

Ginecologia ed Adolescentologia

Presidente: Roberto Sassi

Moderatori: Attilio Romano, Massimo Ummarino

Adolescente e ciclo mestruale

Sergio Bernasconi

XXIV Congresso Nazionale
Società Italiana di Pediatria
Preventiva e Sociale

BAMBINI DI VETRO

12 - 15
Settembre
2012
Grand Hotel
Vanvitelli
Caserta



CLINICA PEDIATRICA

DIPARTIMENTO MEDICINA CLINICA E SPERIMENTALE

UNIVERSITA' DI PARMA



- **1) richiami di fisiologia della pubertà**
- **2) ciclo mestruale**
- **3) storia “naturale” del ciclo**
- **4) alterazioni più frequenti**
 - **approccio clinico e terapeutico**



- **1) richiami di fisiologia della pubertà**
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 - **approccio clinico e terapeutico**

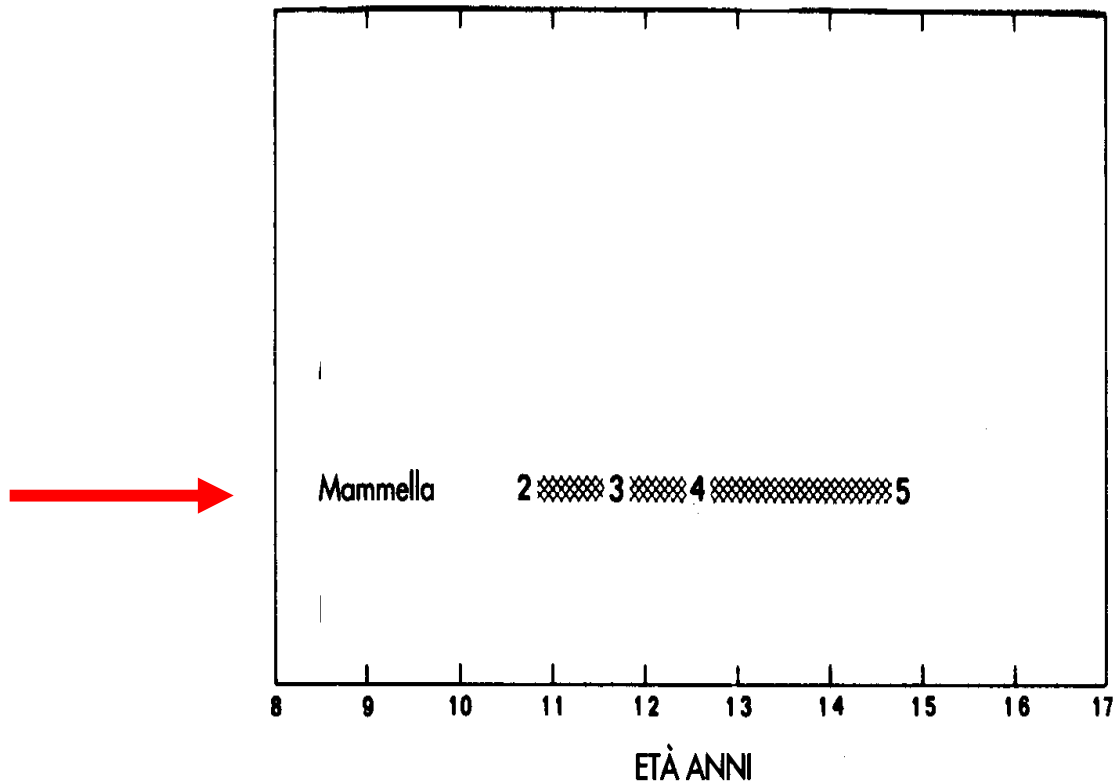


- **1) richiami di fisiologia della pubertà**

- **segni clinici**



PUBERTA' : clinica



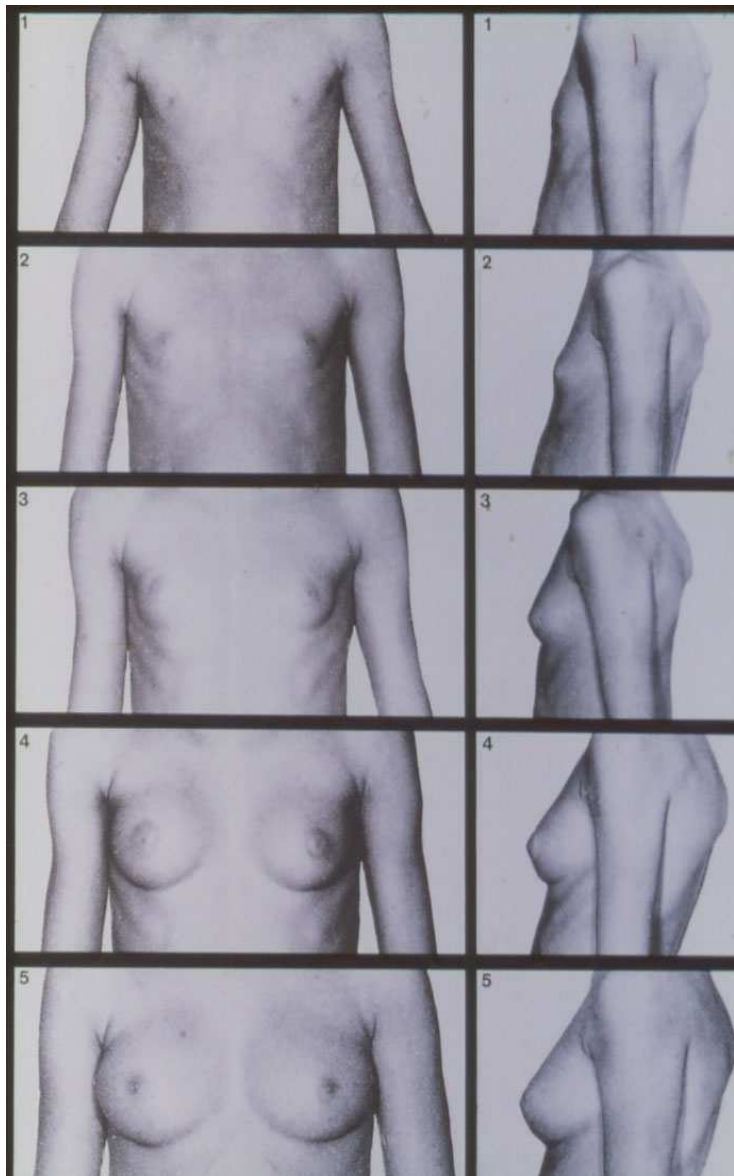
Stadi puberali nella femmina secondo Tanner et al

Adolescente e ciclo mestruale
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TELARCA

PREPUBERE



Stadio B1

→ *Stadio B2*

Stadio B3

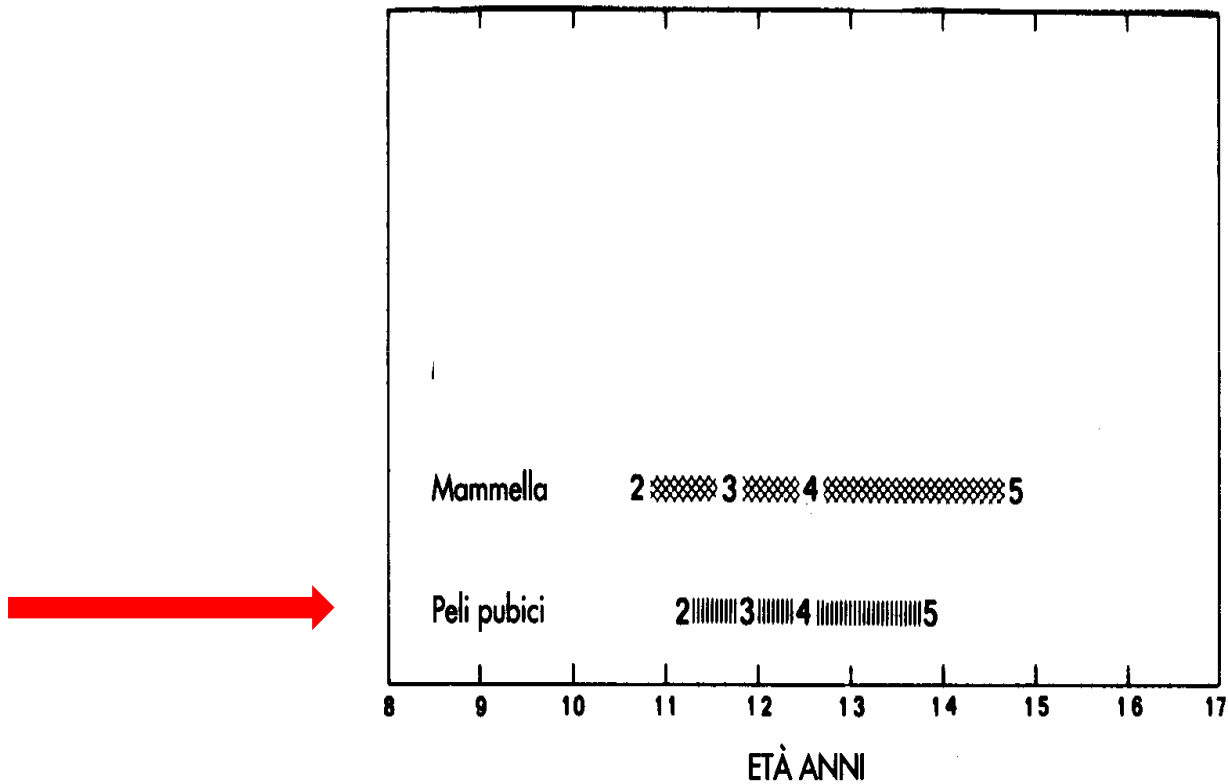
Stadio B4

Stadio B5

ADULTO

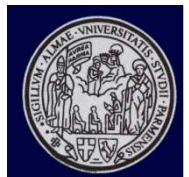


PUBERTA' : clinica

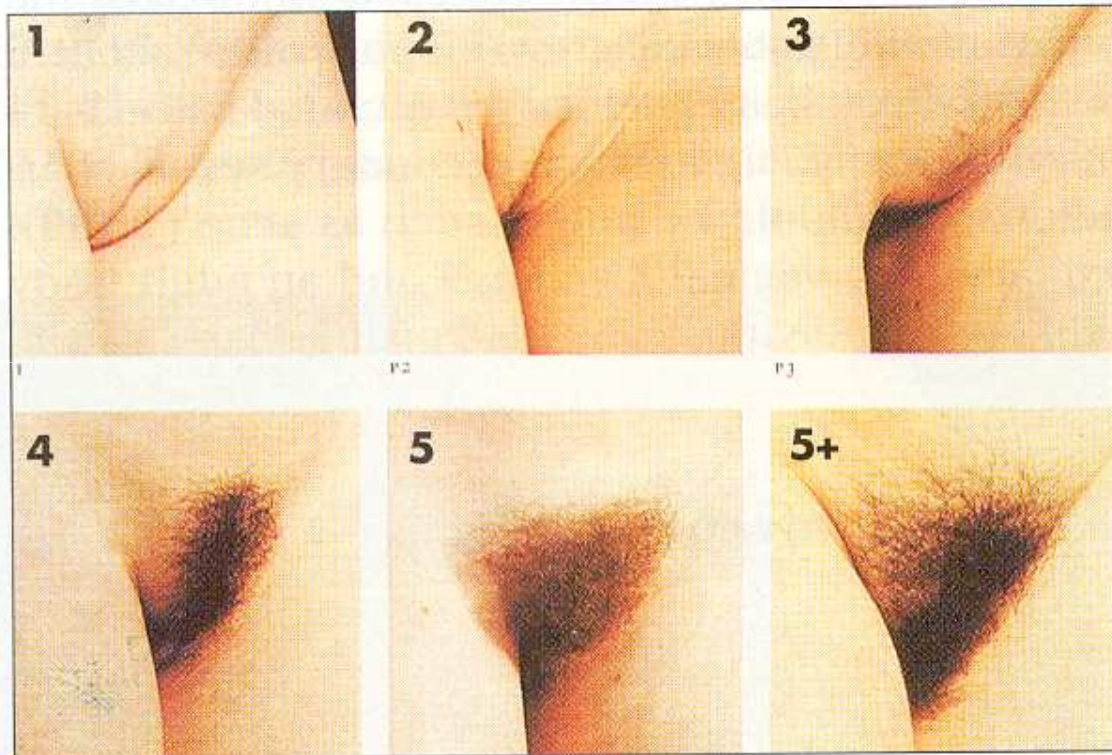


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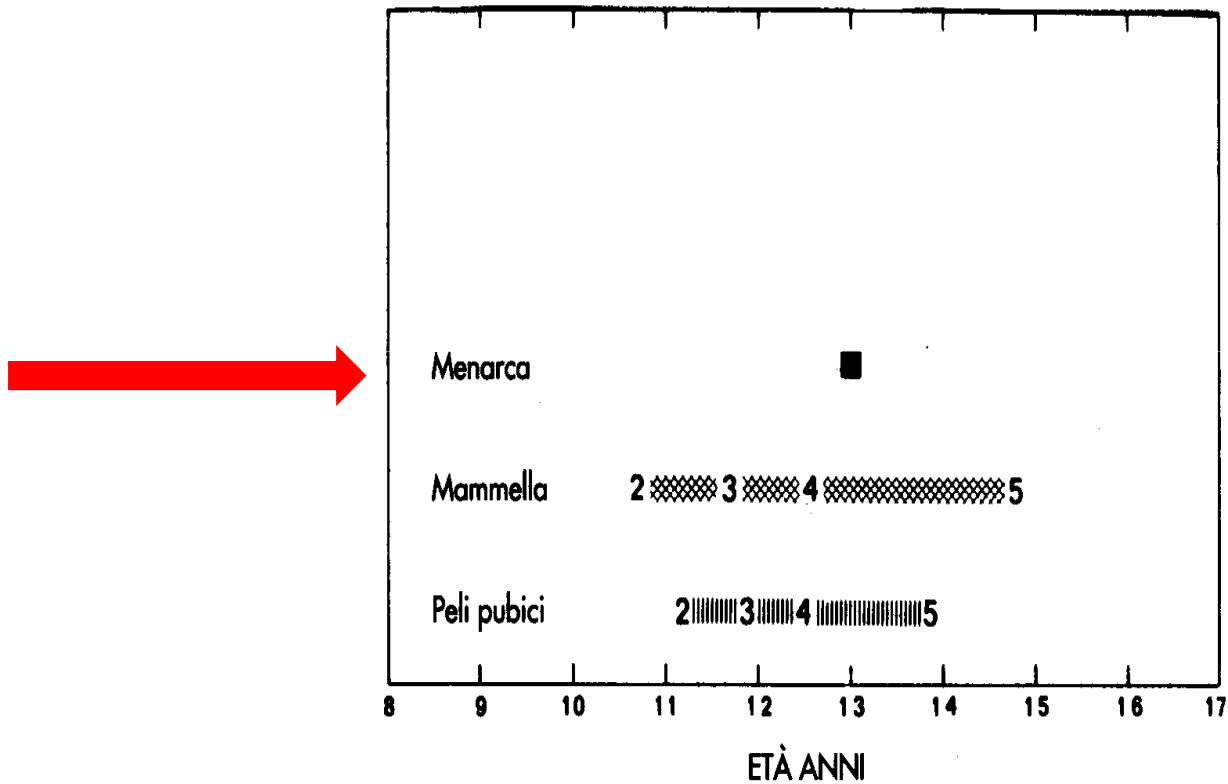
PUBARCA



1.96 Female pubic hair stages 1-5+.



PUBERTA' : clinica

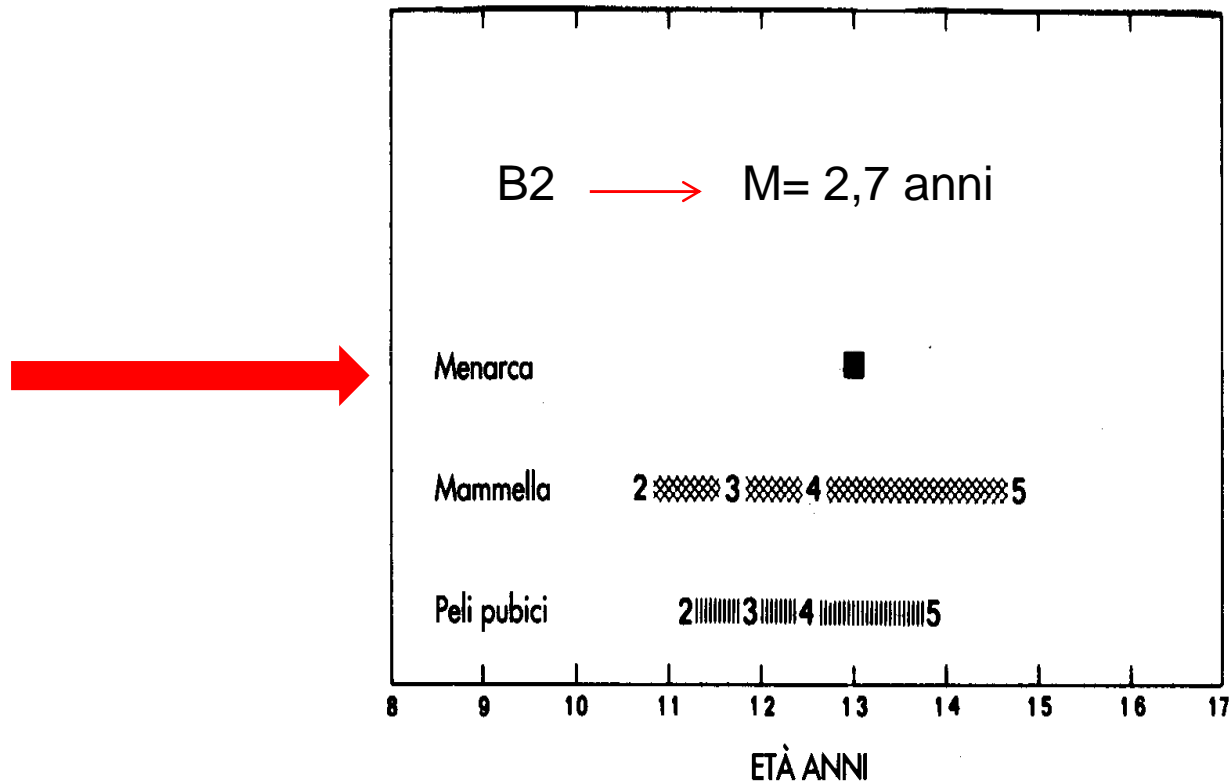


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PUBERTA' : clinica

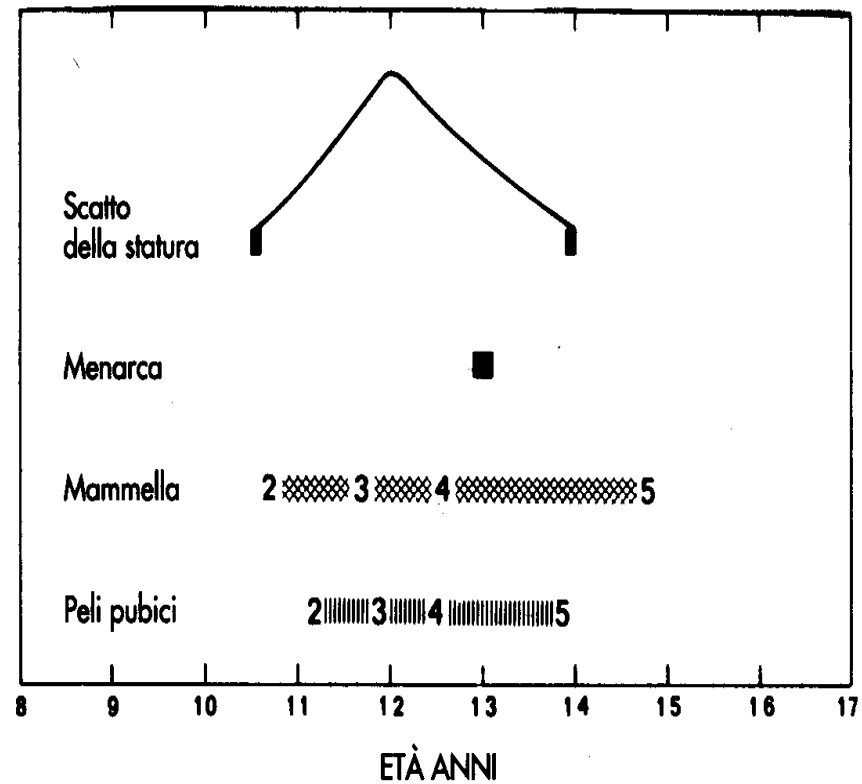


Stadi puberali nella femmina secondo Tanner et al

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PUBERTA' : clinica

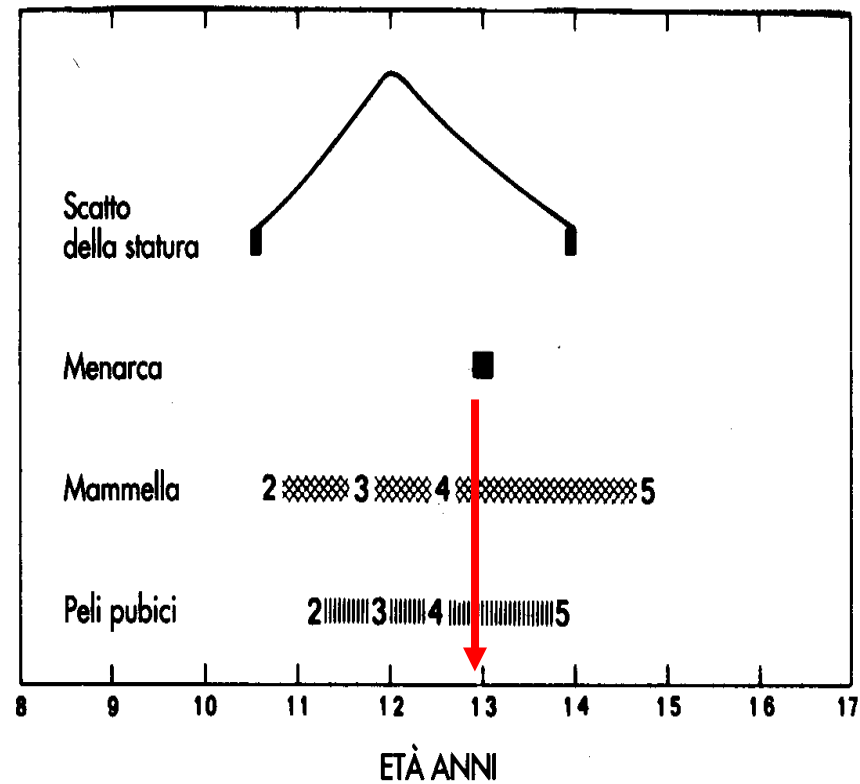


Stadi puberali nella femmina secondo Tanner et al

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PUBERTA' : clinica



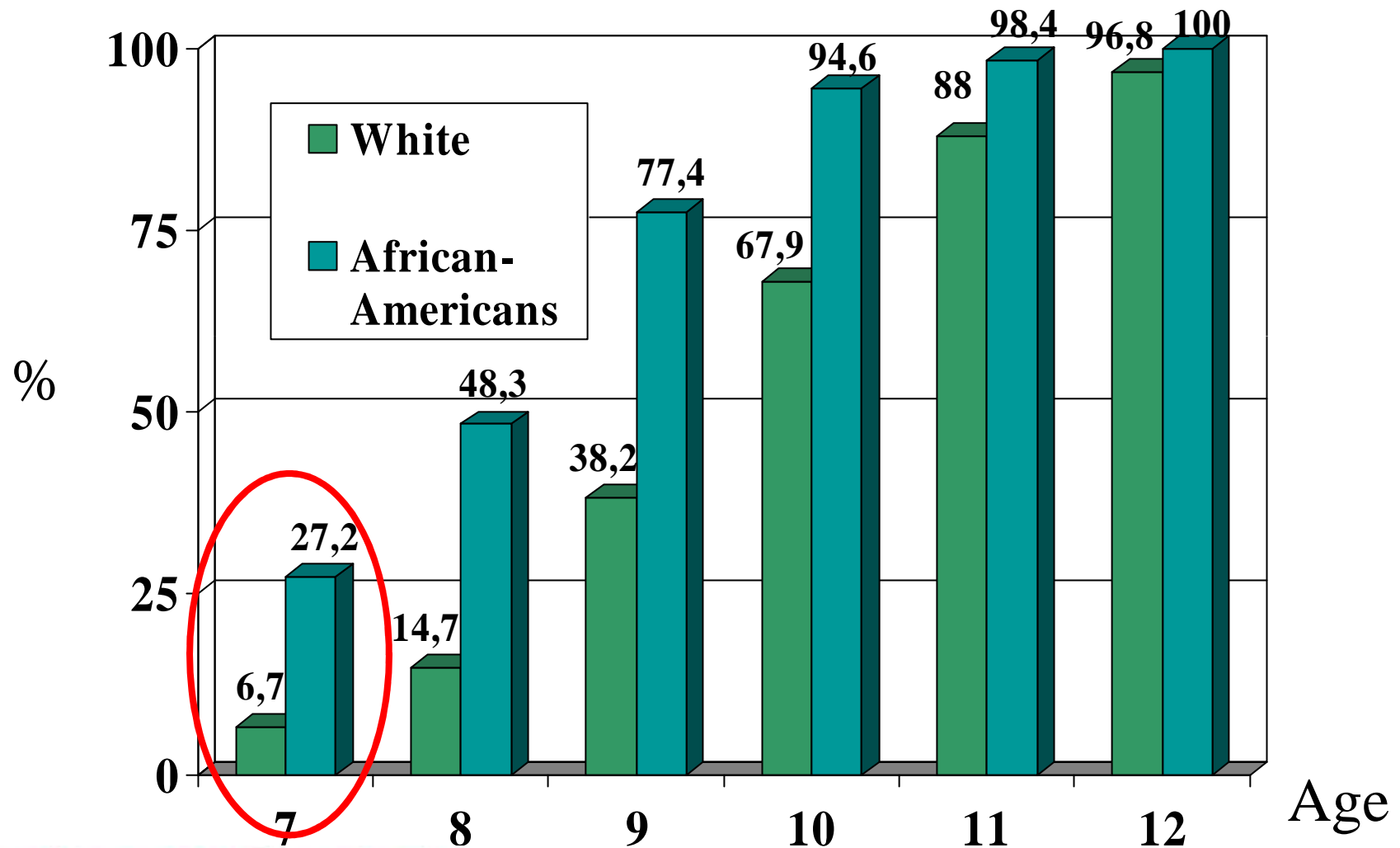
Stadi puberali nella femmina secondo Tanner et al

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Secular trend

Prevalence of breast and/or pubic hair development at Tanner stage 2 or greater (17,077 girls)



Adolescente e ciclo mestruale
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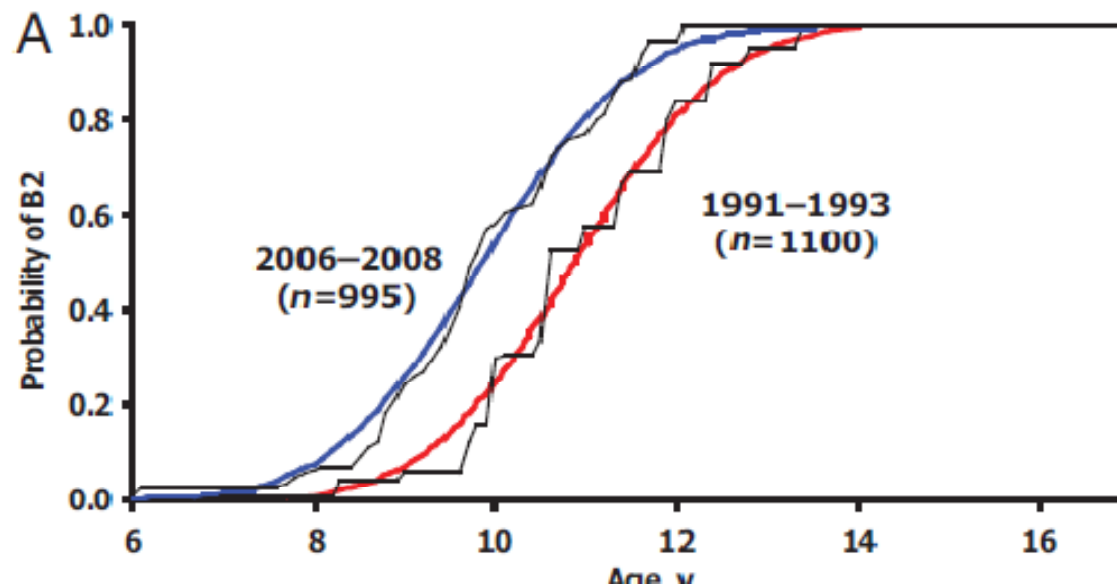
Herman – Giddens ME et al., Pediatrics, 1997

TELARCA

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

Lise Aksglaede, Kaspar Sørensen, Jørgen H. Petersen, Niels E. Skakkebaek and Anders Juul

Pediatrics 2009;123:e932



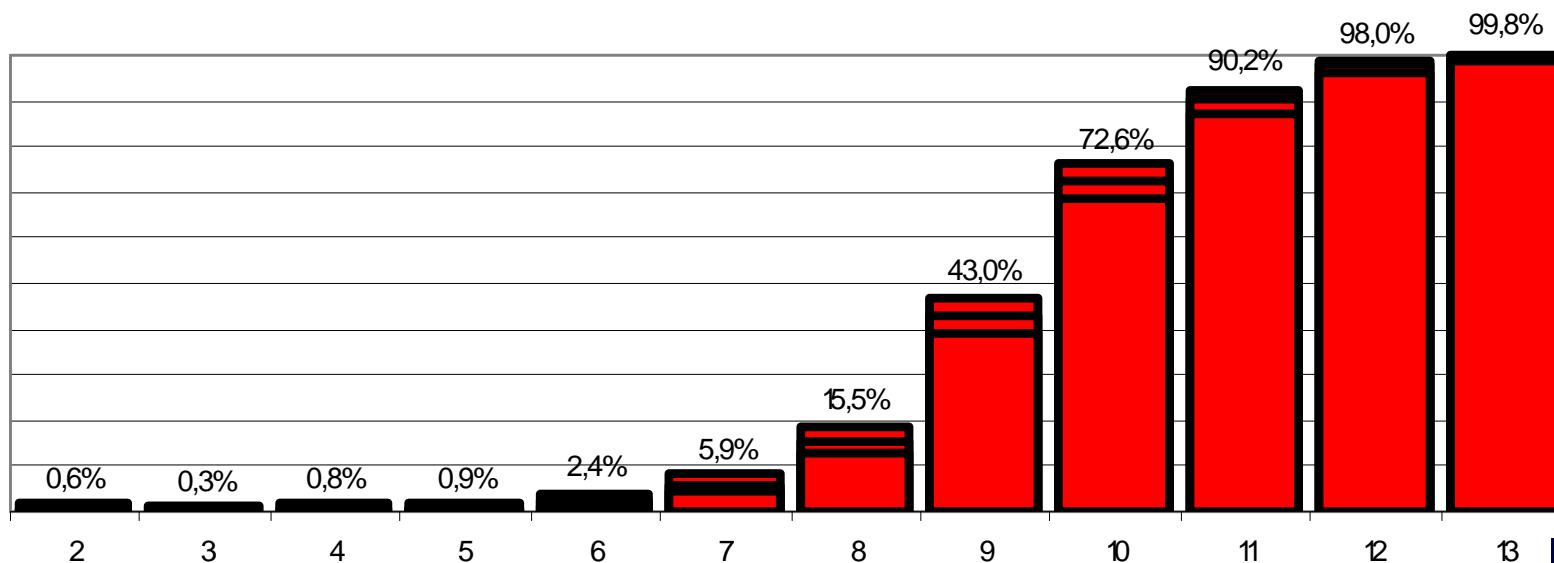
Adolescente e ciclo mestruale
Sergio Bernasconi



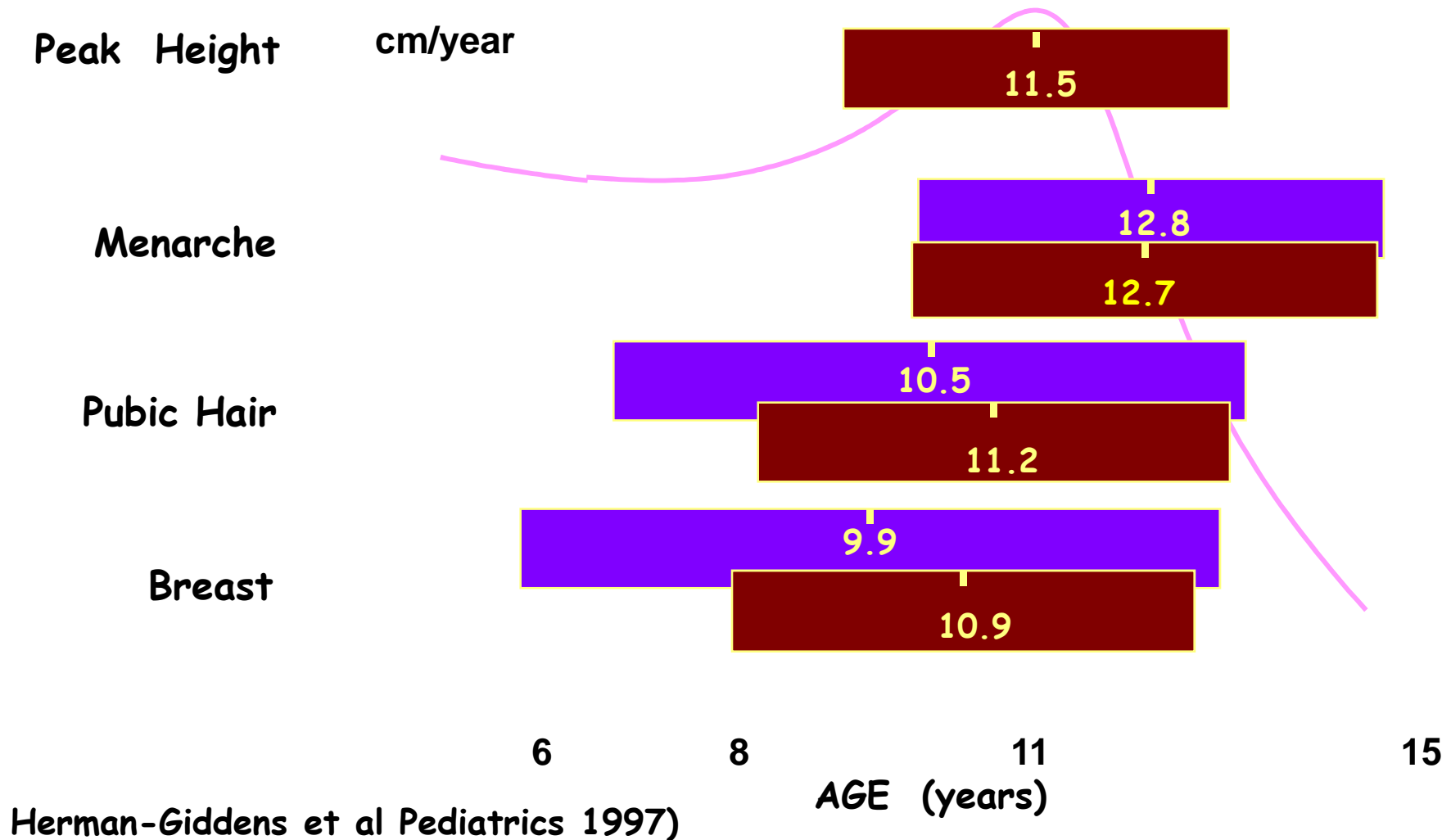
TELARCA

- 2 DS	media	+ 2 DS
7.09 aa	9.73 aa	12.36 aa

Prevalenza dello sviluppo puberale M stadio ≥ 2 (con IC al 95%)



Comparison between "OLD" (■) & "NEW" (■) data on the Appearance and Sequence of Pubertal Signs in the Female

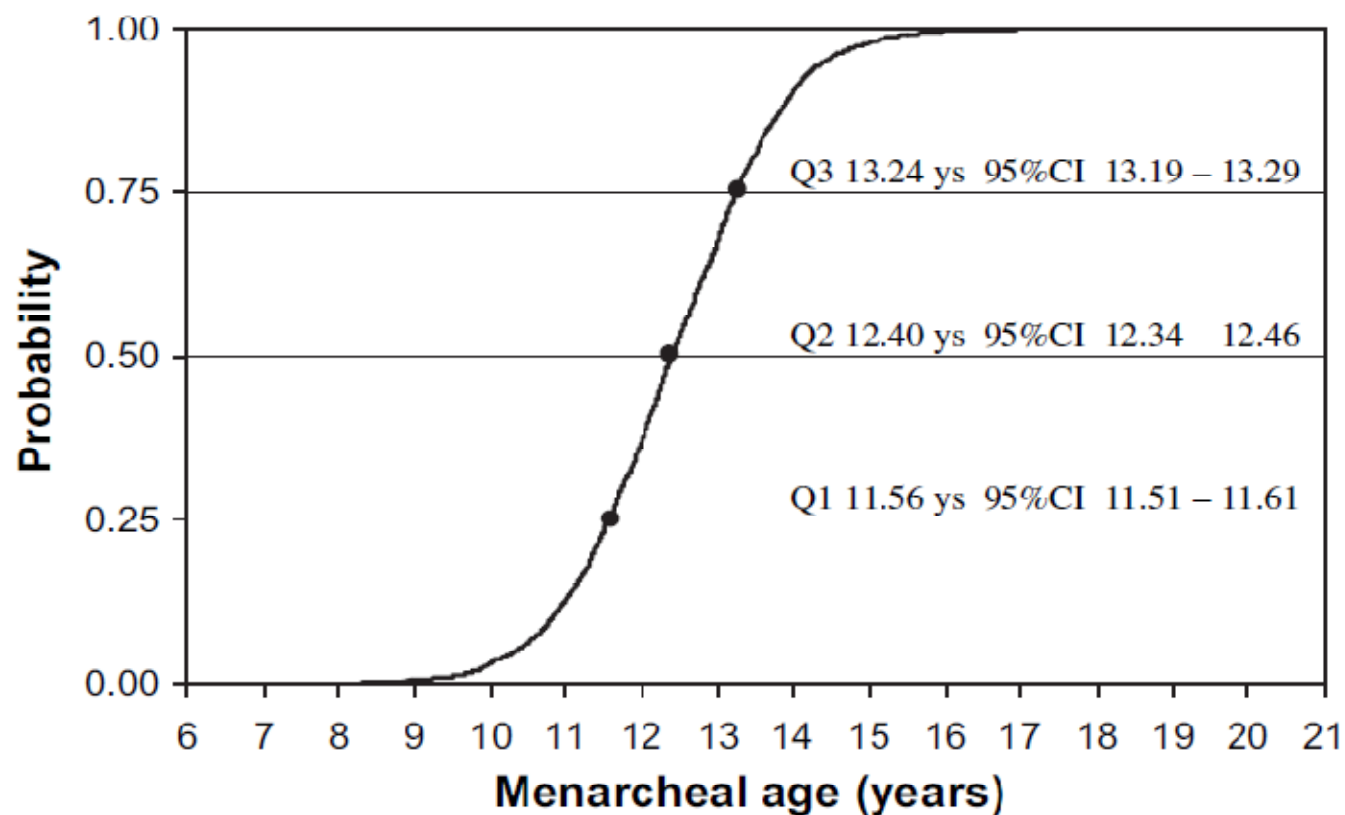


Update on Age at Menarche in Italy: Toward the Leveling Off of the Secular Trend

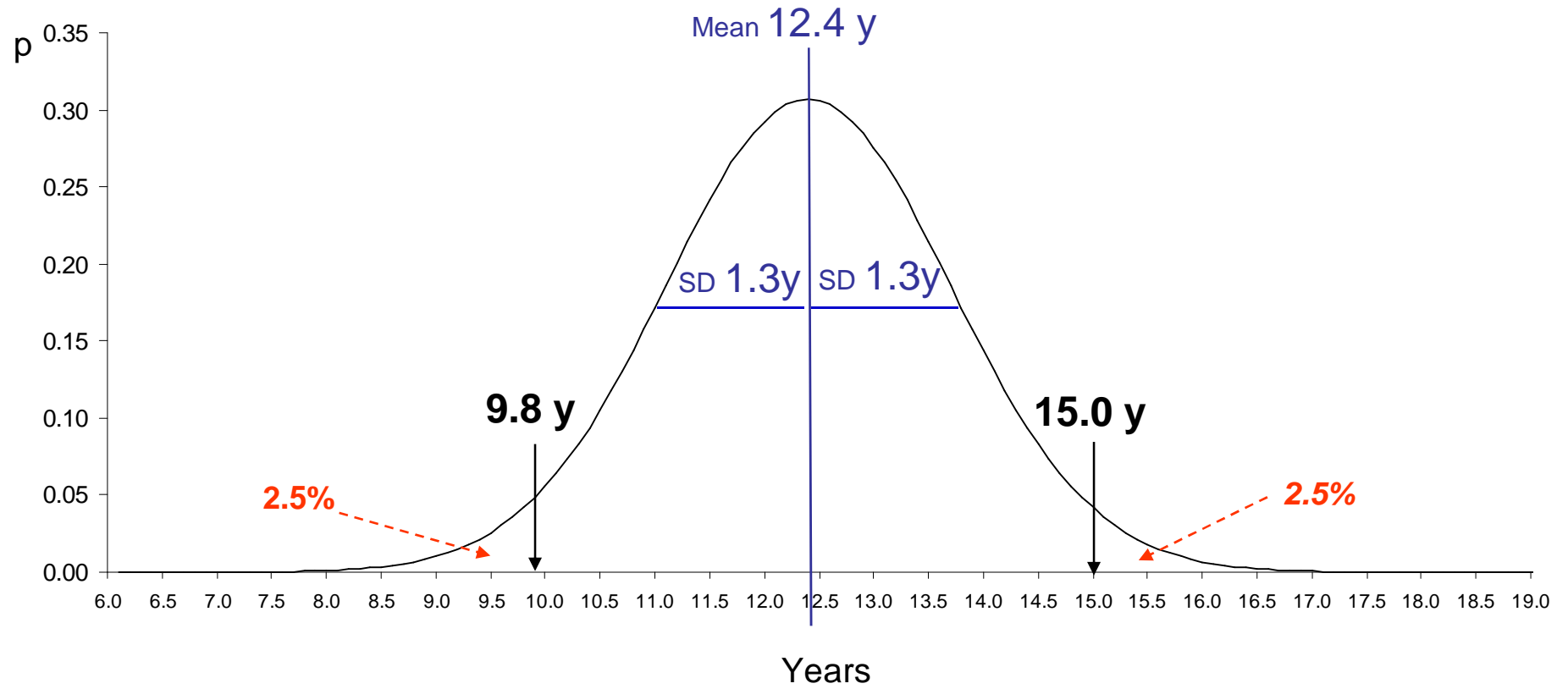
Franco Rigon, M.D.^a, Luigi Bianchin, M.D.^b, Sergio Bernasconi, M.D.^c, Gianni Bona, M.D.^d, Mauro Bozzola, M.D.^e, Fabio Buzi, M.D.^f, Alessandro Cicognani, M.D.^g, Carlo De Sanctis, M.D.^h, Vincenzo De Sanctis, M.D.ⁱ, Giorgio Radetti, M.D.^j, Luciano Tatò, M.D.^k, Giorgio Tonini, M.D.^l, and Egle Perissinotto, Sc.D.^{m,*}

Journal of Adolescent Health 46 (2010) 238–244

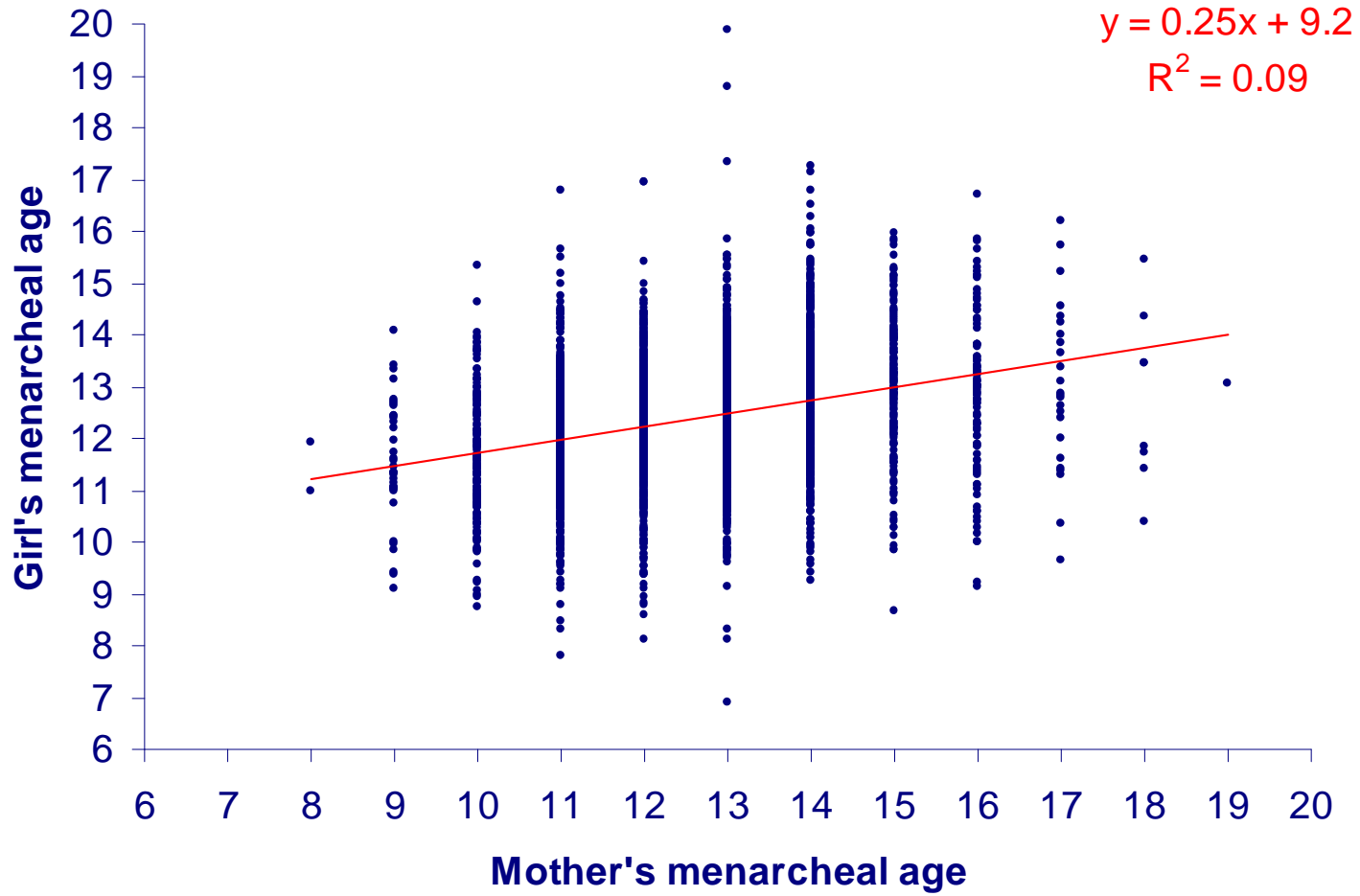
The mean age at menarche was 12.4 years (SD = 1.3), and the median age was 12.4 years (95% CI = 12.34–12.46).



Distribution of Age at menarche



Simple linear regression between mother's and girl's age at menarche



Update on Age at Menarche in Italy: Toward the Leveling Off of the Secular Trend



Franco Rigon, M.D.^a, Luigi Bianchin, M.D.^b, Sergio Bernasconi, M.D.^c, Gianni Bona, M.D.^d, Mauro Bozzola, M.D.^e, Fabio Buzi, M.D.^f, Alessandro Cicograni, M.D.^g, Carlo De Sanctis, M.D.^h, Vincenzo De Sanctis, M.D.ⁱ, Giorgio Radetti, M.D.^j, Luciano Tatò, M.D.^k, Giorgio Tonini, M.D.^l, and Egle Perissinotto, Sc.D.^{m,*}

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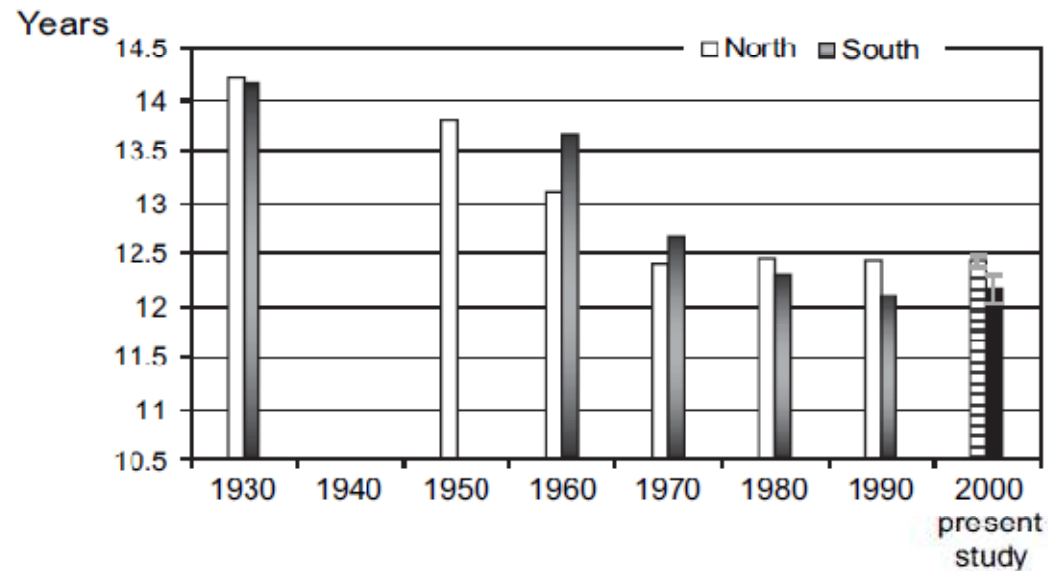


Figure 2. Secular trend for age at menarche in northern and southern Italy. Grey vertical lines represent 95% CI for the results of the present survey.

- **1) richiami di fisiologia della pubertà**

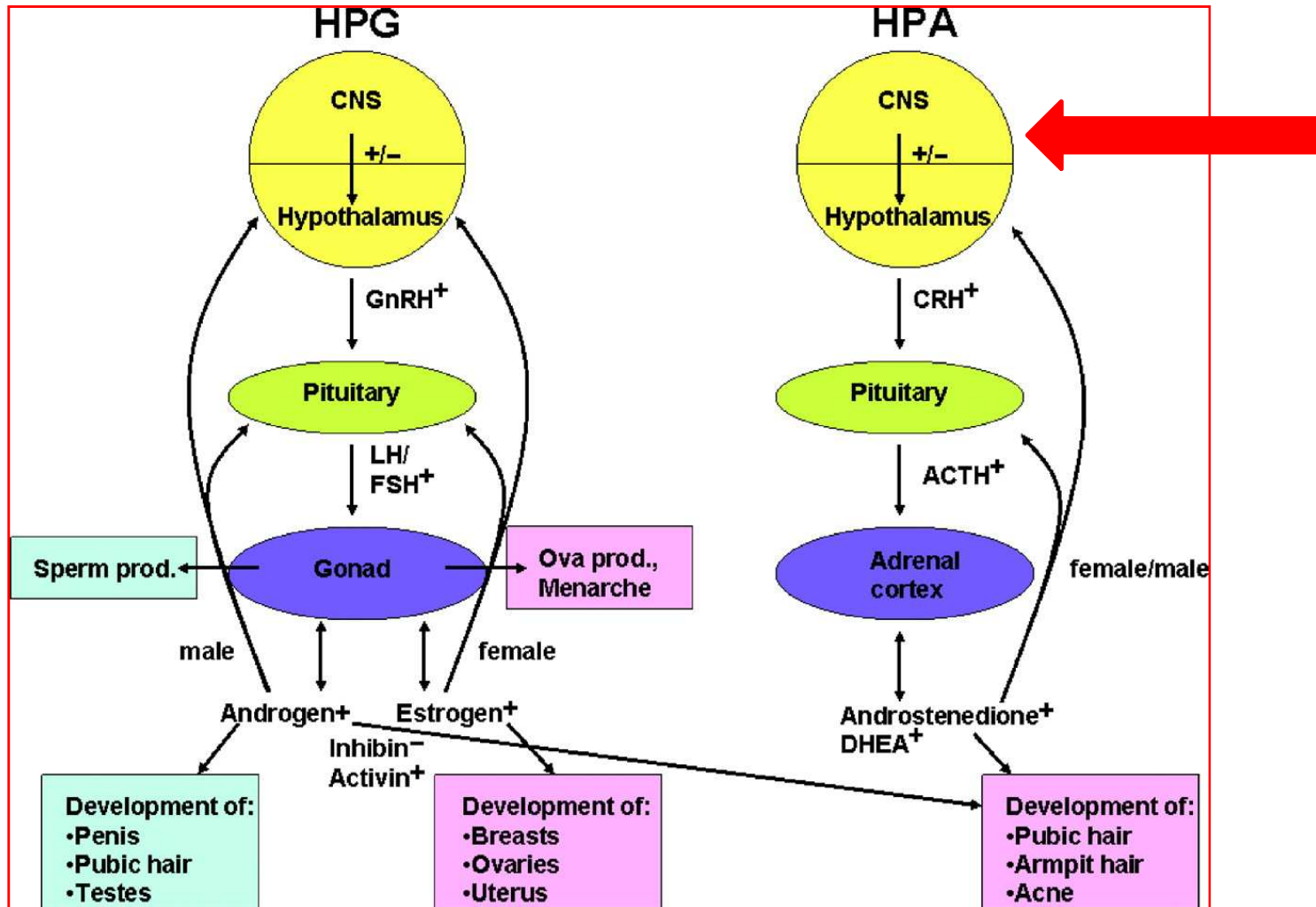
- **segni clinici**
- **meccanismi neuroendocrini**



Environmental Factors and Puberty Timing: Expert Panel Research Needs

Pediatrics 2008;121;S192

Germaine M. Buck Louis, PhD*, L. Earl Gray, Jr, PhD*, Michele Marcus, PhD, MPH, Sergio R. Ojeda, DVM*, Ora H. Passovitz, MD*,
 Selma Feldman Witchel, MD, Wolfgang Sippell, MD, PhD, David H. Abbott, PhD*, Ana Scios, MD, Rochelle W. Tyl, PhD,
 Jean-Pierre Bourguignon, MD, PhD*, Neils E. Skakkebaek, MD, DMSc, Shanna H. Swan, PhD*, Marit S. Gokub, PhD*, Martin Wabitsch, MD, PhD*,
 Jerma Toppert, MD, PhD*, Susan Y. Furlong, PhD*

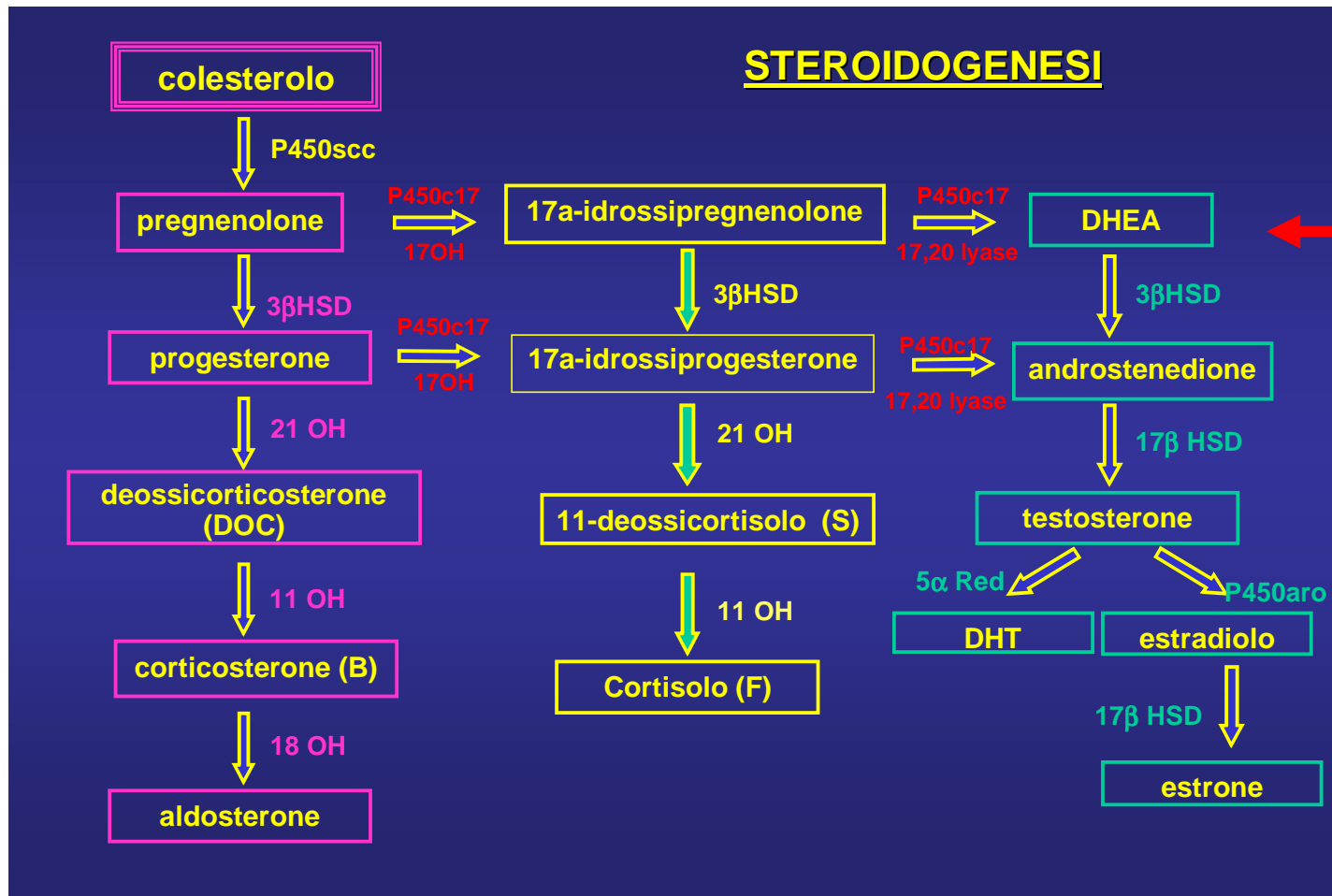


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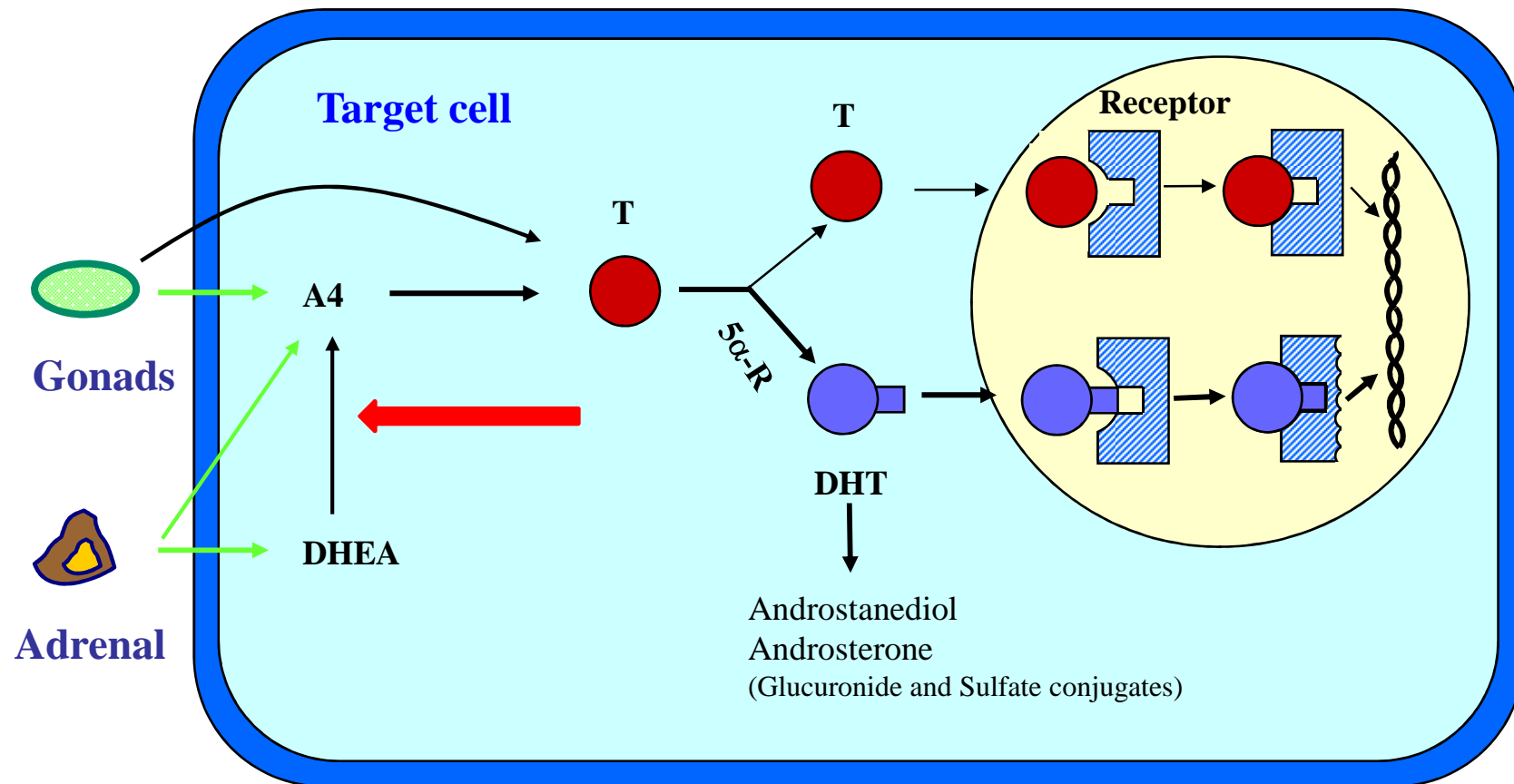
These physical changes are preceded by biochemical adrenarche, which has been described to begin physiologically as early as ages 5–6 yr and consists of increased Zona Reticularis production of 5 steroids, principally dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS).



PUBARCA



ANDROGEN METABOLISM AND MECHANISM OF ACTION



PUBARCA

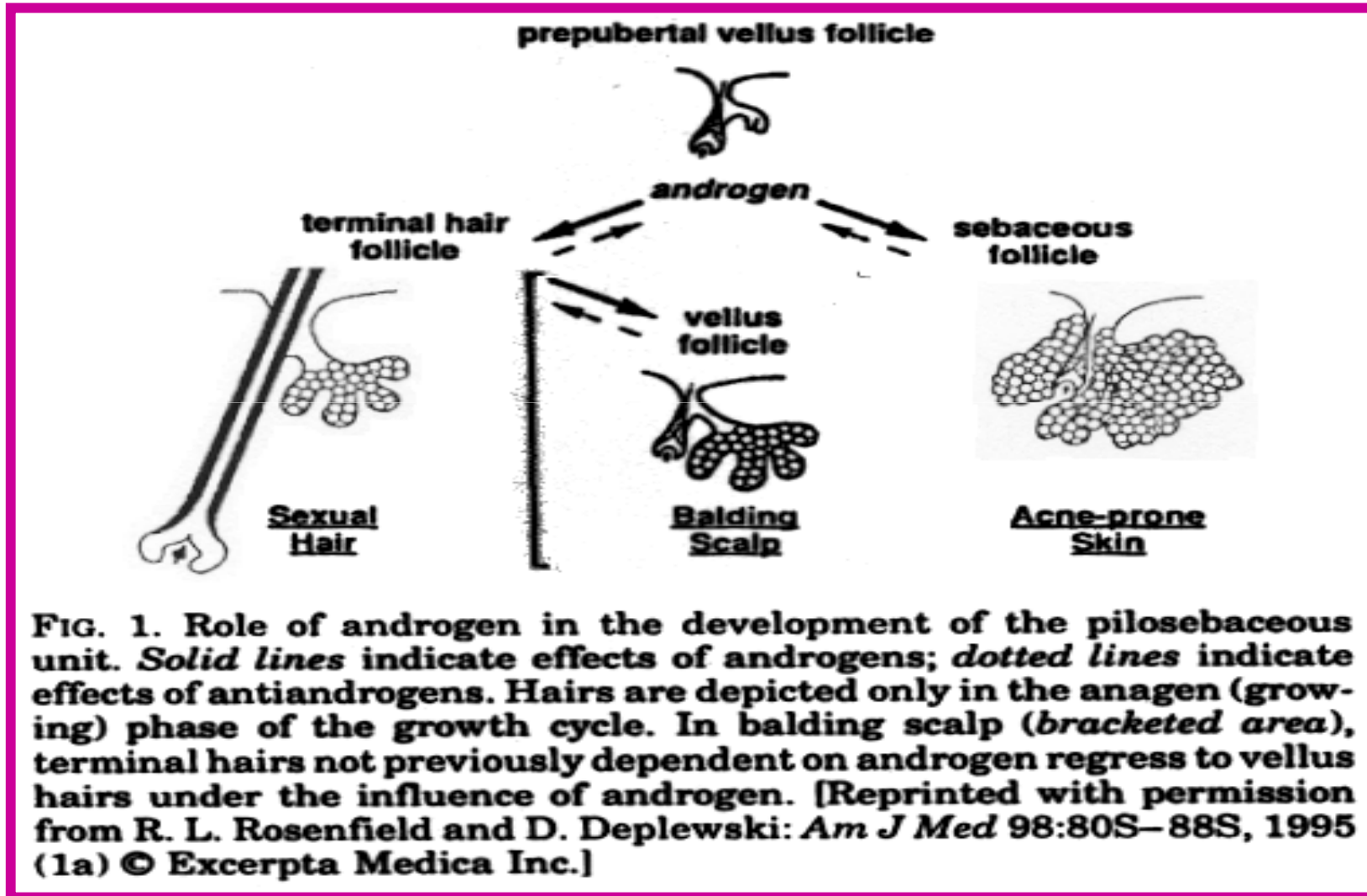
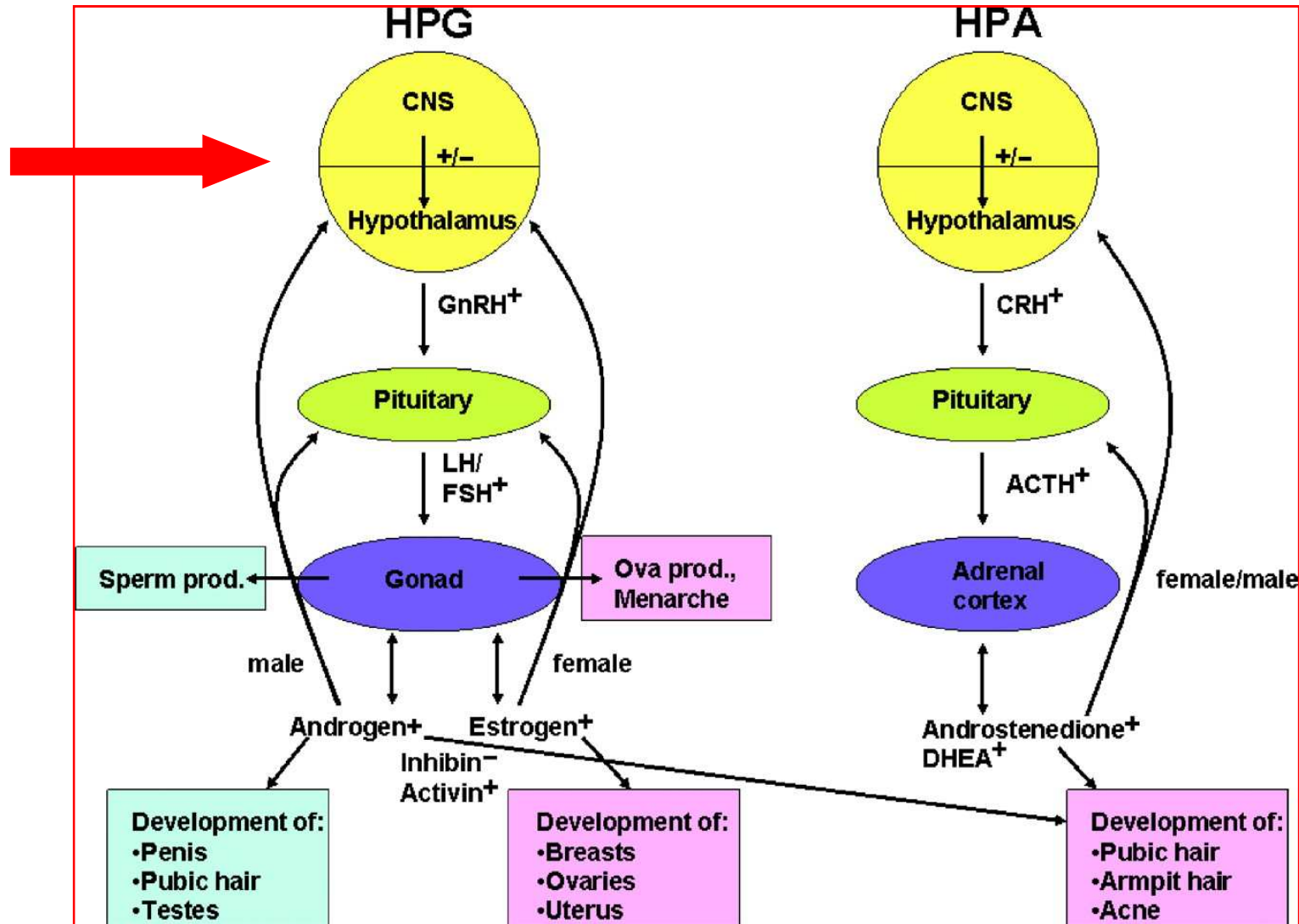
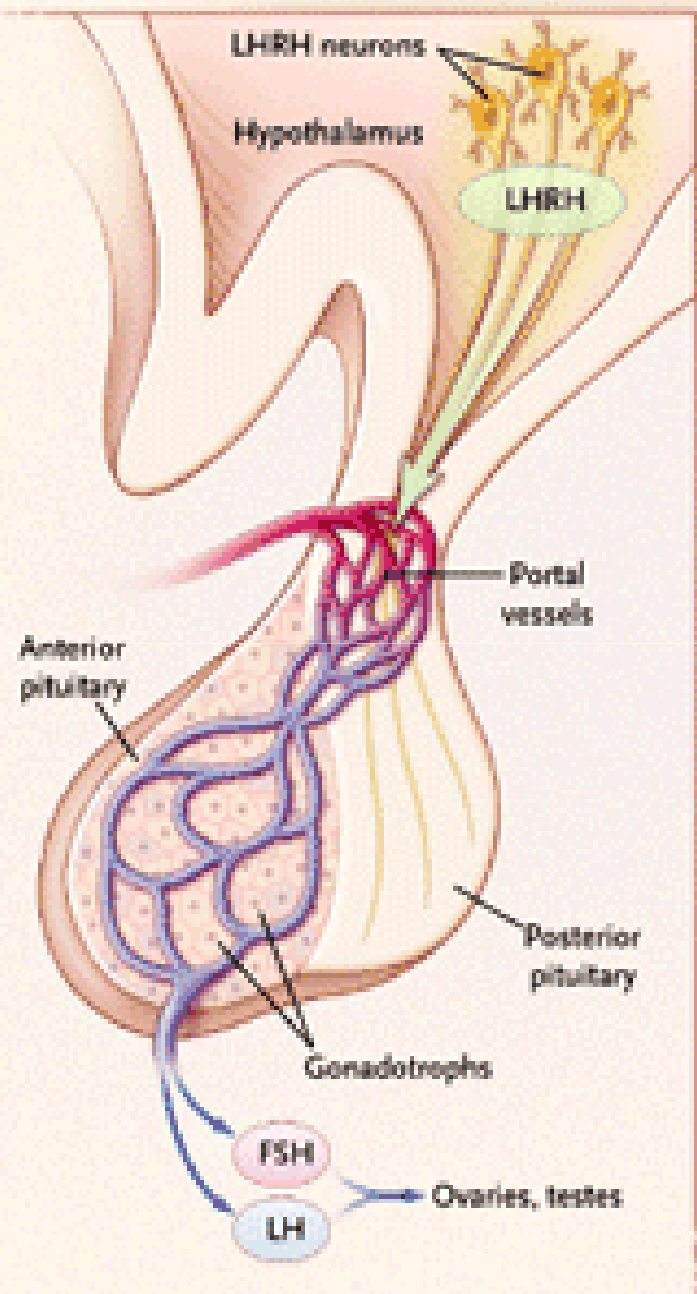


FIG. 1. Role of androgen in the development of the pilosebaceous unit. Solid lines indicate effects of androgens; dotted lines indicate effects of antiandrogens. Hairs are depicted only in the anagen (growing) phase of the growth cycle. In balding scalp (bracketed area), terminal hairs not previously dependent on androgen regress to vellus hairs under the influence of androgen. [Reprinted with permission from R. L. Rosenfield and D. Deplewski: *Am J Med* 98:80S–88S, 1995 (1a) © Excerpta Medica Inc.]

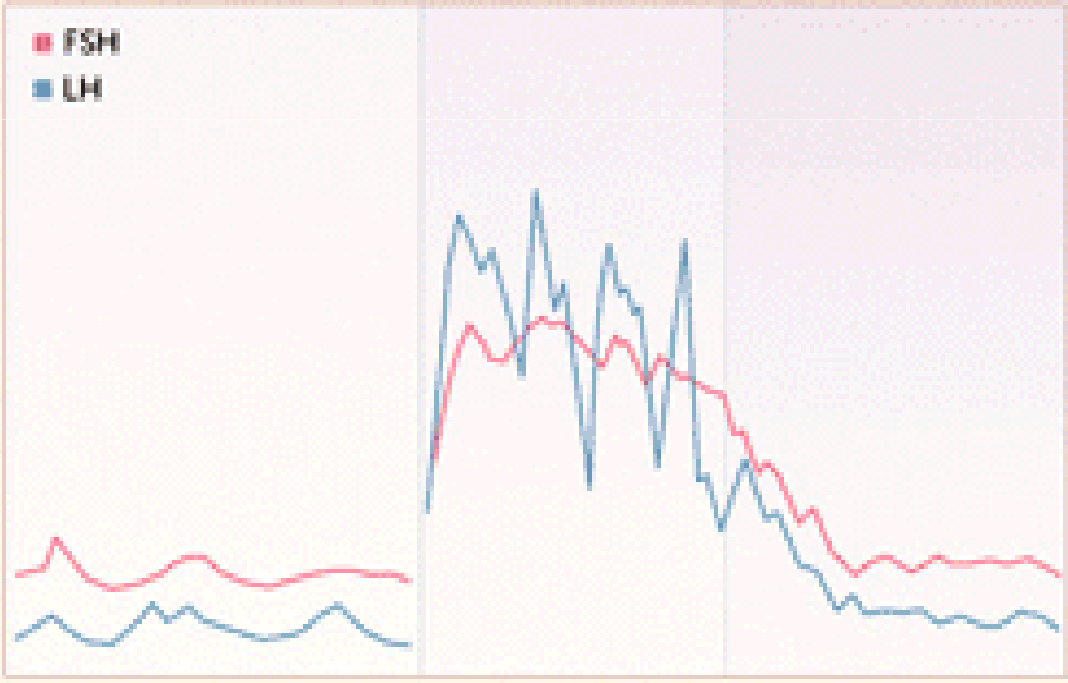
Environmental Factors and Puberty Timing: Expert Panel Research Needs

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 Jerma Toppert, MD, PhD*, Susan Y. Finkel, PhD*





Prepuberty	Puberty	
Low, infrequent LHRH pulses	Increased frequency and amplitude of LHRH pulses	Suppression of LHRH pulses with long-acting LHRH analogue



Neurobiological Mechanisms of the Onset of Puberty in Primates*

End Rev 2001

EI TERASAWA AND DAVID L. FERNANDEZ†

Department of Pediatrics (E.T.), Wisconsin Regional Primate Research Center (E.T., D.L.F.), and Center for Neuroscience (E.T.), University of Wisconsin-Madison, Madison, Wisconsin 53715-1299

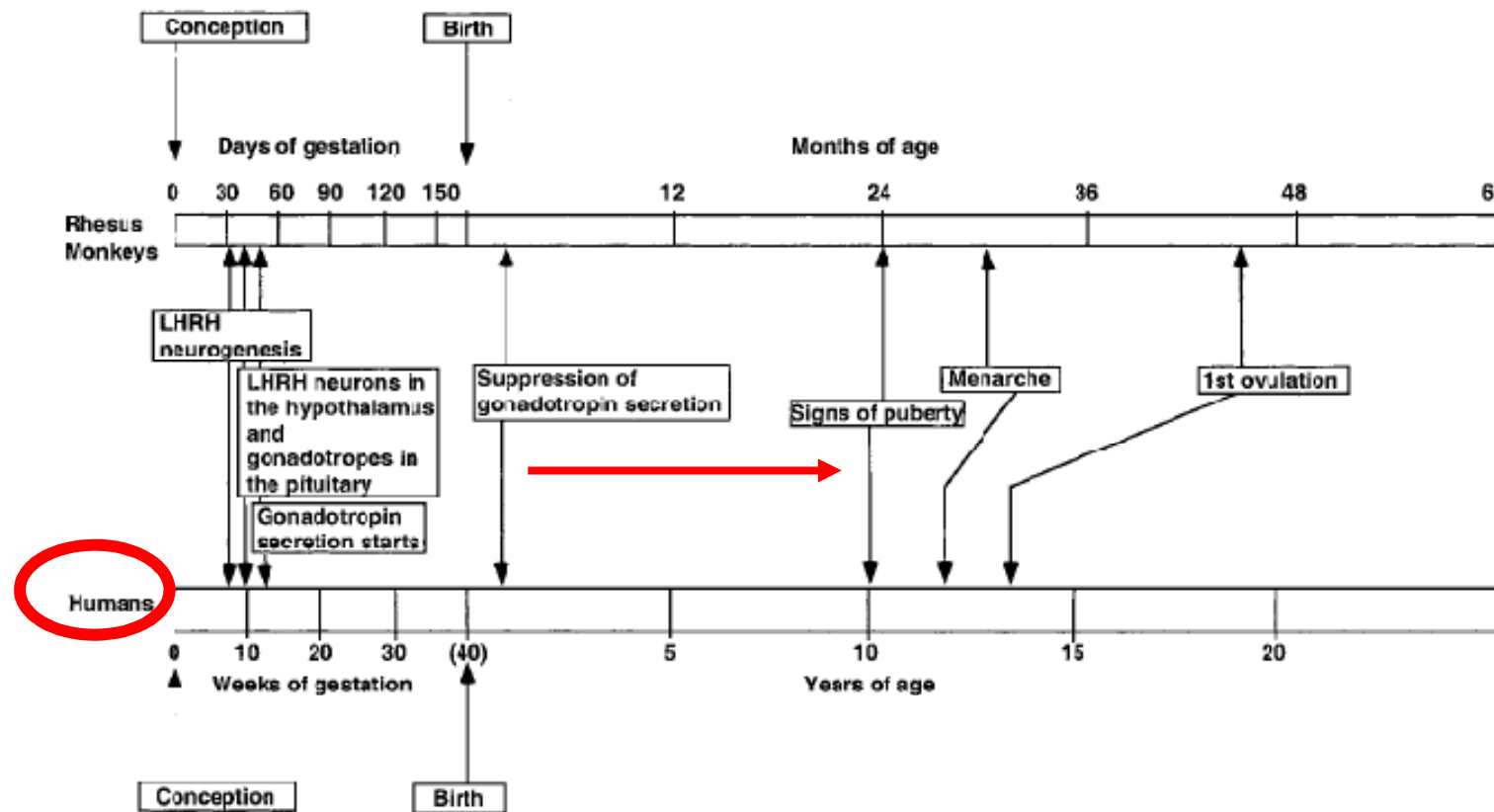


FIG. 1. Ontogeny of the LHRH-pituitary-gonadal system before birth until after the onset of puberty in female rhesus monkeys (*top*) and in female humans (*bottom*). Days and months are used as the scale for the gestational period and after birth in monkeys, respectively, whereas weeks and years are used as the scale in humans. The age of events indicated in this figure is approximate.

Pubertal Development and Menarche

SARA A. DiVALL AND SALLY RADOVICK

Ann. N.Y. Acad. Sci. 1135: 19-28 (2008)

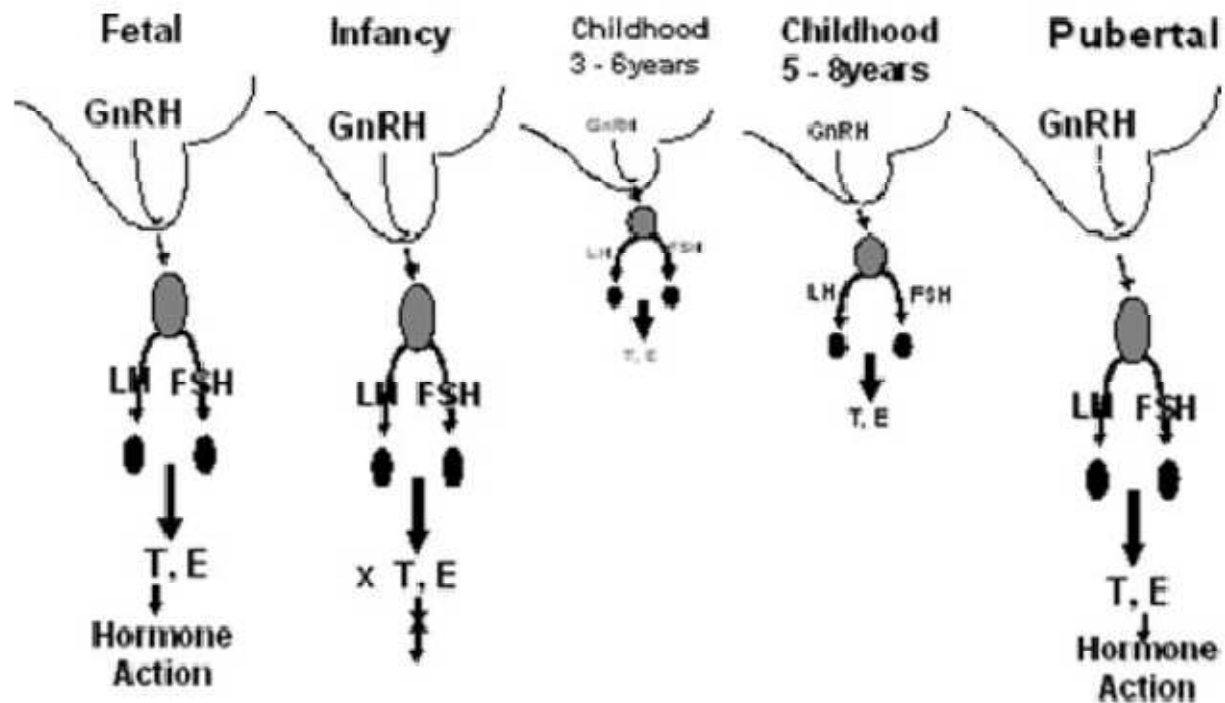


FIGURE 1. Schematic of the hypothalamic-pituitary-gonadal axis during developmental stages of childhood. The axis is active in fetal life and infancy, becoming quiescent at 1 year of age. In early childhood, the axis is minimally active, but becomes increasingly active in later childhood. Finally, at the time of puberty, the axis fully “reawakens” to mature to the activity present in adults.

Adolescente e ciclo mestruale
Sergio Bernasconi



Neurobiological Mechanisms of the Onset of Puberty in Primates*

End Rev 2001

EI TERASAWA AND DAVID L. FERNANDEZ†

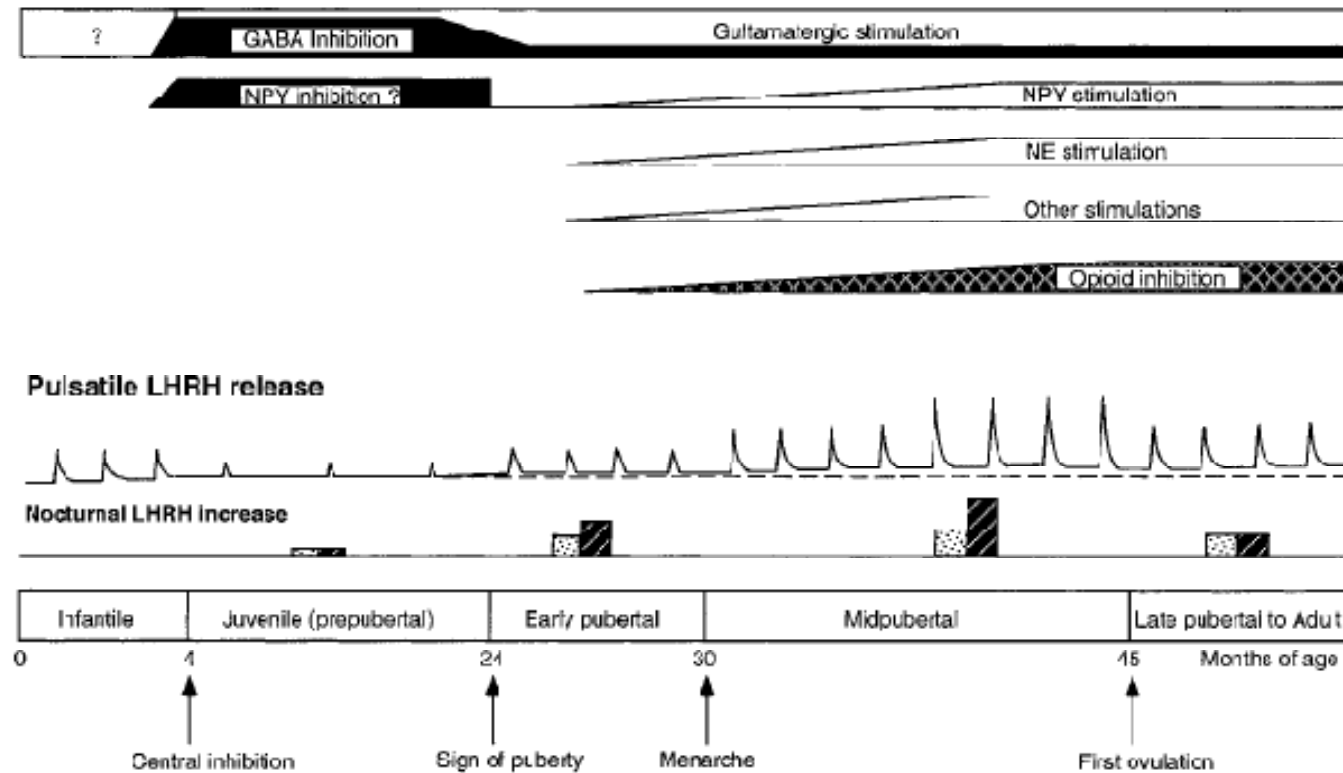


FIG. 2. Schematic illustration of postnatal changes in LHRH release and neurotransmitter events that occur in the hypothalamus in association with puberty in nonhuman female primates. The LHRH neurosecretory system appears to be active during the infantile period, but is suppressed by an inhibitory mechanism comprising GABA neurons. At the onset of puberty, a reduction in GABA inhibition and a subsequent increase in glutamate excitation of LHRH neurons result in the pubertal increase in the pulse frequency, pulse amplitude, and baseline levels of LHRH, which trigger puberty. Furthermore, a higher nocturnal level of LHRH release, shown by *hatched bars*, becomes particularly prominent. After the onset of puberty, other stimulatory neurotransmitters such as NPY and NE take part in control of LHRH neurons, resulting in further increases in the pulse amplitude and baseline level of LHRH release, until the time of first ovulation. The nocturnal increase in LHRH release and LHRH pulse amplitude are reduced to the adult level, perhaps due to participation of inhibitory neurotransmitters, such as opioids. *Stippled bars* indicate morning levels of LHRH. In males the LHRH neurosecretory system is fully mature during the infantile period, but is suppressed completely during the juvenile period. Recently, it has been hypothesized that NPY is an inhibitory neurotransmitter before puberty in males. (See text for details.)

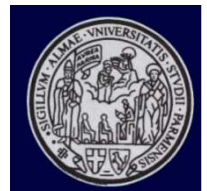
FISIOLOGIA DELLA PUBERTA'

1) Nuovi Peptidi agenti sul pulse generator



FISIOLOGIA DELLA PUBERTA'

- **Kisspeptin, encoded by the KISS1 gene**, is secreted as a precursor peptide, kisspeptin-1, which is submitted to proteolytic processing followed by amidation of its carboxy-terminal domain
- Seems to be the exclusive ligand of KISS1R
- **Is the most potent known stimulator of GnRH dependent LH secretion**



New *frontiers* in kisspeptin/GPR54 physiology as fundamental gatekeepers of reproductive function

Juan Roa ^{a,c}, Enrique Aguilar ^{a,c}, Carlos Dieguez ^{b,c}, Leonor Pinilla ^{a,c},
Manuel Tena-Sempere ^{a,c,*}

Frontiers in Neuroendocrinology 2008

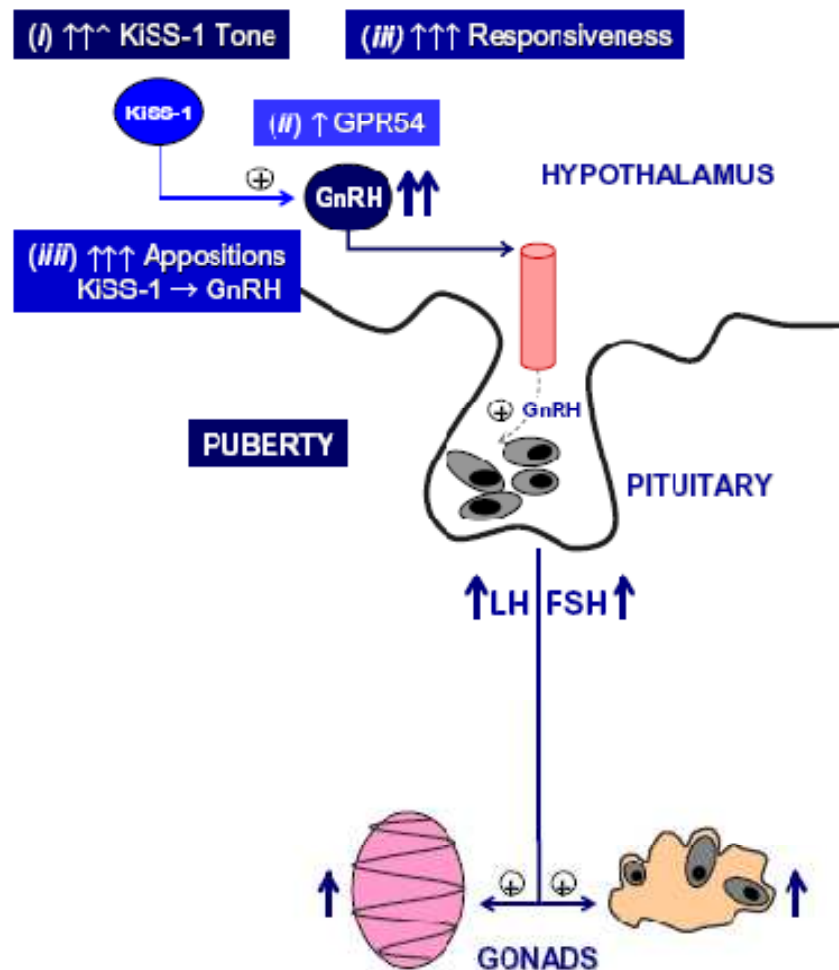


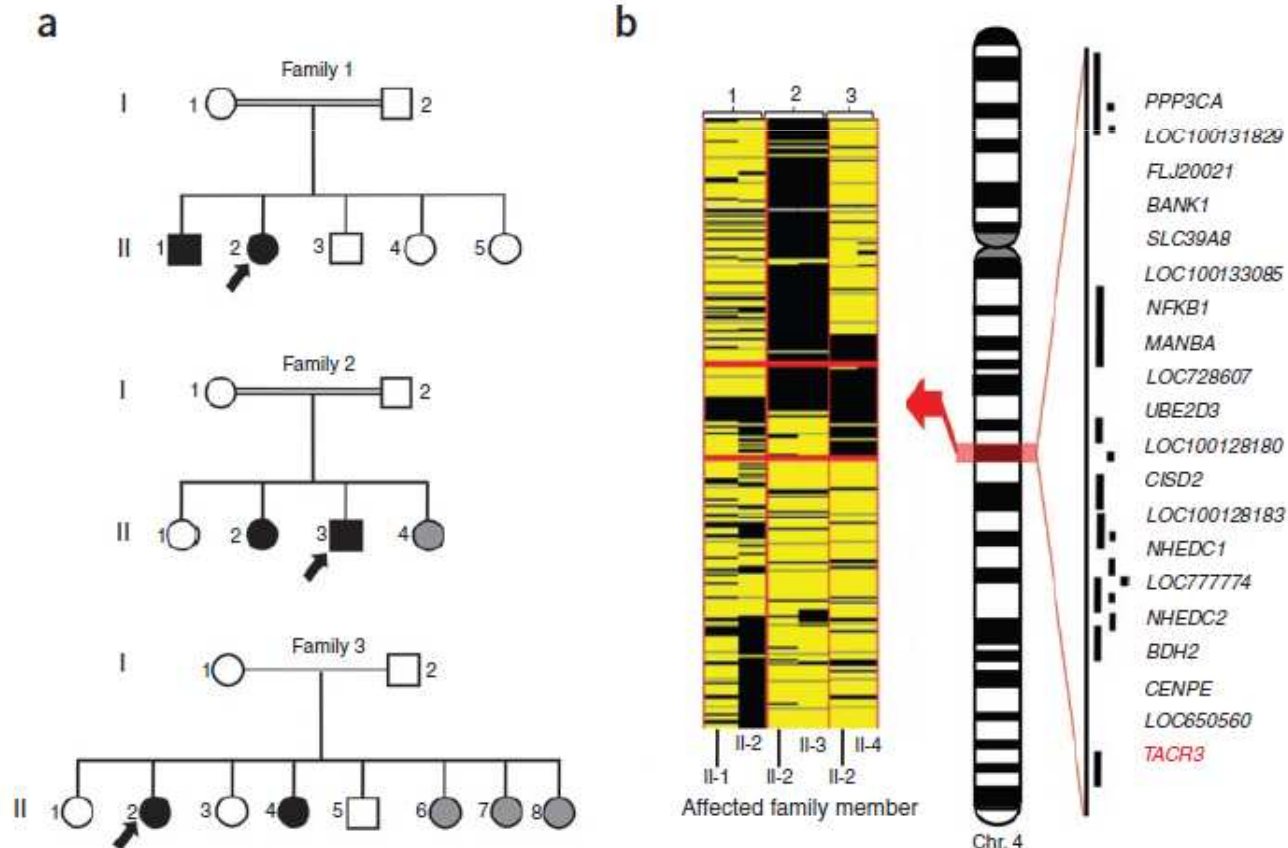
Fig. 4. Tentative model for the mechanisms potentially involved in the activation of GnRH neurons by kisspeptins and GPR54 at the time of puberty. These might include: (i) increase in endogenous kisspeptin tone at certain hypothalamic nuclei—likely AVPV; (ii) enhancement of the expression of GPR54, of lower magnitude than the ligand; (iii) increase in the sensitivity/responsiveness to the stimulatory effects of kisspeptin linked to augmentation of the efficiency of GPR54 coupling to its signaling systems; and (iv) increase in the number of appositions between KiSS-1 neurons (*projections*) and GnRH neurons. Overall, the enhancement in the activity of KiSS-1 system likely operates as a major driving signal for the full activation of the GnRH pulse generator (denoted by *arrows*), and subsequently gonadotropin secretion and gonadal function, at the time of puberty. For further details, see Section 4.3.

FISIOLOGIA DELLA PUBERTA'

TAC3 and *TACR3* mutations in familial hypogonadotropic hypogonadism reveal a key role for Neurokinin B in the central control of reproduction

VOLUME 41 | NUMBER 3 | MARCH 2009 | NATURE GENETICS

A Kemal Topaloglu^{1,7}, Frank Reimann^{2,7}, Metin Guclu³, Ayse Serap Yalin⁴, L Damla Kotan⁵, Keith M Porter⁶, Ayse Serin⁵, Neslihan O Mungan¹, Joshua R Cook⁶, Mehmet N Ozbek¹, Sazi Imamoglu³, N Sema Akalin⁴, Bilgin Yuksel¹, Stephen O'Rahilly⁶ & Robert K Semple⁶



FISIOLOGIA DELLA PUBERTA'

- **Neurokinin B, encoded by the TAC3 gene** is a member of mammalian tachykinins family of excitatory neurotransmitters, composed of evolutionary and conserved peptides widely distributed within the peripheral and central nervous system (Pinto et al., 2004).

The best known members of this family are substance P, neurokinin A, neurokinin B and, more recently, endokinins and hemokinins

- The NK3 receptor (NK3R), encoded by the TAC3R gene is the most selective of the tachykinin receptors with highly preferential binding and activation by NKB
- **In rodents, NK3R is highly expressed in GnRH and kisspeptin-expressing neurons in the hypothalamus**



FISIOLOGIA DELLA PUBERTÀ'

- 1) Nuovi Peptidi agenti sul pulse generator**
- 2) Rapporto tra stato nutrizionale/energetico e pubertà**



FISIOLOGIA DELLA PUBERTÀ'

Review

Insulin and NPY pathways and the control of GnRH function and puberty onset

François P. Pralong*¹

Molecular and Cellular Endocrinology 324 (2010) 82–86

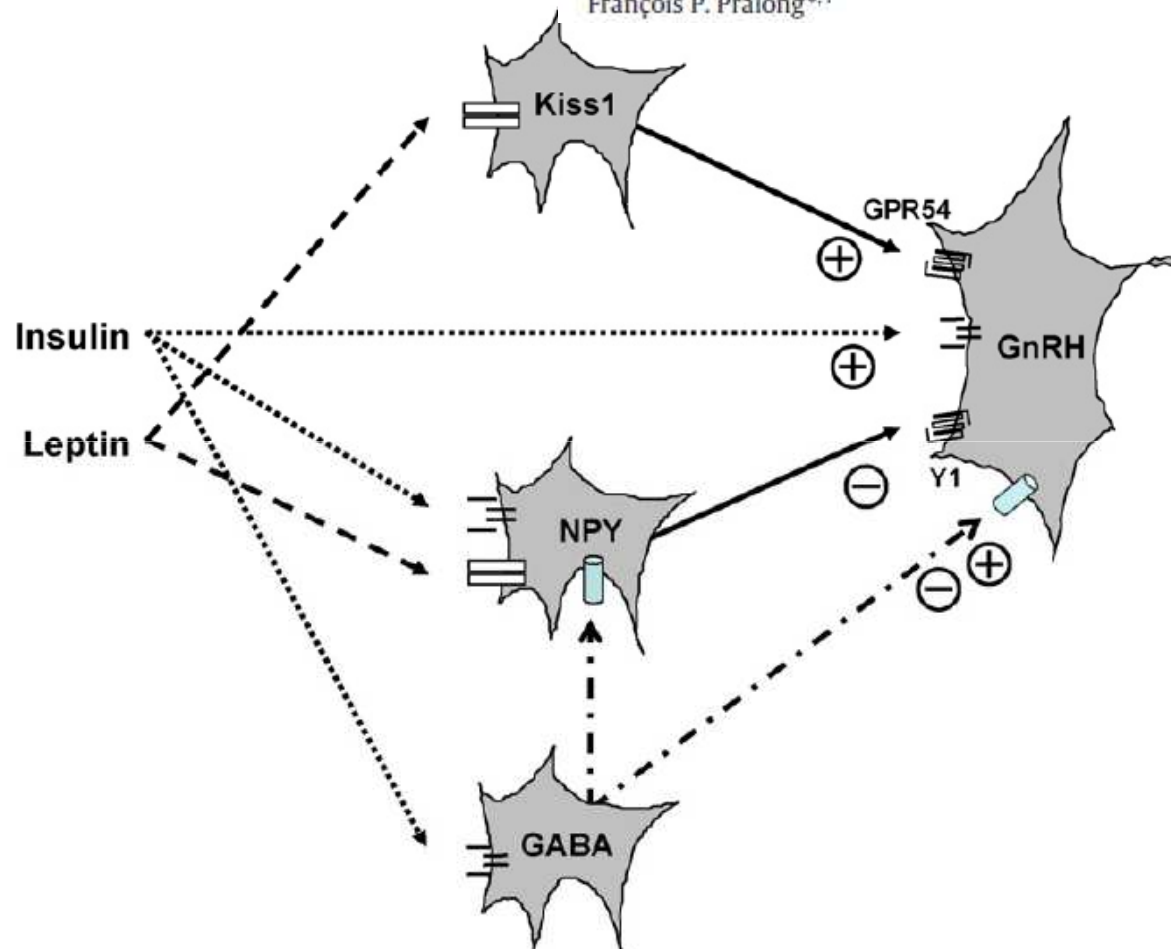


Fig. 1. Schematic representation of possible hypothalamic pathways involved in insulin and leptin signaling for neuroendocrine reproductive modulations. GnRH neurons can be modulated either directly or indirectly via first-order neurons like NPY- or KISS-1 expressing neurons, as well as GABA-ergic neurons. According to our working hypothesis, insulin can activate GnRH neurons either directly or indirectly, whereas leptin is acting exclusively via a modulation of first-order neurons. In unfavorable metabolic conditions, elevated NPY levels are exerting a predominantly inhibitory effect on GnRH, at least partially via Y1. In contrast, KISS-1 stimulates the activity of GnRH neurons which express GPR-54. Finally, GABA has been shown to exert stimulatory or inhibitory effects, depending on the pubertal status of the animals.

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- 3) storia naturale del ciclo
- 4) alterazioni più frequenti del ciclo
 - approccio clinico e terapeutico



Period problems: disorders of menstruation in adolescents

A Peacock, N S Alvi, T Mushtaq

Arch Dis Child 2012;**97**:554–560.

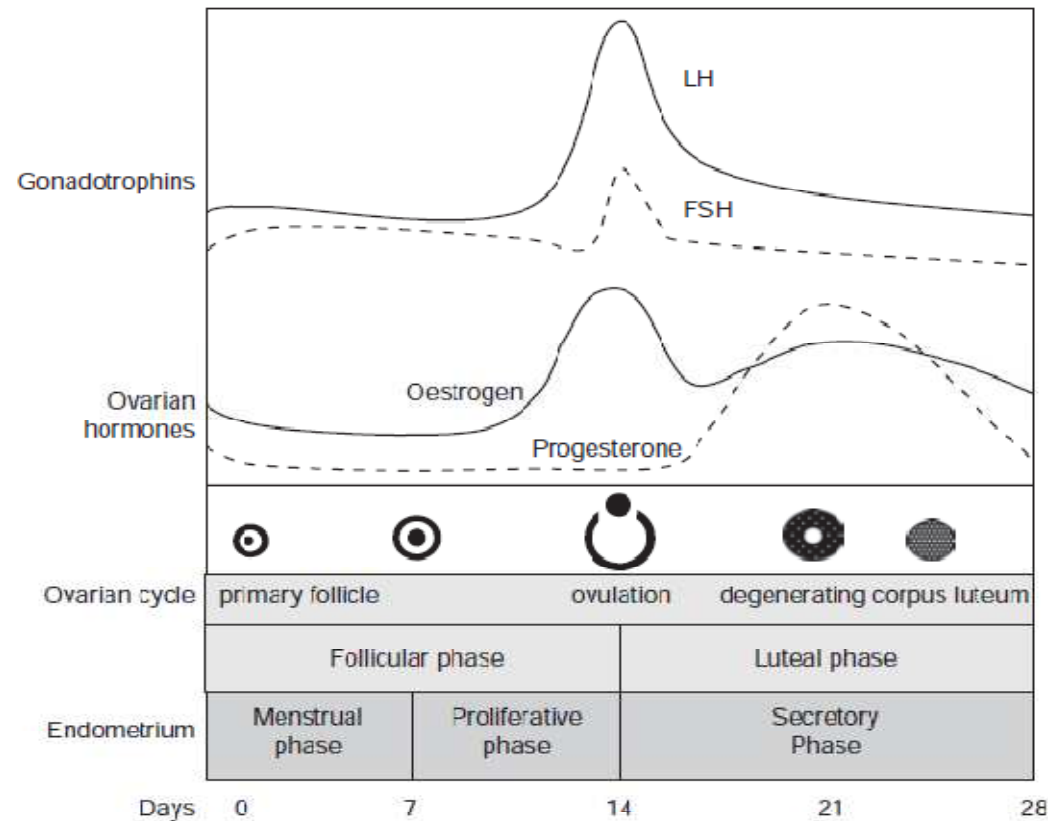


Figure 1 Hormone levels, follicular development and endometrial changes in the normal menstrual cycle. This ovarian follicular stage is characterised by increases in the size of the ovarian follicles and selection of a dominant follicle that progresses to full maturity. Once circulating levels of oestradiol reach a critical concentration, they induce the LH surge that leads to ovulation around day 14 of the menstrual cycle. After ovulation, the remaining granulosa cells become the corpus luteum that produces progesterone.

Adolescente e ciclo mestruale
Sergio Bemascori

Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding?[†]

Ian S.Fraser^{1,5}, H.O.D.Critchley², M.G.Munro³ and M.Broder⁴

Human Reproduction Vol.22, No.3 pp. 635–643, 2007



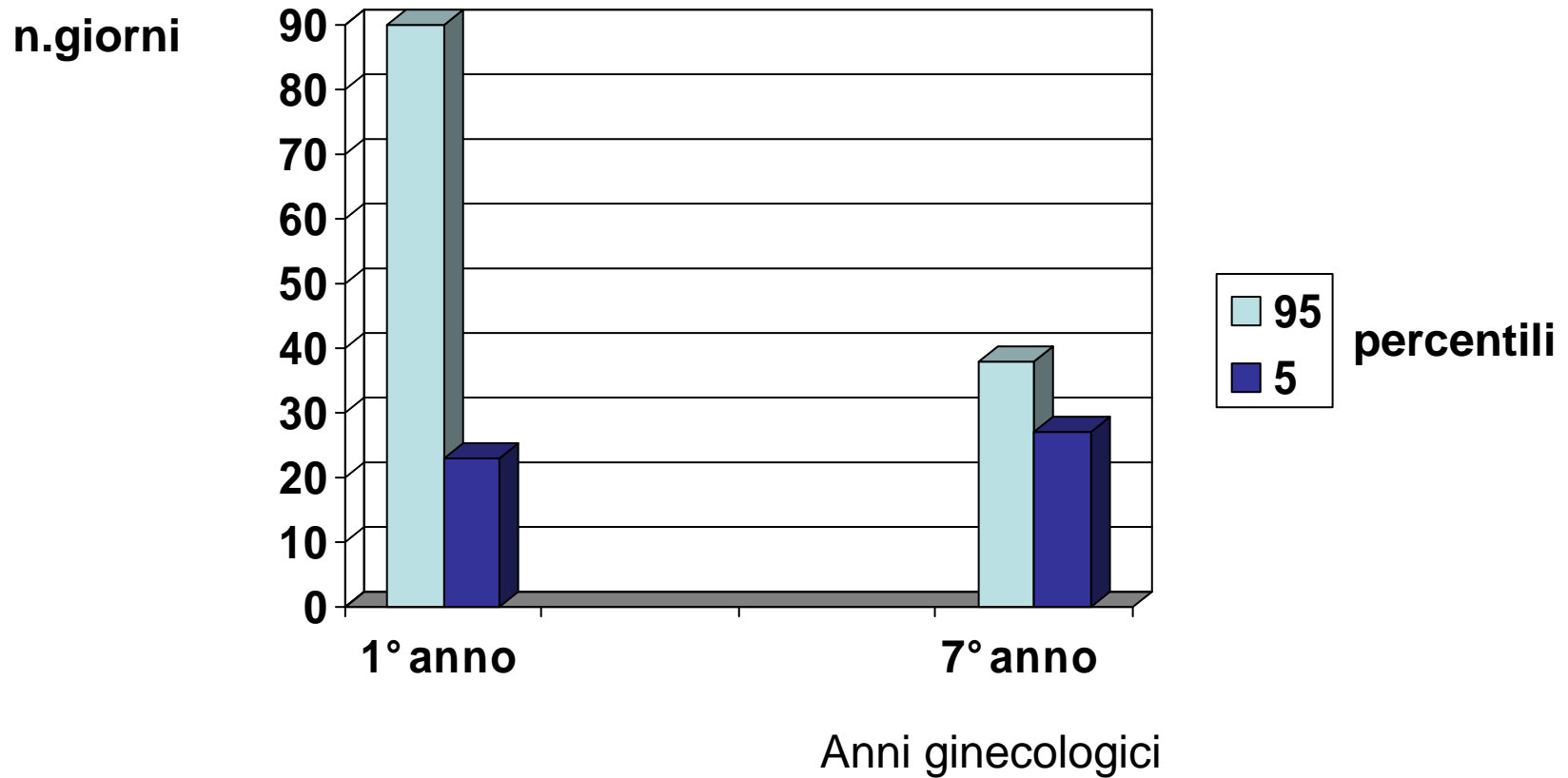
Table VII. Suggested normal limits for menstrual parameters in the mid-reproductive years

	Normal limits (5th–95th percentiles)
Frequency of menses (days)	24–38
Regularity of menses (cycle to cycle variation over 12 months; in days)	Variation \pm 2 to 20 days
Duration of flow (days)	4.5–8.0
Volume of monthly blood loss (ml)	5–80

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Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign
American Academy of Pediatrics, Committee on Adolescence, American College of Obstetricians and Gynecologists and Committee on Adolescent Health Care
Pediatrics 2006;118:2245
DOI: 10.1542/peds.2006-2481



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 - **approccio clinico e terapeutico**
 - **amenorrea primaria**



1) AMENORREA PRIMARIA

Period problems: disorders of menstruation in adolescents

A Peacock, N S Alvi, T Mushtaq

Arch Dis Child 2012;**97**:554–560.

Primaria = assenza di menarca a 16 anni in adolescenti con normale crescita e presenza di caratteri sessuali secondari :

- 40% da endocrinopatie
- 60% su base funzionale.

1) AMENORRHEA PRIMARIA

Table 1 Causes of primary and secondary amenorrhoea

Causes of amenorrhoea

Primary

Systemic

- Chronic disease and weight loss
- Excessive exercise

Hypothalamus/pituitary

- Tumours and cranial irradiation
- Hyperprolactinaemia and hypopituitarism

Endocrine disease

- Thyroid disease and Cushing syndrome

Uterus/ovary

- Mullerian agenesis
- Gonadal dysgenesis (eg, Turner syndrome)
- Premature ovarian failure (eg, galactosaemia)
- Imperforate hymen
- PCOS

Disorders of sexual differentiation

- Androgen insensitivity syndrome
 - 5 α reductase deficiency
-

Period problems: disorders of menstruation in adolescents

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Arch Dis Child 2012;**97**:554–560.



1) AMENORREA PRIMARIA

- 1) **Eco pelvica**
- 2) **LH, FSH, E2 (basali e successivamente tests funzionali)**
- 3) **TSH, FT4**
- 4) **PRL (pool)**
- 5) **Androgeni (17OHP, DHEA-S, T)**
- 6) **Cariotipo o altra indagine genetica**



1) AMENORRREA PRIMARIA

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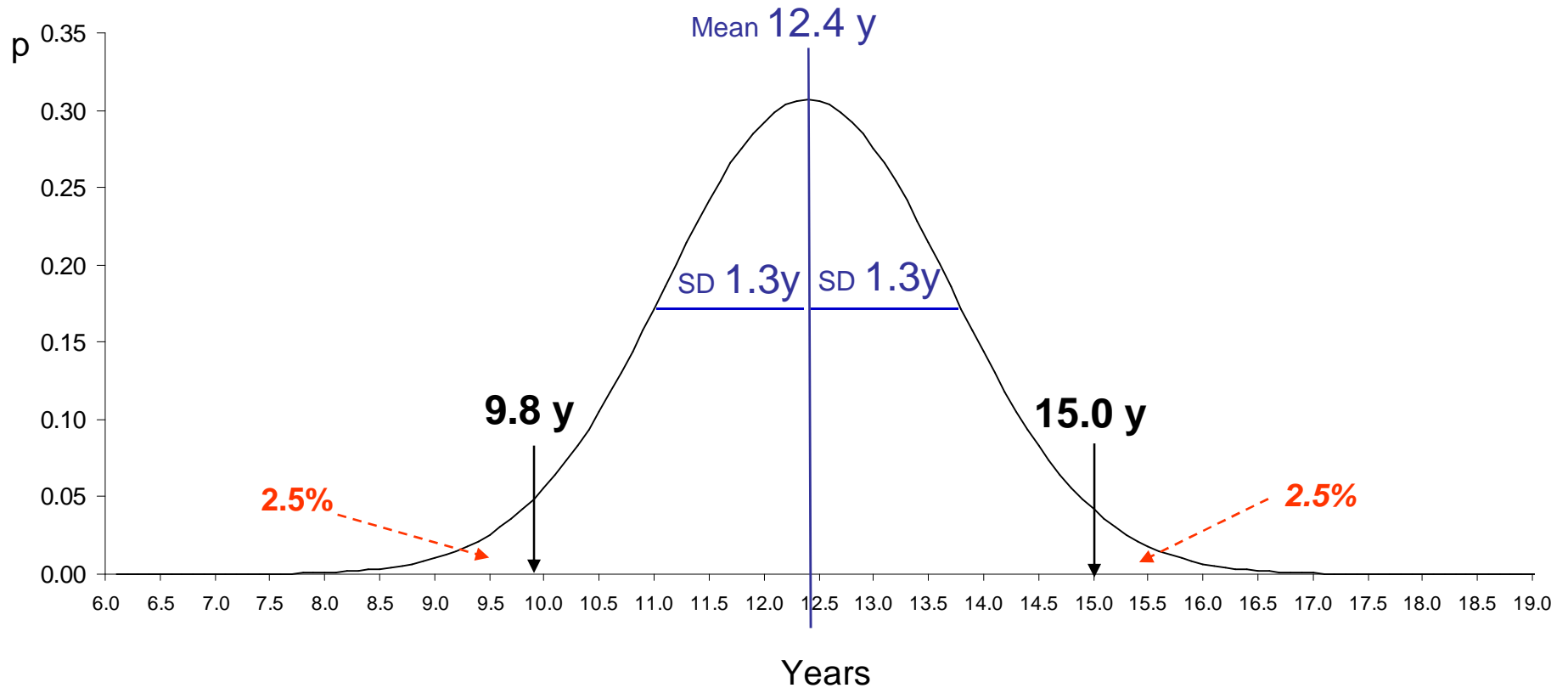
TABLE 3 Menstrual Conditions That May Require Evaluation

Menstrual periods that:

- Have not started within 3 years of thelarche
- Have not started by 13 years of age with no signs of pubertal development
- Have not started by 14 years of age with signs of hirsutism
- Have not started by 14 years of age with a history or examination suggestive of excessive exercise or eating disorder
- Have not started by 14 years of age with concerns about genital outflow tract obstruction or anomaly
- Have not started by 15 years of age



Distribution of Age at menarche



Journal of Adolescent Health 46 (2010) 238–244

Update on Age at Menarche in Italy: Toward the Leveling Off of the Secular Trend

Franco Rigon, M.D.^a, Luigi Bianchin, M.D.^b, Sergio Bemasoni, M.D.^c, Gianni Bona, M.D.^d,
Mauro Bozzola, M.D.^e, Fabio Buzi, M.D.^f, Alessandro Cicognani, M.D.^g, Carlo De Sanctis, M.D.^h,
Vincenzo De Sanctis, M.D.ⁱ, Giorgio Radetti, M.D.^j, Luciano Tatò, M.D.^k, Giorgio Tonini, M.D.^l,
and Egle Perissinotto, Sc.D.^{m,*}

- 1) richiami di fisiologia della pubertà
- 2) ciclo mestruale
- 3) storia “naturale” del ciclo
- **4) alterazioni più frequenti**
 - **approccio clinico e terapeutico**
 - **amenorrea primaria**
 - **altre anomalie**



2) ALTRE ANOMALIE CICLO MESTRUALE

1) Difficoltà di classificazione uniforme



2) ALTRE ANOMALIE CICLO MESTRUALE

Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding?[†]

Human Reproduction Vol.22, No.3 pp. 635–643, 2007

Ian S.Fraser^{1,5}, H.O.D.Critchley², M.G.Munro³ and M.Broder⁴

Table VII. Suggested normal limits for menstrual parameters in the mid-reproductive years

Clinical dimensions of menstruation and menstrual cycle	Descriptive terms	Normal limits (5th–95th percentiles)
Frequency of menses (days)	Frequent	<24
	Normal	24–38
	Infrequent	>38
Regularity of menses (cycle to cycle variation over 12 months; in days)	Absent	—
	Regular	Variation \pm 2 to 20 days
	Irregular	Variation greater than 20 days
Duration of flow (days)	Prolonged	>8.0
	Normal	4.5–8.0
	Shortened	<4.5
Volume of monthly blood loss (ml) (Hallberg <i>et al.</i> , 1966)	Heavy	>80
	Normal	5–80
	Light	<5

Based primarily on Hallberg *et al.*, 1966, Treloar *et al.*, 1967, Snowden and Christian 1983, Belsey *et al.*, 1997.



2) ALTRE ANOMALIE CICLO MESTRUALE

1) Perdite ematica eccessiva – Heavy Periods





Menstrual pattern and menstrual disorders among adolescents: an update of the Italian data

Italian Journal of Pediatrics 2012, **38**:38 doi:10.1186/1824-7288-38-38

Adolescente e ciclo mestruale
Sergio Bernasconi

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Garofolo" and University of Trieste*

Franco Rigon, Dep. of Pediatrics, University of Padova

*L Egle Perissinotto Dep. of Cardiac, Thoracic and Vascular Sciences, Unit of Biostatistics,
Epidemiology and Public Health, Univ. of Padova*

Indagine sulla salute mestruale nelle giovani

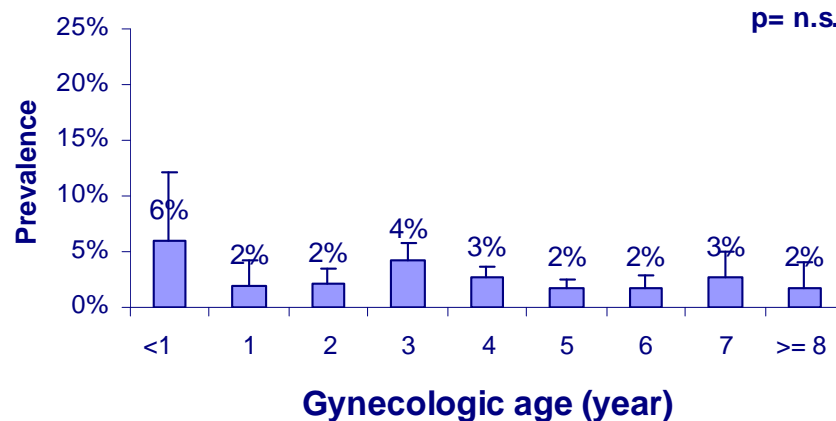


- Studio Multicentrico Trasversale che valuta lo 'status quo'
- Lo studio include solo ragazze nelle quali il menarca si è già verificato.
- Campione osservato di n=4992 ragazze delle scuole secondarie di 16 città Italiane, costruito secondo una strategia di uguale allocazione e ottenuto campionando circa il 5% della popolazione scolastica target in ciascuna città

Perdita ematica eccessiva

- **POLIMENORREA:** lunghezza del ciclo inferiore a 21 giorni (1,2)

Polymenorrhea



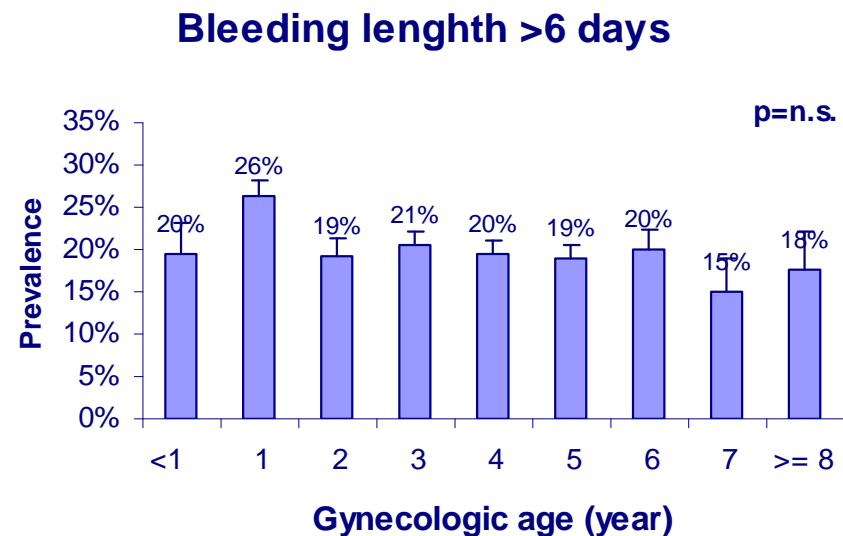
1. Petrozza J, Poley K. *Dysfunctional uterine bleeding*. In: Curtis MG, Hopkins MP (Eds). *Glass's office gynecology*. 5th edn. Baltimore: Williams & Wilkins, 1999; 241-64.
2. Speroff L, Glass RH, Kase NG (eds). *Dysfunctional uterine bleeding*. In: *Clinical Gynecologic Endocrinology and Infertility*. 5th edn. Baltimore: Williams & Wilkins, 1994; 575-93.



Perdita ematica eccessiva

PERDITE EMATICHE ANOMALE: sanguinamenti della durata superiore a 6 giorni

(3,4,5)



3. Flug D, Largo RH, Prader A. Menstrual patterns in adolescent Swiss girls: a longitudinal study. *Ann Hum Biol.* 1984; 11(6):495–508.
4. ACOG Committee on Adolescent Health Care. Menstruation in girls and adolescents using the menstrual cycle as a vital sign. *Obstet Gynecol.* 2006; 108(5):1323-1328.
5. Fraser IS, Critchley HO, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? *Hum Reprod.* 2007; 22(3):635-643.





Management of heavy menstrual bleeding in adolescents



Nancy Sokkary and Jennifer E. Dietrich

Curr Opin Obstet Gynecol 2012, 24:000–000

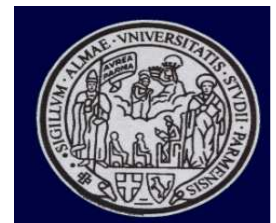
KEY POINTS

- Anovulation and blood dyscrasias are the two most common causes of HMB in the adolescent population.

Durante i cicli anovulatori aumenta FSH, il follicolo comincia a produrre E , manca il picco di LH e quindi l'ovulazione, non si forma il corpo luteo, non si produce P e l'endometrio continua a proliferare senza fase secretoria. Il follicolo poi va verso un'involuzione e diminuisce la sintesi di E con ulteriore effetto sull'endometrio

Perdita ematica eccessiva

Nel 10-50% dei casi riconducibile a turbe della coagulazione (piastrinopatie e/o penie, von Willebrand) soprattutto se compare in coincidenza con il menarca.



Perdita ematica eccessiva

Bleeding Disorders in Adolescents

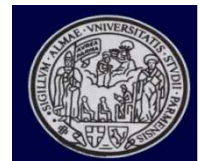
Obstet Gynecol Clin N Am 36 (2009) 153–162

Adolescente e ciclo mestruale
Sergio Bernasconi

Table 1
Bleeding disorders associated with menorrhagia in adolescents

	N	Site	% VWD	% Platelet Dysfxn	% Low Factor	% Low Platelets
Claessens and Cowell, 1981 ⁵⁴	59	Inpatient	5	2	—	—
Smith et al, 1998 ⁵⁵	46	Inpatient	11	—	—	—
Oral et al, 2002 ⁵⁶	25	Inpatient	8	—	—	20
Bevan et al, 2001 ⁵⁷	71	ED, inpatient	8	3	—	13
Philipp et al, 2005 ¹⁸	25	Outpatient	4	44	8	—
Jayasinghe et al, 2005 ⁵⁸	106	Inpatient, outpatient	5	6	—	—
Mikhail et al, 2007 ⁵⁹	61	HTC	36	7	—	—

Abbreviations: ED, Emergency department; HTC, Hemophilia treatment center; Plt Dysfxn, Platelet dysfunction.





Management of heavy menstrual bleeding in adolescents



Nancy Sokkary and Jennifer E. Dietrich

Curr Opin Obstet Gynecol 2012, 24:000–000

KEY POINTS

- Anovulation and blood dyscrasias are the two most common causes of HMB in the adolescent population.
- A thorough evaluation to rule out pregnancy, infection, hormone imbalance and anatomic abnormalities should be considered in adolescents with HMB.

Perdita ematica eccessiva

Common menstrual problems in adolescence

Diana J Fothergill

antifibrinolitico

Antinfiammatorio non steroideo



Table 1 Treatment options for menorrhagia

Treatment	Dose	Comments and contraindications
Tranexamic acid	1 g orally three to four times daily on days of heavy loss	Well tolerated, do not use if history of thromboembolic disease
Mefenamic acid	500 mg orally three times daily during period	Also helps pain. Asthma may worsen, care in renal disease, do not use if bleeding disorder. Gastrointestinal side effects
Medroxyprogesterone acetate	10 mg twice daily from day 16 for 10 days	Missed tablets will lead to bleeding, may put on weight, care in liver disease
Norethisterone	5 mg three times daily for 3 weeks	Missed tablets will lead to bleeding, may put on weight, care in liver disease, androgenic side effects
OCP	Once daily for 3 or 9 weeks	Avoid if liver disease, migraine or raised BMI, increased risk of thromboembolism
DDAVP	150–300 µg intranasally daily during period	On advice of haematologist in Von Willebrand's disease
LNG-IUS	Lasts 5 years	Initial spotting may last several months, GA to insert, caution in liver disease
DMPA	Intra muscular injection monthly until menses cease, then incrementally increase interval to maintenance at 12 weekly	Can cause erratic spotting and weight gain. Avoid in liver disease

Arch Dis Child Educ Pract Ed 2010;**95**:199–203.

Adolescente e ciclo mestri
Sergio Bernasconi

GA, general anaesthesia.



KEY POINTS

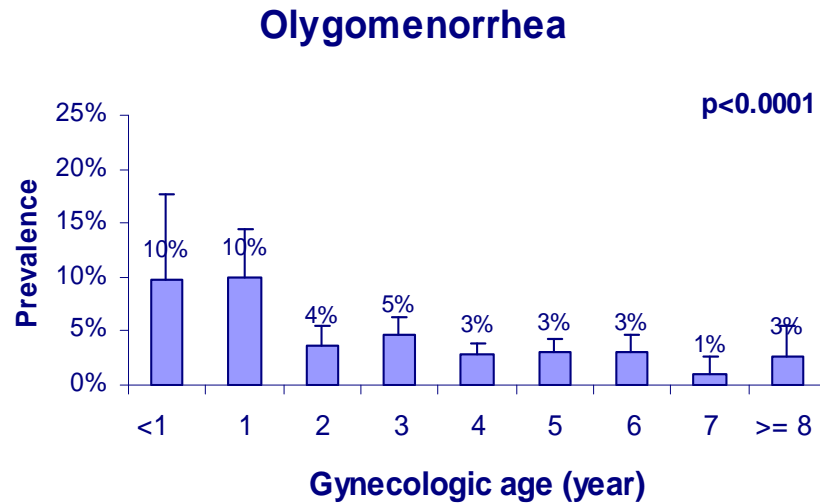
- Anovulation and blood dyscrasias are the two most common causes of HMB in the adolescent population.
- A thorough evaluation to rule out pregnancy, infection, hormone imbalance and anatomic abnormalities should be considered in adolescents with HMB.
- A von Willebrand panel should be considered in any adolescent with HMB.
- Hormonal contraception and antifibrinolytics are safe, effective, and well studied therapies for this population.

2) ALTRE ANOMALIE CICLO MESTRUALE

- 1) **Perdite ematica eccessiva – Heavy Periods**
- 2) **“Infrequent menses”**



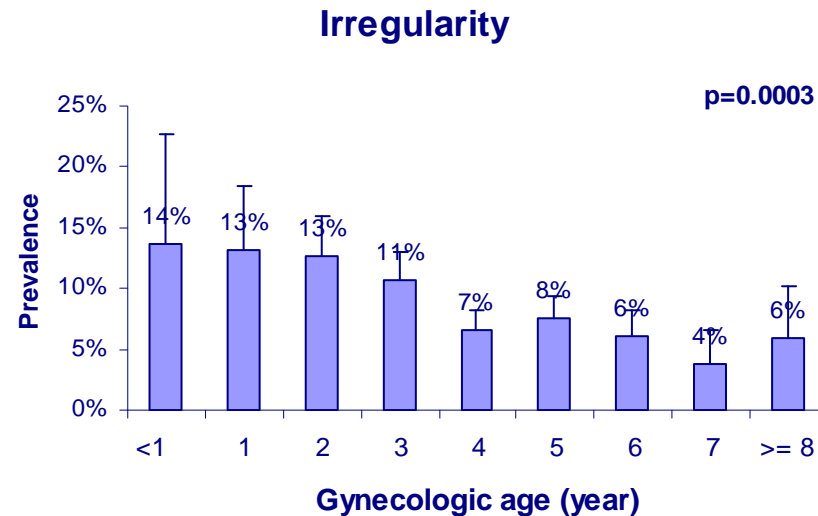
-OLIGOMENORREA: lunghezza del ciclo superiore a 35 giorni (1,2)



1. Petrozza J, Poley K. *Dysfunctional uterine bleeding*. In: Curtis MG, Hopkins MP (Eds). Glass's office gynecology. 5th edn. Baltimore: Williams & Wilkins, 1999; 241-64.
2. Speroff L, Glass RH, Kase NG (eds). *Dysfunctional uterine bleeding*. In: Clinical Gynecologic Endocrinology and Infertility. 5th edn. Baltimore: Williams & Wilkins, 1994; 575-93.

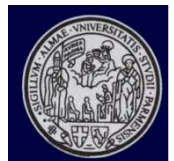


- **IRREGOLARITA'**: cicli mestruali senza lunghezza fissa (3,4,5)



3. Flug D, Largo RH, Prader A. Menstrual patterns in adolescent Swiss girls: a longitudinal study. *Ann Hum Biol.* 1984; 11(6):495–508.

4. ACOG Committee on Adolescent Health Care. Menstruation in girls and adolescents using the menstrual cycle as a vital sign. *Obstet Gynecol.* 2006; 108(5):1323-1328.



Infrequent menses

Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign

American Academy of Pediatrics, Committee on Adolescence, American College of Obstetricians and Gynecologists and Committee on Adolescent Health Care
Pediatrics 2006;118:2245
DOI: 10.1542/peds.2006-2481

TABLE 2 Causes of Menstrual Irregularity

Pregnancy
Endocrine causes
Poorly controlled diabetes mellitus
Polycystic ovary syndrome (PCOS)
Cushing disease
Thyroid dysfunction
Premature ovarian failure
Late-onset congenital adrenal hyperplasia
Acquired conditions
Stress-related hypothalamic dysfunction
Medications
Exercise-induced amenorrhea
Eating disorders (both anorexia and bulimia)
Tumors
Ovarian tumors
Adrenal tumors
Prolactinomas



Infrequent menses

Limiti per una valutazione

1) dopo il secondo anno ginecologico

2) Amenorrea per 3 mesi o intervallo superiore al 95° percentile (65 gg anche nel primo anno ginecologico).



Infrequent menses

Menstruation in Girls and Adolescents: Using the Menstrual Cycle as a Vital Sign

American Academy of Pediatrics, Committee on Adolescence, American College of Obstetricians and Gynecologists and Committee on Adolescent Health Care
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Ovarian tumors
Adrenal tumors
Prolactinomas



The diagnosis of polycystic ovary syndrome in adolescents

Enrico Carmina, MD; Sharon E. Oberfield, MD; Rogerio A. Lobo, MD

Am J Obstet Gynecol 2010

TABLE

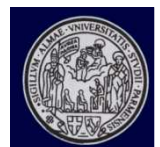
Diagnostic criteria for polycystic ovary syndrome in adolescents

Criterion	Hyperandrogenism ^a	Chronic anovulation ^b	Polycystic ovaries ^c
Diagnosis of PCOS	+	+	+
Diagnosis of PCOS probable but not confirmed	+	+	–
Diagnosis of PCOS not possible during adolescence	+	–	+
Diagnosis of PCOS not possible during adolescence	–	+	+
Not PCOS	+	–	–
Not PCOS	–	+	–
Not PCOS	–	–	+

PCOS, polycystic ovary syndrome.

^a Hyperandrogenemia is primary criterion—acne and alopecia are not considered as evidence for hyperandrogenism—hirsutism may be considered sign of hyperandrogenism only when it has been documented to be progressive; ^b Oligomenorrhea (or documented anovulation) has to be present for at least 2 years; ^c Diagnosis of polycystic ovaries by abdominal ultrasound has to include increased ovarian size (>10 cm³).

Carmina. The diagnosis of PCOS in adolescents. *Am J Obstet Gynecol* 2010.



Polycystic Ovary Syndrome in Adolescents

R.F. O'Brien, MD and S.J. Emans, MD

Division of Adolescent/Young Adult Medicine Children's Hospital Boston, and Harvard Medical School, Boston, Massachusetts, USA

J Pediatr Adolesc Gynecol 2008

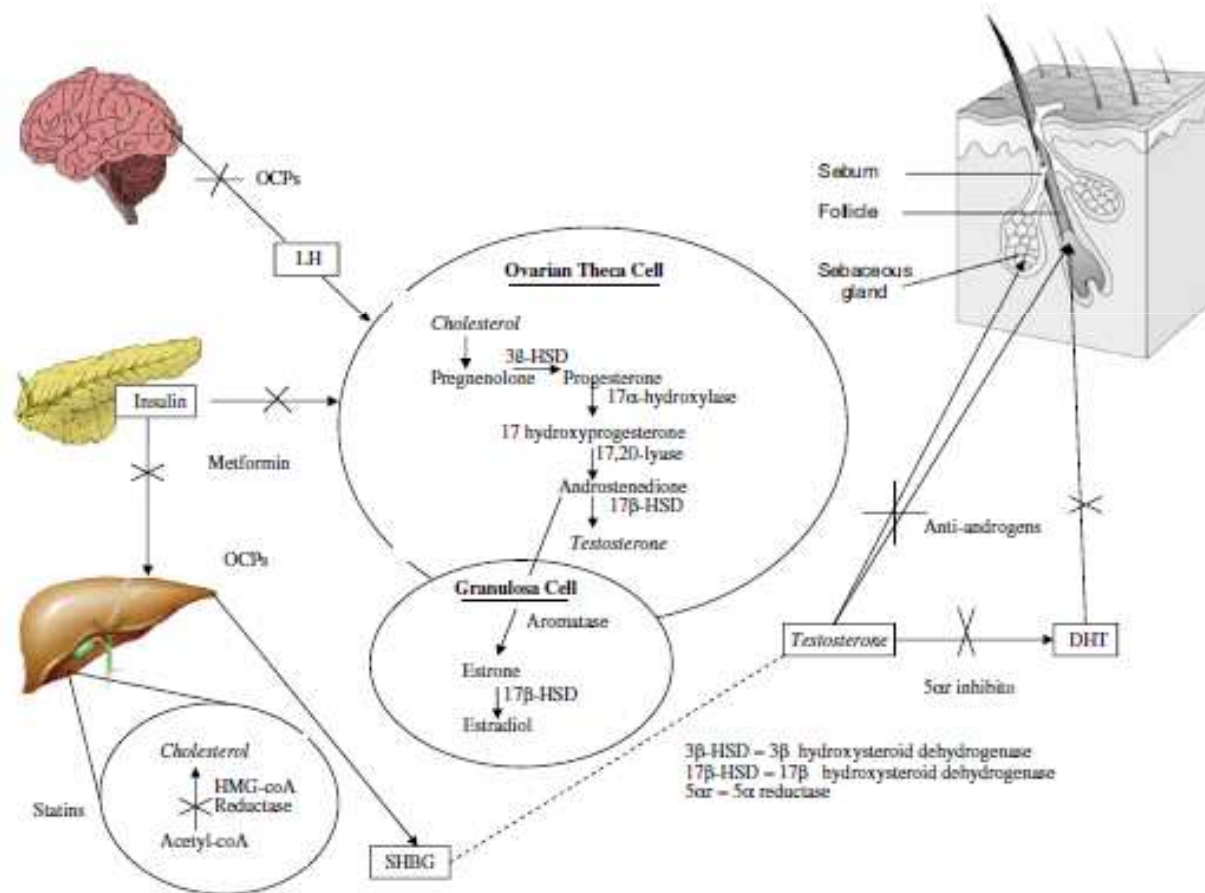


Fig. 1. Schematic of pathophysiology of polycystic ovary syndrome and mechanism of therapeutic drugs. DHT=dihydrotestosterone; LH=Leutenizing hormone; SHBG=sex hormone binding globulin; OCPs=oral contraceptive pills. Adapted from Hassan A, Gordon. Polycystic ovary syndrome in adolescence. Curr Opin Pediatr 2007; 19(4): 389 with permission.



Beth W. Rackow

Curr Opin Obstet Gynecol 2012, 24:000–000

KEY POINTS

- Adolescents with menstrual irregularity, hirsutism and obesity should be evaluated for PCOS.
- The criteria for diagnosing PCOS in adolescence are unclear; the use of all three Rotterdam criteria is recommended to limit inappropriate diagnosis.
- Adolescent PCOS is associated with insulin resistance, hyperinsulinemia, obesity, metabolic syndrome and sleep disorders.
- Lifestyle modification is the most important treatment for PCOS and may be most effective when initiated in young adolescents.
- Further research on metformin therapy in adolescents is necessary, but this intervention may be effective for adolescents with a range of PCOS phenotypes.

2) ALTRE ANOMALIE CICLO MESTRUALE

- 1) **Perdite ematica eccessiva – Heavy Periods**
- 2) **“Infrequent menses”**
- 3) **Dismenorrea**



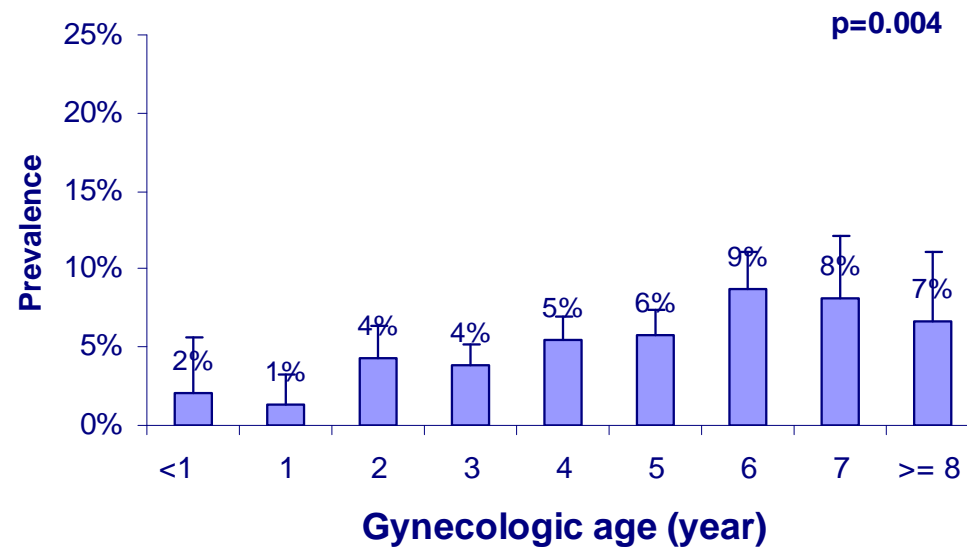
- **DOLORE ADDOMINALE:** il dolore addominale è stato categorizzato su quattro livelli (1,2) .
 - dolore addominale assente/lieve
 - dolore addominale moderato/severo senza uso di farmaci e/o limitazione delle attività
 - dolore addominale moderato/severo con uso di farmaci e/o limitazione delle attività durante le perdite ematiche
 - dolore addominale moderato/severo con uso di farmaci e/o limitazione delle attività prima delle perdite ematiche (**DISMENORREA**)

1. World Health Organization: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision. Geneva, Switzerland: World Health Organization; 1992.

2. World Health Organization: Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, Ninth Revision. Geneva, Switzerland: World Health Organization; 1977.



Dysmenorrhea



KEY POINTS

- Adolescents with dysmenorrhea severe enough to interfere with activities of daily living require evaluation for endometriosis.
- Endometriosis in adolescents has an atypical appearance at laparoscopy.
- More research is required to determine whether postoperative medical treatment should be routinely prescribed or that intervening in the adolescent population prevents disease progression.



The menstrual disorder of teenagers (MDOT) study: determining typical menstrual patterns and menstrual disturbance in a large population-based study of Australian teenagers

MA Parker,^a AE Sneddon,^a P Arbon^b

DOI: 10.1111/j.1471-0528.2009.02407.x
www.bjog.org

‘Typical’ menstruation (approximately 75%)

‘Typical’ menstruation may be characterised by mild to moderate pain managed with analgesia, low interference with life activities, minimal school absence and manageable menstrual symptoms. Minimal treatment is required.

Menstrual disturbance (approximately 25%)

Menstrual disturbance may be characterised by: moderate–severe pain associated with menses; multiple menstrual symptoms; school absence; and high interference with life activities.

Treatment could involve optimizing first-line conservative measures, including the effective use of simple analgesics, such as NSAIDs with or without paracetamol in combination, and with or without hormonal medication. Lifestyle factors may be modified, such as diet and optimising bowel function, exercise and sleep patterns. Recording



The menstrual disorder of teenagers (MDOT) study: determining typical menstrual patterns and menstrual disturbance in a large population-based study of Australian teenagers

MA Parker,^a AE Sneddon,^a P Arbon^b

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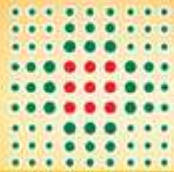
Further investigation is required if symptoms are suggestive of endometriosis, that is, severe pain that may include bowel or bladder, dyspareunia, poor response to simple analgesia and/or hormonal medication, and significant interference with life activities. Adolescents with endometriosis may also present with acyclical pain.^{12,13}

Although uncommon, endometriosis has been found in young girls investigated for severe pelvic pain prior to menarche, but post thelarche.^{14,28}

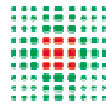




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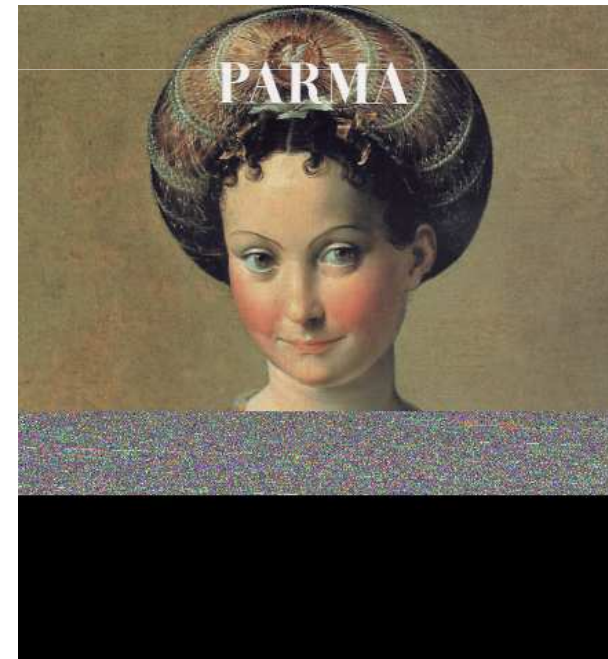
SERVIZIO SANITARIO REGIONALE
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Azienda Ospedaliera di Reggio Emilia
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia
Istituto di Ricovero e Cura a Carattere Scientifico

Ambulatorio di ginecologia adolescenziale

- G.B La Sala , Dr. G. Tridenti**
- S. Bernasconi, Dr.ssa M. Street**

GRAZIE PER L'ATTENZIONE





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TABLE 1 Normal Menstrual Cycles in Young Females

Menarche (median age): 12.43 years

Mean cycle interval: 32.2 days in first gynecologic year

Menstrual cycle interval: typically 21–45 days **21-34 days**

Menstrual flow length: ≤ 7 days

Menstrual product use: 3–6 pads/tampons per day **35 ml di media (5-80 ml)**



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