

# **PHYSIOLOGY OF REPRODUCTION**

*Life is a dynamic system with focused behavior, with*

***autoreproduction***, *characterized by flow of substrates,*

*energy and information.*

## Reproduction in mammals (humans)

- 1) Sexual reproduction
- 2) Selection of partners
- 3) Internal fertilization
- 4) Viviparity
- 5) Eggs, resp. embryos – smaller, less, slow development, placenta
- 6) Low number of offspring, intensive parental care

Pregnancy (days)	
Mouse	20
Rat	23
Rabbit	31
Dog	63
Cat	65
Lion	107
Pig	114
Sheep	149
<b>Human</b>	<b>260 - 275</b>
Cow	285
Rorqual	360
Elephant (Indian)	609

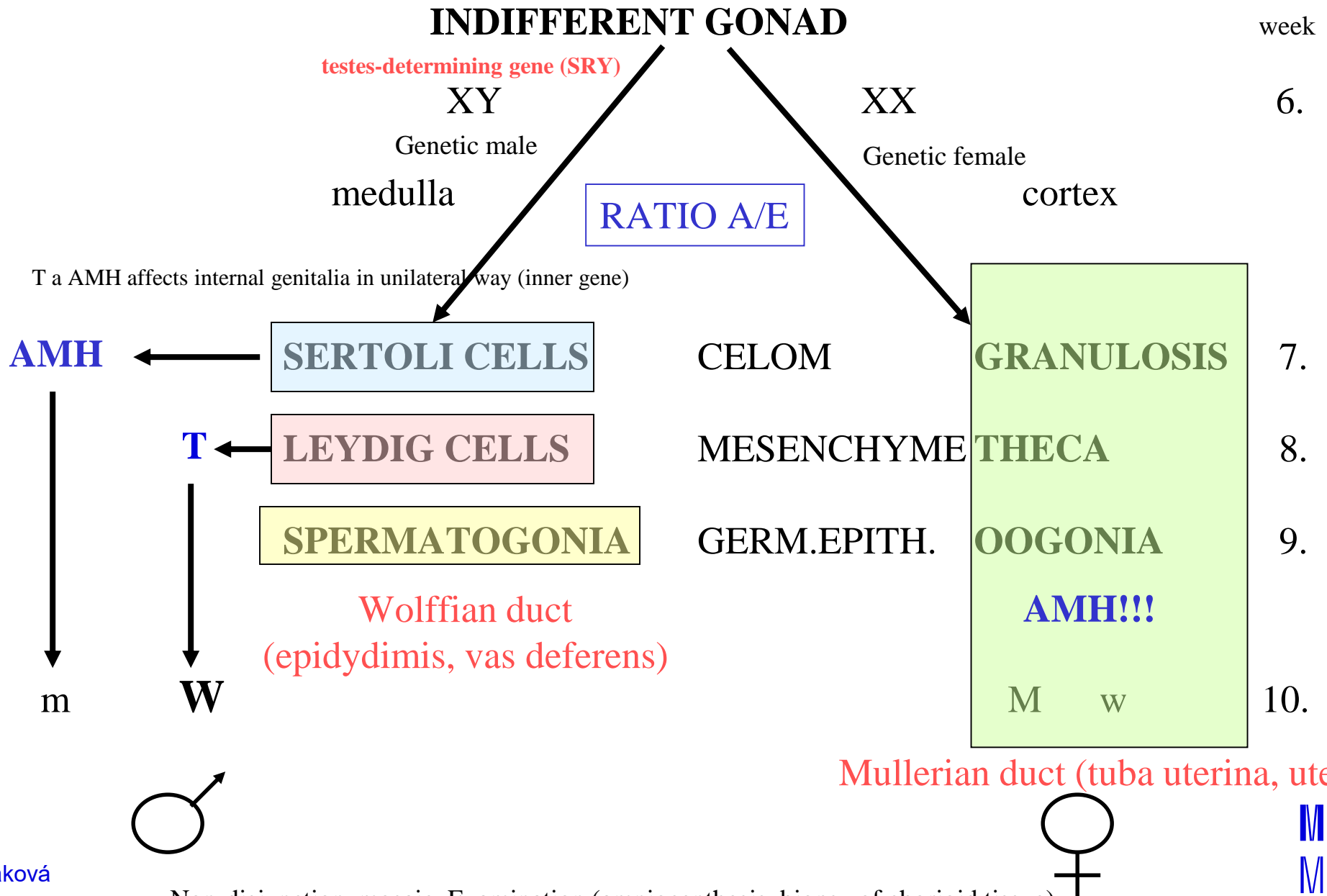
**High investment, low-volume reproduction strategy !**

## Reproduction in humans – gender comparison

- 1) Both male and female are born immature (physically and sexually)
- 2) Sex hormones are produced in significant amount in men also during prenatal  
and perinatal periods, not in women!
- 3) Reproduction period significantly differs – puberty, climacterical
- 4) Character of hormonal changes significantly differs – cyclic vs. non-cyclic

- Meiosis occurs only in germ cells and gives rise to male and female **GAMETES**
- Fertilization of an oocyte by an X- or Y-bearing sperm establishes the zygote's **GENOTYPIC SEX**
- Genotypic sex determines differentiation of the indifferent gonad into either an **OVARY** or a **TESTIS**
- The testis-determining gene is located on the Y chromosome (testis-determining factor, sex-determining region Y)
- Genotypic sex determines the **GONADAL SEX**, which in turn determines **PHENOTYPIC SEX** (fully established at puberty)
- Phenotypic differentiation is modified by endocrine and paracrine signals (testosterone, DHT, AMH)

# SEX DIFFERENTIATION



## AMH (MIH, MIF, MIS, MRF) – ANTIMÜLLERIAN HORMONE

1940, TGF- $\beta$ , receptor with internal TK activity

**Source:** Sertoli cells (5<sup>th</sup> prenatal week) or embryonal ovary (36<sup>th</sup> prenatal week)

In adult women – granulosa cells of small follicles (NO in antral – under influence of FSH - and atretic follicles)

### Role in men:

- Regression of müllerian duct
- Marker of central hypogonadism

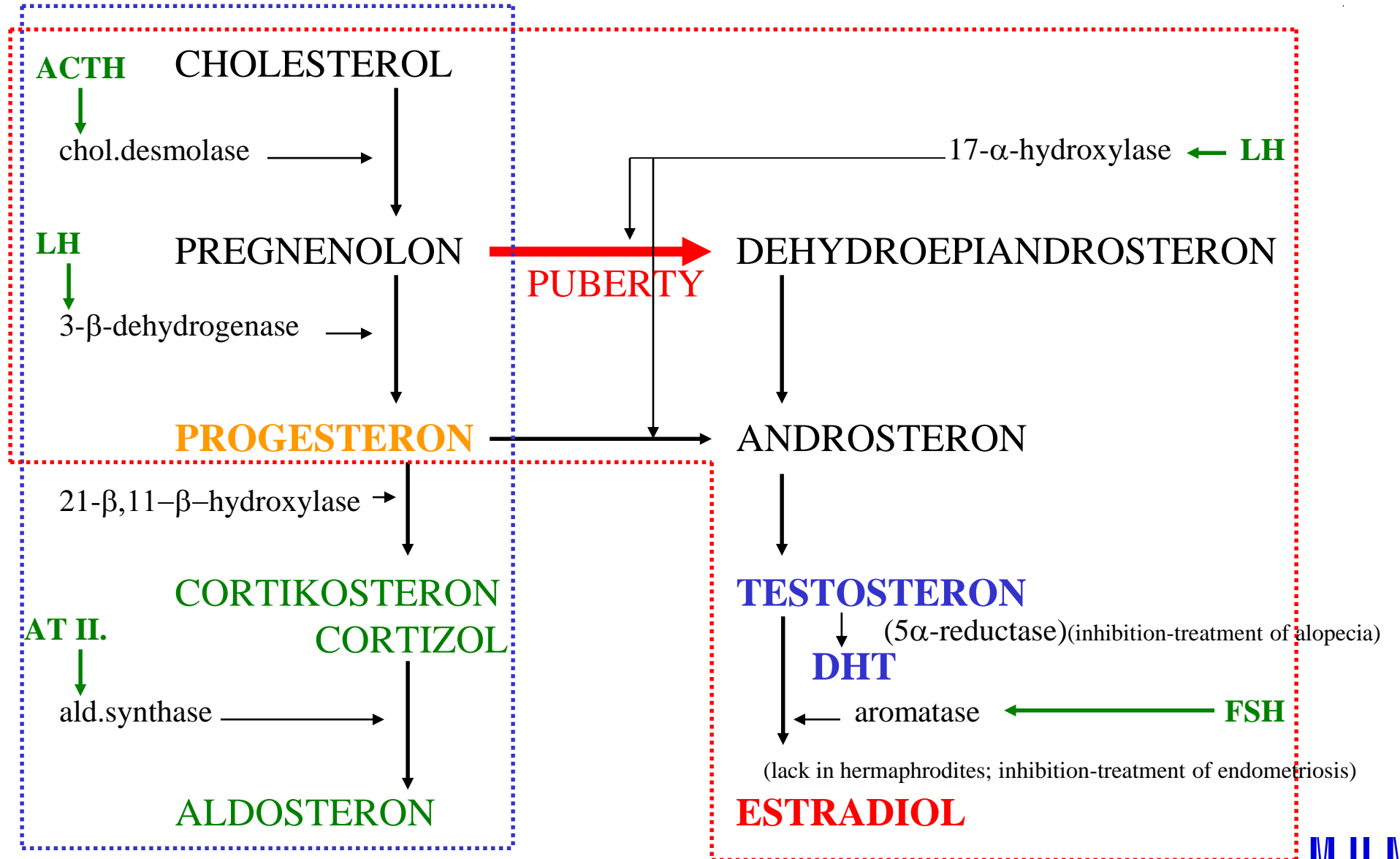
**TUMOUR MARKER**

### Role in women:

- Lower plasmatic levels (by one order), till climacterical
- Estimation of ovarian reserve (AMH level corresponds to pool of pre-antral follicles)
- Marker of ovarian functions loss (premature climacterical)
- Diagnosing of polycystic ovaria syndrome

# BIOSYNTHESIS OF STEROID HORMONES

Impact of androgens on CNS!





## CRITICAL DEVELOPMENTAL PERIODS

- 1) Birth
- 2) Weaning
- 3) Puberty (adolescence)
- 4) Climacterical (menopause)

**Critical body mass** (critical amount of adipose tissue/nutritional state)

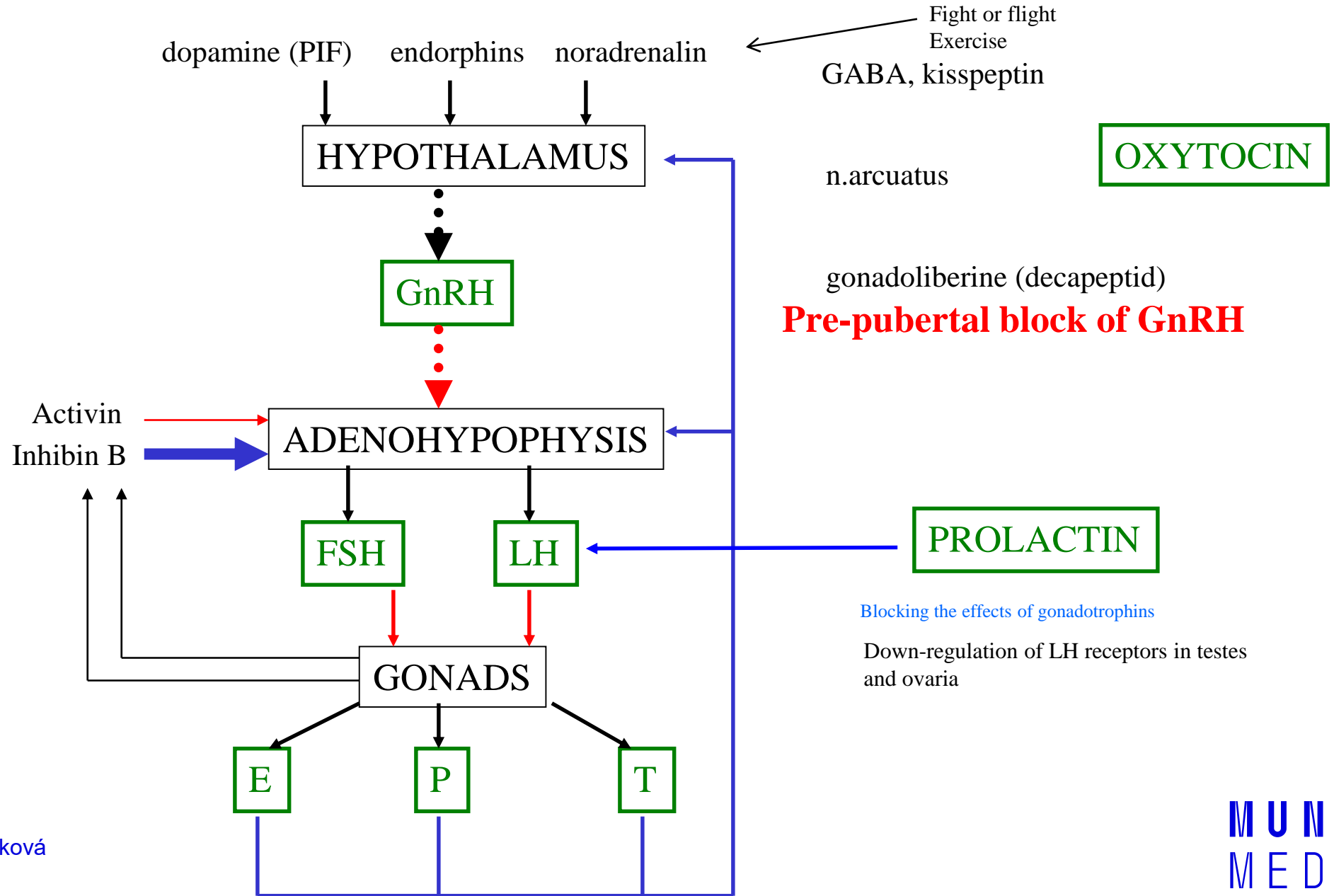
### ***Puberty***

- *Adrenarche*
- *Pubarche*
- *Telarche*
- *Menarche*

Pubertas praecox (central)  
Pseudopubertas praecox (peripheral)

Late puberty

# REGULATION OF SEX HORMONES SECRETION – simplified scheme

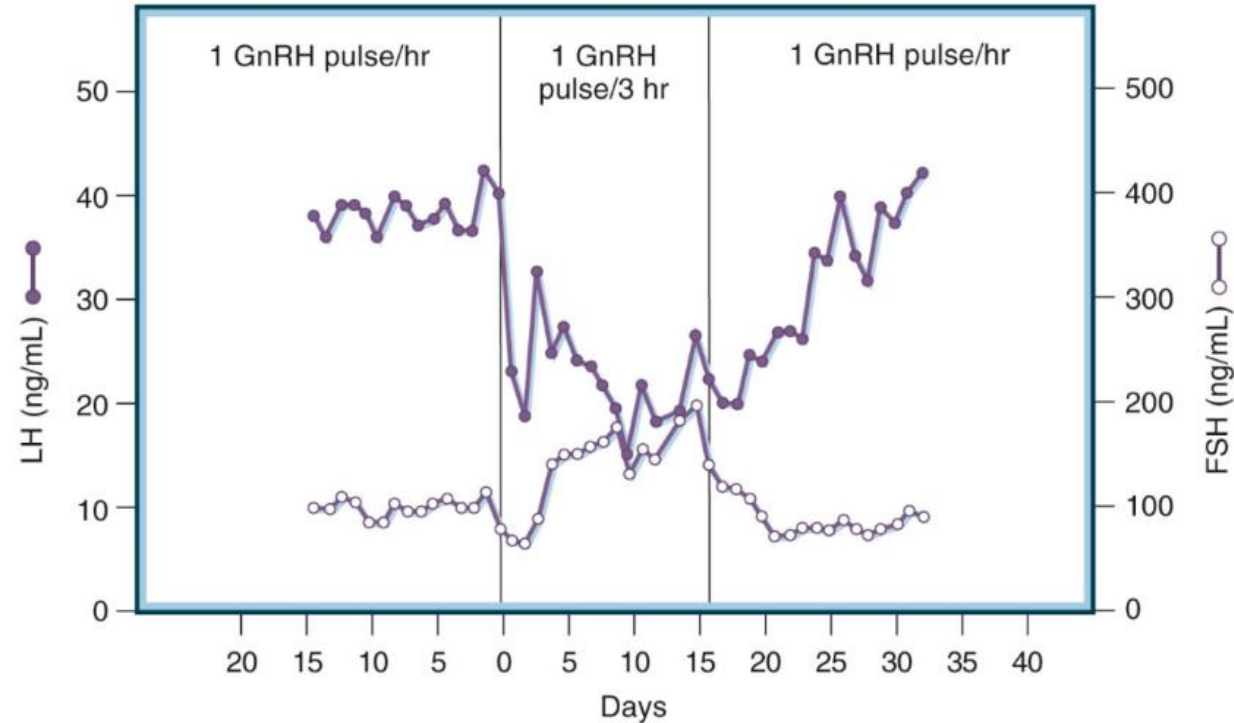


# GONADOLIBERIN (GnRH, GONADOTROPIN-RELEASING HORMONE)

- Specific origin of GnRH neurons out of CNS
- GnRH-I, GnRH-II, (GnRH-III) –  $G_{q/11}$  (PKC, MAPK)
- Important up and down regulation (steroidal hormones, gonadotrophs)
- **Down regulation** – malnutrition, lactation, seasonal effects, aging, continual GnRH
- **Up-regulation** – effect of GnRH on gonadotrophs (menstrual cycle)
- *GNRH1* – hypothalamus; *GNRH2* – other CNS areas

## Hypothalamo-hypophyseal axis

- FSH, LH
- Significance of GnRH pulse frequency (**glycosylation**)
- Menstrual cycle, puberty and its onset

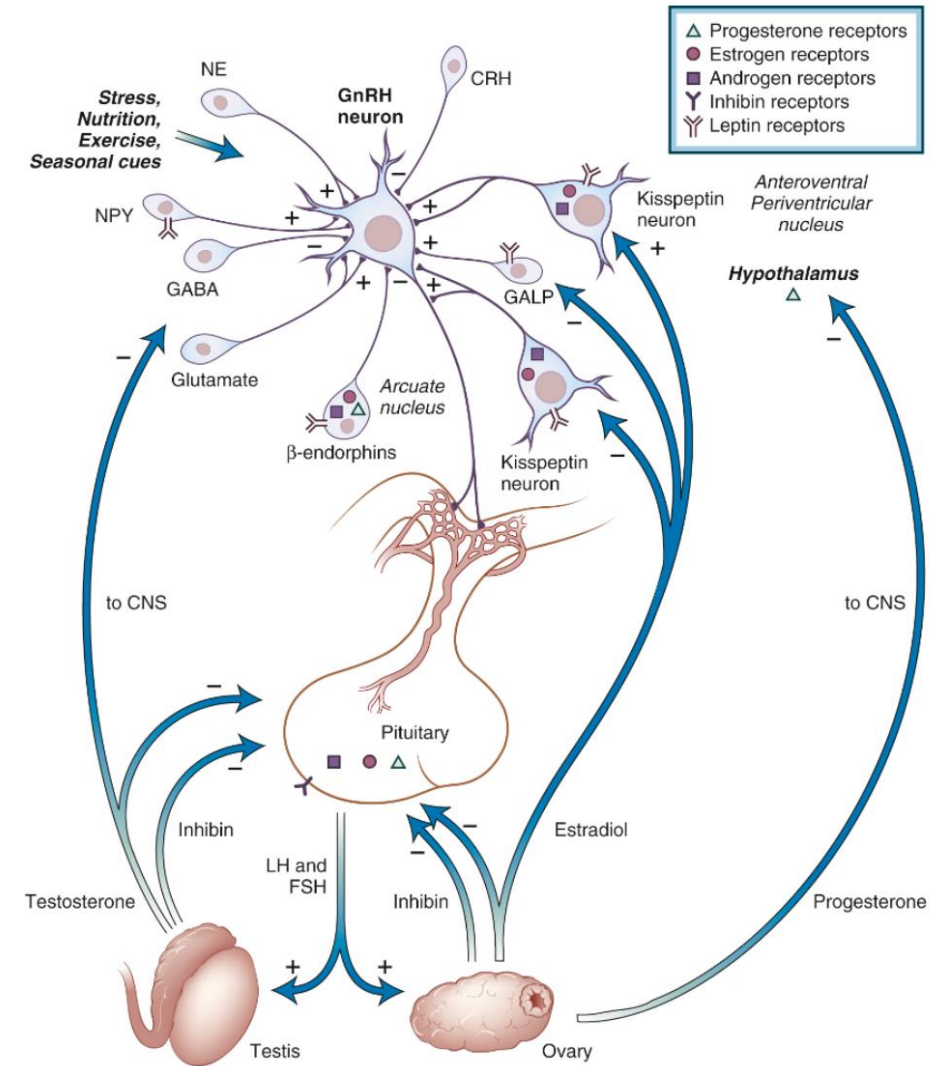


- Other functions and places of production
- CNS – neurotransmitter (area preoptica)
  - Placenta
  - Gonads
  - Tumours (prostate, endometrium)

} Unknown function

# GONADOLIBERIN – REGULATION OF SECRETION

- Inputs from various CNS areas (pons, limbic system)
- Dominating inhibitory effect of sex hormones with exception of estradiol (**negative-positive-negative feedback**)
- Kisspeptin in women
- Inhibitory effect of PRL
- Effect of circulating substrates (FA, Glu)
- Leptin (NPY, kisspeptin)
- **Stress** of various origin
  - **Acute** – MC impairment without effect on fertility
  - **Chronic** – impaired fertility, decreased levels of circulating sex hormones

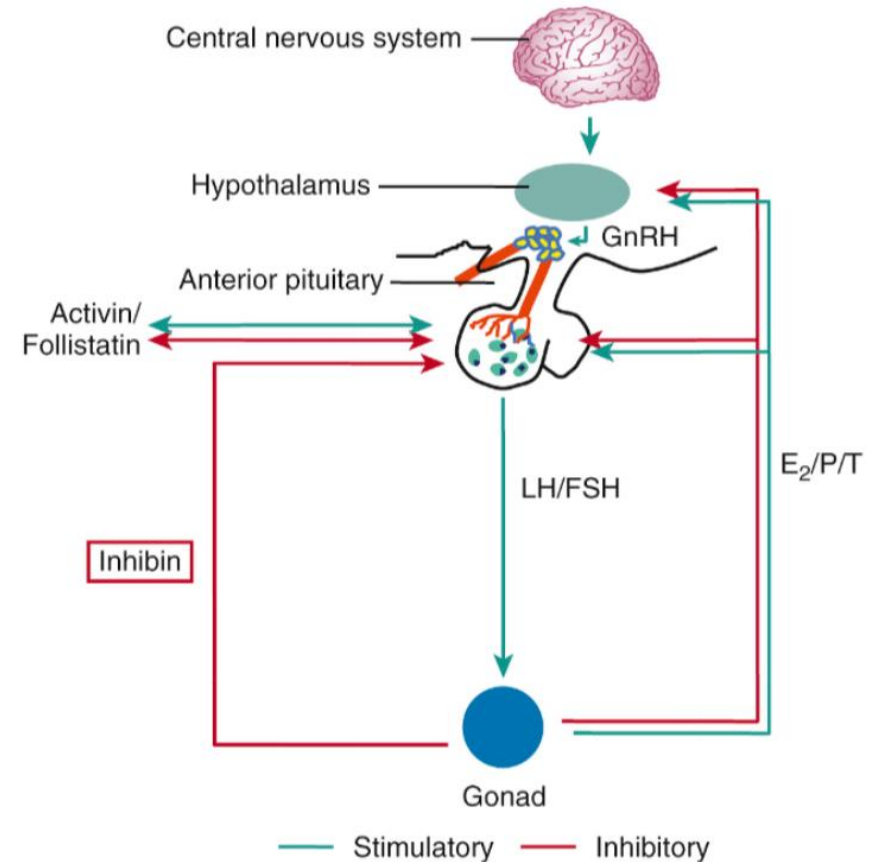


# GONADOTROPHINS - FSH and LH

- Glycoproteins
- Heterodimer, different expression of subunits, **glycosylation**
- Structurally close to **hCG** (placenta)

## Regulation of secretion

- Gonadal hormones, local factors – paracrine (activins, inhibins, follistatin)
- (+) – glutamate, noradrenaline, **leptin**
- (-) – GABA, **opioids**
- Key role of kisspeptins, neurokinin B and substance P in GnRH secretion – FSH/LH
- Estrogens, progesterone, androgens – direct influence on gonadotrophs, indirect influence through GnRH
- Different half-life for circulating LH and FSH



# FSH and LH - functions

## FEMALES

### FSH

- Growth and development of **follicular cell (maturation)**
- **Biosynthesis of estradiol**
- Regulation of inhibin synthesis during follicular phase
- **Upregulation of LH receptors** (preovulatory follicles)
- **Selection of dominant follicle**
- **Recruitment of follicles for next cycle**

### LH

- Stimulation of **estrogen synthesis** at various levels (theca)
- **Oocyte maturation** (preovulatory follicle)
- Rupture of ovulatory follicle, **ovulation**
- Conversion of follicle wall to **corpus luteum**

## MALES

### LH

Intratesticular **synthesis of testosterone** (Leydig cells)

### FSH

**Spermatogenesis** (Sertoli cells)

# ACTIVINS and INHIBINS

## Inhibins

- dimeric peptides ( $\alpha + 1$  or two  $\beta_A$  or  $\beta_B$ )
- circulating hormones produced by gonads
- inhibin A – dominant follicle, corpus luteum
- **inhibin B** – testes, luteal and early follicular phase of ovarian cycle

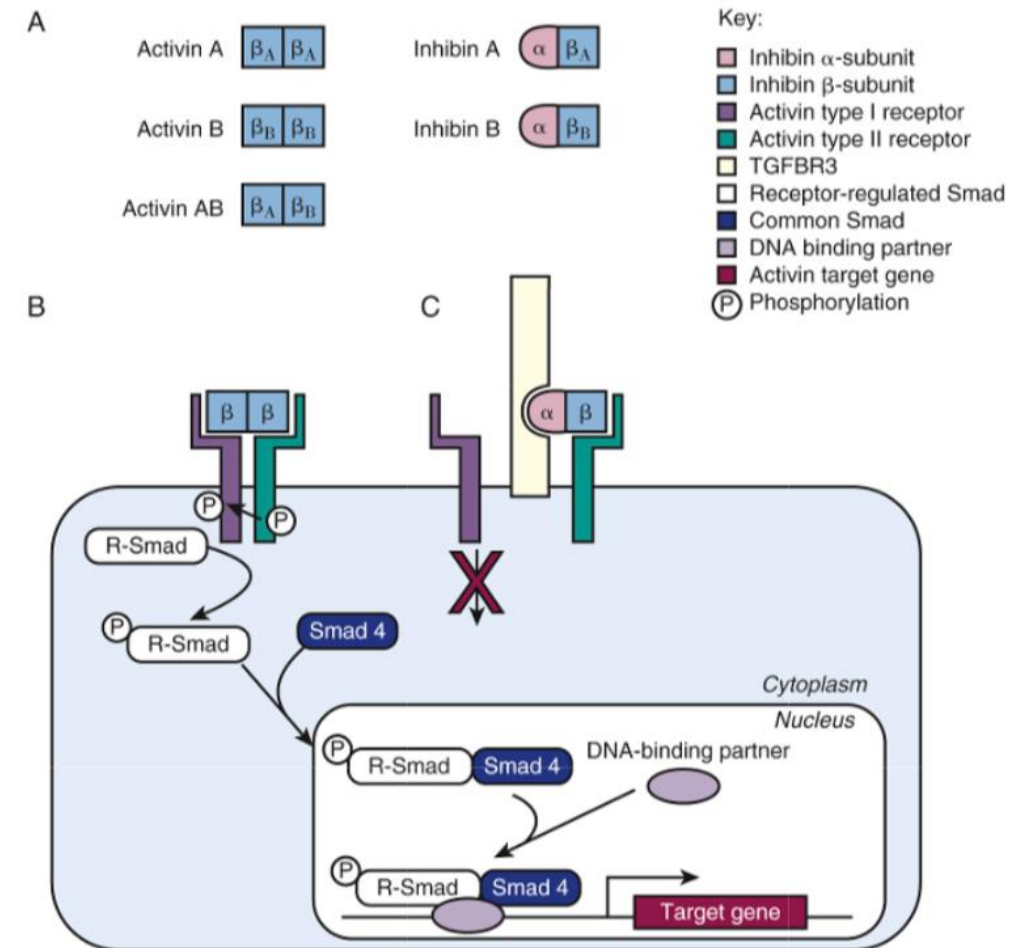
## Activins

- dimeric peptides – dimers of  $\beta$  subunits
- FSH stimulation
- autocrine/paracrine factors
- other tissues – growth and differentiation

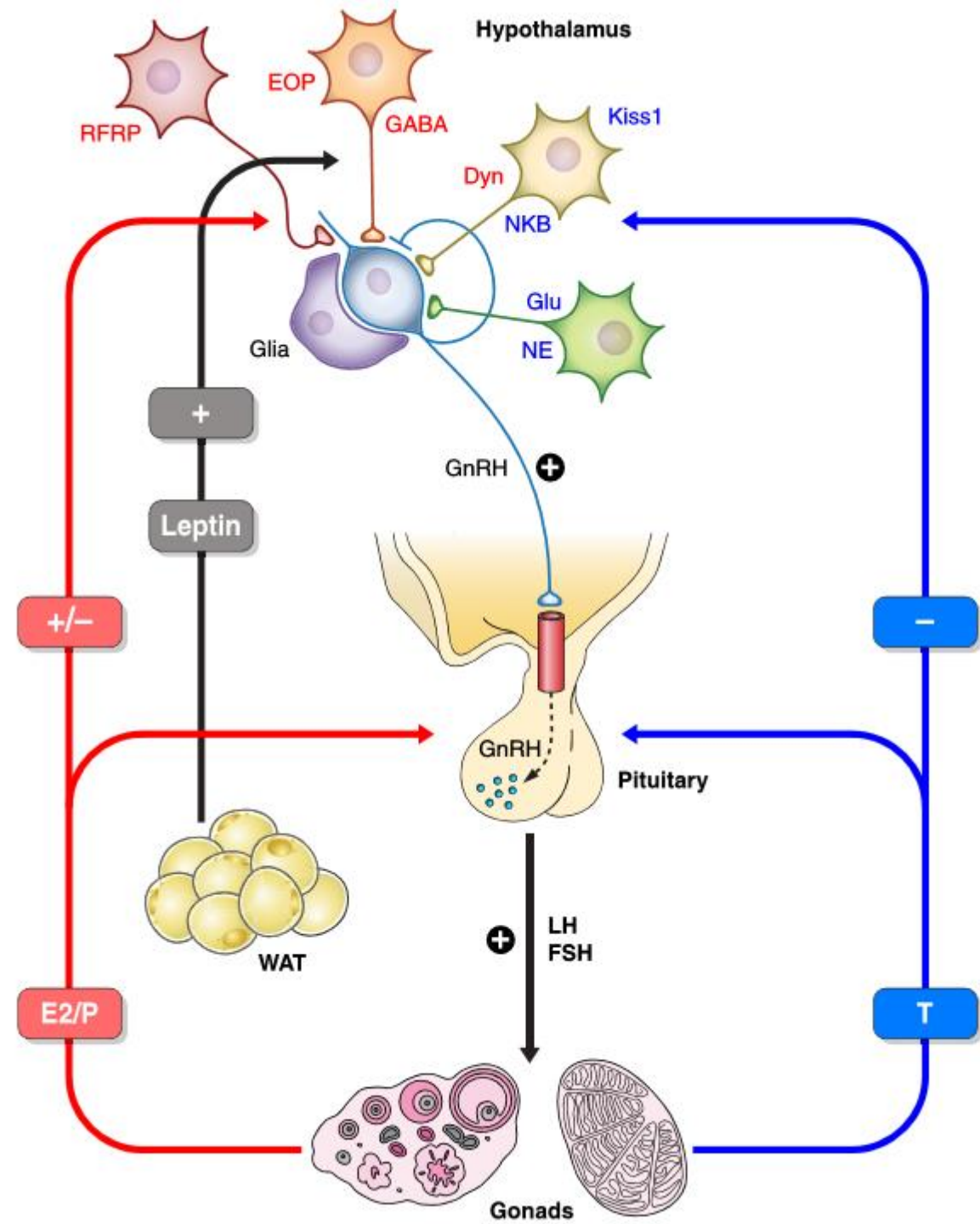
## Follistatin

- monomeric polypeptide
- **FSH inhibition**

- „additional“ regulation of FSH and LH secretion



# REGULATION OF SEX HORMONES SECRETION



Pinilla et al., Phys Rev 92: 1235- 1316, 2012



## LEPTIN A REPRODUCTION

Activation of reproductive system does not depend on age, but on nutritional state of organism.

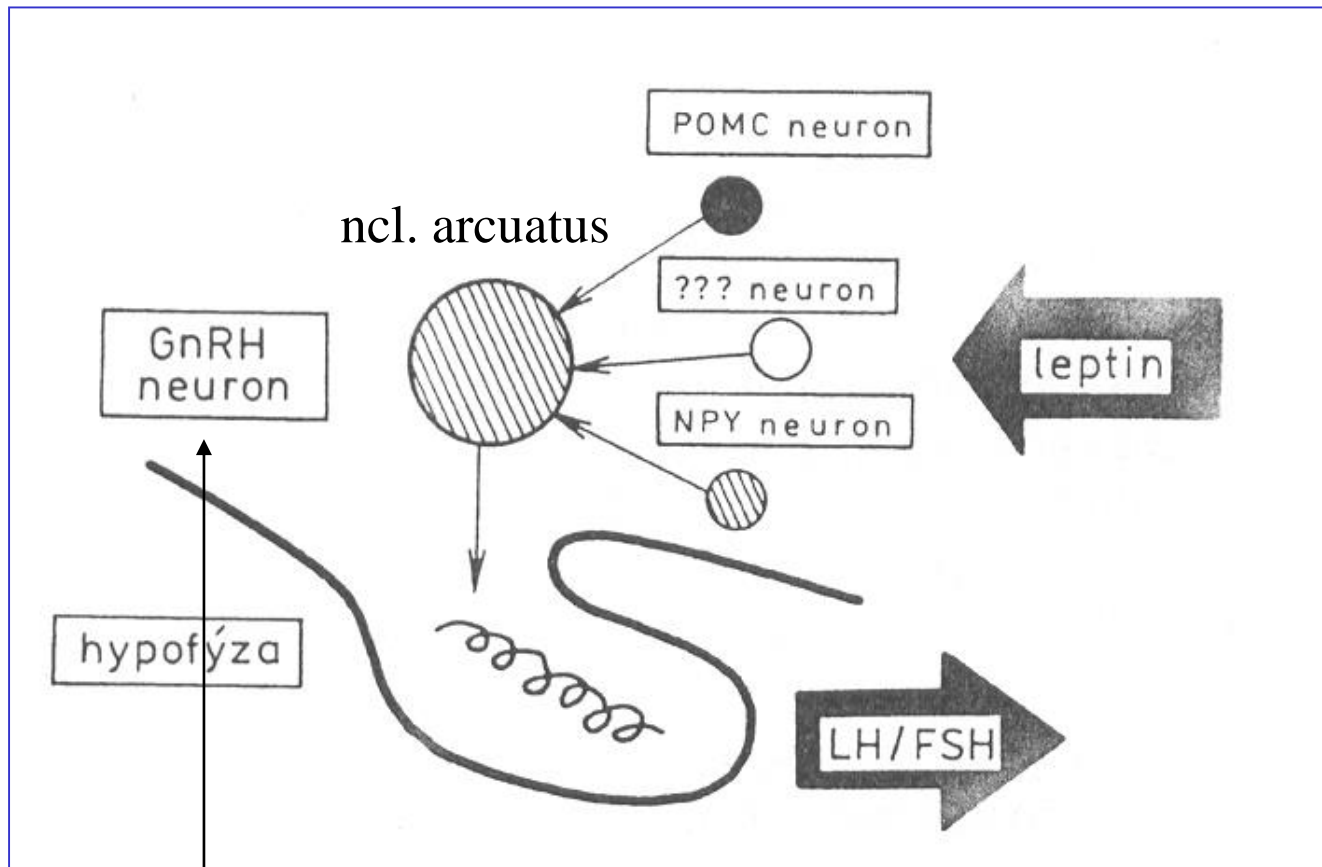
**LEPTIN**: ob-protein, ob-gen, 7.chromosome  
„λεπτος“ = thin, slim  
polypeptide, 176 AA

Bound in **hypothalamus**: n.paraventricularis, suprachiasmaticus, arcuatus a dorsomedialis

Produced in: **adipocytes**, **placenta**, stomach, **mammal epithelium** (???)  
Leptin plasmatic levels are sex-dependent (less in males) and do not depend on nutritional state

Leptin receptor: gene on 4.chromosome, 5 types of receptor, A-E  
Receptor B – effect in **gonads and hypophysis**

*Leptin is not only a factor of body fat amount, but affects also the regulation of neuroendocrine functions, including hypothalamo-hypophyseogonadal axis.*



area preoptica - reproduction

**??? Critical amount of adipose tissue – leptin – hypothalamus – LHRH – puberty ???**

Effects of leptin on **testes** are not fully elucidated yet.

**Testosterone** and **dihydrotestosterone** suppress production of leptin in adipocytes!

## **REGULATION OF PUBERTY ONSET BY LEPTIN**

Critical body mass (**critical nutritional state**).

Leptin plasmatic levels in pre-pubertal children are sex-independent.

Pre-pubertal „leptin resistance“ (relative).

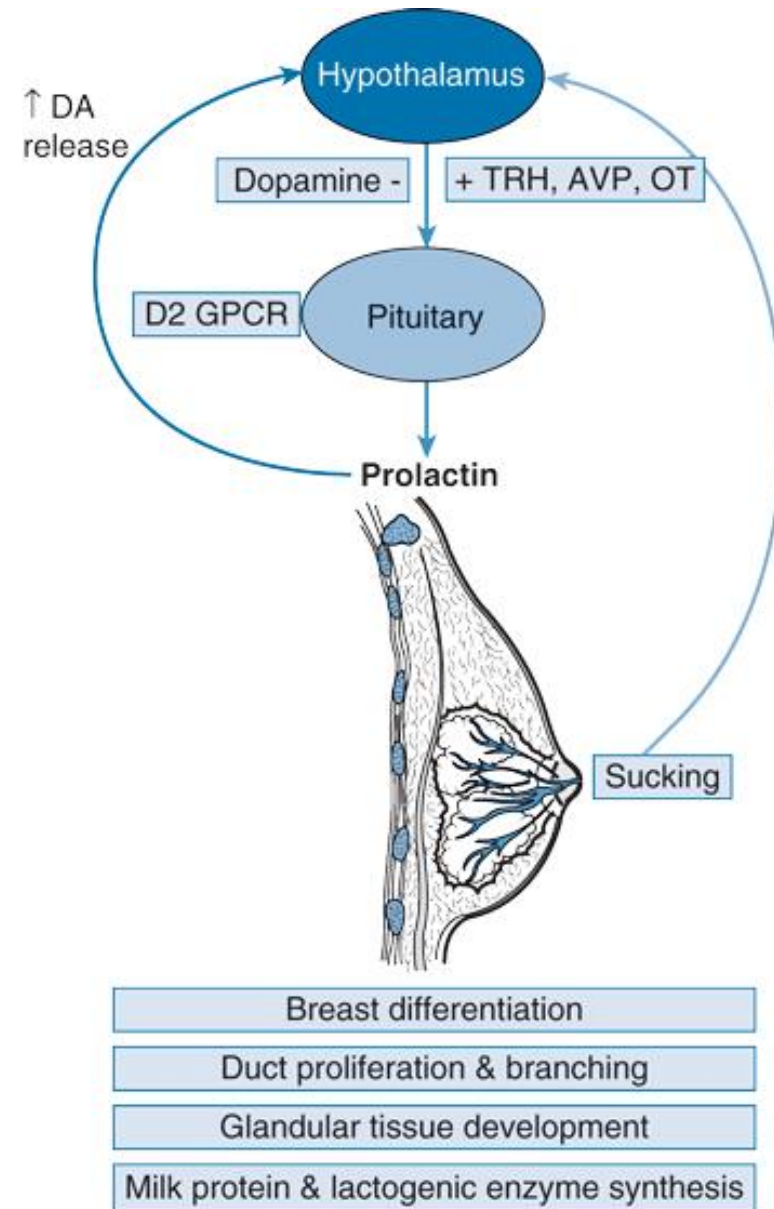
In puberty, girls produce 2x more leptin per 1kg of adipose tissue than boys.

# PROLACTIN - PRL (Co-hormone)

- Protein
- **Lactotropic** cells (only PRL)
- **Mammotroph** cells (PRL and GH)
- Hyperplasia – **pregnancy and lactation**
- Expression regulated by oestrogens, dopamine, TRH and thyroid gland hormones
- **PRLR** – mamma, adenohypophysis, suprarenal gland, liver, prostate, ovary, testis, small intestine, lungs, myocardium, SNS, lymphocytes

## Regulation of secretion

- **Pulsatile secretion**: 4 – 14 pulses/day
- Highest levels during **sleep**
- Lowest levels between 10:00 and 12:00
- Gradual decrease of secretion during **aging**
- TIDA cells – dopamine (-, D2R)
- Paracrine – endothelin-1, TGF- $\beta$ 1, calcitonin, histamine (-)
- FGF, EGF (+)
- TRH, oestrogens, VIP, serotonin, GHRH at higher concentrations (+)
- CCK - ?



# PROLACTIN - functions

**MAIN FUNCTION:** Milk production during pregnancy and lactation  
= „survival“ function

**Other functions** – metabolic, synthesis of melanin, maternal behaviour

## Breast development a lactation

- **Puberty** – mamma development under the effects of GH a IGF-1
- Effect of oestrogens and progesterone
- Age of 8 – 13
- **During pregnancy** – proliferation of alveoli and proteosynthesis (proteins of milk and colostrum)
- During the **3<sup>rd</sup> trimester** – production of colostrum (PRL, oestrogens, progesterone, GH, IGF-1, placental hormones)
- **Lactation** – increase in PRL post-partum, without sucking drop after approx. 7 days
- Milk accumulation prevents further PRL secretion
- Role of oxytocin – ejection of milk !!!

## Reproductive function of PRL

- Lactation = amenorrhea and secondary infertility
- Inhibition of GnRH secretion
- Significance of kisspeptin neurons (PRLR)
- Putative role of metabolic factors

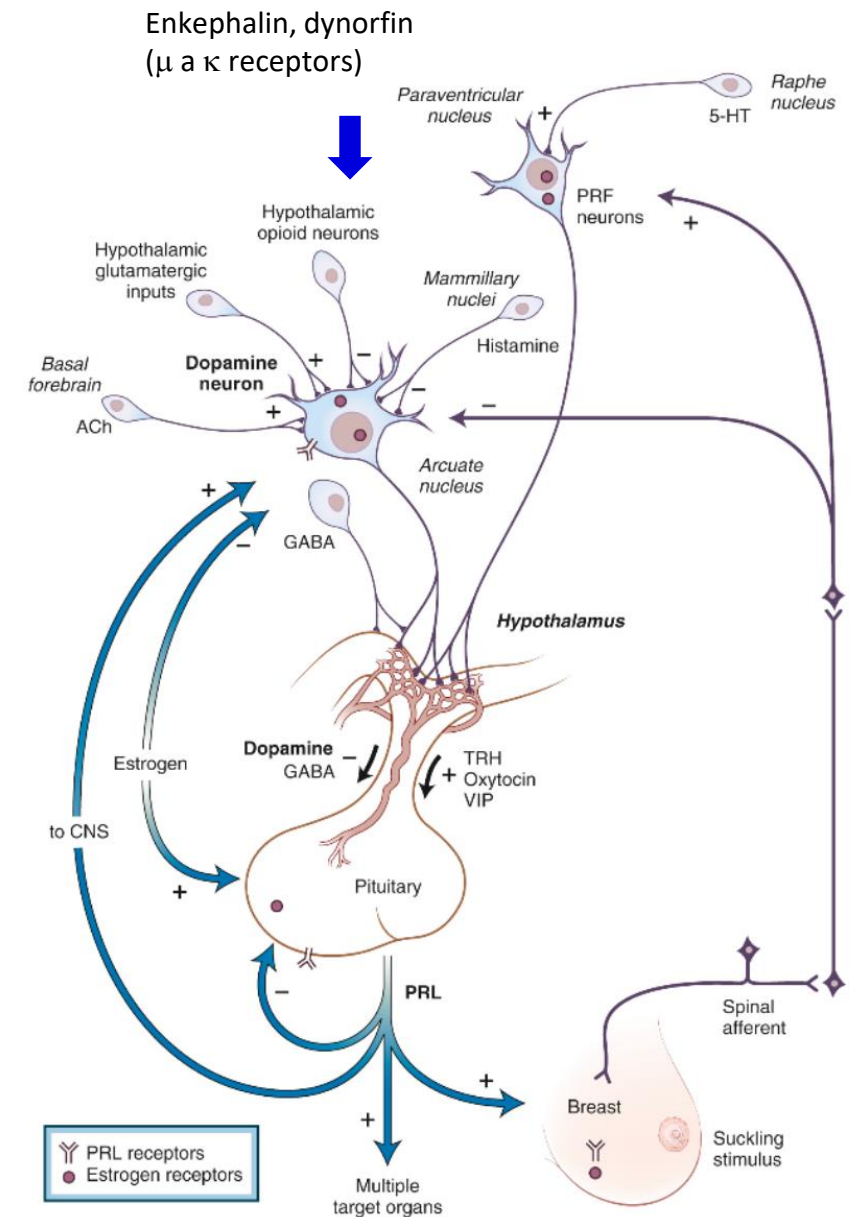
# DOPAMINE – REGULATION OF SECRETION

## PROLACTIN-RELEASING FACTORS (PRF)

- TRH, oxytocin, VIP
- under specific conditions ADH, ATII, NPY, galanin, substance P, GRP, neurotensin
- *prolactin-releasing peptide* (PrRP) – stress, satiety (other parts of CNS)

- Important feedback mechanism (**short loop**) of PRL secretion regulation
  - **Circadian rhythm** (maximum in the morning)
  - **Nipple stimulation** (1-3 min, peak 10 – 20 min)

- **Relevance of studying PRL secretion and its regulation - psychopharmaceutics!**



# DOPAMINE (PIH, prolactin-inhibiting hormone)

## Characteristics

- D2R (G protein inhibition, AC, cAMP decrease, inhibition of shaker type K<sup>+</sup> channels, MAPK, PAK – proliferation!)
- D1R (activation)

## Hypothalamo-hypophyseal axis

- **Inhibition of PRL (D2R) secretion** – lactotropic cells
- ! Lactotrophs with continual high PRL production
- PRL secretion regulated also at adeno-hypophyseal level (paracrine, autocrine)
- Neuroendocrine regulation of PRL secretion – pregnancy, lactation, menstrual cycle, sensory inputs

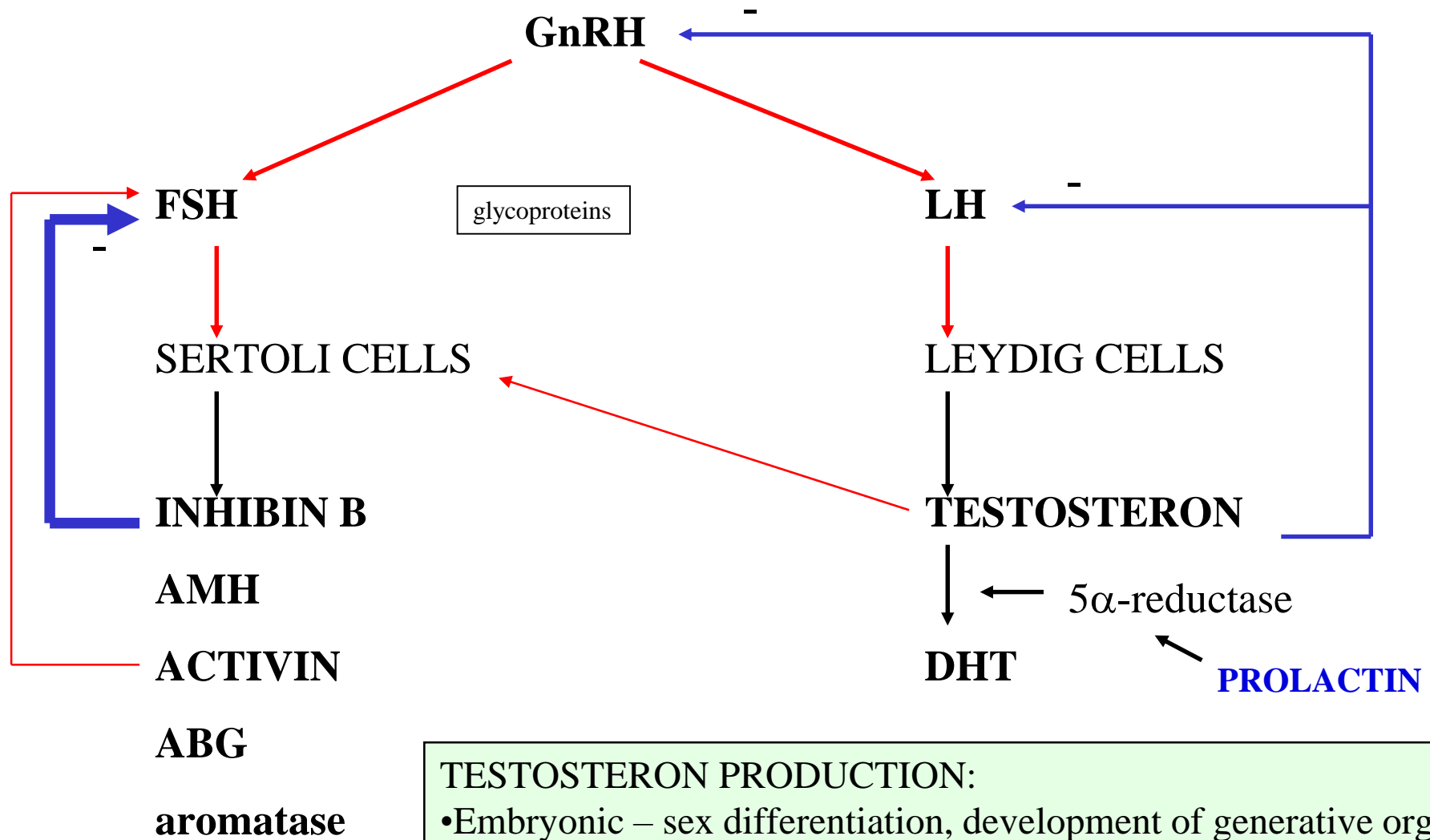
## Other functions and places of synthesis

- Blood vessels – vasodilatation (physiological concentrations)
- Kidneys – sodium secretion
- Endocrine pancreas – decrease in insulin secretion
- GIT – lower motility
- Effect of dopamine on immune system

# MALE REPRODUCTION SYSTEM

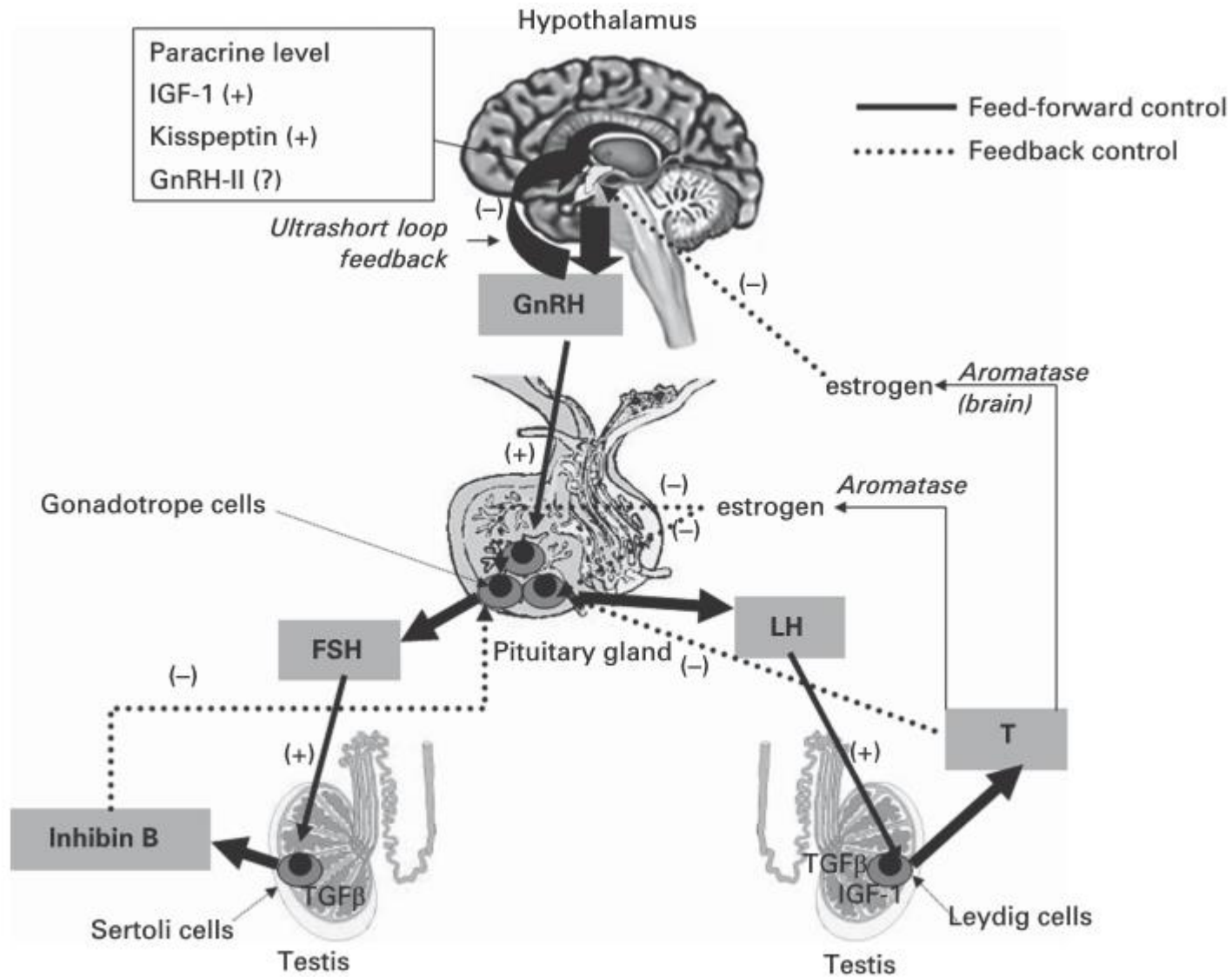


# HUMOURAL CONTROL OF REPRODUCTIVE FUNCTIONS IN MAN



**TESTOSTERON PRODUCTION:**

- Embryonic – sex differentiation, development of generative organs
- Perinatal – descensus testis (?)
- Fertile period – LH pulsation
- Ageing – decrease of sensitivity to LH



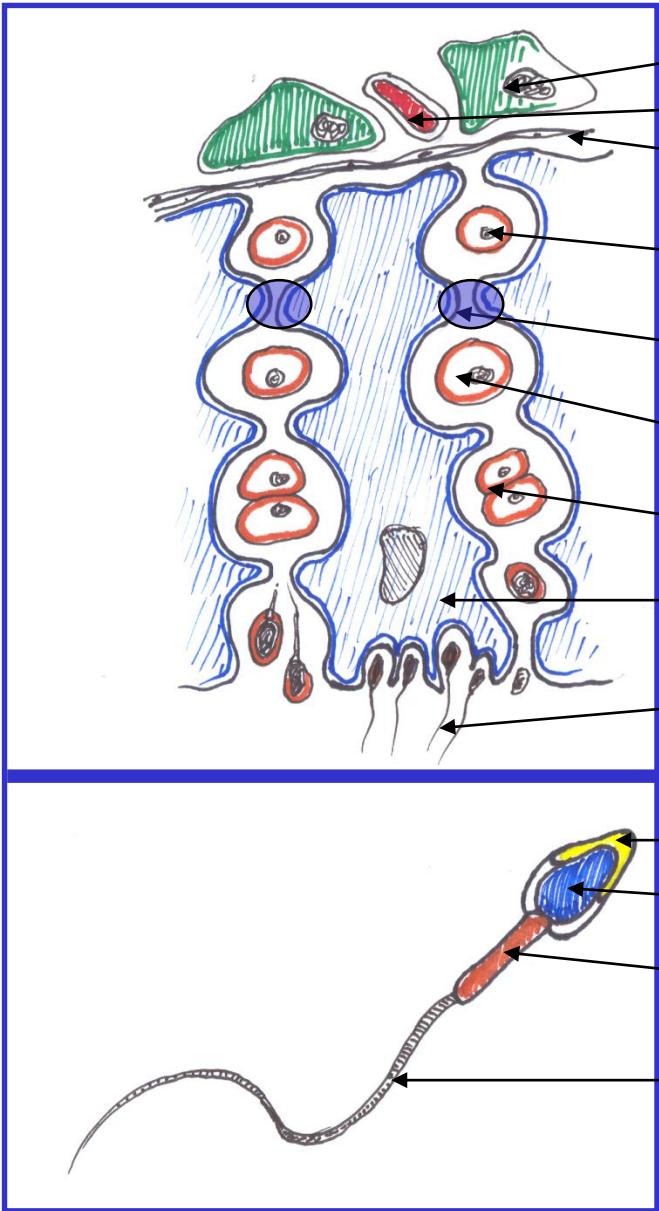
An Introduction to Male Reproductive Medicine  
 Edited by Craig Niederberger

**Table 1.1** Regulation of hypothalamic–pituitary–gonadal axis hormone release

Hormone	Autocrine regulation	Paracrine regulation	Endocrine regulation
GnRH	GnRH itself (–)	GnRH II (+), IGF-1 (+), kisspeptin (+)	Testosterone (–), estrogens (–), neurotensin (+), norepinephrine (+)
FSH	–	Activin (+), follistatin (–)	GnRH (+), estrogens (–), inhibin B (–)
LH		Activin (+), follistatin (–)	GnRH (+), testosterone (–)
Testosterone	–	IGF-1 (+), GH(+), CRH (–), TGF- $\beta$ (–), IL-1 $\alpha$ ( $\pm$ )	LH (+)

+ Stimulatory effect, – Inhibitory effect. Transforming growth factor- $\beta$  (TGF- $\beta$ ), corticotropin-releasing hormone (CRH), interleukin 1 $\alpha$  (IL-1 $\alpha$ ), growth hormone (GH), insulin-like growth factor 1 (IGF-1).

# SPERMATOGENESIS



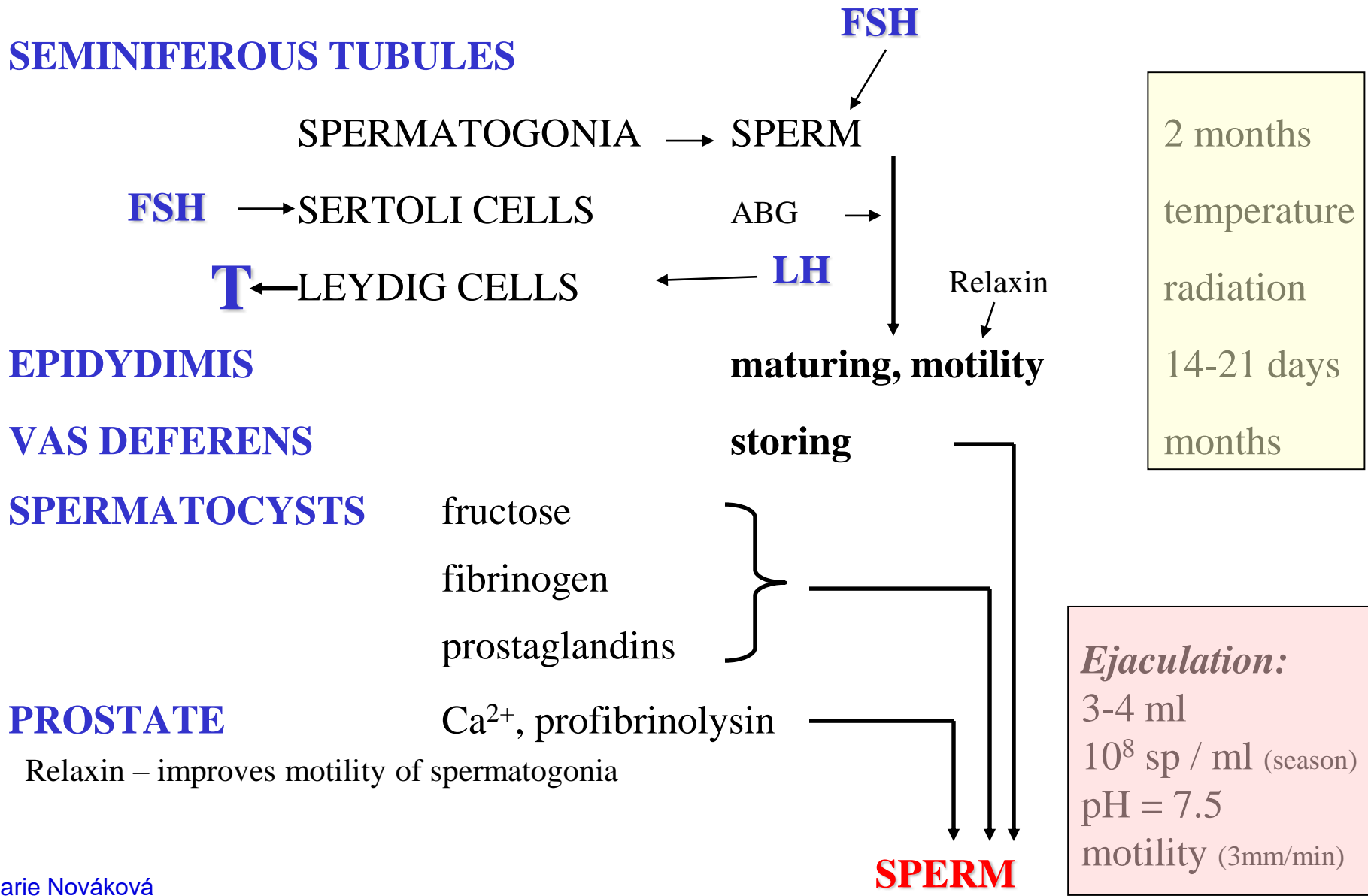
- Leydig cell
- Capillary
- Basal membrane
- Spermatogonium
- Tight junction**
- Spermatocyte
- Spermatide (haploid)
- Sertoli cell (contraction)
- Spermia

70 days  
 1-64 (6 divisions)  
 Temperature < 35°C

- Acrosom (enzymes)
- Head (nucleus, DNA)
- Body (mitochondria)
- Flagella (microtubules, 9+2)

Lumen:  
 androgens, estrogens  
 glutamate, aspartate  
 inositol

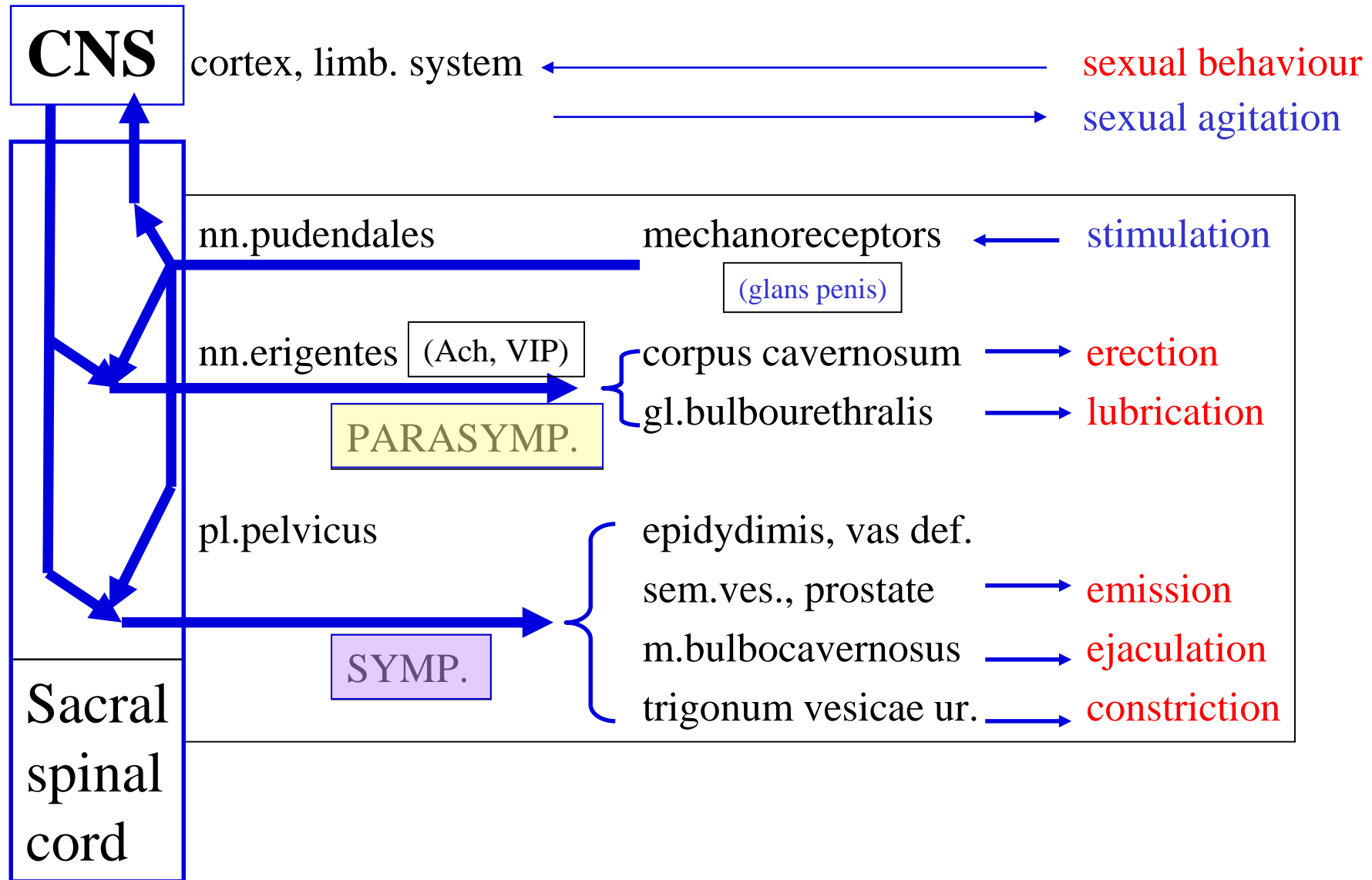
# PRODUCTION OF SPERM



## SPERMIOGRAM

Volume	1,5 - 2,0
pH	7,2 - 8,0
Concentration of sperm	20 mil/ml
Total number of sperm	40 mil and more
Motility	50% and more in category A+B, above 25% in A
Morphology	30% and more of normal forms
Vitality	75% and more of living sperm
Leukocytes	up to 1 mil/ml
Autoagglutination	< 2 (scale 0 - 3)

# SEXUAL REFLEXES



# FEMALE REPRODUCTION SYSTEM



# O O G E N E S I S

## DEVELOPMENT

6-8 weeks

GERMINAL EPITHELIUM

Hormonally  
independent

O O G O N I A  
mitotic division

F O L L I C L E  
P R I M O R D I A L

24 weeks

O O C Y T E S I .

$7 \times 10^6$

1. meiosis  
prophase

$2 \times 10^6$

birth

Hormonally  
dependent  
(cyclic)

puberty

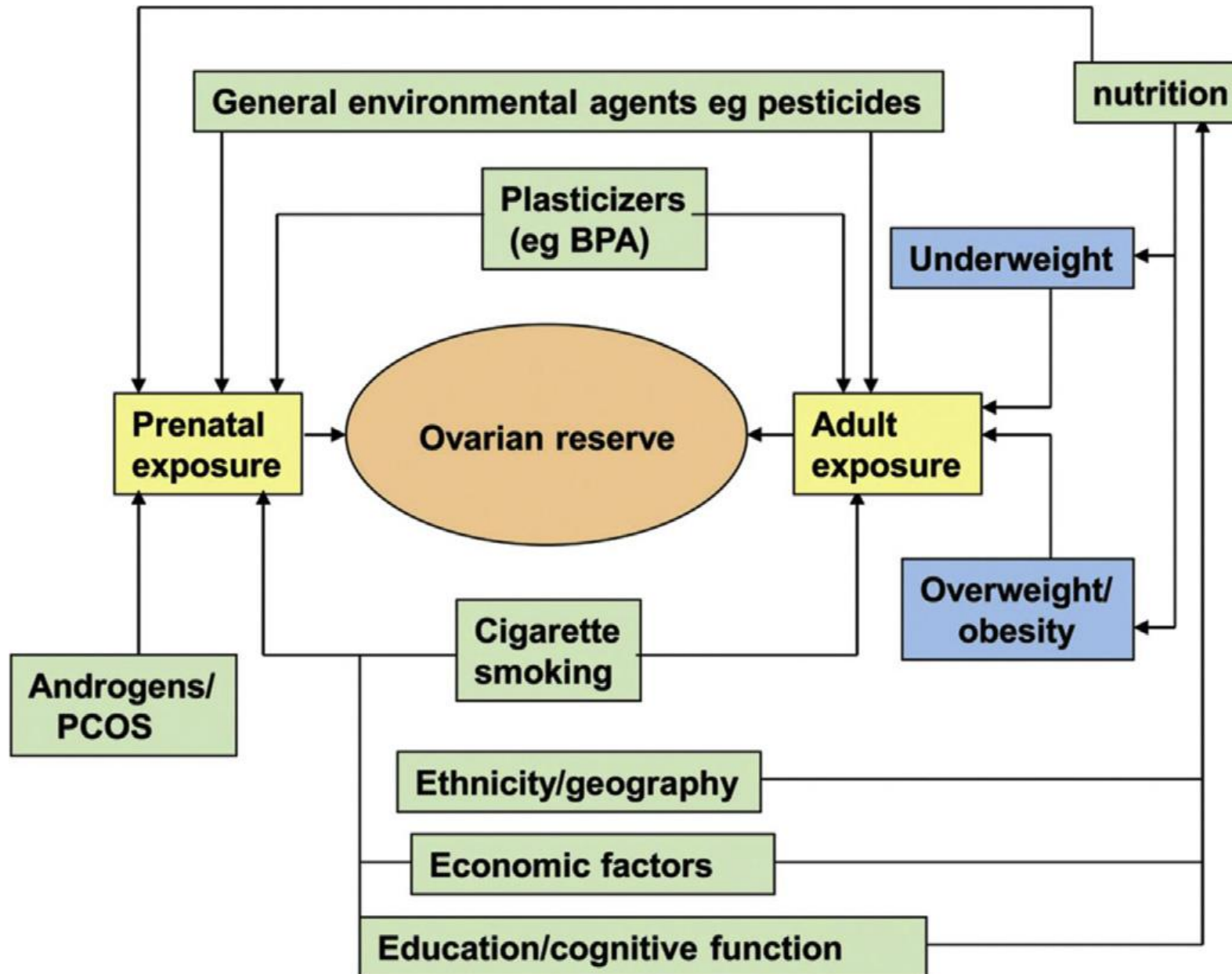
O O C Y T E S I I .  
haploid  
2. meiosis  
metaphase  
O V U M

$3 \times 10^5$   
D O M I N A N T  
A T R E T I C  
G R A A F  
O V U L A T I O N

2. meiosis – end

menopause

0



Daan and Fauser, Maturitas 82 (2015) 257–265

# CYCLIC CHANGES

ovarian

uterine

+ vagina/cervix uteri

+ mamma

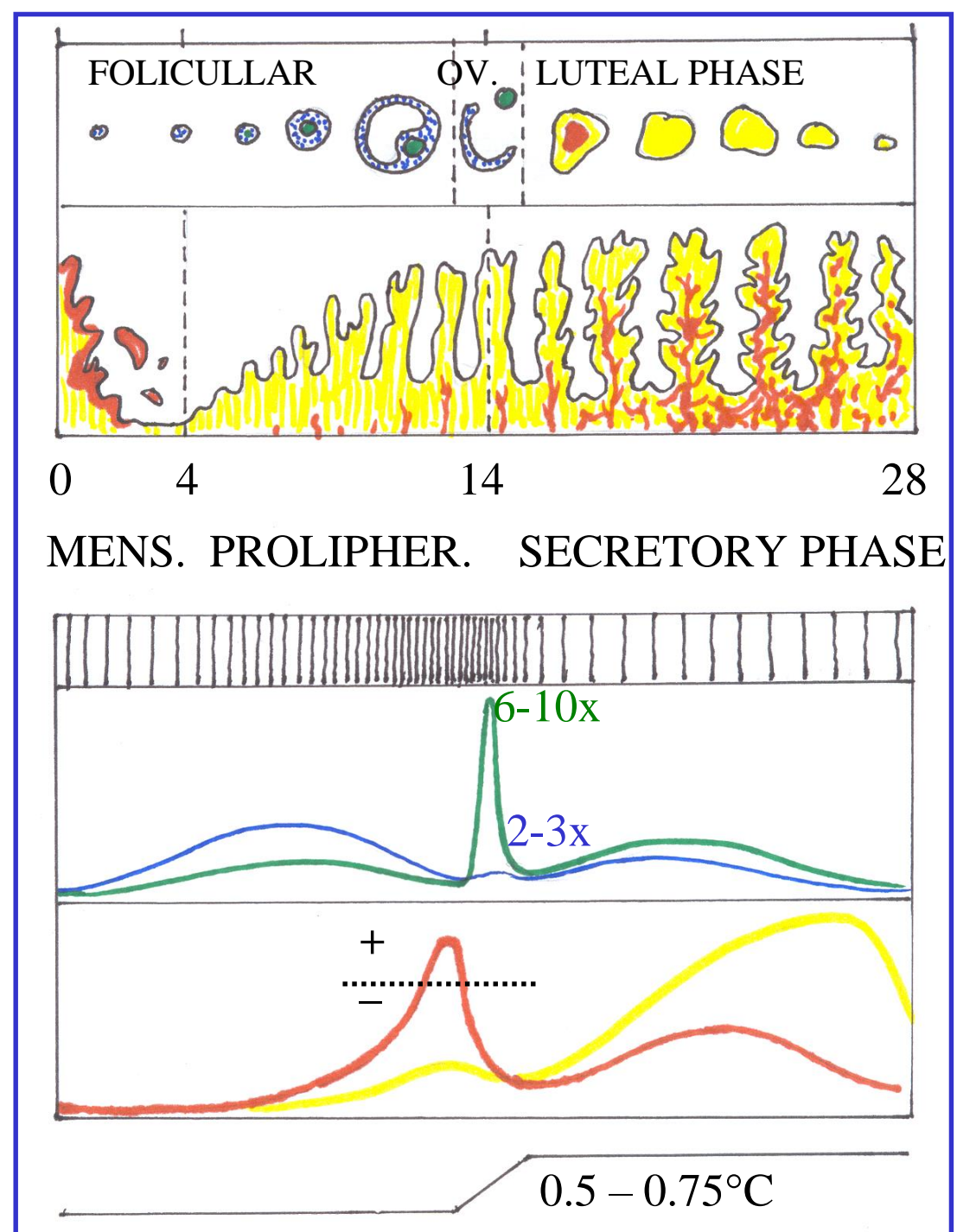
GnRH

FSH, LH

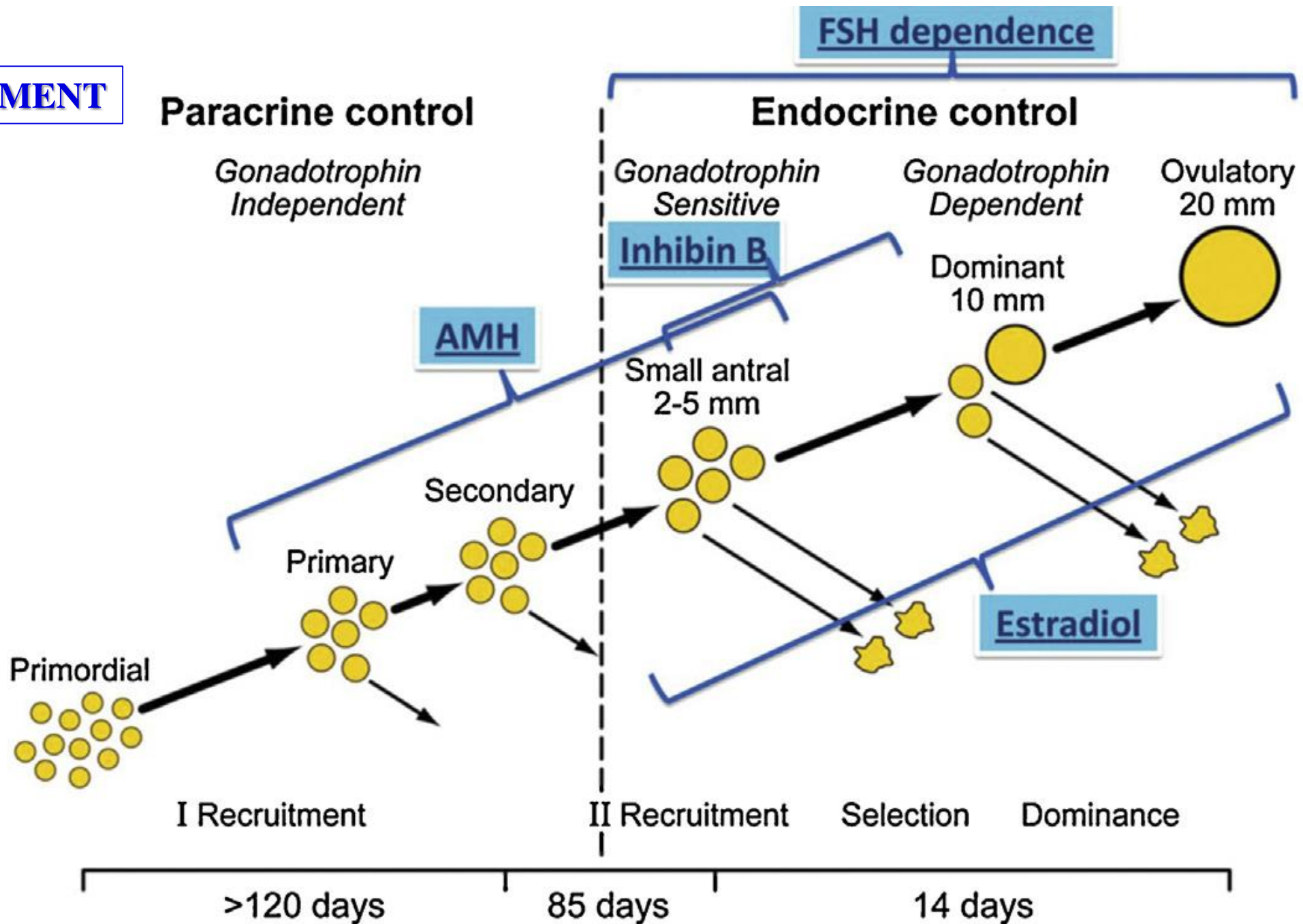
estradiol

progesteron

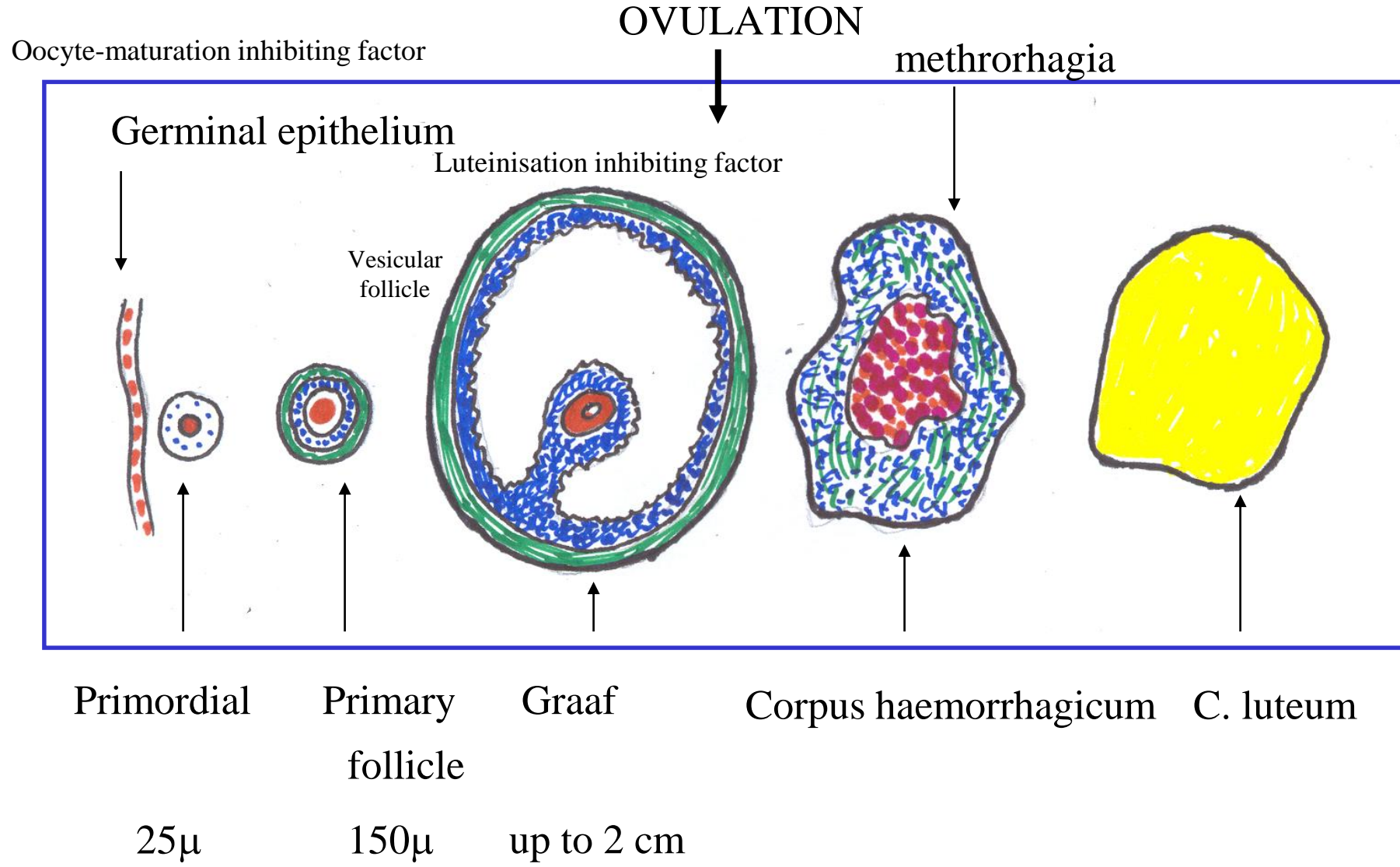
basal temper.



# RECRUITMENT



# OVARIAN CYCLE



# VESICULAR FOLLICLE

## PRIMARY FOLLICLE - FSH

Growth acceleration of primary follicle – change into vesicular follicle:

1) estrogens released into follicle stimulate granul. cells



**UP REGULATION** of **FSH receptors** and **intrinsic positive feedback** (higher sensitivity for FSH!!!)

2) **UP REGULATION** of LH receptors (estrogens and FSH) – another acceleration of growth due to „higher sensitivity“ to LH (**positive feedback**)

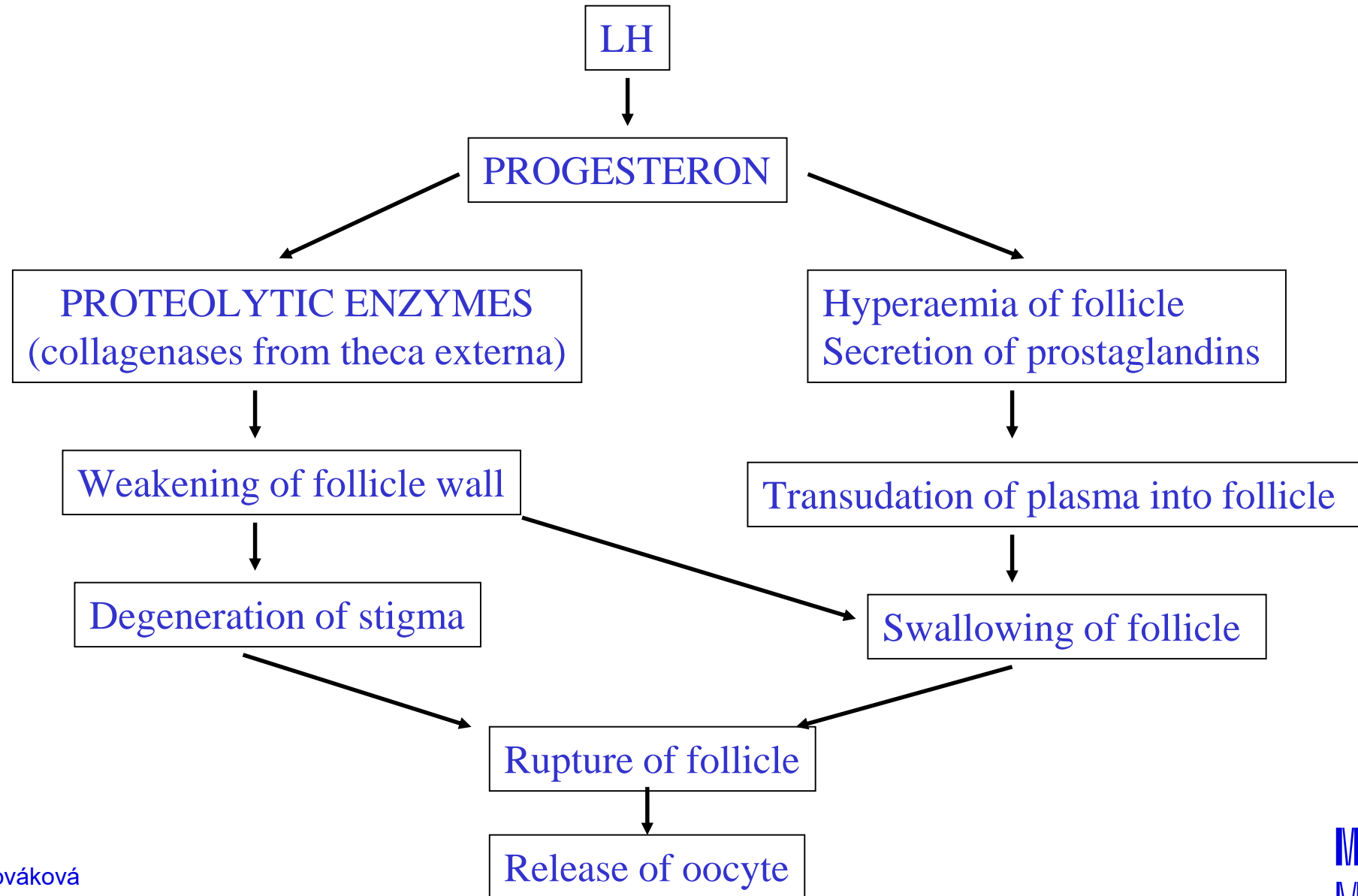
3) Increased estrogens and LH secretion accelerates growth of theca cells, secretion is increased

→ **explosive growth of follicle**

## DOMINANT FOLLICLE

1. High levels of **oestrogens** from the fastest-growing follicle
2. **Negative** feedback on FSH production from adenohypophysis
3. Gradual decrease in **FSH** secretion
4. „**Dominant** follicle“ continues in growing due to **intrinsic positive** feedback
5. Other follicles grow slowly and subsequently become **atretic**

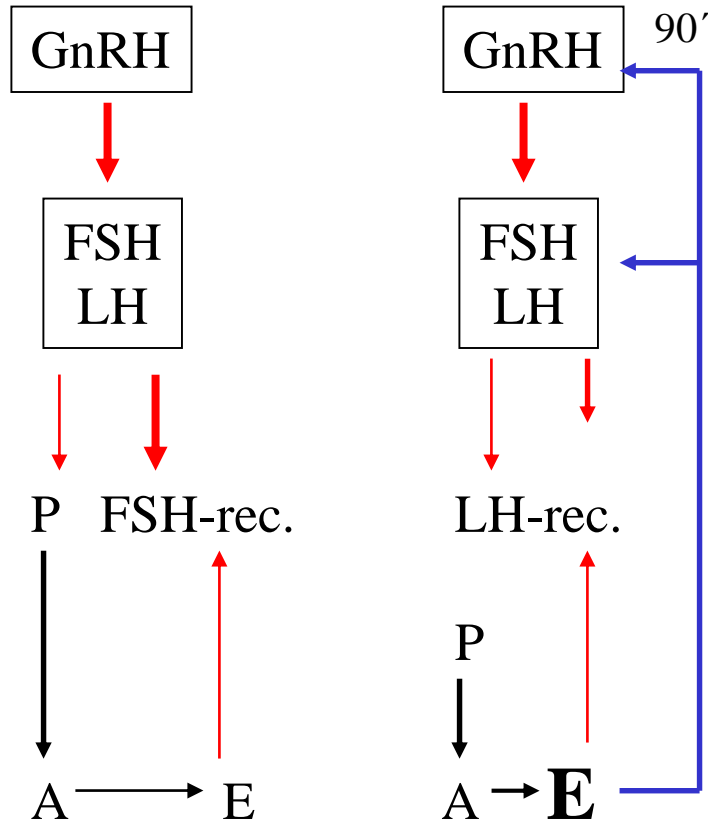
# MECHANISMS OF OVULATION





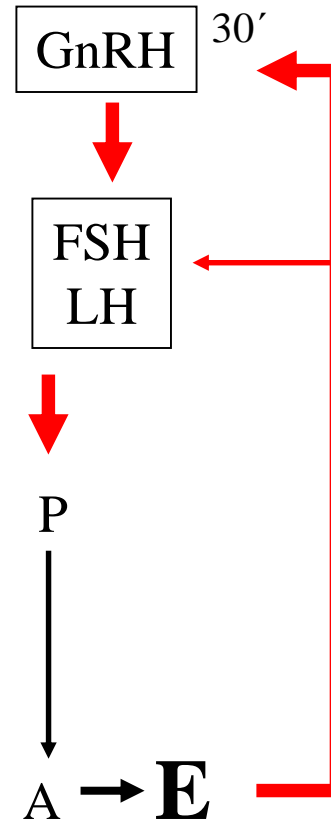
# HUMOURAL REGULATION OF THE CYCLE

Follicular phase



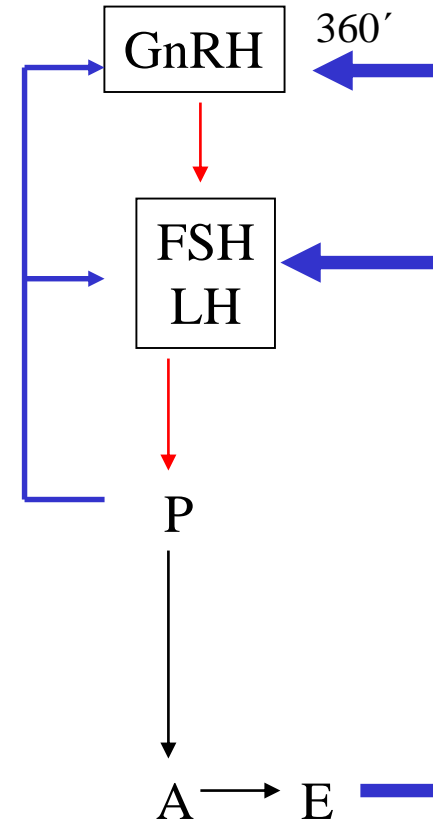
Artesia of follicle (but one!)

Ovulation



Feedback -/+/-

Luteal phase



Involution of corpus luteum

# EFFECTS OF OVARIAN HORMONES

**E**

**Secondary sexual signs** +

Adipose tissue: store (predilection), (critical amount)

Bone tissue: **absorption**

closure of fissures

development of pelvis

Total water retention: +

Sexual behaviour: +

**P**

-

-

-

-

-

+

-

Ovaries: **maturation of follicles**

Hysterosalpinx: **motility**

Uterus: **proteosynthesis**

**vascularisation and proliferation of endom.**

**EXCITATION**

**motility**

**proteosynthesis**

**secretion of endom. glands**

**glycogen**

**RELAXATION**

Cervix: **colliquation of „plug“**

Vagina: **cornification of epithelium**

Mamma: **growth of terminals**

**creation of „plug“**

**proliferation of epithelium**

**growth of acines**

## ASSISTED REPRODUCTION

1. STIMULATION OF OOGENESIS (maturation of more follicles) –  
pharmacologically
2. STIMULATION OF SPERMIOGENESIS – life style, diet, glycaemia, vitamin E
3. INSEMINATION - treated sperm, applied deeply into the uterus
4. IVF (*in vitro* fertilization) – ovarian stimulation, timed obtaining of the oocytes,  
extracorporeal fertilization, cultivation, assisted hatching, embryotransfer,  
substitution therapy

## CONTRACEPTION (BIRTH CONTROL)

- RHYTHM METHOD
- SPERMICIDE SUBSTANCES
- COITUS INTERRUPTUS
- CONDOM, PESSARY
- IUD (intra-uterine device)
- **HORMONAL CONTRACEPTIVES** – risk of failure less than 1%
- VASECTOMY AND LIGATION OF HYSTEOSALPINX

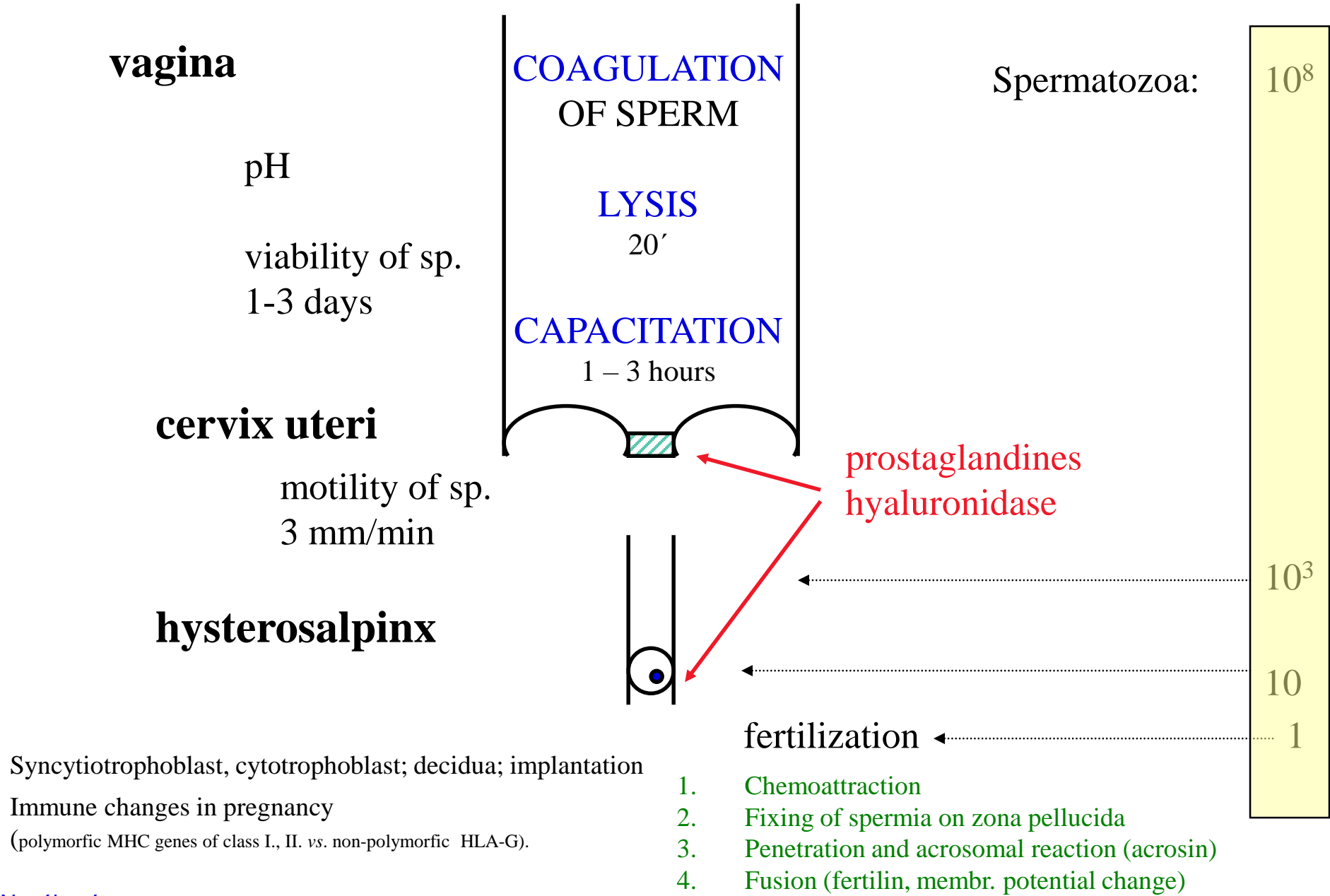
*Hormonal curettage (excochleation). Substitution therapy in climacterium.*

## HORMONAL CONTRACEPTION

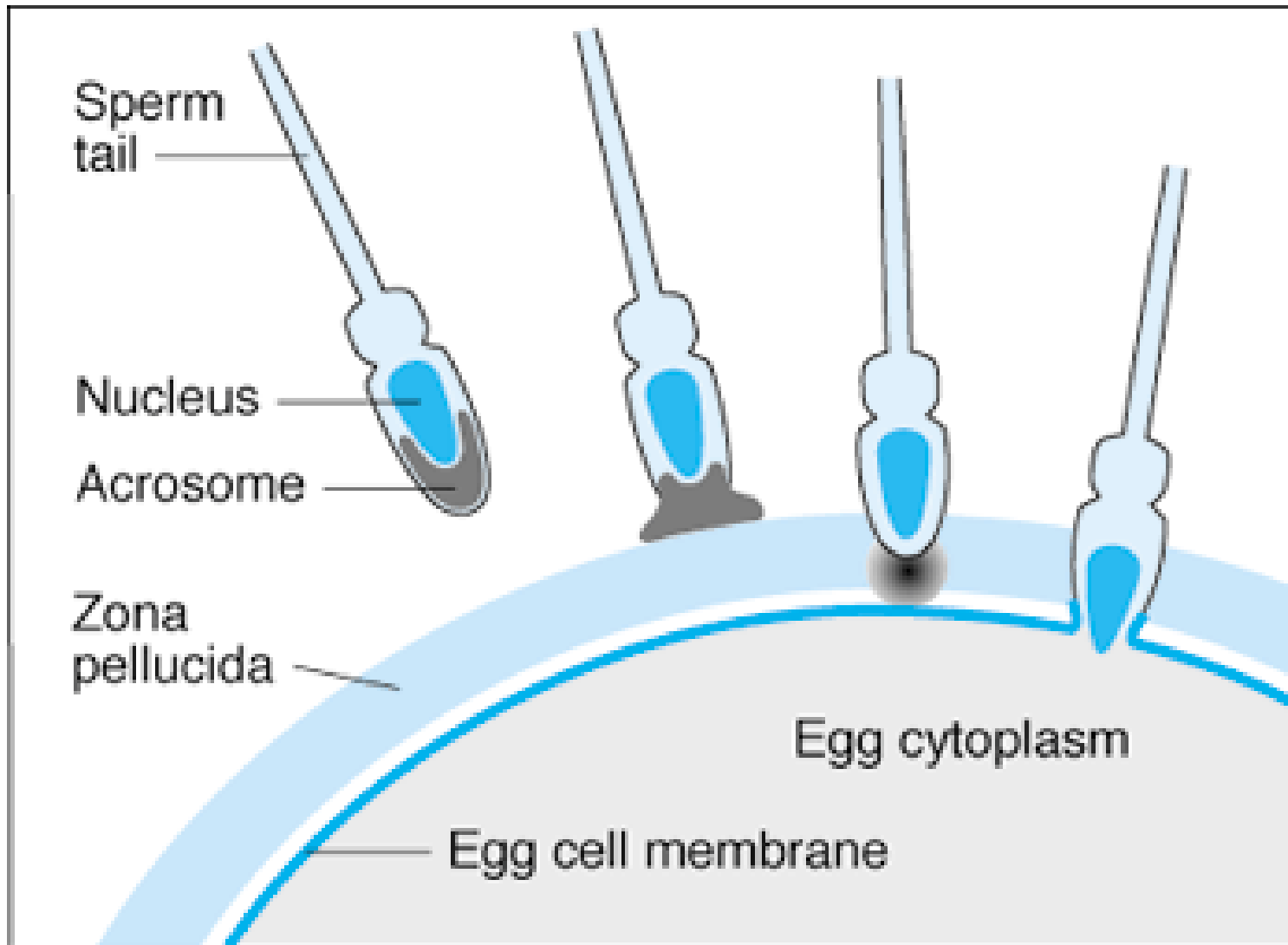
- substitution with gonadal hormone(s) at the lowest possible concentration in order to keep negative feedback to hypothalamus and adenohypophysis
- block of ovulation by suppression of hypothalamic releasing hormones (block of preovulatory surge of LH)
- changes of character of cervical plug (progestin thickens mucus)
- changes of endometrium (suppression of its growth)
- changes of hysterosalpinx motility

# **PREGNANCY, PARTURITION, LACTATION**

# FERTILISATION PROCESSES



Syncytiotrophoblast, cytotrophoblast; decidua; implantation  
 Immune changes in pregnancy  
 (polymorphic MHC genes of class I, II. vs. non-polymorphic HLA-G).





**HORMONAL PROFILE DURING PREGNANCY**

(8<sup>th</sup> week!!!)

*Corpus luteum graviditatis*

*Placenta*

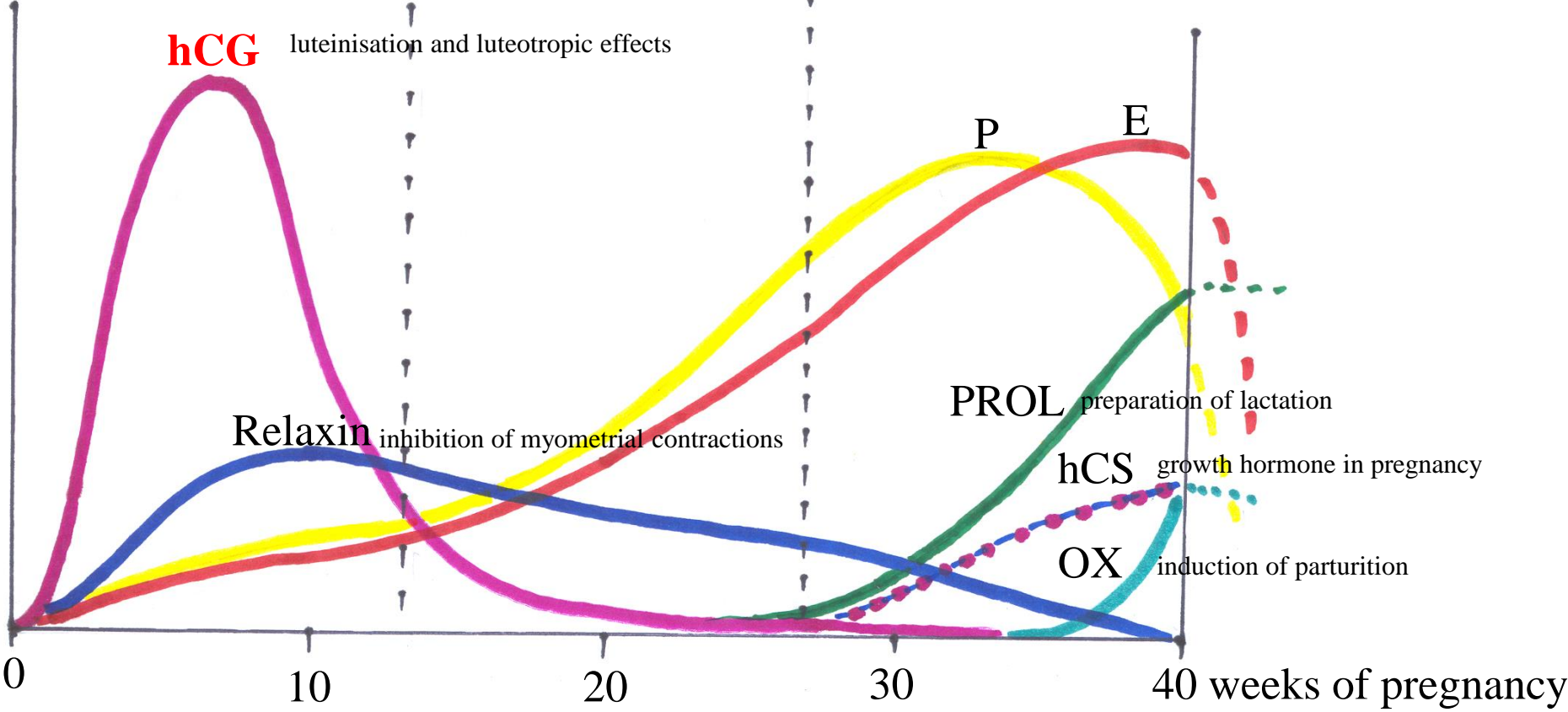
↓  
E, P, Relaxin

↓  
hCG, hCS, E, P

I.

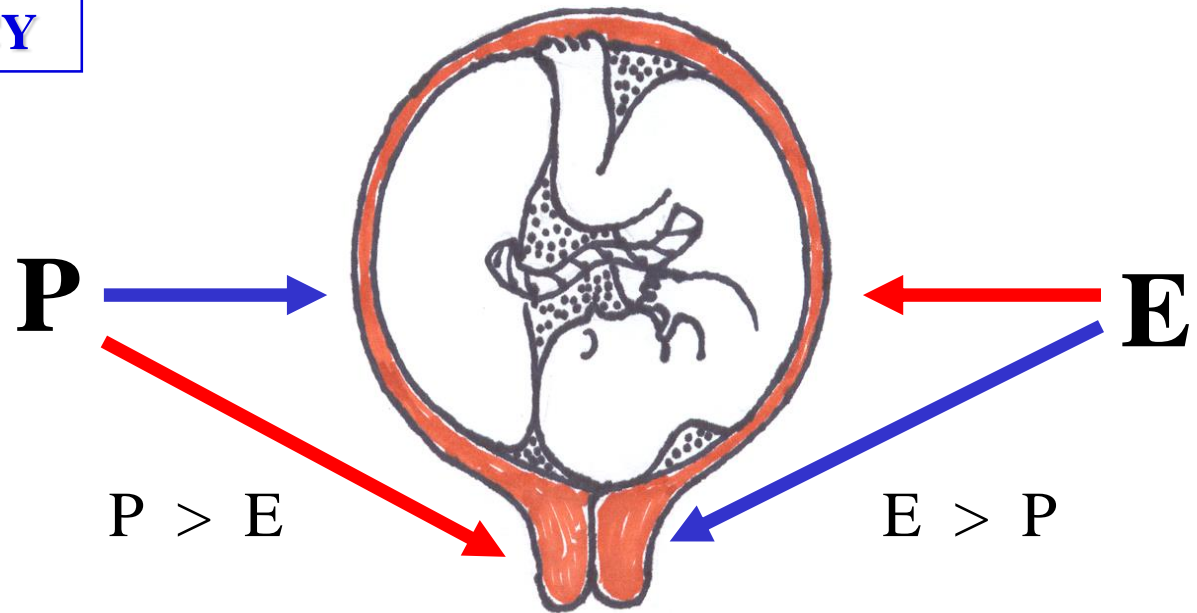
II.

III. trimester



- STH
- TSH
- ACTH
- INS
- KORT
- ALD
- T<sub>4</sub>
- PTH

**RELATIONSHIP BETWEEN P:E IN PREGNANCY**



Foetal-placental unit

MOTHER	PLACENTA	FOETUS
cholesterol	pregnenolone	DHEAS 16OH-DHEAS
	progesterone	cortisol aldosterone
DHEAS	estradiol Estriol	

Excretion of estriol in urine  
– index of foetal status

# PHYSIOLOGICAL CHANGES DURING PREGNANCY

## Changes of reproduction organs

- **Uterus**
  - Growth (from 60 g to 1000 g), change of position
  - Hyperaemia
  - Functional differentiation of myometrium
- **Cervix**
  - Changes of colour, consistency; shortening
  - Hypertrophy a hyperplasia of glandules – mucus plug
- **Vagina**
  - Changes of colour, increase of secretion
- **External genitals**
  - Vascularization, vasocongestion (changes of colour)

## Somatic changes

- **Breasts**
  - Growth – alveolar as well as ductal part
  - Enlargement and hyperpigmentation of mammillae and areolas
- **Skin**
  - Increase in subcutaneous fat
  - Changes in connective tissue
  - Hyperpigmentation

## Endocrine and metabolic changes

## Immunological changes

## Psychic changes

# ENDOCRINE and METABOLIC CHANGES DURING PREGNANCY

## Endocrine glands

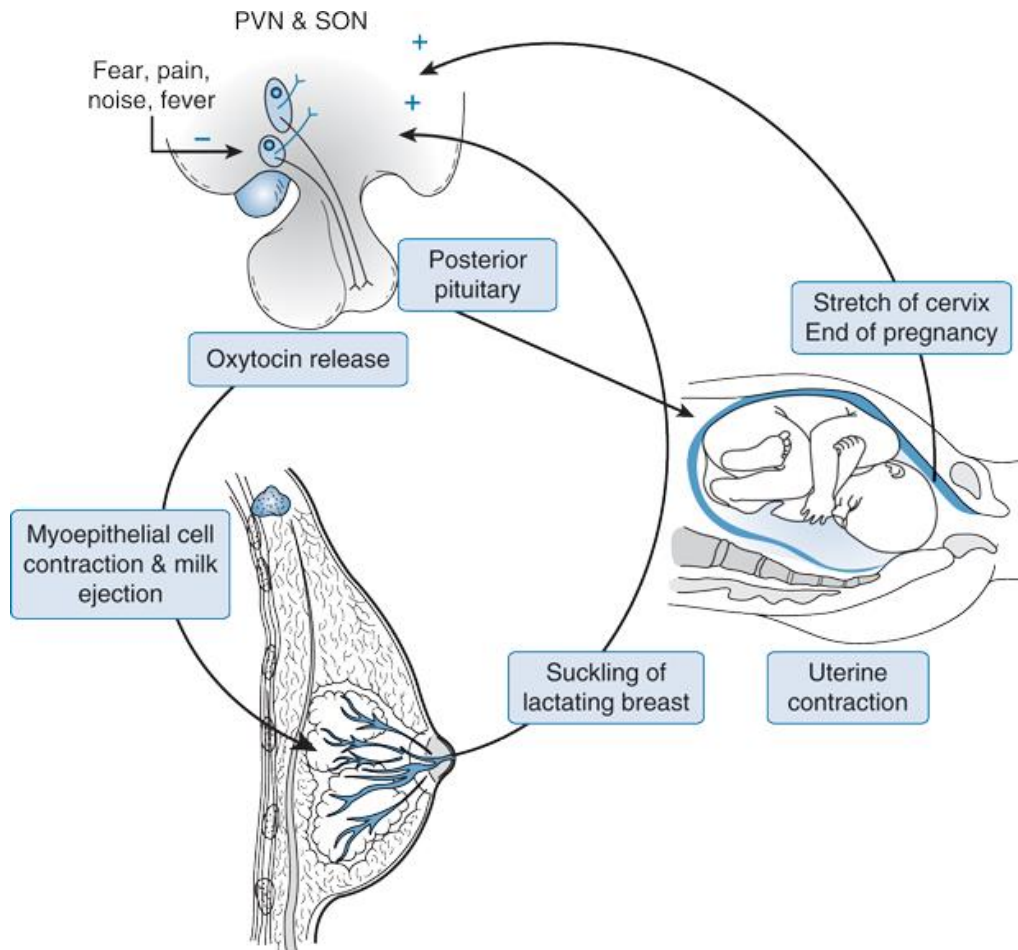
- **Thyroid gland**
  - Slight hypertrophy (E), increase in thyroxine production, in III. trimester BEE +25%
- **Parathyroid glands**
  - Increase in production of parathormone
- **Adrenal glands**
  - Increase in production of aldosterone
- **Pancreas**
  - Hyperplasia of Langerhans islets

## Anterior pituitary gland

## Metabolism

- **Weight gain:** 12-15 kg
- **Glycaemia**
  - Glc – main energetic source for foetus
  - Prohyperglycemic state
  - Decrease of renal glucose reabsorption, increase in glomerular filtration - glycosuria
  - Gestational diabetes
- Increased demand for **Ca** (1300 mg), **P** (1200 g) and **Fe** (18 mg/day)
- **Water retention:** + 6.5 l

# OXYTOCIN



- **Mechanoreceptors/tactile receptors**
- **Magnocellular neurons** (PVN, SON)
  - inhibition by endogenous opioids, NO, GABA
  - Autocrine (+ ZV)
  - Prolactin, relaxin (-), Estrogens (+)
- OXT receptors ( $G_{q/11}$ ) – effect of up/down regulation
- Acts together with prolactin and sex hormones

## Functions

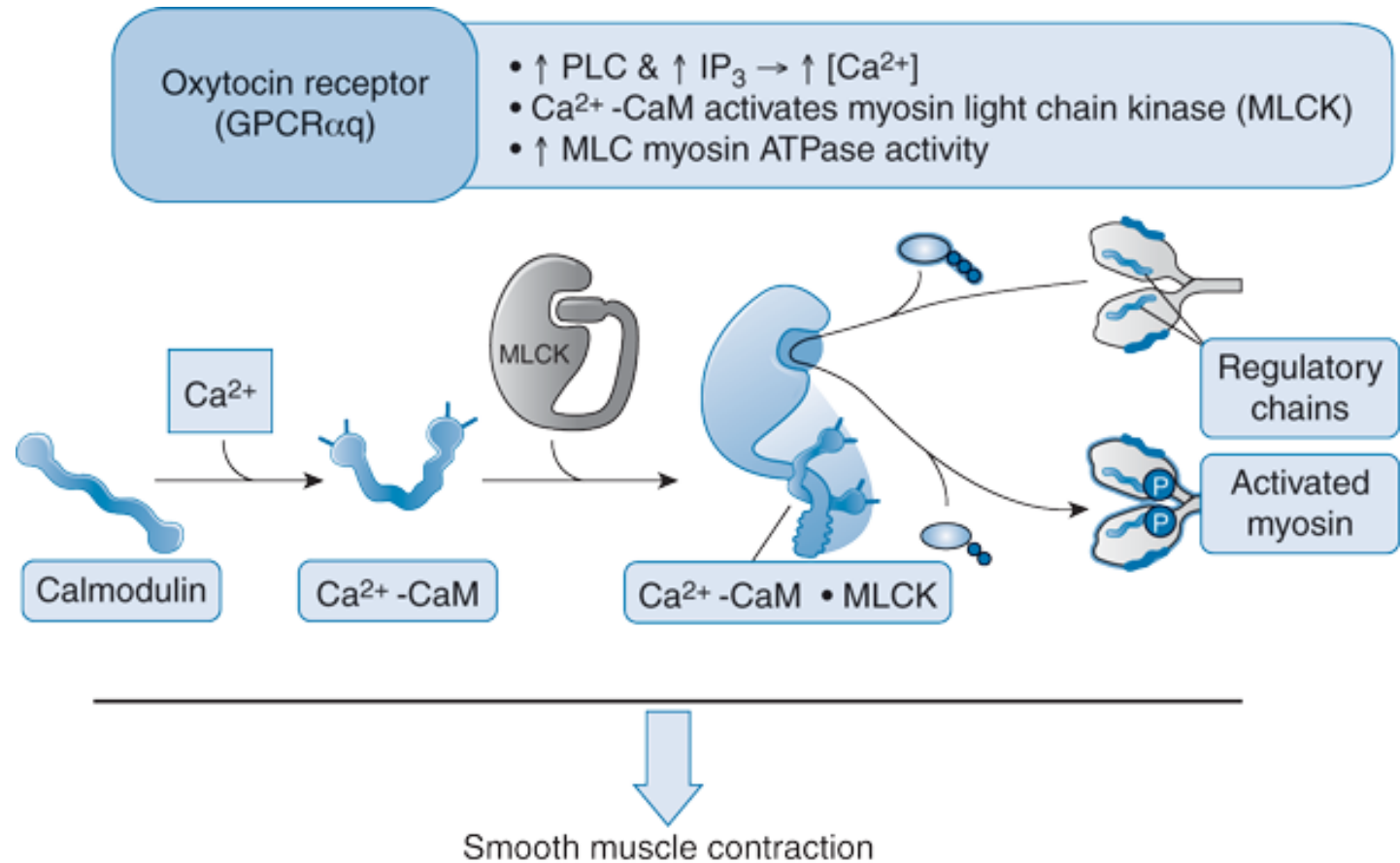
- Lactation (under 1 min) – **MILK EJECTION**
- Parturition
  - rhythmical contractions of smooth muscles (gap-junction, stimulation of prostaglandin synthesis – extracellular matrix)
  - postpartum bleeding
  - uterus involution
- Ejaculation (males)
- Behavior

## Other functions and places of synthesis

- CNS
  - Stimulation of ACTH secretion through CRH
  - Stimulation of ADH/induced vasoconstriction
  - Stimulation of prolactin secretion
  - Memory traces recollection inhibition
  - Maternal behavior

# OXYTOCIN RECEPTORS

- OXT receptors ( $G_{q/11}$ )
  - Myoepithelial cells
  - Myometrium
  - Endometrium
  - CNS
- PLC,  $IP_3$ ,  $Ca^{2+}$
- Target molecule – MLCK (myosin light chain kinase)



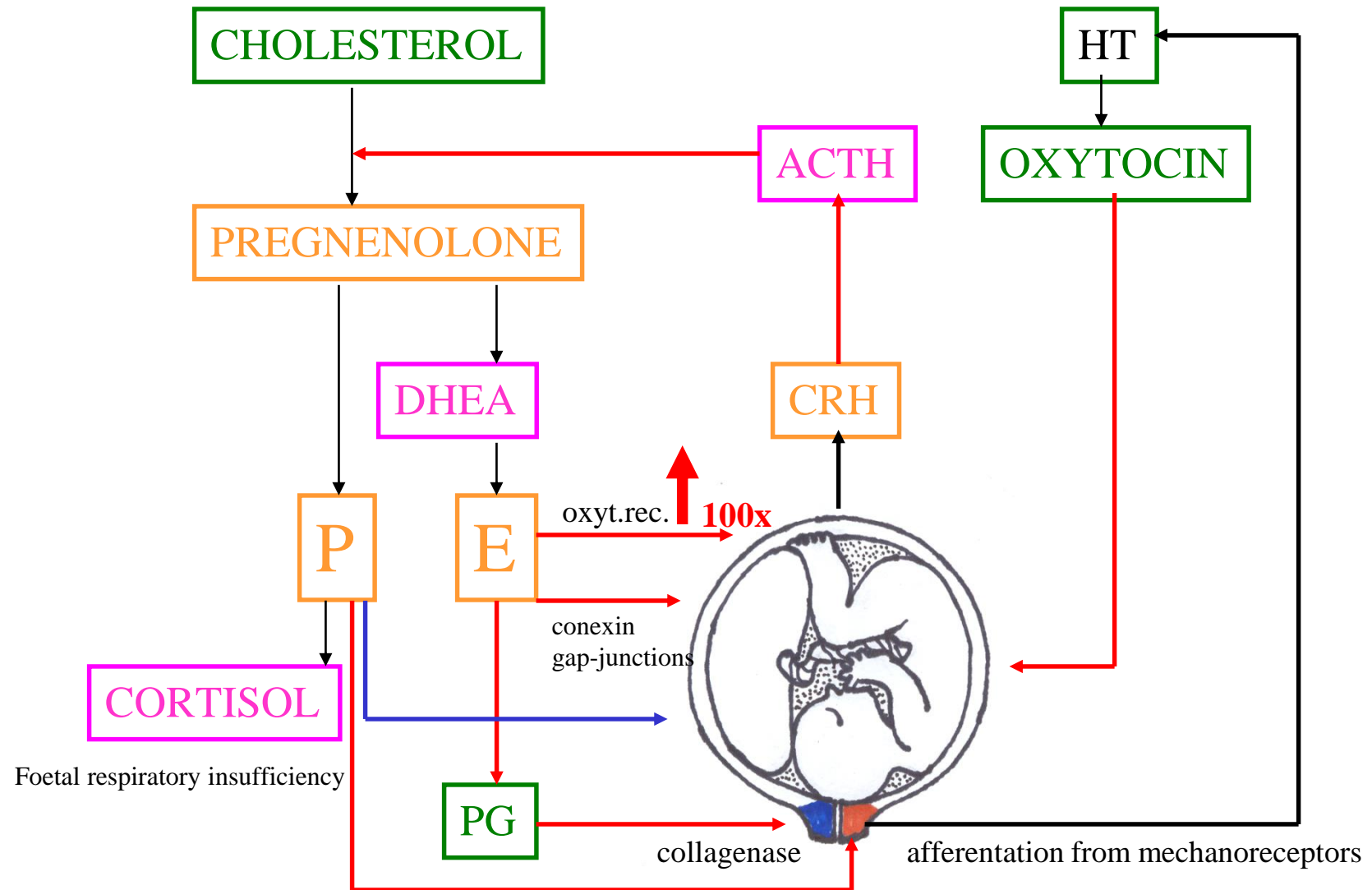
# OXYTOCIN

- 9 AA, differs from ADH in 3. a 8. AA
- Precursor molecule is synthesized in the same location as ADH (*nucleus paraventricularis*)
- Stimulus for synthesis: dilatation of birth path caused by pressure of foetus and stimulation of mechanoreceptors at breast nipple
- **Reflex release**: during breast-feeding, orgasm
- Main effects – on reproduction system:
  - **Uterokinetic effects** (induction of parturition), milk ejection, involution of uterus
  - In men: probably increases contractions of smooth muscle in *ductus deferens*
- Regulation of water and mineral metabolism – natriuretic effect, potentiation of ADH effect
- **Effect on memory**: opposite to ADH effect – inhibits forming of memory and its recollection
- Note: Melanocytes inhibiting factor – from oxytocin, modulates certain types of receptors, modulation of melatonin effects (melatonin – epiphysis, together with glomerulotrophin and DMT, circadian/circannual biorhythms, controlled by hypothalamus, information from retina)

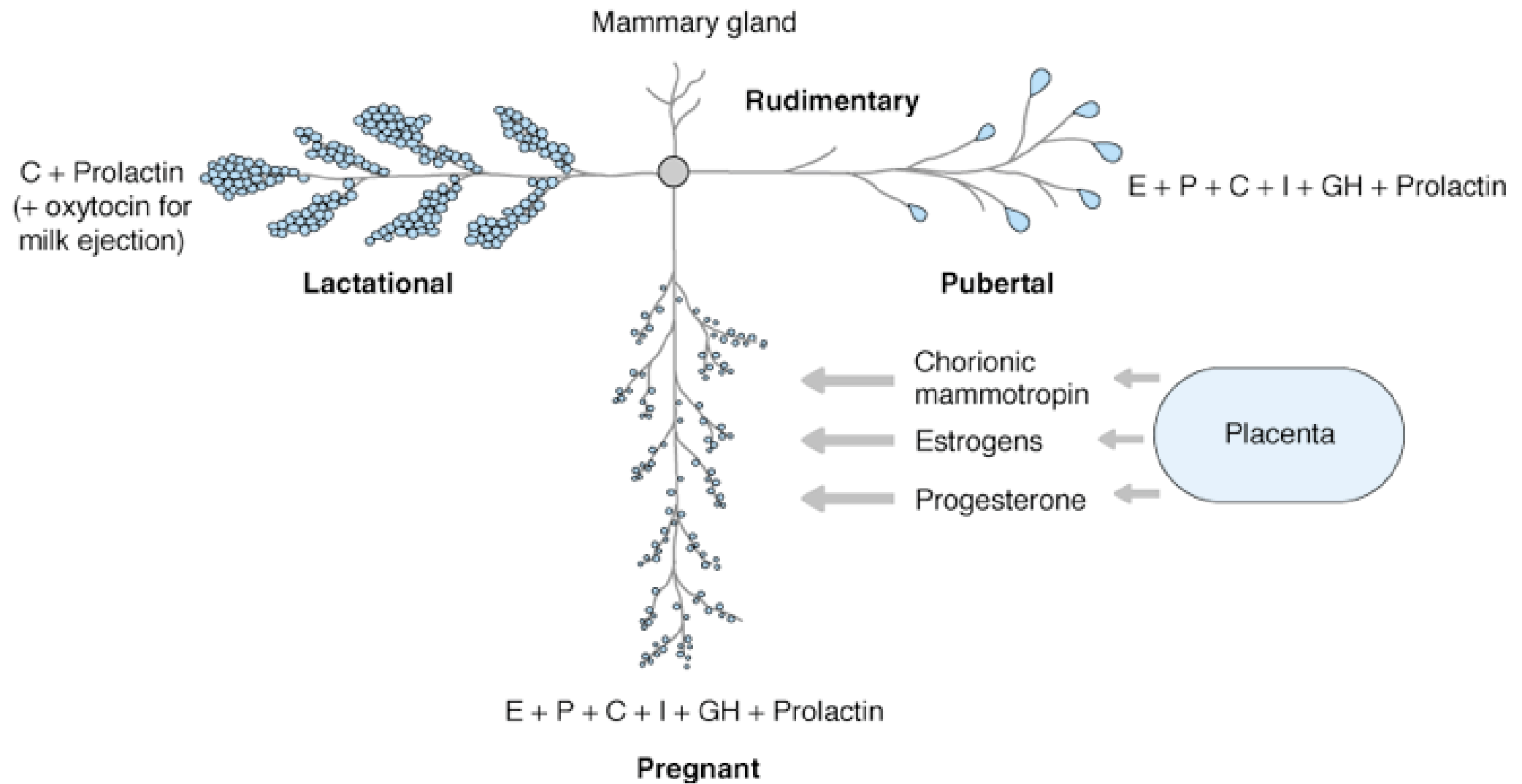
# INDUCTION OF PARTURITION

P > E → E > P

maternal  
placental  
foetal

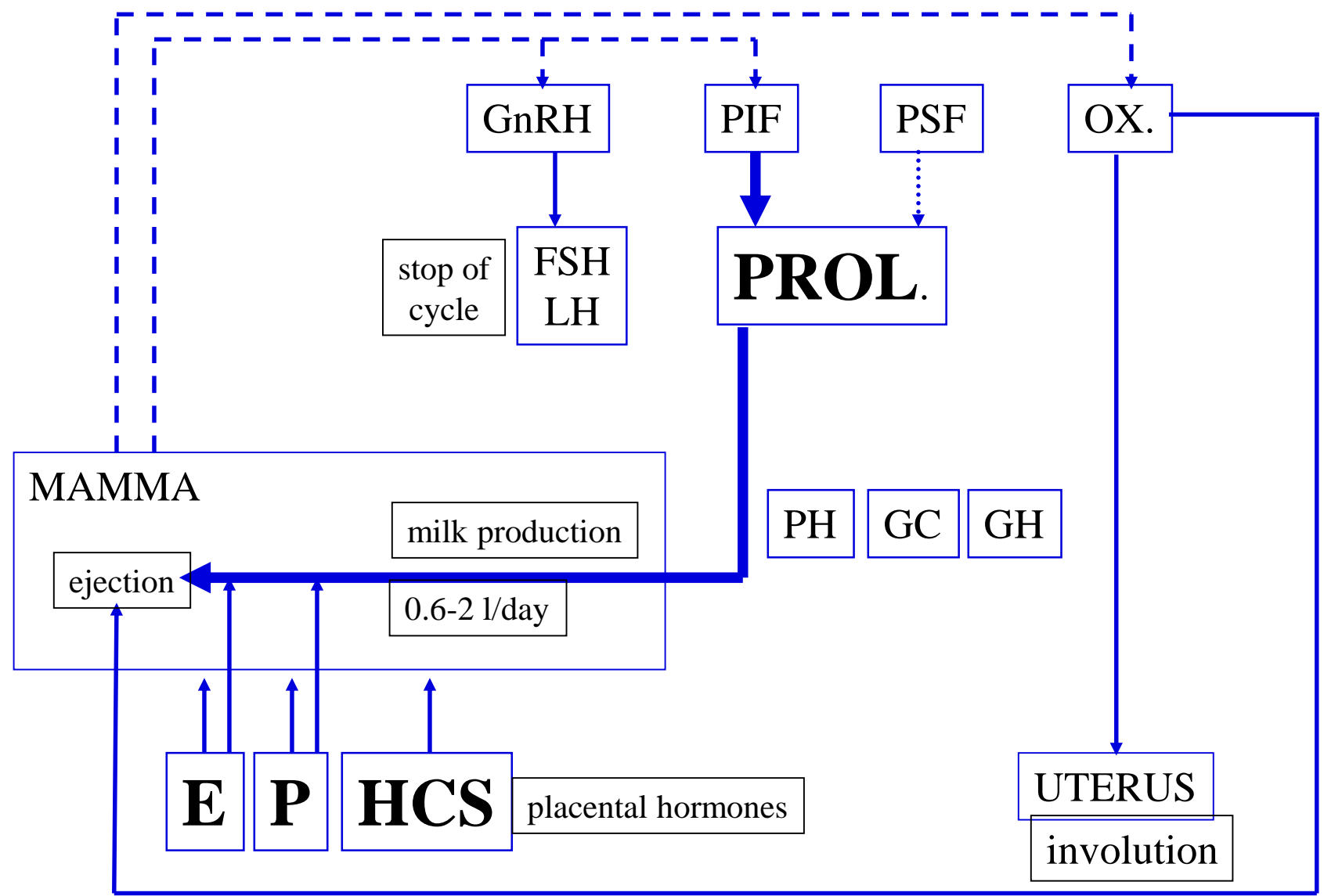






# LACTATION

1 – 3 days after birth; initiated by decrease of oestrogens' concentrations *post partum*



Composition of milk: water (88%), fat (3,5%), lactose (7%), proteins (1%)  
 trace minerals (Ca), vitamins, antibodies

(hyperprolactinaemia)

# LEPTIN AND REPRODUCTIVE FUNCTIONS

## LEPTIN IN PREGNANCY

Synthesised by placenta from the 18<sup>th</sup> week of pregnancy.

Dramatic increase in maternal blood after the 34<sup>th</sup> week.

Synthesis in placenta, foetal adipose tissue and growing maternal adipose tissue.

**BUT** leptin plasmatic levels in non-pregnant women do not correspond to adipose tissue amount (BMI).

Decrease after delivery down to the levels typical for non-pregnant women.

Leptin may play a role in proliferation and function of trophoblast, and thus affects foetal growth.

## LEPTIN IN NEWBORNS

Plasmatic levels of leptin correspond to newborn body mass and BMI.

Blood of newborn contains maternal and foetal leptin.

Girls have higher levels of leptin than boys.

It is supposed, that sex differentiation of plasmatic levels of leptin is already genetically given, since it is not affected postnatally by sex hormones.