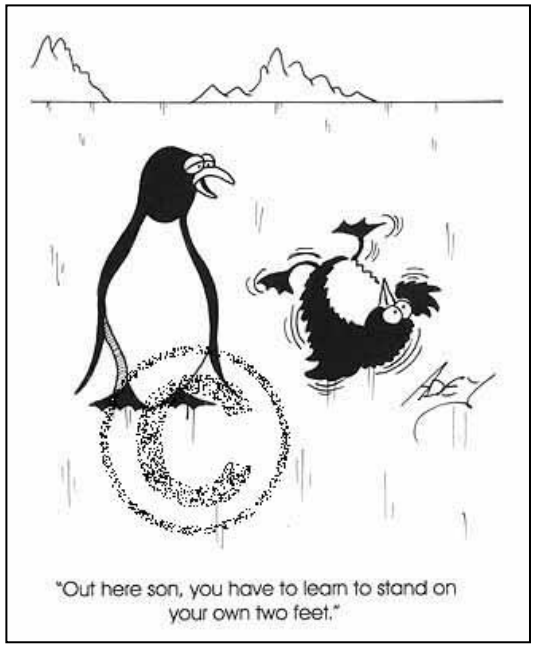
Puberteit

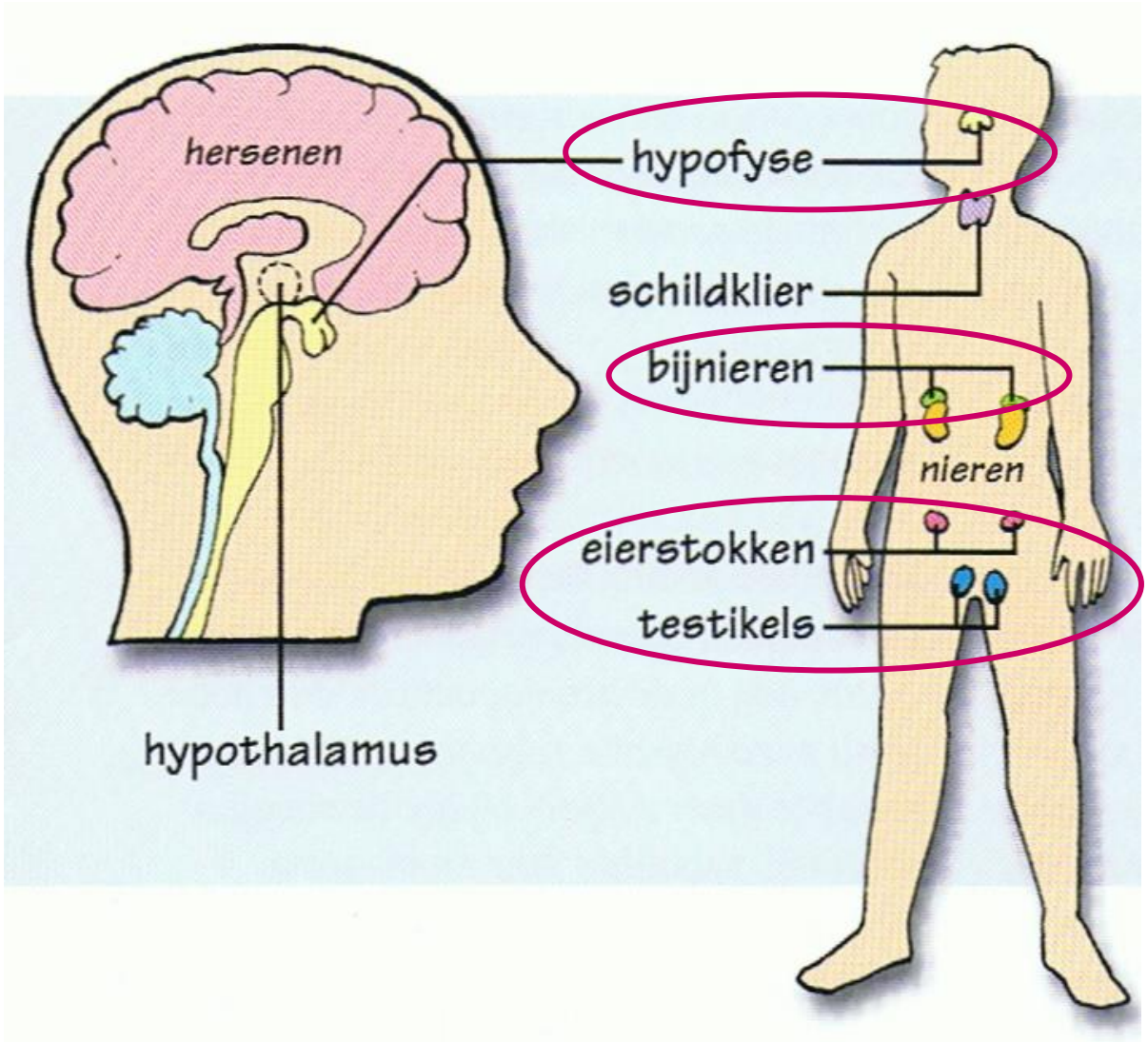
K. De Waele

Puberteit

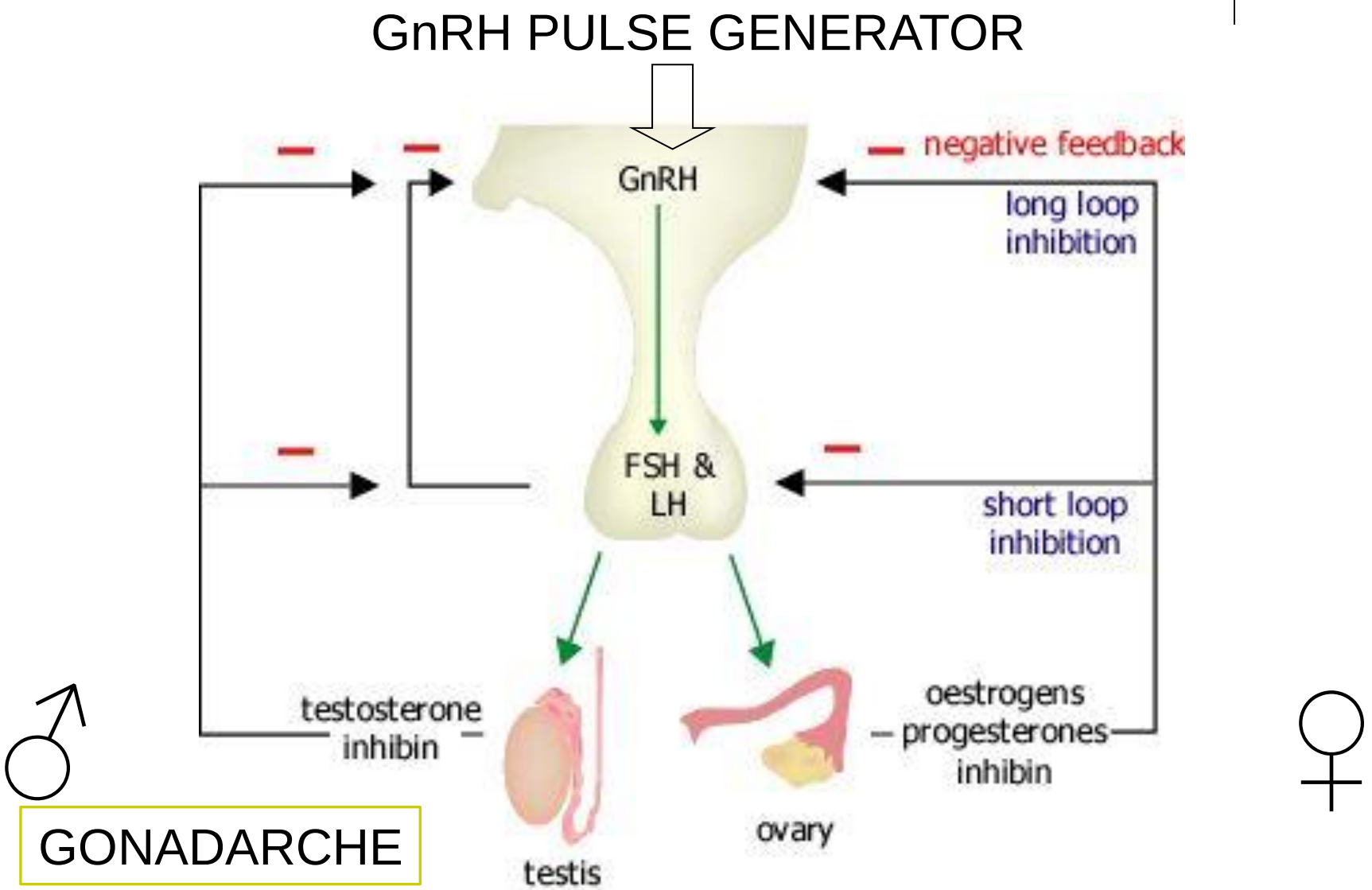
- “levensperiode tussen kinderjaren en volwassenheid waarin de seksuele rijping plaatsvindt”



Puberteit

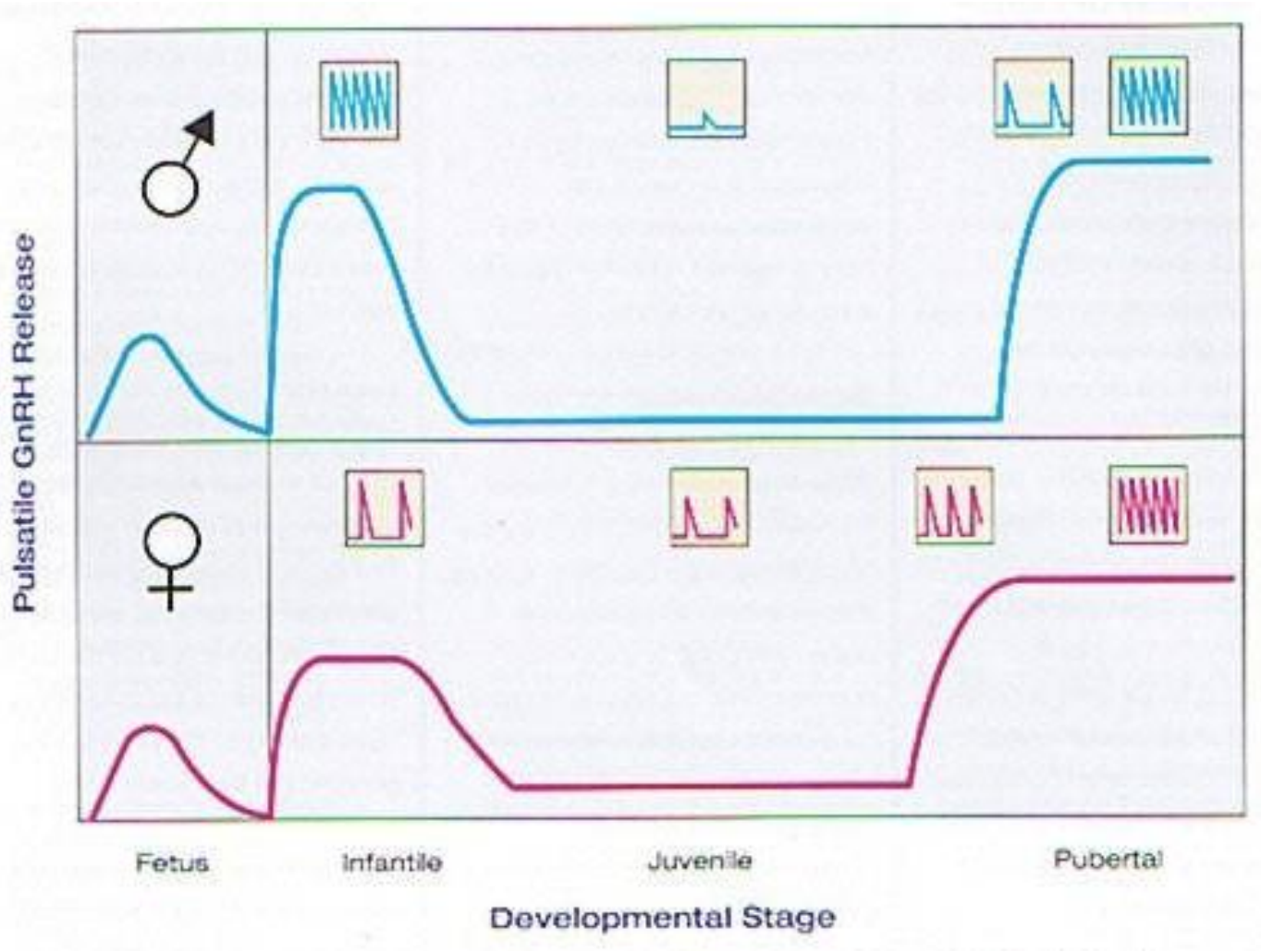

hersenen
hypofyse
schildklier
bijnieren
nieren
eierstokken
testikels
hypothalamus

Hypothalame-hypofysaire-gonadale as

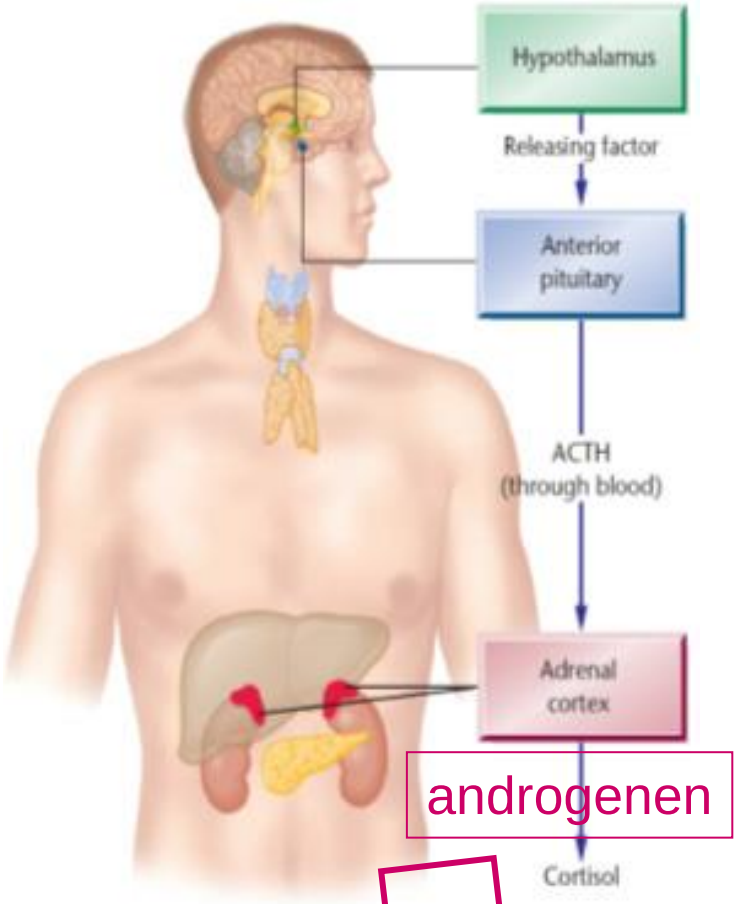


GONADARCHE

Pulsatiele GnRH secretie



Hypothalame-hypofysaire-bijnieras



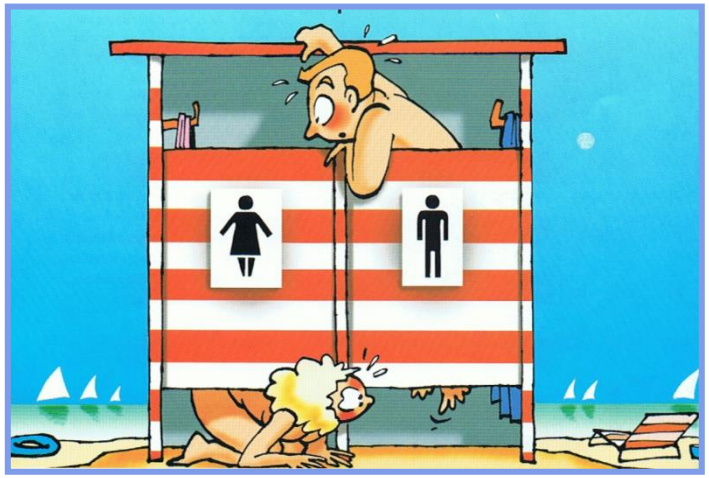
ADRENARCHE

acne
pubis/okselbeharing

Puberteit

- klinische veranderingen
  - groeispurt

  → verschillen tussen jongens en meisjes …
  - secundaire geslachtskenmerken



Puberale groeispurt

- wanneer ?
  - meisjes: gemiddelde ‘piek’ rond 12 jaar
  - jongens: gemiddelde ‘piek’ rond 14 jaar
    - aan begin van puberteit: 6 à 7 cm groter
- maximale groeisnelheid ?
  - hoger bij jongens dan bij meisjes
- hoeveel cm ? duur ?
  - 15 tot 30 cm (gemiddeld 20 à 25 cm)
  - periode : jongens > meisjes

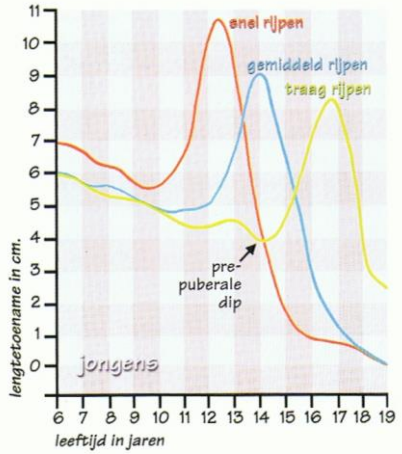


Fig. A: Puberale groeispurt bij jongens.

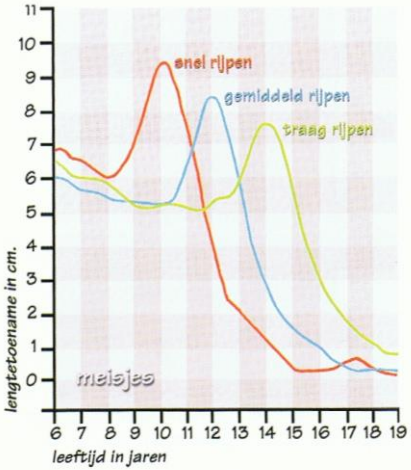


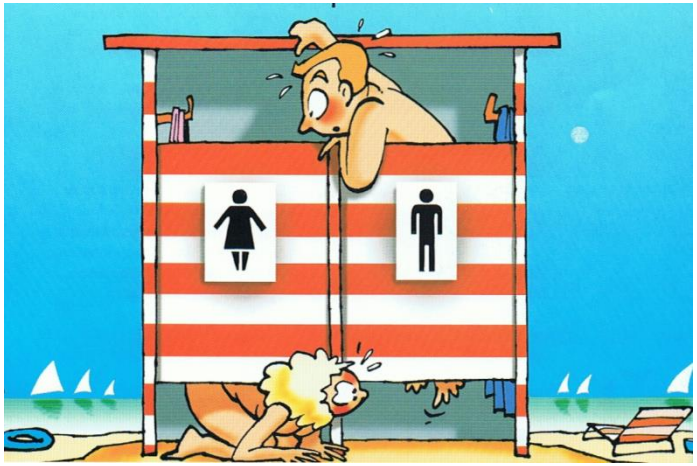
Fig. B: Puberale groeispurt bij meisjes.

- volwassenen: ♂ gemiddeld 13 cm groter dan ♀

Puberteit

- klinische veranderingen
  - groeispurt

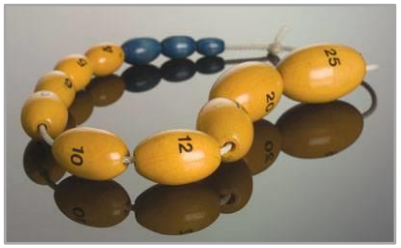
  → verschillen tussen jongens en meisjes …
  - secundaire geslachtskenmerken



Secundaire geslachtskenmerken

<u>evaluatie van puberteit volgens TANNER</u>

- ♀ M of B 1-5 P 1-5 A 1-2
- ♂ G 1-5 P 1-5 A 1-2
  - + testikelgrootte/volume



Archives of Disease in Childhood, 1970, **45**, 13.

Variations in the Pattern of Pubertal Changes in Boys

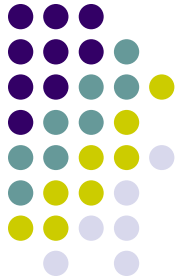
W. A. MARSHALL and J. M. TANNER
From the Department of Growth and Development, Institute of Child Health, University of London

Arch. Dis. Childh., 1969, **44**, 291.

Variations in Pattern of Pubertal Changes in Girls

W. A. MARSHALL and J. M. TANNER
From the Department of Growth and Development, Institute of Child Health, University of London

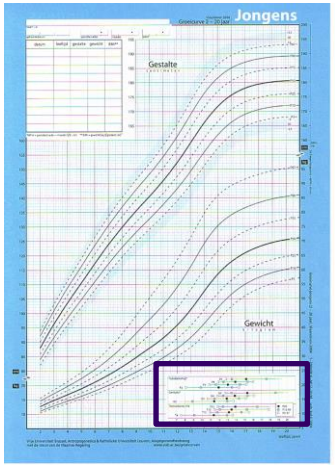
Wat gebeurt er en wanneer ?

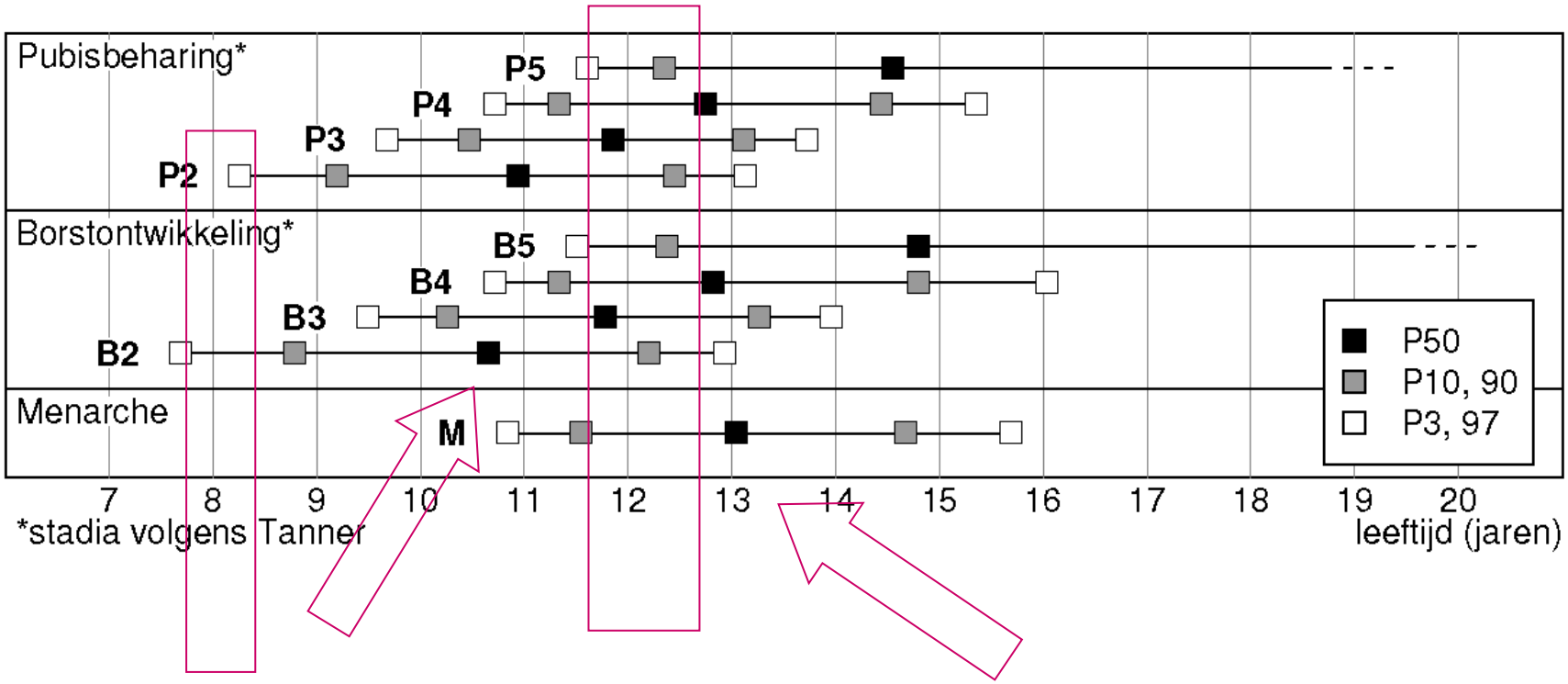


- variatie
  - tijdstip
  - tijdsduur
    - anderhalf tot 5 jaar

- vast patroon/volgorde van optreden van de verschillende puberteitskenmerken

Groeicurve meisjes

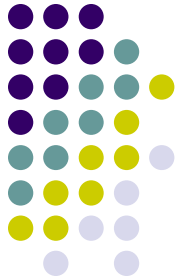




Te vroege puberteit
Pubertas praecox

- te vroege puberteit (pubertas praecox (PP))
  - ontwikkeling van secundaire geslachtskenmerken
    - ♀ borstontwikkeling vóór de leeftijd van 8 jaar
      - of menarche vóór 10 jaar
    - ♂ testes > 4 ml vóór de leeftijd van 9 jaar

Premature thelarche



- geïsoleerde borstontwikkeling (immature tepel, areola)
- geen tekenen van adrenarche
- geen groeiversnelling
- meestal regressie

- prepubertair oestrogeengehalte (licht ↑)
- botleeftijd ~ CA

- normaal tijdstip puberteit

Premature adrenarche/pubarche

- begint tussen 4 en 6 jaar
- pubis/okselbeharing, zweetgeur
- geen groeiversnelling

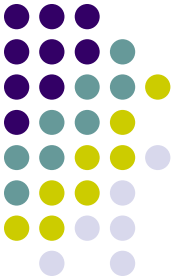
- DHEAS licht ↑ (~ Tanner stadium)
- BL licht voorop (~‘height age’)

Te late puberteit (pubertas tarda)

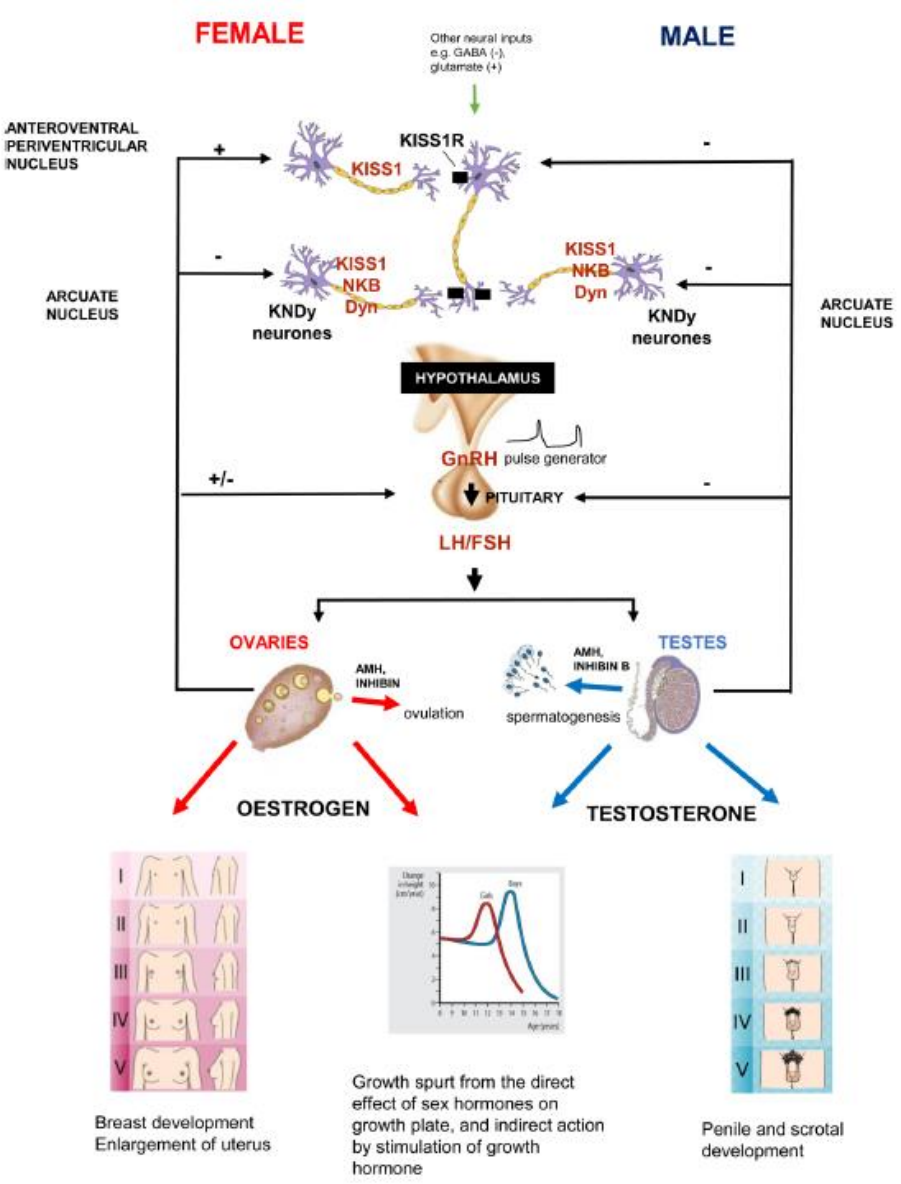
- ♀ : afwezigheid van secundaire geslachtskenmerken na de 13e verjaardag

- ♂ : afwezigheid van secundaire geslachtskenmerken na de 14e verjaardag

Wat verklaart de fysiologische variatie in onset/timing?



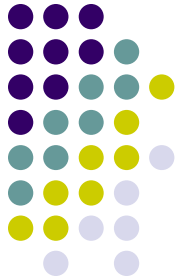
- >>> genetische factoren
  - 50 tot 80 % herediteit
- intra uteriene factoren
- nutritie
- chronische ziekten
- omgevingsfactoren (blootstelling EDC)
- …



Key: AMH - Anti-Mullerian Hormone, Dyn- Dynorphin, FSH – Follicle-Simulating Hormone, GABA- gamma-Aminobutyric acid, GnRH- Gonadotrophin-releasing Hormone, KISS1- Kisspeptin, KISS1R- Kisspeptin Receptor, KNDy – Kisspeptin/Neurokinin/Dynorphin, LH- Luteinising Hormone, NKB- Neurokinin B,

Arch Dis Child 2016 101:481-488

Genetische regulatie
Welke genen ?

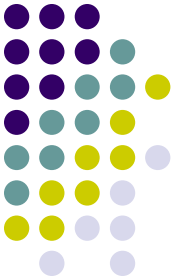


- GnRH receptor (de Roux et al, NEJM 1997)
- KAL (Franco B et al, Nature 1991)
- Leptin en leptin receptor (Clement et al, Nature 1998)
- PC1 (Jackson RS et al, Nat Genet 1997)
- DAX-1 (Zanaria et al, Nature 1994)

- FGFR1 (Pitteloud et al, JCEM 2005)
  - autosomaal dominant Kallman syndroom
  - fenotypisch spectrum van anosmie tot late puberteit tot IHH

- GPR54 (Semple et al, JCEM 2005)
  - geïsoleerd hypogonadotroop hypogonadisme

Wat verklaart de fysiologische variatie in onset/timing?

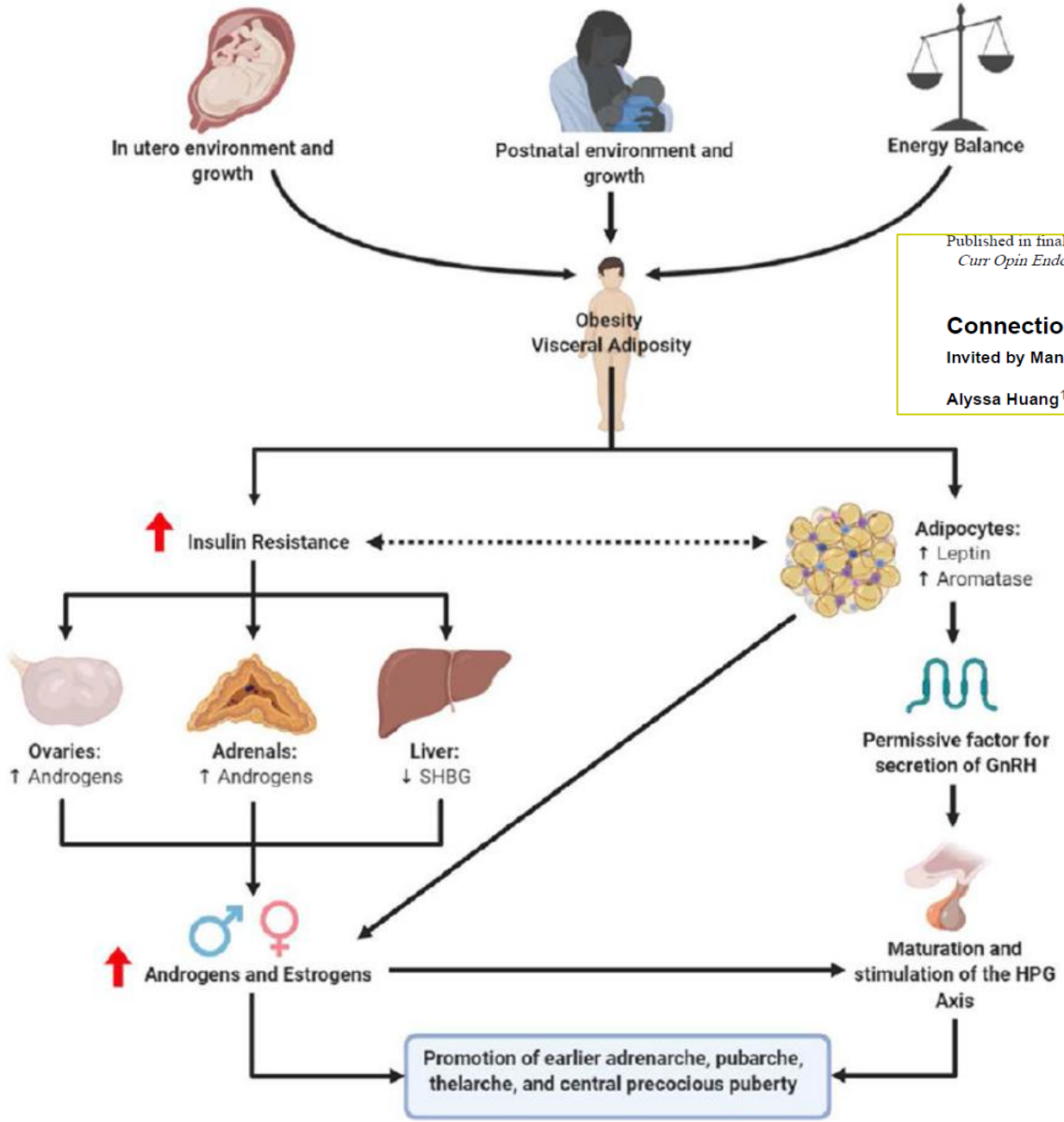


- >>> genetische factoren
  - 50 tot 80 % herediteit
- intra uteriene factoren
- nutritie
- chronische ziekten
- blootstelling aan EDC
- …

(over)gewicht en puberteit

- overgewicht/obesitas ~ timing puberteit
  - meisjes
    - hogere BMI ~ vroegere start van de puberteit
    - hogere BMI ~ ↑tempo/vroegere menarche
  - jongens
    - minder eenduidige bevindingen in ≠ studies
      - jongens met overgewicht (vroeg) ⇿ obese jongens (laat)
      - jongens met overgewicht/obese jongens: vroege gonadarche

Busch AS, Hojgaard B, Hagen CP, and Teilmann G, "Obesity Is Associated with Earlier Pubertal Onset in Boys," J Clin Endocrinol Metab, vol. 105, no. 4, 4 1 2020



Published in final edited form as:
Curr Opin Endocr Metab Res. 2020 October ; 14: 160–168. doi:10.1016/j.coemr.2020.08.004.

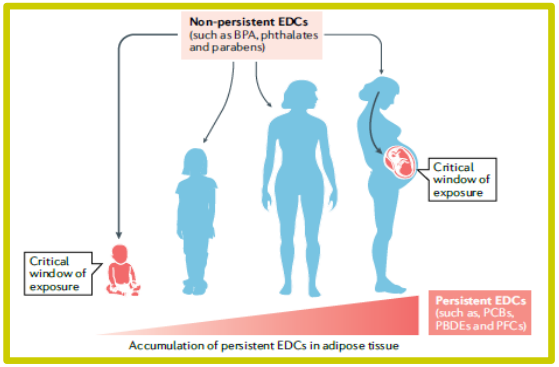
Connections Between Obesity and Puberty:

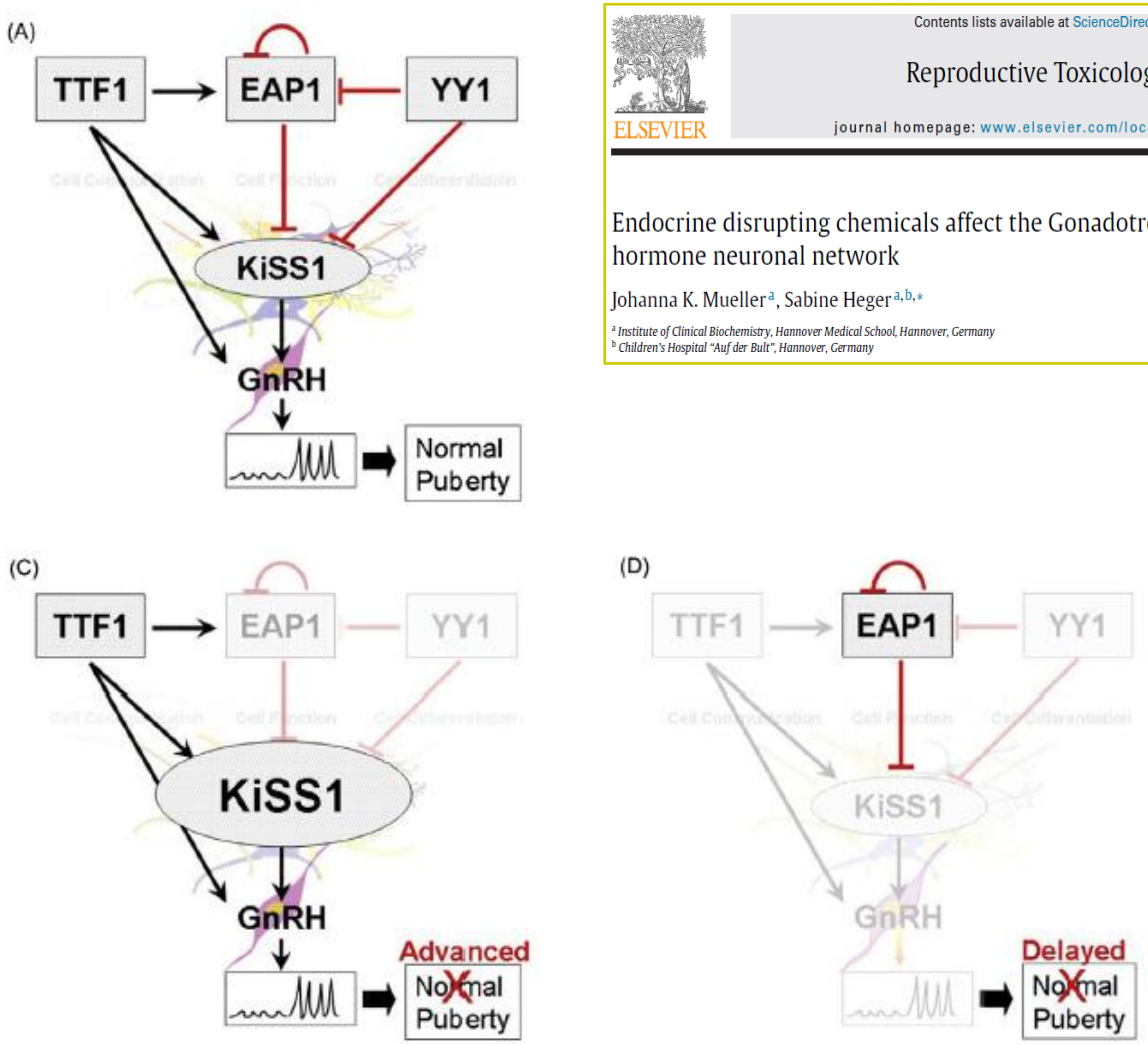
Invited by Manuel Tena-Sempere, Cordoba

Alyssa Huang[1], **Thomas Reinehr**[2], **Christian L Roth**[1,3]

Endocrine disrupting chemicals (EDC)

- the fetal and pubertal developmental windows are very sensitive to EDC exposure
  - timing of puberty
  - sexual maturation
  - reproductive function
- animal studies are very important to determine causal relationships and involved mechanisms
  - neuroendocrine versus peripheral mechanisms





Contents lists available at ScienceDirect

Reproductive Toxicology

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

Endocrine disrupting chemicals affect the Gonadotropin releasing hormone neuronal network

Johanna K. Mueller[a], Sabine Heger[a,b,*]

[a] Institute of Clinical Biochemistry, Hannover Medical School, Hannover, Germany
[b] Children's Hospital "Auf der Bult", Hannover, Germany

Fig. 11. Schematic representation depicting the alteration of the GnRH network by EDCs in regard to proposed pubertal onset. (A) In the normal situation, *KiSS1*, the main stimulatory neurotransmitter of GnRH, is regulated by stimulatory (TTF1) and inhibitory factors (EAP1, YY1) resulting in physiological timing of GnRH secretion. (B) Exposure to Genistein increases *EAP1* and *KiSS1* expression, while YY1, the repressor of puberty is inhibited, assuming that the net *KiSS1* expression is enhanced, suggesting an advancement of pubertal onset. (C) Exposure to BPA, an ubiquitous EDC, diminished the expression of both repressors (*EAP1*, *YY1*), while stimulating the *KiSS1* gene expression assuming that BPA exposure advances puberty as observed in animal studies. (D) Dioxin is a highly potent and persistent EDC, which was shown to delay pubertal onset in rodents. The functional and expressional analysis revealed that Dioxin inhibits all components of the GnRH neuronal network except EAP1.

Seculaire trends

“Schaamhaar op 5 en borsten op 7 jaar: kinderen puberen steeds vroeger”

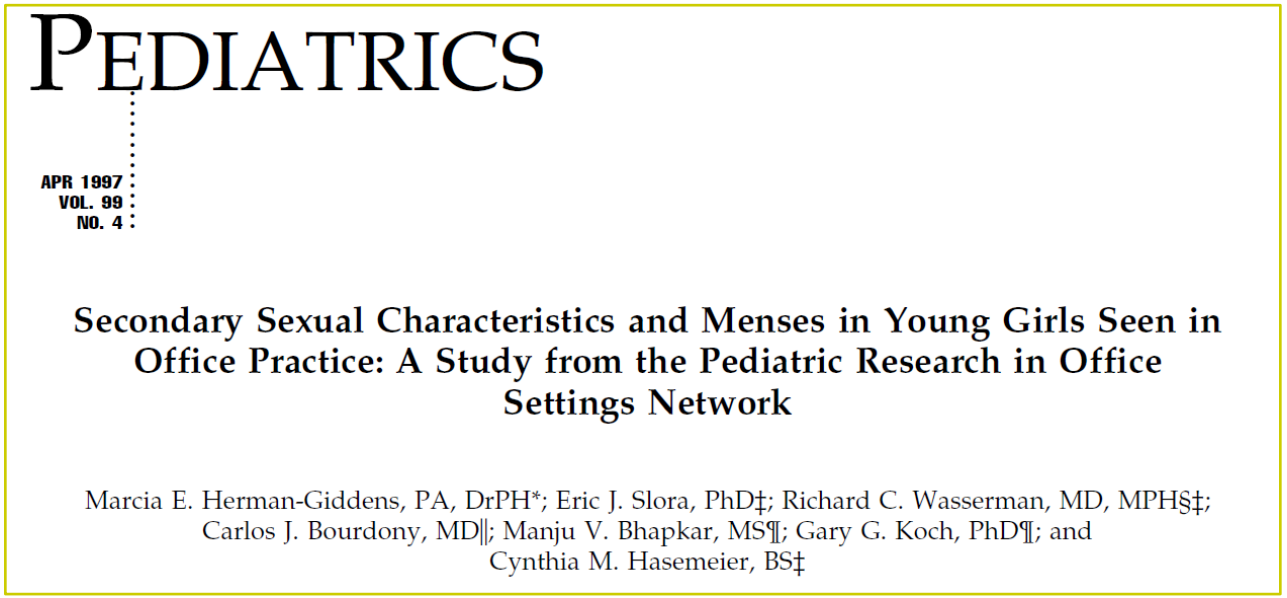
HUMO

Seculaire trends

- gemiddelde leeftijd van menarche
  - daalde uniform tot jaren ’60
    - variatie tussen verschillende landen
    - Europa : Noord – Zuid gradiënt
  - studies NA 1960
    - minder ‘uniforme’ data
    - België: lichte ↑ leeftijd menarche (+ 0.03 jaar/decade)

Seculaire trends

- start borstontwikkeling B2
  - USA PROS Study 1997
    - ondergrens B2 op 7 jaar?
    - ondergrens B2 in Afro-Amerikaanse meisjes op 6 jaar?



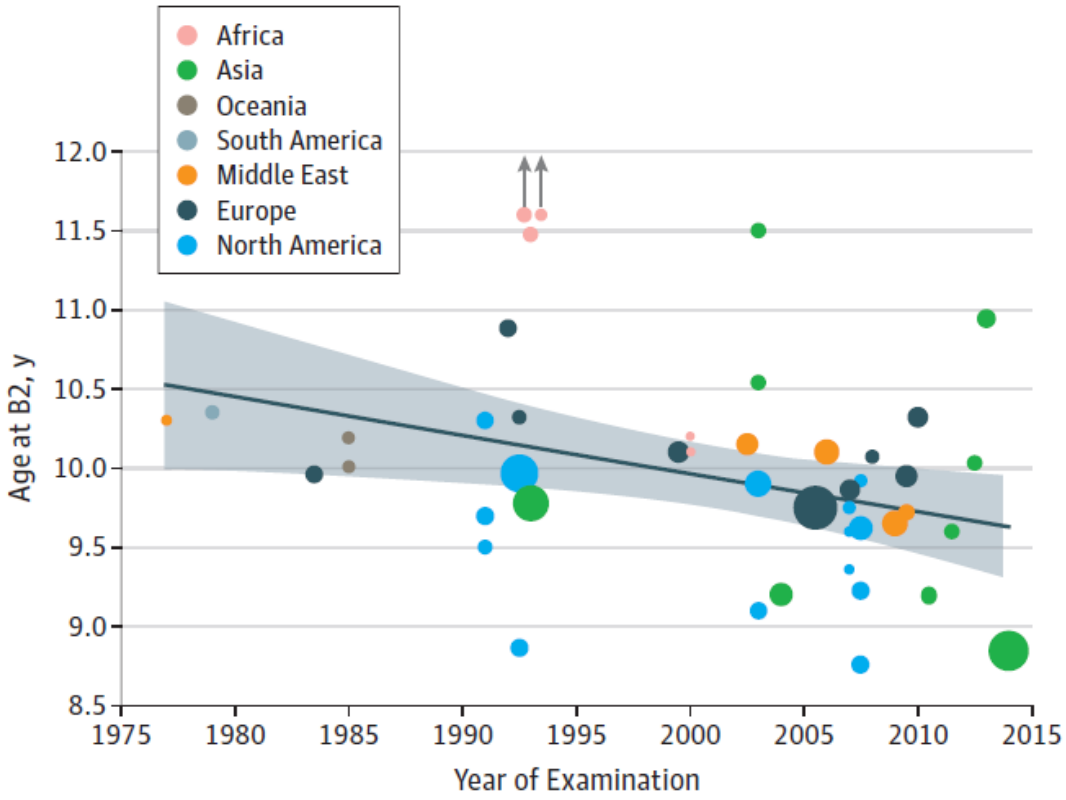
PEDIATRICS

APR 1997
VOL. 99
NO. 4

Secondary Sexual Characteristics and Menses in Young Girls Seen in Office Practice: A Study from the Pediatric Research in Office Settings Network

Marcia E. Herman-Giddens, PA, DrPH*; Eric J. Slora, PhD‡; Richard C. Wasserman, MD, MPH§‡; Carlos J. Bourdony, MD‖; Manju V. Bhapkar, MS¶; Gary G. Koch, PhD¶; and Cynthia M. Hasemeier, BS‡

Figure 2. Secular Changes in Age at Onset of Tanner Breast Stage 2 (B2) From 1977 to 2013 Around the World According to Year of Study



JAMA Pediatrics | Original Investigation

Worldwide Secular Trends in Age at Pubertal Onset Assessed by Breast Development Among Girls

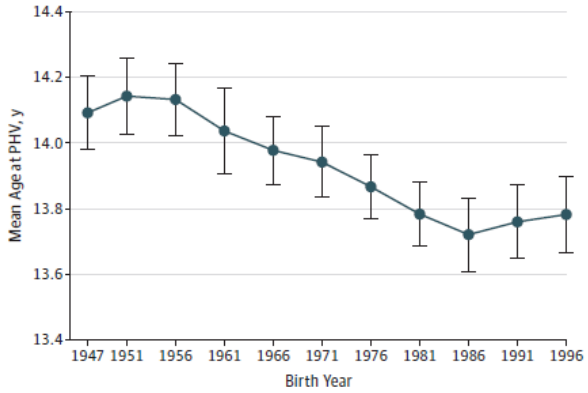
A Systematic Review and Meta-analysis

Camilla Eckert-Lind, MB; Alexander S. Busch, MD, PhD; Jørgen H. Petersen, PhD; Frank M. Biro, MD; Gary Butler, MD; Elvira V. Bräuner, PhD; Anders Juul, MD, DMSc, PhD

Seculaire trends in jongens

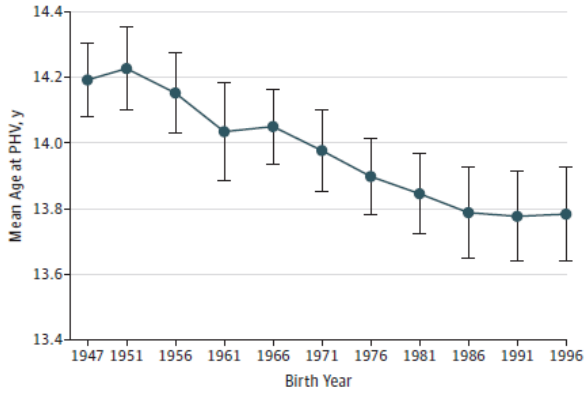
- veel minder robuste data in jongens

Figure 3. Mean Age at Peak Height Velocity (PHV) Adjusted for Childhood Body Mass Index (BMI) for Boys Included in the BMI Epidemiology Study Cohort Born From 1947 to 1996



Values are presented as mean (95% CI). The *P* for trend is <.001.

Figure 4. Mean Age at Peak Height Velocity (PHV) Among a Subgroup of Boys Born From 1947 to 1996 in Sweden and With Parents Born in Sweden



Values are presented as mean (95% CI). The *P* for trend is <.001.

JAMA Pediatrics | Original Investigation

Secular Trends in Pubertal Growth Acceleration in Swedish Boys Born From 1947 to 1996

Claes Ohlsson, MD, PhD; Maria Bygdell, MSc, PhD; Jimmy Celind, MD; Arvid Sondén, MSc; Anders Tidblad, MD; Lars Sävendahl, MD, PhD; Jenny M. Kindblom, MD, PhD

- start genitale ontwikkeling G2
  - geen evidentie van (veralgemeende) significante daling

Rethinking the definition of ‘normal’ age and milestones of puberty…