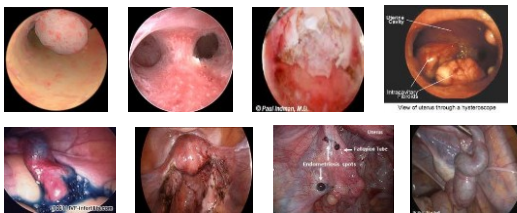
- Laparoscopy for infertility: 38%
- Laparoscopy for pelvic pain: 20-70%
- Laparoscopy for a pelvic mass: 0-5%
- Incidental finding 2-18%
- In the general population 7-10%

*Canadian Consensus on Endometriosis, SOGC 1999
ACOG Guidelines*

Gold standard(s)

- **Tubal Factor: Laparoscopy/Chromotubation:**
- Cost/Benefit analysis does not favour global approach in all couples.
- HSG compared to Lap/CTB
 - FP 12.5%, FN 11.2%
- SHG compared to Lap/CTB
 - FP 10.3%, FN 6.7%
- **Hysteroscopy:**
 - Advantage of site, endometrial evaluation, treatment
 - Evidence of enhanced IVF outcomes following scope.
 - < 6months, Best < 50 days.

Hystero-laparoscopy



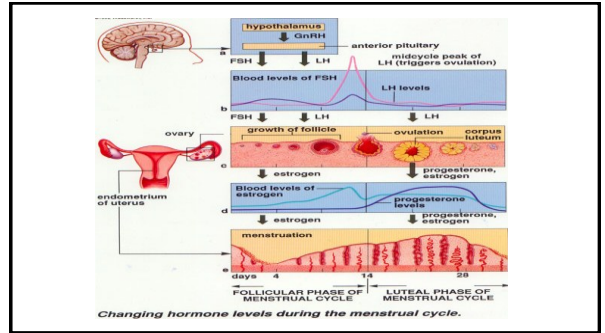
Egg

30-35% of all infertile couples

Basic infertility workup

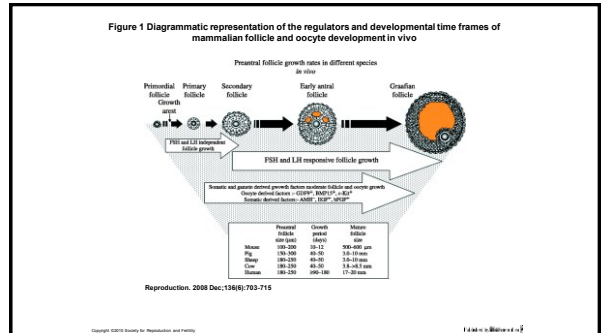
Egg

- ✓ Assess folliculogenesis and ovarian reserve
 - Menstrual history
 - Day 3 Hormonal profile: FSH, LH, Estradiol
 - TSH , Prolactin
- ✓ Document ovulation
 - Day 21 progesterone
 - BBT, LH kits



How many eggs are we dealing with?

- 5 months in utero: 2-5 million primordial follicles arrested at prophase I of meiosis.
- Birth: 1-2 million
- Puberty: 300-500 000
 - Majority will be lost to atresia
- Ovulate: 400-500 lifetime cycles
- Menopause: < 1000



Ovarian reserve tests

- ✓ Intended to help predict future fecundability and provide help in predicting likelihood of successful IVF
- Day 3 FSH (normal <10)
 - Normal FSH < 10mIU/mL
 - Borderline FSH 10-15mIU/mL
 - High FSH 15-25mIU/mL
- Day 3 Estradiol level:
- Day 3 ultrasound antral follicle count
- AMH



Tests Utilized

- Antral Follicle Count (AFC):
 - Usually measured Day 3
 - US to measure follicles (2-10mm)
 - Poor AFC: 4-10 total
 - In poor AFC: Anytime of cycle is equally prognostic
 - Not predictive:
 - Oocyte quality
 - Pregnancy outcome

Anti-Mullerian Hormone

- AMH is expressed by granulosa cells of the ovary during the reproductive years
- Produced by small pre-antral and early antral follicles prior to the attainment of FSH responsiveness
- In essence, produced by the pool of follicles that are ready for recruitment each cycle (ovarian reserve)
- Level independent of the cycle, can be measured any day



Tests of Ovulation

- **Ovulation Kits**
 - Urine detection of LH (approx. 1-2 days of the true surge)
 - Web-based temperature charts
 - Retrospective of the true surge by at least 2 days
 - Do not increase chance of conceiving over regular timed intercourse
- **Day 21 Progesterone:**
 - Indicative of ovulation (Don't produce Progesterone without CL)
 - Ultrasound/blood work monitoring

Male Factor

35% of infertility couples

Basic infertility workup

Sperm

- ✓ *Semen analysis*
 - 2 to 5 days of abstinence
 - Sample in the lab within 45 minutes
 - In Canadian weather, has to be kept warm
 - Always repeat if borderline result

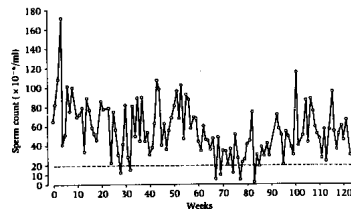


Semen analysis

Parameter	Result
Volume	1.5-5.0 ml
pH	>7.2
Concentration	> 15 x 10 ⁶ /ml
Total sperm count	> 40 x 10 ⁶
motility	> 50%
Morphology	>30% normal forms

WHO 2010 criteria
 >32% PM WHO 1992 criteria
 >14% strict Krueger WHO 1999 criteria

Variability in sperm count in one individual!



Male Factor

- Advanced Semen analysis (Monash)
 - 20-30% discordant from CBSA
 - Separation of sperm from semen
 - Motility
 - Morphology
 - Predicts success in ART



Follow up (6 weeks)

- Go over:
 - D3, D21 bloodwork
 - Tubal Tests
 - Sonohysterogram
 - SA
- Or findings from hysteroscopy, laparoscopy, tubal dye tests

ART

- IUI (10-25%)
- IVF (40-50%)
- IVF +/- ICSI (40-50%)

The major discriminator is sperm quality!

The minor discriminators are:

- Cost
- Female parameters (TP, Age)
- not anovulation

Tubes open, Sperm normal, Not ovulating

Options:

1. Oral ovulation (Clomiphene Citrate, Letrozole) + TI
 - ovulating: allow 6 months
 - not-ovulating: increase dose, add metformin
 - Still not ovulating: LOD (80%) or IUI
1. IUI (PO or SC ovulation medication)

Tubes open, Sperm normal, ovulating (unexplained infertility 5-20%)

Options:

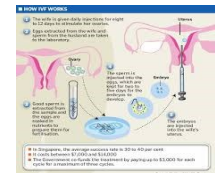
1. Investigate for endometriosis and treat
2. IUI



Tubes open, Sperm abnormal, +/- ovulating

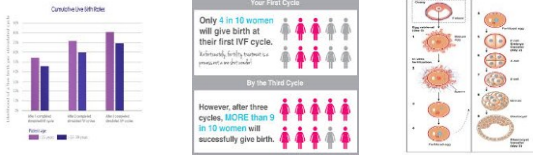
Options:

1. Refer to urology: search and treat a correctable factor
2. IVF +/- ICSI
3. IVF with Donor Sperm
4. IUI with Donor Sperm



Tubes Blocked, sperm/ovulation +/- normal

- IVF



Uterine Anomalies

- Minor: correct
- Major: Gestational Carrier
 - IVF with both parents gametes

Advanced Reproductive Age, no eggs

- Donor eggs: Known or anonymous
- Embryo Adoption
- Child Adoption

Thank You

- Questions?

