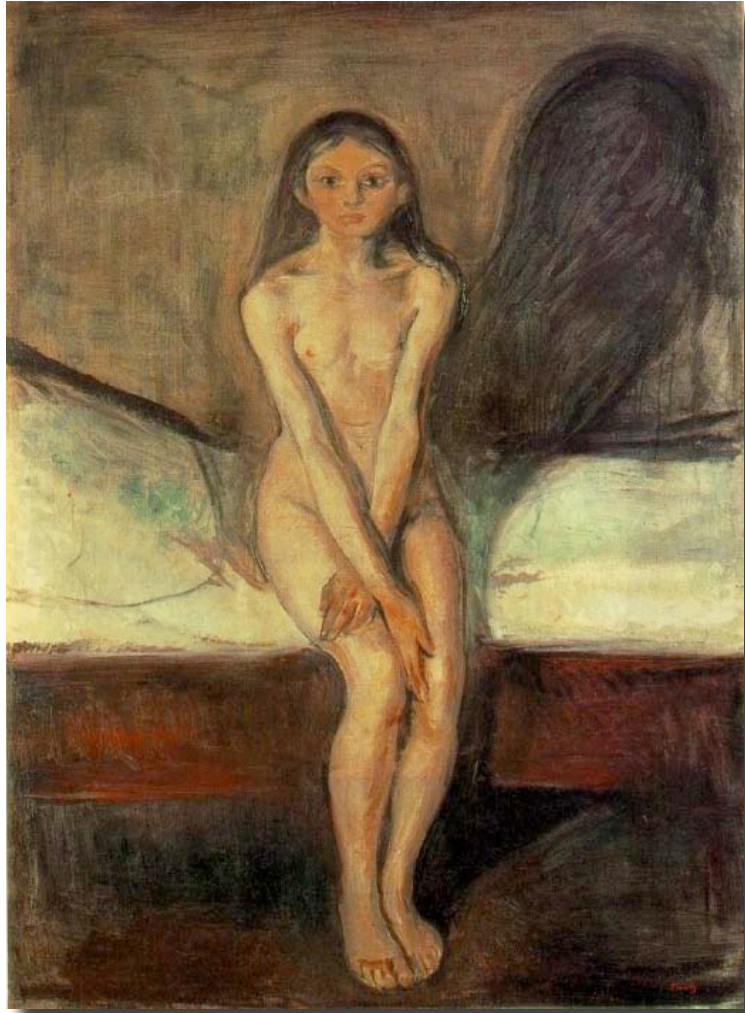
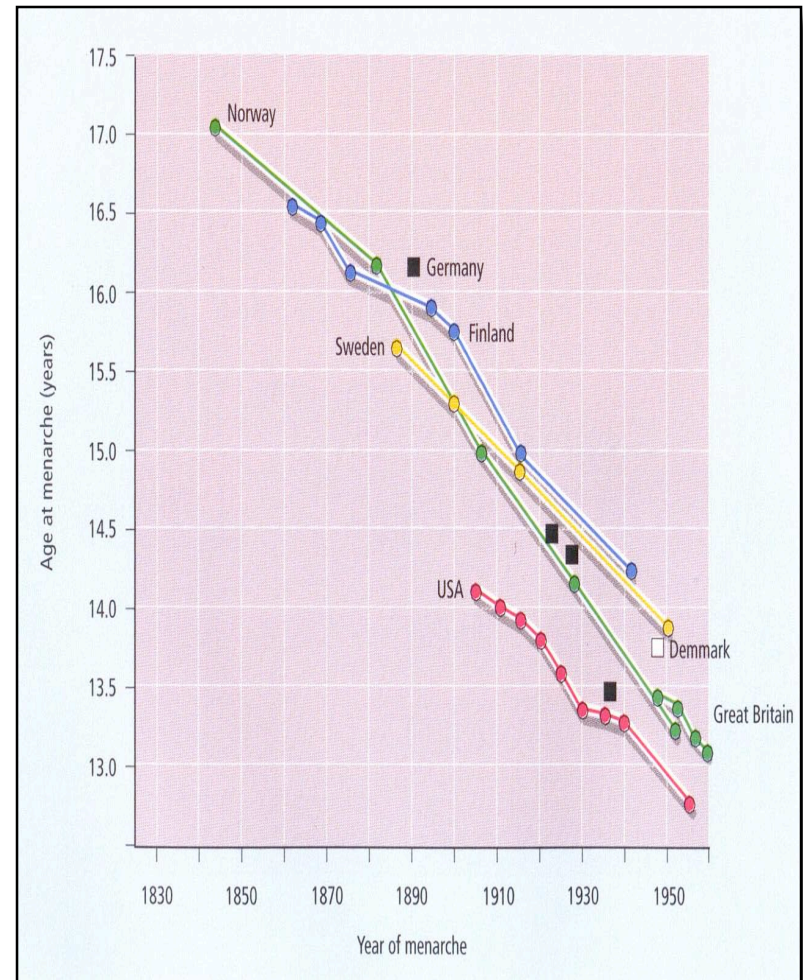


Puberty



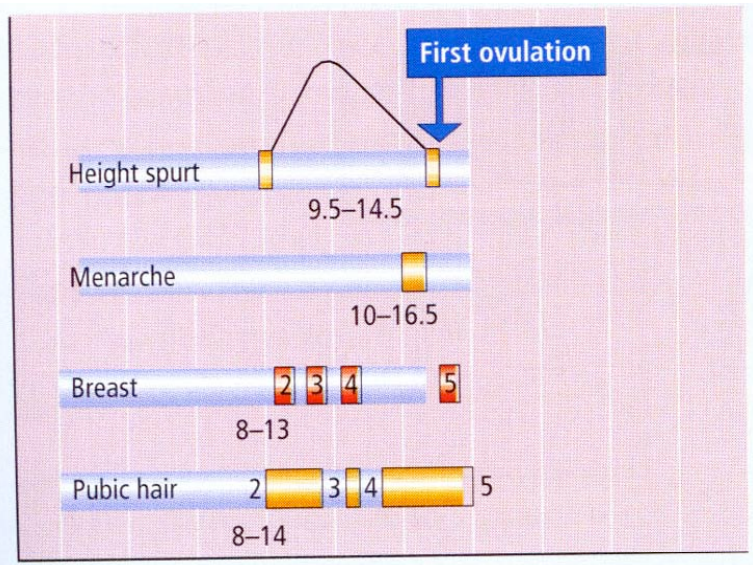
'Puberty'
1894
Munch



Puberty - sexual maturation

- transition from sexually immature child to sexually mature adult
- puberty from Latin 'pubes' meaning hair
- varies with age, weight
- in humans, begins earlier in females than males
- in western Europe and USA, clear trend toward earlier puberty in girls and boys

Females - human

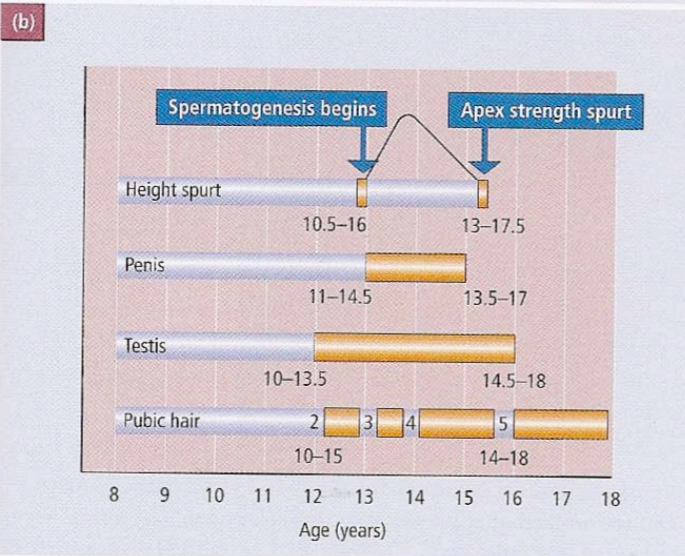
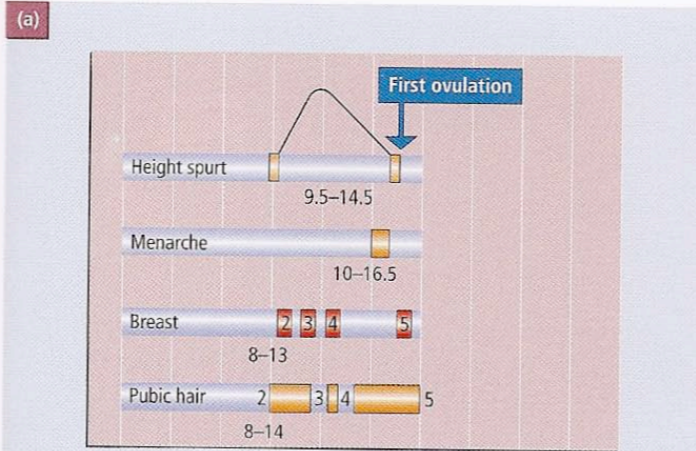


- 1st menstruation (menarche)
12 years (7 - 19 yr)
- 1st ovulation
 - then or as much as 2 yrs latter
 - 1st menarche can be anovulatory
- menarche and ovulation are steps in a series of changes
- development of 2nd sex characteristics

Secondary sex characteristics- Female

- uterus, oviducts and vagina grow and mature
- pelvis grows
- pubic and axillary hair
- breast development
- sweat and sebaceous glands increase activity
- decrease in voice
- increase in metabolic rate
- fat deposition especially in hips and breasts
- skeletal growth (usually ends about 16 years of age)

Females

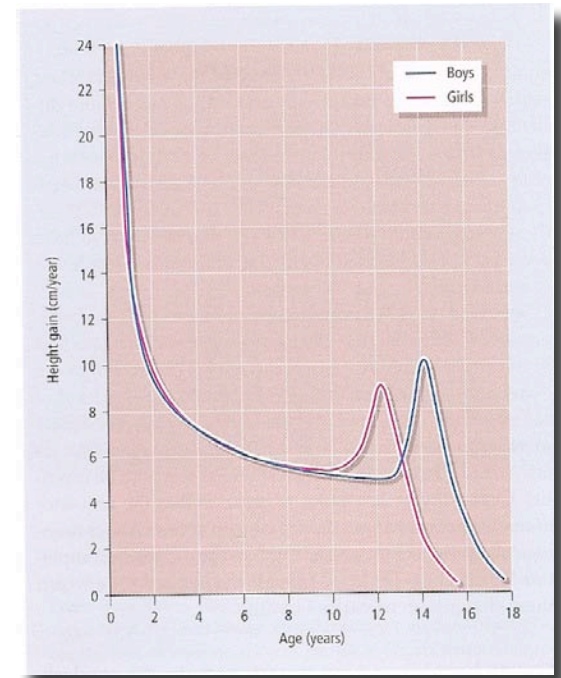


Males

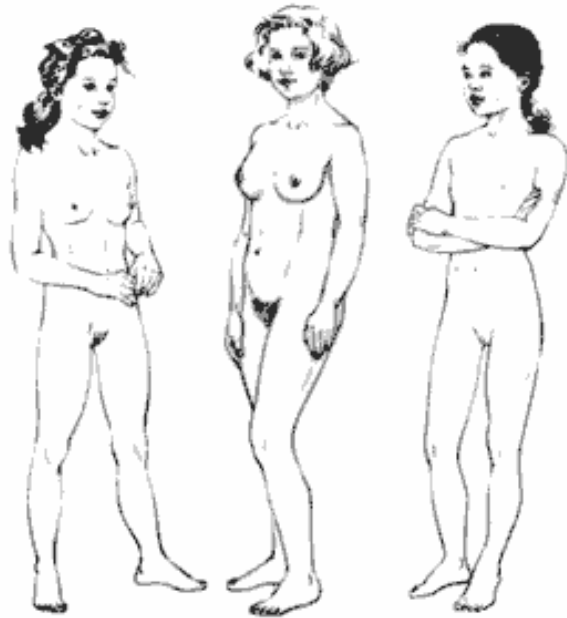
Fig. 7.6 Summary of the sequence of events during puberty in (a) girls and (b) boys. The figures below each symbol represent the range of ages within which each event may begin and end. The figures within each symbol refer to the stages illustrated in Figs 7.2–7.4.

Males - human /1

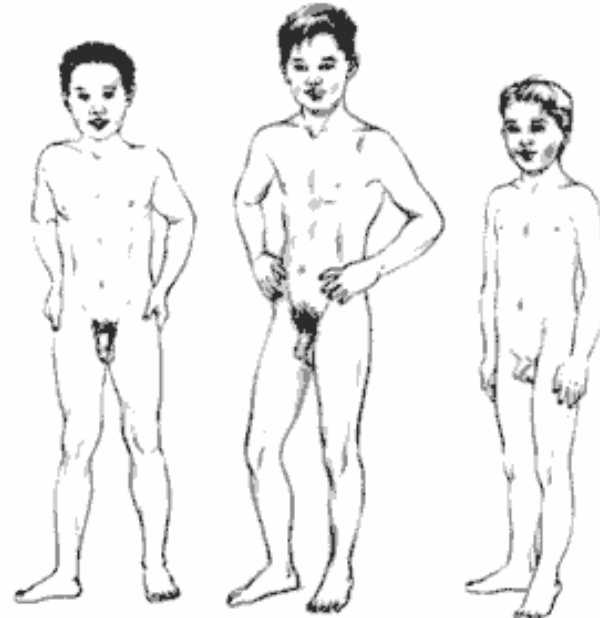
- growth spurt and fat deposition
 - 10-13 yr girls taller & more developed than same age boys
 - later stimulation of growth due to increasing testosterone
- testes and secondary sex characteristics
 - pubic hair and axilla, chest, facial and extremities
 - sweat glands become active in scrotum, face, back and chest
 - areola darkens and widens
 - vocal cords double in length = dramatic deepening of voice



Great Variation Among Individuals



All three of these young women will be 13 in three months - their bodies are developing at different rates.

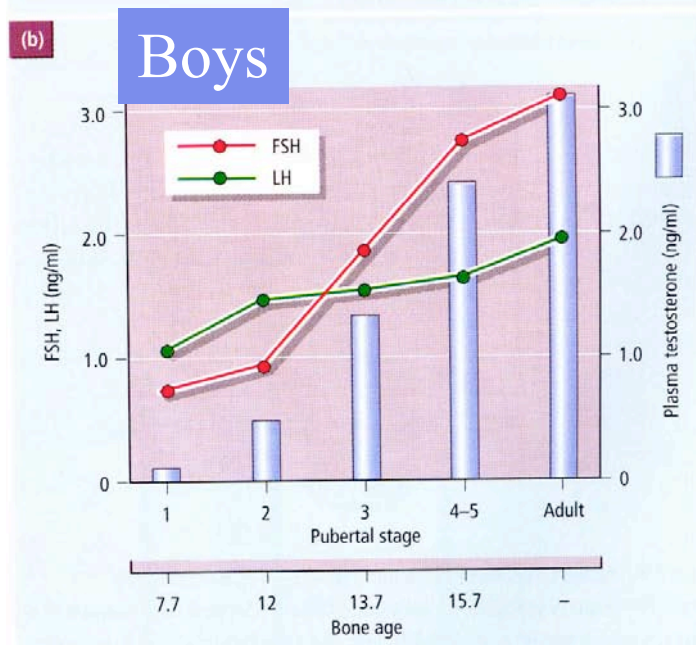
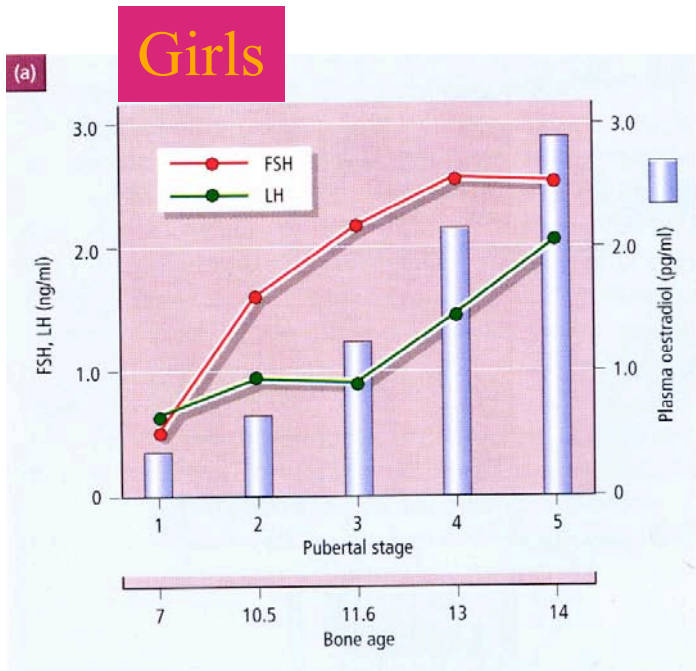


All three of these young men will be 13 in three months - their bodies are developing at different rates.

Males - human /2

- scrotum, penis growth
 - spontaneous erections increase in frequency
 - occur in infants and fetuses
- nocturnal emissions/ejaculation
 - Normal
 - do not indicate abnormal behavior or physiology
 - both spontaneous erections and nocturnal emissions decrease after puberty

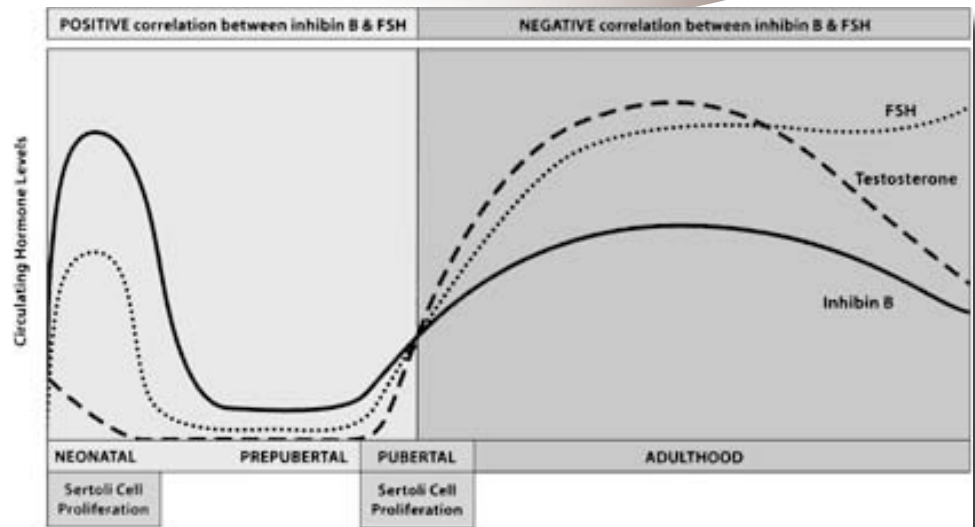
FSH/LH



- Children
 - FSH & LH not elevated and no gonadal stimulation until puberty

Neonatal Gn and Androgen

- however, FSH & LH
 - can be at or near adult levels soon after birth and for first 2 years of life
 - neonatal (0-5 months) boys have elevated T levels responsible for Leydig & Sertoli cell mitosis and future sperm count



Hormones - Birth to Puberty

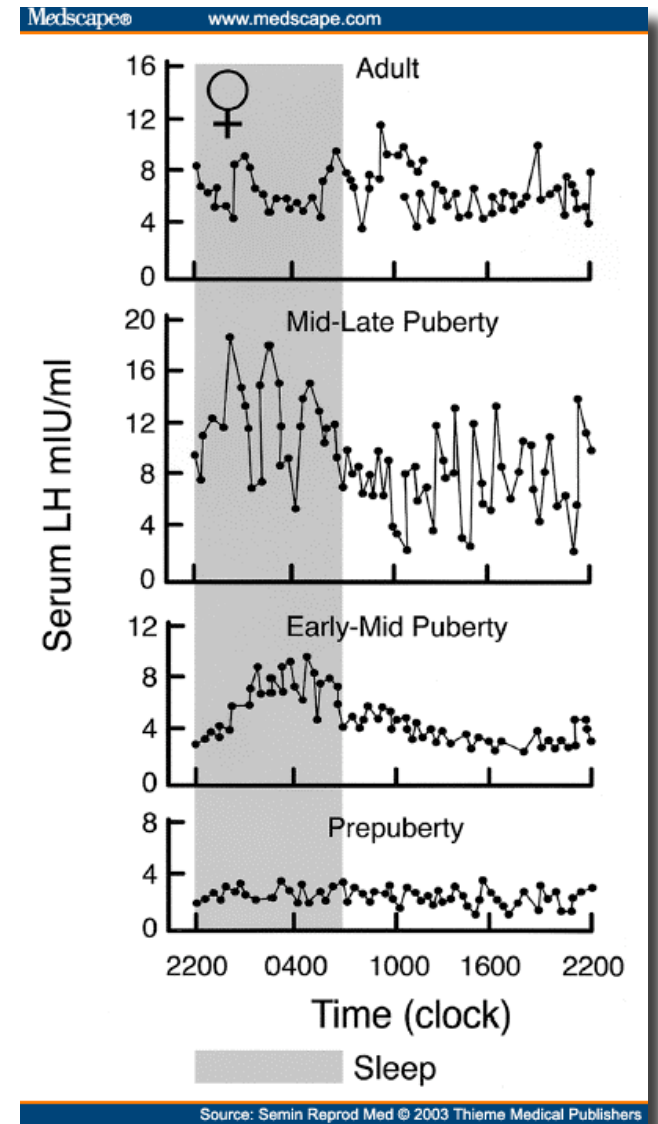
Early Puberty

- 9-12 yrs =
 - FSH then LH rise
 - occurs in females 1 - 2 yrs earlier than males
 - Prolactin rises in females but not males
 - possibly due to rising estradiol

Hormones - Birth to Puberty

FSH & LH

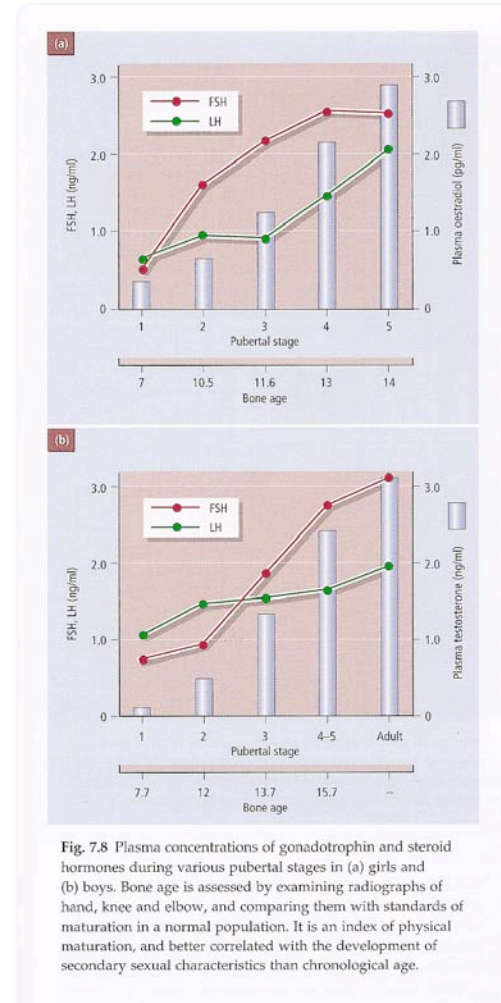
- During puberty fluctuation in LH and FSH great
 - role unknown
 - dramatic rise at night
 - daily cycle in not seen in adults or children
 - from early to mid puberty dramatic rise in magnitude and frequency of LH surges
 - sleep augmented LH secretion
 - in late puberty
 - daytime surges also increase, but still less than nighttime
 - continues until adult-noncyclic-levels achieved



Hormones - Birth to Puberty

Testosterone /1

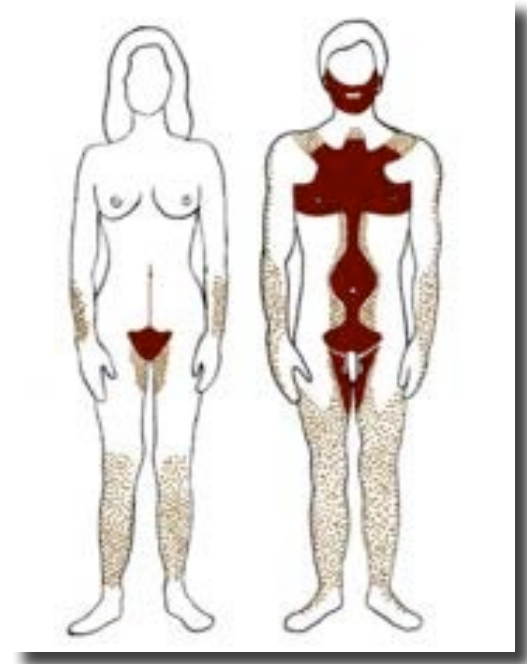
- Testosterone rises in boys with increasing LH
 - elevated at night
 - sleep augmented LH secretion
 - during mid puberty, T can also be elevated during day
 - females show similar increases but not the same elevation as in males



Hormones - Birth to Puberty

Testosterone /2

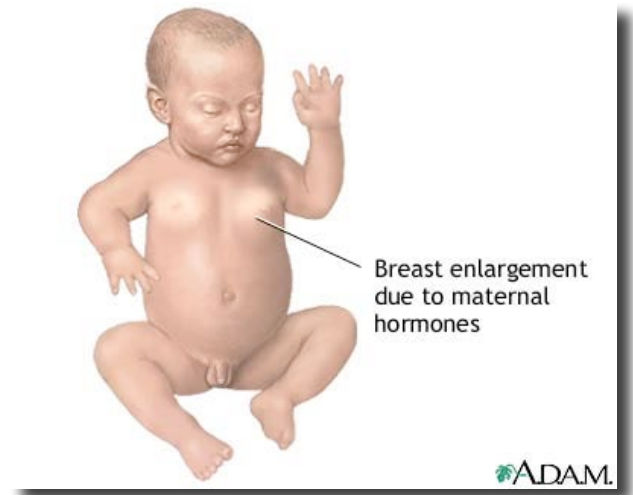
- Roles in males and females:
 - pubic and axillary hair growth
 - vocal cord growth
 - development of sebaceous glands
 - growth of long bones
 - protein anabolism - muscle growth
 - sex drive



Hormones - Birth to Puberty

Estrogens /1

- estrogens are extremely high in both males and females at birth
 - ~5000 pg/ml
 - Placental/maternal in origin
 - infants can show breast budding and 'witches milk'
 - levels drop soon after birth until puberty



Hormones - Birth to Puberty

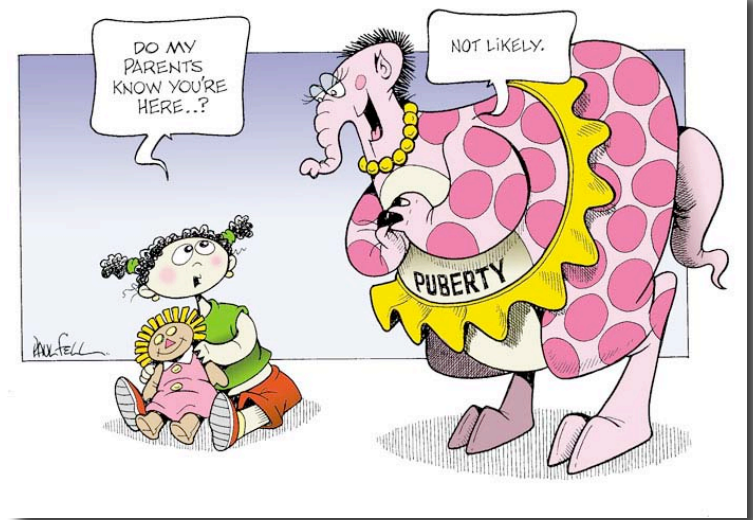
Estrogens /2

- in females
 - estrogens rise thru puberty until adult levels, follows LH secretion
- in boys
 - estrone higher than estradiol
 - both lower than in girls, but rise with puberty
- in males
 - half of estradiol from extraglandular aromatization of testosterone
 - a quarter or less from testicular synthesis

Hormones - Birth to Puberty

Estrogens /3

- Roles in males and females:
 - bony pelvic growth
 - initial mammary gland growth
 - gynecomastia in some boys - lost in 1-2 yrs
 - onset of fat deposition
 - long bone closure
- In females
 - growth of external genitalia
 - growth oviduct and uterus
 - continued growth of mammary glands



Hormones - Birth to Puberty

Adrenal Hormones

- earliest detectable changes
 - preceding gonadotropins and sex steroids
- progressive increase in adrenal androgens
 - dehydroepiandrosterone (DHEA)
 - DHEA sulfate
- glucocorticoids and mineralocorticoids do not increase

Hormones - Birth to Puberty

ADRENARCHE

- Increasing adrenal steroids = ADRENARCHE
 - starts at about age 8
 - continues until 13 - 15 yr age
- DHEA/DHEA sulfate
 - orders of magnitude higher in plasma concentration than sex steroids
 - role unknown but they do promote pubic and axillary hair
- growth spurt is not dependent on these androgens
- not involved with timing puberty

Puberty is...

- not a gonadal-pituitary phenomenon but a CNS maturation event

Mechanisms Underlying Puberty

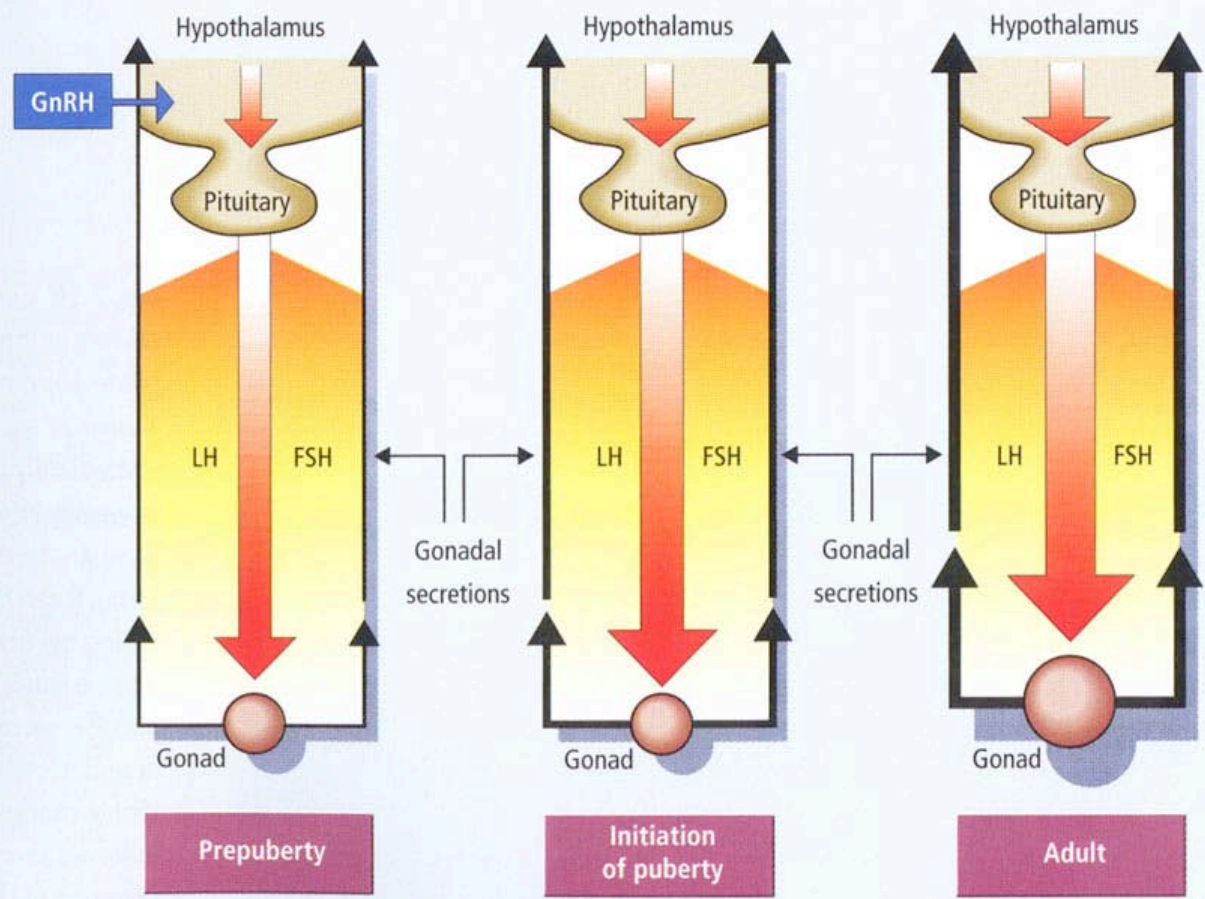
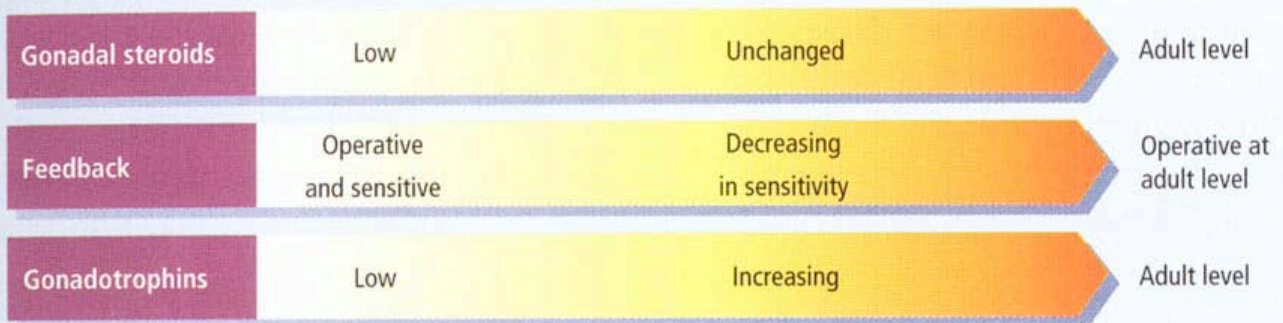
- Two hypotheses that are not mutually exclusive
 - gonadostat hypothesis
 - hypothalamic maturation

Gonadostat Hypothesis /1

- negative feedback of FSH and LH on the pituitary and hypothalamus is very sensitive [low threshold]
- very sensitive negative feedback = low concentrations of steroids
- at puberty, set point is increased, becoming less sensitive to steroids - thus, steroids in the plasma rise

Gonadostat Hypothesis /2

- pituitary response to steroids does change with puberty
- however, changing steroids do not drive change
- positive feedback established late in puberty
 - >50% of the cycles in early post-puberty are anovulatory
 - decreases to one fifth after 5 years



Hypothalamic Maturation /1

- currently accepted hypothesis
 - maturation of the CNS and increased output of GnRH drives puberty
- requires only changes in the GnRH neurosecretory neurons
 - no changes in negative and positive feedback required

Puberty - Genes

- Puberty is controlled by genetic and environmental factors
- 17 different single-gene mutations
 - Mutation leads to delayed or absent puberty in humans
 - Several of these genes
 - involved in the development of the olfactory nervous system,
 - result in anosmia/hyposmia and hypogonadotropic hypogonadism
 - otherwise known as Kallmann syndrome.
 - Development of the gonadotropin-releasing hormone (GnRH) neurons
 - responsible for regulating fertility
 - intricately associated with development of the olfactory system
- single-gene mutations are presently estimated to account for approximately 30% of individuals with disorders of puberty

Hypothalamic Maturation /2

- pulsatile LH release at onset of puberty
 - even in gonadectomized monkeys
- in male rhesus gonadectomized at birth
 - pulsatile LH release
 - levels normal for first 10 weeks of life (as in controls)
 - no release for 2.5 yrs - juvenile hiatus
 - pulsatile secretions begin on time and transition to adult levels normally in absence of testes

Hypothalamic Maturation /3

- thus, puberty is ability to release pulses of GnRH
- adult levels of steroids do not turn on GnRH pulse system
- clinical studies confirms that humans are similar
 - first 6 months associated with fluctuating, often high plasma FSH, LH, T (boys), E (girls)
 - by 1-2 yr age, system exhibits juvenile hiatus
 - Turner's syndrome girls - agonadal
 - start puberty at correct time

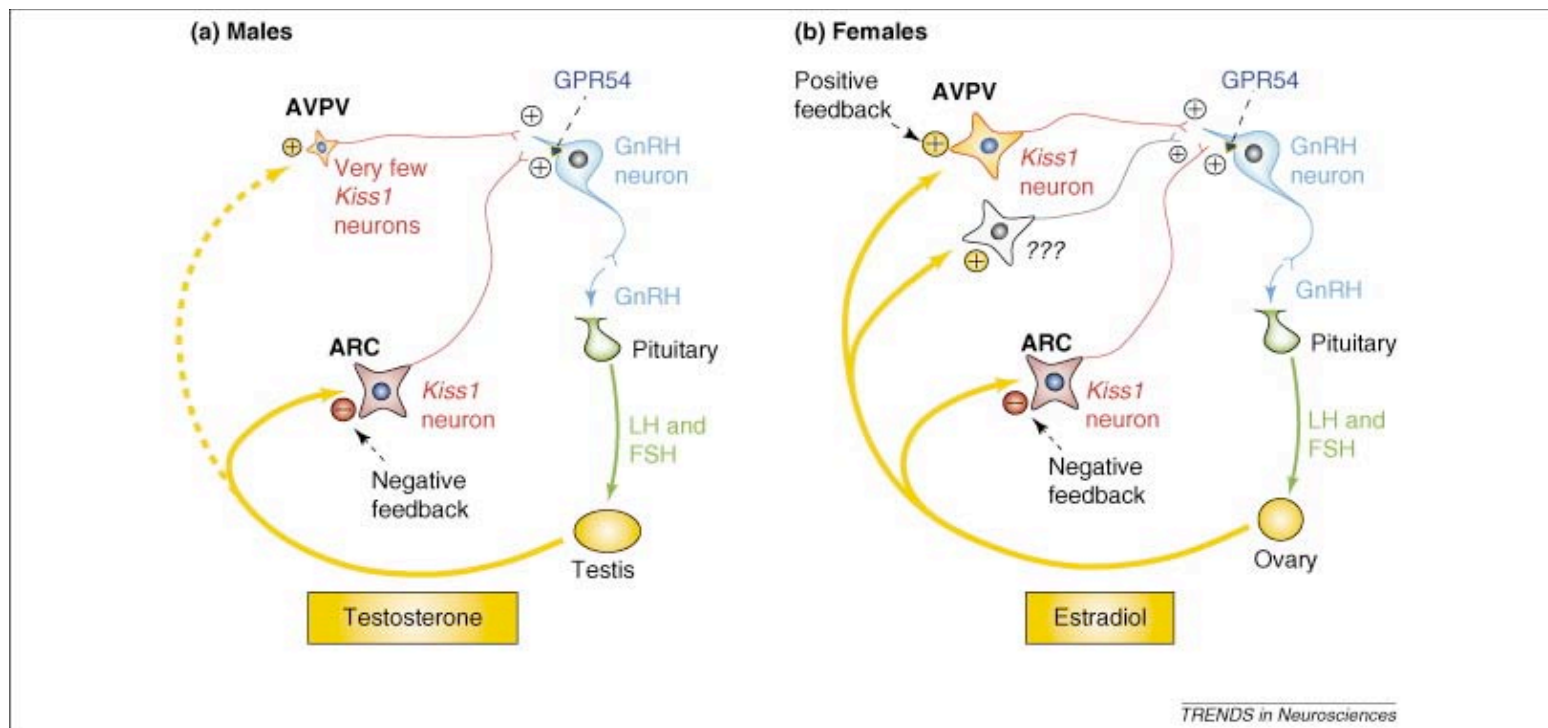


Puberty - Kisspeptin

- product of the gene *Kiss1*
- G-protein coupled receptor ligand for *GPR54*
- *Kiss1* was originally identified as a human metastasis suppressor
- *Kiss-1* mRNA and steroid receptors
 - Are coexpressed in *KiSS-1* neurons
 - are direct target for the action of sex steroids
 - *KiSS-1* mRNA and/or *GPR54* mRNA expression increase with puberty
 - electrophysiologic response of *GnRH* neurons to kisspeptins increase over the course of puberty

Puberty - Kisspeptin

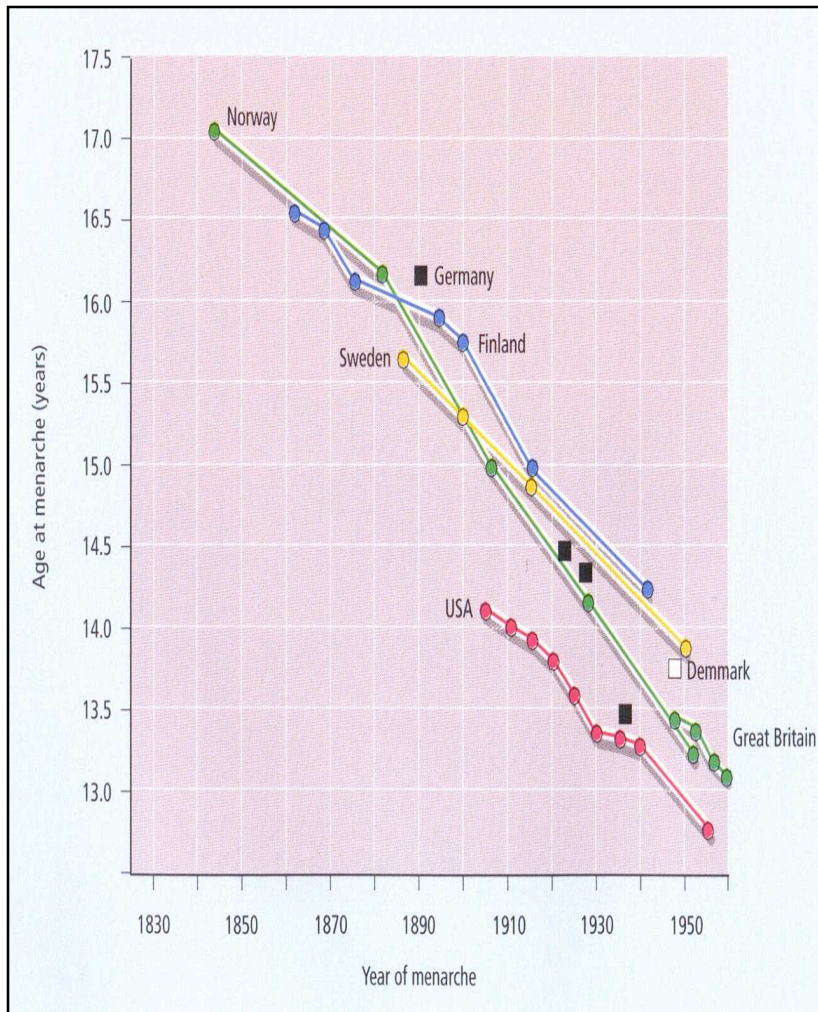
- Kisspeptin-GPR54 signalling system
 - affect puberty by directly or indirectly modulating the functioning of the GnRH neurons and pituitary gonadotrophs



Precocious Puberty

- precocious puberty
 - can occur as young as 2 yr age
 - pituitary and gonads can function in adult manner
 - usually CNS tumor
 - But, has become more common
 - not due to tumor
 - Environmental factors?

Timing of Puberty



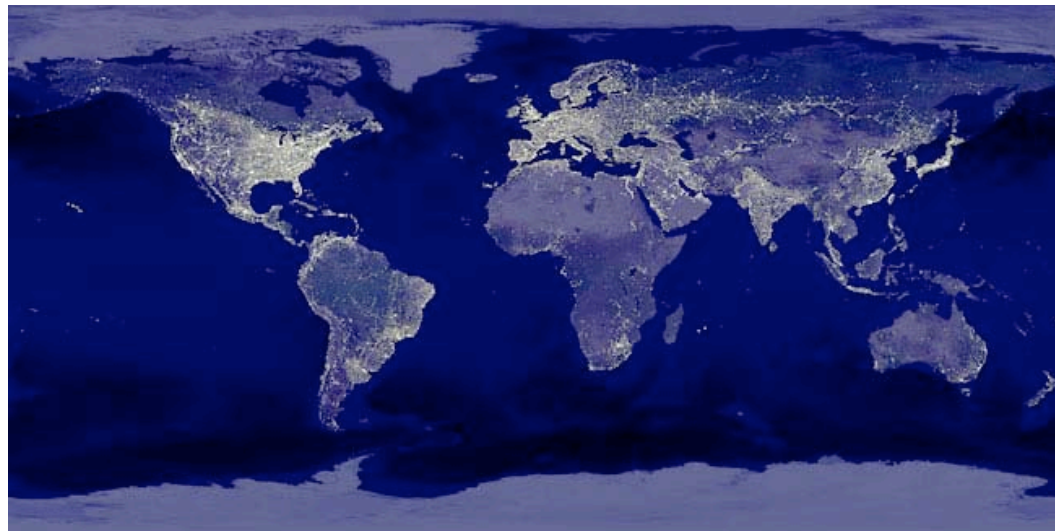
- Decreasing age in developed countries
- Variation does occur in population
- Various factors controlling puberty onset

Environment & Puberty

- Environmental Factors
 - health care
 - personal health improvements
 - living conditions
 - socioeconomic standards
- major factors:
 - photoperiod
 - nutrition

Photoperiod & Puberty

- **Photoperiod** -
 - electricity = 'long days' or a constant summer
 - light in domestic setting probably not intense enough to influence photosensitive neural mechanism in GnRH pathways
 - little data to support this hypothesis in humans or primates



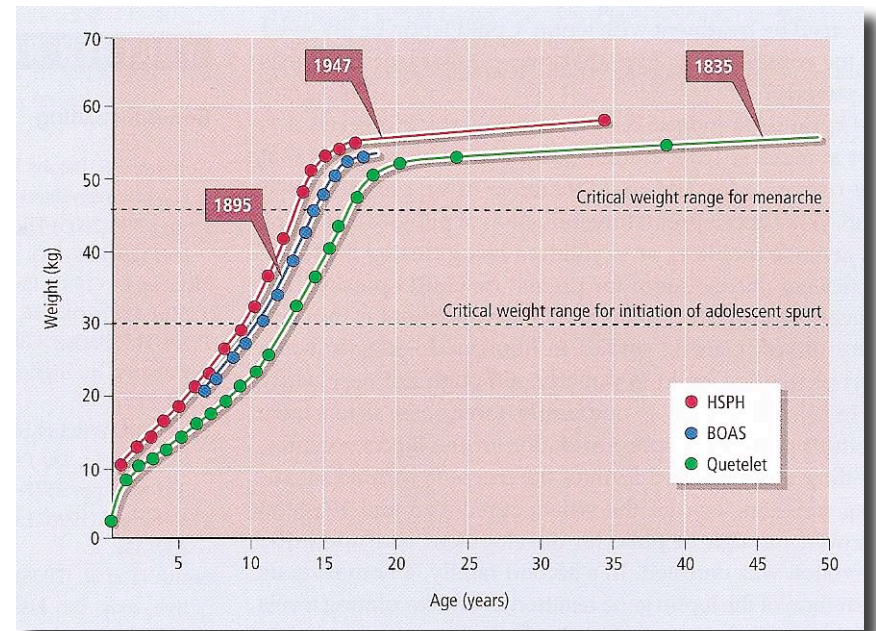
Nutrition & Puberty

- Nutrition has changed dramatically in last century
- nomadic peoples - Lapps/Saami
 - no changes in onset of menarche from 1870-1930
 - changes occur in villages
- diet influences menarche / normal menstruation
 - women athletes with low fat/muscle ratio stop menstruation
 - young girls involved in similar activities with low fat/hi protein diets show delayed menarche or irregular menstrual cycles



Body Mass & Puberty

- onset of menarche is at 47 kg and has remained apparently unchanged
- critical weight must be attained before activation of hypothalamo-pituitary-gonadal axis
- suggests 55 kg for boys



Body Mass & Puberty /2

- **problem**
 - based on total weight
 - (lean body wt + fat, + water)
 - can this be true?
 - other factor(s) involved?
 - most of these studies are retrospective
 - very difficult to predict puberty by body weight
 - menarche /other obvious events occur 'late'
 - like the gonadostat hypothesis, this may be a consequence of puberty not its trigger

Health and Early Puberty

1900's

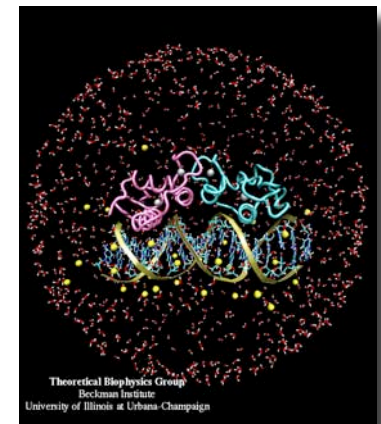
16 yr - 45 yr = 29 years reproductive lifetime

2000 $29 \text{ yr} \times 12 \text{ cycles/yr} = 348$

12 yr - 50 yr = 38 years reproductive lifetime

$38 \text{ yr} \times 12 \text{ cycles/yr} = 456$

Difference = +108 cycles



Health and Early Puberty

348 cycles - (6 pregnancies + 5 lactations)

- 348 - (6 X 9 mo + 5 X 12 mo)

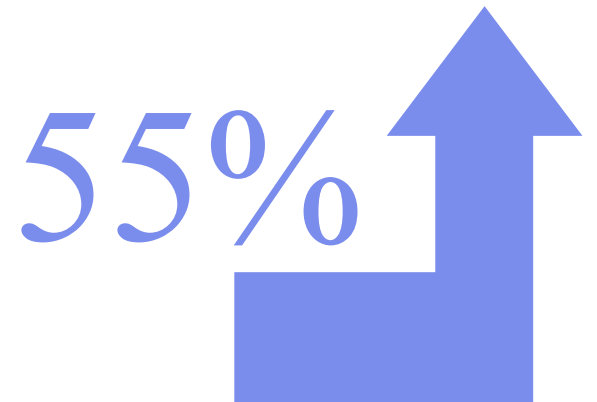
$$348 - (54 + 60) = 234$$

456 cycles - (2 pregnancies + 2 lactations)

- 456 - (2 X 9 mo + 2 X 6 mo)

$$456 - (18 + 12) = 426$$

Difference = + 192 cycles



Estrogens and Disease

- Endometriosis
- Fibroids/Polyps
- Breast Cancer
- Endometrial Cancer



Puberty

Comparative Studies /1

- **Comparative Studies**
 - many studies examine puberty in various domestic species
 - similar observations of elevated LH/FSH
 - support for CNS hypothesis
 - few studies examining puberty in wild species

Puberty

Comparative Studies /2

- alligator - male juveniles show clear change in plasma T at 75 cm TL
 - sexual maturity at 1 meter SVL
- seasonal variation in plasma T also seen
 - not all males of this size exhibit elevated T
 - not uncommon for individuals of a given population to begin puberty at differing ages or body sizes

Puberty

Comparative Studies /3

- Few studies have examined seasonal variation in plasma sex steroids in wild non-mammalian juvenile animals.
- The majority of species examined
 - (e.g., rodents, salmon, chickens, sheep)
 - relatively short lives
 - thus, puberty occurs within a few days or months and seldom stretches over a year