Diagnostic et traitement des pubertés précoces

Charles Sultan

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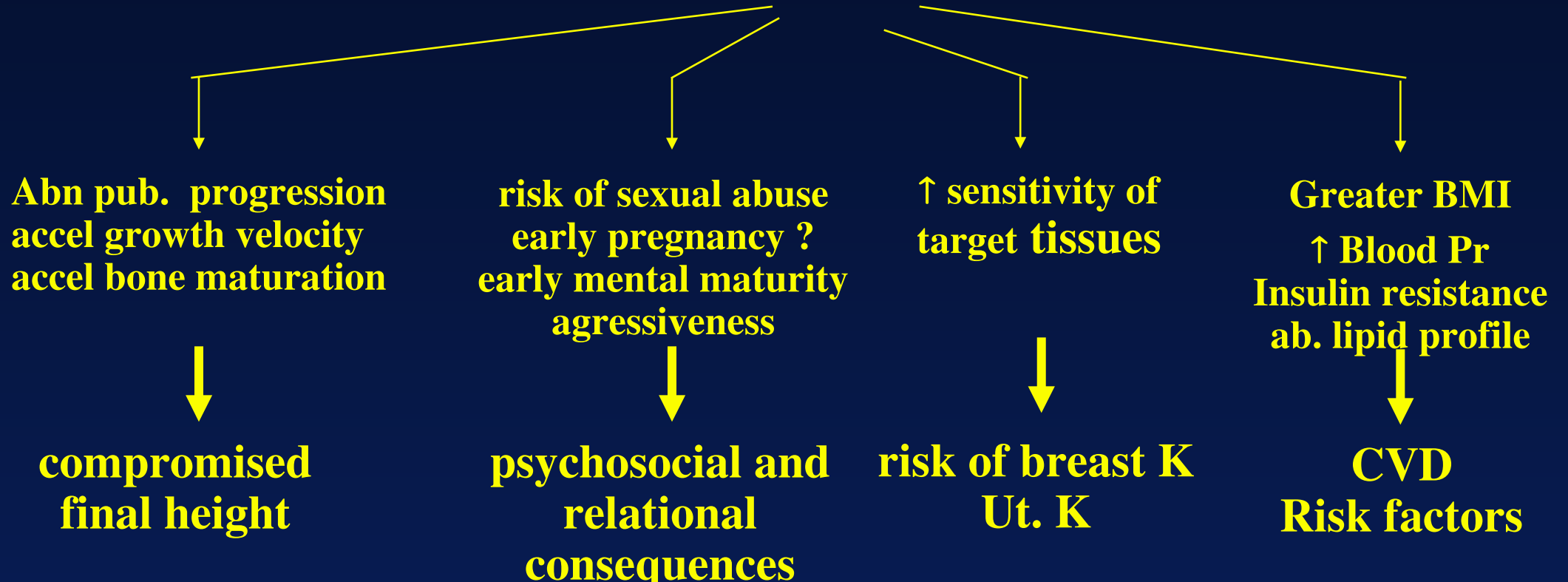
AES, Agadir, Maroc , 29 Juin 2013

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens



Diagnostic et traitement des pubertés précoces

Questions

1 - What are the physiological limits - When does pathology begin ?

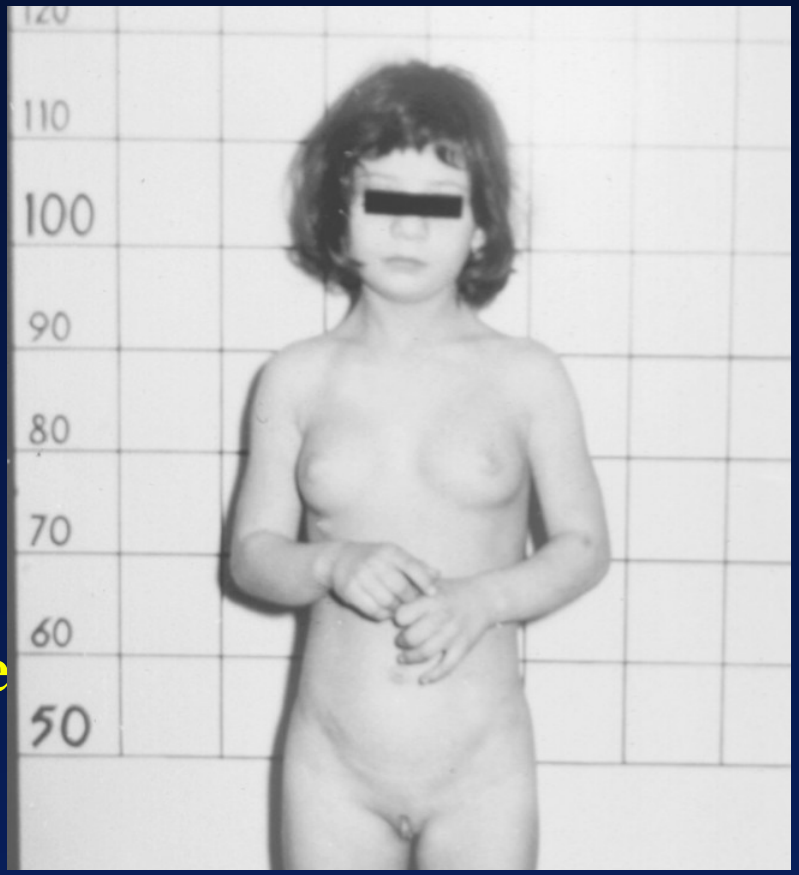
2 - Complete (central),
incomplete (partial)
or peripheral precocious puberty ?

3 – Assessment of sexual precocity

4 – Diagnosis

5 – Management : optimizing the outcome

6 - Conclusions



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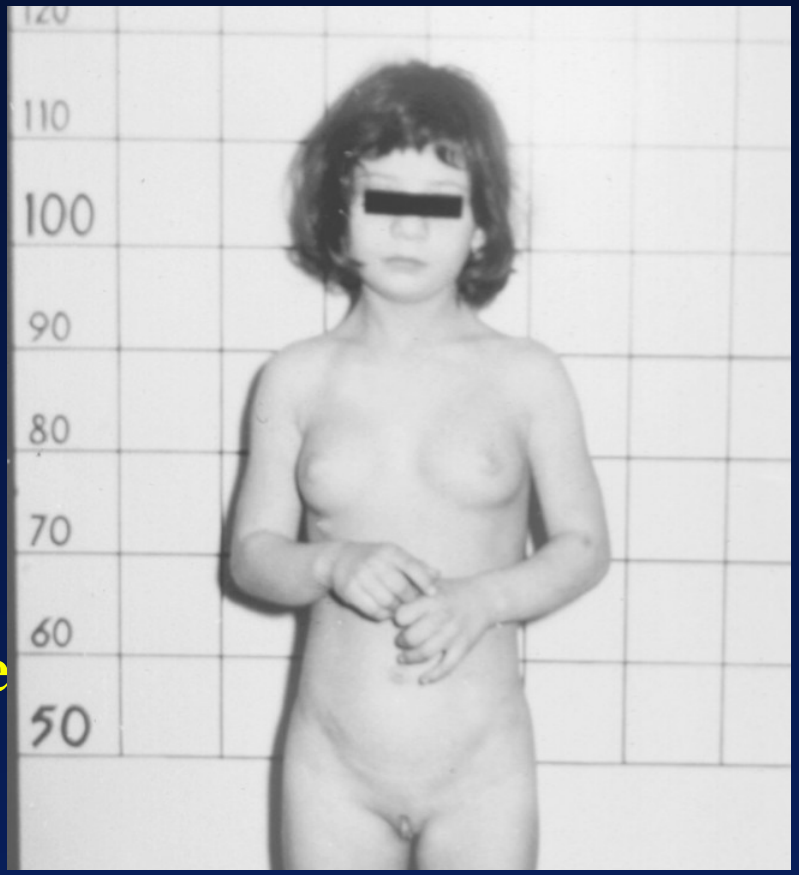

1 - What are the physiological limits - When does pathology begin ?

1 – Secular trends towards

- earlier breast development

- ie early onset of puberty

↳ have been observed during the 2nd past decades

2 – Continuing changes in environmental influences and interactions with genetic determination are involved in the pubertal process

3 – Pubertal process appears to be influenced by fetal life conditions

↳ Pubertal timing = an adaptative mechanism

1 - What are the physiological limits - When does pathology begin ?

Precocious puberty has traditionally been defined as the development of breasts < 8 years

= B_2 (Normal) ≈ 10.9 yrs

*** Herman-Giddens (17 000 girls) - B_2 : 10 yrs (white)**
9 yrs (black)

- 7% of white
- 27% of black
} **B2 < 8 y**

*** A. Juul (Denmark) - B_2 : 9.8 yrs**

*** G. Liu (China) - B_2 : 9.2 yrs**

→ **Recommendations to change the age limits**

for precocious puberty to < 7 yrs in white girls ?
< 6 yrs in black girls ?

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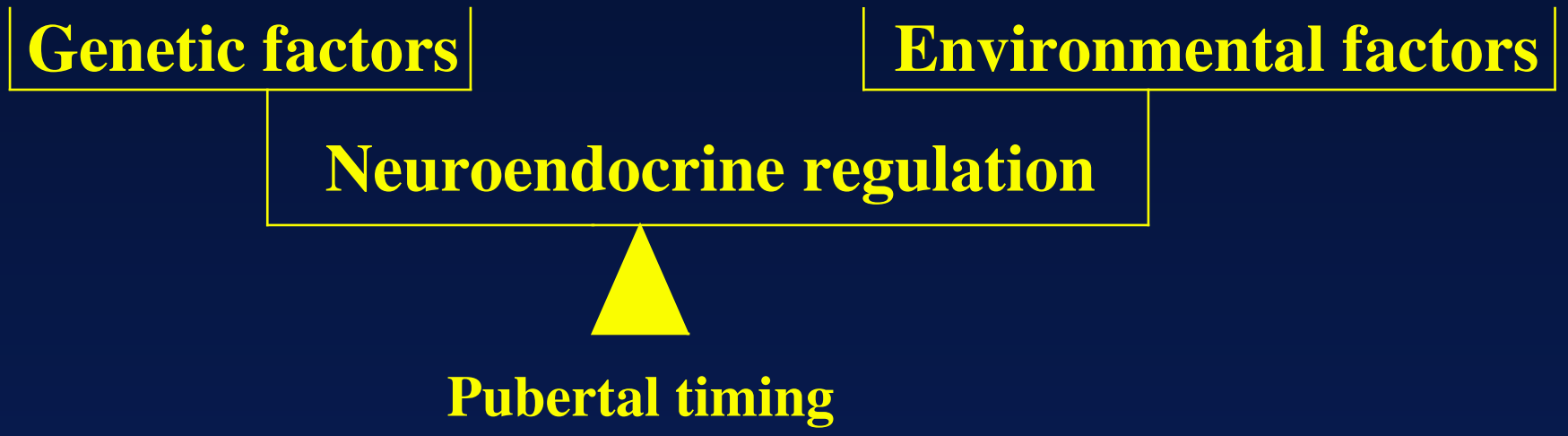

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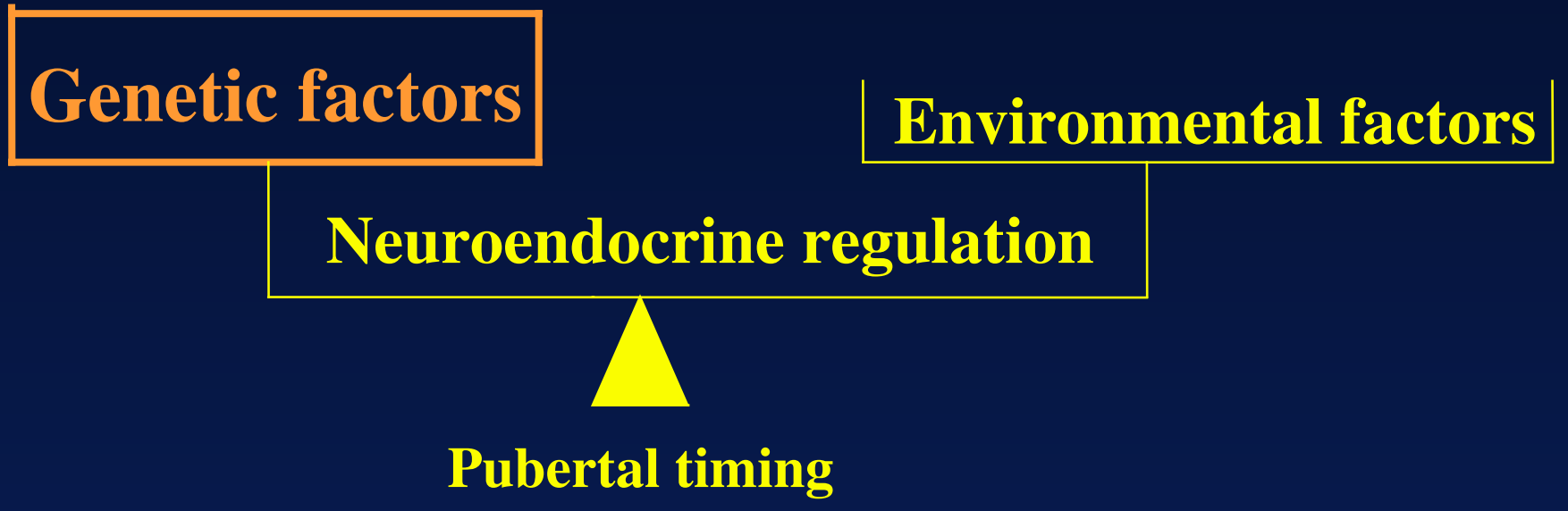


Genetic factors

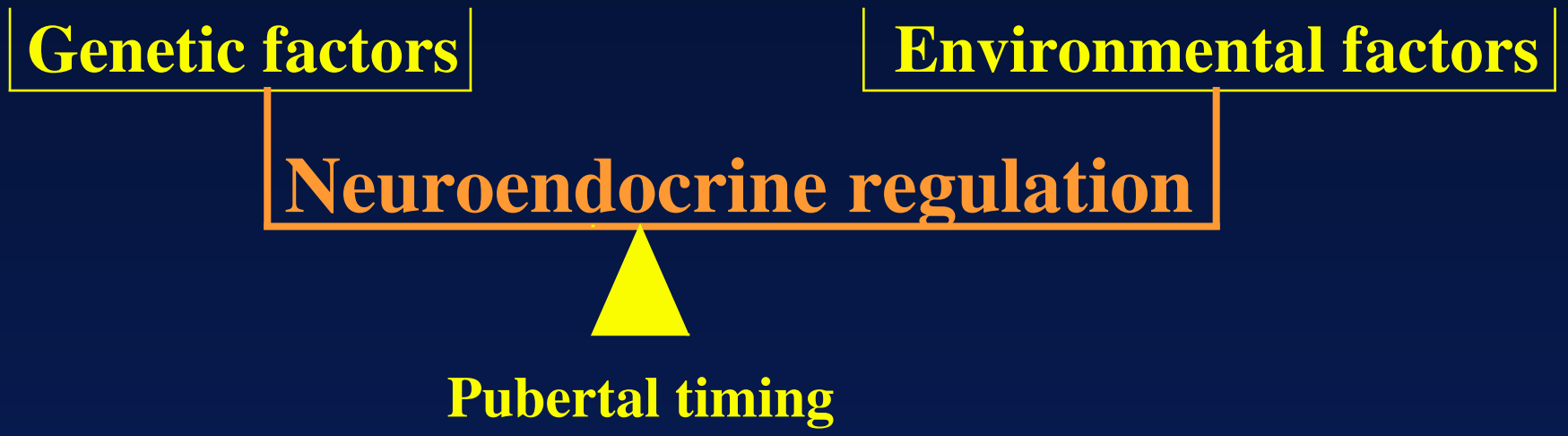
Evidence from genetic regulation (50 – 70%)

- racial / ethnic population groups
- families
- monozygotic vs dizigotic twins

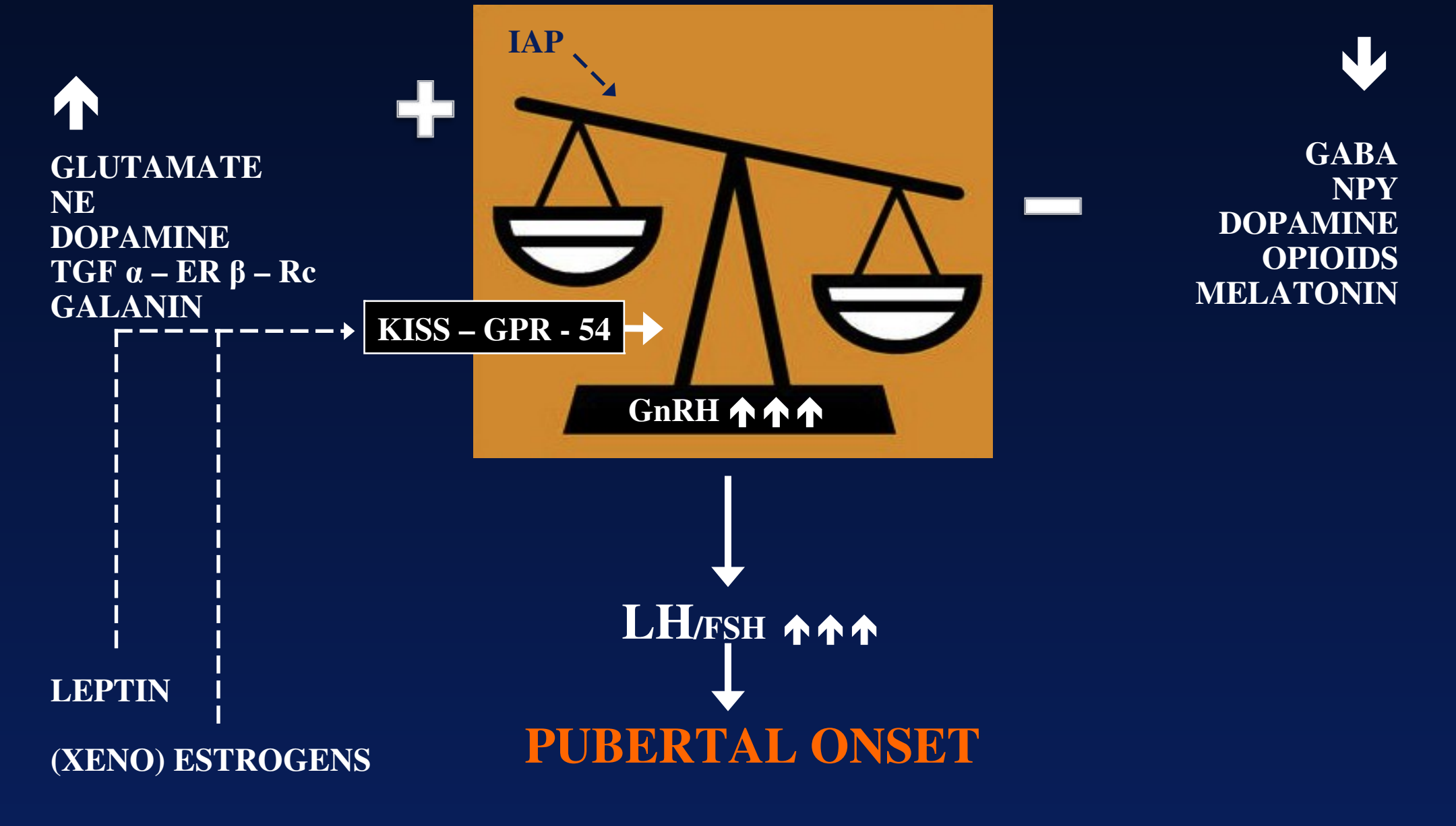
Identifying genetic factors

- resequencing of candidate genes
- genome-wide linkage analysis (22q11)
- Association studies (menarche = CYP17, COMT, ERα, SHBG, AR)
- single gene disorders (GnRH, GnRH-R, KAL, GPR-54, FGF-R1, PRO-K2, PRO-K2-Rc, LEP, LEP-Rc)

Diagnostic et traitement des pubertés précoces



Neuroendocrine regulation of Pubertal Onset



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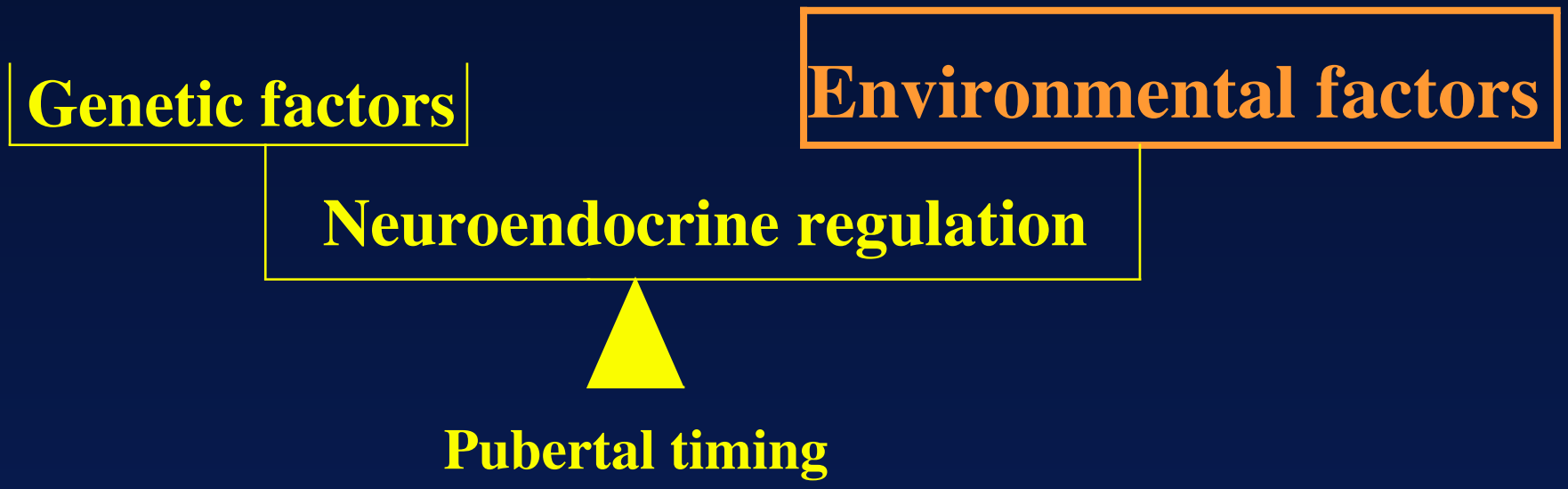


Environmental factors

1 - Nutrition (post natal vs prenatal effects)

- early menarche / BMI ↑
- intra-uterine nutrition = IUGR + precocious pubarche / early puberty

- short stress ↑ onset of puberty

4 - Environmental endocrine disruptors

"increasing use of plastics, insecticides …. (environmental disrupting chemicals) should be investigated in relation to the earlier onset of puberty" M. Herman-GiddensPediatrics 1997, 99, 4, 505

Environmental factors

. Environmental endocrine disruptors

1 - Pesticides (DDT…), herbicides, fungicides …..

2 - PCB (coolants in transformers, electrical equipment)

3 – Plastics = Bisphenol A (plastic, chemicals, containers, …), Phtalates (surfactants for packaging, storing plasticisers, medical equipment, toys …. Solvents, detergents, cosmetics ….)

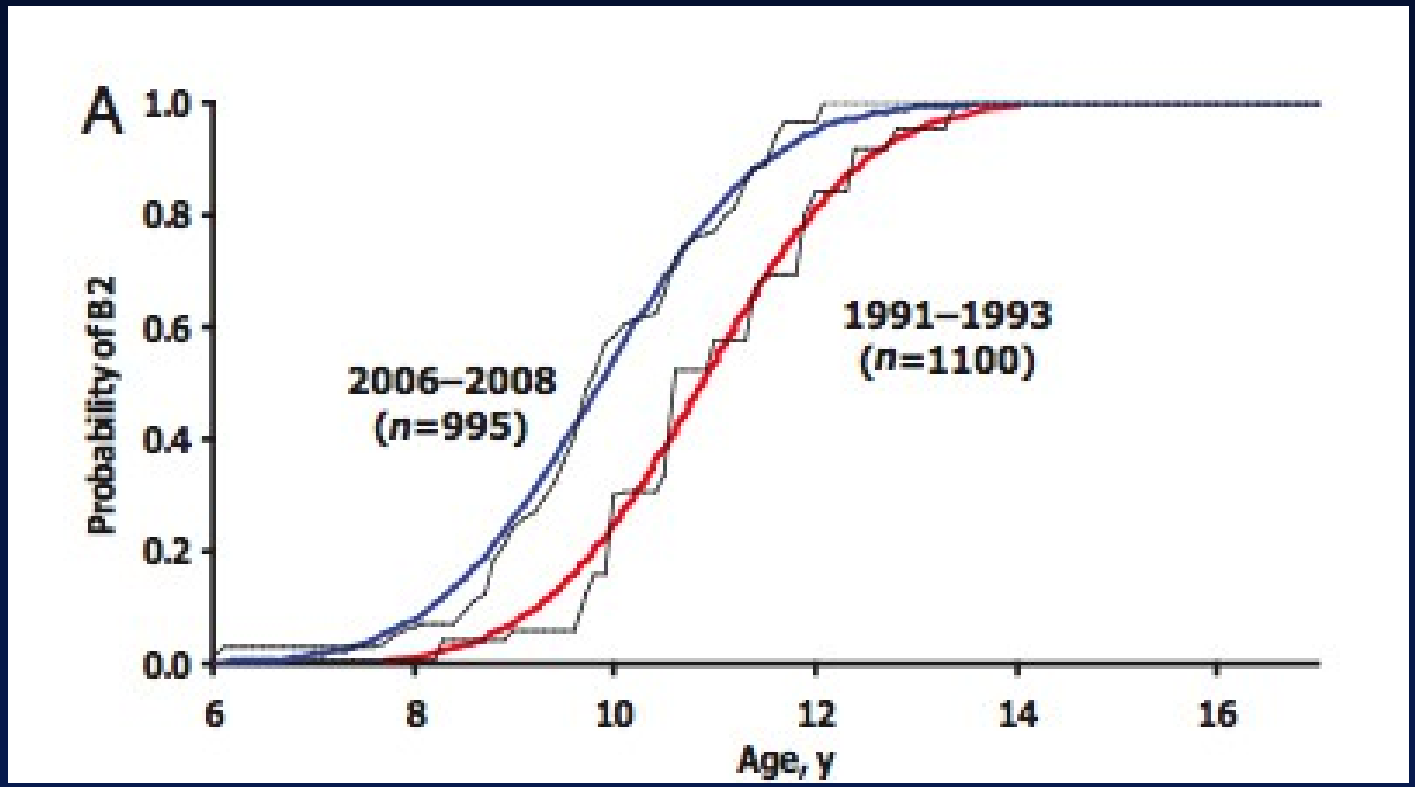
4 - Residual hormones (E2) in meat and milk …..

5 - Cosmetics, skin care products containing E2 : placenta)

6 - Phytoestrogens (soy formulas, soy milk …..)

Recent Decline in Age at Breast Development: The Copenhagen Puberty Study

Lise Aksglaede, MD[a], Kaspar Sørensen, MD[a], Jørgen H. Petersen, PhD[a,b], Niels E. Skakkebæk, MD, DMSc[a], Anders Juul, MD, DMSc[a]



Pediatrics, 2009

Pubertal Assessment Method and Baseline Characteristics in a Mixed Longitudinal Study of Girls

AUTHORS: Frank M. Biro, MD,[a] Maida P. Galvez, MD, MPH,[b] Louise C. Greenspan, MD,[c] Paul A. Succop, PhD,[d] Nita Vangeepuram, MD,[b] Susan M. Pinney, PhD,[d] Susan Teitelbaum, PhD,[b] Gayle C. Windham, PhD,[e] Lawrence H. Kushi, ScD,[f] and Mary S. Wolff, PhD[b]

RESULTS: The baseline cohort included 1239 girls. The proportion of girls who had attained breast stage 2 varied by age, race/ethnicity, BMI percentile, and site. At 7 years, 10.4% of white, 23.4% of black non-Hispanic, and 14.9% of Hispanic girls had attained breast stage ≥2; at 8 years, 18.3%, 42.9%, and 30.9%, respectively, had attained breast stage ≥2. The prime determinant of height velocity was pubertal status.

CONCLUSIONS: In this multisite study, there was substantial agreement regarding pubertal staging between examiners across sites. The proportion of girls who had breast development at ages 7 and 8 years, particularly among white girls, is greater than that reported from studies of girls who were born 10 to 30 years earlier.

Pediatrics, 2010

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Molecular and Cellular Endocrinology 324 (2010) 39–44

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journal homepage: www.elsevier.com/locate/mce

Review

Trends in puberty timing in humans and environmental modifiers

Jorma Toppari [a,b,*], Anders Juul [c]

[a] Department of Physiology, University of Turku, Kiinamyllynkatu 10, FI-20520 Turku, Finland
[b] Department of Paediatrics, University of Turku, Kiinamyllynkatu 10, FI-20520 Turku, Finland
[c] Department of Growth and Reproduction GR, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

. Environmental signals = chemical (EDCS)

Mechanisms of action

1 - Activation of transcription of estrogen-dependent genes

2 - Reduction of transcriptional activity induced by androgens

3 - Transcriptional repression of downstream genes

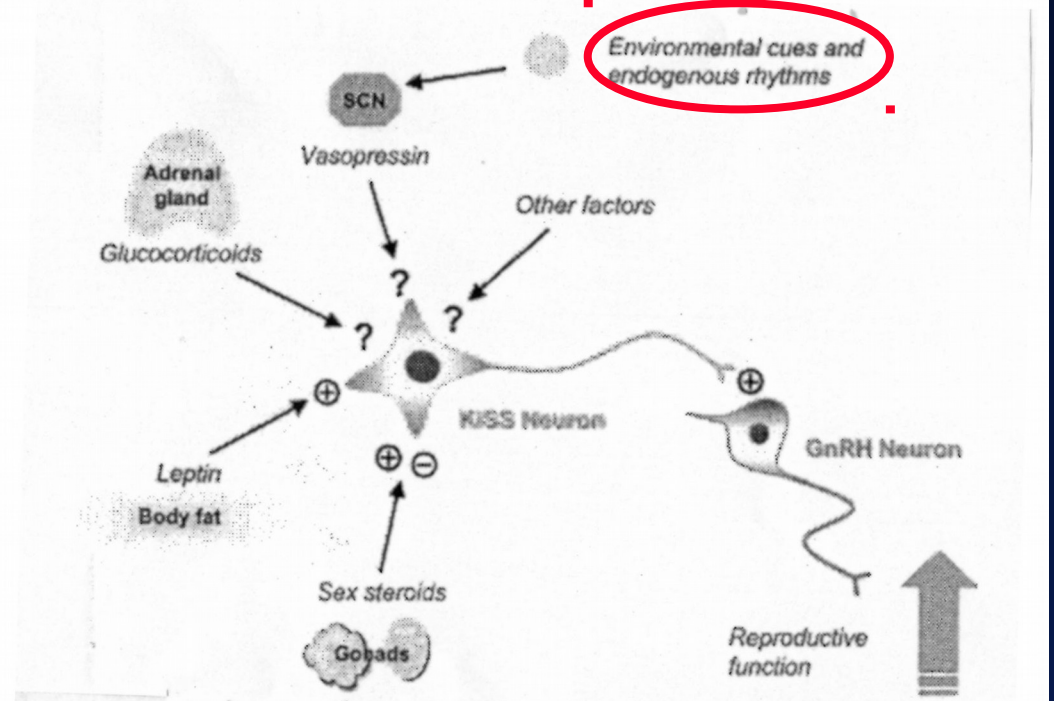
4 – Impact on the Kiss-GPR-54 system

5 - Oncogenic effect

6 - Transgenerational impact

7 - Adipose tissue +

Kisspeptin neurons as central processors in the regulation of GnRH secretion / onset of puberty



Kisspeptin neurons may act as central processors for relaying signals from the periphery to GnRH neurons. Metabolic and environmental factors regulate reproductive function, which ensures that reproduction proceeds only when metabolic and environmental conditions are favorable.

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Estrogen-like endocrine disrupting chemicals affecting puberty in humans – a review

Jonathan R. Roy[1], Sanjoy Chakraborty[2], Tandra R. Chakraborty[1]

Effects of EEDC on reproduction of prenatal and pubertal girls.

EEDC	Exposure	Type of Action	Findings	Reference
DDE	Pubertal girls	Estrogen mimicker/blocker	Earlier menarche	Vasiliu et. al. 2004, [20]
Dioxin	Pubertal girls	Estrogen blocker	Abnormal breast dev	Den Hond et. al., 2002 [42]
Bisphenol A	Prenatal girls	Estrogen blocker	Precocious puberty	Howdeshell et. al., 1999 [62]
PCB	Pubertal girls	Estrogen mimicker/blocker	No significant effect	Vasiliu et. al.. 2004 [20]
PBB	Prenatal girls	Estrogen mimicker	Earlier menarche and earlier pubic hair stage	Blanck et. al., 2000 [61]
Phthalate esters	Pubertal girls	Estrogen mimicker	Causes de-feminization	Colon et. al., 2000 [63]

Med Sci Monit, 2009

Diagnostic et traitement des pubertés précoces

** Epidemiological studies in girls*

(1) Michigan cohort (4000 individuals) : PCB

. Breast-fed daughters of mothers with a high serum PCB = earlier menarche 11.6 years

vs non-breastfed girls 12.5 years

(2) The great lakes cohort

. DDE (DDT) = lowers age of menarche

Précocités pubertaires : un nouveau regard

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** Epidemiological studies in girls*

(3) BOURGUIGNON (2001) = adopted girls with CPP

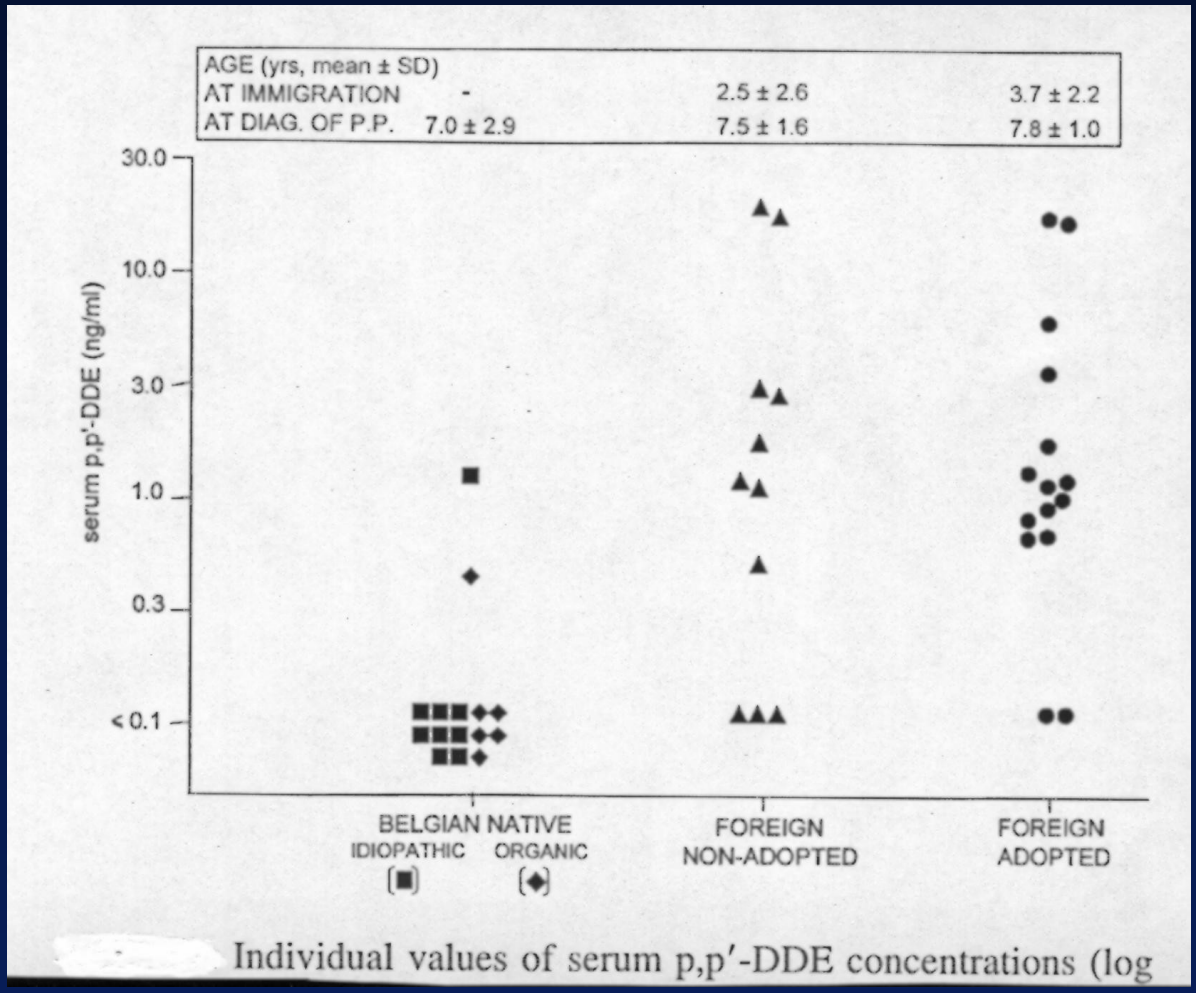
= DDE levels : 5 to 10 tms higher / native belgium girls

(4) WANG (2005) National Children's study

= exposure to EDCS in utero can alter

- **the growth of mammary glands**
- **the age of onset of puberty of the offsprings**

Environmental disruptors and precocious puberty in adopted girls (M. Kristewska et al, 2001)



Individual values of serum p,p′-DDE concentrations (log

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Précocités pubertaires : un nouveau regard

** Epidemiological studies in girls*

(5) COLON (2000) = premature thelarche in girls / phtalates
= phtalate levels x 5 (adipose tissues)

(6) MASSART (2005) = Precocious puberty in girls from Toscany

= Prevalence of CPP 16/10 000 / intensive agricultural area

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Gynecol Endocrinol, 2013; 29(8): 1–5
 DOI: 10.3109/09513590.2013.801448

informa healthcare

ORIGINAL ARTICLE

Increased serum estrogenic bioactivity in girls with premature thelarche: a marker of environmental pollutant exposure?

Françoise Paris[1,2]*, Laura Gaspari[1,2]*, Nadège Servant[2], Pascal Philibert[2], and Charles Sultan[1,2]

[1]Unité d'Endocrinologie-Gynécologie Pédiatriques, Departement de Pédiatrie, Hôpital Arnaud-de-Villeneuve, CHU Montpellier et Université Montpellier 1, Montpellier, France and [2]Service d'Hormonologie (Développement et Reproduction), Hôpital Lapeyronie, CHU Montpellieret Université Montpellier 1, Montpellier, France

Diagnostic et traitement des pubertés précoces

Précocité pubertaire / fille

. Observation personnelle privilégiée : Clara, 3 mois, précocité pubertaire

- S3
- menstruations
- estrogènes ultrasensibles x 10
- LHRH test = plat
- échographie pelvienne = utérus L = 69mm !

Puberté précoce périphérique

* ATCD = famille vit dans une propriété (Lodève) où sont stockés x ~~tonnes de pesticides~~

Gaspari et al, Gynecol Endocrinol. 2011 Sep;27(9):721-4

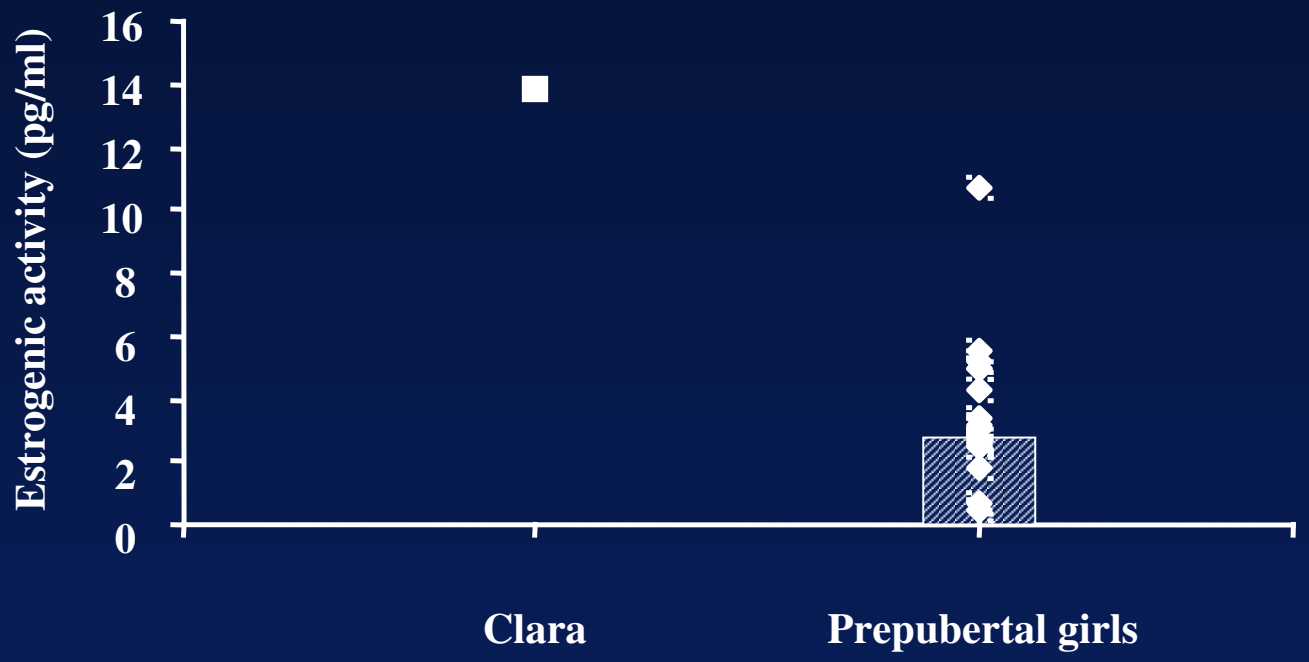
Neonatal peripheral precocious puberty

3 month-old girl

Lives in an area of pesticides storage

Father 38 years old, decreased libido

EA = 13,7 pg/ml vs 3,5 +/- 2,2 pg/ml

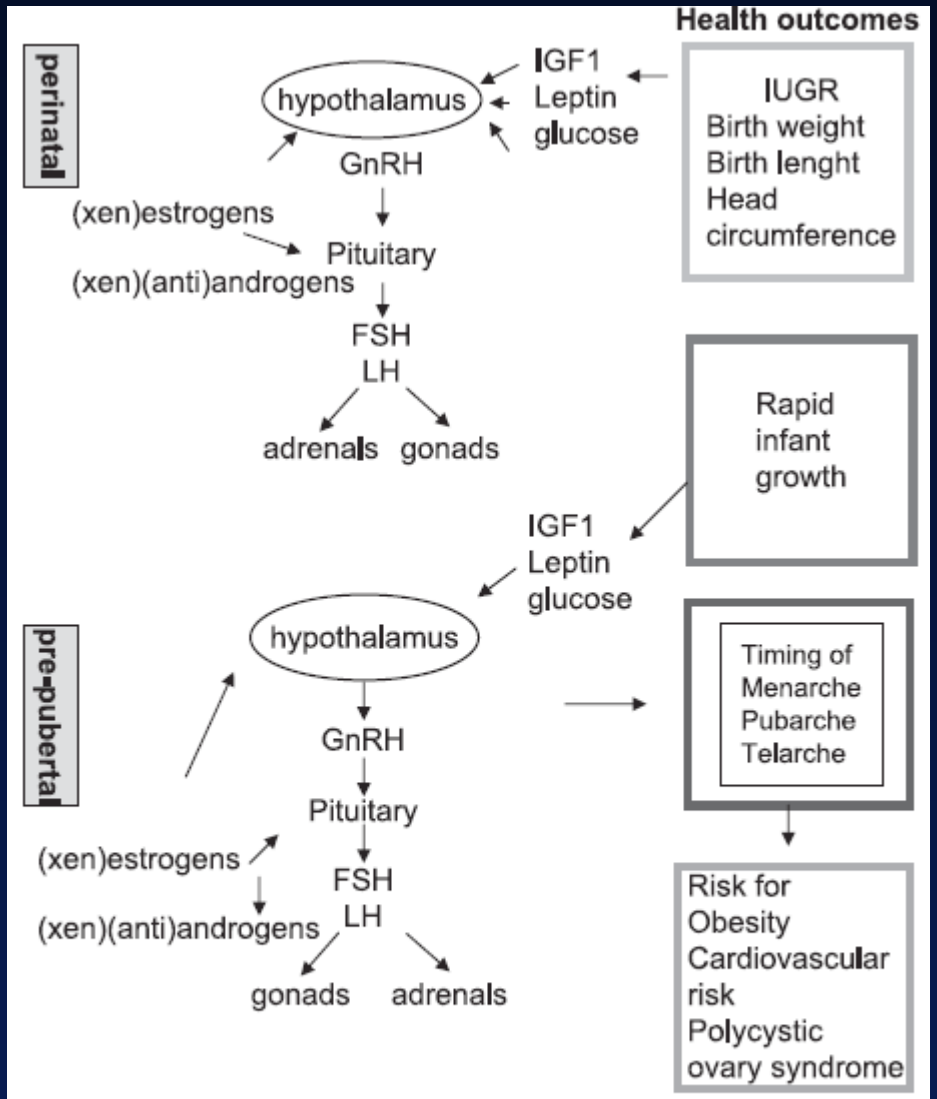


Précocités pubertaires / fille

.Observation personnelle

Etude des pesticides (N. Oléa, Grenade)

Clara	***Père***	***Mère***	***sol (propriété)***
Lindane		**Lindane**	**Lindane**
p,p'-DDD		**p,p'-DDD**	**m,p-DDD**
p,p-DDT			**o,p'-DDT**
Endosulfan-sulphate	**Endosulfan-sulphate**		



Schematic illustration of perinatal and postnatal targets for endocrine-disrupting chemicals (EDC) in relation to possible health outcomes.

Schoeters, 2008

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Diagnostic et traitement des pubertés précoces

Consequences of early maturation of girls

1 - Greater weight and BMI

2 – Insulin resistance

3 – Metabolic syndrome

4 - PCOS

5– Cardio-vascular diseases

6 – Breast cancer risk ++

Diagnostic et traitement des pubertés précoces

Consequences of early maturation of girls

1 – Lower self-esteem during adolescence
2 – Lower level of body satisfaction
3 – Greater likewood of depression
4 – Greater likewood of earling disorders
5 – Greater perceived stress
6 – Greater vulnerability to peer pressures
7 – Younger age of sexual initiation
8 – Younger age of smoking and drug use
9 – Lower life-long academic achievement

Precocious Puberty in Adolescent Girls: A Biomarker of Later Psychosocial Adjustment Problems

Line Tremblay, PhD
Laurentian University, Department of Psychology
Sudbury, Ontario, Canada
Jean-Yves Frigon, PhD
University of Montreal, Department of Psychology
Montreal, Quebec, Canada

Early maturing girls : at risk for

1 – psychosocial adaptation problems

2 – depression and anxiety

3 – problem behaviors / delinquency

4 – physical aggression, hostility, hyperactivity

5 – earlier sexual behaviors

6 – sex transmitted diseases

7 – pregnancy (↓ contraceptive methods)

« Puberty acceleration hypothesis «

***Child Psychiatry and Human Development*, 2005**

Coup de gueule

La « pédomode » selon « Vogue »

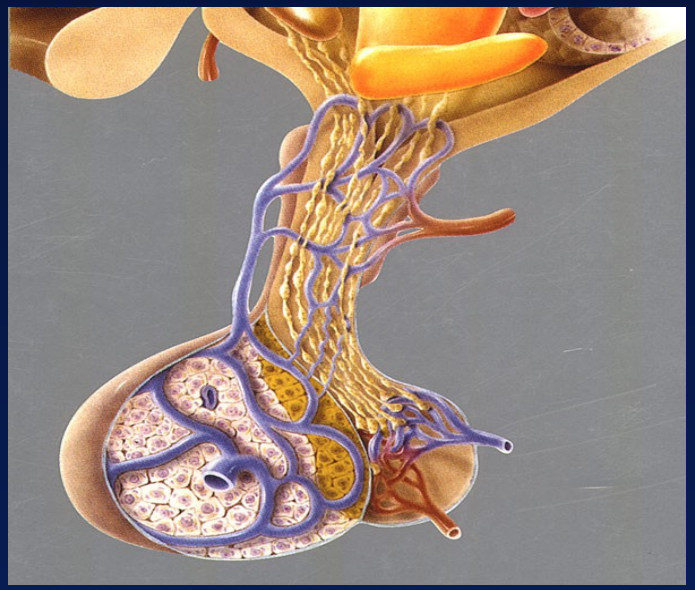
Des Lolita de 10 ans à peine, posant lascivement en tenues sexy, pour vendre des articles de luxe : le numéro de *Vogue France*

FACTEURS GENETIQUES

FACTEURS ENVIRONNEMENTAUX

50- 75% ?

25-50 %?



Puberté

Diagnostic et traitement des pubertés précoces

1) What are the physiological limits - When does pathology begin ?

⟶ **Precocious puberty**

B2

< 8 yrs (< 9 yrs)

P2

Diagnostic et traitement des pubertés précoces

Questions

1 - What are the physiological limits - When does pathology begin ?

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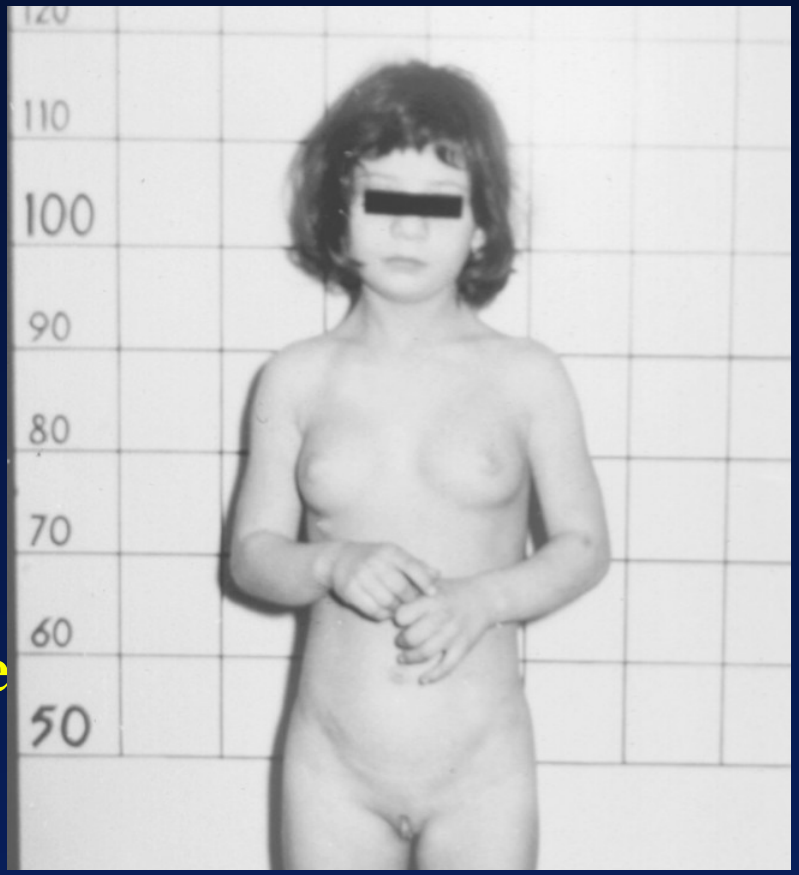


Diagnostic et traitement des pubertés précoces

2) Complete (central), incomplete (partial) or peripheral precocious puberty

= excess estrogens (girls)

1 - activation of HPO axis ? **= central, <u>complete</u> PP**

2 - estrogen effect from anyother sources ? **= peripheral PP**

Diagnostic et traitement des pubertés précoces

2 - Complete (central), incomplete (partial) or peripheral precocious puberty

1 - Central, complete precocious puberty (true CPP)

A - Idiopathic CPP

B - Neurogenic

C - Ass / other anomalies

2 - Complete (central), incomplete (partial) or peripheral precocious puberty

2 - 1 Central, complete precocious puberty (true CPP)

A - idiopathic

1 - sporadic

= rapidly progressive puberty + growth spurt

= deterioration of height potential

2 - very precocious puberty

3 - slowly progressive CPP

4 - spontaneously regressive CPP

5 - adopted girls

6 - early puberty

* familial CPP

2 - Complete (central), incomplete (partial) or peripheral precocious puberty

2 -1 Central, complete precocious puberty (true CPP)

B - neurogenic ----------→ Very precocious puberty

1 - CNS abnormalities

- hypothalamic hamartoma, other tumors
- hydrocephalus
- neurofibromatosis (glioma)

2 - Acquired CNS damage

- radiation therapy
- head trauma
- infection (encephalitis, meningitis …)

Précocités pubertaires : un nouveau regard

2 - Complete (central), incomplete (partial) or peripheral precocious puberty

2-2 – Incomplete (partial) or peripheral precocious puberty (pseudo pp)

a) Definition

. No premature and permanent activation of the gonadotropic axis

2 - Complete (central), incomplete (partial) or peripheral precocious puberty ?

2-2 - incomplete (partial)

- Premature thelarche
- Premature adrenarche
- early menarche

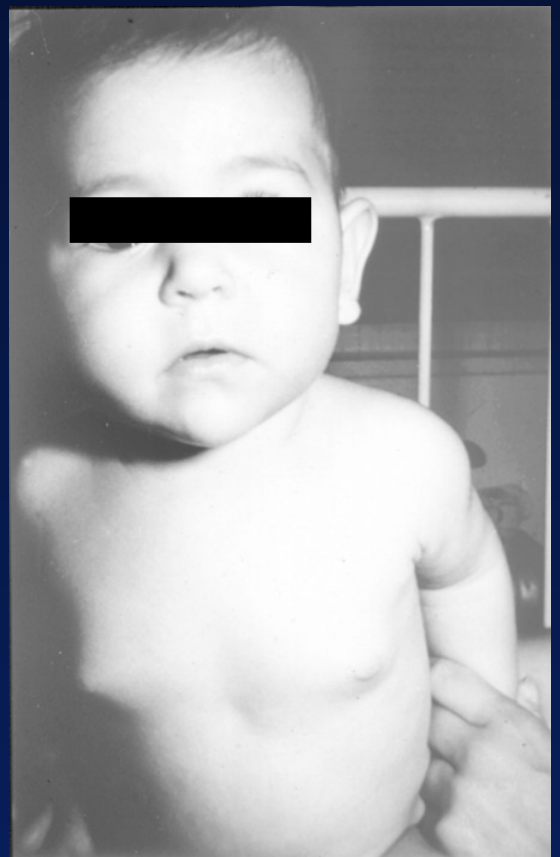
Incomplete PP ?

- recurent ovarian cysts)
- ovarian tumor
- adrenal tumor
- environmental disruptors chemicals

Peripheral PP ?

2 - Complete (central), incomplete (partial) or peripheral precocious puberty?

2 - 2 Incomplete (partial) precocious puberty

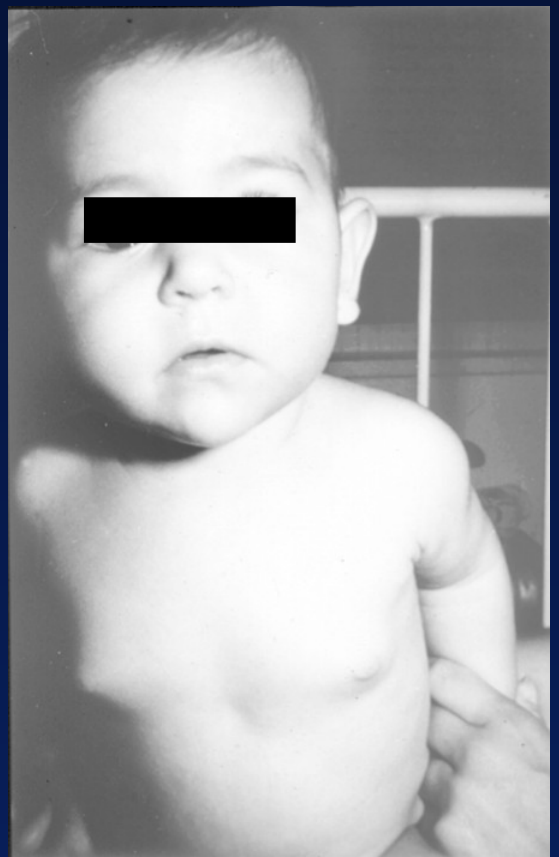


A - Premature thelarche

= Is premature thelarche truly a « normal variant » ?

2 - Complete (central), incomplete (partial) or peripheral precocious puberty?

2 – 2 Incomplete (partial) precocious puberty



A - Premature thelarche

= Is premature thelarche truly a « normal variant » ?

1 - isolated premature thelarche (classical) :

2 - non classical, atypical forms (geographical cluster)

3 - thelarche variant = slowly progressive PP

4 - ovarian tumor !

Diagnostic et traitement des pubertés précoces

2 - Complete (central), incomplete (partial) or peripheral precocious puberty?

2 - 2 Incomplete (partial) precocious puberty

B - Premature adrenarche / Pubarche

= Is premature adrenarche truly a « normal variant » ?

Diagnostic et traitement des pubertés précoces

2 - Complete (central), incomplete (partial) or peripheral precocious puberty?

2 - 2 Incomplete (partial) precocious puberty

B - Premature adrenarche / Pubarche

= Is premature adrenarche truly a « normal variant » ?

- late onset 21 OH Def 10 - 20%
- adrenal tumor !

Diagnostic et traitement des pubertés précoces

2 - 3 incomplete (partial) or peripheral precocious puberty (pseudo PP)

Classification / causes

1. Ovarian autonomous hyperactivity

. McCune-Albright syndrome

. granulosa cell tumor

2. Adrenal tumors : adenomas / carcinomas

3. Environmental pollution (xenoestrogens) /

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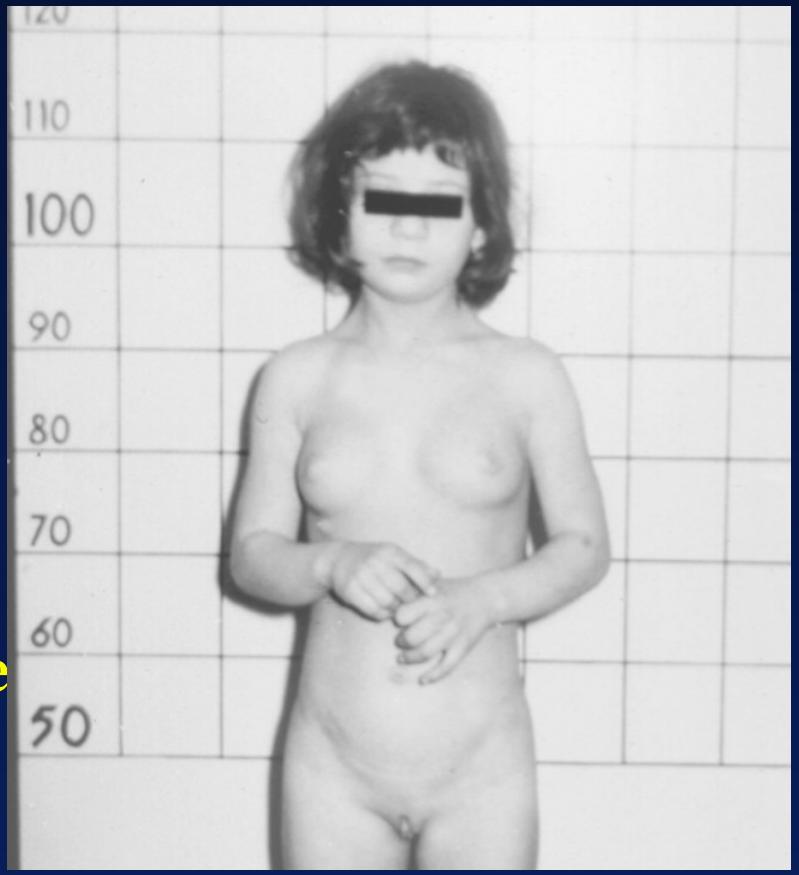


Diagnostic et traitement des pubertés précoces

3 - Assessment of sexual precocity

1 - History

- familial history of age of puberty onset
- CNS trauma, anomalies, infections
- exposure to exogenous estrogens
  (environment ?)
- history of first manifestation of puberty
- signs and how fast they progressed
- growth rate over last 12 months

Diagnostic et traitement des pubertés précoces

3 - Assessment of sexual precocity

2 - Physical examination

- pubertal maturational staging (Tanner)
- height, height velocity
- weight
- body proportions
- acne, skin pigmentation
- abdominal bimanual examination

Diagnostic et traitement des pubertés précoces

3 - Assessment of sexual precocity

3 - Radiological assessment

- bone age
- ratio of ΔBA / CA
- pelvic US
  - uterine length > 35 mm
  - ovarian structure - ov. cysts
  - ov. tumor ?

± . Uterine ant-post diameter > 8 mm

. Ut. Transverse diameter > 15 mm

. Ut. Volume > 2 cm3

. Endometrial thickness > 0.2 mm

. Ovarian circumference > 5 cm

Diagnostic et traitement des pubertés précoces

3 - Assessment of sexual precocity

4 - hormonal evaluation

-plasma levels of E2, FSH, LH (?)

- LHRH test =↑ LH > 7 mUI.ml
  LH/FSH > 1

- ↑ IGF1

- TSH ↑(?)

Diagnostic et traitement des pubertés précoces

3 - Assessment of sexual precocity

5 - Psychosocial and behavioral consequences

- distressing findings for families / girls
  = 2 major concerns of parents
    . the risk of sex abuse
    . early pregnancy (+)

- girls - difficulty developing social relationships
  - a negative self-concept
  - alteration of body image, self-esteem
  - depression, aggressiveness, socially withdrawn
  - drop in school performance

Diagnostic et traitement des pubertés précoces

Questions

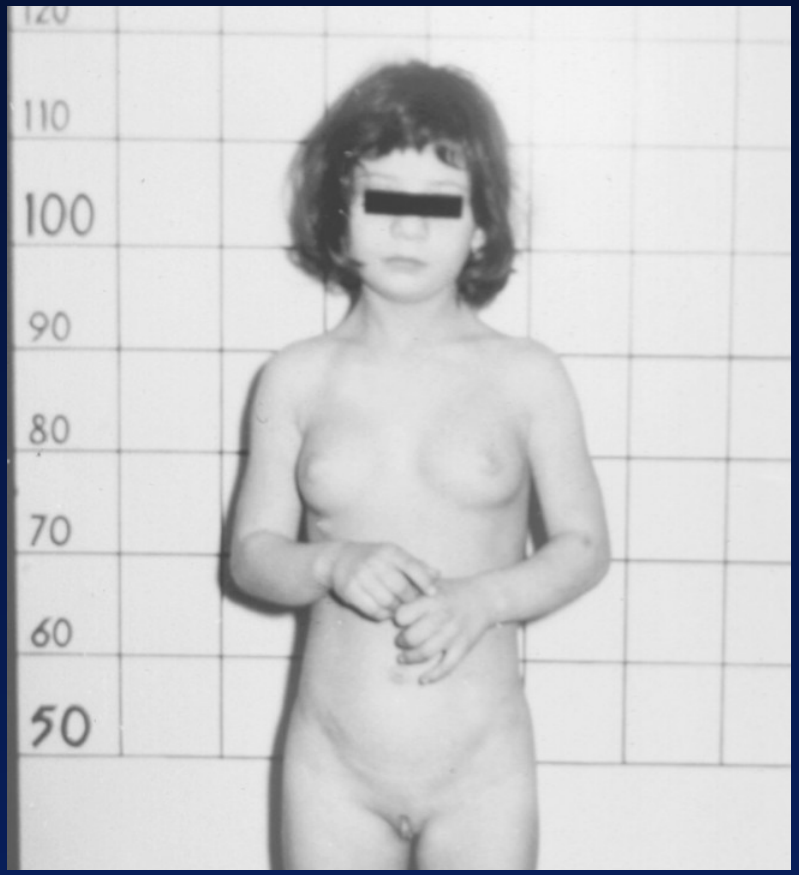
1 - What are the physiological limits - When does pathology begin?

2 - Complete (central),
incomplete (partial)
or peripheral precocious puberty ?

3 – Assessment of sexual precocity

4 – Diagnosis

5 - Conclusions



Diagnostic et traitement des pubertés précoces

4 - Diagnosis of girls presenting with signs of sexual precocity (personal experience)

1 - Central precocious puberty (25%)

- sec / CNS tumor, lesion (5%)
- idiopathic (15%)
- adopted girls (5%)

2 - Precocious puberty "variants" (25%)

- transient CPP
- undulating CPP
- slowly progressive CPP

3 - Premature thelarche (40%)

- isolated (30%)
- thelarche variant (10%)

Diagnostic et traitement des pubertés précoces

4 - Diagnosis of girls presenting with signs of sexual precocity (personal experience)

4 - Premature pubarche (10%)

- idiopathic adrenarche (8%)
- late onset CAH (2%)

5 - Peripheral precocious puberty (10%)

- ovarian cysts
- MAS
- Granulosa cell tumor (2%)

* Early and fast puberty (2/10)

Diagnostic et traitement des pubertés précoces

4 - Diagnosis

1 - Central precocious puberty (25%)

- sec / CNS tumor, lesion
- idiopathic

↓

Premature activation of GnRH secretion

1. LHRH test = predominant LH response
2. Pelvic US = uterine volume
   endometrial thickness | ↑ E2 production
   ovarian morphology = multicystic
3. Bone age > 12, 18 months
   ratio of ΔBA/CA > 1.2
4. MRI of CNS

Diagnostic et traitement des pubertés précoces

4 – Diagnosis

2 - Central precocious puberty "variants" (15%)

-transient CPP

- undulating CPP

- slowly progressive CPP

1 LHRH test

2 Pelvic US

3 Bone age

Investigation

*** repeated after a 6-month- observation period**

*** progression of pubertal maturation ?**

Diagnostic et traitement des pubertés précoces

4 – Diagnosis

3 - Premature thelarche (40%)

-isolated

- thelarche "variant"

Difficult to distinguish from CPP

= complete spectrum of GT secretion between FSH and LH dominance !

1. LHRH test ±

2. Pelvic US

3. Bone age = not advanced

Diagnostic et traitement des pubertés précoces

4 – Diagnosis

4 - Peripheral precocious puberty (10%)

- **ovarian cysts (isolated)**
- **ovarian cysts (recurrent)**

1. **Pelvic US**
2. **LHRH Test = negative**
3. **Mol genetics of Gsα gene (MAS) ?**

Diagnostic et traitement des pubertés précoces

4 – Diagnosis

4 - Peripheral precocious puberty (10%)

- granulosa cell tumor

. pl E2 + Androg + Inhibin / AMH

. Pelvic US: Ovarian tumor ?

. LHRH test : negative

. Mol genetics: somatic Gsalpha

Diagnostic et traitement des pubertés précoces

Questions

1 - What are the physiological limits - When does pathology begin ?

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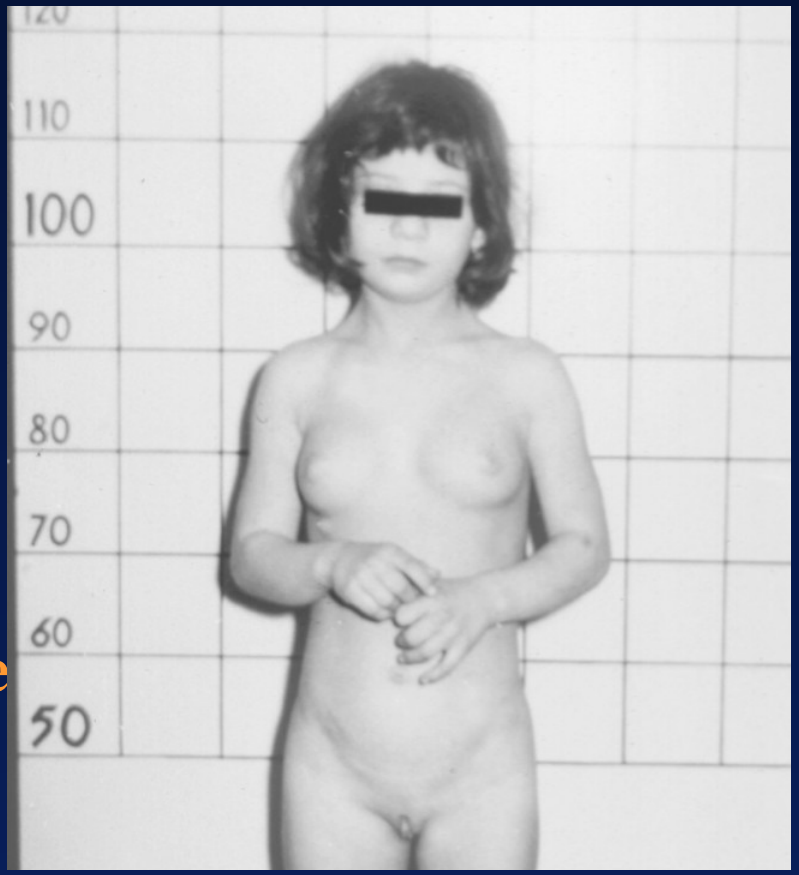
4 – Diagnosis

5 – Management : optimizing the outcome

6 - Conclusions



Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

= therapy for precocious puberty depends first and foremost on the cause of hyperestrogenism

→ Medical / surgical suppression of hyperestrogenism

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

1 - From peripheral origin

- MAS
- Granulosa cell tumor
- Environmental xenoestrogens

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

1 - From peripheral origin **- MAS**

1 - cystectomy
2 - ovariectomy
3 - aromatase inhibitors
4 - anti-estrogens (estrogen antagonists)

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

1 - From peripheral origin

- MAS

1 - cystectomy

- large ovarian cyst(s)
- early life
- isolated ppp

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

1 - From peripheral origin

- granulosa cell tumor

→ Surgery

- tumorectomy
- ovariectomy

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

1 - From peripheral origin

- environmental xenoestrogens

→ **Reduce inhalation**
ingestion
transdermal exposure to EDC !

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin

- neurogenic (tumor) CPP

  - surgery
  - radiation
  - chemotherapy

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin **- idiopathic CPP**

*** indications for treatment**

1. Complete (and rapidly progressive) CPP
2. Abnormal height potential
   - height prediction < 3SD
   - height SDS for BA < -2

3 - Behavioral and psychological disturbances

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

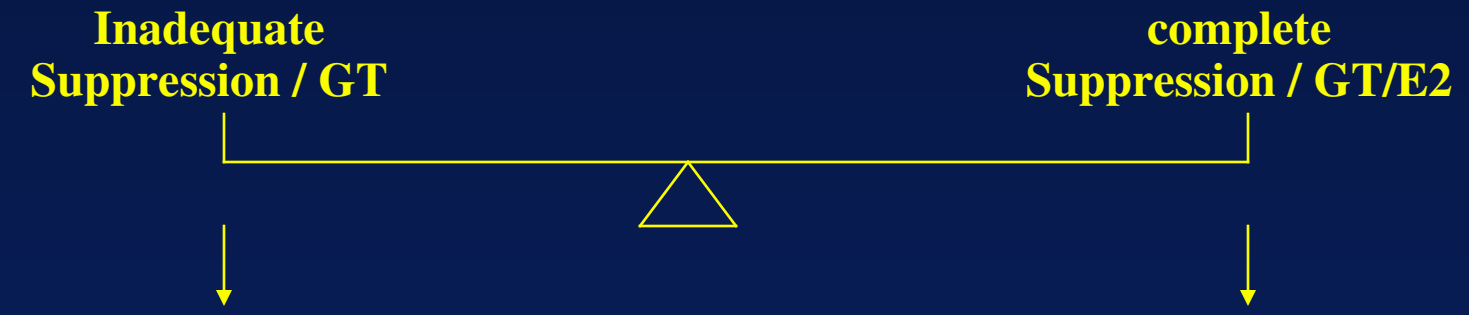
2 - From central origin **- idiopathic CPP**

2- Which regimen? (reliable suppression of GT, compliance)

3- When to start the treatment ?

4- When to stop the treatment ?

5- Long term outcomes ?



Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin — **- idiopathic CPP**

1- Therapeutic option → **depot GnRH analogs (GnRHa)**

- **. one month**
- **. three months**
- **. One year**

regimens

→ **GnRHa + GH ?**

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin **- idiopathic CPP**

2- Which regimen ? ⟶

*** depot Leuprolide : the drug of choice**

. US : the recommended starting dose = 0.3mg.kg.month

7.5 mg ⟶ 15 mg / month

*** depot Leuprolide = 11.25 mg every 3 months (1 year)**

. France (2006) = suppression of the pit. ovarian axis

. US (2006) = suppression of the pit. ovarian axis

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin **- idiopathic CPP**

→

*** Histerelin Subdermal Implant (50 mg) / 1 year**

E. Eugster (2007) = excellent suppression of peak LH / E2 levels for 1 year

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin **- idiopathic CPP**

3- When to start the treatment ?

. 60 girls with CPP + GnRHa 3.75 mg / month

. Discontinuation of treatment
. CA : 11 - 11.5 y

. BA : 12 - 12.5
. GV < 4cm / y

38 diagnosed **CA > 6 - 8 yr**

Girls treated > 6 yr **. ↓ post-treatment height gain**
. compromised final height

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin - idiopathic CPP

4- When to stop the treatment ?

The policy of many (pediatric) endocrinologists is to interrupt GnRHa

at CA 11 - 11.5 yr
at BA 12 - 12.5 yr

→ to anticipate a similar percentage of residual height gain

<u>Question</u> : Should GnRHa treatment be withdrawn when BA closer to 11 that 12 y to allow a more robust post-treatment growth spurt ?

Diagnostic et traitement des pubertés précoces

Premature exposure to estrogens

2 - From central origin - idiopathic CPP

5- Long term outcomes ? (PASQUINO, JCEM, 2008)

1. Impact on adult height = m 161 cm (-4cm / TH)

2. Impact on BMI = overweight (14.3%), obese (9.1%)

3 - Impact on BMD = lower than control (lumbar spine) during treatment

> complete resumption of gonadal activity = mean BMD = N

4 - Reactivation of the gonadotropic axis > 3 - 4 months

menarche = 1 y

Diagnostic et traitement des pubertés précoces

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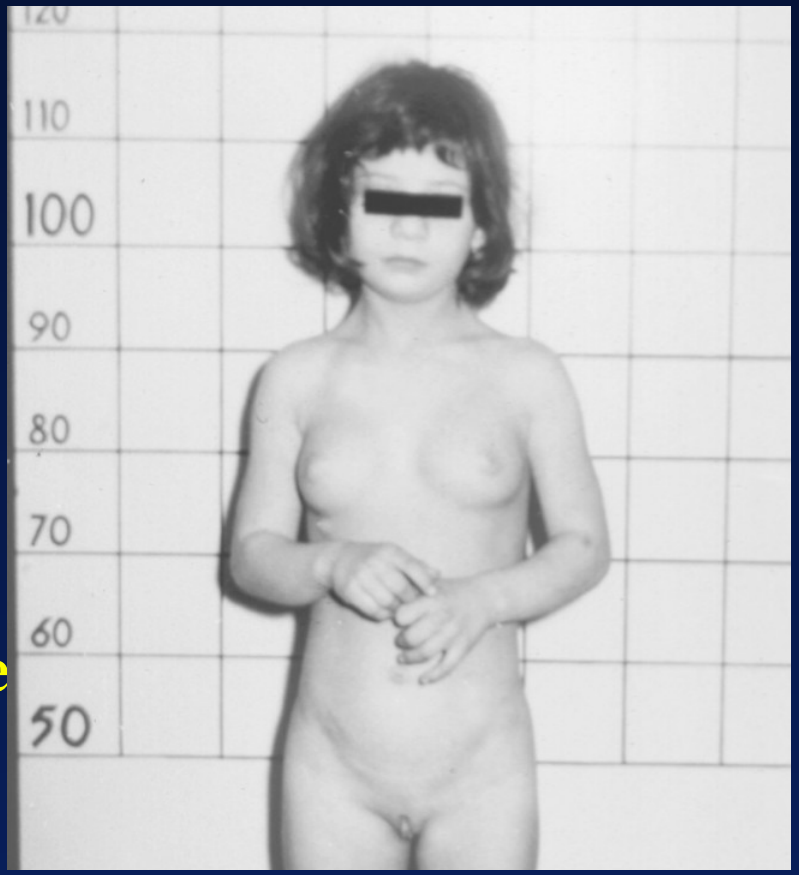


Diagnostic et traitement des pubertés précoces

Conclusion (1)

1. Starting treatment > 6 y : worsen final height ?
2. Stopping treatment : BA < 12 : increase post treatment growth spurt ?
3. Should regimen be modulated (f.) : -growth response ?
   - pubertal response ?
4 - How much should psychological problems be taken into consideration for treatment decision ?
5 - Any consensus or individualized treatment ?

Diagnostic et traitement des pubertés précoces

Conclusion (2)

- Female precocious puberty is very common.

- It is difficult to know how far to push the investigations.

- Sometimes it is within the physiological limits and sometimes it is an early sign of underlying pathology.

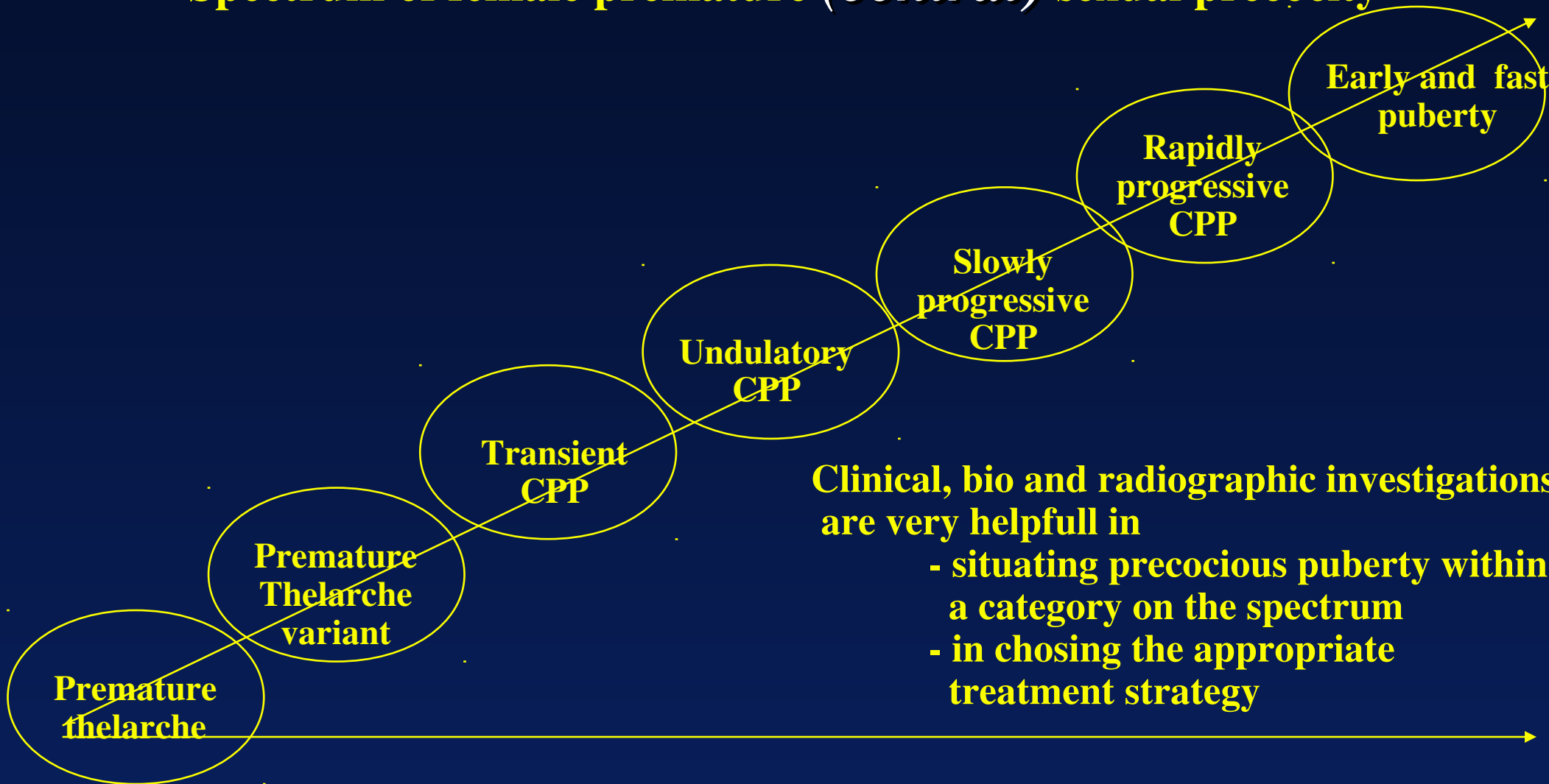
- (Pediatric) Endocrinologists and Gynecologists do have the key role in determining a realistic strategy of investigation.

- Central and peripheral puberty cover a very wide spectrum.

Diagnostic et traitement des pubertés précoces

Conclusion (3)

Spectrum of female premature *(central)* sexual precocity



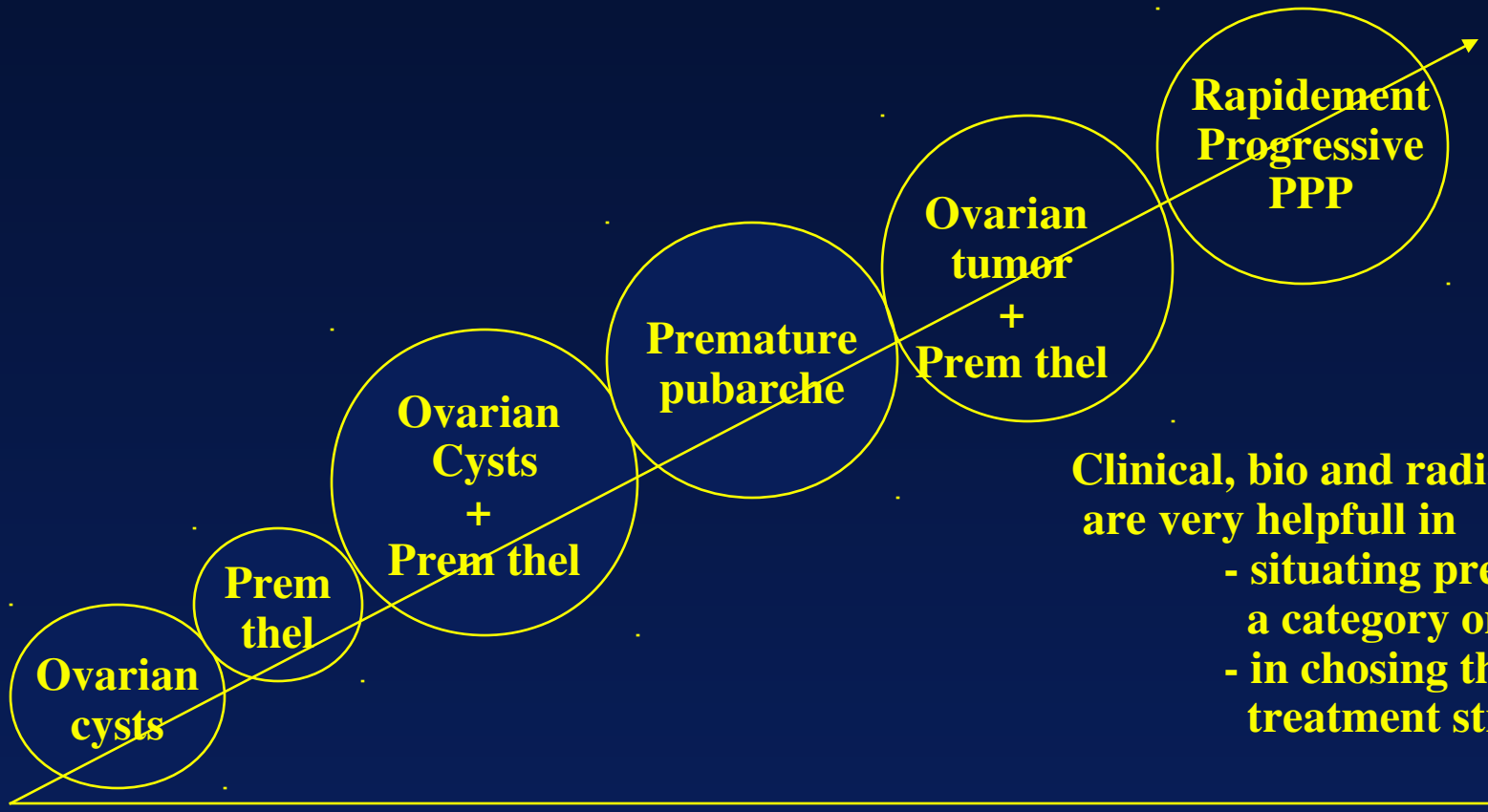
Clinical, bio and radiographic investigations are very helpfull in

- situating precocious puberty within a category on the spectrum
- in chosing the appropriate treatment strategy

Diagnostic et traitement des pubertés précoces

Conclusion (4)

Spectrum of female *peripheral* sexual precocity

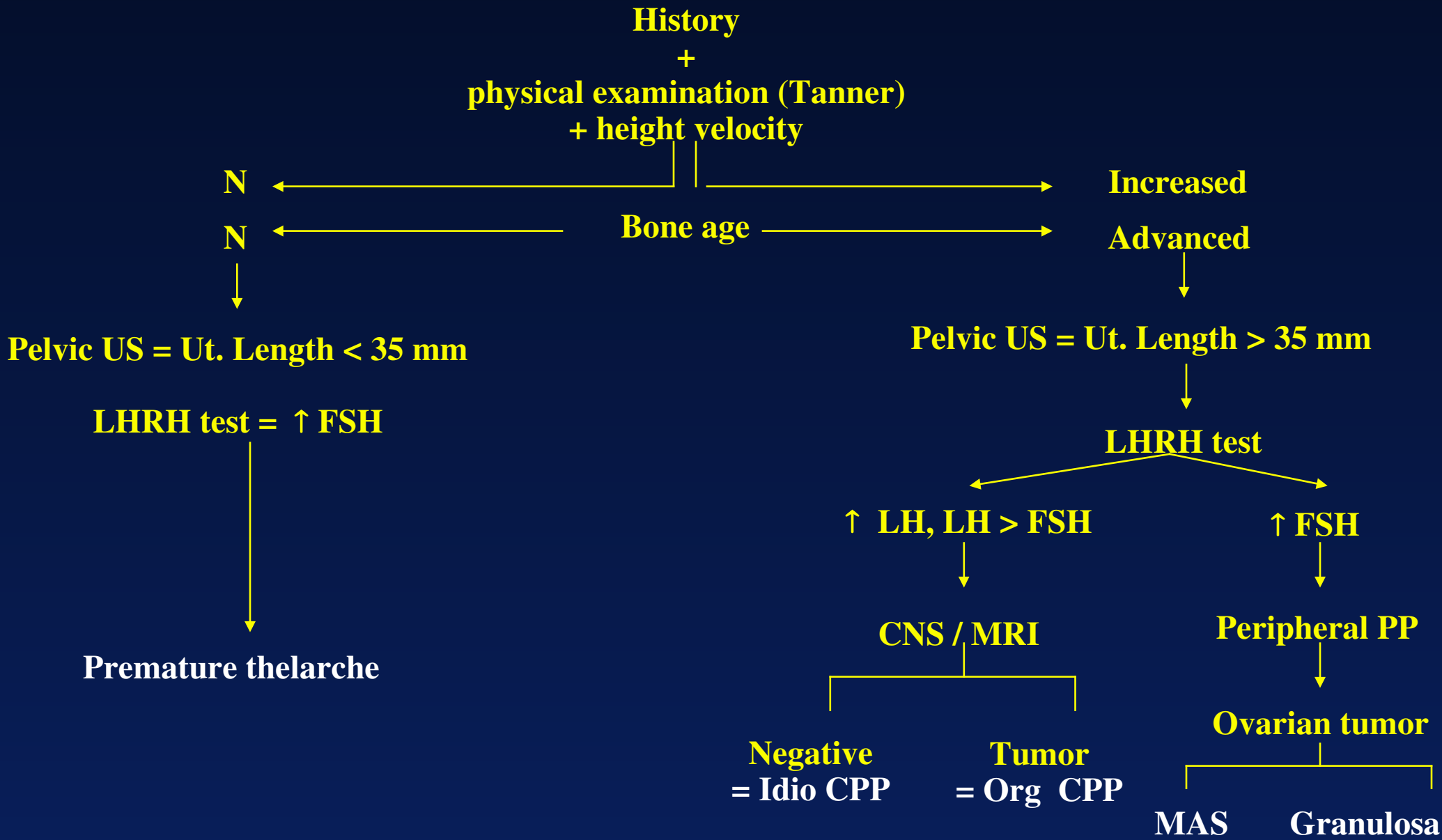


Clinical, bio and radiographic investigations are very helpfull in

- situating precocious puberty within a category on the spectrum
- in chosing the appropriate treatment strategy

Conclusion (5)

Algorithm evaluation of girls with sexual precocity



Thank you for your attention