



# Abnormalities of the HPOE axis

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Reproductive system module (phase II)



# Learning objectives

- The physiology of the HPOE axis
- The importance of the HPOE axis
- Pathophysiology of HPOE axis abnormalities
- Evaluation of HPOE abnormalities
- Treatment of specific causes of HPOE abnormalities.



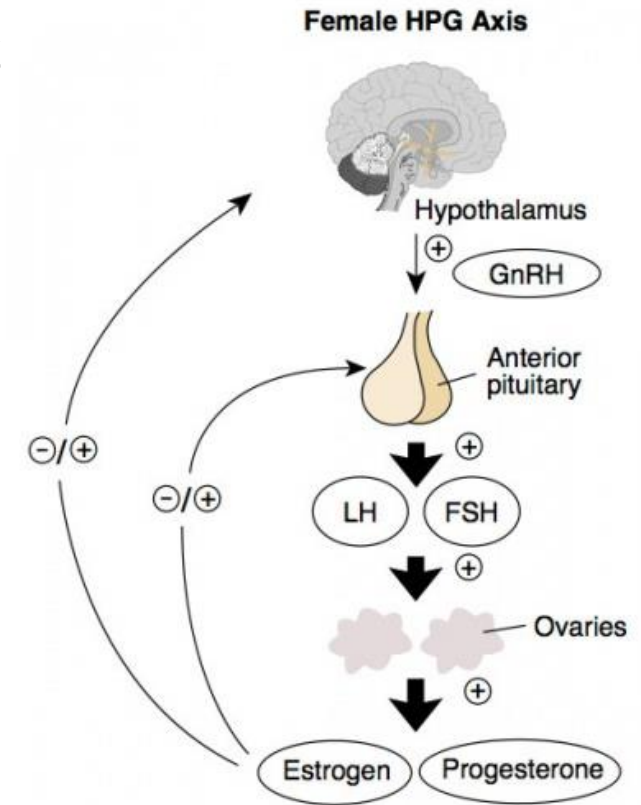
# What is HPOE axis

- The endocrine pathway of controlling gonadal function
- Also known as HPG axis
- Responsible for the function of 2 end-organs
  - Ovaries
  - Endometrium
- HPG axis common to both male and female
  - HPOE is in the female

# The physiology of the HPOE axis

- Initiated by the hypothalamus
- Under the control of CNS
- Negative / positive feedback mechanisms in controlling the normal function

- Follicle development
- Uni-follicle development
- Ovulation
- Endometrial development





# Activation and functioning of axis

- Pubertal change
  - Not completely understood
  - Pre-pubertal hypothalamus is sensitive to very low levels of oestrogen
    - Negative feedback
  - Around puberty this sensitivity is lost
    - Pulsatile secretion of GnRH begins
- With depletion of follicles in ovaries, the ovarian response diminishes
  - Menopause



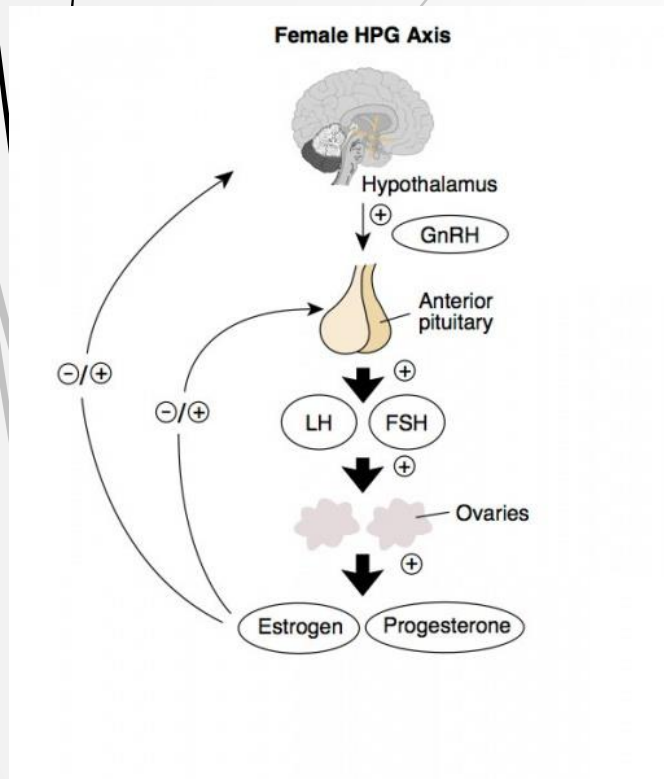
# Clinical importance of HPOE axis

- Anovulatory infertility
  - Ovulation induction
- Assisted reproductive techniques (IVF)
  - Superovulation
- Contraception
  - Ovulation inhibition
- Management of other hormone dependent conditions
  - Eg. Endometriosis, PMS

# Pathophysiology of HPOE axis abnormalities

## ■ Hypothalamic causes - Abnormal GnRH secretion

- Congenital – Isolated, Kallman synd.(Anosmia)
- Lesions – Craniopharyngiomas, Germinomas, Gliomas,
- Secondary causes – Sarcoidosis, TB, head injury
- Exercise induced – Athlete amenorrhea
- Weight related – Eating disorders
- Stress induced
- Chronic illness – Renal disease, liver disease



***Hypogonadotropic hypogonadism***

# Pathophysiology of HPOE axis abnormalities

- Pituitary causes - Abnormal FSH/LH secretion

- Hyperprolactinaemia

- Commonest pituitary cause

- Prolactin secreting tumour or loss of dopamine inhibitory action

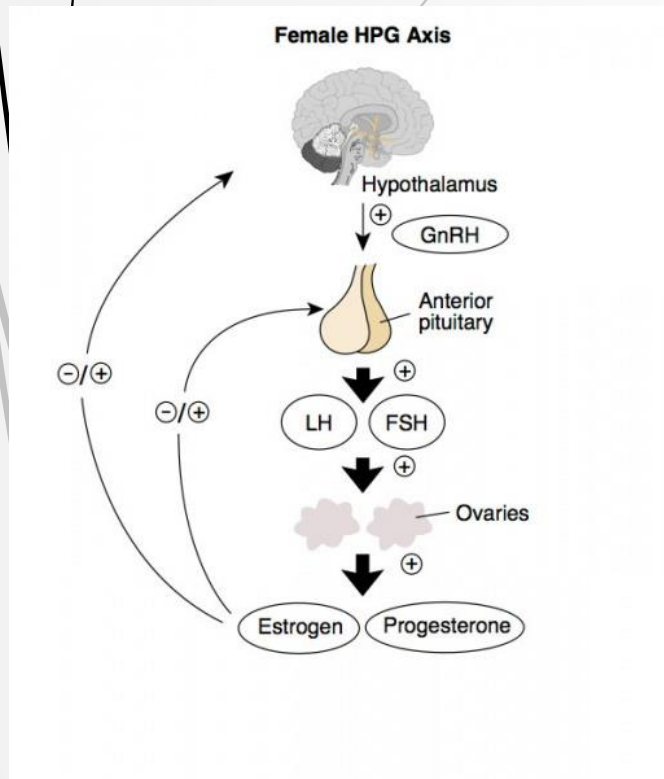
- Macroadenoma (>10mm) or microadenoma (<10mm)

- Macro-very high prolactin levels, Pressure effects

- Panhypopituitarism

- Isolated FSH/LH deficiency

***Hypogonadotropic hypogonadism***





# Pathophysiology of HPOE axis abnormalities

## ■ Ovarian causes

### ■ Polycystic ovary syndrome

■ Commonest cause of anovulation

■ Main features

■ Anovulation

■ High androgen levels –Clinical / biochemical

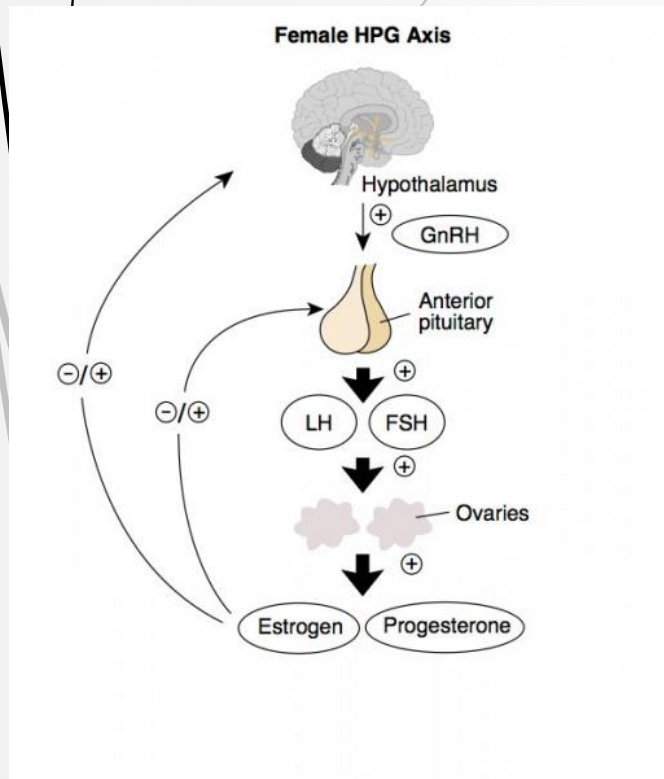
■ Polycystic ovaries

***Normogonadotropic hypogonadism***

### ■ Premature ovarian failure

■ Idiopathic, genetic, autoimmune, iatrogenic

***Hypergonadotropic hypogonadism***





# Presentations of HPOE axis abnormalities

- Delayed puberty
  - Absent secondary sexual characteristics
  - Primary amenorrhea
- Anovulatory infertility
- Secondary amenorrhea
- Other presentations - rare
  - Galactorrhea
  - Visual field defects
  - Growth abnormalities

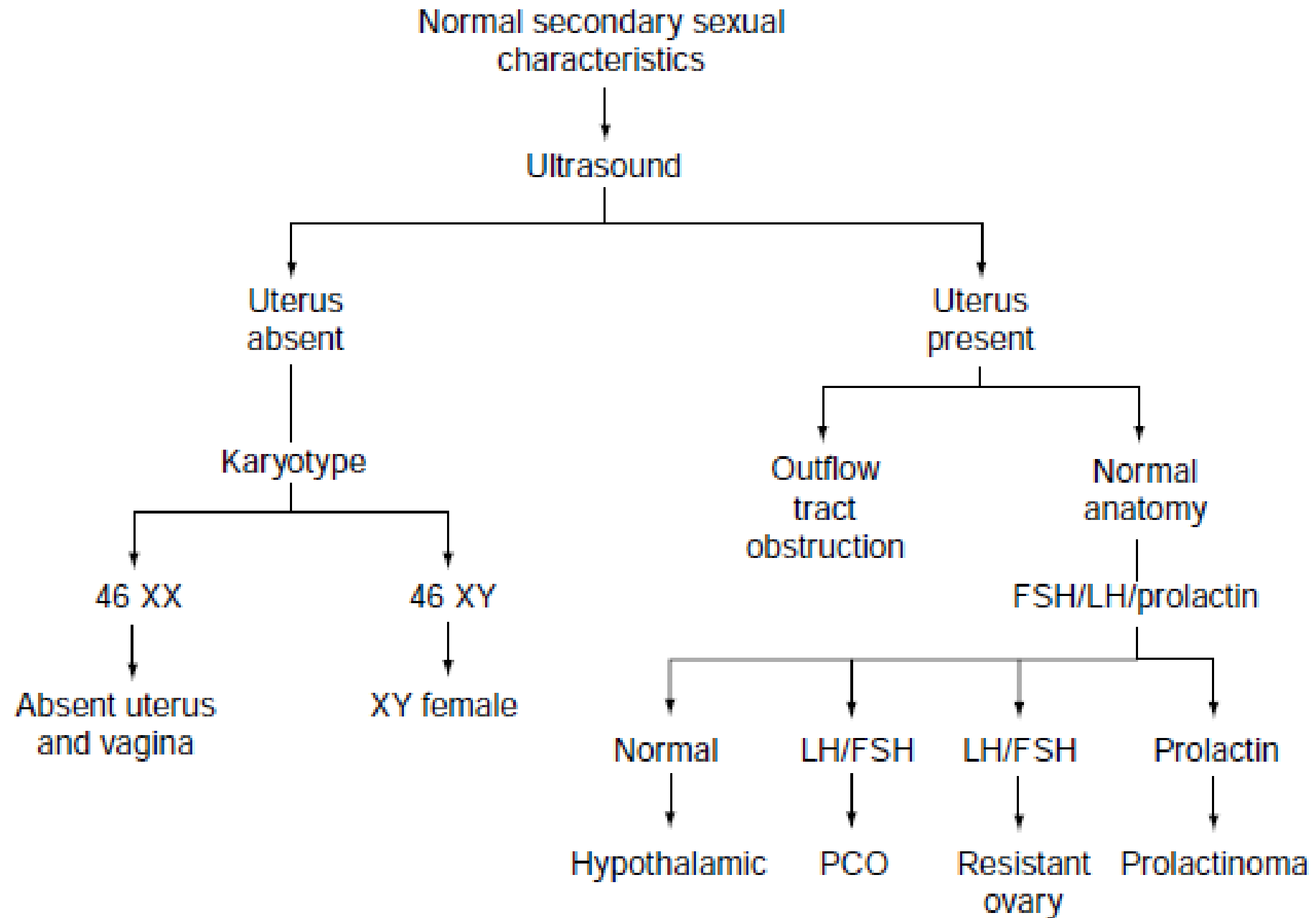


# Evaluation of HPOE axis abnormalities

- History and examination
- Investigations
- Logical approach
- Minimise the investigations
- Less invasive to more invasive
- Cost effectiveness

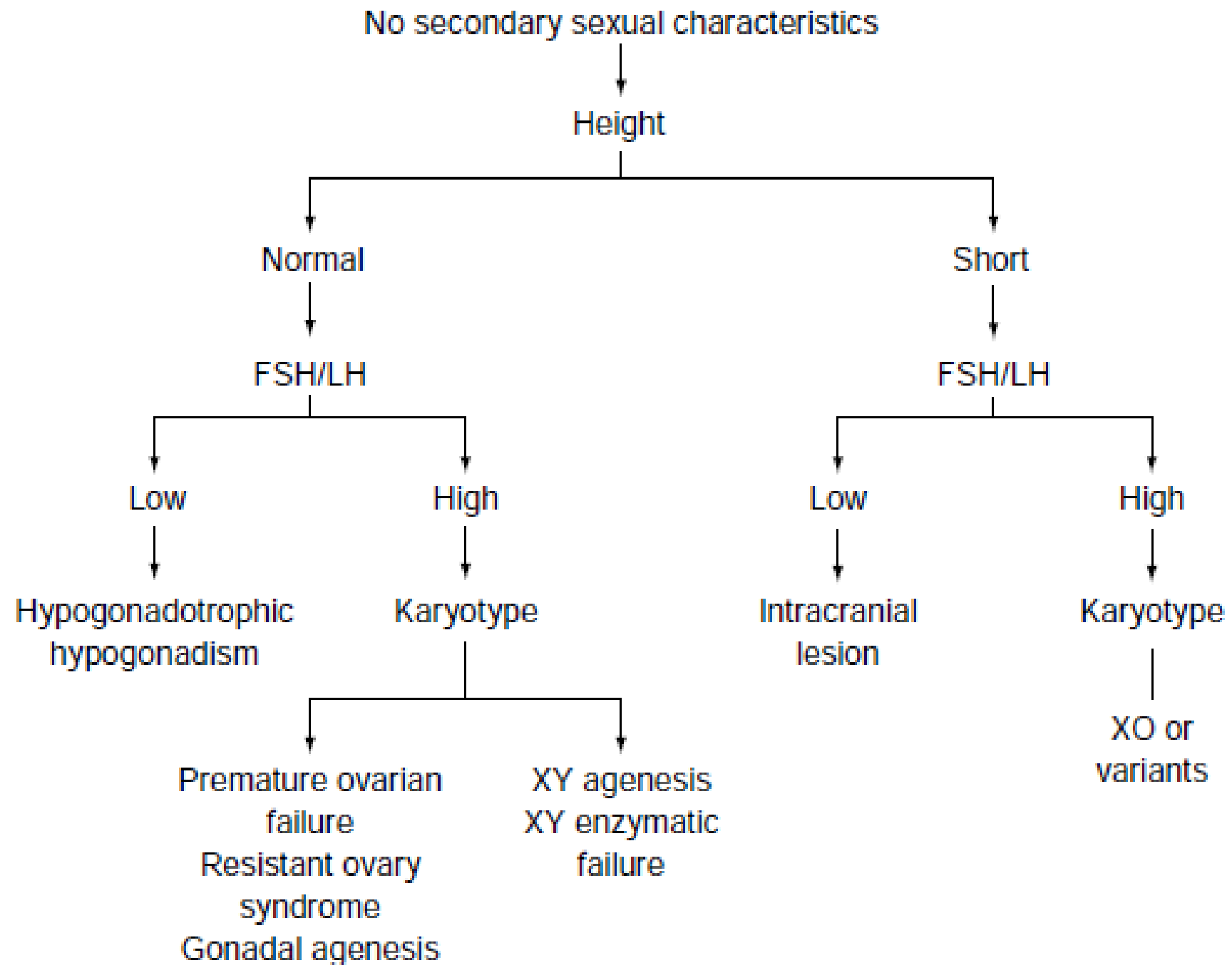
# Evaluation of HPOE axis abnormalities

- Primary amenorrhea with 11<sup>ry</sup> sexual charac.
  - ? Presence of uterus - USS
    - Absent – Mullerian agenesis / Intersex conditions
      - Do Karyotype
    - Present
      - Outflow tract obstruction
        - Imperforated hymen, Vaginal septum
      - Normal anatomy
        - Hypothalamic – FSH/LH
        - PCOS – FSH/LH, USS for ovarian morphology
        - Prolactinaemia / pituitary conditions – FSH/LH, Prolactin



# Evaluation of HPOE axis abnormalities

- Primary amenorrhea without 1<sup>ry</sup> sexual charac.
  - ? Growth spurt
    - Normal
      - Low FSH/LH levels – Pituitary causes
      - High FSH/LH levels – Ovarian failure / Gonadal agenesis
    - Short stature
      - Low FSH/LH – Panhypopituitarism, Intracranial lesions
      - High FSH/LH – 45XO (Turner syndrome)



# Evaluation of HPOE axis abnormalities

- Secondary amenorrhea (Exclude pregnancy)
  - FSH/LH levels
    - High –Premature ovarian failure
    - Normal – PCOS
    - Low – Hypothalamic conditions, Pituitary conditions, Eg. Sheehan synd
  - Prolactin levels, Cranial MRI if high
  - Other pituitary causes
    - Head injury, tumours, irradiation
  - End-organ damage
    - Endometrial damage (Asherman synd)
    - Outflow obstruction (cervical stenosis)



# Treatment of HPOE axis abnormalities

- Hypothalamic causes

- Correction of contributing factors

- Diet, weight, exercise, stress

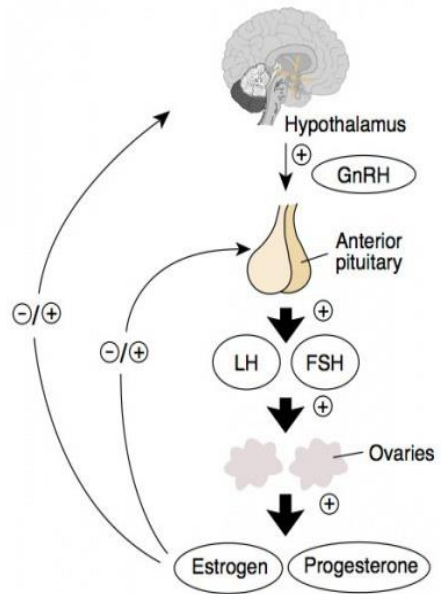
- GnRH def

- GnRH pulsatile administration via pump

- FSH/LH administration

- Oestrogen replacement if fertility not desired

Female HPG Axis



# Treatment of HPOE axis abnormalities

## ► Pituitary causes

### ► Hyperprolactinaemia

- Macroadenoma – Require surgery
- Microadenoma – Medical Eg. Bromocriptine, Cabergollin

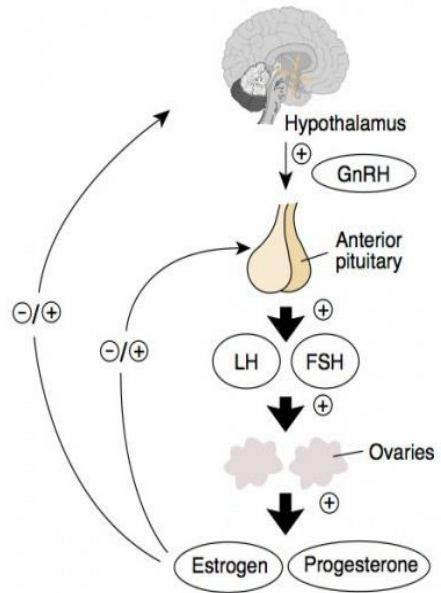
### ► Isolated FSH/LH def

- Replacement of FSH/LH to induce ovulation
- Oestrogen replacement if fertility not desired

### ► Panhypopituitarism

- Replacement of other pituitary hormones also

Female HPG Axis



# Treatment of HPOE axis abnormalities

## ■ Ovarian causes

### ■ PCOS

#### ■ Induce ovulation with

- Anti-oestrogens – Clomifene citrate
- Aromatase inhibitors – Letrozole
- Gonadotropins – FSH

#### ■ Contraceptive pill / withdrawal bleeds- if fertility not desired

### ■ Premature ovarian failure

- Oocyte donation for fertility
- Oestrogen replacement

Female HPG Axis

