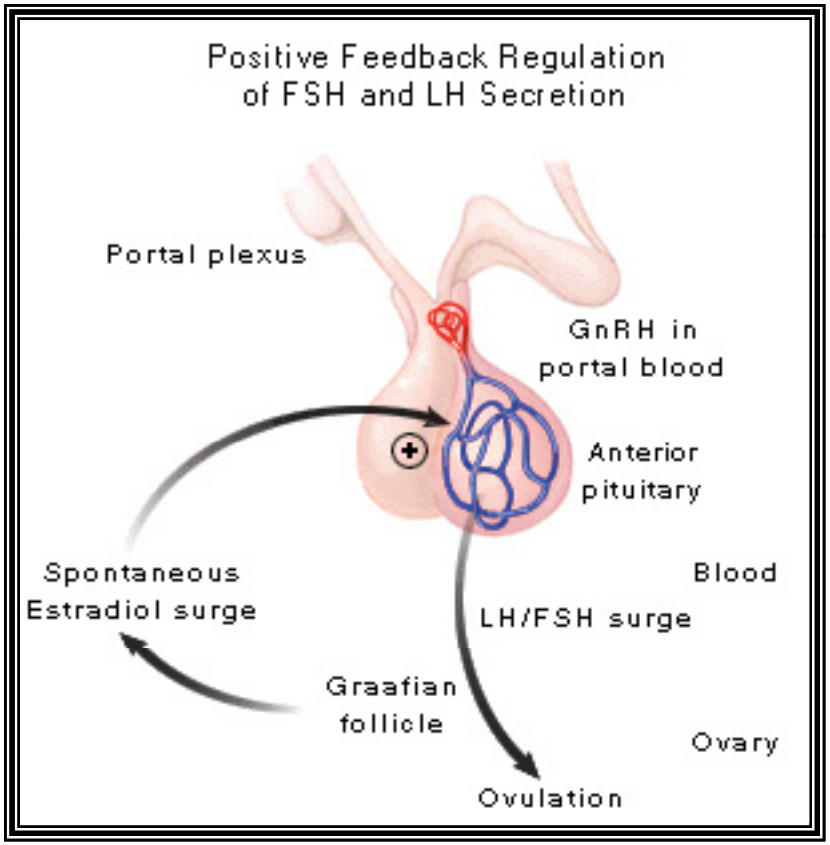
PRECOCIOUS PUBERTY, DIAGNOSIS & TREATMENT

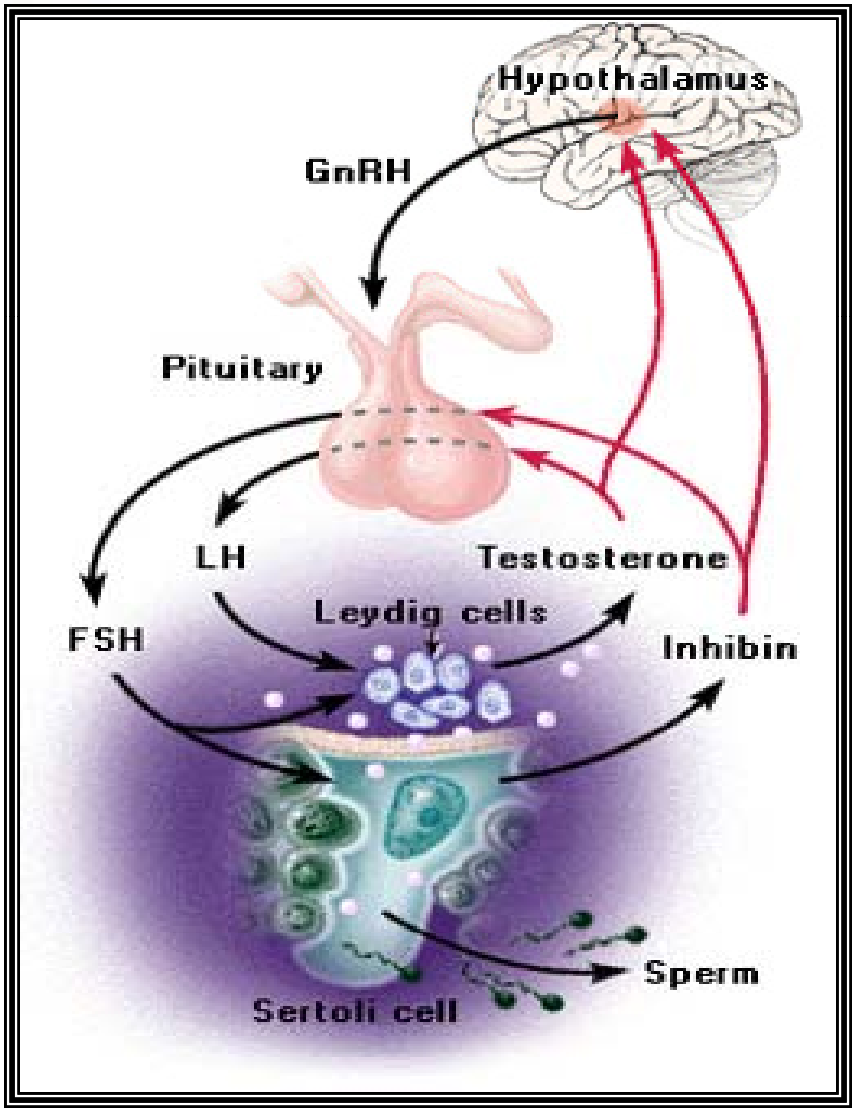
dr. H. Hakimi, Sp.AK
dr. H Charles Darwin Siregar, Sp.A
dr. Melda Deliana, Sp.AK
dr. Siska Mayasari Lubis, Sp.A

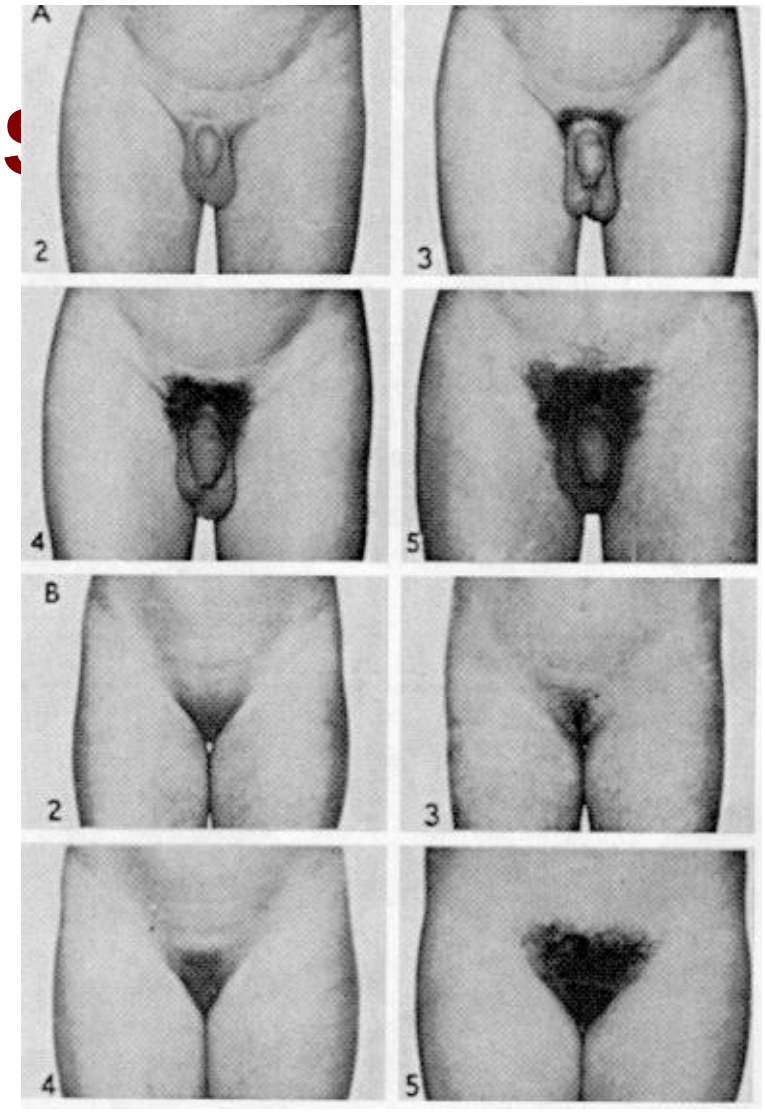
PEDIATRIC ENDOCRINOLOGY
MEDICAL SCHOOL USU/H. Adam Malik HOSPITAL
Medan

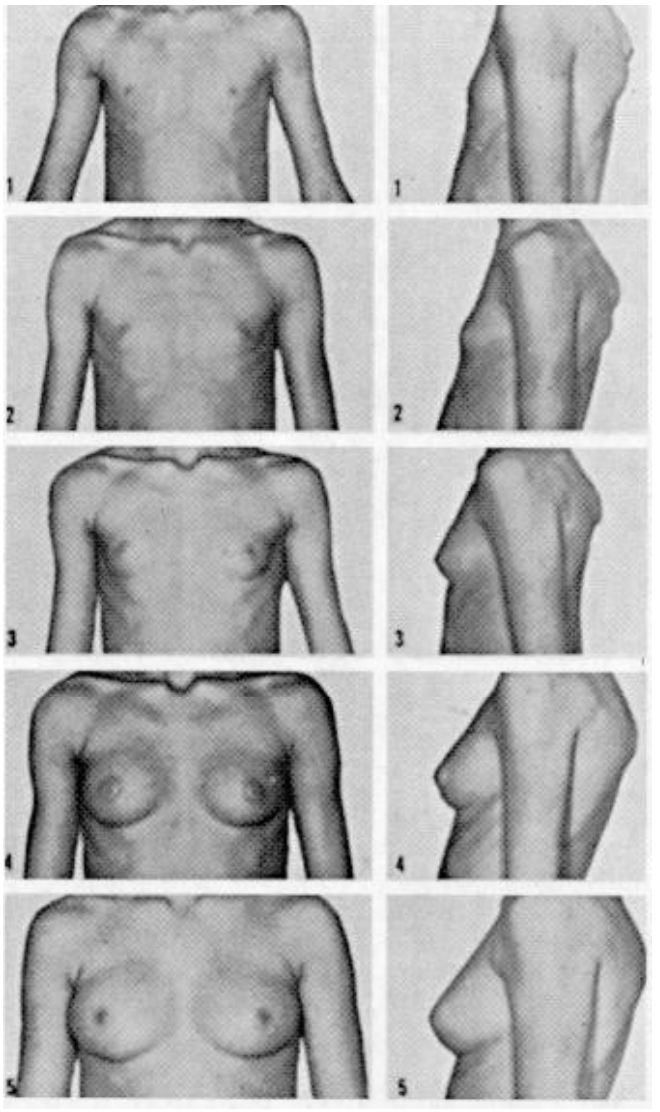
GnRH-LH/FSH-Estrogen AXIS PHYSIOLOGY



GnRH-LH/FSH-Testosteron AXIS PHYSIOLOGY




A
2
3
4
5
B
2
3
4
5

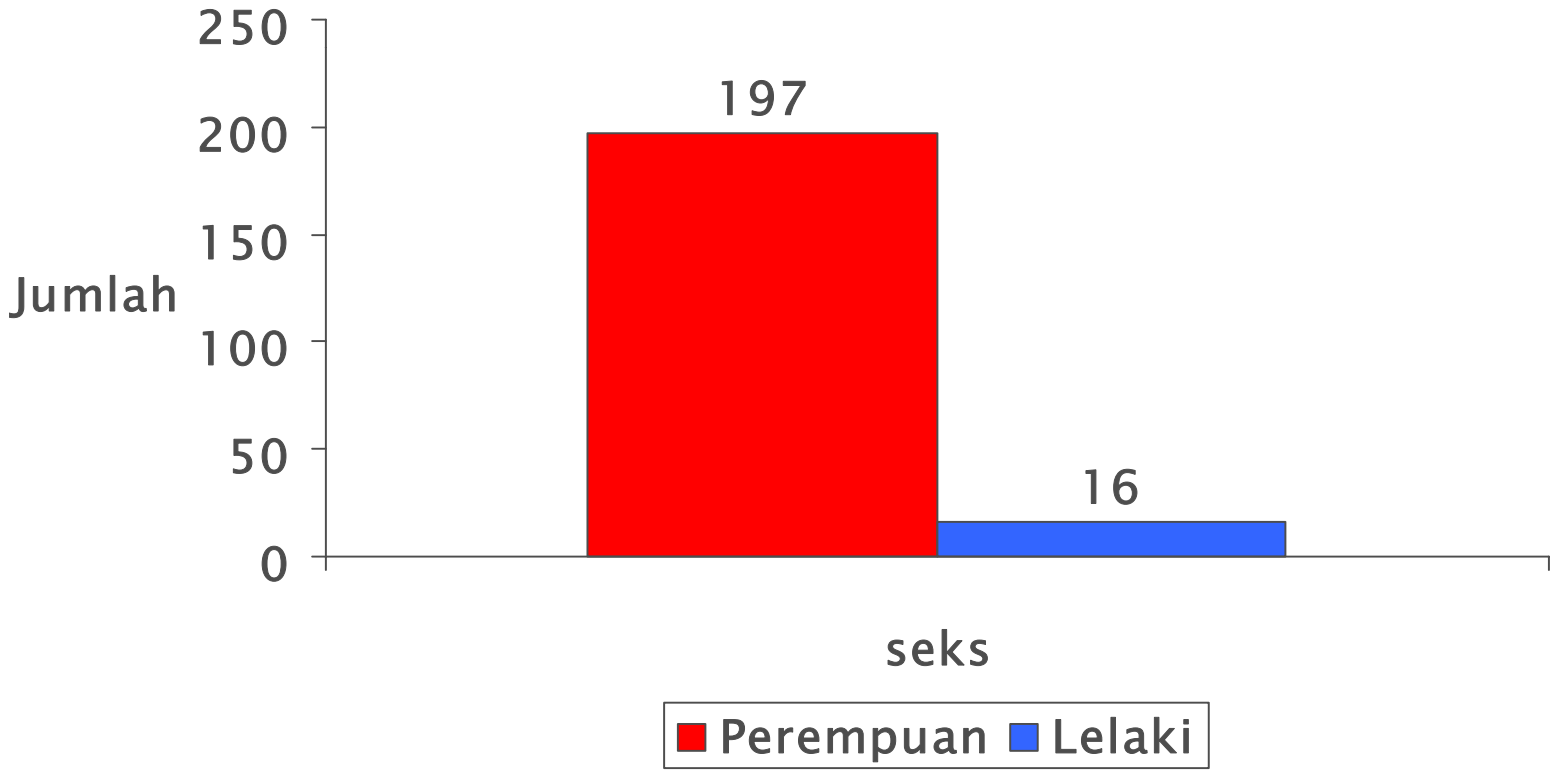

1
1
2
2
3
3
4
4
5
5

DEFENITION

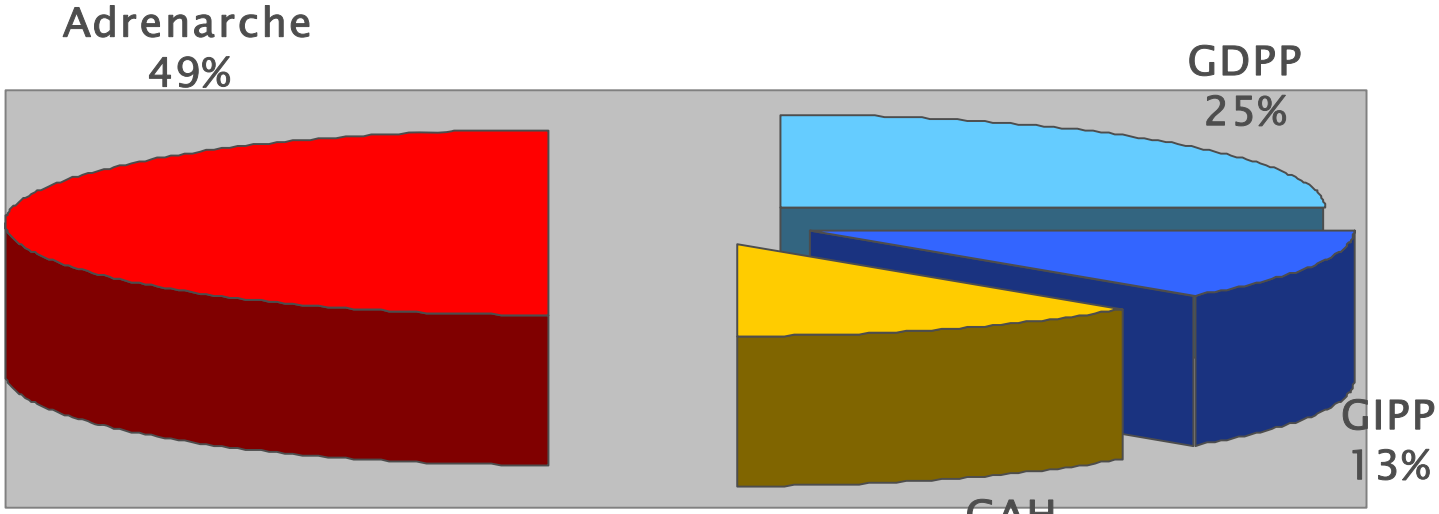
- **APPEARANCE OF SEXUAL MATURATION SIGNS BEFORE**
  - MALE : 9 YRS OLD
  - FEMALE : 8 YRS OLD

EPIDEMIOLOGY

PRECOCIOUS PUBERTY CASES AT Middlesex HOSPITAL(1975 - 1990)

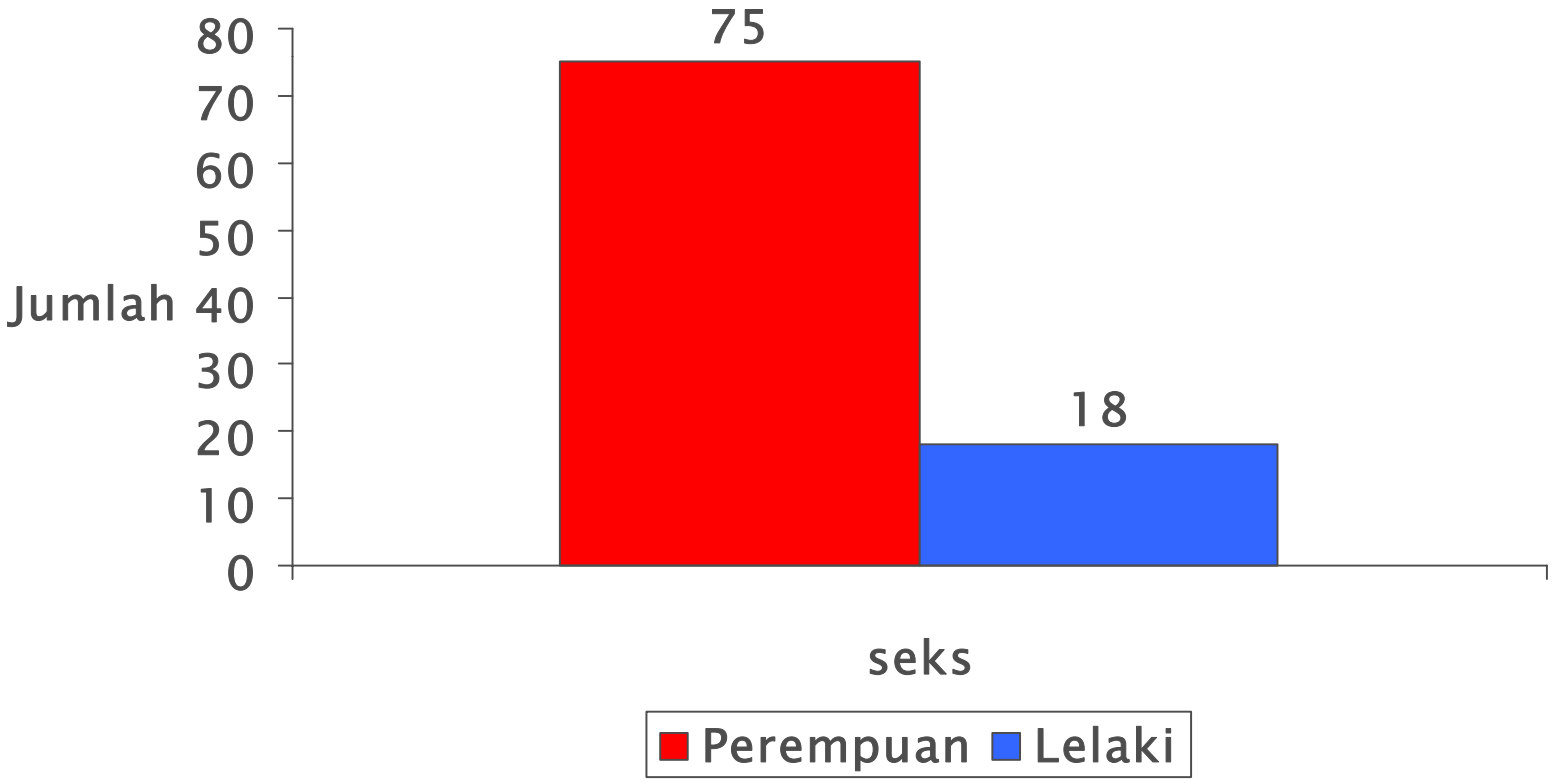


MALE PRECOCIOUS PUBERTY (N=16) AT MIDDLESEX HOSPITAL

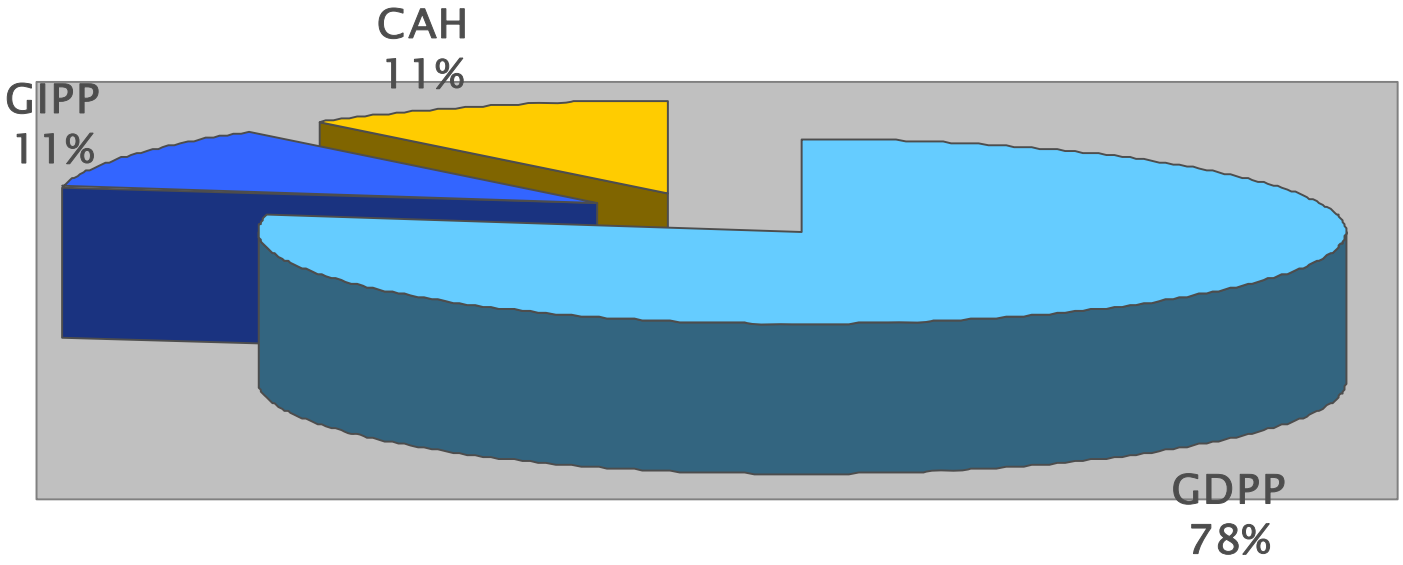


Catatan: GDPP = Gonadotropin Dependent Precocious Puberty; GIPP = Gonadotropin Independent Precocious Puberty; CAH = Congenital Adrenal Hyperplasia

PRECOCIOUS PUBERTY AT St. VINCENT HOSPITAL (1971 – 1977)



PRECOCIOUS PUBERTY AT St. VINCENT HOSPITAL (N=18)



Note : GDPP = Gonadotropin Dependent Precocious Puberty; GIPP = Gonadotropin Independent Precocious Puberty; CAH = Congenital Adrenal Hyperplasia

EPIDEMIOLOGY

- More frequent in female
- Female
  - **Mostly idiopatic**
- Male
  - **Mostly caused by significant CNS**

Precocious Puberty Classification

- ***GnRH dependent*** **(central) : early reactivation of Hypothalamus-pitutary- gonad axis**
- ***GnRH independent*** **(peripheral): autonom sex steroid , not affected by Hypothalamus-pitutary- gonad axis**
- ***Variant***
  - thelarche prematur
  - adrenarche prematur

Precocious Puberty Etiology

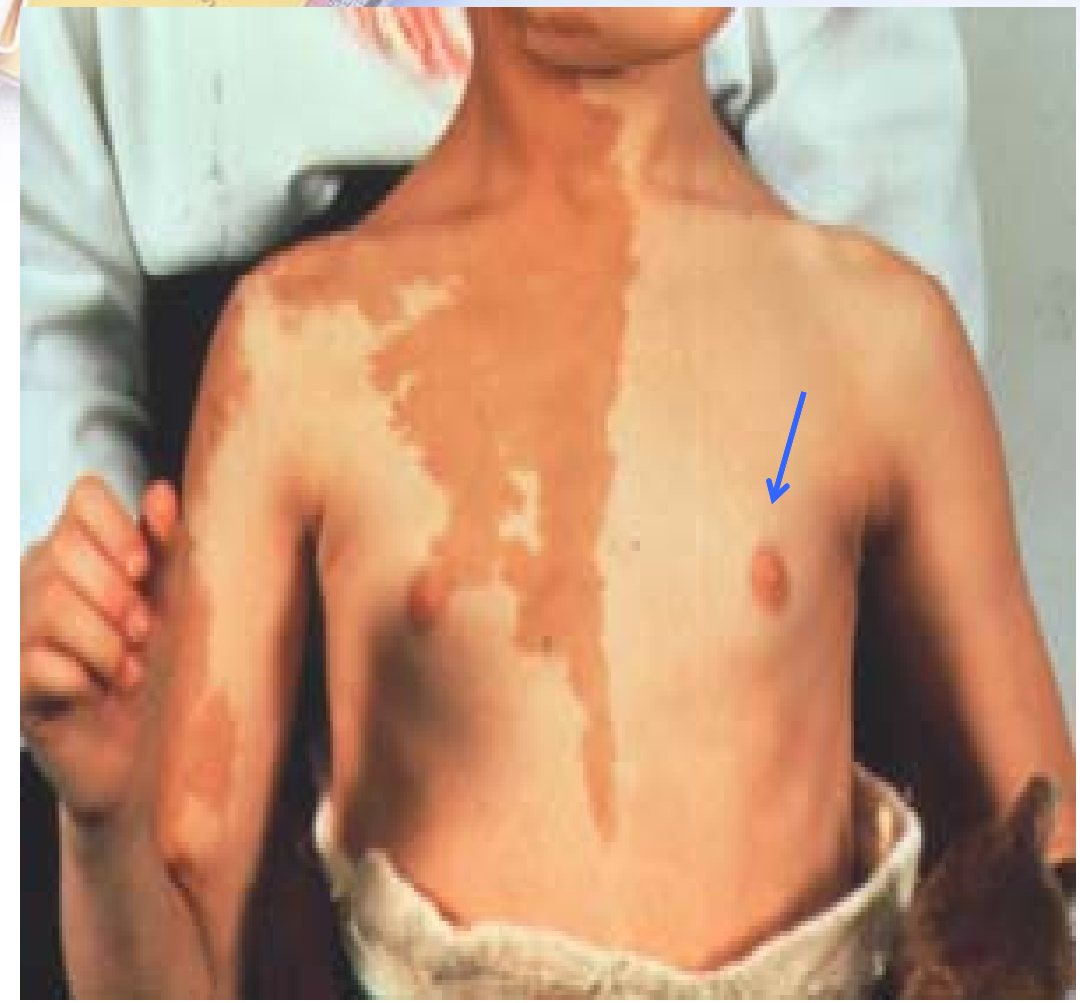
- ***GnRH dependent*** **(central)**
  - **idiopatic**
  - **CNS disorders**
    - tumor
    - non-tumor: post infection, radiation, trauma, congenital
  - **iatrogenic**
  - **Delayed diagnosis on GIPP**

Precocious Puberty Etiology

- ***GnRH independent*** **(peripheral)**
  - **Male (isosexual)**
    - adrenal: tumor, CAH
    - testis : cell Leydig tumor, familial testotoxicosis
    - gonadotropin-secreting tumor:
      - non CNS: hepatoma, germinoma, teratoma
      - CNS: germinoma, adenoma (LH secreting)
  - **heterosexual**
    - Increase peripheral aromatization

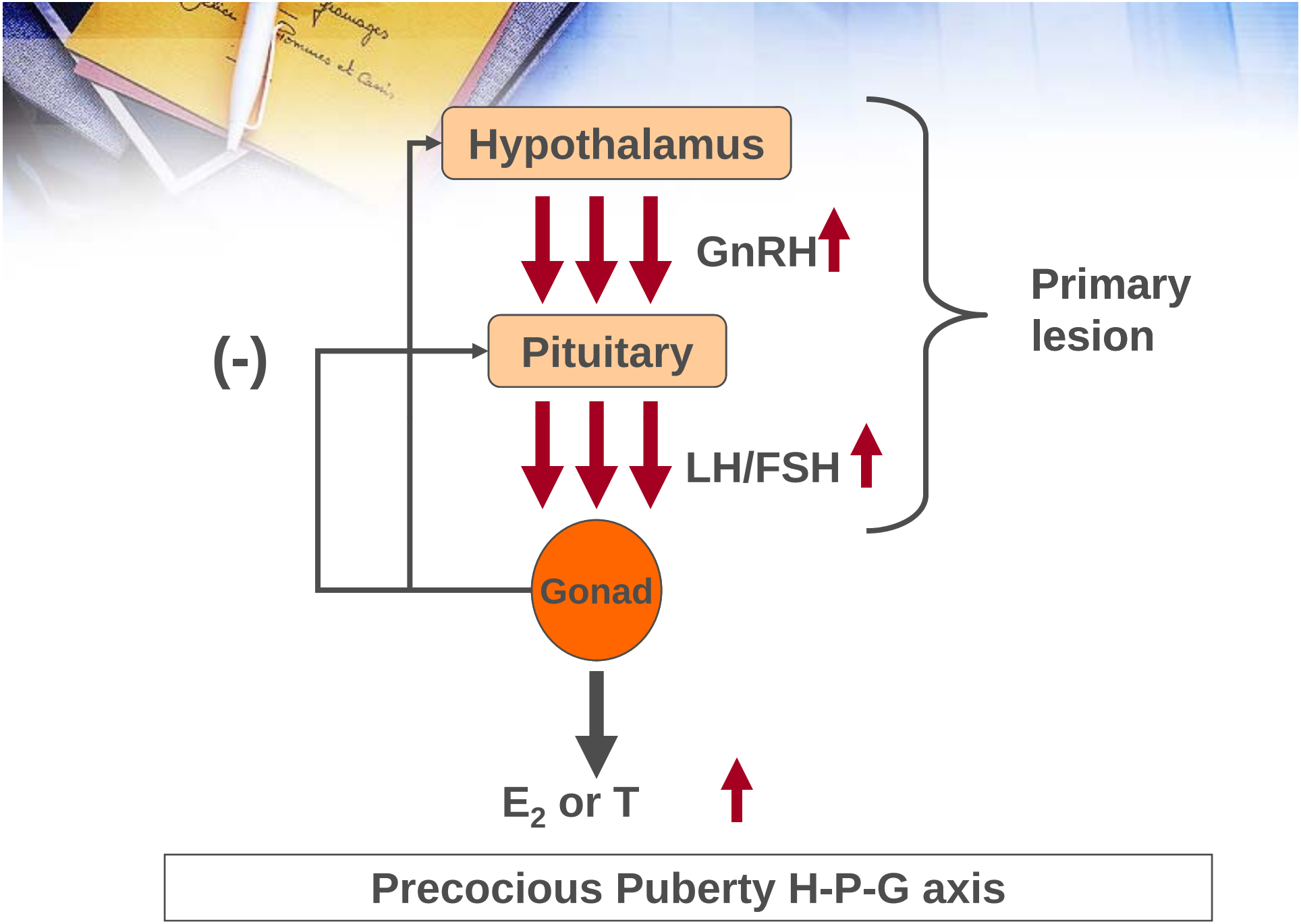
Precocious Puberty Etiology

- ***GnRH independent*** **(peripheral)**
  - **female (isosexual)**
    - McCune Albright
    - Severe hypothyroid
  - **heterosexual**
    - adrenal: tumor, CAH
    - tumor ovarium:arrhenoblastoma



McCune Albright Syndrome

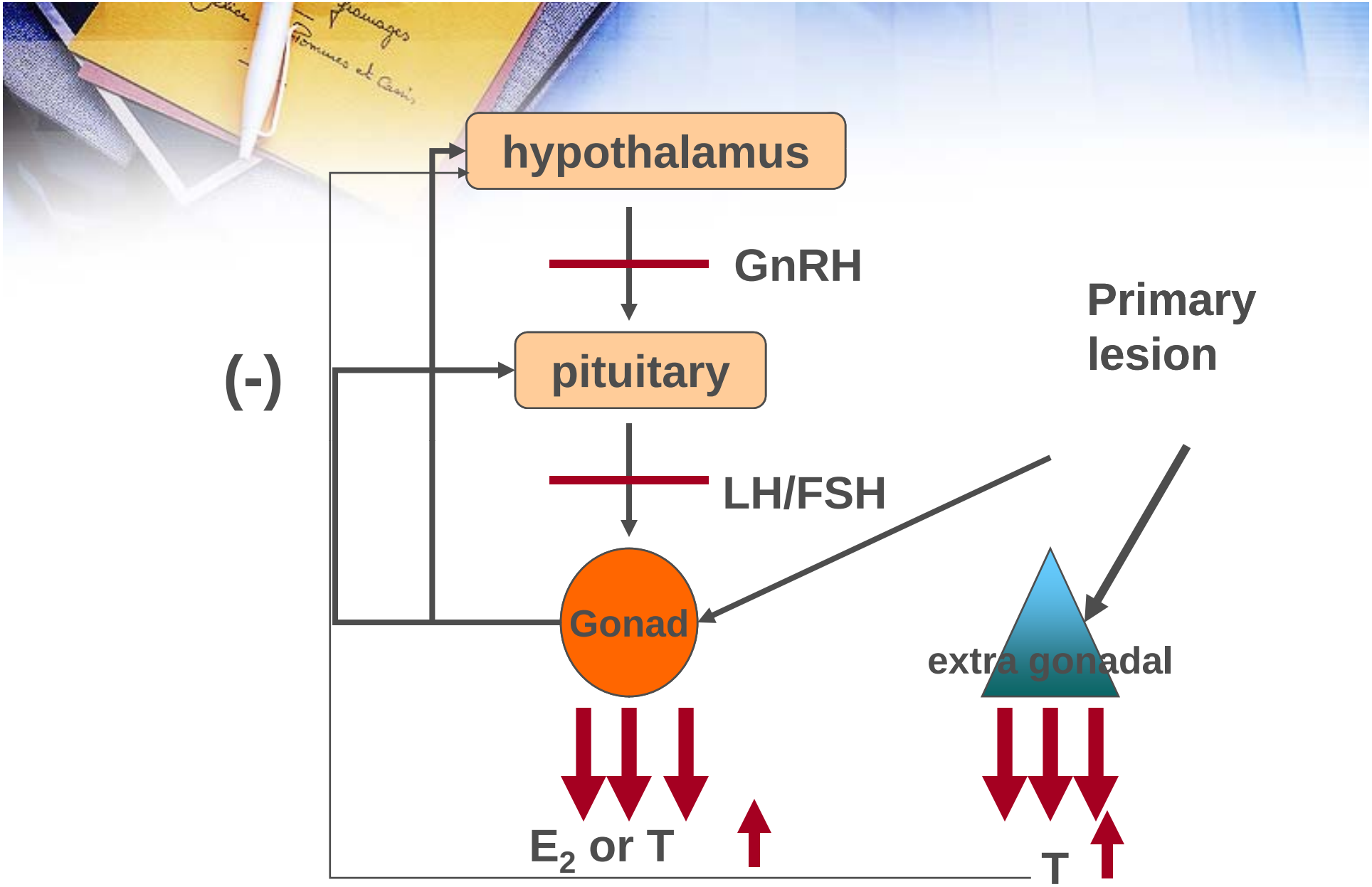
Pathophysiology



Precocious Puberty H-P-G axis

CLINICAL APPEARANCE GDPP

- Always isosexual
- Puberty signs develop as normal puberty pattern
- Hormonal : increase of hormonal at all axis



Precocious Puberty H-P-G axis in GIPP

Clinical appearance of GIPP

- Isosexual or heterosexual (late onset CAH, tumor adrenal)
- Unsinchronized secondary sexual development (testis volume doesn’t suit puberty stage-smaller)
- Sex steroid level increases without increase of GnRH and LH/FSH level

Clinical appearance of sex steroid level increase

- estrogen →
  - **”*tall child but short adult*” – because of early epiphiseal clocsure**
  - **gynecomasty**
- testosteron
  - **hirsutism**
  - **acne**
  - ***male habitus***

Clinical appearance of sex steroid level increase

- General
  - **sexual behavior**
  - **aggresive**

Variant

- Thelarche premature
  - **mammae enlargement only**
  - **normal hormonal features**
  - **Effect of local tissue sensitivity to estrogen**
  - **Benign, onset < 4 yrs old, mostly spontaneous regression**
  - **DD/ beginning of precocious puberty**

DIAGNOSTIC STEPS

History

- Onset, progress (DD/ adrenal tumor), secondary sexual signs (variant or not),
- neurologic symptoms (CNS tumor) and tumor characteristic (hamartoma - *gelactic laughter*)
- Family history (testoxicosis – only in male, CAH)
- Drug usage (hormonal, non hormonal)
- Linier growth history
- CNS disease : ensefalitis, meningitis

PHYSICAL DIAGNOSTIC

- Antropometric ("*tall stature*", obesity) and another condition (mental retardation, blood pressure)
- hormonal excess signs (acne, hirsutism, *moon face*)
- Puberty stage (testis volume - GIPP :remains small; isosexual atau heterosexual)

WORK UP

- LH/FSH level: basal, *stimulated* - GnRH test
- Serum estrogen / testosteron level
- Serum β-HCG level (germinoma) - male
- Based on indication : 17-OH progesteron, etc

WORK UP

- Imaging
  - **Pelvic, adrenal USG**
  - **Head CT / MRI**
  - **Bone Age**
  - **Bone survey (McCune Albright)**

TREATMENT

- Based on etiology
- GDPP idiopathic: GnRH agonist
- GIPP : medroksi-progesteron, ketokonazole, etc
- variant: observation

Prognosis

- Bassed on etiology
- GDPP idiopathic:
  - **Final height = genetic**
  - **Normal fertility**
  - **Minimal psychosocial disorders, regression of secondary sexual signs**
- GIPP :
  - **height < genetic height**
  - **regression of secondary sexual signs ± ↓**

Conclusion

- Puberty disorder is not always pathologic
- Early axis activity must be actively handled
- GnRH agonist is drug of choice for GDPP

THANK YOU