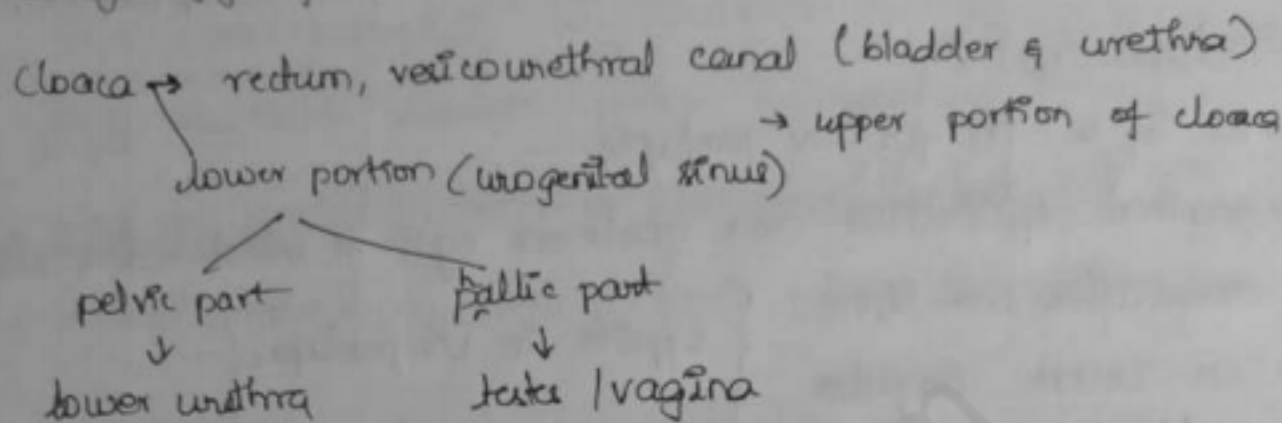


GYNACOLOGY

Disorders of sexual development

Embryology of female genitourinary system



Homologous structures

Embryonal structure

• primordial germ cell

• genital ridge

• sex cords

• Gubernaculum

• Mesonephric tubule

• Mesonephric duct

• Paramesonephric duct

♀

ova

ovary

granulosa cells

round ligament

epoophoron, paroophoron

gartner's duct

uterus, fallopian tube, upper vagina

♂

spermatozoa

testis

seminiferous tubule, sertoli cells

gubernaculum testis

efferent ductule, parastidymis

epididymis, vas deferens, ejaculatory duct

prostatic utricle, appendix of testis, hydatid of Morgagni

→ target gene for SRY $\perp$ favour testis differentiation is SOX9

→ genes $\perp$ favour ovary differentiation are WNT4, Rspo1, DAX1

Gartner's cyst:

- It is a DD for UV prolapse
 - vaginal epithelium over Gartner's cyst is atretic & shiny, rugosities are lost
 - no cough impulse
 - well defined
 - 6 - excision
- { opposite in UV prolapse }

Mullerian fusion defects:

Uterus didelphys

- paramesonephric duct fails to unite completely
- two horns of uterus & 2 cervix
- septum in vagina may be seen

Bicornuate uterus

- incomplete fusion of paramesonephric ducts $\leftarrow$ complete partial

Septate uterus

- similar to bicornuate uterus, but no endometrial tissue in b/w, only septum present $\leftarrow$ complete partial

Arcuate uterus:

- mild indentation in fundus of uterus

Unicorne uterus:

- One paramesonephric duct fails to develop
- only one horn present, other rudimentary horn
- may be communicating or non communicating
- ectopic pregnancy may occur in rudimentary horn

* Modality of choice for investigation → 3D USG

* surgery for bicornuate uterus → Strassman operation
→ 1st → recurrent abortion

* Rx for septate uterus → hysteroscopic septal resection

Mullerian agenesis / MRKH syndrome:

- 1^o amenorrhoea
- 2^o sexual characters well developed
- no ^{uterus} ~~cervix~~ / cervix / vagina
- ovaries are developed
- repair for vaginal agenesis can be done at time of marriage → for coital purpose

STDs:

<u>Bacteria</u>	<u>Viruses</u>	<u>Fungi</u>	<u>Protozoa</u>	<u>Ectoparasite</u>
* Gonorrhoea	* HIV	* candida	* Trichomonas	* Scabies
* Syphilis	* HPV			* Pediculosis
* Chlamydia	* HSV			
* LGV	* molluscum contagiosum			
* H. ducreyi				

Bacterial vaginosis:

- (N) flora $\Rightarrow$ anaerobic $\gg$ aerobic
 $\downarrow$
 eg. Lactobacillus $\rightarrow$ maintains the acidic pH
- pH $\Rightarrow$ 4 to 4.5 (N)
- vaginal cells produce glycogen under the influence of estrogen
- Lactobacillus acts on glycogen & produce lactic acid responsible for acidic pH
- When Lactobacilli are outnumbered by Gardnerella vaginalis, M. hominis, ureaplasma urealyticum, mobiluncus to cause bacterial vaginosis
- presents τ foul smelling, greyish white vaginal discharge
- profuse discharge
- no itching (no inflammation)
- Clue cells are seen in microscopy

Amine test → used to detect fishy odour in bacterial vaginosis

- AMSEL criteria is used to diagnose
- Not transmitted sexually
- RFs → new sexual partner, many partners, douching, smoking, IUCDs.
- Rx → * no need to Rx the partner (X)
* metronidazole 400mg daily BD x 7 days
- Whiff test is aka amine test
- abundance of gram variable coccobacilli may be seen
- discharge doesn't contain any cells, WBCs
- On ex → Cx is (X) = no discharge

Candidiasis

- caused by *C. albicans* > *C. glabrata* > *C. tropicalis*
- occurs at pH < 4.5
- RF: immunocompromised states
- Sx → - curdy white discharge
- vulva is inflamed & red
- severe itching
- Δ → 10% KOH → dimorphic nature of candida seen
- Types → complicated & uncomplicated
 - ↳ single episode, no RF
- longer Rx: > 4 episodes/yr
- duration: ≥ 1 RF
- non candida albicans inf
- easy to Rx
- candida albicans

Rx : -azole group of antifungals (clotrimazole, butoconazole, fluconazole)
 ° for complicated → boric acid capsules

Trichomonas vaginitis

- ° caused by *T. vaginalis*
- ° sexually transmitted
- ° affects female >> male
- ° cause vaginal discharge, cervicitis
- ° Sx → dyspareunia, spotting, discharge, urethritis, proctitis
- ° males are asymptomatic
- ° discharge is frothy green & itching present
- ° Δ : swab + 10% KOH → motile organisms seen
- ° Speculum examination → strawberry cervix (X)
- ° Rx → metronidazole
- ° Rx the partner too

Sequale

- ° Bacterial vaginosis → pregnancy : PTL, PROM
- ° pelvis surgery : infection of cuff
- ° marker of other STDs

TB of genital tract

- ° caused by *M. tuberculosis* (95%) & *M. bovis* (5%)
- ° m/c in childhood TB
- ° becomes symptomatic by puberty

- Involve fallopian tube & uterus & vagina & vulva
- Cause → infertility, ectopic pregnancy (fallopian tube inv)
 - menorrhagia foll by amenorrhoea (endometrium)
 - ulcers (cx, ovary, vagina)
- Δ → moth eaten appearance of tube on HSG
 - aka beaded appearance / leopard spot appearance
 - clubbed ends of fimbriae
- R → ATT (doesn't cure infertility)
 - gold ↓ club appearance
 - tobacco pouch appearance

PID:

- infection of upper genital tract
- causative → N. gonorrhoeae, Chlamydia trachomatis (m/c)
 - Ⓢ vaginal flora too

Δ

- Minimum criteria →
- uterine tenderness
 - cervical motion tenderness
 - adnexal tenderness

Additional criteria →

- white discharge PV
- fever $> 101^{\circ}\text{F}$
- ↑ CRP, ↑ ESR
- NAAT (N gonorrhoea & chlamydia)

- Gonorrhoea → Sx develop in 3-7 days
 - cervicitis, urethritis, PID
- Chlamydia → no direct pathogenic effect on genital organs
 - presents w/ sequelae of PID
 - delayed hypersensitivity → damage of → PID tubes

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NACO

- syndromic m/m → KIT ±
- lower abd pain → KIT 6 → cefixime, metro & doxy
 - gonorrhoea
 - BV
 - chlamydia

- pt may present w tubo-ovarian abscess $\rightarrow$ do laparoscopy, obtain cultures from fallopian tube
- most sensitive test for chlamydia $\rightarrow$ NAAT (PCR)
- Doc for chlamydia in pregnancy is erythromycin

Genital ulcers

- Syphilis → 1° chancre
 - 14 - 21 days after sexual contact
 - a single ulcer on vulva / vagina / cx
 - painless ulcer & raised indurated border
 - base of ulcer is clean & non infected ; deep
 - disappears after some time
- H. ducreyi → cause chancroid
 - red beefy, extremely painful ulcer
 - occurs on vulva / vagina / cx
 - single lesion
- Herpes, HSV 2 → ◦ extremely painful, numerous ulcers
 - Hb previous episodes
 - occurs on vulva / vagina
 - occurs in crops
 - Rx → acyclovir / ganciclovir → ↓ no of ulcers / recurrence
- LGV → buboes are present

Sex & intersexualityPuberty:

- 1st sign $\rightarrow$ thelarche (breast budding)
- 2nd $\rightarrow$ pubic/axillary hair $\rightarrow$ pubarche/adrenarche
- 3rd $\rightarrow$ menarche $\leq$ is just preceded by a growth spurt

* GnRH $\rightarrow$ pulsatile secretion (night > day) $\rightarrow$ responsible for pubertal growth $\rightarrow$

$\downarrow$
LH > FSH

$\downarrow$
GnRH pulse throughout day

$\downarrow$
FSH & LH $\rightarrow$ ovary $\rightarrow$ follicle development $\rightarrow$ estrogen

$\downarrow$
• estrogen for 1 yr $\rightarrow$ 1^o ovulation $\rightarrow$ progesterone $\rightarrow$ menarche (priming of endometrium)

• precocious puberty $\rightarrow$ ~~early~~ 2^o sexual characters before 8 yrs of age

• absence of 2^o sexual characters & menstruation at 14 yrs

$\&$
absence of menstruation even in presence of 2^o sexual characters at 16 yrs

$\rightarrow$ both needs evaluation i.e. delayed puberty

Abn^o pubertal development

① precocious puberty (PP) $\left\{ \begin{array}{l} \text{central} \rightarrow \text{aka gonadotrophin dependant precocious} \\ \text{peripheral} \rightarrow \text{m/c is idiopathic} \end{array} \right.$ puberty

Central PP causes $\rightarrow$ hypothalamic hamartoma, optic glioma (in NF), radiation, head trauma, CNS anomalies, infections

causes of precocious puberty → autonomous ovarian cyst, adrenal estrogen producing tumours, exogenous estrogen

* Hypothalamic hamartomas present - gelastic seizures / laughing fits

• precocious puberty → F > M

• delayed puberty → M > F

→ m/c is constitutional → hypogonadotropic hypogonadism

→ gonadal failure : hypergonadotropic hypogonadism

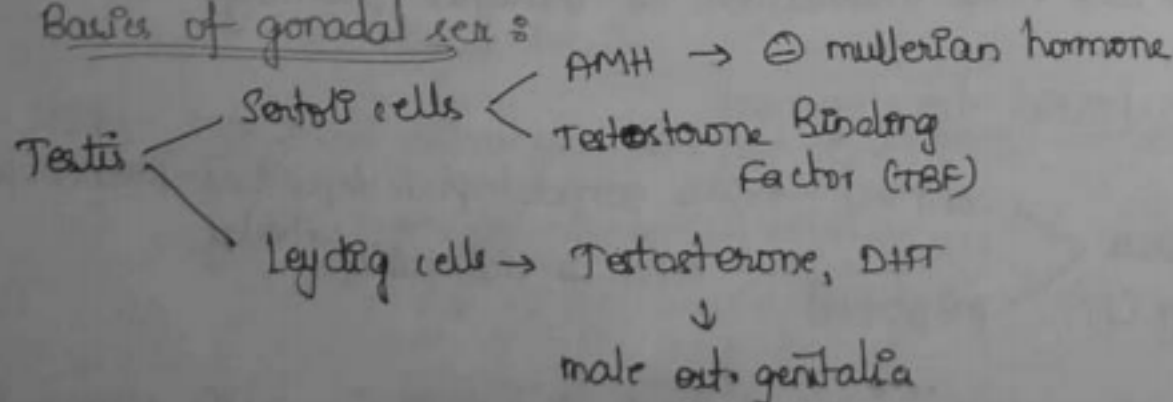
McCune Albright syndrome :

- Precocious puberty
- Café au lait pigmentation
- Polyostotic fibrous dysplasia of bone
- somatic mutation in GNAS1 gene
- girls > boys

Basis of @ menstruation :

@ hypothalamus, pituitary, ovary / gonads, endometrium

Basis of gonadal sex :



De novo sex → ♀

Classification of disorders of sexual development:

◦ Sex chromosome disorders:

- 45 XO Turner
- 47 XXY Klinefelter

◦ 46 XY disorders

- pure gonadal dysgenesis (Swyer syndrome)
- partial gonadal dysgenesis

◦ 46 XX disorders

* m/c of 1° amenorrhoea → Turner > müllerian agenesis > testicular feminizing syndrome

Cryptomenorrhoea:

- Dr imperforate hymen / transverse vaginal septum / cervical atresia
- pt presents w 1° amenorrhoea

Imperforate hymen

- 1° amenorrhoea, monthly abd. pain
- O/E → bulging bluish membrane
- USG → hematocolpos (blood in vagina), hematometra (blood in uterus)
 - blood may sometimes spill into abdominal cavity
- Rx → create incision in hymen

Amenorrhoea

1°
 2° → +ve progesterone challenge test

- Kallman syndrome →
 - delayed menarche / puberty + anovulation
 - defect in anosmin gene
 - defective hypothalamus
 - hypogonadotropic hypogonadism
- Withdrawal bleeding following administration of progesterone indicates progesterone deficiency &
 - Ⓝ oestrogen secretion
- Androgen insensitivity / testicular feminisation syndrome = (AIS / TFS)
 - 46 XY chromosome
 - though ~~testosterone~~ testosterone is produced, testosterone receptors are absent
 - failure of testicular descent → inguinal swelling ±
 - external female genitalia
 - Ⓝ breast development
 - absent pubic / axillary hair, 1° amenorrhoea

Reifenstein syndrome :

- almost like a lesser degree of AIS
- male + some degree of feminization
- buried scrotum, hypospadias
- partial androgen insensitivity syndrome
- Other syndromes + delayed puberty → Prader Willi syndrome, Lawrence Moon Biedl syndrome

Sheehan's syndrome

- Pituitary necrosis/apoplexy d/t severe hyp PPH
- 2° amenorrhoea
- 2° amenorrhoea is seen in persons w/ systemic diseases leading debility, anorexia nervosa etc. → it is hypogonadotropic
- m/c of congenital adrenal hypoplasia → 21 OH deficiency

MCOs

- Fitz Hugh Curtis syndrome → violin string adhesions between
(R) fallopian tube & undersurface of liver

Menopause & HRT

- d/t loss of ovarian follicular activity
- cessation of ~~menopause~~ menstruation for 12 months
- avg age $\Rightarrow$ 45 to 55 yrs (50 yrs)
- before 40 $\rightarrow$ premature ovarian failure
- Menopausal transition $\rightarrow$ begins w/ menstrual irregularity & extends to 1 yr after permanent cessation of menses
 $\rightarrow$ average of 47 years & lasts 4-7 years
- classification of female reproductive aging is called STRAW

Prediction of approaching menopause:

- Fall in the level of inhibin B $\rightarrow$ $\uparrow$ FSH
- fall in anti-müllerian hormone (AMH) suggest low ovarian reserve & low antral follicular count
- $\uparrow$ LH (but $<$ FSH)
- Study of FSH level on ~~2nd day~~ day 2-5 after last menstrual period detects premenopausal stage

Markers of $\downarrow$ ovarian reserve:

- Day 3 serum FSH $>$ 10-15 IU/L
- day 3 serum estradiol $>$ 60-80 pg/ml
- low AMH (0.2-0.7 ng/ml)
- low serum inhibin B
- antral follicular count (N-20 to 150)
- ovarian volume

AMH

- AMH is secreted by Sertoli cells (in ♂) & granulosa cells (in ♀)
- peptide hormone
- in ♂, AMH secreted by 7th week of IUL till puberty
- in ♀, AMH secreted after puberty
- $\text{level} \approx 2-6.8 \text{ ng/ml}$
- Helps in follicular development & oocyte maturation
- Level reflects no. of growing follicles

In postmenopausal period:

- $\uparrow \text{FSH}$, $\uparrow \text{LH}$, $\uparrow \text{estrone}$
- $\downarrow \text{AMH}$, $\downarrow \text{androstenedione}$

* No. of oocytes at menopause $\rightarrow 1000$

Sx of menopause:

- | | |
|--------------------------|-------------------------------|
| ◦ menstrual sx | ◦ urinary stress incontinence |
| ◦ hot flashes | ◦ osteoporosis |
| ◦ dyspareunia | ◦ neurological |
| ◦ $\downarrow$ ed libido | ◦ psychological |

* Hot flashes $\rightarrow$ are d/t $\downarrow$ ed estrogen & $\uparrow$ ed noradrenaline

$\rightarrow$ peripheral vasodilatation $\rightarrow$ skin temp $\uparrow$, esp in fingers & toes

$\downarrow$
sweating, $\uparrow$ BP

$\rightarrow$ d/t rapid fluctuation in estrogen levels

$\rightarrow$ altered vasotonic levels

- Rate of bone loss after menopause is 3-5%

Perimenopausal osteoporosis:

- Bone mass measured by DEXA (dual energy x-ray absorptiometry)
- gives i) T score (compares your results to a healthy young adult 20-35)

* expressed as std deviations from mean

* 0 score $\rightarrow$ (N)

* -1.5 to -2.4 $\rightarrow$ indicate osteopenia

ii) Z score $\rightarrow$ compares your results to a person of the same gender & age as yourself

* score -2.5 indicate osteoporosis

- all menopausal women should be given 1g Calcium (if not on HRT)

- If on HRT $\Rightarrow$ 500mg Calcium is given

- pH of vagina is maximum during menopause (pH 6-7.5)

- androstenedione is converted to ~~est~~one

* most potent oestrogen is estradiol (E_2) $\rightarrow$ reproductive age

estrone (E_1) $\rightarrow$ menopause

estriol (E_3) $\rightarrow$ pregnancy (least potent)

[potency $\rightarrow E_2 > E_1 > E_3$]

- There is 50% reduction in androgen production & 66% reduction in oestrogen at menopause

- estrogen level $\rightarrow$ 10 to 40 pg/mL
- estrogen level >40 pg/mL exerts bone & cardioprotective effect
& <20 pg/mL predispose to osteoporosis & IHD
- Serum FSH >40 is diagnostic of menopause

HRT

- Tx $\rightarrow$ vasomotor Sx,
vaginal atrophy,
osteoporosis prevention or Rx
- re-evaluation of need for HRT at 6-12 month intervals
- prescribed in lowest possible dose for shortest period
- HRT is not useful in CAD
- Estrogen causes $\rightarrow$ $\downarrow$ LDL, $\downarrow$ cholesterol, $\uparrow$ HDL, $\uparrow$ TGs,
 $\uparrow$ coagulation factors, $\uparrow$ lithogenicity of bile (stone forming capacity)
- progesterone causes $\rightarrow$ $\uparrow$ LDL, $\downarrow$ HDL

Drugs for postmenopausal osteoporosis:

- Antiresorptive agents:
 - estrogen
 - SERM - raloxifene
 - Bisphosphonates
 - Denosumab $\rightarrow$ mab against RANK-L
 - Calcitonin
 - vit D
- Anabolic agents (stimulate bone formation)
 - Teriparatide (recombinant human parathormone)

[Raloxifene $\rightarrow$ for bone, tamoxifen $\rightarrow$ for breast]

- Raloxifene → ↓ incidence of osteoporosis
 - * ↓ # rate,
 - * doesn't cause endometrial hyperplasia / breast carcinoma
 - * SE → hot flushes
 - * C/I in renal disease

* progesterone is added to estrogen in HRT only if uterus is present to prevent endometrial cancer; ∴ not given in pts who have undergone hysterectomy

* Hot flushes

→ hormonal agents

- estrogen - CEE, 17βE₂
- progestin - MPA
- combined E & P
- TSEC : CEE + BZA

[conjugated equine estrogen - CEE
Tissue selective estrogen complex
Bazedoxifene - BZA]
-TSEC

Non hormonal

- SSRIs
- SNRIs
- clonidine
- gabapentine

C/I for HRT

- Thrombosis
- ~~PE~~
- undiagnosed abt genital bleeding
- known / suspected H/o Ca breast
- Any estrogen dependant neoplasia
- TE
- stroke / MI
- liver d/s

- DOC for ↓ libido - androgens
- HRT ↓ Alzheimer, colorectal Ca

Abnormal uterine bleedingCharacteristics of (N) menstrual cycle

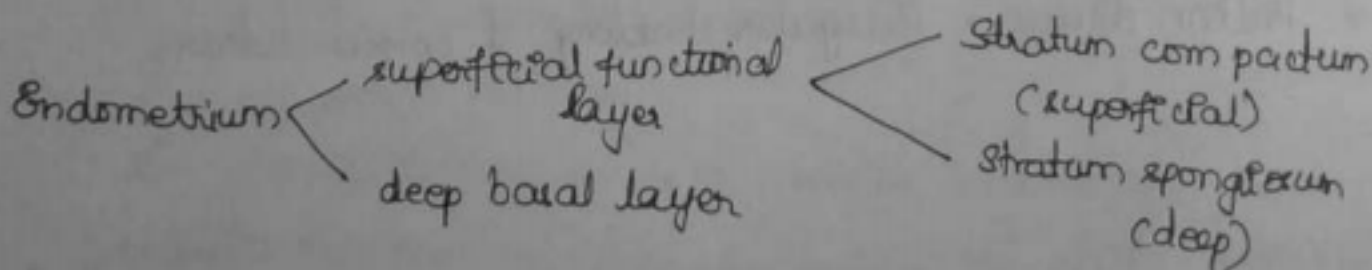
- (N) length of cycle : 24 to 35 days
- avg " - 28 days (seen only in 15%)
- No. of days of bleeding : 2-7 d
- Avg. no. of days of " - 4 to 5 d
- (N) blood loss : 5-80 ml
- Avg " " : 30 ml

Definitions in ab(N) uterine bleeding :

- Menorrhagia → cyclic bleeding at (N) intervals; the bleeding is either excessive in amount ($>80\text{ml}$) or duration (>7 days) or both
- Metrorrhagia → irregular, acyclic bleeding
- Oligomenorrhoea → occur less frequently i.e. more than 35 days apart
- Hypomenorrhoea → scanty bleeding, last <2 days

Causes of metrorrhagia

- Fibroid polyp
- Co Cr & Co endometrium
- uterine ~~sub~~ conuade
- IUCD
- decubitus ulcers
- withdrawal bleeding in pill users



- The superficial functional layer is hormone sensitive whereas deep basal layer is hormone insensitive & contain stem cells.
- After every menstruation, regeneration occurs from deep basal layer

AUB

Anatomical causes (PALM)

- Polyp
- Adenomas
- Leiomyoma < submucosal others
- Malignancy & hyperplasia

Functional causes (COEIN)

- Coagulopathy
- Ovulatory dysfunction
- Endometrial
- Trophogenic
- Not yet classified

Causes of AUB:

General causes

- Blood dyscrasia
- Coagulopathy
- Thyroid dysfunction
- genital TB

Pelvic causes

- PID, pelvic adhesions
- uterine fibroids
- endometrial hyperplasia
- adenomyosis
- feminizing tumor of ovary
- endometritis
- pelvic congestion
- varicose veins in pelvis

Contraceptive use

- IUCD
- post-tubal sterilization
- POPs

Hormonal DUBs

- ovulatory - Irregular shedding / bleeding
- Anovulatory - resting endometrium - 80%
- metropathia hemorrhagica

* Halban disease → irregular shedding of corpus luteum

- Rule out coagulopathy, pelvic lesions, hypothyroidism
- m/c is anovulation > blood dyscrasias
- Rx of PCOS $\rightarrow$ drospirenone acetate
- Rx of puberty menorrhagia $\rightarrow$ progesterone, OCPs, GnRH analogues
- m/c endometrial pattern in DUB is (N)

M/m of AUB

• Young women

- * progestogens
- + combined OCPs
- * NSAIDs
- * Tranexamic acid
- * GnRH analogues

• in older women who have completed family

- * hysterectomy
- * endometrial ablation

In AUB $\rightarrow$ 1st investigation is TVS

1st is endometrial bx

- m/c of postmenopausal bleeding $\left\{ \begin{array}{l} \text{globally} \rightarrow \text{ca endometrial} \\ \text{India} \rightarrow \text{ca cx} \end{array} \right.$

Dysmenorrhea - cramping pain during menstruation

$\left\{ \begin{array}{l} 1^{\circ} \rightarrow \text{no pelvic pathology} \\ 2^{\circ} \rightarrow \text{pelvic pathology} \end{array} \right.$

- $\rightarrow$ eg. fibroids, adenomyosis, PID, endometriosis
- Spasmodic dysmenorrhea $\rightarrow$ cramping pain on 1st & 2nd day, most prevalent
- Congestive " $\rightarrow$ manifest as trig pelvic pain
- Anovulatory bleeding is painless

ENDOMETRIOSIS

Theories of endometriosis:

- * Sampson's retrograde menstruation theory - most accepted & oldest
- * Meyer & Ivanoff's coelomic metaplasia theory
- * stem cell theory
- * lymphatic or vascular spread

Common sites of endometriosis in decreasing frequency

- ovary
- cul de sac (pouch of Douglas)
- uterosacral ligaments
- vermiform appendix
- recto sigmoid colon
- ureters
- urinary bladder

- * Endometriosis doesn't occur in spleen
- * Endometriosis is hormone dependant
- * 1st method of Δ is laparoscopy, $\bar{\Delta}$ or without Bx or histology Δ
(gold std)

RF:

- infertility
- nulliparity
- pelvic pain
- high socioeconomic status, late child birth
- low BMI
- white women > other races
- red hair

Sx

male Sx

- o/e :- retroverted & fixed uterus may be seen
- o cobblestone feel of uterosacral ligament is seen

Scar endometriosis:

- o Painful & tender swelling over the scar
- o usually not a/w pelvic endometriosis
- o can occur at episiotomy sites, hysterectomy/caesarean scar, myomectomy/tubectomy
- o cannot be treated w/ hormones
- o scar should be excised
- o implantation theory explains its entity

Classification:

- o American Society for reproductive medicine classification: (ASRM v)

- * stage I - minimal
 - II - mild
 - III - moderate
 - IV - severe

- * menorrhagia may be seen
- * Pain w/ endometriosis is diff PG in peritoneal fluid
- * Depth of penetration is more related to sx than spread
lesions penetration > 5mm are responsible for pain, dysmenorrhea & dyspareunia

Examination findings

- o pelvic tenderness
- o bluish or blackish spots in posterior fornix & are tender
- o U/L or B/L chocolate cysts (adnexal mass) of varying sizes

- Early lesions: papules & red vesicles filled with hemorrhagic fluid & surrounding flame like lesions
- with age → dark red, bluish or black cystic areas
- powder burnt areas are inactive old lesions scattered over pelvic peritoneum
- Healed areas are seen as small peritoneal defects (windows) or white patches

Chocolate cyst

- mostly SL
- lined by columnar epithelium
- pseudoxanthoma cells are large macrophages or scavenger cells & brown colour is due to hemosiderin in them

Rx:

M/m of pain

Drug Rx:

- OC
- mifepristone (RU-486)
- progestogens
- androgens
- GnRH
- letrozole
- RU-486

Laparoscopy

- destruction by cautery, laser vapourization
- excision of cyst
- adhesiolysis
- presacral neurectomy
- LUNA (laparoscopic uterine nerve ablation)

Laparotomy

- incision of chocolate cyst & removal of lining
- salpingo-oophorectomy
- hysterectomy & U/L or SL
- salpingo-oophorectomy
- excision of scar endometriosis

Infertility:

clomiphene, letrozole (high doses)

• Danazol causes abn^l liver enzymes

LNG IUCD - noncontraceptive uses
(Mirena)

• Menorrhagia / DUB

• dysmenorrhoea

• premenstrual syndrome

• endometriosis

× lifespan of mirena → 5 yrs

• adenomyosis

• leiomyoma

• endometrial hyperplasia

• endometrial ca

• HRT

Adenomyosis:

• It is ingrowth of endometrium both stromal & glandular components directly into myometrium

Etiology: vigorous curettage, repeated childbirth / excess estrogen

CF: • women above age 40, parous women

• menorrhagia (70%), dysmenorrhoea (30%), urinary frequency, dyspareunia, infertility

M/m: • surgery is TxC

• hormonal therapy is not much effective

Leiomyoma

- Commonest benign tumor of uterus & commonest benign solid tumor in female
- Histologically, composed of smooth muscle & fibrous connective tissue.
- each myoma is derived from smooth muscle cell nests, either from vessel wall or uterine musculature
- derived from single progenitor myocyte

Classification:

- Subserous
- Interstitial / Intramural
- Submucous
- cervical
- Intraligamentary

* m/c site $\rightarrow$ posterior wall of uterus

* m/c sx $\rightarrow$ abn^o bleeding

* m/c degeneration $\rightarrow$ hyaline degeneration

* incidence of sarcomatous degeneration $< 0.5\%$

* intermenstrual bleeding - submucous fibroid

Leiomyoma subclassification

SM - submucosal $\rightarrow$ 0 - pedunculated intracavity

1 - $< 50\%$ intramural

2 - $\geq 50\%$ intramural

0 - other $\rightarrow$ 3 $\rightarrow$ contacts endometrium; 100% intramural

4 - intramural

5 - subserosal; $\geq 50\%$ intramural

6 - subserosal ~~pedunculated~~ $< 50\%$ intramural

7 - subserosal pedunculated

8 - other (eg: cervical, parasitic)

* Broad ligament fibroid is related to ureter

RF:

- Age
- African American race
- sustained hyperestrogenic environment
 - anovulation
 - PCOS
 - obesity
 - $\uparrow$ BMI
 - early menarche
- Family history

Reduced risk:

- smoking
- combined OCPs ($\downarrow$ risk / no risk)
- post menopausal state
- 1st parity

* Fibroids are mostly asymptomatic

Pregnancy & fibroids:

- incidence in pregnancy 2%
- 80% of fibroids $\downarrow$ in size / show no change in size
- when they $\uparrow$, it is rarely $> 25\%$
- Complications
 - * preterm labor
 - * obstruction
 - * malpresentation
 - obstructed labour, CS delivery
 - PPH
 - 2nd trimester abortion

often confused with adrenal mass. MRI can be done after T3

Red degeneration:

- occurs in large fibroid, mainly during 2nd half of pregnancy & puerperium
- cause is vascular (no infection)
- Raw beef appearance - cystic spaces
- Fishy odour d/t fatty acids & colour is d/t hemolyzed red cells & Hb
- scope → evidence of necrosis present, vessels are thrombosed
- USG may be helpful, but not diagnostic
- Rx → analgesia, conservative

Degeneration of fibroids:

- ① Calcareous degeneration - phosphates & carbonates of lime are deposited in periphery along course of vessels. Form "coral stones"
- ② Hyaline degeneration
- ③ Cystic
- ④ Fatty
- ⑤ Red

Sx:

- asymptomatic (80-90%)
- bleeding
- pressure & pain → urinary frequency, incontinence, constipation, dysmenorrhea, dyspareunia, noncyclical pelvic pain, uterine obstruction
- infertility & pregnancy wastage & hydronephrosis

Rare presentation

- Myomatous erythrocytosis syndrome: d/t excessive erythropoietin production by kidneys or leiomyomas themselves
- Pseudo Meigs' syndrome
- Hereditary leiomyomatosis & RCC (HLRCC) syndrome
 - d/t fumarate hydratase (FH) gene mutations.
 - characterised by cutaneous & uterine leiomyomas & RCC

Δ:

- Pelvic ex: uterine enlargement, irregular contours
- TVS: if tumor within or just above pelvis
- TAS: for large masses
- Saline infusion sonography & hysteroscopy → submucous fibroid
- Fibroid + infertility: HSG or hysterosalpingo contrast sonography
- MRI rarely needed - for more accurate Δ
- CT scan Δ of no use

M/m:

- asymptomatic → observation ± annual pelvic ex
- symptomatic → expectant m/m → surgery
- Medical m/m

- Sex steroid hormones
- mifepristone: max of 3-6 months, can cause endometrial hyperplasia
 - ulipristal acetate
 - danazol, gestrone

GnRH receptor agents

→ leuprolide acetate

- goserelin, triptorelin, nafarelin

- GnRH receptor antagonists: cetrorelix, ganirelix

Non hormonal

- tranexemic acid

- anastrozole, letrozole

Radiological interventions

- uterine A embolization

- Magnetic Resonance guided focused USG (MRgFUS or MR-HIFU)

Laparoscopic

- laparoscopic uterine A occlusion

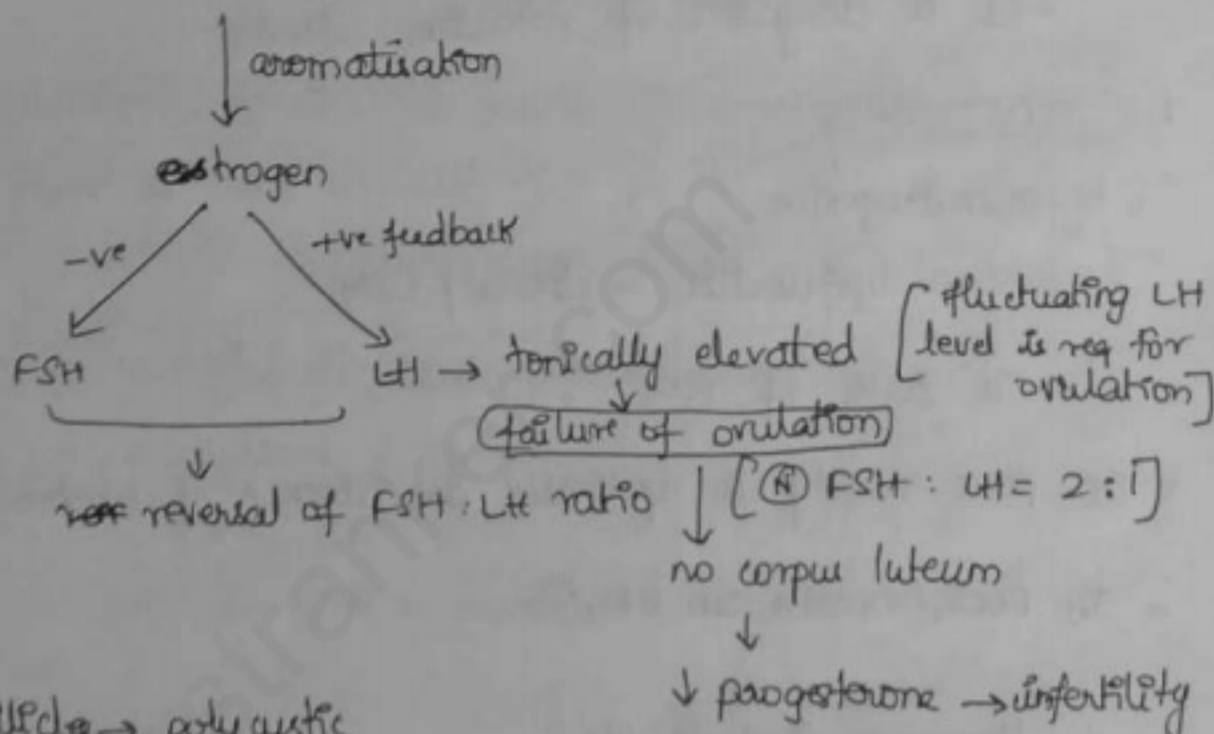
- laparoscopic myolysis

m/c of hirsutism in young ♀ → idiopathic

m/c pathological c/o hirsutism in young ♀ → PCOS

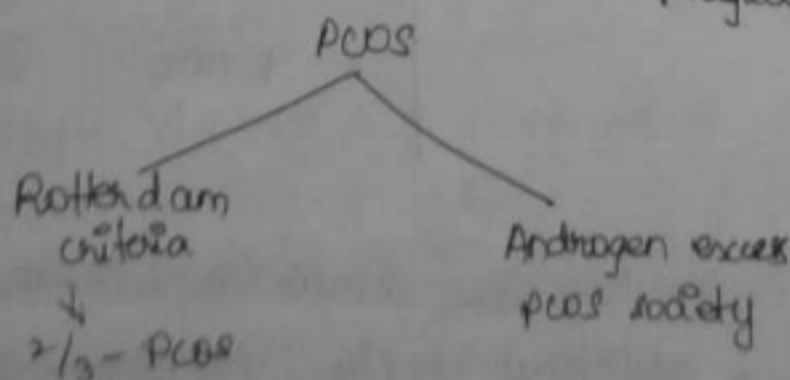
m/c c/o rapid onset hirsutism — testosterone producing tumour

PCOS → ↑ androgen



big follicles → polycystic

continuous proliferation d/t estrogen ↑
no ^{secretory} phase d/t ↓ progesterone } → endometrial hyperproliferation
↓
menometrorrhagia ← inadequate blood supply



Rottendam criteria

- 1) Hyperandrogenism $\rightarrow$ clinically / biochemically
- 2) Ovulatory dysfunction $\rightarrow$ amenorrhea / anovulation
- 3) USG features of PCOS $\rightarrow$
 - ≥ 12 follicles 2-9mm
 - in one or both ovaries $\pm$
 - ovarian volume of $\geq 10cc$

2/3 is diagnostic of rottendam criteria

AE-PCOS criteria

- hyperandrogenism
- ovarian dysfunction - clinical / USG

2/2 is Dx of PCOS

* AE-PCOS society is applicable in absence of androgenic tumour

* In PCOS, ovaries can be $\odot$

Hormones $\uparrow$ ed in PCOS

- 1) androgen (testosterone, androstenedione, DHEA, DHEAS)
- 2) estrone
- 3) $\uparrow$ LH
- 4) $\uparrow$ prolactin
- 5) $\uparrow$ LDL / TGs

Hormones $\downarrow$ ed in PCOS

- $\downarrow$ FSH
- $\downarrow$ progesterone
- $\downarrow$ SHBG (sex hormone binding globulin)
- $\downarrow$ HDL

Associated syndromes

- HAIR AN synds $\rightarrow$ hyperandrogenism, insulin $\odot$, acanthosis nigricans
- Metabolic X syndrome $\rightarrow$ abdominal obesity, TG ($>150mg/dl$), HDL ($<50mg/dl$), BP $\geq 140/90$, diabetic status

- obesity
- insulin $\uparrow$ / hyperinsulinemia
- hyperandrogenism

* insulin $\downarrow$ es SHBG $\rightarrow$ hyperandrogenism

* insulin $\textcircled{R}$ = $\frac{\text{Serum fasting glucose}}{\text{serum fasting insulin}}$

◦ Acanthosis nigricans is the marker of insulin $\textcircled{R}$ in PCOS

◦ $\therefore$ 2hr OGTT is done in all PCOS pts $\rightarrow$ 35% of PCOS have impaired glucose tolerance & 10% have DM

◦ Hirsutism $\rightarrow$ modified ferriman gallway scoring

$\rightarrow$ max score : 36

score ≥ 8 - mild

≥ 15 - moderate to severe hirsutism

M/m of PCOS

- weight reduction
- low dose OCPs (for irregular periods)
- metformin (m/c Ad/E - GI upset
dangerous Ad/E - lactic acidosis)

◦ ovulation induction using clomiphene citrate, synthetic LH & FSH

M/m of hirsutism:

- androgen in PCOS is LH dependant (LH stimulate theca cells to produce androgen)
- low dose OCPs for hirsutism τ desogestrel, gestodene & norgestimate
(3rd gen progestogens)

• m/c of vesicovaginal fistula < globally → gynaec surgery
India → obstructed labour

- most appropriate method for collecting urine for culture in case of vesicovaginal fistula is - Foley's catheterisation
- ~~uterovag~~ uterovaginal fistula { may present w/ cyclical hematuria bladder endometriosis }

Vesicovaginal fistula

- presents w/ continuous dribbling of urine from vagina, no urination thro' urethra
- 3 swab test - middle cotton swab is wet w/ urine & dye
- I/O - cystourethroscopy
- M/M → Latzko repair
- Timing of repair - after 3 months in obstetric fistula, post surgery → within 24 hours + immediate repair
late recognition → 3 months later

Uterovaginal fistula

- D/t hysterectomy
- continuous dribbling of urine from vagina & (N) filling of bladder
- 3 swab test - upper most cotton plug is wet w/ urine but not w/ dye
- further evaluation - iv ~~ce~~ CECT in excretory phase / IVP
- M/M - ureteric reanastomosis to be carried out as early as possible

~~ure~~ = ureterovaginal fistula - upper most swab soaked $\pm$ urine but not $\pm$ dye. Lower 2 swabs remain dry

• vesicovaginal fistula - upper & lower swabs remain dry but middle swab stained $\pm$ dye

• urethrovaginal fistula - upper two swabs dry, lower swab stained $\pm$ dye

* Chassai-Mayer technique $\rightarrow$ repair vesicovaginal fistula

* most useful investigation in vesicovaginal fistula $\rightarrow$ cystoscopy

* m/c site of obstetric injury leading to ureterovaginal fistula $\rightarrow$ below cardinal ligament where uterine artery crosses

* Causes of retention of urine in reproductive age group

$\rightarrow$ cervical fibroid

$\rightarrow$ retroverted gravid uterus

$\rightarrow$ severe UTI

* Retroverted uterus

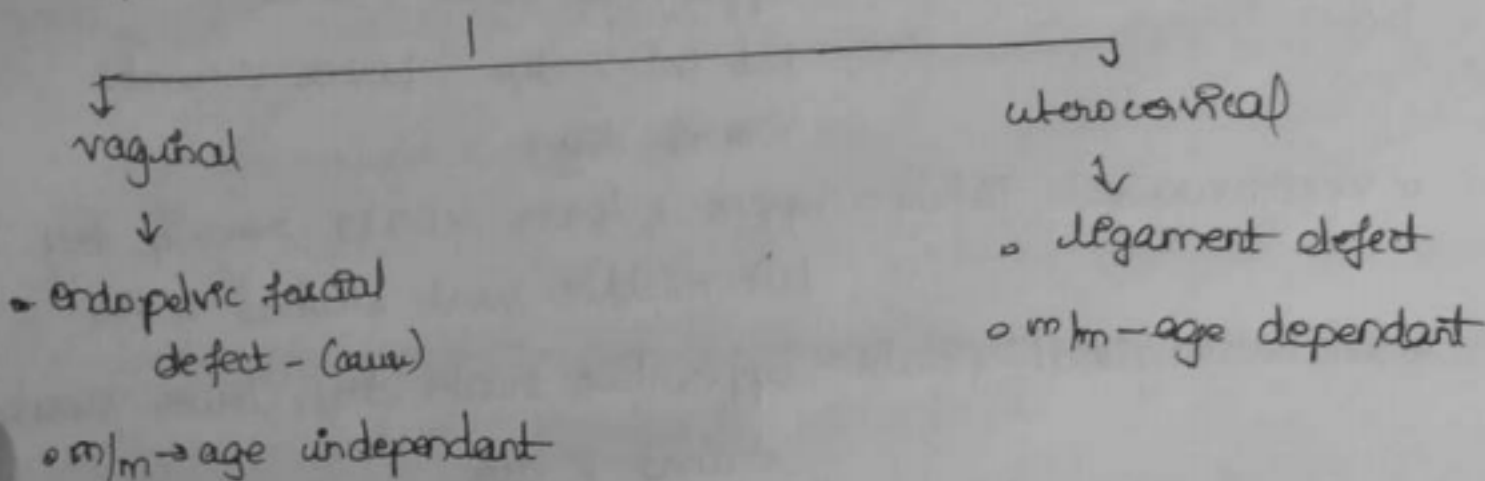
$\rightarrow$ may be a/w endometriosis, PID

$\rightarrow$ may be a/w infertility

$\rightarrow$ may cause menorrhagia

* Kegel's exercise

$\rightarrow$ should be started 24 hrs after delivery (once the pt is pain free)



Vaginal prolapse

DeLancey's vaginal supports

level 1 → apex → uterosacral & Mackenrodt's

• 2 → middle ~~and~~ 3rd → paravaginal attachment

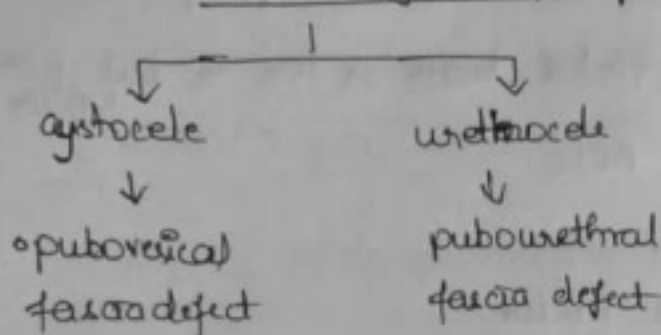
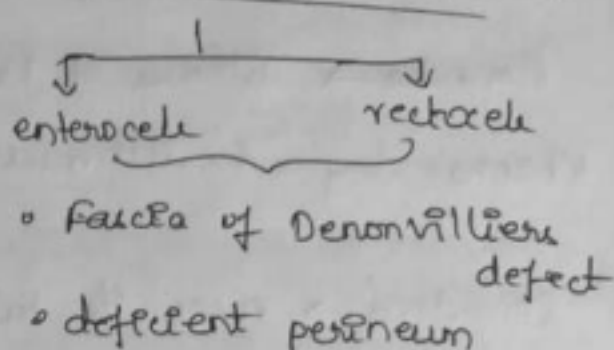
• ~~2~~ → ~~transverse~~ i) arachnoid tendinous fascial pelvis
ii) " " rectovaginalis

• 3 → lower 3rd → perineal membrane, muscle & body

* Defect in level 1 supports → enterocele, apical prolapse, descent of cx, ~~vag~~ vault prolapse

" 2 support → cystocele & rectocele

" 3 " → gaping introitus, deficient or lax perineum, ~~urethro~~ enterocele

Anterior vaginal prolapsePosterior vaginal prolapseManagement:

cysto & urethrocele → anterior colporrhaphy

rectocele → posterior colpoperineorrhaphy

enterocele → Moscovitz surgery + posterior colpo
perineorrhaphy
↓
(purse string suture of POD)

lax perineum / deficient perineum → perineorrhaphy

↓
interval tightening surgery

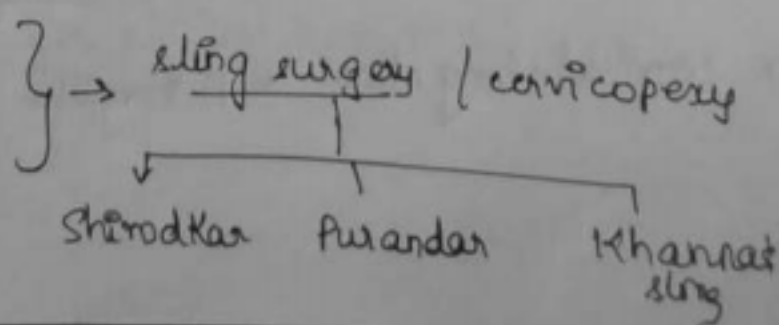
Uterine prolapse

True ligament → Mackendrot's, uterosacral & pubocervical

False " → round, broad ligament, ovarian ligament,
angulation & serosa

M / m

- < 40 yrs, infertility,
recurrent pregnancy
loss



Shandker → Isthmus of Cx to sacrum → most preferred

Purandara → Isthmus of Cx to rectal sheath → less % but more failure

Khanna's sling → Cx Isthmus to ASIS

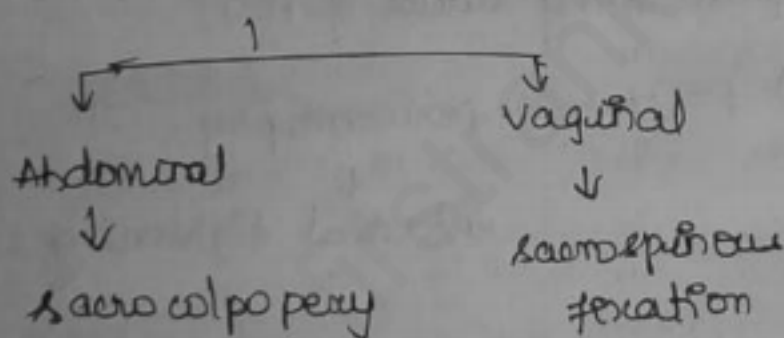
Shandker → more % but less failure

Khanna's → ad/le → chronic proctitis

* >40, completed family → vaginal hysterectomy + vault suspension

* prolapse in pregnancy / perimenopause → ring pessary

* vault suspension



Ⓡ side preferred as Ⓢ side sigmoid colon may be damaged

* elderly, unfit for surgery → LeFort's surgery (colpocleisis)
(ring pessary is preferred)

* cervical elongation → Fothergill's or Manchester operation

• 9 measurements - hymen as reference point

• 3 x 3 grid

i) Aa → points on Anterior vagina 3cm proximal to external urethral meatus (midline)

ii) Ba → most dependant portion btw Aa & anterior fornix

Aa & Ba are marker of anterior vaginal prolapse

iii) Ap → posterior vagina midline 3cm proximal to hymen

iv) Bp → most dependant portion btw Ap & posterior fornix
(Ap & Bp - marker of post-vaginal prolapse)

v) C → Cx or vaginal cuff → marker of uterine prolapse of uterine cervix length - ①
corresponds to

vi) D → apex of vagina / vault → uterosacral & Mackendroff

D is marker of enterocele

vii) Genital hiatus → distance btw external urethral meatus to posterior hymenal remnant
(GH)

viii) Perineal body - posterior hymen to middle of anal opening
(PB)

ix) Total vaginal length → hymen to point D
(TVL)

Aa	Ba	C
GH	PB	TVL
Ap	Bp	D

⇒ 3 x 3 grid

$$GH \propto \frac{1}{PB}$$

GH $\rightarrow$ (N) 4-5 cm ; TVL (N) $\rightarrow$ 9 cm

PB $\rightarrow$ 3-4 cm

uterocervical length $\rightarrow$ (N) 3 inches

- All 9 measurements are done $\pm$ full vulva except TVL & is done after reducing the prolapse.

Staging

Type 0 $\rightarrow$ no demonstrable prolapse

1 $\rightarrow$ > 1 cm above the hymen (ie $\bullet$ < -1 i.e. -2, -3)

2 $\rightarrow$ $\bullet$ -1 to +1

3 $\rightarrow$ more than stage 2, but 2 cm less than TVL

4 $\rightarrow$ $\bullet$ more than TVL - 2

-3
-2
-1
0 $\rightarrow$ hymen
+1
+2
+3

Max measurement of Aa & Ba $\rightarrow$ +3

" " " Ap & Bp $\rightarrow$ +3

Classification

- Temporary → barriers, natural methods, pills, IUDs
- permanent → surgeries

Natural methods1) Rhythm method

- * calendar method (Ogino-Knaus theory)
 - * 1st unsafe day $\Rightarrow$ length of shortest cycle - 20 days
 - * last unsafe day $\Rightarrow$ length of longest cycle - 10 days
- * Temperature method $\rightarrow$ abstinence until 3rd day of rise of temp (temp. $\uparrow$ is d/t progesterone)
- * Mucus method (Billings method): abstinence on all days of noticeable mucus & for 3 days thereafter
- * Symptothermal method: 1st day of abstinence predicted from calendar or mucus method. End of fertile period detected by ABT method

2) withdrawal method (coitus interruptus)

a) Breastfeeding

b) Persona - oestrogen - 3 glucuronide & LH testing in urine

✓) Cycle beads

- * Ectopic pregnancy may be a complication of calendar method

- No method $\rightarrow 85$
- natural $\rightarrow 25$
- withdrawal $\rightarrow 27$
- lactational amenorrhoea $\rightarrow 2$
- condom, $\sigma^7 \rightarrow 15$
 $\text{♀} \rightarrow 21$
- Implanton $\rightarrow 0.01$
- Vasectomy & tubectomy $\rightarrow 0.15$
- Norplant $\rightarrow 0.05$
- Cu T 380 A $\rightarrow 0.8$
- LNG 20 $\rightarrow 0.1$
- combined OCP $\rightarrow 0.1$
- POP $\rightarrow 1$
- DMPA & NET injectables $\rightarrow 0.3$

⑧ Pearl index =
$$\frac{\text{no. of accidental pregnancies} \times 1200}{\text{no. of pt observed} \times \text{months of use}}$$

$\downarrow$
indicate contraceptive failure

Barrier methods:

- Condoms, spermicidal agents (nonoxonyl-9)
- occlusive diaphragms -
 - dutch cap/diaphragm
 - cervical cap
 - female condom
 - today (cerv sponge)

Female condom:

- prevents STDs

Diaphragm

- not suitable in pelvic organ prolapse
- proper sizing
- additional spermicide after each episode of coitus
- can cause TSS if left > 24 hours

Sponge (today)

- consists of a nonoxonyl 9-impregnated polyurethane disc that can be inserted for upto 24 hrs prior to intercourse
- disc is moistened
- for efficacy, should be kept in place for 6hrs after intercourse & no longer than 30 hours
- * contact dermatitis is m/c problem also use of condom
- * c/I of diaphragm → recurrent UTI, uterine prolapse, herpes vaginitis
- * Spermicidal jelly acts by disruption of cell membrane

Combined hormonal contraceptives

- ethinyl (estradiol (10-50 mcg) + progesterone
- mono / multiphase
- MOA: * $\downarrow$ of ovulation by suppression of release of FSH & LH
estrogen suppress FSH & stabilises endometrium to prevent intermenstrual bleeding

- * progestins $\ominus$ ovulation $\rightarrow$ $\rightarrow$ renders endometrium unfavourable for implantation & fertilization
- * uterine & tubal contractions may be modified to disfavour fertilization
- * 3rd gen ocp $\rightarrow$ contain norgestimate & gestodene $\pm$ estrogens $\rightarrow$ more lipid friendly

Choice of progestins

- 1st gen pills $\rightarrow$ ethinyl E₂ + norethindrone
- 2nd gen $\rightarrow$ " + norgestrel & LNG
- 3rd $\rightarrow$ " + desogestrel, gestodene, norgestimate
- 4th $\rightarrow$ ethinyl E₂ + drospirenone

- * Drospirenone $\rightarrow$ has antiandrogenic & antimineralocorticoid properties. useful in acne, premenstrual syndrome, $\uparrow$ in renal / adrenal insufficiency & hepatic dysfunction. Can cause hyperkalemia

Non contraceptive benefits of ocp

- $\downarrow$ endometrial & ovarian Ca
- fewer ectopic pregnancies
- more regular menses
- less salpingitis
- $\uparrow$ bone density
- less endometriosis
- $\downarrow$ benign breast disease
- probably less RA
- protection against atherosclerosis
- $\downarrow$ fibroids
- $\downarrow$ ovarian cysts
- $\downarrow$ PID

o OCPs does not $\downarrow$ Ca ex

o combined OCPs $\uparrow$ chlamydia & candida infections

c/i for OCPs (WHO MEC category 4)

o impaired liver fn

o Ca breast (known/suspected)

o $\uparrow$ TG / cholestasis

o undiagnosed vaginal bleeding

o smoken over 35yr

o past/present/family H/o TE

o mod to severe HT

o diabetes & vascular disease

o migraine & aura

Amount of estrogen in Mala D is 30mcg

Mala D $\Rightarrow$ LNG 0.15 mg + ethinyl E2 30mcg (21+7 Iron tabs)

Drug Interactions $\pm$ OCPs (Drugs $\downarrow$ long $\downarrow$ efficacy)

o Rifampicin (if EE $<$ 50 mcg)

o Griseofulvin

o phenytoin, phenobarbitone, primidone, carbamazepine, ethosuximide

o Tetra, doxy, penicillins, E-pro, ofloxacin

o antiretrovirals

DMPA

NOA - $\uparrow$ Cr mucous viscosity, endometrium unfavourable for implantation & $\ominus$ ovulation (v)

o 150mg i.m every 90 days (104mg s.c)

o Notable effects $\rightarrow$ * irregular vaginal bleeding

* prolonged ovulation suppression after inj have been stopped

* $\downarrow$ Bone mineral density

* $\uparrow$ cervical carcinoma in situ

* $\downarrow$ ovarian & endometrial Ca

LNG-IUS (Mirena)

- T shaped polyethylene structure is stem encased by a cylinder containing polydimethylsiloxane & LNG
- 52 mg LNG eluting 20 mcg daily
- approved for 5 yrs use, but evidence for 7 yrs
- Noncontraceptive uses:
 - ↓ menstrual blood loss,
 - ↓ dysmenorrhea, ↓ PID, HRT in perimenopause
- ↓ menorrhagia

CuT

- Cu 380A approved for 10 yrs use, but can be used upto 20 yrs
- Mechanism - intense local inflammatory response induced in uterus by Cu containing devices leads to lysosomal activation & other inflammatory actions that are spermicidal.
 - if fertilization occurs, inflammatory action against blastocyst.
 - endometrium becomes hostile for implantation
 - ↑ motility of tubes, induces endometrial atrophy

Contraindications for CuT:

- puerperal sepsis / postabortal sepsis
- unexplained vaginal bleeding
- GTN
- current PID / STD within past 3 months, known pelvic TB
- Ca Cx
- Ca endometrium

- If pt becomes pregnant & IUCD, the IUCD should be removed to ↓ Rto infection

Managing IUCD

- PV

↓
UCD / erect X-ray abd AP / lateral & sound

↓
hysteroscopy

↓
laparoscopy

- Emergency contraceptive doesn't interfere & early pregnancy

↓

- CuT, LNG & OCP's can be used

- POP → LNG 0.7mg / LNG 1.5mg → ⊕ / delay ovulation

- SPRM (ulipristal acetate) - 30mg

- COC - EE 0.1mg + LNG 1mg - Yuzpe method

- CuT - 380A

* all are preferred within 72hrs, can be used upto 120 hrs
Permanent methods

- Eligibility criteria

* married

* > 22 & < 49

* atleast one child & yr age unless medically indicated

* female (her partner must not have undergone sterilisation in past)

* consent in sound state of mind

♀ sterilization

- Hysterolap methods → ^{used} Pomeroy, Irving, uchida, fimbriectomy/
Knoeven's tech, Parkland tech
↳ used
- Laparoscopy → falope rings (m/c used),
Hulka clamped clips,
silicone titanium clip (fixative clip)
- * ~~least method~~ effective method → vaginal fimbriectomy
- * max chance of reversal → laparoscopic methods =
clip or ring
- * tubes are ligated at isthmus
- * reversal of tubal ligation → isthmo-isthmic anastomosis
- * No scalpel vasectomy is done now; ~~fast~~ involves
ligation & division of spermatic cord; partner may
be on DMPA for 3 months
- * Contraceptive implants → norplant, implanon, ~~medroxy~~
fadelle

Urinary incontinence & hyperprolactinemia

- ① post. urethrovaginal angle $\rightarrow 100^\circ$
- initial desire to void $\rightarrow 150$ ml
strong " $\rightarrow 250$ ml
residual $\rightarrow 50$ ml
bladder capacity $\rightarrow 400-600$ ml
flow rate $\rightarrow 15$ ml/sec
- intra vesicle pressure $\rightarrow 10 \text{ cm}^2 \text{ H}_2\text{O}$
intra urethral " $\rightarrow 20-50 \text{ cm}^2 \text{ H}_2\text{O}$
dit urethral sphincter mechanism
- upper $2/3^{\text{rd}}$ of bladder neck $\rightarrow$ above levator ani muscle
- urethral mobility mech $\rightarrow$ when pt coughs, pressure equally transmitted to bladder wall & upper $2/3^{\text{rd}}$ bladder neck
 $\downarrow$
(70-75% of urinary incontinence)

Urinary incontinence

m/c $\rightarrow$ stress urinary incontinence (SUI) > detrusor instability urge incontinence

SUI

- Involuntary passage of urine $\circ$ to $\uparrow$ intra abd. pressure in absence of detrusor instability

Features $\rightarrow$

- leak on cough
- small amount
- leak only till $\uparrow$ intra abd pressure
- no urge / frequency / nocturia / dysuria

- other mech of SUI → urethral mobility & mech abn
- * intraurethral pr > intraurethral pr
- * upper 2/3rd bladder neck below levator ani
- Causes : age, multiparity, obesity, chr cough, constipation, menopause, surgeres in bladder neck

Δ : clinical

diagnostic tests → stress test (pt in lithotomy position → cough
↓
sprinkling of urine)

- ii) tip test → done in empty bladder
- tipped swab introduced thro urethra & asked to cough
 - when tipped swab move more than 30° → +ve test

iii) Bonney's test → 2 fingers in para urethral region push up & ask to cough.

• if SUI corrected → +ve test

iv) Marchetti test → 2 allie forceps used instead of finger

M/m of SUI

- Abdominal surgeres → Burch colposuspension, Marshall marchetty Krantz

Not done now
• Cole →

Burch colposuspension

Marshall

→ proximal urethra

bladder neck suspended

• Cooper's ligament

• pubic bone

• C/c - osteitis pubis

Vaginal SurgeriesTVT (tension free vaginal tape)

- mid urethra is suspended in both
- both are day case surgeries

- mesh tape placed behind midurethra

(retro space entered where blades is present, chance of injury +)

- cystoscopy must be done at end of procedure

TOT (^{trans}obturator tape)

- tape passed thro' both obturator foramen

◦ don't enter space of Retro, no bladder injury

* TOT is the best method among all 4.
(TOT > TVT)

Urge incontinence

- detrusor overactivity & parasympathetic overactivity

Features → ◦ frequency (>7 times/day)

- urgency
- nocturia
- dysuria

- m/c is UTI (∴ medical m/m)

- CNS causes should be ruled out (eg: parkinson, MS, alzheimer etc)

◦ structural similarity to GH & human chorionic somatomammotropin

◦ $t_{1/2} \rightarrow 20 \text{ mins}$

◦ ↑ed by stress, sleep, nipple stimulation, pregnancy

◦ drugs ↑ing it $\rightarrow$ antipsychotics, dopamine antagonists, α methyl dopa, verapamil

◦ pathological $\uparrow \rightarrow$ pituitary adenoma, trauma, infection

◦ TRH $\rightarrow \uparrow$ prolactin ($\therefore$ in hypothyroidism $\rightarrow$ prolactin ↑ed)

◦ hyperprolactinemia $\rightarrow$ treat of amenorrhoea, infertility & galactorrhoea

◦ in $\sigma \rightarrow$ erectile dysfunction, hyperlipidemia, stroke, MI

◦ NOA of prolactin

$\rightarrow$ prolactin has -ve feedback of GnRH

$\therefore \downarrow$ FSH & LH $\rightarrow$ no folliculogenesis $\rightarrow$ no ovulation

◦ $\beta \rightarrow$ bromocriptine in medical m/m

◦ $\textcircled{A} \Rightarrow 15 \text{ to } 25 \text{ ng/ml}$

◦ Protocol for $\uparrow$ prolactin

* 1st do UPT $\xrightarrow{+ve}$ ARC deficit
 $\downarrow -ve$

* Rule out stress, sleep deprivation, drug intake
 $\downarrow -ve$

* Rule out hypothyroidism $\rightarrow \beta$ accordingly
 $\downarrow -ve$

* CT/MRI $\rightarrow$ pituitary adenoma $\rightarrow \beta$ accordingly
 $\downarrow \textcircled{A}$

Repeat prolactin levels after 6 weeks

Infertility

- 1 year is needed for Δ of infertility
- Types - 1° & 2°
- Infertility attributed to ♀ in 1/3rd, ♂ in 1/3rd & both in 1/3

Causes (↓ in order)

- Ovarian → anovulation, corpus luteum insufficiency
- Tubal → blockade d/t inf, surgery
- unexplained
- PCOD anovulation
- Uterine → Fibroid, synechiae, TB, malformations
- pelvic → endometriosis, adhesions
- cervical factor → lack of mucus, Abs in mucus

Testing

- Ovulatory dysfunction → ovulation predictor test
 - early follicular FSH ± estradiol level (ovarian reserve)
 - ± AMH
 - ± serum TSH, prolactin, androgen
 - ± ovarian USG (antral follicle count)
- Tubal / pelvic disease →
 - HSG
 - laparoscopy + chromotubation
- Uterine factors →
 - HSG
 - TVS / saline infusion sonography (SIS)
 - ± MRI
 - Hysteroscopy ± laparoscopy
- ♂ factor → semen analysis

Asherman syndrome:

- Intrauterine adhesions / Asherman synd. is d/t destruction of endometrium in response to ovarian steroids
- Endometrial damage occurs d/t vigorous curettage following
 - PPH
 - miscarriage
 - elective abortion complicated by infection
- Δ: HSG / SIS
- Pt/m → hysteroscopy

• Best investigation for tubal patency → laparoscopic chromotubation

HSG

- Rubin's cannula / Foley's catheter is inserted into Cx & a radiopaque dye (usually 50% iodine + polyvinyl alcohol) is instilled into uterine cavity.
- performed on 9th / 10th day of cycle
- cannot diff b/w cornual spasm & tubal block

Laparoscopic chromotubation

- done ~ diagnostic laparoscopy & a dye is injected thro Cx
- free flow can be demonstrated at fimbrial ends
- Ix:
 - HSG showing abn finding
 - prior to planning tuboplasty
 - prior to IVF
 - prior to induction of labour

- removal of hydrosalpinx prior to IVF
- PCOS to puncture the cysts to improve pregnancy rate of ART & avoid hyperstimulation syndrome
- suspected endometriosis

Sonosalpingography

- under USG, a Foley catheter is inserted, ~~then~~ a 200ml of saline injected into uterine cavity
- flow of saline along tube is visualised
- USG shows presence of free fluid in pouch of Douglas if tubes are patent

M/m of tubal factor infertility

- proximal (cornual) block → tubal cannulation / catheterisation
- distal block - IVF, fimbrioplasty
- midsegmental block - resection & anastomosis
- Tubal recanalisation

- reversal best < clips > fallope rings > modified Pomeroy's > cautery
- length of final tube: 4 cm
- isthmo isthmie anastomosis has best results

Post coital test : (Cx mucous is examined)

- antisperm antibodies
- cervical factor ab (N)
- penetration of sperm in Cx mucous - Miller-Kuznetsov test
- sperm count & ab (N)

- Abnormalities - cryosurgery / LEEP / conization
cervical infection

(cervical mucus is permeable to sperm only during mid cycle)

- Evaluation - post vital test / Sims Huhner test

- * couple req. to have intercourse on day of ovulation
- * a subsequent sample of cervical mucus is ~~also~~ evaluated for elasticity (Spermbarrel) & no. of motile sperm per high power field

- M/m → intrauterine insemination

Male infertility

Ante testicular

- Endocrine deficiency
- psychosexual
- drugs → anti-hypertensives, antipsychotics
- genetic → Klinefelter's, Y chr. deletion, single gene mutations

Testicular

- Immobile cilia
- cryptorchidism
- infection
- toxins
- varicocele
- immunogenic
- 1° testicular failure

Post testicular

- obstruction of efferent duct:
 - cong. absence of vas deferens (cystic fibrosis)
 - acquired w/
 - surgery (vasectomy, hemiorrhaphy)
- ejaculatory failure
- retrograde ejaculation
- hypospadias
- bladder neck surgery

* aspermia → complete absence of semen

* oligospermia / oligozoospermia → sperm count < 20 million / ml

* polyzoospermia → > 350 million / ml

* azoospermia → no sperm in semen

- **asthenozoospermia** - reduced sperm motility
- **leucocytospermia** - ↑ white cells in semen
- **neurozoospermia** → spermatozoa are dead / motionless
- **teratozoospermia** → > 70% sperm = abn morphology
- **oligoastheteratozoospermia** → disturbance of all 3 variables

Semen analysis

- volume - > 1.5 ml
- count - > 15 million/ml
- Total motility > 40%
- morphology > 4%
- WBCs < 1 million / ml
- Round cells < 5 million / ml

In depth analysis

◦ Serum FSH, LH, testosterone, prolactin, TSH

* testicular dysfn → ↑ FSH & LH

* ↓ FSH & LH → hypogonadotropic hypogonadism

* Leydig cell dysfn → low testosterone & high LH level;
elevated level d/t pituitary adenoma

◦ absence of fructose in seminal fluid → cong. absence of
seminal vesicle or portion of ductal system / both

◦ Testicular Bx → Bx material is sent in Bouin's soln

M/m of infertility

- ovulation induction
- IVI
- IVF-ET
- ICSI → Intracytoplasmic sperm injection

ICSI

- I₁ → severe oligospermia (5 million sperm/ml)
 - azoospermia / teratozoospermia
 - sperm Abx
 - obstruction of efferent duct system
 - cong. Abx absence of vas
 - failure of fertilization in IVF

* Aspiration of sperm from testis is done by

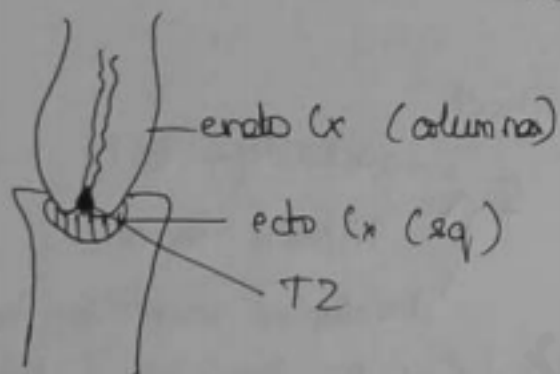
- i) Testicular sperm aspiration (TESA)
- ii) " " extraction (TESE)
- iii) Percutaneous epididymal aspiration (PESA) → trauma to epididymis may occur
- iv) Microsurgical epididymal ^{sperm} aspiration (MESA)

Tx of IVI

- * cervical factor infertility
- * unexplained infertility
- * oligoasthenospermia

Anatomy of Cx:

- 2 parts → endocervix (part close to uterine) - columnar
 ectocervix → part $\subseteq$ projects into vagina, squamous epi
- squamocolumnar junction transformation zone
- original SCT is at external os, but rarely restricted to it



SCT:

- endo Cx → red
 ecto Cx → pink
 TZ → white
- TZ moves out during pregnancy, puberty, OCP
 moves in into endo Cx w/ age
- In all ♀, columnar epithelium of endo Cx changes to sq. epithelium of ecto Cx. This metaplasia - physiological, in all ♀
- m/c site of Ca Cx - TZ
- m/c variety of Ca Cx - sq. cell Ca
- as endo Cx is lined by columnar, adenocarcinoma of Cx can also occur
- m/c site for adenocarcinoma of Cx → endo Cx

- m/c cell in menopausal ♀ → basal & parabasal cells
- In pregnancy & 2nd 1/2 of menstrual cycle → intermediate cells predominate
- in 1st half of menstrual cycle → superficial cells predominate

Superficial cells → large ~~eosinophilic~~ basophilic cell & pyknotic nucleus

Intermediate cells → basophilic cells & smudged outline

parabasal cells → basophilic, smaller cells & large nucleus

Ca Cx :

- m/c Ca in Indian ♀ → Ca breast
- m/c Ca of genital tract in ♀
 - globally - Ca Cx
 - India - Ca Cx
 - developed countries - Ca endometri^{um}
- infection of Cx leads to dysplasia in few ♀ & leads to
- Ca formation & takes 10 to 30 yrs
- N:C ratio ↑ in dysplastic cell

Classification

- < 1/3rd epithelium is dysplastic → CIN I
- > 1/3 but < 2/3 → CIN II
- > 2/3 → CIN III
- whole epithelium dysplastic but overlying epithelium intact - CIS
- overlying epithelium broken → invasive Ca

Bethesda classification

◦ CIN 1 $\Rightarrow$ LSIL (low grade squamous intraepithelial lesion)

2, 3 $\Rightarrow$ HSIL

◦ CIS - no longer used

RF for CIN / Ca Cx:

- early age of intercourse
- " " " 1st child birth
- multiparity
- low SES
- multiple partners

◦ all STDs

◦ smoking (RF for SCC)

◦ OCP (for adenocarcinoma)

◦ HPV infection - most (X)

* Early menarche & late menopause are RF for endometrial & ovarian Ca, not Ca Cx

◦ Ca Cx has no familial inheritance

◦ age group for CIN - 20-30 yrs

CIS - 30-35 yrs

invasive Ca - 35-39 yrs & 2nd peak at 5th to 6th decade

[endometrial & ovarian Ca are more common in nulliparous]

+ all estrogen dependant conditions are more common in nulliparous women

* HPV affects basal epithelial cells (epitheliotropic)

The cytological changes are called koilocytosis
koilocyte $\rightarrow$ enlarged nucleus + perinuclear halo

- High risk HPV → 16, 18 (70% cases)
→ 31, 33, 45, 52, 58 (30% cases)
- Low risk → 6, 11 → genital warts / condyloma acuminata
- Babies born to ♀ w/ genital warts have laryngeal papillomatosis, hence CS done

* Viral protein responsible for malignant transformation

- E6 & E7

• E6 affects gene p53

E7 " retinoblastoma gene

* Viral proteins req for viral replication - E1 & E2

* m/c HPV a/w Ca cx → HPV 16

SCC Ca → HPV 16

most sensitive HPV a/w c Ca cx → HPV 16

" specific " " " " " → HPV 18

m/c HPV a/w adenoc Ca cx → HPV 18

Cancers by HPV

- ♀ → Ca cx, vagina & vulva
- ♂ → oral, anal & penile Ca

* HPV vaccines are made from inactivated capsid proteins

i) Cervarix → bivalent vaccine → protects against HPV 16, 18
given to ♀ only

given to ♂ & ♀ { ii) Gardasil → quadrivalent → 16, 18, 6, 11

iii) Gardasil-9 → 9 valent → 16, 18, 6, 11, 31, 33, 45, 52, 58

• Ideal age of vaccines → 11-12 yrs (9-26 yrs)

• most ♂ ad IE → synovial effusion

• ✓ during pregnancy

• can be given to HPV +ve ♀

• protection rate of $\left\{ \begin{array}{l} \text{gardasil} \rightarrow 75\% \\ \text{gardasil-9} \rightarrow 90\% \end{array} \right.$

• screening should continue after vaccine

Screening test → Pap smear

• start by 21 yrs

• universal screening, done 3yrlly till 30 yrs

• and then if Pap test ~~negative~~ +ve, HPV DNA testing
- 5 yearly

• only pap smear - 3yrlly

• HPV DNA testing in ♀ > 30 yrs

• method - PCR / hybrid capture tech / southern blot

• screening continued ~~if~~ for 65 yrs if last 10 pap @

HPV 75 if last 10 yrs pap suspicious

- After hysterectomy for benign cases - stop
- In HIV +ve ♀, annual screening till 3 (N) results & then 3 yearly screening
- Sampling instruments → Cx brush, cytobrush, plastic spatula, wooden spatulae (Ayer's spatula)
- 1st slide → smear from TZ
- 2nd " → endocervix
- 3rd slide → control slide → post. wall of vagina
- For hormonal study → lateral wall of vagina
- cytology → post. " " "
- Fixative used → 95% ethanol + 5% ether
- Liquid based cytology → done w/ Cervical brush
 - better than conventional pap
 - fixative is methanol

Alternative to Pap in rural areas

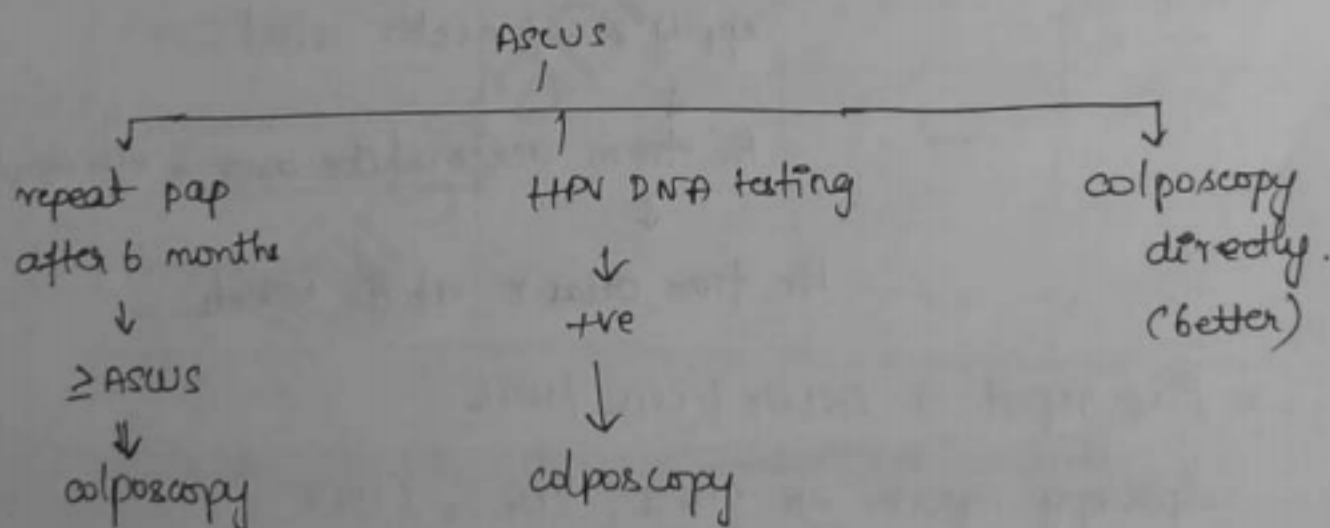
- VIA - visual inspection w/ 5% acetic acid - white stained areas ab (N)
- VILI → visual " w/ Lugol's Iodine - unstained yellow areas (stained areas are black-brown) ab (N)
- Lugol's Iodine - 5%
- Schiller's Iodine - 0.3%

- Pap smear detects - *Trichomonas*, *Candida*, *HSV*, *HPV*, *actinomyces*
- doesn't detect - gonorrhoea, chlamydia

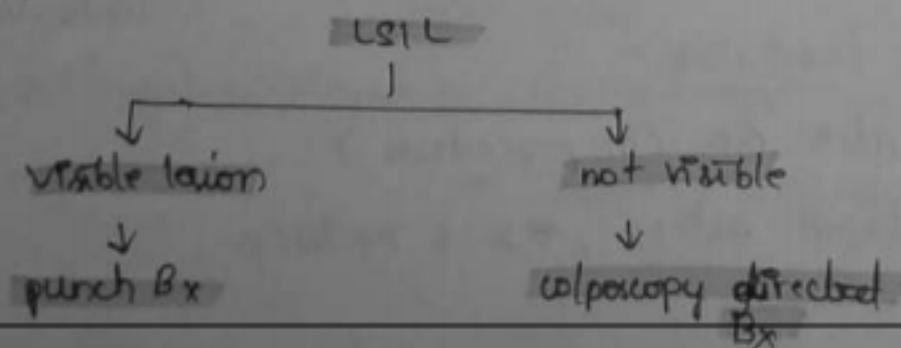
Result of pap smear

- (N)
- Infection $\rightarrow$ $R = \text{Abx}$
- reactive changes
- atypical squamous cells of unknown significance - ASCUS
- LSIL $\rightarrow$ enlarged, dark nuclei than ASCUS, $\bar{c}$ fair amount of cytoplasm
- HSIL - nuclei wrinkled & dark, very little cytoplasm

ASCUS $\rightarrow$ cells ~~cells~~ $\bar{c}$ slightly enlarged & darker nuclei compared to other (N) cells



• 10% of LSIL $\rightarrow$ HSIL $\xrightarrow{10\%}$ Ca Cx



• HSIL → colposcopy directed Bx + endocervical curettage

• mild erosion of cx & pap smear shows dysplasia → ABx & repeat Pap after 3 months

Colposcope:

• minimum magnification → 5 times
max → 30^x

- OPD procedure, no anaesthesia
- disadvantage → cannot visualize endo cx

Bx from any rough area / area appearing white before applying acetic acid - leukoplakia

↓
apply 3-5% acetic acid

↓
Bx from aceto white area → Ht dysplasia

↓
Bx from areas w abn vessels

• Pap report → ASCUS / LSIL / HSIL

colposcopy report → CIN 1, CIN 2, CIN 3

• If pap smear → HSIL & colposcopy - (N) ⇒ cone Bx / conization done

Cone biopsy (conization)

• done under GA (OT procedure)

• Bx from ecto cx, +2 & endo cx

Diagnostic Tx:

- unsatisfactory colposcopy
- discrepancy b/w pap & colposcopy
- pap report is HSIL & are endocervical curettage
- suspicion of microinvasion
- " " adenoca

Therapeutic Tx:

- treat CIS or stage 1A1 of Ca cx in young ♀

Lifecycle of CIN

	CIN 1	CIN 2	CIN 3
Regression	60	40	30
Persistence	30	35	50
progression to CIN III / CIS	10	20	
Progression to invasion	<1	5	20

CIN 1 → HPV DNA + pap smear yearly



If persists ≥ 2 yrs



cryosurgery

CIN 2 & CIN 3 → LLETZ (large loop excision of TZ)

OR LEEP (loop electro excisional procedure)

Gyrosurgery

• N_2O is passed at 20° temp $\rightarrow$ destroys cell

• m/c c/c $\rightarrow$ cx discharge

• orate c/c $\rightarrow$ cx stenosis & cx incompetence

• never 1/2 cervical bleeding

• destroys epithelium upto 5mm deep

laser $\rightarrow$ " " " 7mm deep

• for CIN $\leq$ extends to vaginal fornices i.e. CIN + VAIN

LEEP / LLETZ

• OPD procedure under LA

• diagnostic & therapeutic

• stainless steel wire used $\rightarrow$ thin wire + high power

• upto 10mm depth

Indications for hysterectomy in CIN

• recurrent CIN

• suspected adenocarcinoma & family of pt complete

• associated pelvic pathology for $\leq$ hysterectomy has to be done like fibroid

• pt cannot come for followup

Ca Cx

◦ m/c variety → SCC → large cell keratinizing (m/c)

→ " " non "

→ small cell → worst prognosis

◦ adeno Ca → m/c site as endo Cx

* seen in young ♀

* more common in OCP use

* 9/10 HPV IS

◦ m/c complaint in Ca Cx → irregular bleeding

most specific complaint → post coital bleeding.

m/m : * post coital bleeding only → pap smear ⁺⁺⁺ → colposcopy

* post coital bleeding ± growth → punch Bx

m/c in Ca Cx

◦ age - 35 - 39 yrs / 5th - 6th decade

◦ m/c route of spread - lymphatic

◦ site of met - obturator LN

◦ sentinel LN - paracervical / ~~uterine~~ uterine LN

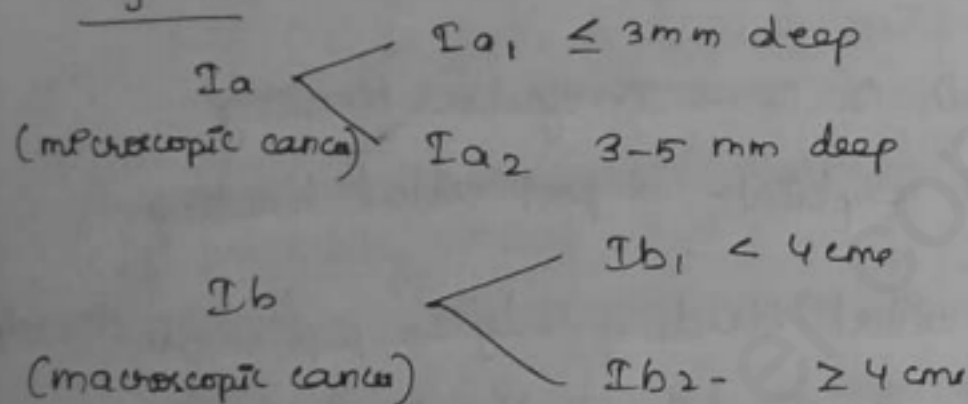
◦ m/c site of met in hematogenous spread - lungs

* sentinel LN assessment is very useful in → vulval carcinoma

FIGO staging

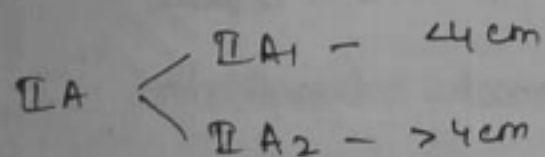
- Investigations not recommended by FIGO $\rightarrow$ USG, MRI, CT, PET
- CT approved only to look for hydronephrosis
- Investigations like X ray, IVP etc are recommended by FIGO

Stage I $\rightarrow$ cancer confined to cx



Stage II - cancer involving upper $\frac{2}{3}$ of vagina

IIA - parametrium not involved



IIB $\rightarrow$ parametrium involved

Stage III - Ca involving lower $\frac{1}{3}$ of vagina

IIIA - pelvic sidewall ~~involved~~ not involved

IIIB - pelvic sidewall involved / hydronephrosis / hydroureter

IV A - local spread - bladder / bowel

B → distant met / inguinal LN involved

↓

only LN τ $\leq$ staging is changed

- Ca Cr rarely spreads to ovaries → no need of oophorectomy
- m/c of death in Ca Cr - uremia / renal failure
- ureter & kidney are involved in stage 3B of Ca, but bladder in stage 4A
- Met $\otimes$ prognostic marker in Ca Cr - stage > LN

Types of hysterectomy

structures removed

- Simple / type 1 → ~~total~~ uterus + Cr
- Wertheim / type 2 } → uterus + Cr + 1 cm vagina +
modified radical } medial half of cardinal & uterosacral
ligament + uterine artery after it has
given branch to ureter + selective
removal of enlarged LN
- Type III / melage / radical → uterus + Cr + 2 cm vagina + whole
of cardinal & uterosacral ligament +
whole uterine artery + pelvic & para
aortic lymphadenectomy

④ Type IV → same like type 3 but upper $3/4^{\text{th}}$ of vagina removed + perineal fissure + superior vesical A.

⑤ Type V (rarely done) → Type 4 + distal ureter & bladder also removed

* Highest R/o ureteric injury is Wertheim's hysterectomy
ureteric injury is m/c in simple hysterectomy

M/m of Ca Cx :

• all stages are radiosensitive, but Sy can be done only upto stage 2A.

• Stage 1A1 - 1B1 ⇒ Sy

1A1 → conization / simple hysterectomy

1A2 → Wertheim's

1B1 → radical hysterectomy

Advantage of Sy - ovaries preserved, less vaginal fibrosis, coital fn retained

• m/c Sy done is radical / Wertheim's

• Radical trachelectomy - removal of 80% Cr, parametria, 1cm vaginal cuff + pelvic LN. later if the p becomes pregnant, deliver by CS as vagina & uterus left are stitched

Radical trachelectomy is an option for women in stage 1A1, 1A2 & 1B1 disease if Ca is $< 2\text{cm}$ in who desire uterine preservation & fertility

from stage 1B2 - IV

- Radiotherapy & cisplatin as radiosensitiser
- So TCC - chemoradiation
- CIS & stage 1A1 & LVSI absent
 - Young ♀ → conization
 - old → simple hysterectomy (TAH + BSO)
- Stage 1A1 & LVSI present & stage 1A2
- * Family not complete - radical trachelectomy & pelvic lymphadenectomy
- * Sy - Wertheims + pelvic lymphadenectomy (PL)

Stage 1B1

- Family complete → Type 3 / merge (radical + PL & paraaortic sampling)
- Not complete $\left\{ \begin{array}{l} \text{tumor } < 2\text{cm} - \text{trachelectomy} \\ \text{big} - \text{hysterectomy} \end{array} \right.$

Postoperative m/m - done in all cases except stage 1A1

- If 3P's present → i) involvement of parametria
ii) +ve LN
iii) +ve margin

post op m/m of choice → chemoradiation

o If 3S are present

- large tumor size
- stromal invasion > 1 cm
- LV ≤ 1 (lymph vascular space invasion)

post op m/m of choice $\rightarrow$ radiotherapy

Radiotherapy for Ca Cy

① Teletherapy (EBRT)

- * go to ↓ size of tumor foll by brachytherapy
- * isotope used - cesium

② pelvic radiation -

① extended field rdn includes pelvic & para aortic LN

⑤ Brachytherapy

- isotope $\rightarrow$ low dose rate tech - cesium 137
- high " " " - iridium 192

	Point A	Point B
location	2cm above & 2cm lateral to external os	2cm above & 5cm lateral to external os
structures present	paracervical / parametrial LN	obturator LN
Dose	early stage 80 Gy to 85 Gy locally advanced $\rightarrow$ 85-90 Gy	50 - 55 Gy $\rightarrow$ early stage 55 - 60 Gy $\rightarrow$ late stage

o If 1st Ca Rx by surgery, recurrent is Rx by chemoradiation

o If 2nd Ca " " chemo ? radiation $\rightarrow$ recurrent Ca

- operable $\rightarrow$ pelvic exenteration
- Inoperable $\rightarrow$ palliative chemotherapy - cisplatin & paclitaxel

Endometrial hyperplasia & carcinomaEndometrial hyperplasia

- Estrogen dependant (long term unopposed estrogen is most (X) cause)

Utter cause of postmenopausal bleeding (PMB):

i) endometrial atrophy (m/c) ii) endometrial hyperplasia

iii) HRT

iv) endometrial polyps

v) endometrial Ca

→ corpus cancer syndrome

RF: late menopause, nulliparous, PCOS, obesity, DM, HT, tamoxifen, unopposed estrogen therapy, family history of breast, ovary, colon/endometrium, rdn menopause

Types:

◦ simple (cystic without atypia)

— 1

◦ complex (adenomatous without atypia)

— 3

◦ simple (cystic + atypia)

— 8

◦ complex (adenomatous + atypia)

— 29

progression to Ca (%)

Histopathology:Simple hyperplasia

- glands large, cystic + ↑ gland to stromal ratio
- glands lined by columnar
- stroma - sparsely cellular
- scanty mitosis

characteristics of atypia

- cells large & irregular
- loss of polarity
- hyperchromatic nucleus + prominent nucleolus
- altered nuclear cytoplasmic ratio

Complex hyperplasia

- glands → ↑ in size & no.
- overcrowding of glands
- pseudostratified columnar
- stroma - densely cellular
- numerous mitoses

Δ :

$S_x \rightarrow$ AUB or PMB

$\Delta \rightarrow$ fractional curettage & histology

R_0 : depends on age & type

Simple/complex hyperplasia without atypia

R/O progression to Ca is low

Young $\rightarrow$ cyclic progestogen therapy for 6 months

- MPA for 21 days a month 3-6 months

- progesterone IUD

o follow up after 6 months by endometrial sampling

peri & post menopausal $\rightarrow$ o cyclic/continuous progestin therapy or
o hysterectomy

Simple/complex $\bar{e}$ atypia: (Also malignancy - high)

postmenopausal $R_0 \rightarrow$ hysterectomy^a

young women $\rightarrow$ o high dose progestin therapy (Megestrol)^a
o endometrial sampling every 6 months

Role of screening (not as effective as CIN)

methods $\rightarrow$ TVS, endometrial aspiration (Bx), vaginal pool smears

Endometrial carcinoma

• genital malignancy in developed countries $\rightarrow$ Ca endometrium > ovary
developing $\rightarrow$ Ca cx > ovary > endometrium^a

• mostly in post menopausal (55-70 yrs)

• 10% $\bar{e}$ PMB have Ca endometrium (EM)

RF: same as for endometrial hyperplasia + atypical EM hyperplasia^a

Protective factors: OCPs, progesterone therapy, multiparity, physical exercise

Mode of spread:

- Direct spread → myometrium, serosa, adnexa, Cx, parametrium
- Lymphatic " → occurs late to pelvic & para aortic nodes
- LN involvement is most (X) prognostic factor
- Inguinal nodes - involved in stage IV

CF:

- m/c Sx in perimenopausal → Irregular vaginal bleeding
- " " " post " → PMB
- watery offensive discharge → hydrometra / pyometra
- Referred pain in hypogastric region - Sampson's pain
- BME - uterus atrophic / (N) size / enlarged

Δ:

- HPE of endometrium → diagnostic
- 1st inv in PMB → TVS

Features suggestive of Ca

- endometrial thickness $\geq 5\text{mm}$ (ET)
- fluid within cavity
- echogenic EM
- red vascularity
- ✦ ET $< 5\text{mm}$ → review after 3 months / If bleeding recurs
- ✦ ET $\geq 5\text{mm}$ → EM sampling

Methods for EM sampling

- EM aspiration - OPD procedure
- Fractional curettage → gold std
→ endometrial curettage foll by dilatation & EM curettage
- Hysteroscopic Bx → direct visualisation & targeted Bx
→ Tx = focal lesions / focal thickening

• Pap smear → not reliable in 10% of cases

HPE types

- adenocarcinoma (endometrioid 80%) - m/c
- adenosquamous Ca - 15%
- papillary serous Ca (5-10%)
- mucinous adenocarcinoma (5%)
- clear cell adenocarcinoma (<5%) → most malignant = worst prognosis

Other inv → CT - myometrial invasion & LN mets
MRI → best inv for "

Staging

- FIGO revised staging (2009)
- changes in all stages except stage IV
- surgical pathological staging

Stage I → tumor confined to uterus

IA → $< 1/2$ of myometrial invasion

IB → $\geq 1/2$ of " "



Stage II → invades cervical stroma, not beyond uter

II → local and/or regional spread of tumor

IIA → invades serosa of uterus &/or adnexae

IIB → vaginal &/or parametrial involvement

IIIC → mets to pelvic &/or para aortic LN

Stage IV → involves bladder &/or bowel mucosa &/or

IVA → invasion of bladder &/or bowel mucosa

IVB → distant mets, including intraabdominal mets &/or inguinal LN

Diagnostic factors

- Metastasis in LN mets
- age ↑, stage of dis, histologic type <
 - adeno Ca → good prognosis
 - clear cell Ca → worst
- histological grade - grade III - poor prognosis
- myometrial involvement & extension to Cx → poor prognosis
- tumor size > 2cm → ↑ LN mets
- hormone receptor status (+ve → better)
- ploidy status (aneuploid tumors → poor prognosis compared to diploid)
- HER-2/neu → poor prognosis
- +ve peritoneal cytology → controversial role (removed now)

Management

- Surgical staging
 - TAH + BSO + pelvic & para aortic LN sampling &
 - clear cell & papillary serous Ca → omentectomy & peritoneal Bx in addition &
- most pts Pd in early stages → Sy is 1st line &
- adjuvant RT following Sy to prevent recurrence &
- Tx for pelvic & para aortic LN sampling &
 - clear cell, papillary serous, squamous Ca
 - adeno Ca Gr III
 - > 1/2 of myometrial invasion
 - extra uterine spread
 - tumor size > 2cm (only pelvic lymphadenectomy in absence of others)
- stages & tx:
 - Endometrioid Ca stage Ia (Gr I & II) → TAH + BSO + pelvic & paraaortic LN sampling. No post op therapy req

- Endometroid & stage Ia (Gn II), Ib $\rightarrow$ TAH + BSO + pelvic & para aortic LN dissection foll by post op RT
- Stage II $\rightarrow$ MRH + pelvic & para aortic LN dissection foll by post op RT
(mod. rad. hysterectomy)
- III & IV $\rightarrow$
 - debulking surgery foll by chemo $\pm$ RT or
 - chemo foll by RT or RT foll by Sy.

choice of post op RT:

- Gn III $\rightarrow$ vaginal vault radn
- adnexa, parametrial, pelvic LN inv $\rightarrow$ whole pelvis EBRT
- para aortic LN inv $\rightarrow$ extended field RT

et drug: cisplatin, carboplatin, adriamycin, paclitaxel

Recurrent EM Ca

- m/c within 1st 2 yrs of Rx
- m/c sites of recurrence $\rightarrow$ vagina & pelvis
- m/c Sy " " $\rightarrow$ vaginal bleeding

M/m:

- Hormone receptor +ve $\rightarrow$ progesterone / tamoxifen
- RT for isolated recurrence
- If local therapy cannot be gn $\rightarrow$ palliative Ct

Ovarian mass

- Non neoplastic & neoplastic

Non neoplastic or Functional cysts

Features :

- related to temporary hormonal disturbances

- not 75-80%
- unilocular
- contains clear fluid
- asymptomatic
- usually regress spontaneously

Functional cysts → follicular cyst (m/c)

corpus luteal cyst

theca lutein & granulosa lutein cyst

Follicular cyst

- m/c
- d/t hyperestrogenism
- < 5 cm
- single / multiple; lined by granulosa cells
- o/w ~~low~~ EM hyperplasia & fibrosis
- OCP prevent formation of new cyst

Corpus luteal cyst

- d/t overactivity of corpus luteum → hemorrhage inside corpus luteum
- may rupture → intraperitoneal hemorrhage (simulate ruptured ectopic)
- USG - cob web appearance
- may p/w amenorrhea / pregnancy
- spontaneous regression

uterine cyst

- a/w excess HCG like molar pregnancy, chorio G, domiphen therapy
- B/L
- local pain
- conservative m/m

Ovarian tumours

- 2nd common genital malignancy
- 80% benign & 20% malign
- 90% malignant tumours are 1° & 10% are 2°
- 80% are epithelial ovarian tumours, 90% of $\leq$ are benign
- 20% " non " " "

Classification

- epithelial ovarian tumour
- germ cell T
- sex cord stromal T

Epithelial tumours → benign / borderline malign / malign

- derived from surface epithelium
- ^(m/c) serous (75%), mucinous (10%), endometrioid (10%), Brenner, clear cell, mixed epithelial

Sex cord stromal T:

- derived from ovarian stroma or mesenchyme
- secrete male or ♀ hormones
- granulosa cell, theca cell T → estrogen secreting
- Sertoli cell, Leydig cell T → androgen "
- gynandroblastomas

- derived from primordial germ cells of ovary
- dysgerminoma, teratoma, yolk sac tumor, chorio ca, embryonal ca, polyembryoma

Benign ovarian T (ovarian cysts)

① Serous cystadenoma

- m/c benign epithelial tumor of ovary
- HPE - psammoma bodies
- arise from surface epithelium of ovary

② Mucinous cystadenoma

- arise from surface epithelium
- 10% BL, 10% malignancy risk
- largest benign ovarian T
- cut section - honey comb pattern
- also pseudomyxoma peritonei

③ Dermoid cyst (teratoma)

- arise from germ cells
- m/c germ cell tumor
- m/c benign ovarian tumour
- m/c " " " in reproductive age
- m/c " " " in pregnancy
- contain derivatives of ecto, endo & mesoderm
- m/c → ectoderm
- contain hair, teeth, bone, cartilage, neural & thyroid tissue
- Rokitansky protuberance - area of localized projection from s. teeth, bone & hair project
- m/c → 15 to 20%
- m/c malign → 1 to 2%

• follicular hyperplasia → hyperechoic nodule
 • white ball app & dot and dash app → d/t hair in cyst

X-ray pelvis → teeth & calcification (radioopaque)

- SCC → m/c malignancy arising in dermoid cyst (1-2% risk)
- m/c c/c → torsion (mostly during pregnancy)
- struma ovarii → contain thyroid tissue
- Struma carcinoid → " serotonin & bradykinin from argentaffin cells
- Meigs syndr - fibroma of ovary + ascites + @ PE
- Pseudo meigs syndr - ascites & PE occur w Brenner's tumor, thecoma & granulosa cell tumor
- Benign solid ovarian T → Brenner's, fibroma (m/c)

c/c of ovarian T:

- Torsion → dermoid cyst & serous cystadenoma
 if gangrenous → ovariectomy
 - intra cystic hemorrhage → rupture d/t trauma/spontaneous/ANE
 - Infection
 - pseudomyxoma peritonei → mucinous ascites 2° mucinous cystadenoma & cystadenocarc of ovary, mucocoele of appendix/GIB
 → poor prognosis
 → recurrence
 → Rx ⇒ TAH + BSO + removal of mucin, peritoneal implants & appendectomy
 - Malignancy (max in papillary serous cystadenoma & least in dermoid)
- M/m of adnexal cyst:
- asymptomatic simple ovarian cysts < 5cm → often physiological & resolve
 - 5-8cm, u/c, mobile, cystic → OCB, follow up in 3-6 months if doubt remains

o cysts > 3cm, Irregular, B/C, fixed, postmenopausal → further imaging & Rx.

Paraovarian cyst

- o arise from vaginal remnants of Wolffian duct in mesosalpinx or from peritoneal inclusion
- o unilocular, contain clear fluid
- o USG → ovary visualised separately from cyst
- o always benign
- o can undergo torsion
- o Rx → enucleation of cyst, ovaries are preserved

Malignant ovarian tumours

- o m/c → epithelial tumour
- o m/c malignant → serous cystadenocarcinoma

o 5-10% hereditary predisposition

- o epithelial tumour → also p53 (aggression & m/c gene) & K-Ras gene mutation

RF: 50-70yrs, early menarche, late menopause, obese, nulliparous, family Hx ovarian, breast, EM & colon CA (hereditary ovarian cancer)

Protective factors: multiparity, Breast feeding, OCPs (used for 5yrs -50% reduction)

o ~~Hereditary~~

* Familial ovarian cancer syndrome

i) Lynch II syndr | HNPCC

ii) hereditary breast-ovarian cancer syndr → also BRCA 1 (chr 17) & BRCA 2 (chr 13)
→ AD inheritance

Malignant epithelial ovarian tumours

- CLF → • present in advanced stages & non specific Sx
- vague Sx → abd discomfort, bloating, dyspepsia, loss of wt & appetite

	Benign	Malign
• age	younger	extremes of age
• duration & progression	slow	fast
• ascitic Sx	-	+
• palpation	smooth, well defined border, cystic, mobile	irregular, ill defined border, variable consistency, restricted mobility
• site	U/L	B/L
• ascites	-	+
• POD deposits	-	+
<u>USG</u>	U/L unilocular thin cyst wall thin septations anechoic no ascites high @ flow in Doppler	B/L multilocular thick thick mixed echogenicity d/t solid areas papillary projections, ascites, EFD low @ flow pattern in Doppler

RMI malignancy index (RMI)

- calculated based on → USG features, menopausal status & CA125 levels
- women & RMI score > 200 → refer to oncology centre (multiply all 3)
- [Reed index is for CA ex]

Pattern of spread:

- m/c → exfoliation of cancer cells & implantation in peritoneal cavity (transcoelomic spread)
- less common — lymphatic & hematogenous

Δ: staging laparoscopy is diagnostic

Tumor markers

- ↑ CA 125 in non mucinous epithelial ovarian tumors ($CA < 35 U/ml$)
also elevated in PID, endometriosis, adenomyosis, genital TB, fibroid, endometrial CA, colon, breast, pancreas, lung CA

FIGO staging (surgical staging)

Stage I: Tumor confined to ovaries

IA → limited to one ovary. No tumor on external surface, capsule intact & -ve ~~intra~~ peritoneal washings

IB → both ovaries, no tumor on same as above

IC → one / both ovaries ± tumor on ext. surface of ovaries / capsule rupture / malign ascites / +ve peritoneal washings

Stage II → Involves 1 or both ovaries ± pelvic extension

IIA → extension to uterus / FT

IIB → other pelvic tissues extension

IIC → IIA / IIB ± tumor on ext surface of ovaries / capsule rupture / malign ascites / +ve peritoneal washings

Stage III - one / both ovaries - important outside peritoneal

retroperitoneal nodes; serosal liver mets equals Stage III

III A → histologically confirmed microscopic deposits of abd / peritoneal surface ± +ve retroperitoneal nodes

III B → macroscopic deposits $\leq 2\text{cm}$

III C → $> 2\text{cm}$

Stage IV → one / both ovaries - distant mets

IV A → PE ± +ve cytology

IV B → parenchymal liver mets $\neq$ or +ve inguinal nodes

Q:

• Stage IA, Gr I (low grade, low risk)

* surgical staging - TAH + BSO + pelvic & para aortic LN sampling ± infracolic omentectomy.
No post op Rx req

* uterus & CL ovary can be preserved in young women
± follow up

• Stage IA (Gr II & III), stage IB & IC (high gr. high risk)

* surgical staging foll by post op ct

* chemo → cisplatin / carboplatin + paclitaxel - 6 cycles

• Stage II, III, IV → 1^o cytoreductive / debulking sy foll by post op chemo for 6 cycles

Optimum debulking / cytoreduction → when diameter of residual tumour nodules is $< 1\text{cm}$

Neoadjuvant chemo → initial chemo foll by interval debulking sy in pts in whom optimum debulking may not be possible

Benefits of cytoreduction

- ↑ chemo sensitivity
- improves immune fn
- post op surveillance - physical ex, CA-125, periodic CT scan
- 2nd look laparotomy → to determine response to therapy in pt with no evidence of disease clinically
- 2nd debulking → done for recurrence / persistent d/s after 1st

Progressive / persistent d/s : disease free interval < 6 months till 1st

Recurrence : > 6 months interval

Other tx : intra peritoneal ct, Immunotherapy (interferons & mab like Herceptin), hormonal therapy → progestogens

- RT → only palliative

Dysgerminoma

- m/c malignant germ cell tumour
- corresponds to seminoma in ♂
- elastic rubbery consistency with smooth capsule
- m/c malign. ovarian T also pregnancy
- highly chemo & radio sensitive
- secretes placental ALP, LDH (X)
- malignant GCT with best prognosis

Mgmt of germ cell tumours (GCT)

- Sy → mainly t/f
- U/L salpingo oophorectomy
- post op chemo → BEP regime - bleomycin, etoposide, cisplatin
- all cases needs post op chemo except stage IA dysgerminoma & stage IA gr I immature teratomas

Sex cord stromal tumours

- least common
- U/L
- m/c in perimenopausal age
- feminizing + → granulosa cell, theca cell T
- androgen secreting tumor - sertoli, Leydig cell T

Granulosa cell tumour

- secretes estrogen
- cf - children - precocious puberty
adults - amenorrhea followed by prolonged bleeding
PMB
- also EM hyperplasia in 25-50% (X)
- HPE - Call Exner bodies & coffee bean nucleus
- m/m → Sy → U/L so in young
 - endometrial sampling
 - ~~post op chemo~~
 - post menopausal → TAH+BSO
 - post op chemo - BEP regime

• Role of conservative surgery in young ♀:

- ULC SO can be done in - Stage I epithelial ovarian cancer (Gr I)
- stage I GCT
- ULC sex cord stromal tumours

Metastatic tumours

- mets to ovary is mostly from 1° in GIT
- mostly BL
- spread is transcoelomic or retrograde lymphatics

Krukenberg's tumour

- met from 1° in stomach > bowel > breast
- always BL
- characteristic signet ring cells in HPE
- mets by retrograde lymphatics
- capsule intact, smooth, no adhesions, freely mobile, solid waxy consistency.

Turner markers

- | | |
|-----------------------------|-------------------------------|
| • dysgerminoma | - placental ALP, LDH |
| • yolk sac T | - AFP, α 1 antitrypsin |
| • embryonal CA | - HCG, AFP |
| • polyembryoma | - HCG, AFP |
| • chorio CA | - HCG |
| • Teratoma | - - |
| • granulosa cell T | - inhibin |
| • non mucinous epithelial G | - CA 125 |
| • mucinous " | - CEA, CA 19-9 |

Histological characteristics

- papillary cystadenoma - psammoma bodies
- Brenner's - Walthard's cell nest (BMW)
- clear cell T - hobnail cells
- Dysgerminoma - large polygonal cells = lymphocyte infiltration, fibrous septa
- Yolk sac T - Schiller-Duval bodies
- Granulosa cell T - call exner bodies, coffee bean nucleus
- Leydig cell T - Reinke's crystal
- Krukenberg tumour - signet ring cells

Borderline ovarian tumours (BOT) / low malignant potential

- 30-50 yrs
- no stromal invasion
- mitotic figures $< 4/10$ HPF
- 90% survival rate
- serous type (m/c) > mucinous

H/m - staging laparotomy

- frozen section → if BOT +ve
- * completed family - TAH + BSO
- * not " " - U/C ovariectomy
- LN sampling not req

H/m in familial ovarian cancer

◦ genetic counselling, BRCA 1 & BRCA 2 genetic mapping

- Follow up w/ TVS & CA125
- OCPs

• family completed at latter 35 yrs → prophylactic SO (X)
most factor

- annual mammography after 30 yrs
- OCPs for ≥ 5 yrs $\rightarrow$ $\downarrow$ risk by 50%
- 2 children + OCPs ≥ 5 yrs $\rightarrow$ $\downarrow$ risk by 70%
- prophylactic oophorectomy on family completion $\rightarrow$ only in familial ovarian cancer