Amenorrhea

Dr. Khalid Akkour
Department of Obstetric and Gynecology
College of Medicine, King Saud University

Objectives.

- To discuss the prevalence & pathogenesis of amenorrhea.
- To discuss the clinical presentation of amenorrhea. •
- To discuss the various types of work-up for amenorrhea.
- To discuss the management for amenorrhea.

Definition

- Primary amenorrhea.
  - Failure of menarche to occur when expected in relation to the onset of pubertal development. • No menarche by age 16 years with signs of pubertal development.
  - No onset of pubertal development by age 14 years.
- Secondary amenorrhea.
  - Absence of menstruation for 3 or more months in a previously menstruating women of reproductive age.

Events of Puberty

- Thelarche – breast development.
  - Requires estrogen.
- Pubarche/adrenarche – pubic hair development.
  - Requires androgens.
- Menarche – the first menses.
  - GnRH from the hypothalamus.
  - FSH and LH from the pituitary.
  - Estrogen and progesterone from the ovaries.
  - Normal outflow tract.

Classification.

- Hypothalamic Amenorrhea.
- Pituitary Amenorrhea.
- Ovarian Amenorrhea.
- Uterine Amenorrhea.
- Other.

Etiology – Hypothalamic.

Primary.

- Congenital GnRH deficiency.
- Weight loss.
- Organic disease.
- Constitutional.

Secondary.

- Weight loss – Anorexia nervosa.
- Exercise.
- Organic disease.
- Emotional stress.
- Pseudocyesis.

Anorexia Nervosa

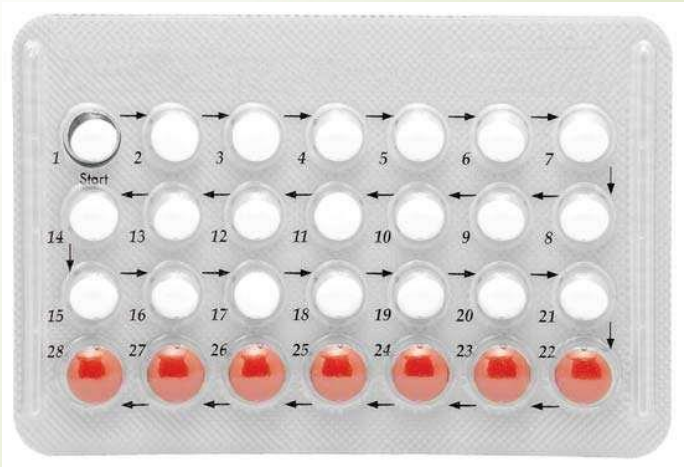
- BMI < 17 kg/m2 -> menstrual irregularity and amenorrhea.
- Hypothalamic suppression.
- Mean age onset (13-14 years)
- Low estradiol -> risk of osteoporosis.

Exercise-associated amenorrhea

- Common in athletic women/ ballet dancers.
- Eating disorders have a higher prevalence in female athletes than non-athletes.
- Hypothalamic disorder caused by abnormal GnRH pulsatility – results in impaired gonadotrophin levels, particularly LH and subsequently low estrogen levels.

Contraception related amenorrhea

- Post pill amenorrhea is not an entity.
- Depot medroxyprogesterone acetate – Up to 80% of women will have amenorrhea after 1 year of use – reversible.
- A minority of women taking the progesterone- only pill may have reversible long term amenorrhoea due to complete suppression of ovulation.



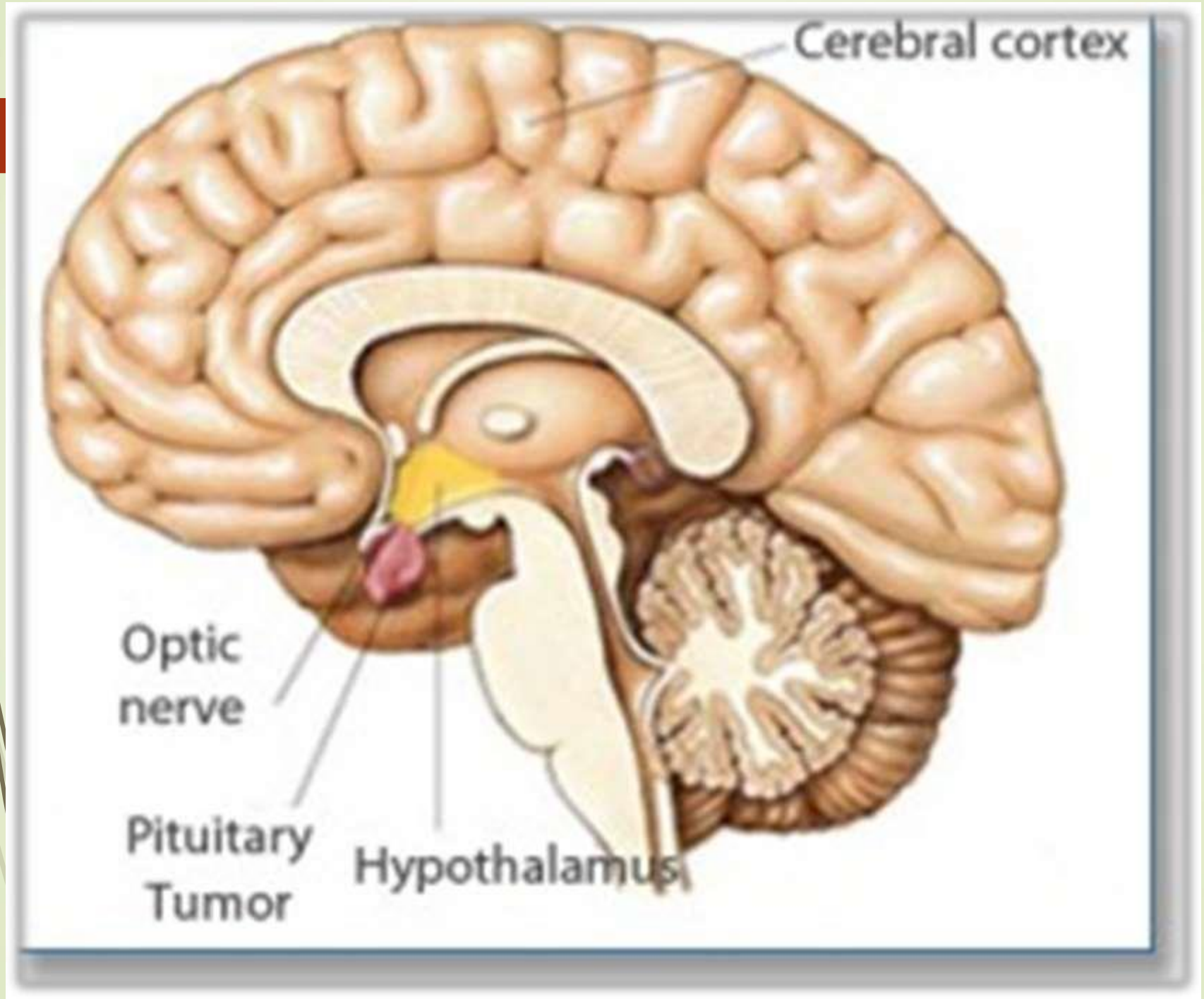
Etiology – Pituitary.

Primary

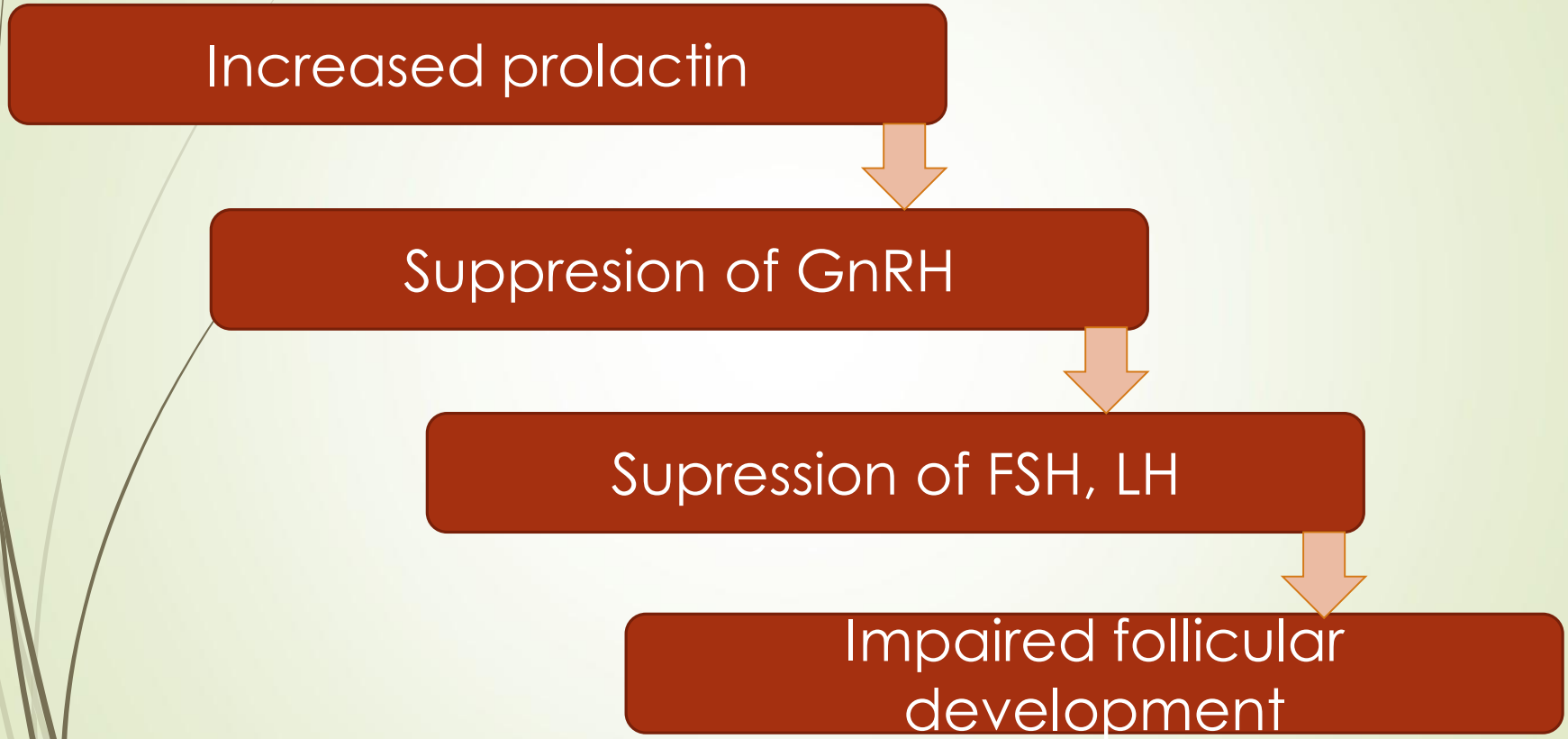
- Hyperprolactinaemia.
- Pituitary failure.

Secondary.

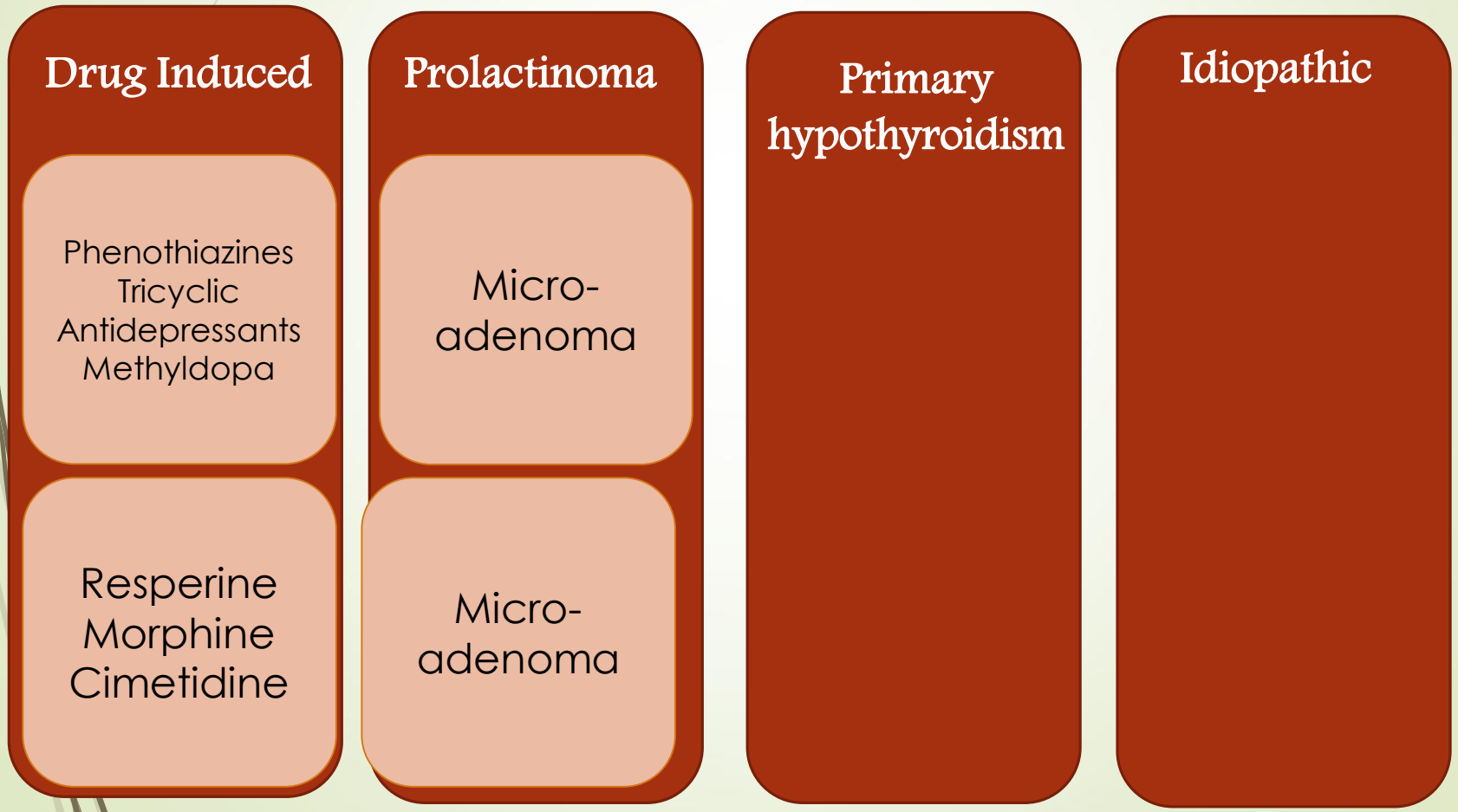
- Hyperprolactinaemia.
- Sheehan's syndrome.
- Organic disease.


Cerebral cortex
Optic nerve
Pituitary Tumor
Hypothalamus

Hyperprolactinaemia.



Hyperprolactinaemia – Causes



Sheehan's syndrome.

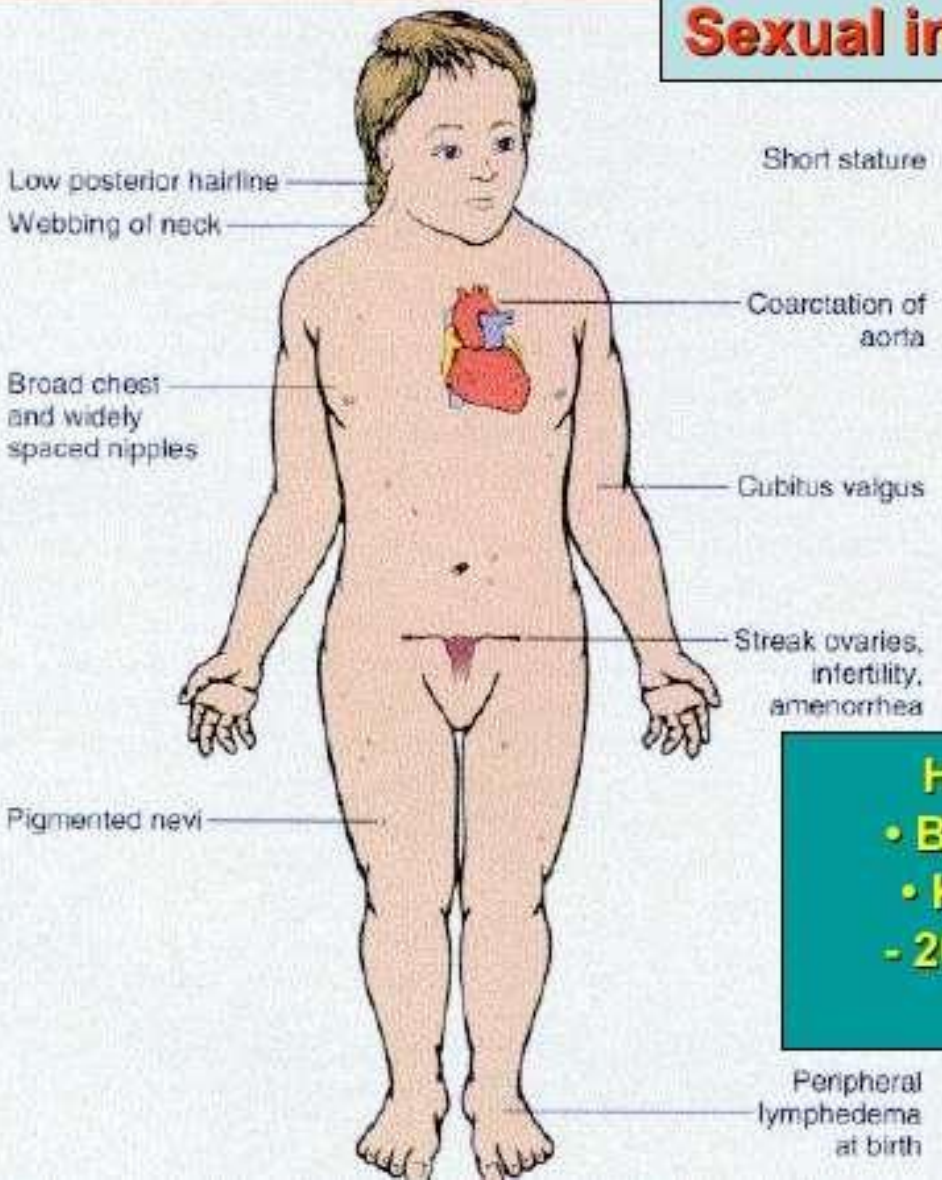
- Pituitary inability to secrete gonadotropins.
- Pituitary necrosis following massive obstetric hemorrhage is most common cause in women.
- Diagnosis.
  - History and E2, FSH, LH + other pituitary deficiencies (Decreased TSH and ACTH)
- Treatment.
  - Replacement of deficient hormones.

Etiology – Ovarian.

Primary.	Secondary.
❖ Gonadal dysgenesis ➢ Chromosomally incompetent. ➢ Turner's syndrome (45X0) ❖ Chromosomally competent ❖ Pure gonadal dysgenesis (46XX) ❖ Ovarian agenesis ❖ Chemotherapy and radiotherapy.	❖ PCOS. ❖ Resistant ovary. ❖ Hormone producing tumours. ❖ Chemo/radiotherapy. ❖ Gonadal dysgensis

Typical features of Turner's Syndrome

Sexual infantilism and short stature



TURNER SYNDROME

Incidence: 1 in 3000 female births

Karyotypes:	
Classic:	45,X
Defective second X chromosome:	46,X,i(Xq) 46,XXq– 46,XXp– 46,X, r(X)
Mosaic type:	45,X/46,XX

High FSH and LH levels.

- **Bilateral streaked gonads.**
- **Karyotype - 80 % 45, X0**
- **20% mosaic forms (46XX/45X0)**

Turner's syndrome

(Classic 45-XO)

Mosaic (46-XX / 45-XO)

Etiology – Uterine.

Primary.	Secondary.
❖ Utero-vaginal agenesis.	❖ Asherman's syndrome.

Mayer-Rokitansky-Kuster-Hauser Syndrome Utero-vaginal agenesis

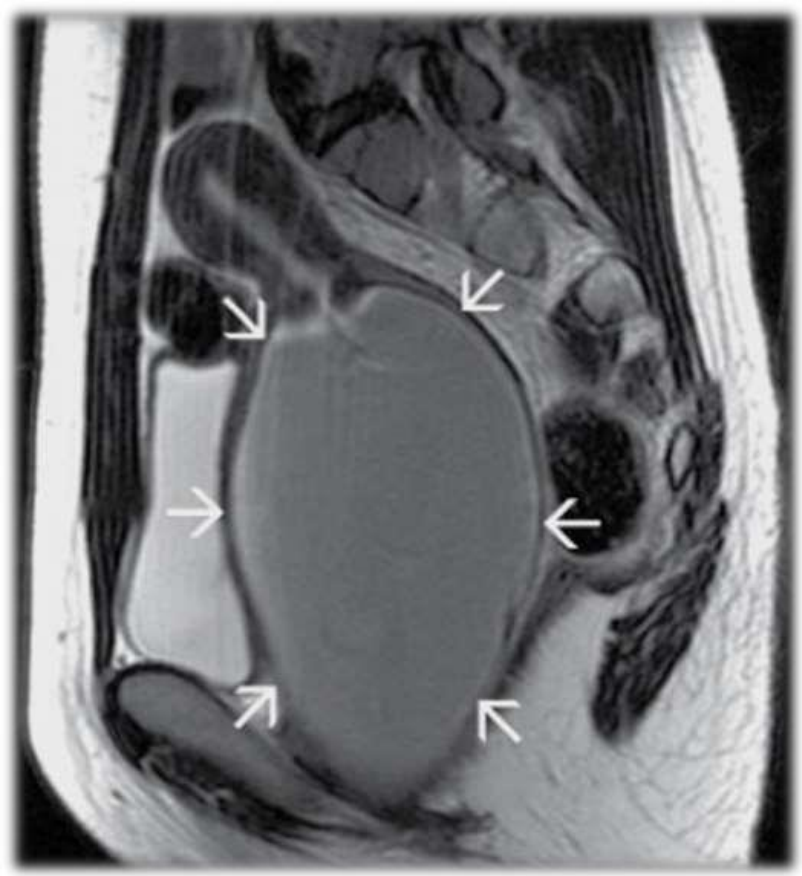
- 15% of primary amenorrhea.
- Normal secondary development & external female genitalia.
- Normal female range testosterone level
- Absent uterus and upper vagina & normal ovaries.
- Karyotype 46XX.
- 15-30% - Renal, skeletal and middle ear anomalies.

Imperforate Hymen

- Congenital disorder.
- Hymen without an opening obstructs the vagina.
- Failure to perforate during fetal development – failure of sinovaginal bulbs to canalize.
- Surgical.

Imperforate Hymen

Haematocolpos & Haematometra



Asherman's syndrome.

- Fritsch syndrome.
- Adhesions/ fibrosis of endometrium associated with dilation and curettage.
- Destruction of stratum basalis of endometrium.
- Diagnosis – Hysteroscopy.
- Treatment – Uterine sound, operating hysteroscopy, IUCD, Estrogen.

Congenital Adrenal Hyperplasia.

- Autosomal recessive trait.
- 21-hydroxylase deficiency.
- +ve Family history.
- Resembles PCOS.
- High 17-OH progesterone blood level.
- Presence of uterus and upper vagina.
- Treatment:
  - Cortisol replacement + Corrective surgery.

Androgen Insensitivity.

- Testicular feminizing syndrome.
- Normal breasts but no sexual hair.
- Normal looking female external genitalia.
- Absent uterus and upper vagina.
- Karyotype 46, XY.
- Male range testosterone level.
- Treatment:
  - Gonadectomy – postpuberty + HRT.

History.

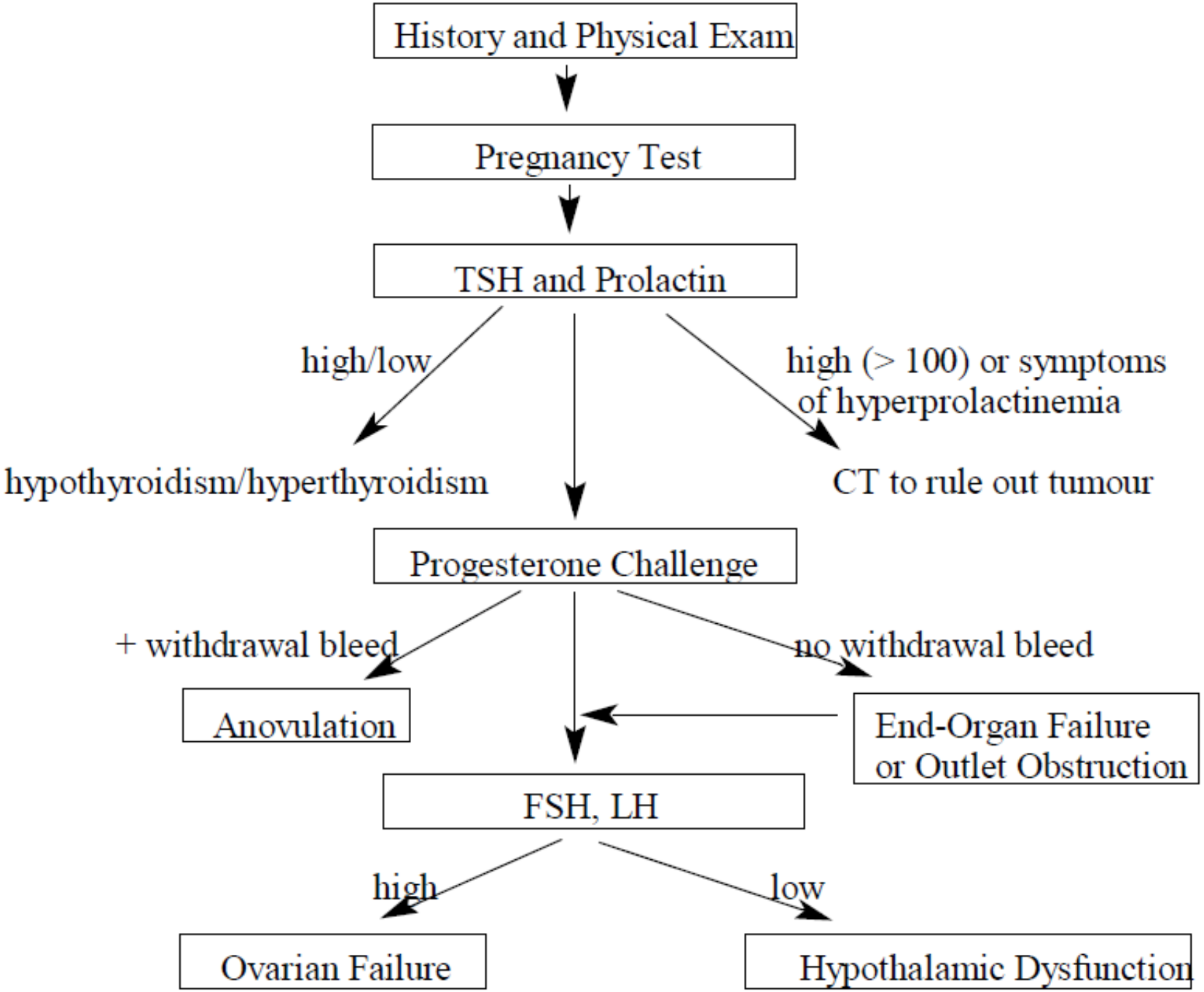
- RULE OUT PREGNANCY.
- Menstrual history: age at menarche, LMP, previous menstrual pattern, diet, medications, stress.
- Galactorrhea, radio/chemotherapy, weight loss/gain.
- Intense exercise/ dieting
- Estrogen deficiency – hot flushes, night sweats.

Physical.

- Tanner staging – breast development, pubic hair distribution.
- Thyroid examination.
- Hair distribution – Androgen excess/ insensitivity
- External genitalia and vagina – atrophy, clitoromegaly, imperforate hymen.
- Palpation of uterus/ ovaries.

Investigations.

- Progesterone challenge to assess estrogen status.
  - Medroxyprogesterone acetate 10 mg for 10 days.
  - Uterine bleed within 2-7 days - +ve test.
  - Withdrawal bleeding occurs – adequate estrogen.
  - No bleeding – hypoestrogenism.
- Bloodwork investigations.
- Ultrasound.
- Karyotype if indicated.


History and Physical Exam
Pregnancy Test
TSH and Prolactin
high/low
high (> 100) or symptoms of hyperprolactinemia
hypothyroidism/hyperthyroidism
CT to rule out tumour
Progesterone Challenge
+ withdrawal bleed
no withdrawal bleed
Anovulation
End-Organ Failure or Outlet Obstruction
FSH, LH
high
low
Ovarian Failure
Hypothalamic Dysfunction

Treatment.

- Hypothalamic dysfunction.
  - Stop drugs, stress manangement, moderate nutrition & exercise.
  - Clompihene citrate if pregnancy desired.
  - OCP to induce menstruation.
- Hyperprolactinemia.
  - Bromocriptine.
  - Surgery for macroadenoma
- Hypoestrogenism.
  - Karyotype.
  - Removal of gonadal tissue if Y chromosome present.
- PCOS.
- Supplemental vitamin D + calcium intake along with moderate weight bearing exercises to combat bone degeneration.

Conclusion

- Primary amenorrhea.
  - The overall reproductive prognosis is grim.
  - Only the patients with idiopathic pubertal delay can be expected to have normal reproductive capacity.
  - It is possible for most patients to achieve satisfying sexual function with appropriate management.
- Secondary amenorrhea.
  - As all fields of clinical medicine, the treatment of patients should be directed against the underlying disease state.
  - Clinical reviews should be held 3~6 months.

Take home points.

To end…

- Primary amenorrhea – absence of menses by age 16.
- Secondary amenorrhea – absence of menses for > 6 months.
- 3 main mechanisms of pathophysiology of amenorrhea.
  - Failure/malfunction of hypothalamic-pituitary-gonadal axis.
  - Absence of end organs.
  - Obstruction of outflow tract.
- Hypothalamic, Pituitary, Ovarian & Uterine classifications of amenorrhea.
- *Test for Pregnancy.
- Progesterone challenge.
- Treat underlying disease state/ symptomatic treatment.

To end…

- PCOS is common – 5~10% of women (reproductive age).
- Anovulation, hirsutism, infertility, obesity, insulin resistance.
- Strong family link.
- Treatment
  - Interrupt self-perpetuating cycle – OCP, weight reduction, clomiphene.
  - Prevent endometrial hyperplasia from unopposed estrogen using progesterone.
  - If pregnancy is desired – medical induction of ovulation.


THANK YOU