Gynae Endocrine

1. Amenorrhea 1

2. Amenorrhea 2

3. Precocious Puberty

4. PCOS

5. Disorders of Sexual Development

Precocious Puberty

DEFINITION

Personal Notes

- Development of secondary sexual characteristics before 8 years of age in a girl or menarche before 10 years of age.
- It is 20 times more common in girls
- 70-80% are idiopathic
- There is early secretion of sex hormones: estrogens or androgens

Types of precocious puberty:

- Central/True/GnRH dependent precocious puberty - It affects the central hypothalamo pituitary ovarian axis. This follows the physiology of normal puberty.
- Peripheral/GnRH independent precocious pseudopuberty - this doesn't follow the rules of physiology

INCOMPLETE PRECIOUS PUBERTY

- Complete puberty: Growth spurt + Thelarche + Adrenarche + Menarche.
- Incomplete puberty:
  - Isolated thelarche <8 years - Due to excess estrogen which may be because of an estrogen secreting tumor.
  - Isolated adrenarche <8 years - Excess androgens due to androgen secreting tumor.
  - Isolated menarche <10 years - Excess estrogen + progesterone.

Causes:

- Most common cause of central precocious puberty is idiopathic.
- Hypothalamic causes - Hypothalamic hamartomas which are often responsible for seizures, developmental delays and laughing/gelastic seizures.
- Causes of Peripheral origin precocious puberty - Ovarian tumors (benign or malignant) which are hormone secreting.
- Benign - McCune-Albright Syndrome which has a triad of precocious pseudopuberty, café-au-lait spots and fibrous dysplasia of bone.
- Malignant - Granulosa cell tumor, theca cell tumors or leydig cell tumors.
- Non classical congenital adrenal hyperplasia
- Adrenal tumors

Evaluation of precocious puberty:

- If the H-P-O axis is intact then most likely it is a complete precocious puberty.
- Hormone secreting tumors - Incomplete precocious puberty.

Personal Notes

- M/c cause is idiopathic so, it is important to take the history of mother or sister, age of menarche.
- Other symptoms like hirsutism, acne, deepening of voice.
- Examine secondary sexual characters and ambiguous genitals.

Lab evaluation:

- If suspecting androgen secondary tumor then check for levels of testosterone, DHEAS or DHT.
- CAH: 17-OHP
- Estrogen secreting tumor: FSH, E2
- GnRH stimulation test

Imaging:

- Bone radiograph of wrist of non dominant hand
- MRI brain to rule out hypothalamic tumors
- Additional imaging - USG pelvis, USG KUB to look at the adrenals.

Treatment:

- Remove the tumor if any, causing hormone secretion
- In case of CAH: exogenous steroids
- In central precocious puberty halt puberty till 11 years of age by giving GnRH analogues, leuprolide, goserelin or triptorelin.

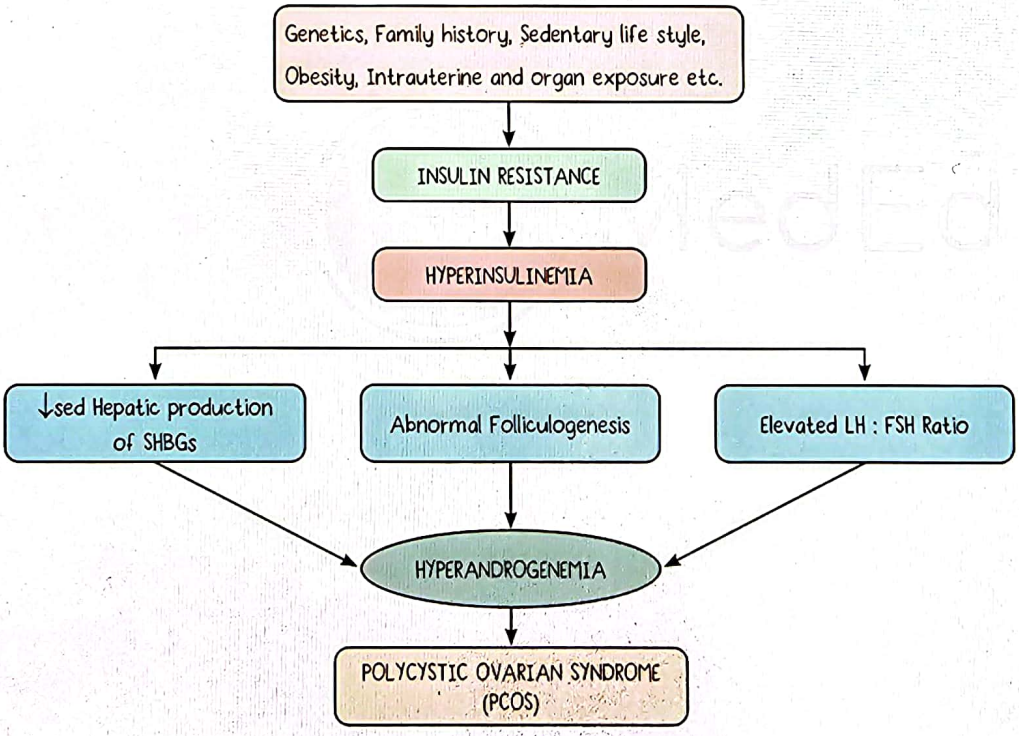
Gynae Endocrine PCOS

POLYCYSTIC OVARIAN SYNDROME

Personal Notes

- Misnomer: No cyst in the ovary
- Syndrome of endocrinological imbalance with increased androgen and E1 (estrone), increase LH and decrease progesterone and FSH.
- Increase in insulin due to insulin resistance
- DM-2, obesity, metabolic disorders overlap with PCOS

PATHOPHYSIOLOGY



Insulin resistance

↓

Increase amount of insulin

↓

Decreased production of SHBG

↓

Less androgen are being bound by the globulin

↓

Free circulating androgen

Insulin like growth factors increased

↓

Hypertrophy of Theca cells of the ovary

↓

LH increased and induces production androgen

↓

Theca cells do not have any mechanism to convert it into estrogen so androgen is transported to the granulosa cell

↓

Due to enzyme aromatase androgens are converted into estradiol but amount of androgen>>>aromatase and less E2 is produced

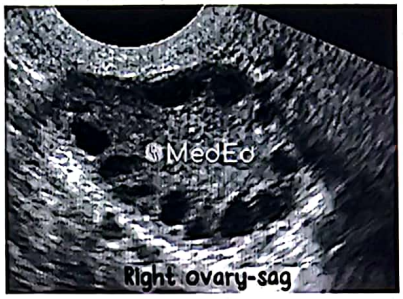
- High LH produces more androgen
- Insulin also stimulates IGF-1 so it produces more androgen
- Androgen goes to adipose tissue which also has aromatase
- Androgen is converted into E1 (estrone)
- More E1 and less E2
- E1 causes endometrial hyperplasia in the uterus
- E1 sending negative feedback to the pituitary and decreasing FSH
- Dominant follicles do not develop due to decreased FSH (anovulation).
- Multiple follicles of small size (low FSH)
- Because of excessive stimulation of Theca cells, ovaries are bulky (Increase size of Theca cells) (Thick central stroma).

CLINICAL FEATURES

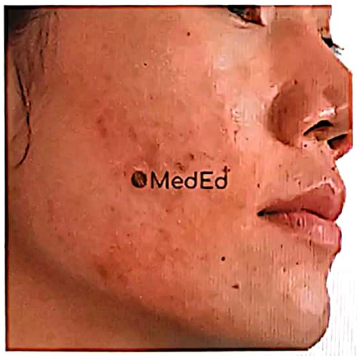
- Decreased FSH and increase E1 and LH
- Anovulation
- E1 will cause endometrial hyperplasia
- Endometrium undergo hyperplasia and keep on growing thicker till the time of blood supply of endometrium no longer able to keep up with this increased growth and this is going to cause a necrosis and sloughing of the endometrium.
- Irregular and infrequent bleeding
- Heavy menstrual bleeding
- Earlier called oligomenorrhea
- Overproduction of androgens causing virilizing features like acne, hirsutism and androgenetic alopecia.
- Metabolic disorders
- USG: bulky ovary more than 10 cc in size and at least have 12 small peripherally arranged follicles and central thick stroma.
- Necklace sign

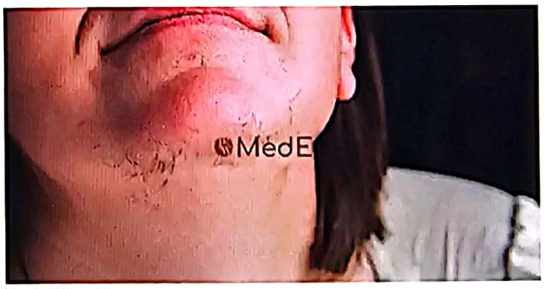
TRIAD OF PCOS

- Oligomenorrhea
- USG features: > 10 cc size and at least 12 follicles and thick central stroma. (string on pearls or necklace sign)
- Hyperandrogenemia (clinically or laboratory values)



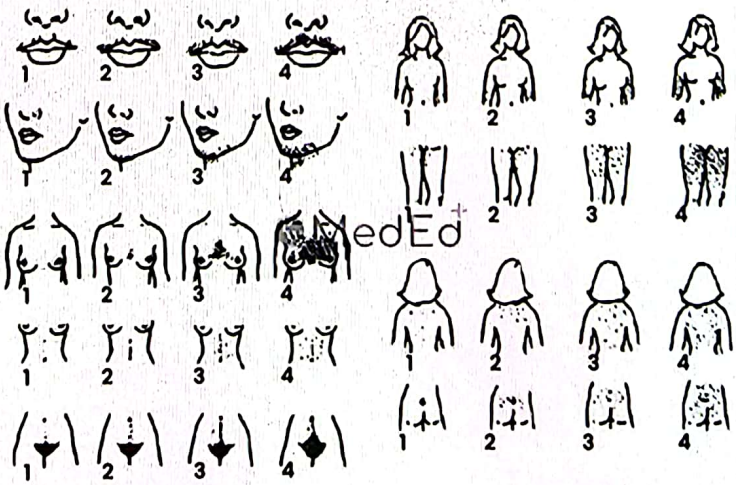
Necklace appearance





DIAGNOSIS

- Rotterdam criteria
- At least 2 out of 3 must be present
- In adolescence, all 3 criteria must be present



Modified FG (ferriman gallery) score

Personal Notes

- Score >8: hirsutism
- 9 area * 4 = 36
- Upper lip
- Chin
- Chest
- Upper abdomen
- Lower abdomen
- Upper back
- Lower back
- arms
- Thighs

PHENOTYPES

- PCOS - A: all three criteria
- PCOS - B: hyperandrogenism + oligomenorrhea
- PCOS - C: hyperandrogenism + USG features
- PCOS - D: oligomenorrhea + USG features

MANAGEMENT

- Lifestyle changes
  - Weight loss
  - Change in diet
  - Exercise (moderate in intensity, at least 30 to 45 minutes per day for at least 5 out of 7 days a week)
- Need to evaluate coexisting metabolic disorders
  - DM
  - HTN
  - Treatment: metformin, myoinositol
- Oligomenorrhea
  - COCs (combined oral contraceptive pills)
  - Acne or hirsutism: 3rd or 4th generation progesterone containing COCs like desogestrel.
  - No acne or hirsutism: MALA - N or any 2nd generation COCs
- Acne:
  - 3rd or 4th generation COCs
  - Dermatology evaluation
- Hirsutism:
  - 3rd or 4th generation COCs.
  - Antiandrogen like flutamide, finasteride
  - Topical preparation called eflornithine (inhibitor of ornithine decarboxylase).

Personal Notes

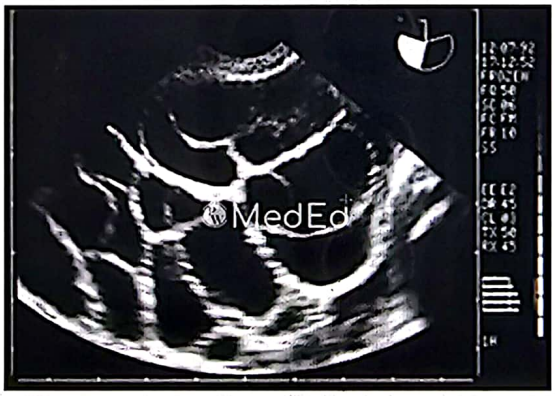
- Pharmacological treatment prevents new conversion of vellus hair to terminal hair but doesnot reduce already transformed hair.
- Already grown hair laser - treatment, epilation, depilation and threading.

- Infertility:
  - Ovulation induction - letrozole- first line
  - Surgical treatment: laparoscopic ovarian drilling

COMPLICATIONS OF PCOS

- Metabolic disorders (DM-2, HTN, obesity)
- Infertility
- Recurrent abortion
- Gestational D
- Endometrial hyperplasia
- Endometrial cancers

OHSS (ovarian hyperstimulation syndrome) is a rare complication of IVF cycles.



Ovarian hyperstimulation syndrome

- Enlarged multiple follicles
- Causative trigger: HCG
- Increased capillary permeability
- Estrogen very high (multiple follicles)
- VEGF increases
- Capillaries become leaky and fluid escapes to tissues leading to hemoconcentration and increased risk of DVT.
- Loss of fluid into third space leading to weight gain and ascites
- Decreased perfusion of kidney due to loss of intravascular fluid which can lead to prerenal acute kidney injury.

1. Mild
2. Moderate
3. Severe
4. Critical

Mild and moderate treated in OPD basis like weight measurement at home, AC measurement, serial hematocrit measurement and encouraging fluid intake.

Severe and critical associated with ascites, AKI, hemoconcentration. Need to be admitted.

Early	Late
o 3-7 days after HCG trigger o This is due to trigger	o 10-15 days later o Due to pregnancy (more HCG) o This needs admission

Prevention:

- Instead of HCG, use GnRH agonists as a trigger
- Cancel the cycle if estrogen is very high, which is more than 3000 pg/ml or more than 20 follicles are present.
- Use the GnRH antagonist protocol

Personal Notes

Gynae Endocrine Amenorrhea Part-1

PHYSIOLOGY OF NORMAL MENSTRUATION

Personal Notes

In girls:

Growth spurt

↓

Thelarche - breast development

↓

Pubarche /adrenarche - development of pubic or axillary hair

↓

Menarche - onset of menses usually happens 2-3 years after the onset of puberty

- Thelarche are primarily under the control of estrogens.
- Pubarche and menarche are primarily under the control of androgens.

AMENORRHEA

- Primary
- Secondary

Primary amenorrhea:

- Never had menstruation
- 15 years - amenorrhoea in the presence of secondary sexual characteristics
- 13 years - no secondary sexual characteristics + primary amenorrhoea

Secondary amenorrhea:

- Prior menses were present now amenorrhea
- When amenorrhea is present since last 6 months or amenorrhoea is present since the equivalent duration of > 3 menstrual cycles.

Causes of amenorrhoea:

- Hypothalamus secretes pulsatile GnRH which is stimulates the pituitary to release FSH and LH.
- It's acting upon ovaries.ovaries produce estrogen that is causing proliferation of endometrium.
- LH surge - ovulation.
- withdrawal of corpus luteum in the absence of pregnancy will cause the withdrawal of progesterone, endometrium will shed and cause menses.
- This process can be disturbed at any level.

- Hormonal imbalance (thyroid or prolactin hormone)
- Level of problem at hypothalamus (hypothalamic cause)
- Level of problem at pituitary (pituitary cause)
- Level of problem at ovary (ovarian/gonadal cause)
- Level of problem at uterus (uterine cause)
- Level of problem at outflow tract outflow tract cause)
- Most common cause of secondary amenorrhea is pregnancy

Approach to amenorrhoea

- History
- Other family members with amenorrhoea
- Any associated symptoms (cyclical abdominal pain)
- Any drug intake or history of any chemotherapy or radiotherapy.
- Personal habits
- Dietary habits
- Age of menarche and menopause in other female members of her family.
- Acne/hirsutism
- Any discharge from the nipple
- Any history of TB/D&C

Examination

- General condition
- BMI - height (short stature, Turner's syndrome) and weight (anorexic).
- Secondary sexual characteristics (any breast development and presence of pubic or axillary hair).
- Local examination: pubic hair and vagina (patent or blind vagina).
- Breast development due to estrogen
- Tanner's staging of breast development
- Any discharge from nipple

Local Examnination

Tanner's staging of pubic hair

Vagina: patent or blind vagina?

Blind or short vagina can be seen in:

- Complete absence of mullerian structure (usually blind vagina, only a dimple)
  - Mullerian agenesis (MRKH)
  - Androgen insensitivity syndrome
- Outflow tract obstruction
  - Imperforate hymen (blind vagina)
  - Transverse vaginal septum (variable vaginal length)
  - Cervical agenesis (vagina may be present or have variable length)
- USG can detect complete mullerian structure
- Outflow tract obstruction causes very severe cyclical abdominal pain.

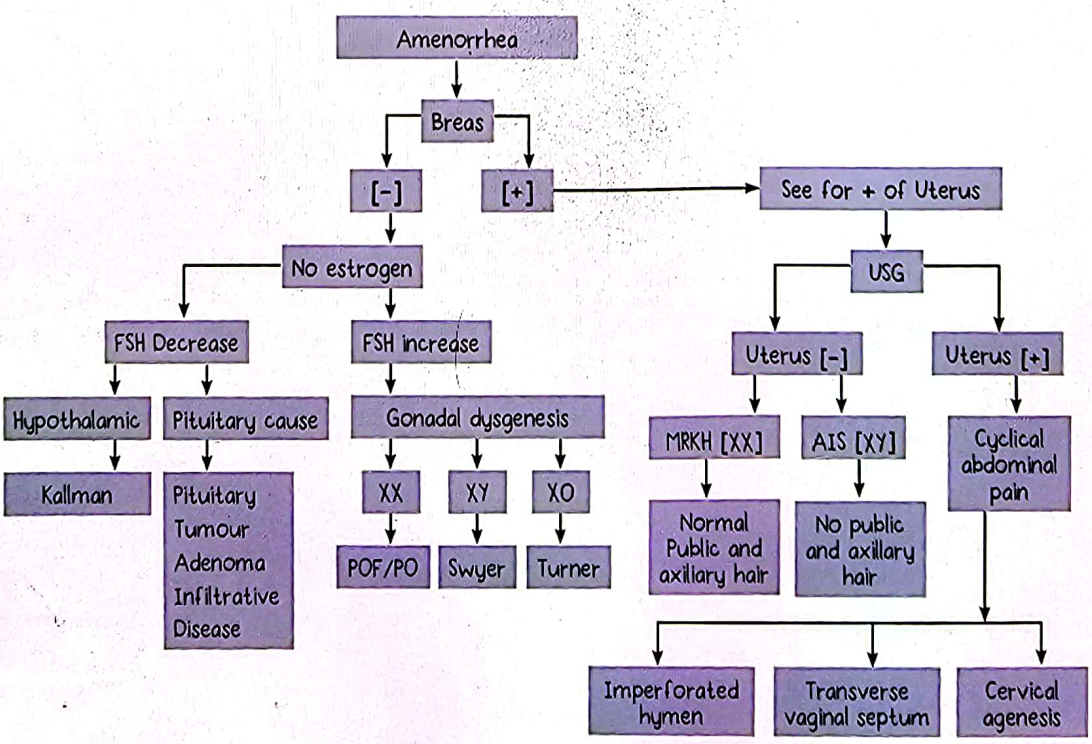
Investigations

- UPT: to rule out pregnancy
- CBC: chronic disease
- FSH and LH: state of pituitary or gonads/ovary.if the pituitary is non functioning low FSH and LH.
- if the gonads are defective, high FSH and LH
- Estradiol: less (problem is at the level of gonads)
- Free and total testosterone dehydroepiandrosterone: hirsutism (PCOS, CAH)
- TSH and prolactin: it will cause menstrual disturbance. after pregnancy, the most common cause of secondary amenorrhoea.
- Karyotype: Turner syndrome, androgen insensitivity, premature ovarian failure.
- Ultrasound pelvis/MRI pelvis: presence or absence of the mullerian structure.
- MRI brain: can detect structural anomalies like pituitary or hypothalamic tumor, empty sella syndrome.

Indications of karyotype testing:

- Diagnosis of Turner's syndrome (XO)
- Swyer syndrome (XY), androgen insensitivity syndrome, LH receptor defect (XY).
- Confusion of karyotype (MRKH-XX vs AIS-XY)
- Premature ovarian failure (before 40 year age)

PRIMARY AMENORRHOEA



Personal Notes

Evaluation of symptomatic primary amenorrhoea

Cyclical abdominal pain with primary amenorrhoea:

- Imperforate hymen:
  - In USG hematocolpos + hematometra
  - P/R examination: swelling anterior to anal verge
  - Treatment: cruciate incision
- Transverse vaginal septum
  - It can be present at any level. Low transverse vaginal septum, mid level or high transverse vaginal septum.
  - P/R examination: bulge will be felt anteriorly at a variable height above the anal verge.
  - In USG hematocolpos + hematometra
  - Treatment: transverse vaginal septum excision with jeffcoat vaginoplasty.
- Cervical agenesis
  - Failure of canalisation of cervical canal
  - Hematometra without hematocolpos. The distended uterus is palpable per abdomen
  - Cyclical abdominal pain
  - Later there can be development of hematosalpinx, endometriosis
  - Highest chances of restenosis after surgery so use foley's catheter or malecot catheter is placed in situ.
  - Treatment: cervico - vaginal anastomosis

MAYER ROKITANSKY KUSTER HAUSER SYNDROME

- Mullerian agenesis
- Absence of fallopian tube, uterus, cervix and upper 2/3 vagina
- Ovaries are normal
- Estrogen is normal
- Breasts are present
- Pubic and axillary hair normal

Examination: blind vagina

USG/MRI: absent uterus also finds renal abnormalities and skeletal abnormalities.

P/R: absent uterus

Reproductive potential:

- Adoption
- Surrogacy
- Counseling regarding prognosis of menstrual function (no menses) and sexual function.
  - McIndoe vaginoplasty
  - Should be planned 2-3 months before marriage
  - Vaginal dilators can also be used

NORMAL DEVELOPMENT OF MALE GENITALIA

Bipotential gonads

↓

To tendency to form ovaries unless Y chromosomes are present.

↓

XY - short arm of this Y chromosome contains the SRY gene which produces protein SOX - 9.

↓

It converts gonads into testes by forming sertoli cells and leydig cells.

↓

Sertoli cells secrete AMH which causes the mullerian duct to regress.

↓

Leydig cells stimulated by LH and secretes testosterone and it forms male internal genitalia.

↓

enzyme 5α-reductase converts testosterone into dihydrotestosterone. It converts bipotential external genitalia to male external genitalia.

SWYER SYNDROME

- Gonadal cells are non functional. (Gonadal dysgenesis)

Testes are not working

↓

Sertoli cells and leydig cells are not working

↓

AMH will not be secreted and AMH causes the regression of the mullerian duct.so mullerian duct persists

↓

Uterus, fallopian tubes, cervix and vagina (female internal genitalia present)

↓

No testosterone due to dysgenetic leydig cells- no male internal genitalia

↓

No DHT- no male external genitalia

↓

Typical presentation: Testes present as labial swelling or swelling in the inguinal canal + female internal genitalia + female external genitalia.

↓

There is some action of adrenal androgen and this leads to formation of axillary and pubic hair.

↓

No breast formation due to absence of estrogen

ANDROGEN INSENSITIVITY SYNDROME

Personal Notes

- Complete
- Incomplete: Clitoromegaly

Testes (present as labial swelling)

↓

Sertoli cells and leydig cells

↓

LH is high so testosterone and DHT is high

↓

End organ insensitivity

↓

There is no male internal genitalia, no male external genitalia, but also no uterus, fallopian tube, cervix and upper vagina (as sertoli cells are producing AMH).

↓

Female external genitalia present due to absence of DHT

↓

Typical presentation: Labial swelling + absence of male or female internal genitalia + absence of uterus, fallopian tube, cervix and upper vagina + presence of female external genitalia.

↓

Because of androgen insensitivity there is a lack of pubic and axillary hair.

↓

breasts develop because testosterone is in large quantities so it goes to adipose tissue and aromatization forms more estrogen.

Treatment:

	AIS	Swyer syndrome
Sex allocation	Prefer to continue as female	Prefer to continue as female
Counseling: Menstrual Sexual	No menses Vaginoplasty	Cyclical E + P causes menses Vagina present
Reproductive potency	Adoption	IVF with donor oocytes.
Retained Testes can form gonadoblastoma. So we need to do gonadectomy.	After puberty	As soon as diagnosis is made.

TURNER'S SYNDROME

- Gonadal dysgenesis (XO)
- Short stature
- Low posterior hairline
- Webbed neck
- Cubitus valgus
- Short 4th metacarpal
- Shield chest
- In USG Very small or atrophic ovaries (streak ovary), Uterus present

Personal Notes

Diagnosis:

- Karyotype

Treatment:

- Growth - GH from around 6 years of age and preferably till 12-13 years of age.
- Amenorrhoea - cyclical E + P
- Reproductive potential - Spontaneous conception in some or IVF with donor oocytes.

PREMATURE OVARIAN INSUFFICIENCY

- Gonadal dysgenesis (XX)
- Both primary and secondary amenorrhoea
- Ovarian reserve is depleted
- Menopausal symptoms

Diagnosis:

- High FSH
- FSH > 25 on 2 occasions at least 4 weeks apart
- Premature (before 40 years age)

Cause:

- Genetic abnormalities or mosaicism, fragile X premutation, autoimmune disease against ovarian antigen (thyroid, adrenal), exposure to chemotherapy or radiotherapy.

Treatment:

- For menses: E + P
- Screen other family members for autoimmune disease and genetic disorder
- IVF with donor oocytes

KALLMANN SYNDROME

- Hypothalamic disease
- Defective migration of GnRH secreting neurons.
- Olfactory neurons usually migrate along with GnRH secreting neurons
- Low GnRH causes low FSH causing amenorrhoea
- History of anosmia

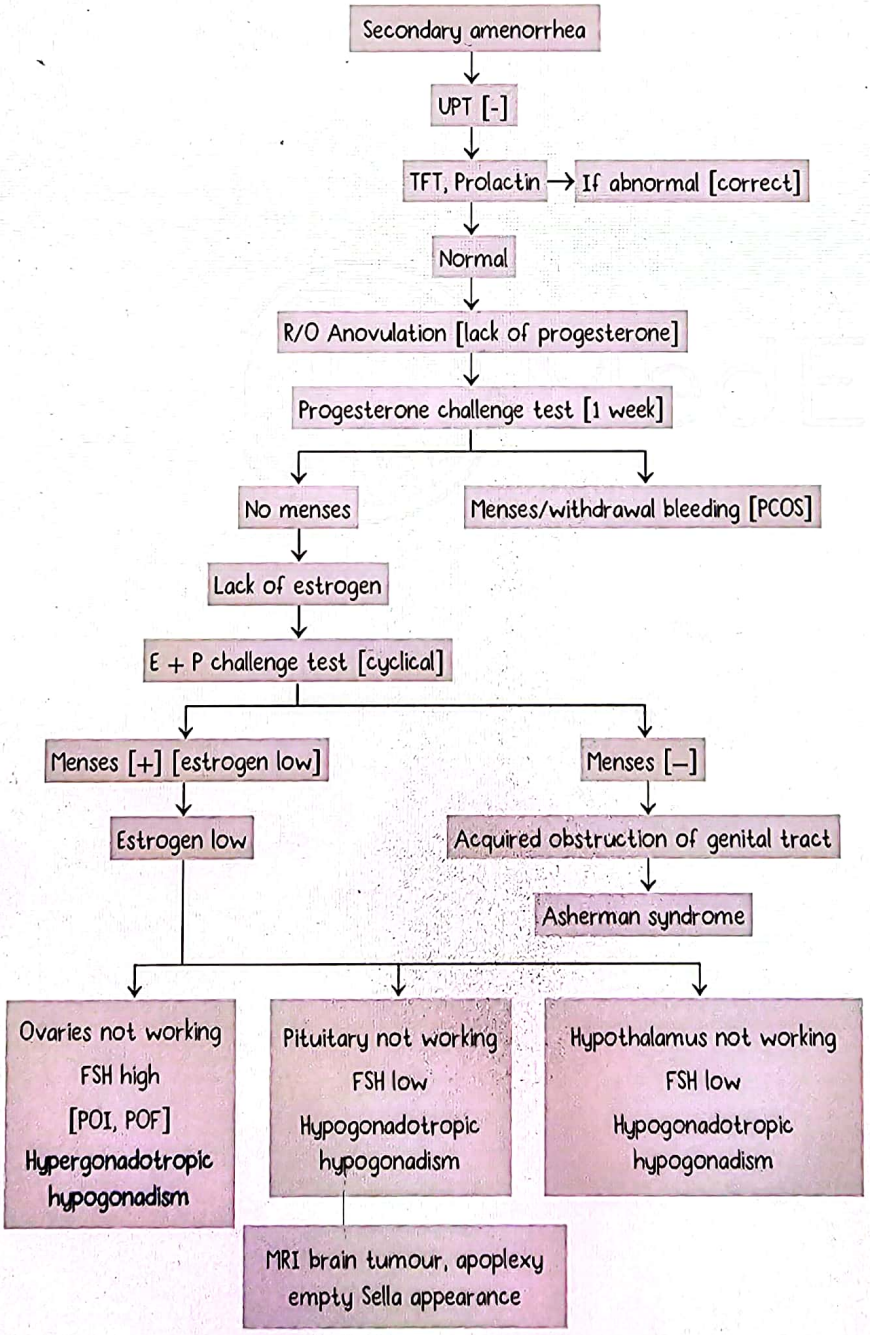
	MRKH	AIS	Swyer syndrome	Turner's syndrome
Breast	+	+	-	-
Public Hair	+	-	+	+
Vagina	Blind	Blind	+	+
Uterus	-	-	+	+
Height	Normal	Increased	Normal to increased	Short
Karyotypr	XX	XY	XY	XO
FSH	Nomral	LH increase	Increase	Increase
Testosterone	Female Level	Male Level	Female Level	Female Level

Gynae Endocrine
Amenorrhea Part-II

SECONDARY AMENORRHOEA

Personal Notes

- In a woman previously m enstruating
- Amenorrhoea > 6 months or > 3 cycles
- Most common cause of secondary amenorrhoea is pregnancy.



Personal Notes

- Hyperprolactinemia (treat with cabergoline), prolactin suppresses GnRH causing amenorrhea.

Hypogonadotropic hypogonadism:

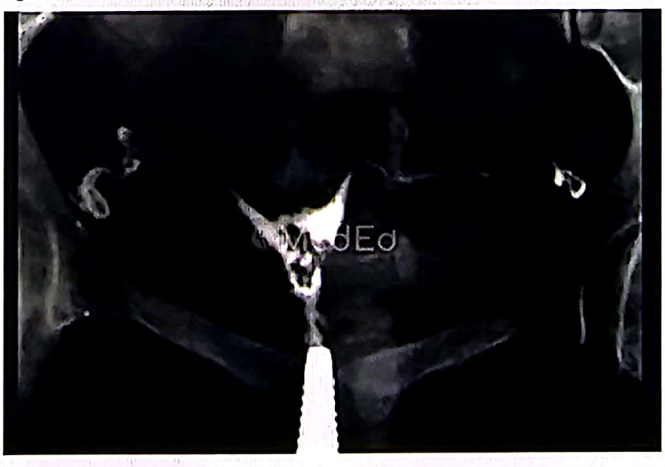
- FSH low
- Estrogen low
- Kallmann syndrome (Primary amenorrhoea)
- Functional hypothalamic causes, tumors of pituitary or hypothalamus, infiltrative disorders like sarcoidosis, pituitary apoplexy - Sheehan syndrome (secondary amenorrhoea).
- Treatment is E + P

Normogonadotropic hypogonadism:

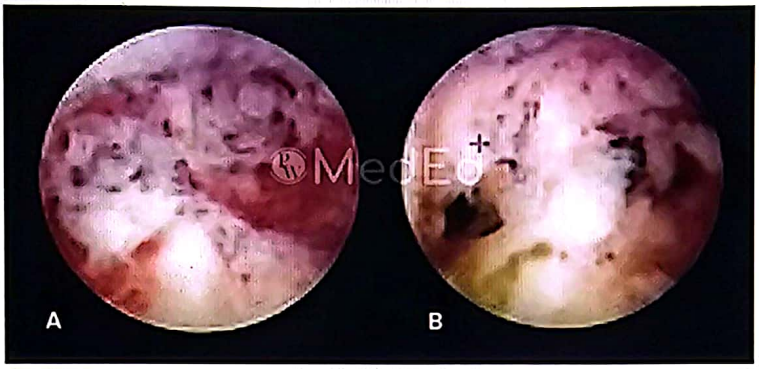
- FSH normal
- PCOS
- Treatment of PCOS is OCPs and lifestyle modification.

Hypergonadotropic hypogonadism:

- FSH high
- Estrogen low
- Premature ovarian insufficiency
- Premature ovarian failure
- < 40 years
- It could be autoimmune, due to chemoradiation, genetic disorders or fragile X permutation.
- Treatment of POI and POF is E+P therapy for amenorrhea. Conception in by IVF with donor oocytes.



Asherman syndrome (HSG) filling defect



Hysteroscopy of asherman syndrome

SHEEHAN SYNDROME

- Pituitary apoplexy
- Post delivery massive PPH there is sudden hypotension in all over the body including pituitary circulation.
- Pituitary has necrosis
- State of panhypopituitarism
- Less FSH, LH, Prolactin, TSH, ACTH
- Failure of lactation first to manifest
- Treatment: administration of exogenous hormones
- MRI: empty sella sign

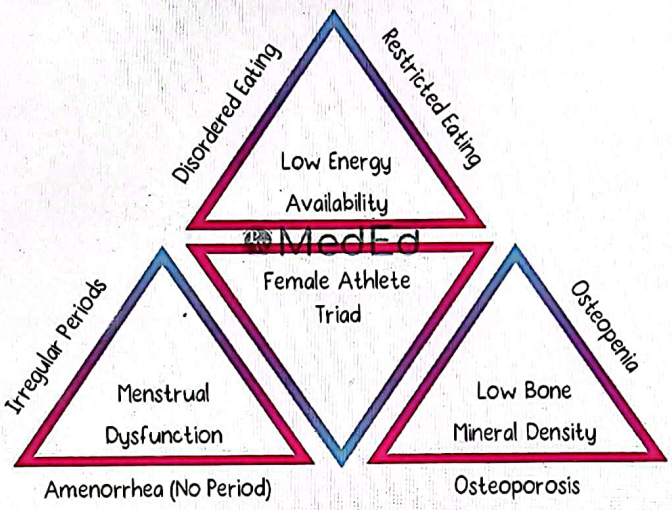
HYPOTHALAMIC CAUSES OF AMENORRHOEA (PRIMARY/SECONDARY)

Functional hypothalamic causes:

- Stress
- Over exercise
- Rapid weight loss
- Poor diet
- This causes decrease GnRH which causes decrease FSH.
- It leads to amenorrhea
- Treatment: remove the trigger
- Anorexia nervosa associated with poor body image
- Self imposed starvation
- Extreme weight loss
- Amenorrhoea
- Electrolyte disturbance
- Downy hair over body
- Treatment: mostly psychiatric treatment with better nutrition

FEMALE ATHLETE TRIAD

Personal Notes



Disorders of Sexual Development

Personal Notes

DSDS (DISORDER OF SEXUAL DEVELOPMENT)

- DSD → discordance between phenotypic sex with either gonadal or chromosomal sex.

	Female	Male
Chromosomal sex	XX	XY
Gonadal sex	Ovaries	Testes
Phenotypic sex (Assigned at birth)	Female external genitalia	Male external genitalia
Gender (not assigned at birth)	Roles that they play	

CLASSIFICATION OF DISORDERS OF SEX DEVELOPMENT

True hermaphroditism	Pseudohermaphroditism		
Ovotestis Or Ovaries one side & testis on other side Or Ovaries on one side & Ovotestis on other side Or Testis on one side & Ovotestis on other side	No ovotestis, single type of gonad		
Mostly XX	46 XX	46 XY	46 XO (Turner's syndrome)
Internal genitalia: variable presentation Wolffian duct on testicular side & Mullerian duct on ovarian side	Gonads are ovaries	Internal genitalia: Gonads are testes, rest internal genitalia may be male or female or absent	Normal female genitalia

External genitalia: Ambiguous genitalia Clitoromegaly ⟷ Ambiguous genitalia	External genitalia: Ambiguous genitalia/ male genitalia/ virilization	External genitalia: Female genitalia	External genitalia: Female
	Most common cause → CAH (congenital adrenal Hyperplasia)	Most common cause → AIS (Androgen insensitivity syndrome)	

Note: Rare cause of 46 XX DSDs:

- Adrenal/androgen hormones exposure in utero
- Theca lutein cyst
- Luteomas

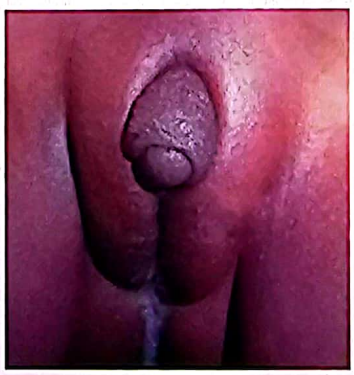
POINTERS TO DSD IN GYNAE CLINIC

- Primary amenorrhea
- Hirsutism
- Hoarseness of voice
- Excessive acne
- Ambiguous genitalia
- Poor or no breast development
- Poor or no pubic/axillary hair development
- Labial masses

GENDER ASSIGNMENT

- Whenever diagnosing DSD:
  - Be sensitive while breaking the news
  - Psychiatry consult
  - Future fertility prospects
  - Treatment plan → proceed according to desired gender identity of the individual

CONGENITAL ADRENAL HYPERPLASIA (CAH)



Personal Notes

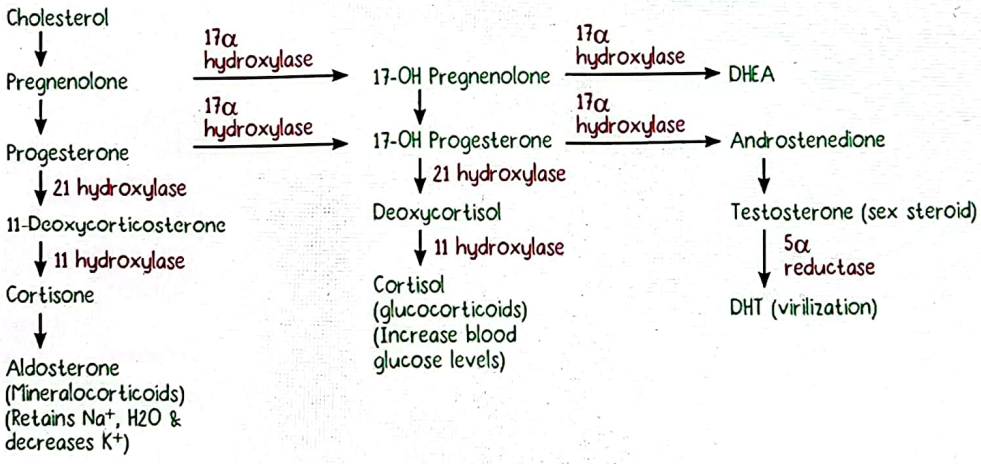
- Most common cause of 46 XX DSDs
- Intrinsic enzyme deficiency → decrease end products
- Hormones secreted by adrenal are not being produced/deficient → increase ACTH production

Personal Notes

Hormones produced by adrenal

- Adrenal medulla → epinephrine & norepinephrine
- Adrenal cortex:
  - Zona glomerulosa → Salt retaining hormones/Mineralocorticoids
  - Zona Fasciculata → Glucocorticoids
  - Zona reticularis → sex hormones (androgens)

Cholesterol produces three lines of hormones



1. Mineralocorticoids (aldosterone):
   - Retains Na+, H2O & decreases K+
2. Glucocorticoids (cortisols):
   - Causes increase in blood glucose levels
3. Sex steroids (testosterone):
   - Testosterone → DHT (by enzymes→ 5 alpha reductase) → causes Virilization

21 hydroxylase deficiency

- Test → 17-OH progesterone (as it accumulates due to enzyme deficiency)
- All shunted to androgen production
- Most common & most dangerous form of CAH
- In female child → Ambiguous external genitalia
- In Classical CAH → severe 21 hydroxylase deficiency
- Most common cause of endocrine related deaths in neonates

- no Aldosterone, no cortisol & lot of Testosterone
- "Salt wasting crisis" in neonate:
- Low sodium, severe dehydration, hyperkalemia & hypoglycemia

- In non classical CAH:
  - Present at puberty with virilizing changes like hirsutism & acne
  - Test for 17-OH progesterone

Note:

- CAH:
  - Classical → most common, present at birth
  - Non classical → present at puberty

17 alpha hydroxylase deficiency

- Decrease in androgens
- Delayed puberty (in male & females)
- In male children → ambiguous external genitalia
- +/- Hypertension

11 alpha hydroxylase deficiency

- 11-DOCA → have 1/20th salt retention power of aldosterone
- In female child → ambiguous external genitalia
- Early onset hypertension due to 11-DOCA

Treatment:

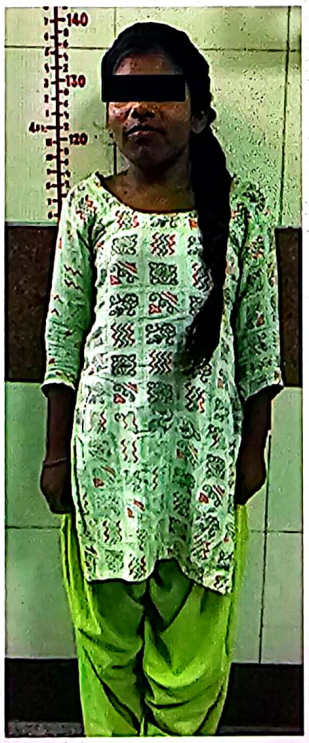
- Goals:
  - Replenish deficient hormones
  - ACTH production which leads to adrenal hyperplasia
- Treatment of choice → Exogenous steroids as they not only replenish deficient hormones but also give a negative feedback to pituitary to decrease ACTH production
- For classical/salt wasting forms of 21 hydroxylase deficiency:
  - Supportive management → IV fluids, salt replenishment, glucose insulin infusion (for hyperkalemia & hypoglycemia)
  - Steroid of choice → Fludrocortisone
- Preconception counseling:
  - Autosomal recessive → 25% having another child with CAH
  - between 4-10 weeks → start on steroids (oral Dexamethasone) → crosses placenta & decreases Fetal ACTH
  - At around 13 weeks → chorionic venous sampling tells us:

1. CAH is present or not
2. Male or female fetus
   - If CAH is not present → stop steroids
   - If CAH is present → continue steroids if it's female fetus & stop it in male fetus, as ambiguous genitalia once formed cannot be reversed

Personal Notes

TURNER SYNDROME

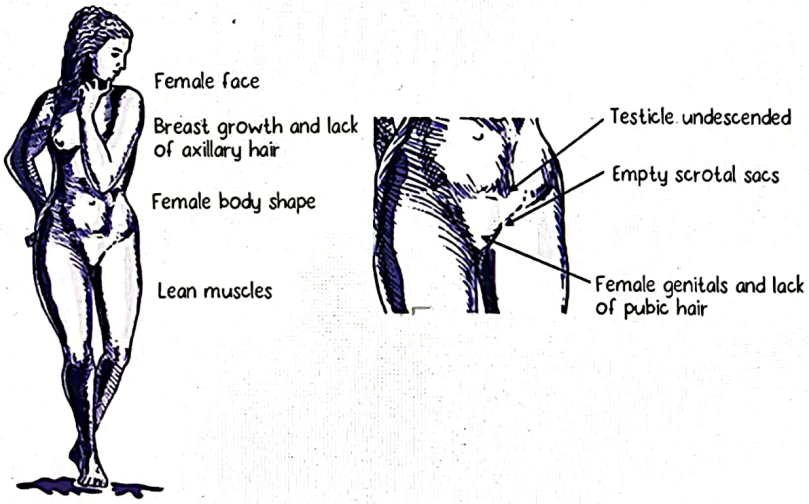
- 46 XO, or mosaic presentation
- Primary amenorrhea
- USG → small/streaky gonads
- Short statured
- Cubitus valgus
- Shield chest
- Webbed neck
- Low posterior hairline
- Other defects → heart & renal anomalies
- Later in life → Infertility due to decreased ovarian reserve
- Treatment:
  - give estrogen first → to build lining of endometrium
  - Followed by Estrogen + progesterone in cyclical fashion → menses
  - Infertility → IVF with donor oocyte
  - Low height → growth hormone supplements



ANDROGEN INSENSITIVITY SYNDROME

Personal Notes

- 46 XY
- Increased testosterone & increased DHT
- Insensitive receptors of target organs →
  - female external genitalia
  - no internal genitalia (either male or female)
  - Gonads → testis



- "Labial swelling"/"Inguinal swelling" (testes)
- Secondary sexual characteristics:
  - Tall, beautiful women
  - Breast development (due to aromatization of testosterone into estrogen in adipose tissue)
  - No pubic/axillary hairs
  - Primary amenorrhea
- AIS spectrum:

1. Complete AIS
2. Incomplete AIS:
   - Present with Clitoromegaly

Treatment:

- Gender assignment
- Blind vagina → mechanical dilators/vaginoplasty
- No uterus → no child bearing
- No ovaries → no surrogacy
- Only recourse is adoption
- Removal of testes (can cause Gonadoblastoma) → after puberty or after 18 years of age

COMPLETE GONADAL DYSGENESIS (SWYER SYNDROME)

Personal Notes

- 46 XY
- No wolffian duct derivatives

Clinical features:

- Primary Amenorrhea
- Female internal genitalia → uterus, fallopian tubes, cervix & vagina
- Female external Genitalia
- Labial/Inguinal swellings (testes) → removed as soon as diagnosis is made
- Sexual infantilism
- No breast development
- Adrenal → androgens → pubic & axillary hairs

Treatment:

- Estrogen first → breast development
- Followed by estrogen + progesterone → for menses
- Reproductive function → IVF with donor oocytes

5 ALPHA REDUCTASE DEFICIENCY

- 5 alpha reductase → converts Testosterone to Dihydrotestosterone
- Absence of DHT → female external genitalia
- Primary amenorrhea
- Male internal genitalia (due to testosterone)
- Spectrum of ambiguous genitalia
- Depending on severity of deficiency of enzyme there may be absolute deficiency leading to female external genitalia or some deficiency(more usual) leading to female external genitalia with clitoromegaly