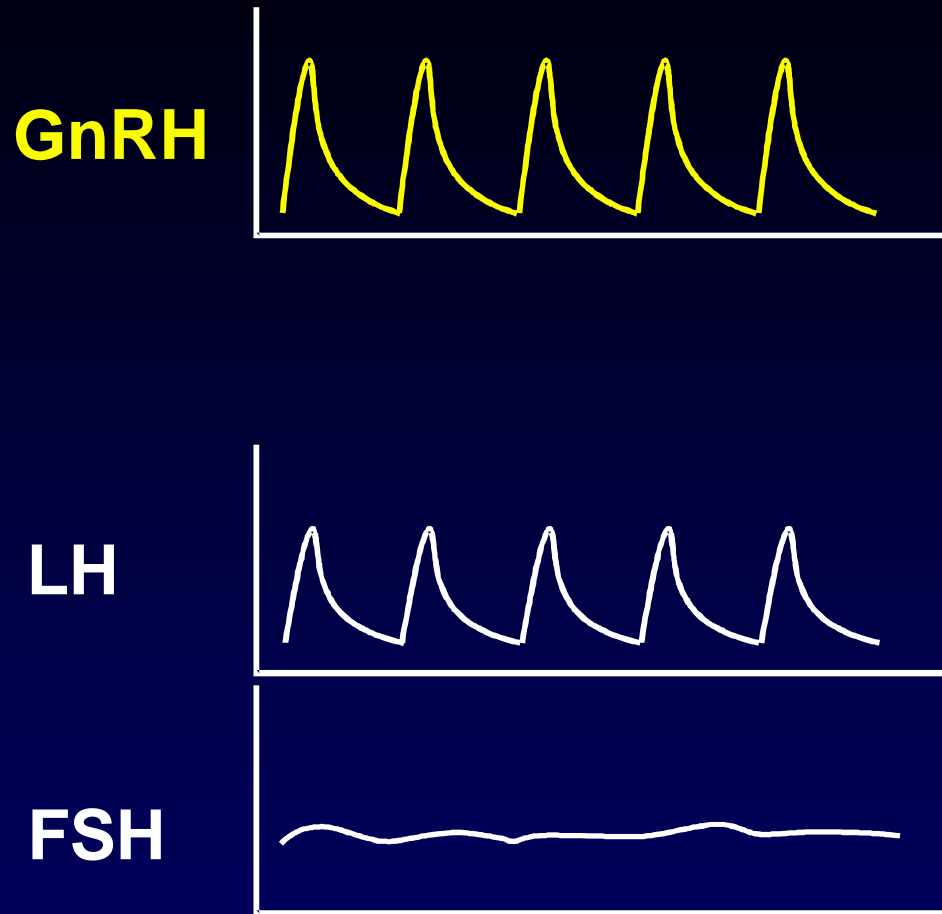
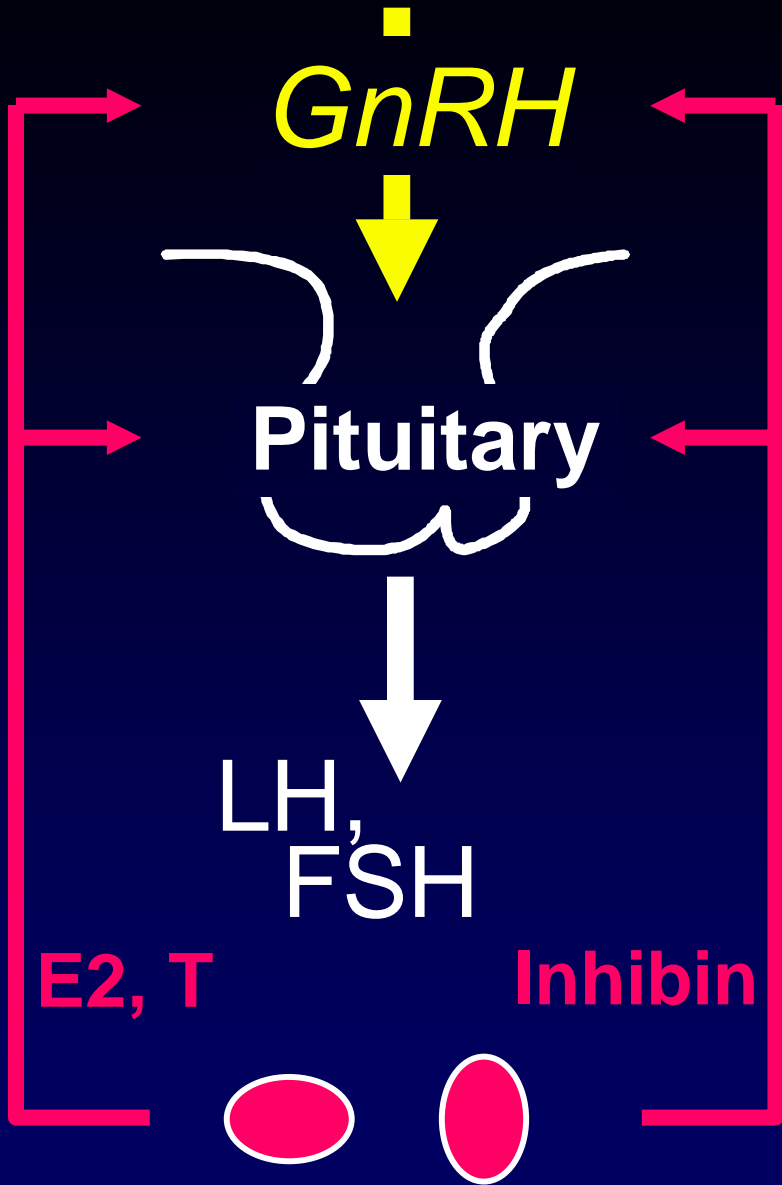
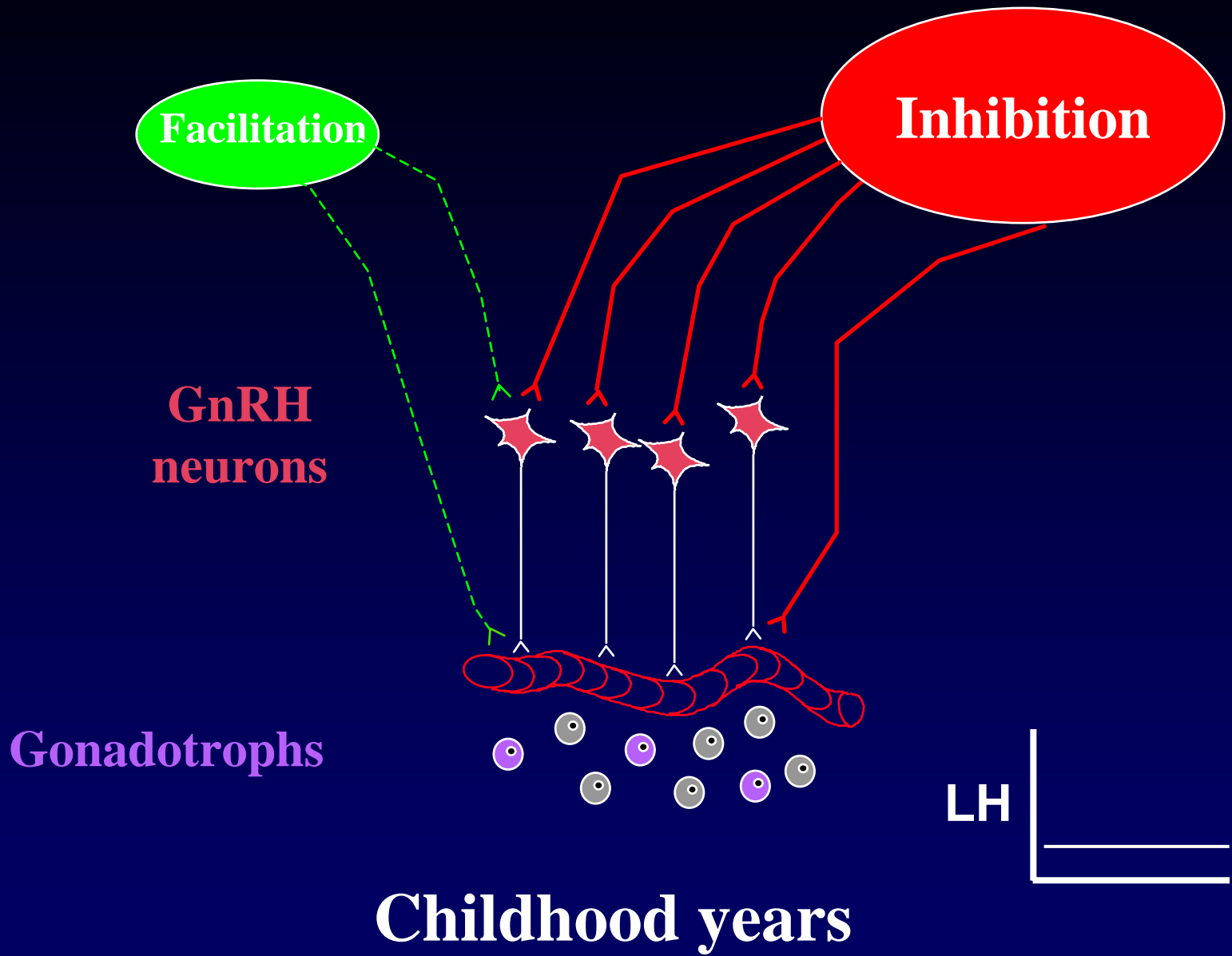


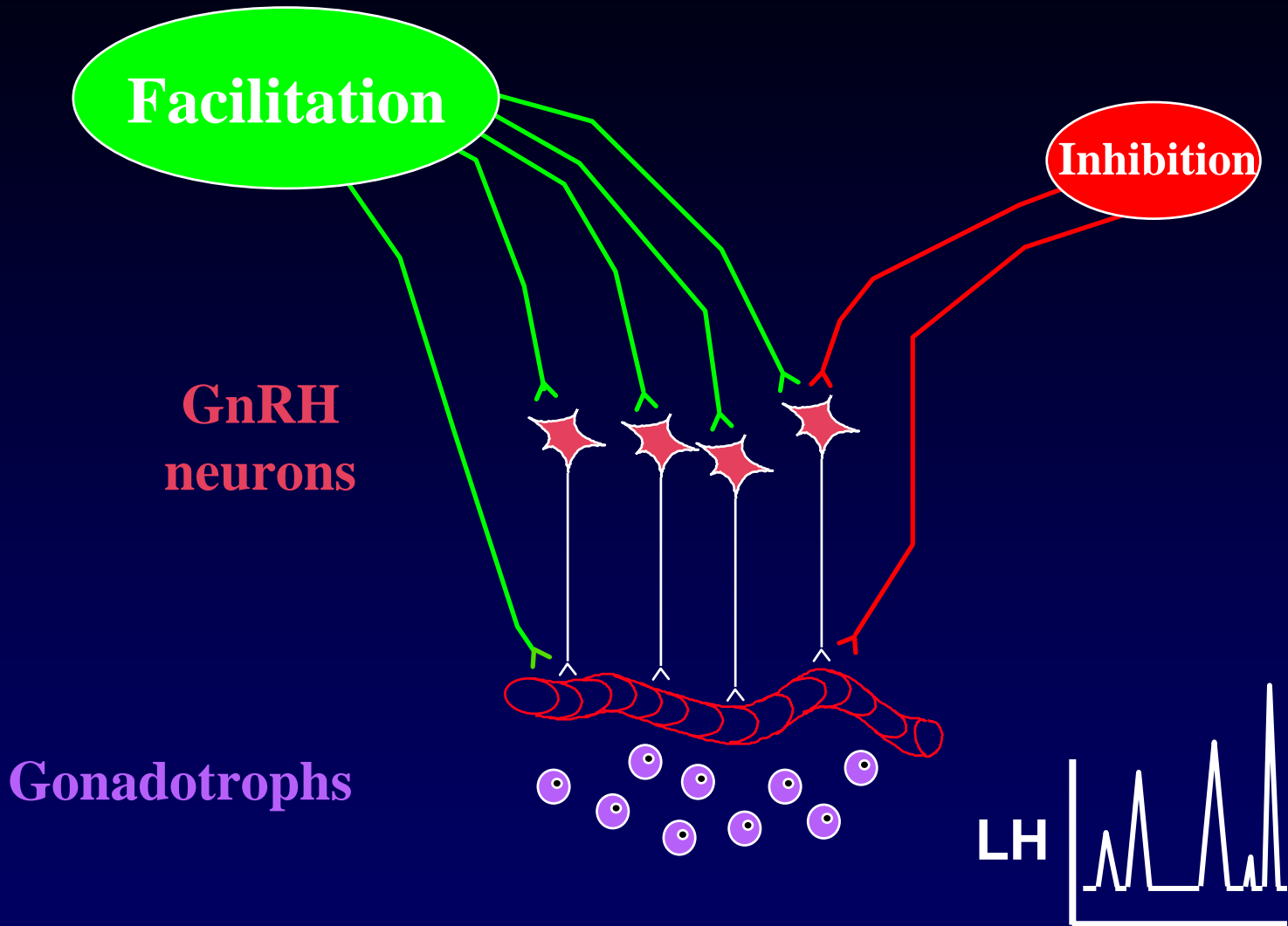
# The Menstrual Cycle

**François Pralong**  
**Service of Endocrinology**









**Facilitation**

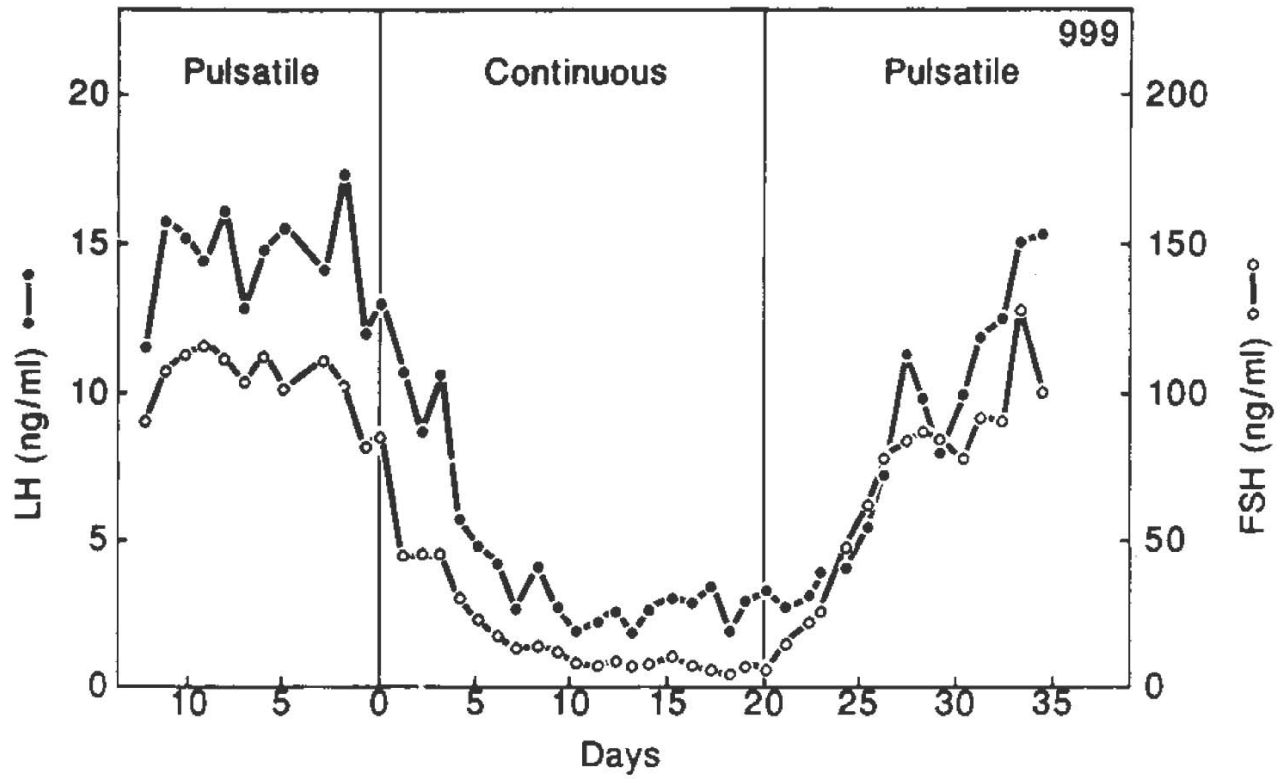
**Inhibition**

**GnRH  
neurons**

**Gonadotrophs**

**LH**

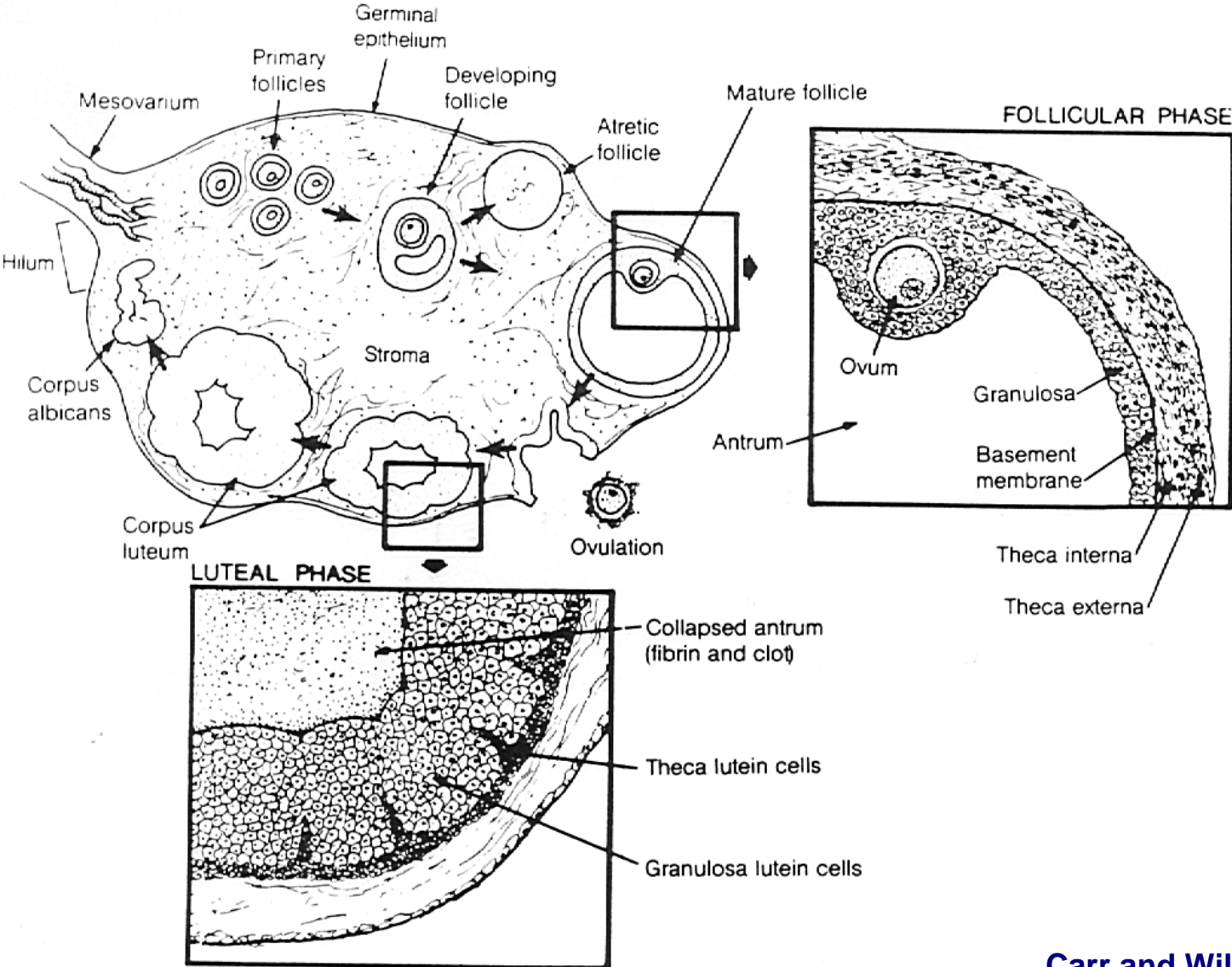
**Post-pubertal Period**



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**Belchetz et al, Science 1978;**

# Functional anatomy of the ovary

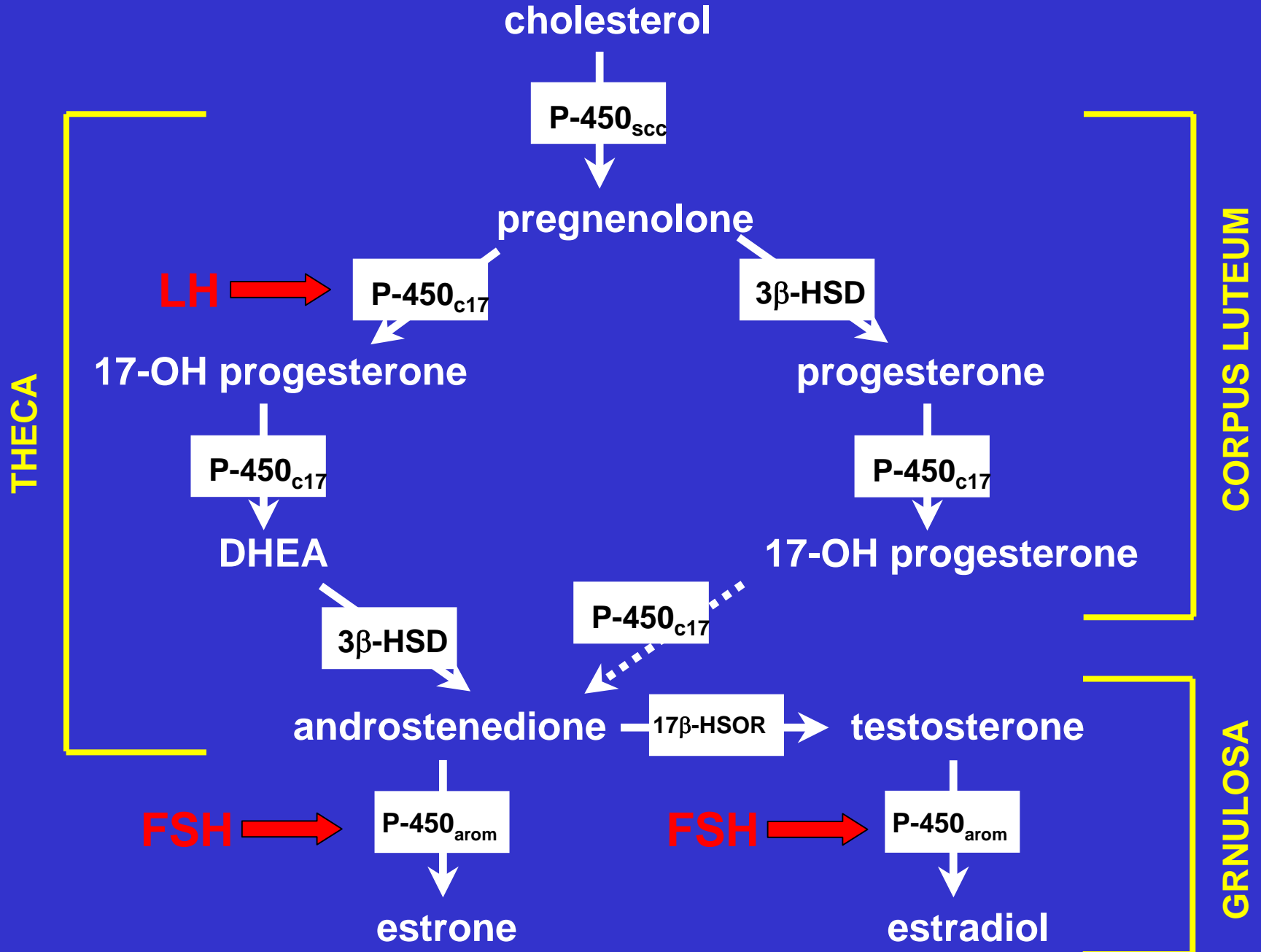


# The Two Functions of the Ovary

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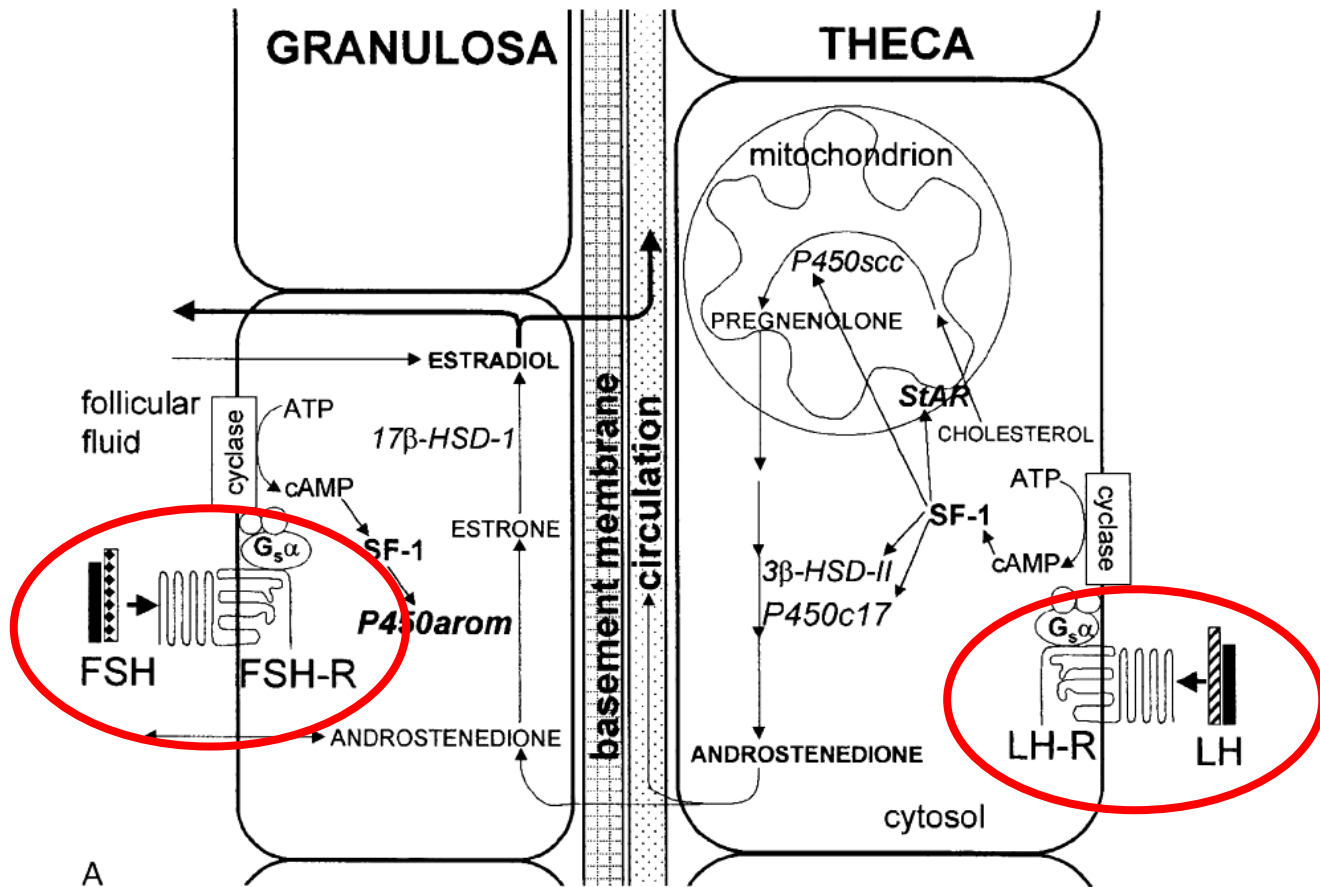
**Gametogenesis**

**Steroidogenesis**

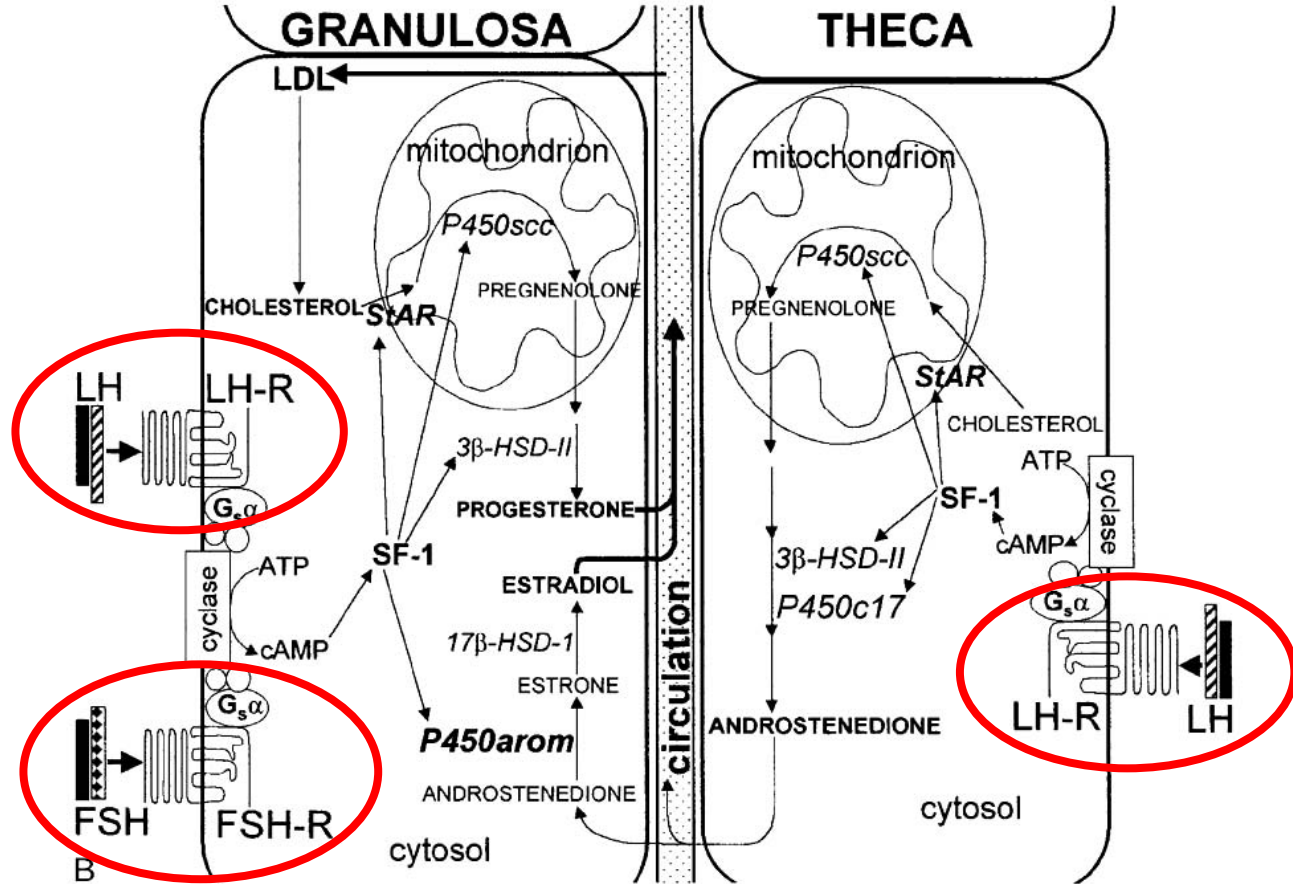




# Two-cell hypothesis in pre-ovulatory follicles

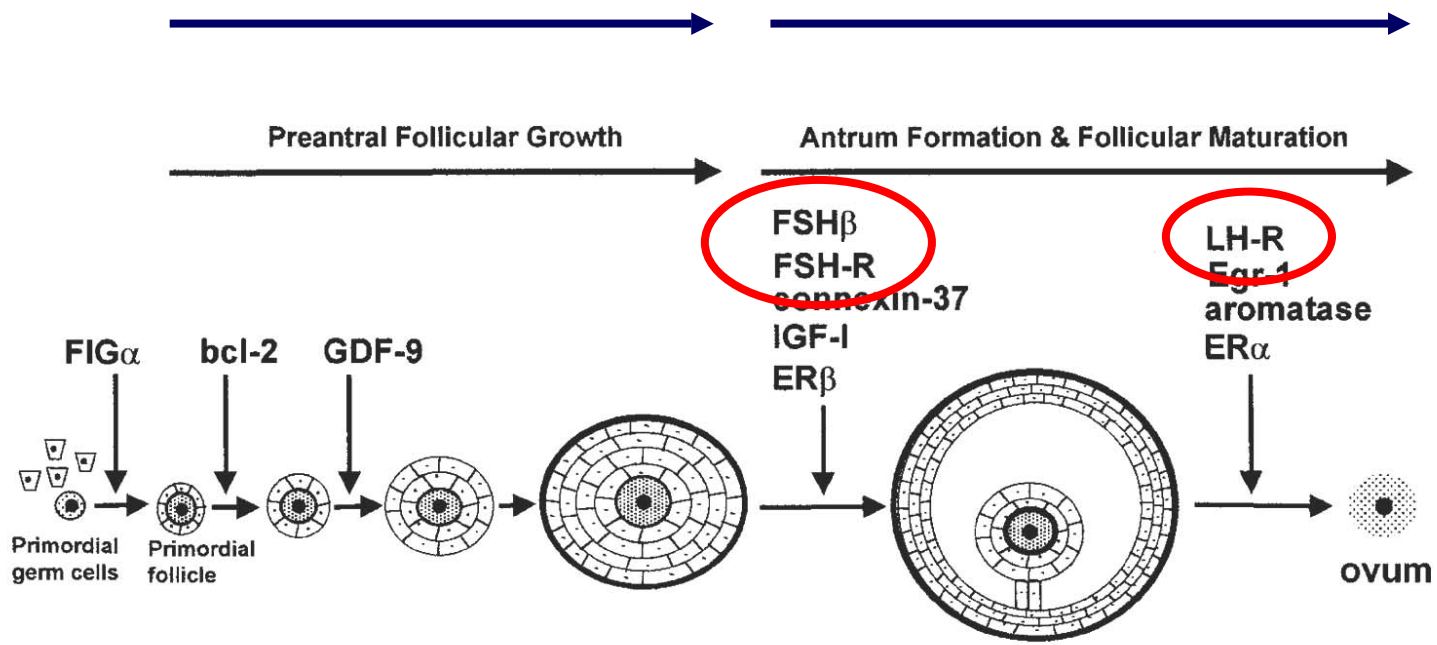


# Two-cell hypothesis in the corpus luteum



# Gonadotropin-independent

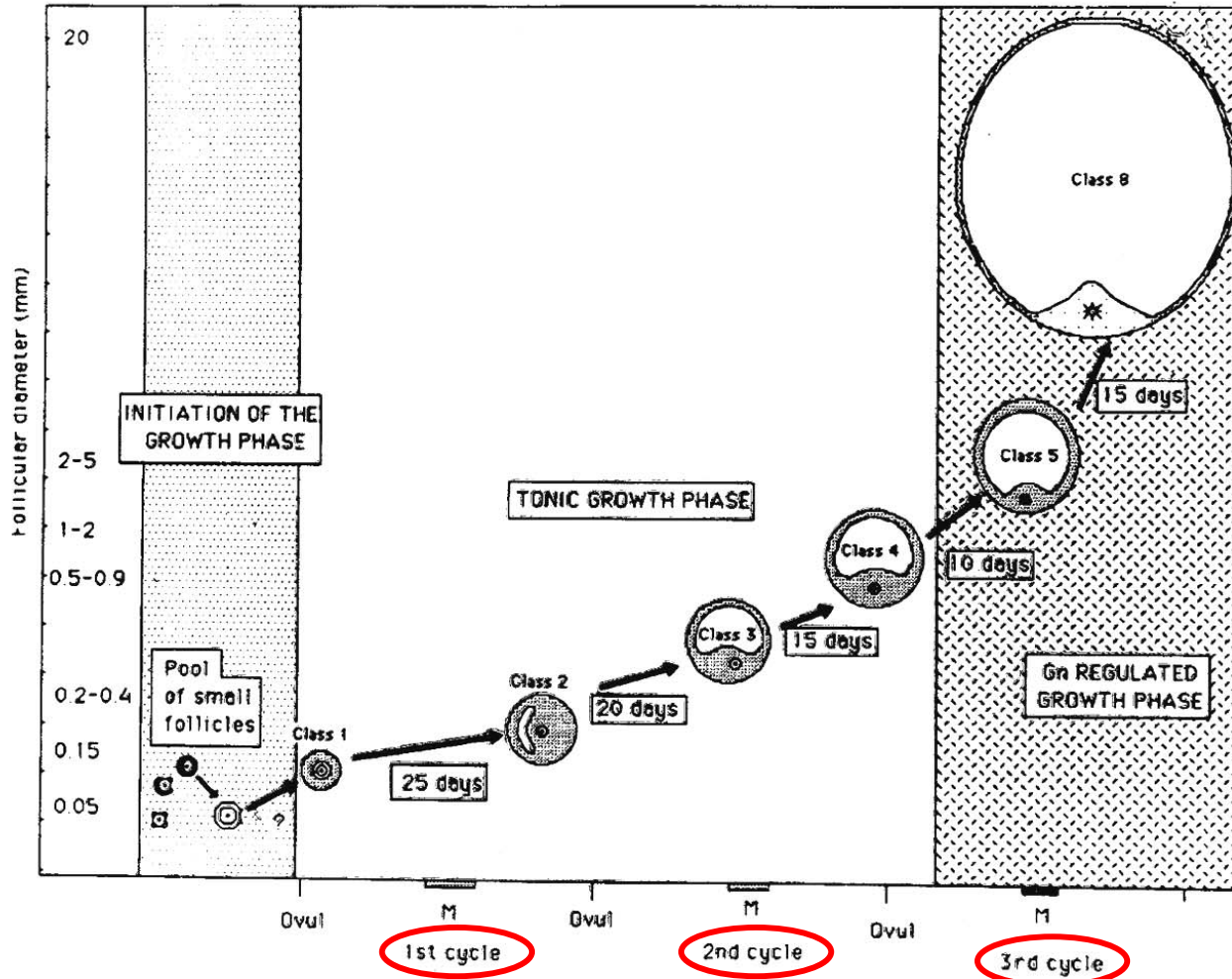
# Gonadotropin-dependent



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Gonadotropin-dependent

Heavily gonadotropin-dependent



# The different types of follicles

## Pre-antral follicles

Primordial follicles: single ovum + uni-cellular layer of granulosa cells

Primary follicles : ovum grows + additional layer of granulosa cells

Primary follicles : ovum grows + granulosa + thecal cells (origin: ovarian stroma)

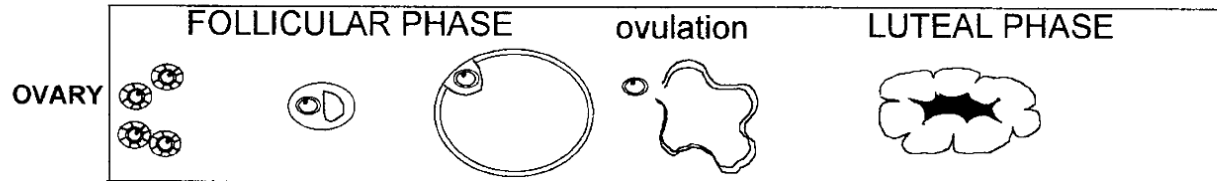
# The different types of follicles

## Antral follicles

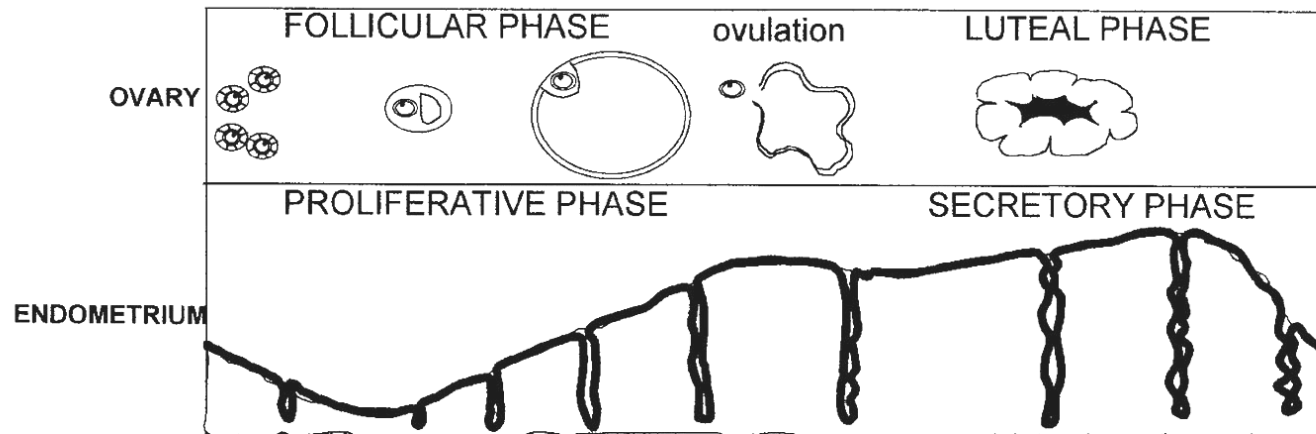
Accelerated growth of theca and granulosa cells, stimulated by gonadotrophins

Secretion of follicular fluid (E2 rich) by theca and granulosa cells: antrum formation

# How does this all end up together?

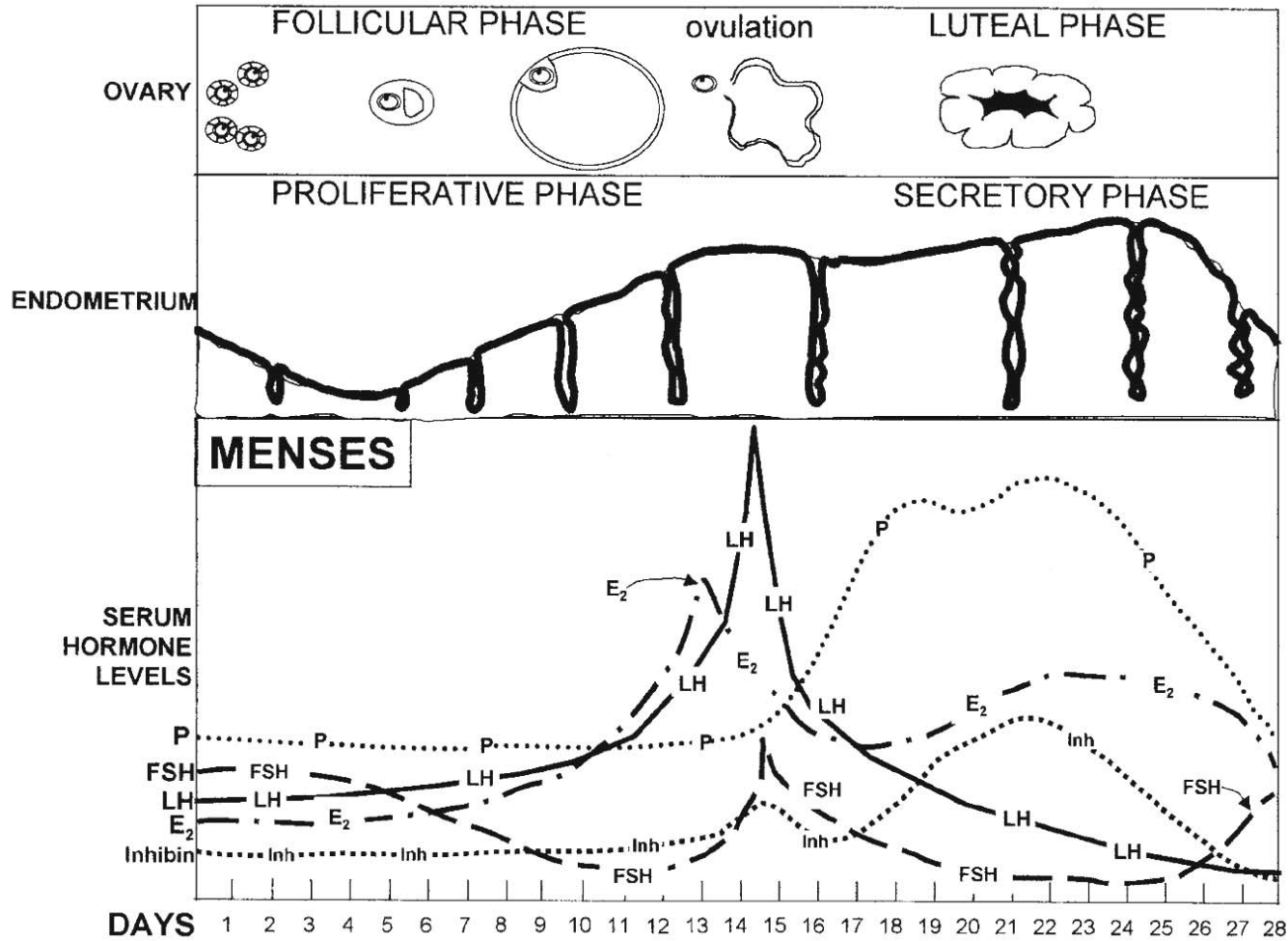


# How does this all end up together?

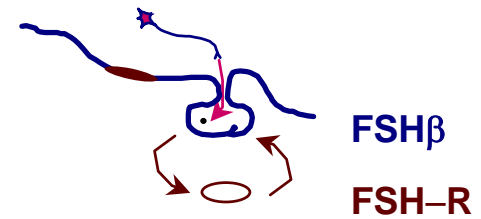




# How does this all end up together?



# FSH Deficiency - Females



## FSH $\beta$

### Three cases described

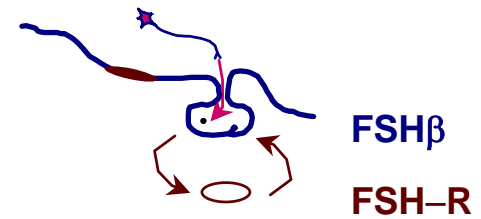
- **Phenotype:**
  - delayed puberty
  - primary amenorrhea
  - normal response to FSH with achievement of fertility

## FSH-R

### Finnish study

- **Phenotype:**
  - primary amenorrhea
  - ovarian dysgenesis with normal karyotype

# FSH Deficiency - Males



## FSH $\beta$

### Two cases described

- **Phenotype:**
  - 1) delayed puberty, low testosterone and absent spermatogenesis
  - 2) normal puberty and virilization, spermatogenic arrest

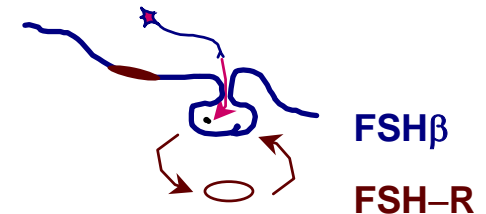
## FSH-R

### Finnish study

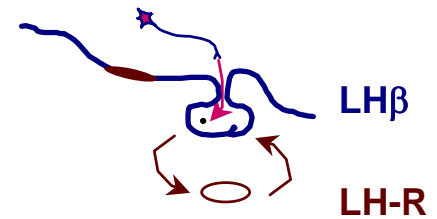
- normal virilization
- decreased testicular volume
- variable suppression of spermatogenesis

# Role of the FSH/FSH-R System

- Important for estrogen production, follicular maturation and fertility
- Role of FSH in spermatogenesis remains unclear:
  - variable spermatogenesis in FSH-R mutations
  - absent spermatogenesis in FSH $\beta$  mutations



# LH Deficiency - Females

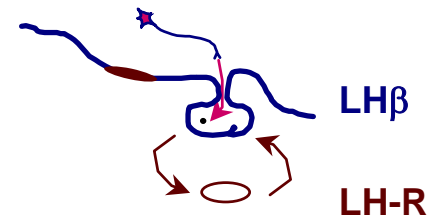


## LH-R

**No LH- $\beta$  mutation yet described in a female patient**

- normal external genitalia
- normal pubertal development
- primary amenorrhea
- **no pre-ovulatory follicles**

# LH Deficiency - Males



LHβ

LH-R

## Two cases described

Bio-inactive LH

Impaired heterodimer

- **Phenotype:**

- normal male
- delayed puberty
- response to hCG:

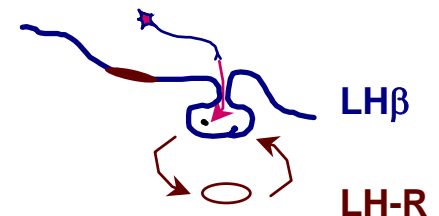
## Broad spectrum of phenotypic expression of inactivating mutations

- pseudohermaphroditism and complete azoospermia
- micropenis, delayed puberty and arrest of spermatogenesis

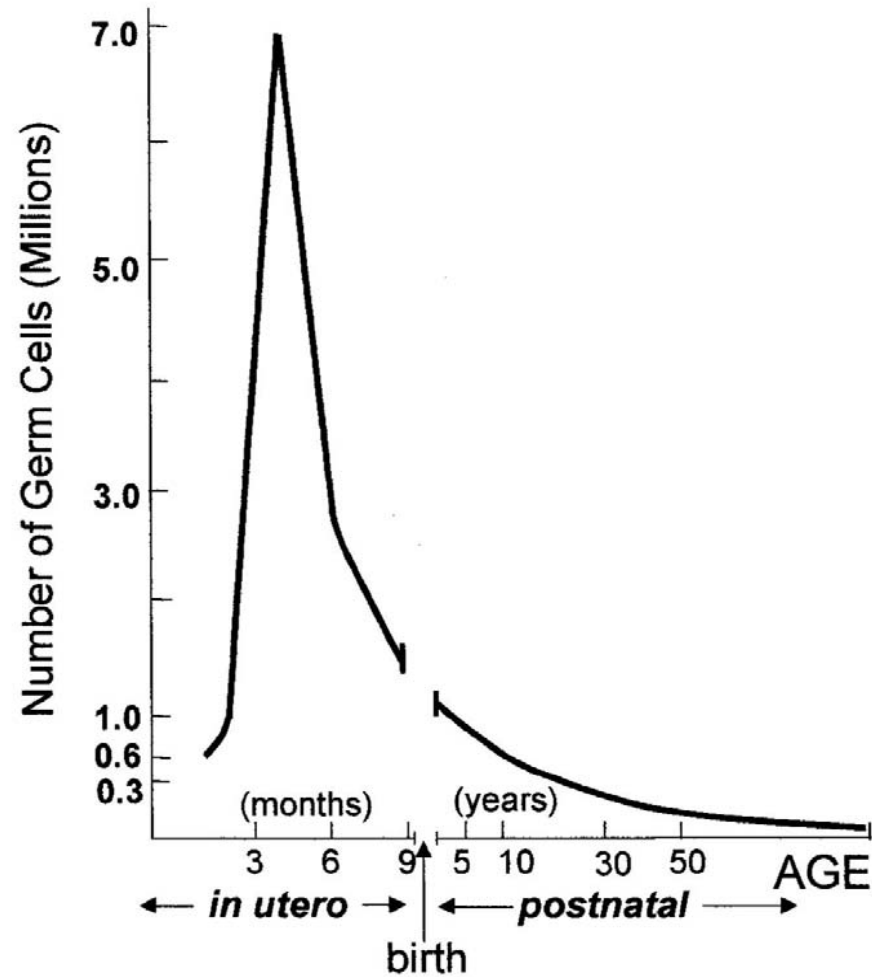
# Role of the LH/LH-R System

- Important for normal male development
- LH-R plays a role in spermatogenesis as well as ovulation

**LH-R is a candidate gene for male as well as female infertility**



# Production de cellules souches germinales par l'ovaire

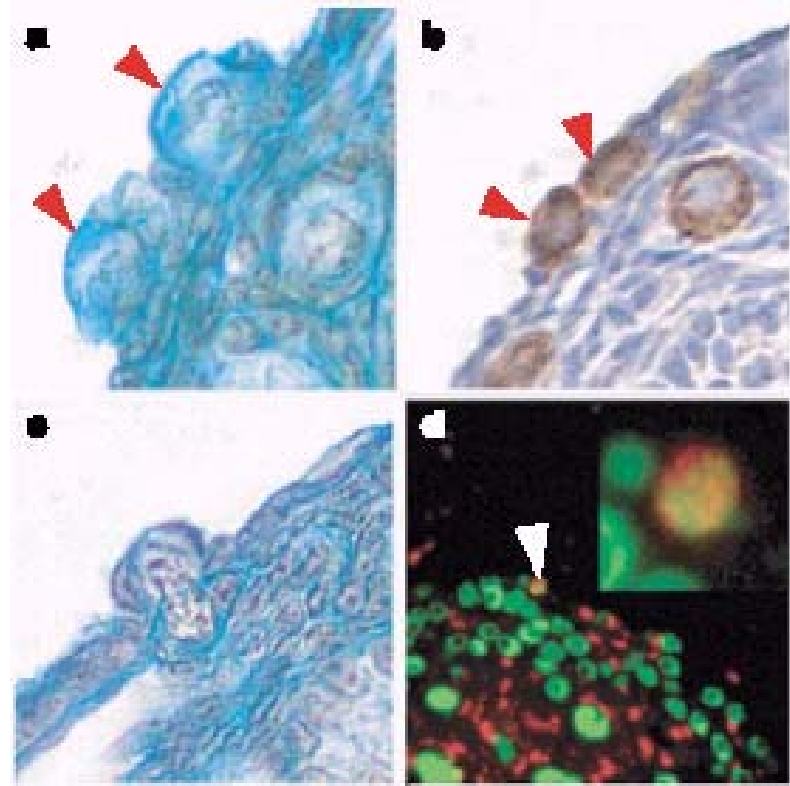




# Germline stem cells and follicular renewal in the postnatal mammalian ovary

Joshua Johnson\*, Jacqueline Canning\*, Tomoko Kaneko, James K. Pru & Jonathan L. Tilly

- Cellules souches germinales présentes dans les ovaires, à l'extérieur des follicules
- Ces cellules souches germinales se divisent



Nature, Mars 2004

# Germline stem cells and follicular renewal in the postnatal mammalian ovary

- Des cellules souches germinales transplantées dans des ovaires receveuses produisent de nouveaux follicules

