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Repromed



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Repromed
Auckland

Saturday, June 10, 2017

(Room 1)

8:30 - 9:25 WS #93: Optimising Fertility - Periconception Management

9:35 - 10:30 WS #105: Optimising Fertility - Periconception Management
(Repeated)



GPCME Rotorua

Optimising the periconception period

10th June 2017

Devashana Gupta

Mrs LM

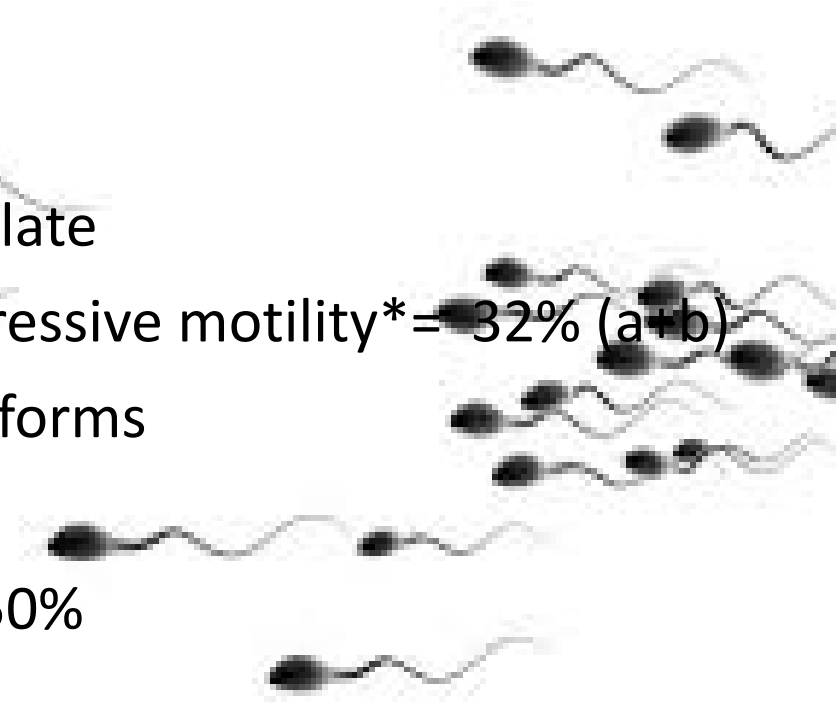


- 28 year old
- 5 years of primary infertility
- Investigations in China- ?bilateral tubal occlusion on HSG.
- Normal menstrual cycles, normal BMI
- Normal pelvic USS
- RSA: reduced motility 28%
- What now? Why are my tubes blocked? Can I unblock them? Is IVF the only treatment I can undergo? What about my partners sperm?



WHO Semen Parameters 2010

- Developed using fertile men with partners TTC <12/12 as reference population
- Lower reference limit= 5th centile
- Volume= 1.5ml
- Concentration = 15M/ml
- Total count* = 39M/ejaculate
- Total motility= 40%; progressive motility* = 32% (a+b)
- Morphology= 4% normal forms
- Vitality= 58% live
- Antisperm antibodies= <50%
- Leukocyte= <1



Tubal disease

- Types:
 - Congenital- rare, e.g. aplasia, segmental atresia, mucosal polyps.
 - Acquired-infection, SIN, tubal adhesion/occlusion and endometriosis.
 - Unknown- 50% due to subclinical Chlamydia. Recent evidence of Mycoplasma genitalium OR 2.43 for tubal infertility
- Impact:
 - Infertility
 - Obstruction to gametes
 - Increased ectopic pregnancies
 - Pelvic pain potentially if bilateral non communicating hydrosalpinx
 - Potential nidus for further infection if fluid present in tubes



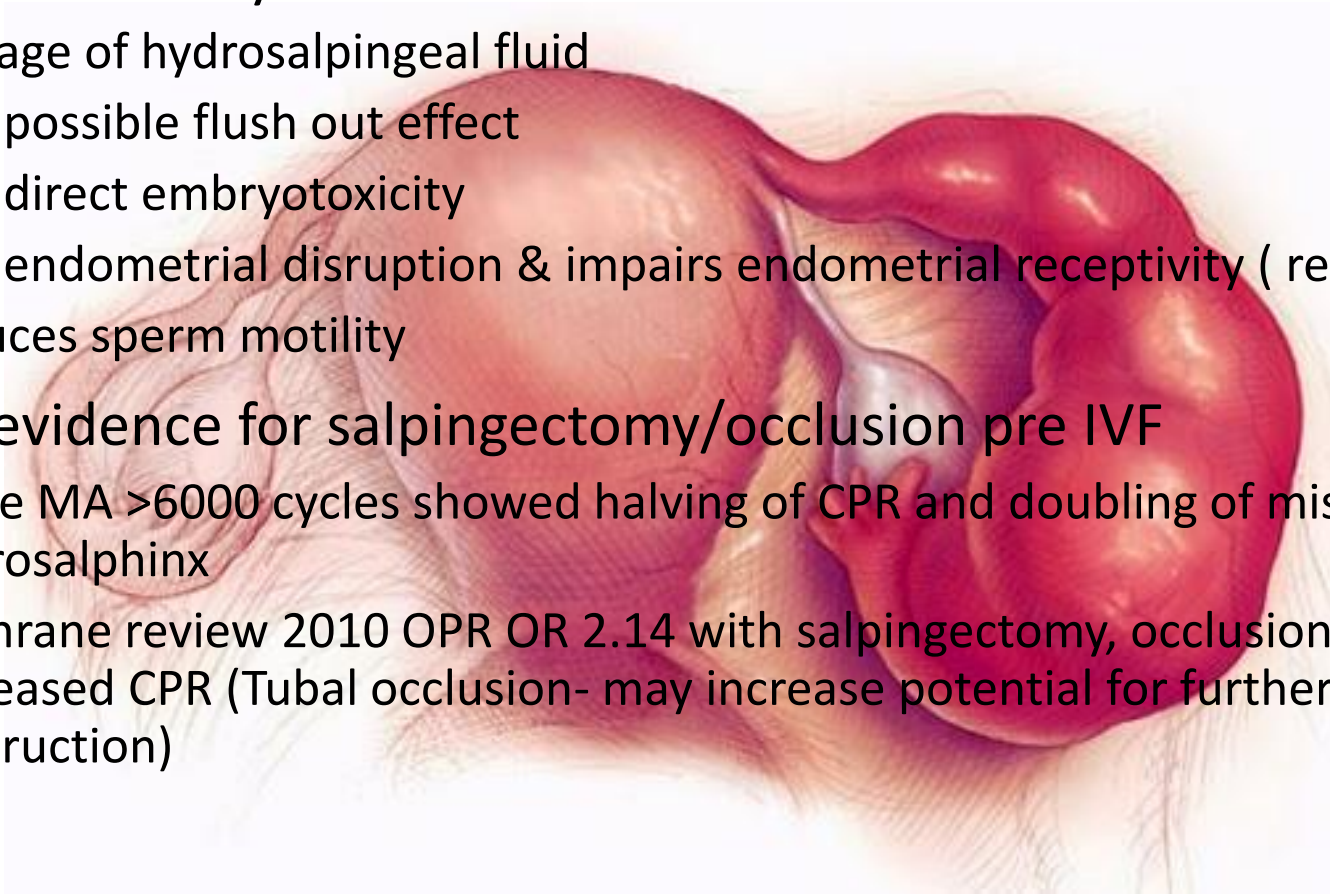
Management

- Assessment: HSG/saline sonohystogram/HyCoSy or laparoscopy & dye
- Surgical versus IVF
- Surgical:
 - Reconstruction- distal* versus proximal disease, bilaterality, age, access to IVF
 - Distal disease- surgery >successful 75-90%. Options of fimbrioplasty versus neosalpingostomy
 - Proximal- success lower, risks of re-obstruction and perforation. Options of hysteroscopic or fluoroscopic cannulation or tubocornual reanastomosis
 - What of tubal ligation reversal?
- IVF has a shorter TTC but eventually achieve a similar pregnancy rate with time.



Salpingectomy pre IVF

- Impact on fertility:
 - leakage of hydrosalpingeal fluid
 - possible flush out effect
 - direct embryotoxicity
 - endometrial disruption & impairs endometrial receptivity (reduced LIF expression)
 - reduces sperm motility
- Level I evidence for salpingectomy/occlusion pre IVF
 - Large MA >6000 cycles showed halving of CPR and doubling of miscarriage rate with hydrosalpinx
 - Cochrane review 2010 OPR OR 2.14 with salpingectomy, occlusion not powered for OPR but increased CPR (Tubal occlusion- may increase potential for further surgery due to non patent obstruction)



What do I offer and to whom?



Surgery	IVF
Young	Cost if not public
Allows NC- cumulative conception	Co-existing male factor
Complementary to IVF	Proximal tubal disease
Cost if not publicly funded as 1 st package	One pregnancy desired
Allows treatment of co-existing disease	
Low AMH??	
Distal disease	

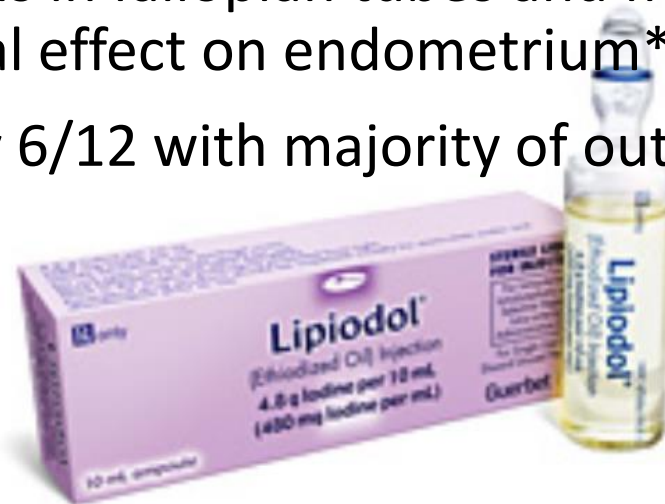
So Mrs LM?



- Recommend repeat RSA for partner- normal
- Wait listed for IVF after discussion of options –IVF versus surgery
- Discussion of assessment of tubal status re hydrosalpinges prior to commencement of IVF ?salpingectomy
- Other benefits of salpingectomy- possible reduction in risks of ovarian cancer
- Tubal occlusion- may increase potential for further surgery due to increased non patent obstruction

Lipiodol

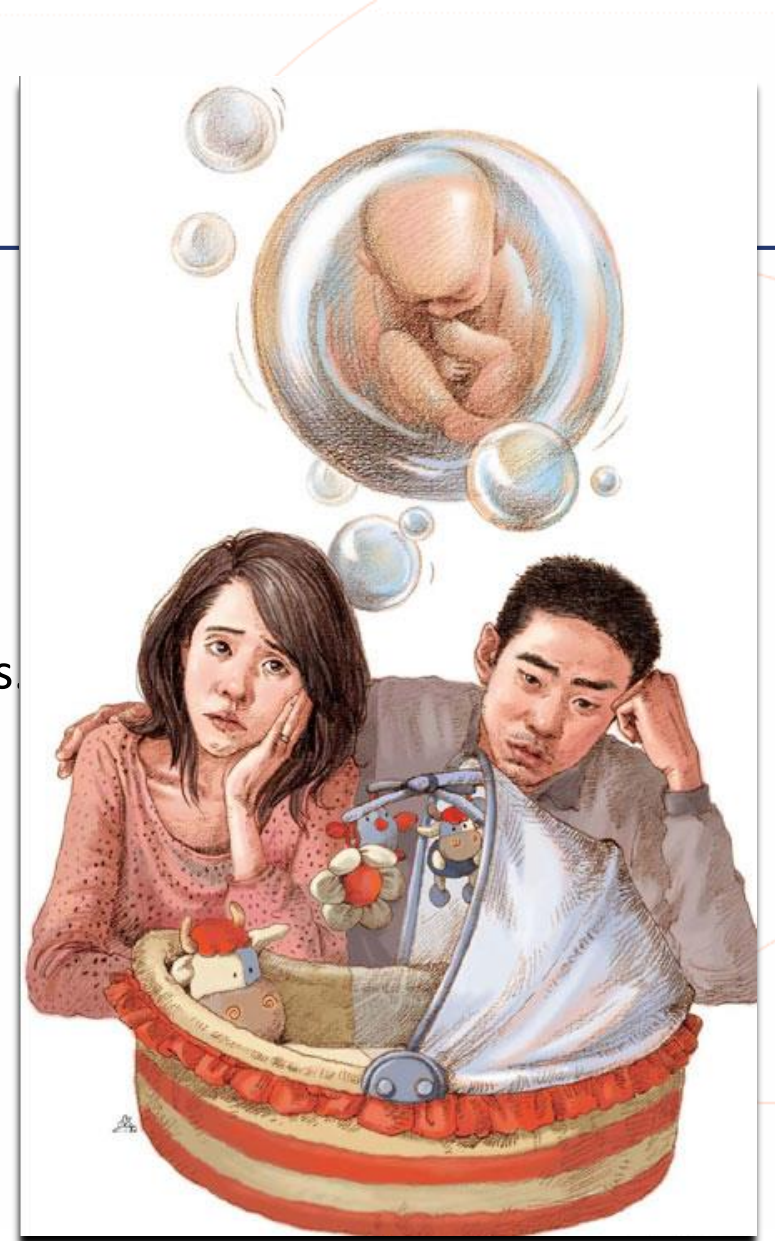
- AKA ethiodized oil, is poppy seed oil
- Standard test until 40 years ago, now making a resurgence
- Effects: dislodging debris in fallopian tubes and flushing out mucous plugs. Also potential immunological effect on endometrium*.
- Benefit lasts potentially 6/12 with majority of outcomes within 4/12



- Beneficial: women with unexplained infertility and mild endometriosis
- H2Oil study- OPR 40% versus 29%/ NNT=10
- Adverse events- theoretic intravasation with subsequent fat embolus

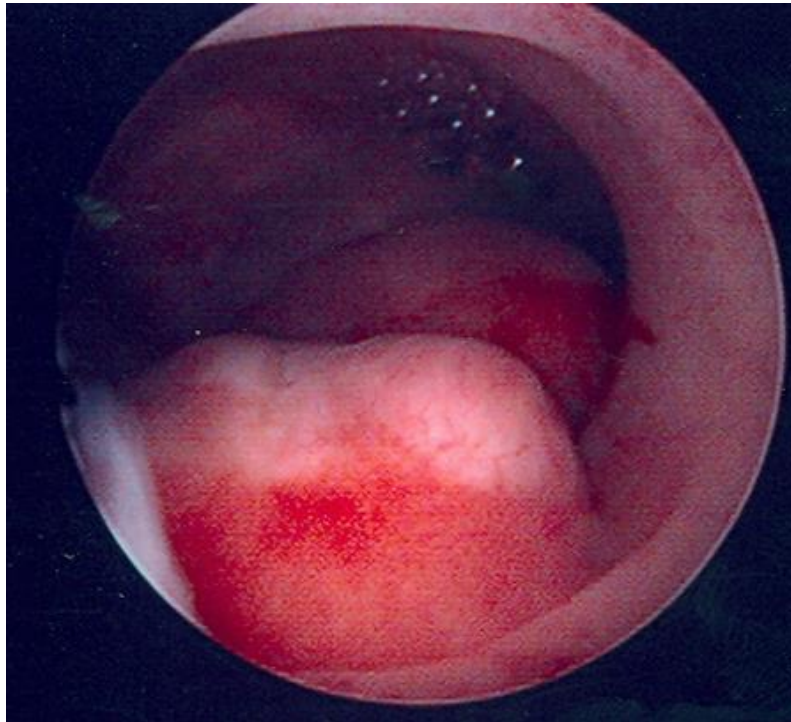
Miss CP

- 39 yr old
- Primary infertility of 8 years, AMH 5pmol/l
- Partner- obese, T2DM and hypertension
- Undergoing publicly funded IVF treatment
 - during ovarian stimulation found to have a large fibroid uterus
- 4 oocytes → 2 injected and 1 ET, none for freeze
- Unfortunately not pregnant
- What now? Proceed with second cycle? What of the fibroid?



Fibroids

- Formal USS assessment
 - large 15cm posterior intramural fibroid plus smaller subserosal fibroid.
 - Cavity distortion difficult to ascertain.



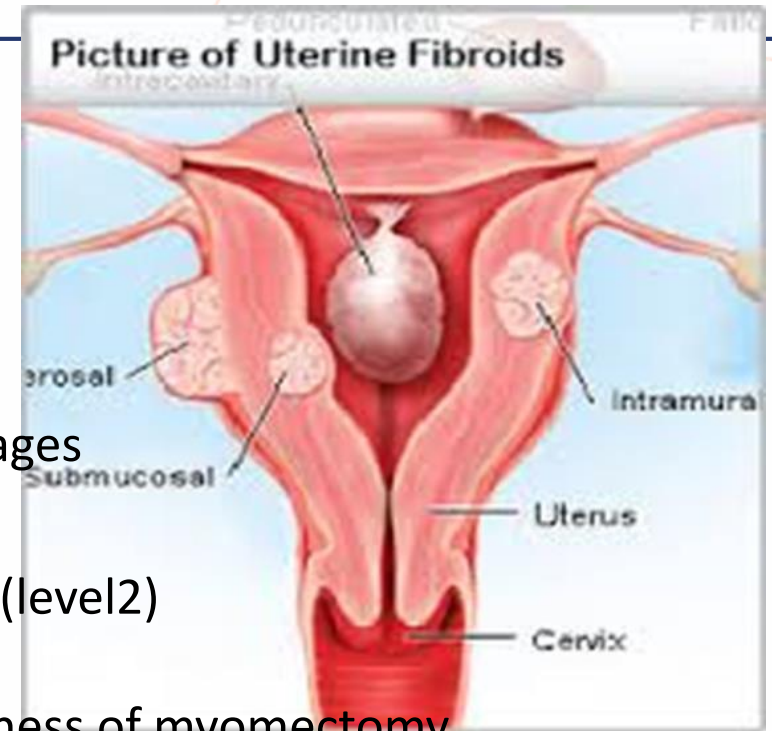
Fibroid classification

- Type 0- pedunculated SM fibroid
- Type 1- SM fibroid with <50% IM extension
- Type 2- SM fibroid with $\geq$ 50% IM extension
- Type 3- IM fibroid that contacts endometrium but 100% IM position
- Type 4- Solely IM
- Type 5- Subserosal with >50% IM location
- Type 6- SS with < 50% IM location
- Type 7- SS pedunculated
- Type 8- other e.g. cervical

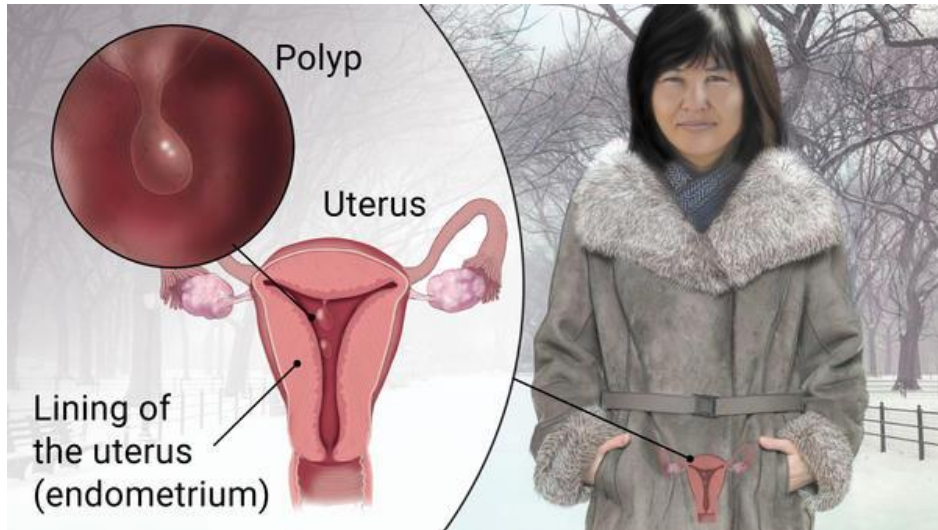


Uterine fibroids

- ACCEPT guidelines 2011
- Effect on fertility (Level 3 evidence)
 - SS don't appear to have an effect
 - IM may be associated with reduced fertility and increased miscarriages
 - SM associated with reduced fertility and increased miscarriages
- Management of fibroids in infertile women
 - Hysteroscopic resection likely to improve fertility outcomes (level2)
 - IM insufficient evidence to determine benefit (Level 2)
 - Fibroid size, number and location may impact on the usefulness of myomectomy
- Indications for myomectomy
 - Infertile woman with SM fibroid (level 2)
 - Infertile woman with symptomatic fibroids (level 4)
 - Previous multiple failed ART cycles with IM fibroids (level 4)



Uterine polyps



- Polyps may interfere with fertility but controversial
- Depends on the size and type of treatment
- CR 2015: OR 2.45 for clinical pregnancy with removal of endometrial polyp prior to IUI treatment
- Lass 1999- 2cm polyps trend to increased pregnancy loss
- Therefore, historically recommend removal of polyps >2-3cm if undergoing IUI/IVF

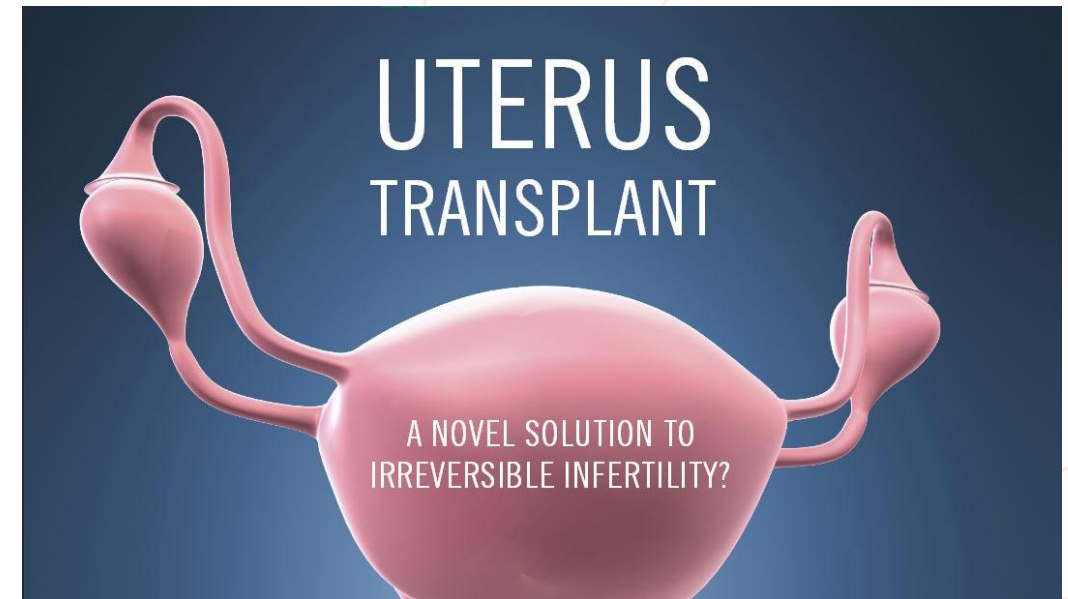
What of uterine septum's?



- Septate uterus: $\geq 1.5\text{cm}$ int. indentation and external cleft $< 1\text{cm}$
- Assess degree of septation- partial versus complete
- Associations such as vaginal septum, renal anomalies
- Poor blood supply of septum- therefore impaired implantation
- Fertility/pregnancy: ?recurrent miscarriage, preterm delivery, malpresentation
- Management- if no other cause found for infertility/miscarriage
- Benefit with resection- uncontrolled studies

Interesting fact!

- Uterine transplant with successful live birth in 2014 in Sweden
- Patient had MRKH syndrome
- Underwent IVF with 11 embryos frozen
- Uterine donation from menopausal friend



Miss CP?

- Discussion of evidence (moderate quality) of myomectomy before next cycle.
- Will be 40 before able to commence cycle. Partner lifestyle modification
- Referred for a myomectomy preceding next IVF cycle
- Risks of potential surgery including hysterectomy discussed
- Indications for myomectomy (ACCEPT)
 - Infertile woman with SM fibroid (level 2)
 - Infertile woman with symptomatic fibroid (level 4)
- UAE
 - Not recommended in women wishing to conceive until safety and effectiveness established

Male infertility

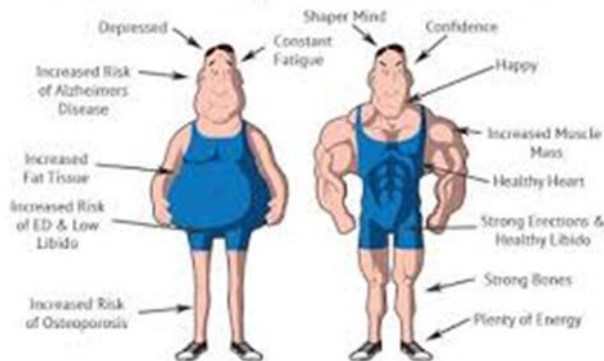
- Mrs JD, 38 yr old and Mr KL, 39 yr old
- PCOS with 3/3 criteria met
- Semen analysis- motility 12%, concentration 5.5 M/ml and morphology 3% normal forms.
- Benign history- no injuries/surgeries.
- Normal genital examination and general examination
- On leaving he mentions he has been on testosterone for a low libido!



Testosterone use in men



Benefits of Optimal Testosterone



Indications:

- Androgen deficiency in men with pituitary/testicular disorders
- Androgen deficiency in men >40 with no disease
- Boys <18 with micropenis, constitutional delay of growth/puberty for pubertal induction
- Androgen deficiency- is a clinical diagnosis with a pathological basis confirmed by hormonal assays (2 * morning T <6nmol/l plus LH 1.5*normal)

Inappropriate use:

- Male infertility
- Sexual dysfunction
- Low energy
- Obesity
- Aging
- Osteoporosis without pathological hypogonadism

Mr KL?

- Cease testosterone use
- Discussed contraceptive effect of Testosterone
- Recommend hormone assay 6 weeks after cessation
- Assessment of cardiovascular status, follow up Hct and PSA
- Repeat RSA 6 months later- normal motility
- Another 6/12 later following OI with Letrozole pregnant!



Ms CN

- 32 yr old
- Recurrent pregnancy losses- G3P0M3
- Karyotype: balanced translocation of 14 for partner
- Referred for discussion of PGD/IVF
- Baseline Ix: elevated TSH 3.9mIU/l, T4 normal
- All else normal

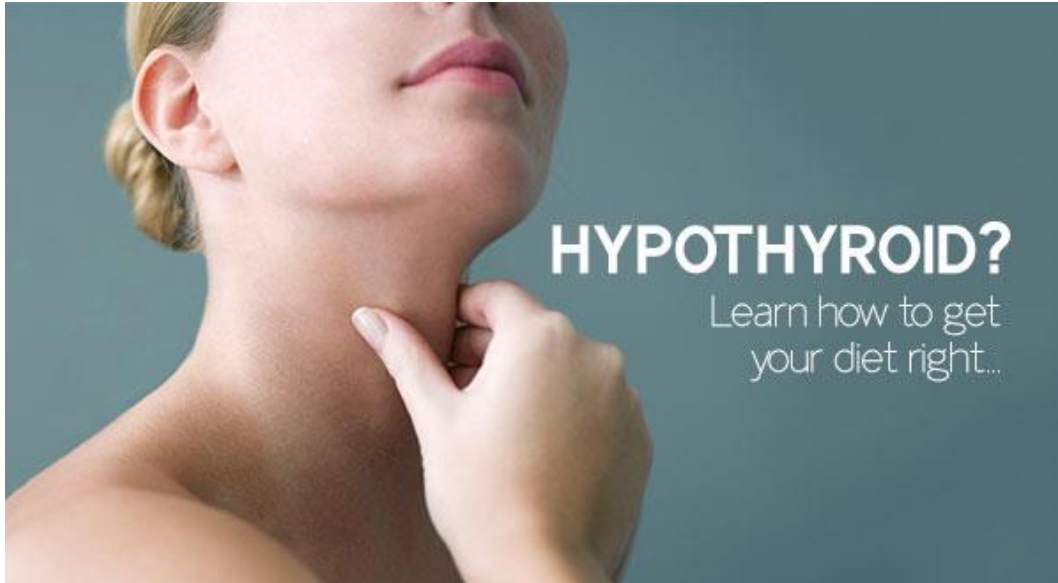


Thyroid disorders



	Hypothyroidism	Hyperthyroidism	Subclinical hypothyroidism
TFT	TSH-high FT4- low	TSH- low FT4- high	TSH- high * ($? > 2.5 \text{ mIU/L}$) FT4 normal
Symptoms	Menstrual irregularity Psychomotor retardation Cold intolerance	Irritability, disturbed sleep Heat intolerance Palpitations	Nil
Signs	Bradycardia Delayed reflexes, dry skin	Tachycardia, warm skin Tremor, Goitre	Nil
Impact on fertility	Subtle effect on ovulation*, decr implantation, incr MR, PTB	Incr MR, PTB, PETER and maternal cardiac failure. Thyroid storm precipitated by stress e.g. labour	Maybe associated with adverse outcomes in TPO positive women e.g. recurrent miscarriages
Treatment	Thyroxine	PTU/Carbimazole	Controversial

Subclinical hypothyroidism



TSH trimester specific guide:
T1 <2.5mIU/l
T2 and T3 <3mIU/l

- Treatment is controversial
- Retrospective studies- improvement in obstetric outcomes with T4 Rx but not proven to modify long term neurological outcomes in children
- 2017 ATA new guidelines:
 - Insufficient data for/against Rx in TPO negative infertile women not undergoing ART
- ES recommendations:
 - T4 Rx in TPO pos/neg women as benefits outweigh risks
- Bottom line- probably best to treat:
 - If TSH >2.5mIU/l and infertile
 - Definitely if commencing ART
 - Definitely if >4.2mIU/l

Ms CN

- Commenced on Thyroxine 50mcg daily
- Repeat TFT a month later: TSH 2.9mIU/l
- IVF with PGD and successful pregnancy following euploid embryo transfer.

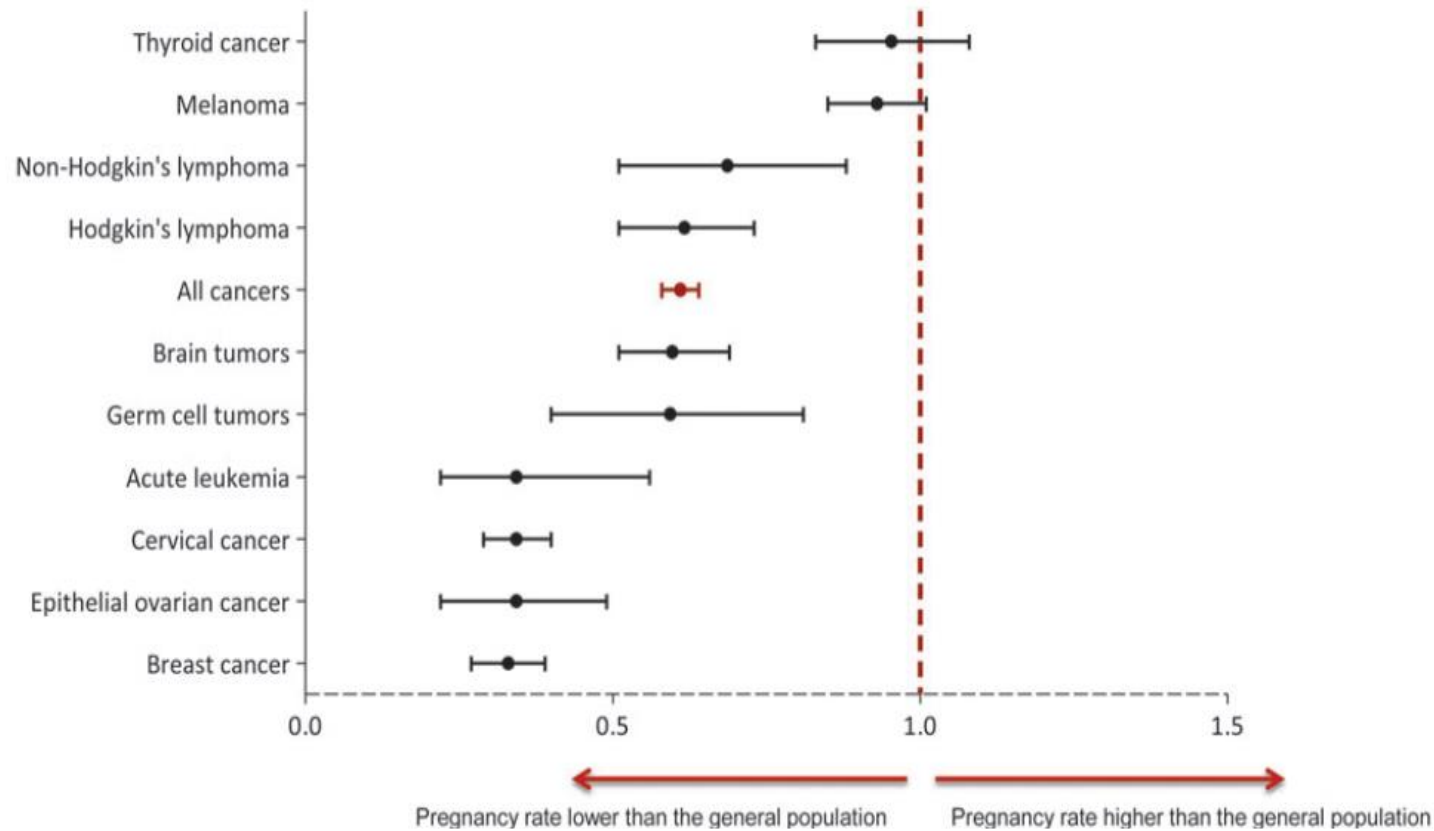


Miss LT

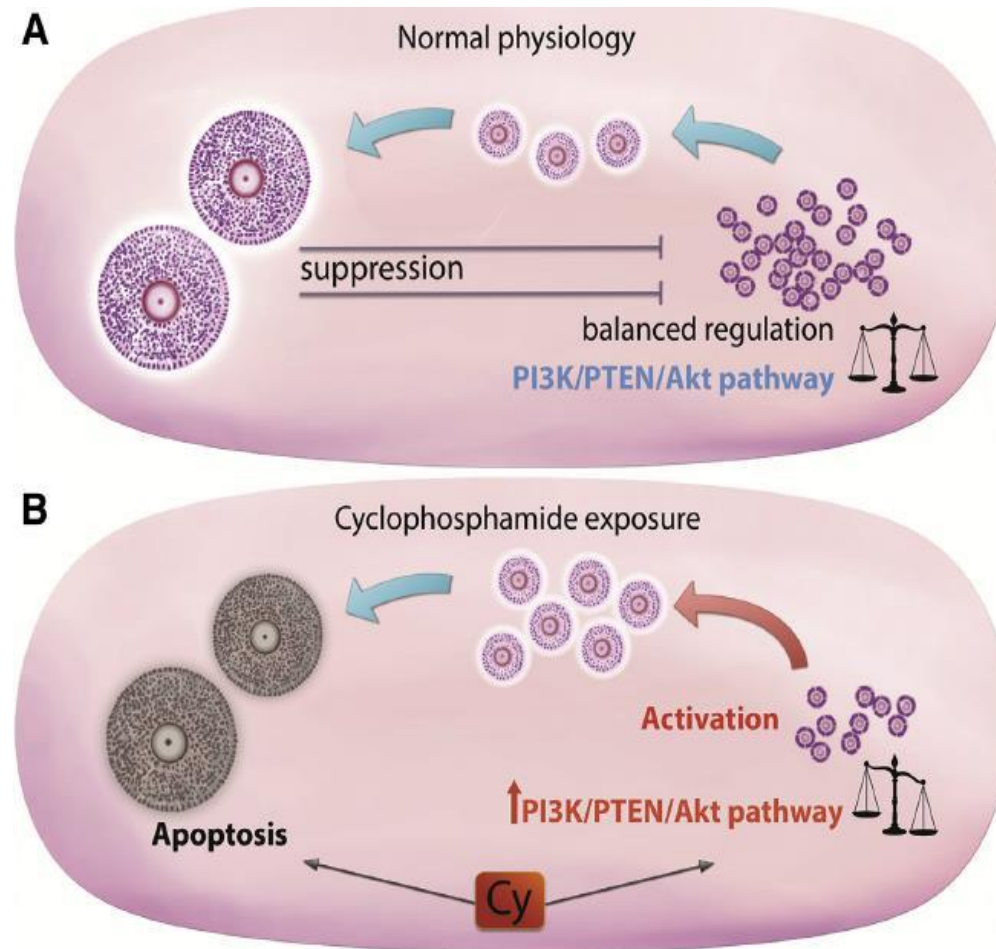
- 32 year old
- Recent diagnosis breast cancer, ER positive
- Planned for lumpectomy and SNB
- Referred for discussion of fertility preservation
- In a relationship for 6/12



Infertility after cancer treatment



Chemotherapy effects on ovaries



Chemotherapy effects

- no effect
- temporary ovarian failure (TOF) with apparent recovery
- permanent ovarian failure (POF)
- later onset premature ovarian failure (LO-POF)

Options for females

- Conservative approach
- GnRHa e.g. Zoladex during treatment
- Oocyte freezing (or IVM)
- Embryo freezing
- Ovarian tissue freezing
- Ovarian transposition
- FPR later in life



Miss LT

- Opted for oocyte freezing
- Protocol for fertility preservation is modified
- Try to maximise egg numbers, minimise harm and treatment burden
- AMH may not be available before commencement
- Random start cycle
- Agonist trigger
- Use of letrozole
- Studies show 15-20 oocytes need to be frozen for 1 successful LB (4% -12% per oocyte)



Thank you



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