

Reproductive Cyclicality

"Reproductive cycles are present so that offspring are presented at a time providing maximal survival"



Proximate Factors

control adult reproductive activity

- photoperiod
- ambient temperature (water/air)
- rainfall
- nutrition
- ion concentration in water



Ultimate Factors

those that enhance offspring survival

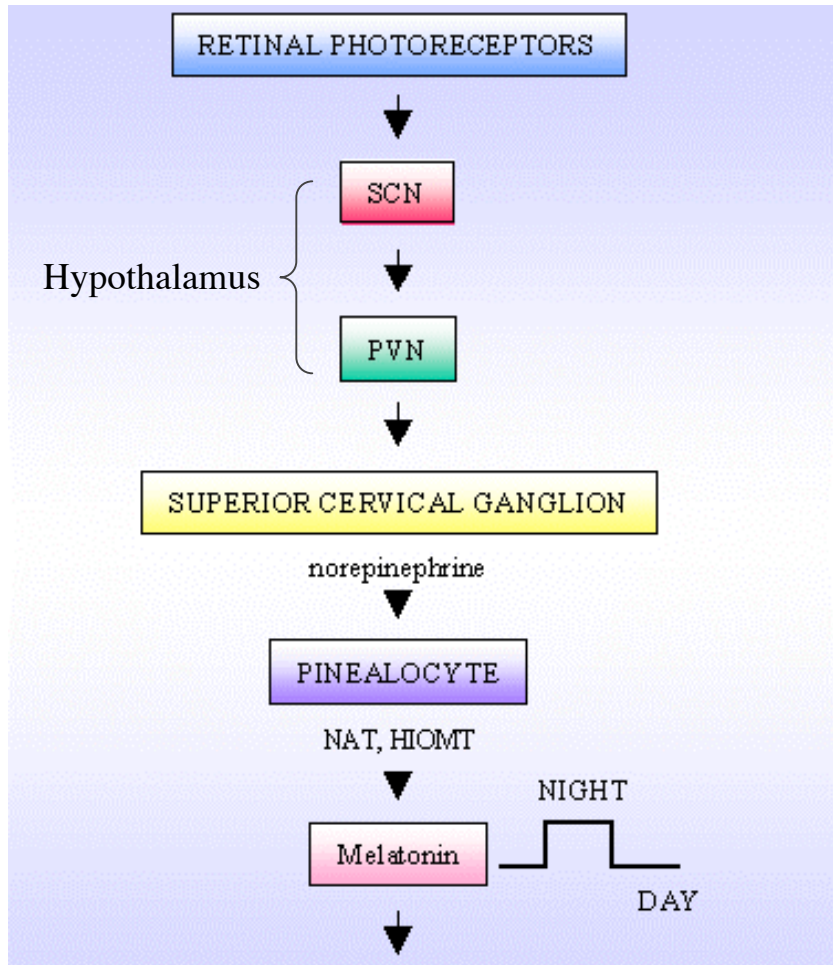
- lower predation
- nutrition for offspring



Endocrinology of Gonadal Cycles

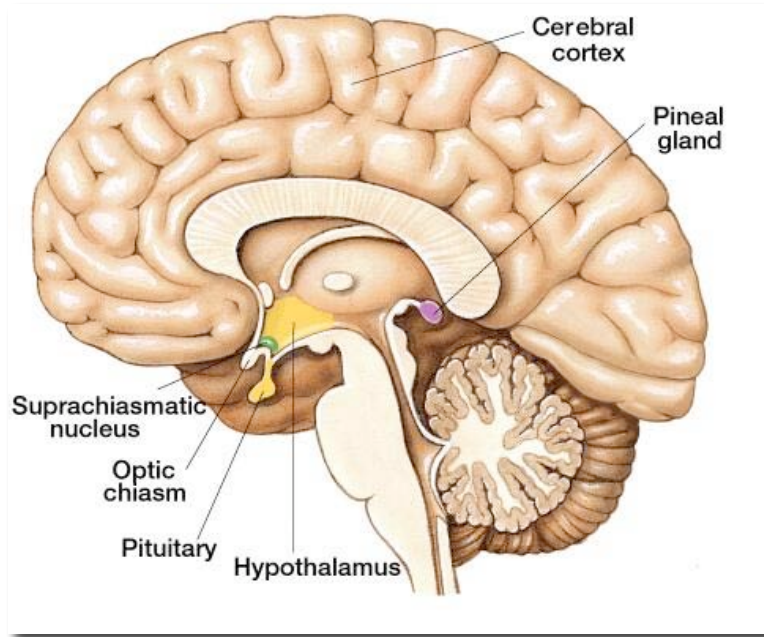
- Hypothalamic control via GnRH
 - GnRH released on environmental cues
- GnRH stimulates release of LH / FSH
 - FSH induces folliculogenesis
 - LH stimulates steroidogenesis

Photoperiod - Melatonin



- Photoperiod detected
- transmitted to the hypothalamus
- neural signal is transduced into a hormonal response
- SCN
 - suprachiasmatic nucleus
 - is an integrative center (ie., neural clock)
 - processes information provided by synchronizing agents (zeitgebers).

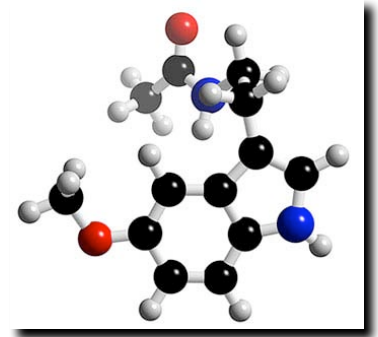
Pineal Gland



- Endocrine organ
- Secretes melatonin
 - Role in 'clock'
 - Role in reproduction



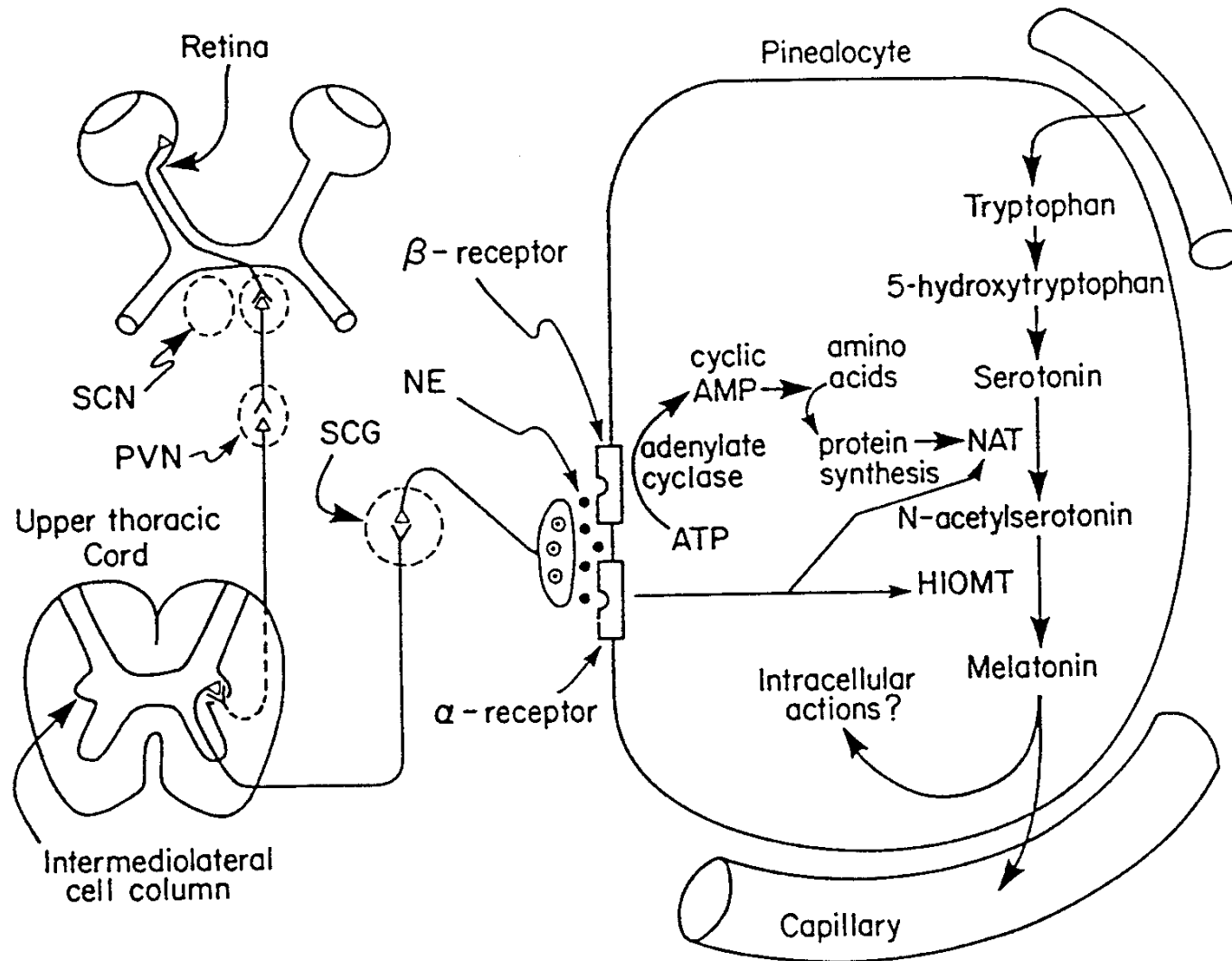
Melatonin



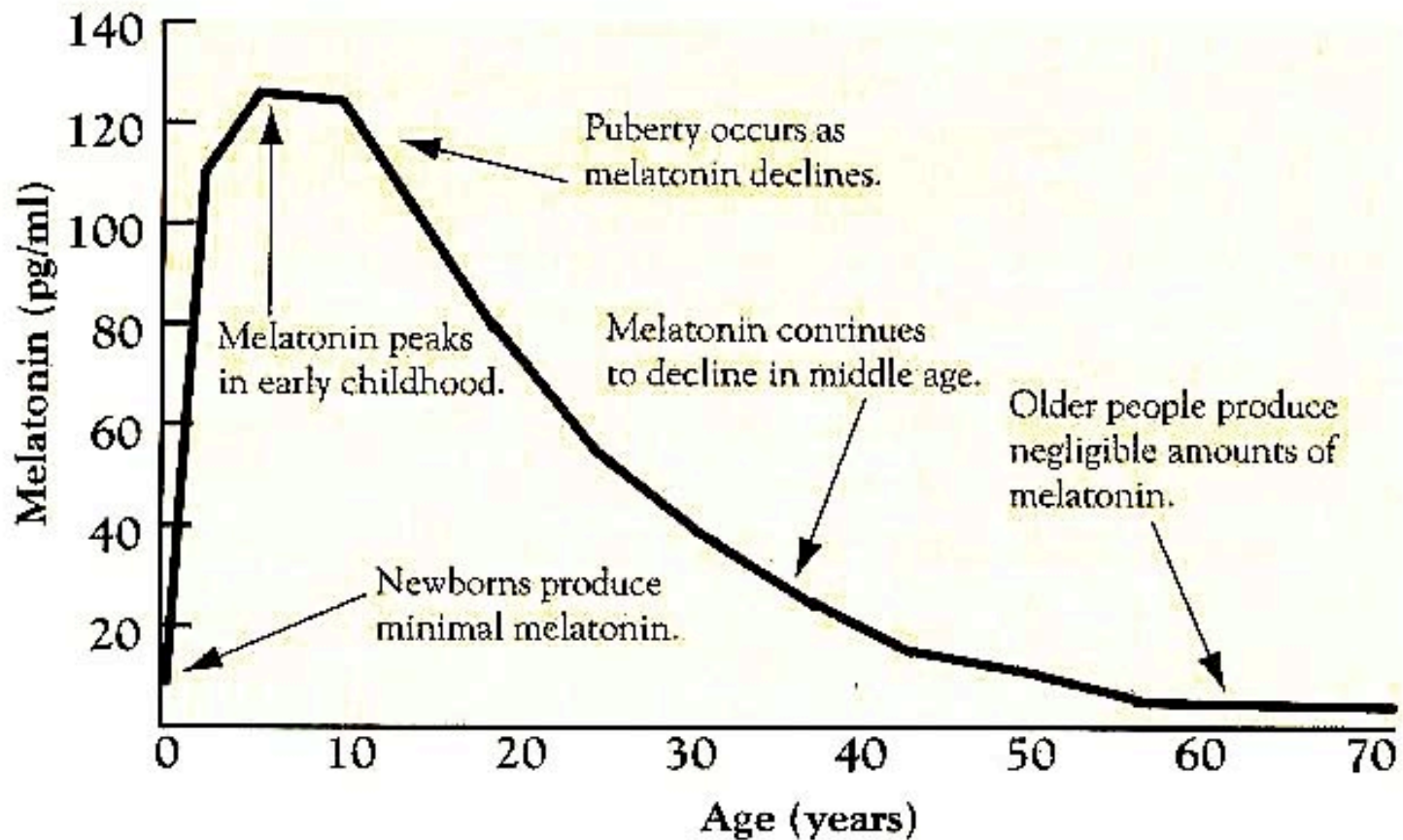
- Circadian (daily) rhythm of melatonin
 - codes the circannual cycle of seasonal reproduction
- Melatonin
 - is synthesized by the pineal gland in the darkness
 - exerts an inhibitory action on secretion of gonadotropins
 - long day -> low melatonin -> more GnRH -> reproduction
- Pinealectomy disrupts
 - the seasonal cadence of reproduction in animals responsive to photoperiod



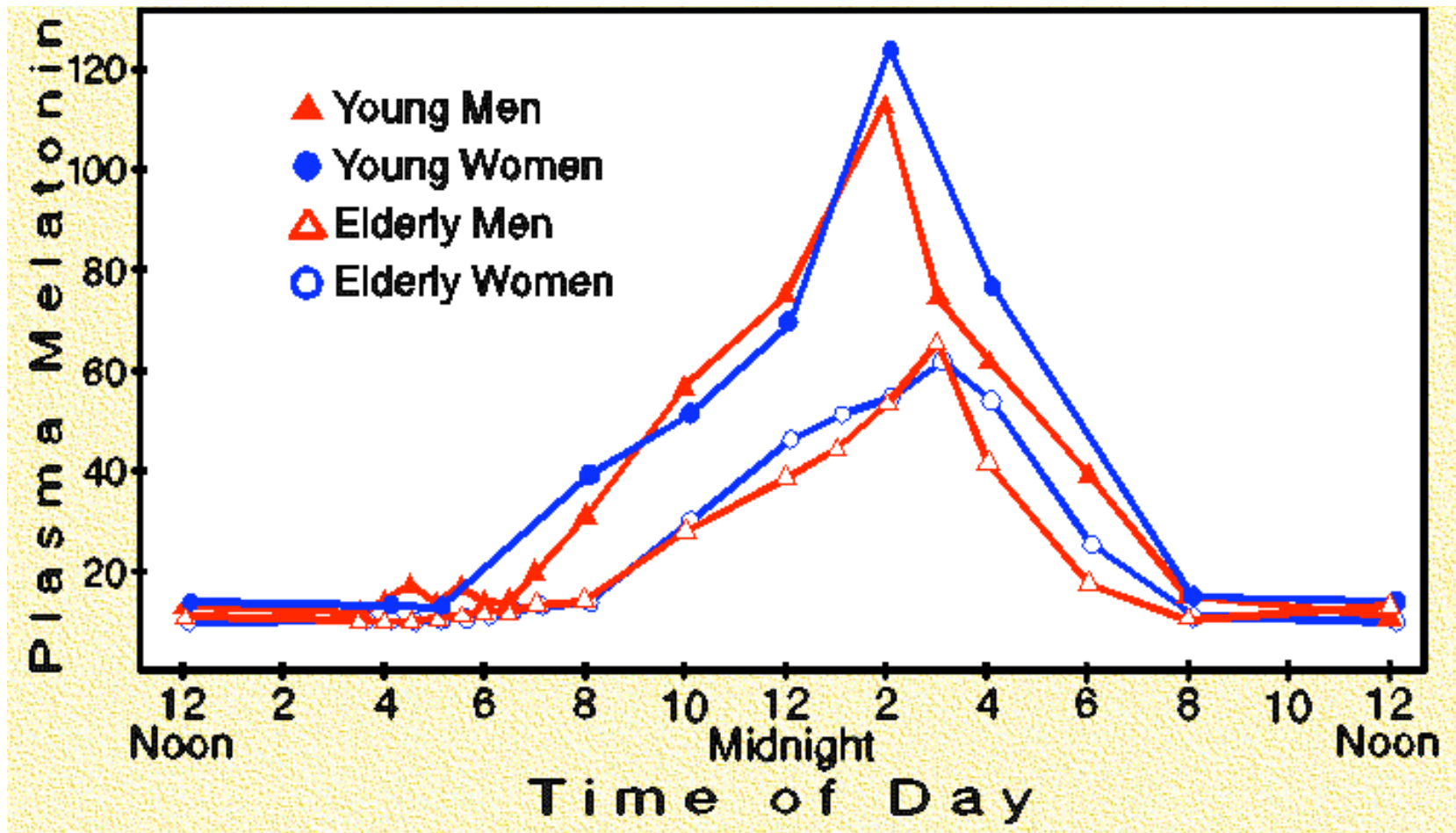
Synthesis of Melatonin



Melatonin and Age



Age and Melatonin



Ovarian Activity

- Can be seasonal or constant
- Two distinct phases
 - Follicular
 - Luteal
 - Pregnant - normal
 - non pregnant - abnormal

Mammals



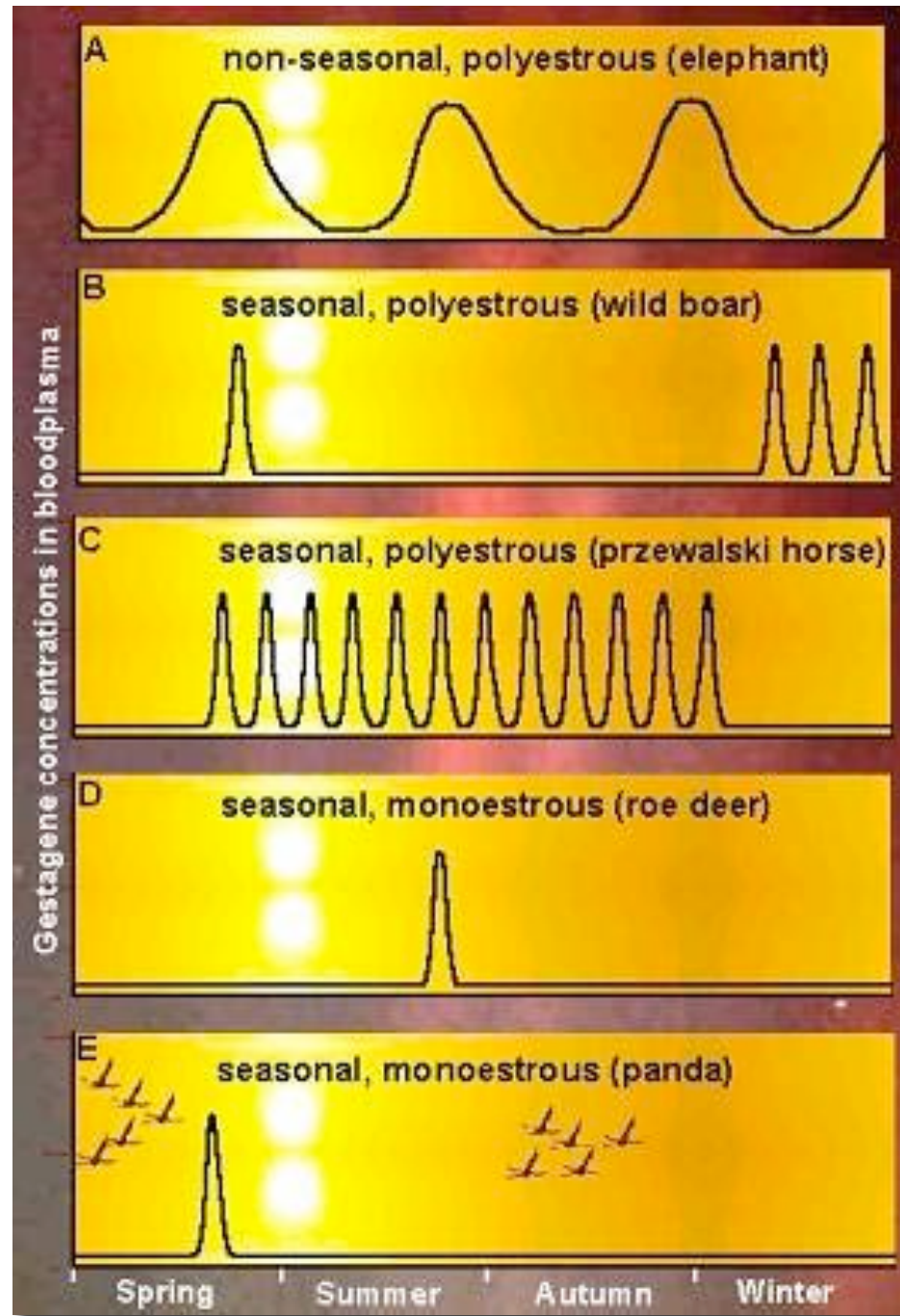
Estrous Cyclicity

- ovarian activity in non-pregnant adult mammals associated with distinct period of sexual receptivity known as **ESTRUS**
- first half of cycle, - prior to ovulation - known as **proestrous**
- **diestrous** - second phase after ovulation
- Note:
 - noun = Estrus -- adjective = estrous

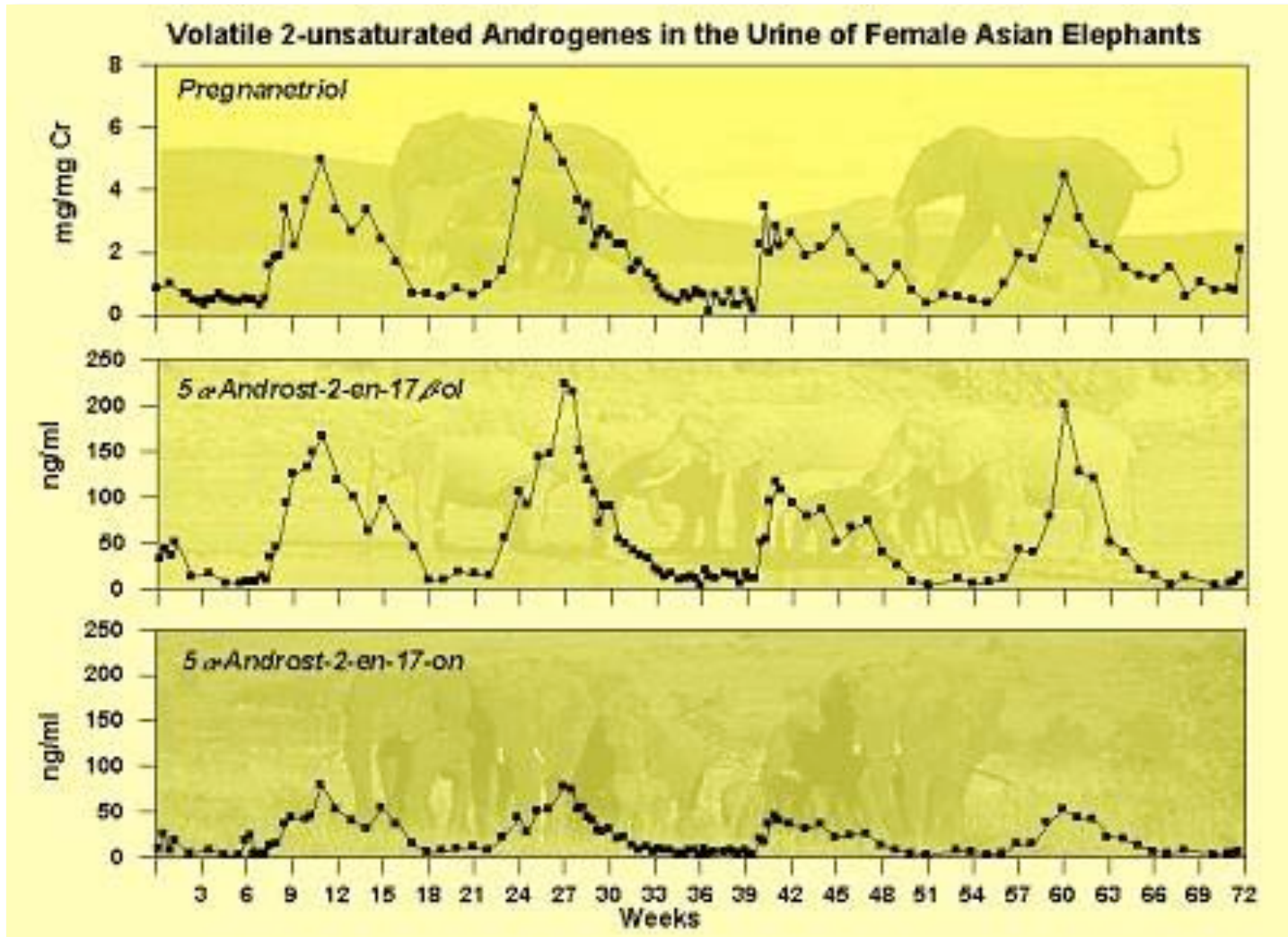
Cycle designation

- **polyestrous** - a series of ovarian cycles
- **seasonally polyestrous** - 2+ estrous cycles in a breeding season
- **seasonally monoestrous** - 1 cycle per season
- **anestrous** - reproductively inactive

Examples of
Seasonal cyclicality
-Mammals-

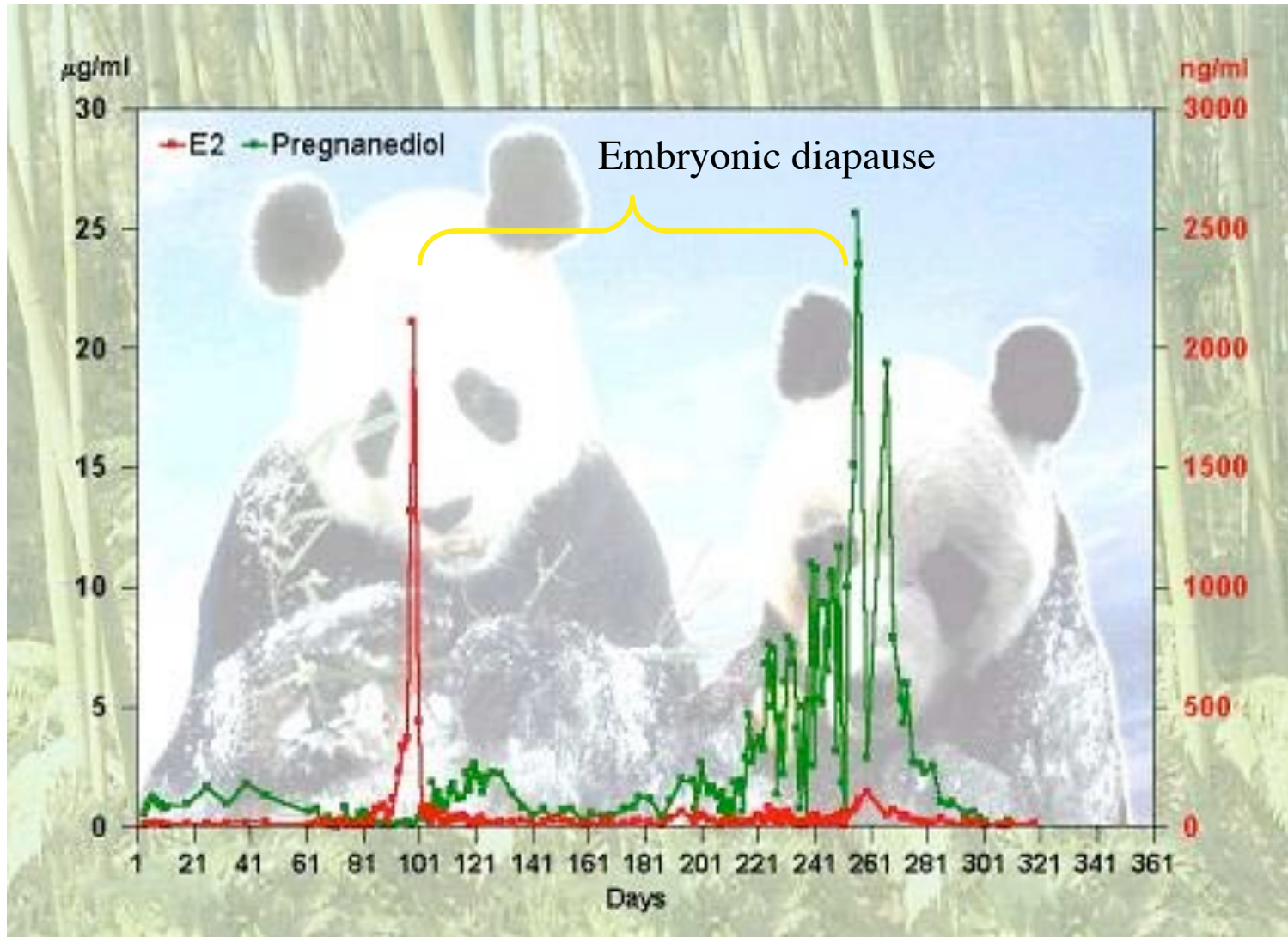


Elephant - polyestrous - 4 cycles - urinary hormones



Denhard et al. *Reproduction* 121, 475-484 (2001)

Panda - monoestrous - cycle



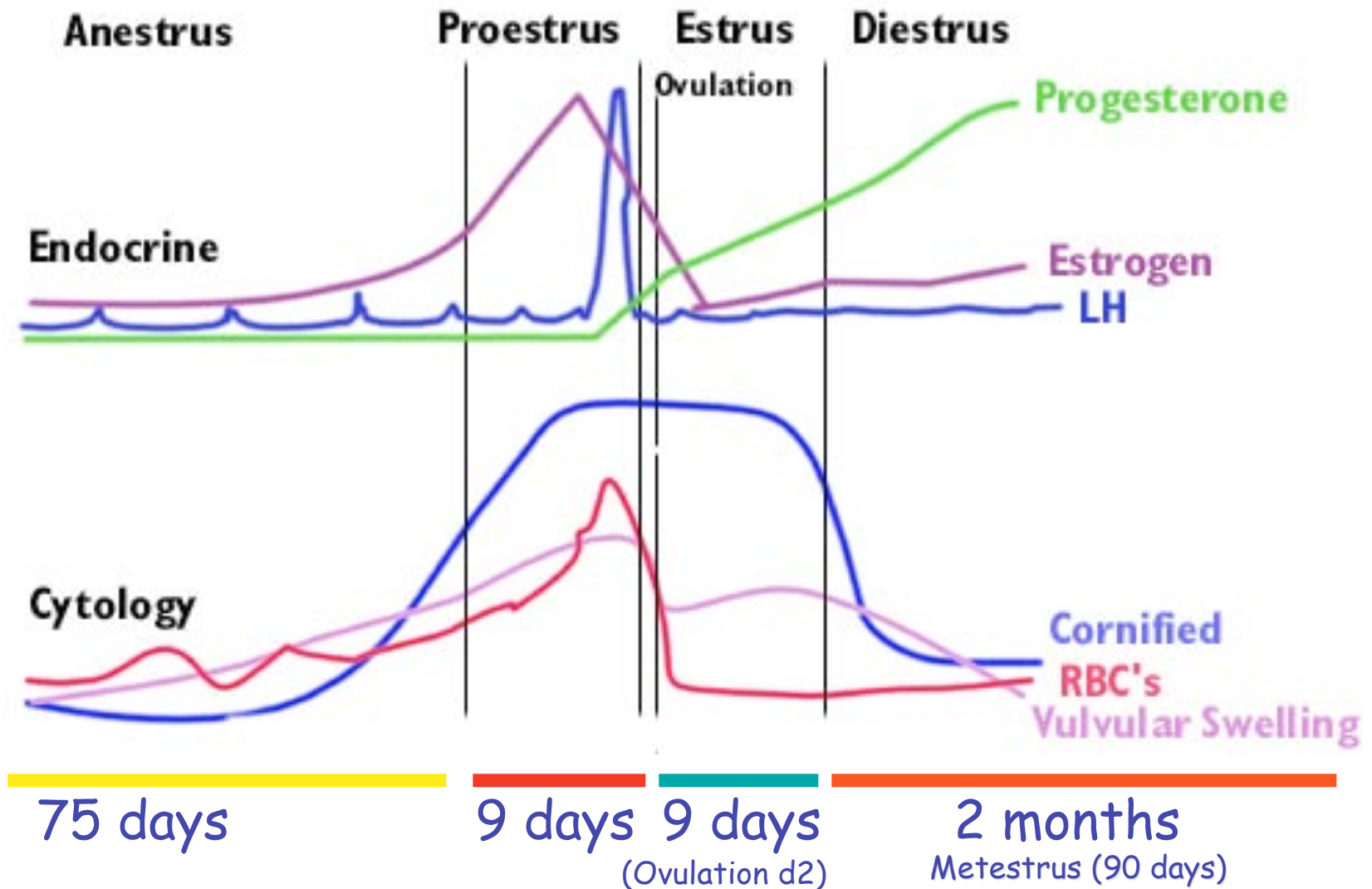
<http://www.izw-berlin.de/en/research/fg4/index.html?reproduktionsmonitoring.html~rechts>

Estrous cycles - Dogs

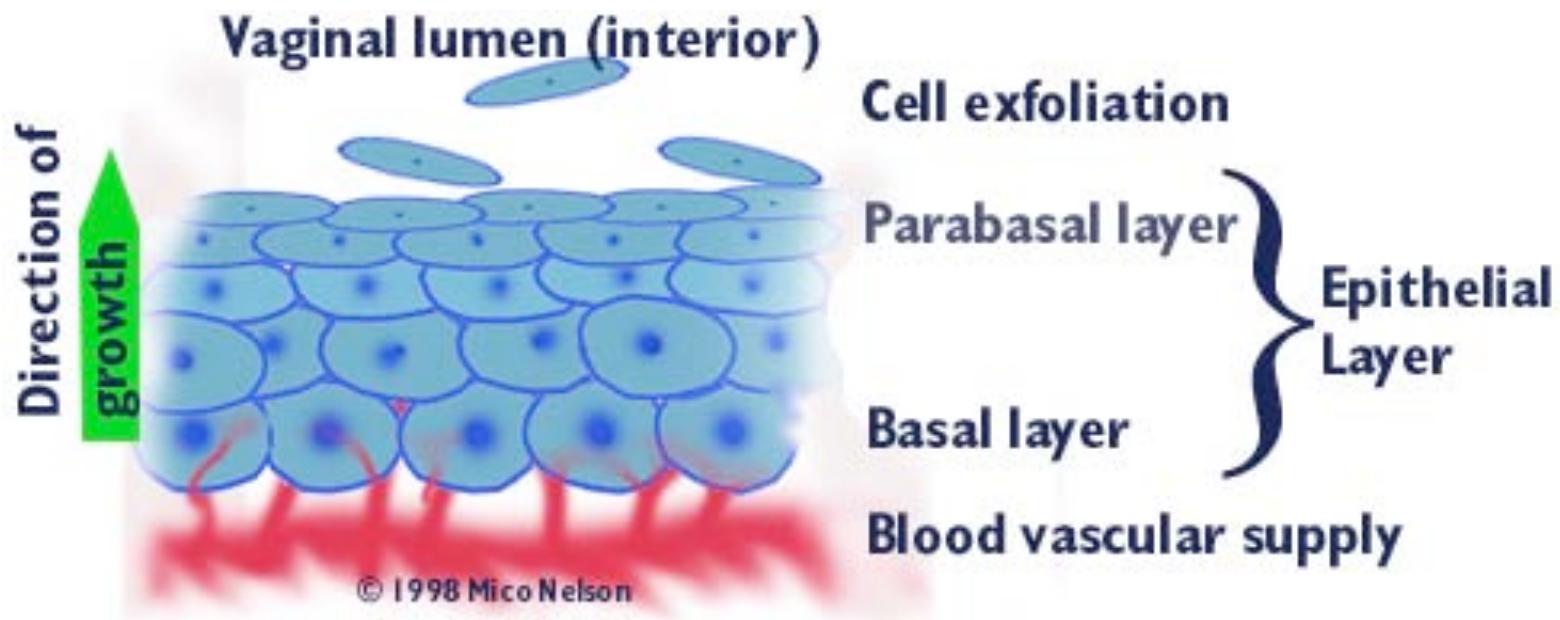
- Dog
 - Female
 - Matures in 6-8 mo
 - 2 estrous cycles/yr
- Wolf
 - Female
 - Matures in 2-4 yr
 - 1 estrous/yr



Estrous cycle in Dog



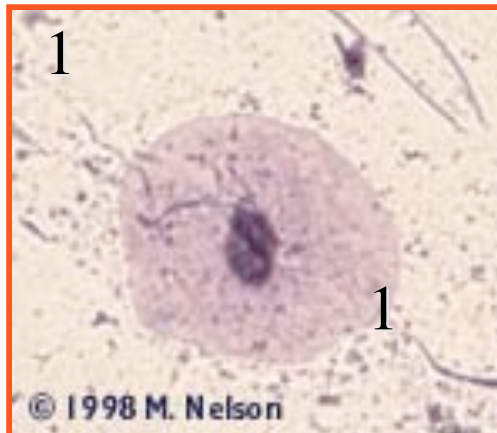
Cytological Changes - Vagina



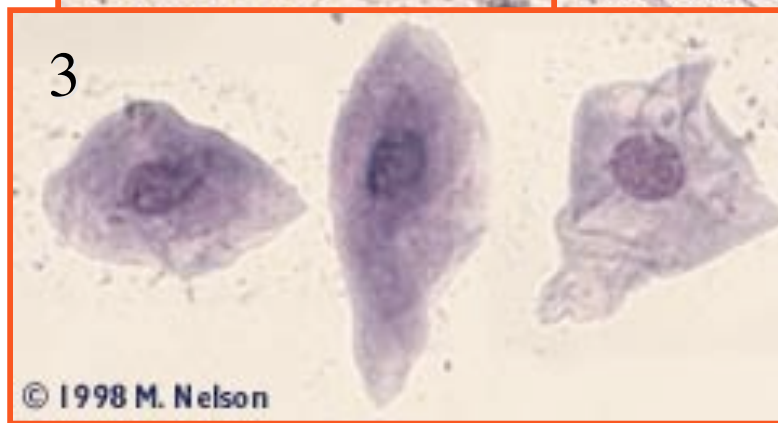
Cytology of Estrus - Dog

Cornification/Keratinization

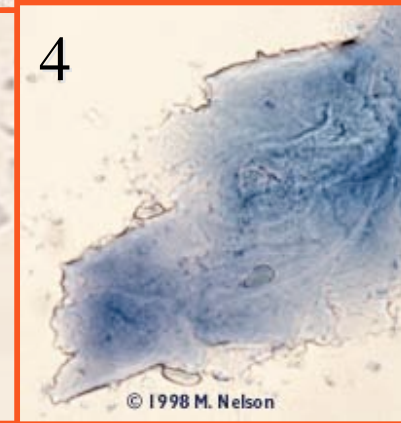
Parabasal
Anestrus -
early proestrus



Transitional



Partly Cornified
proestrus

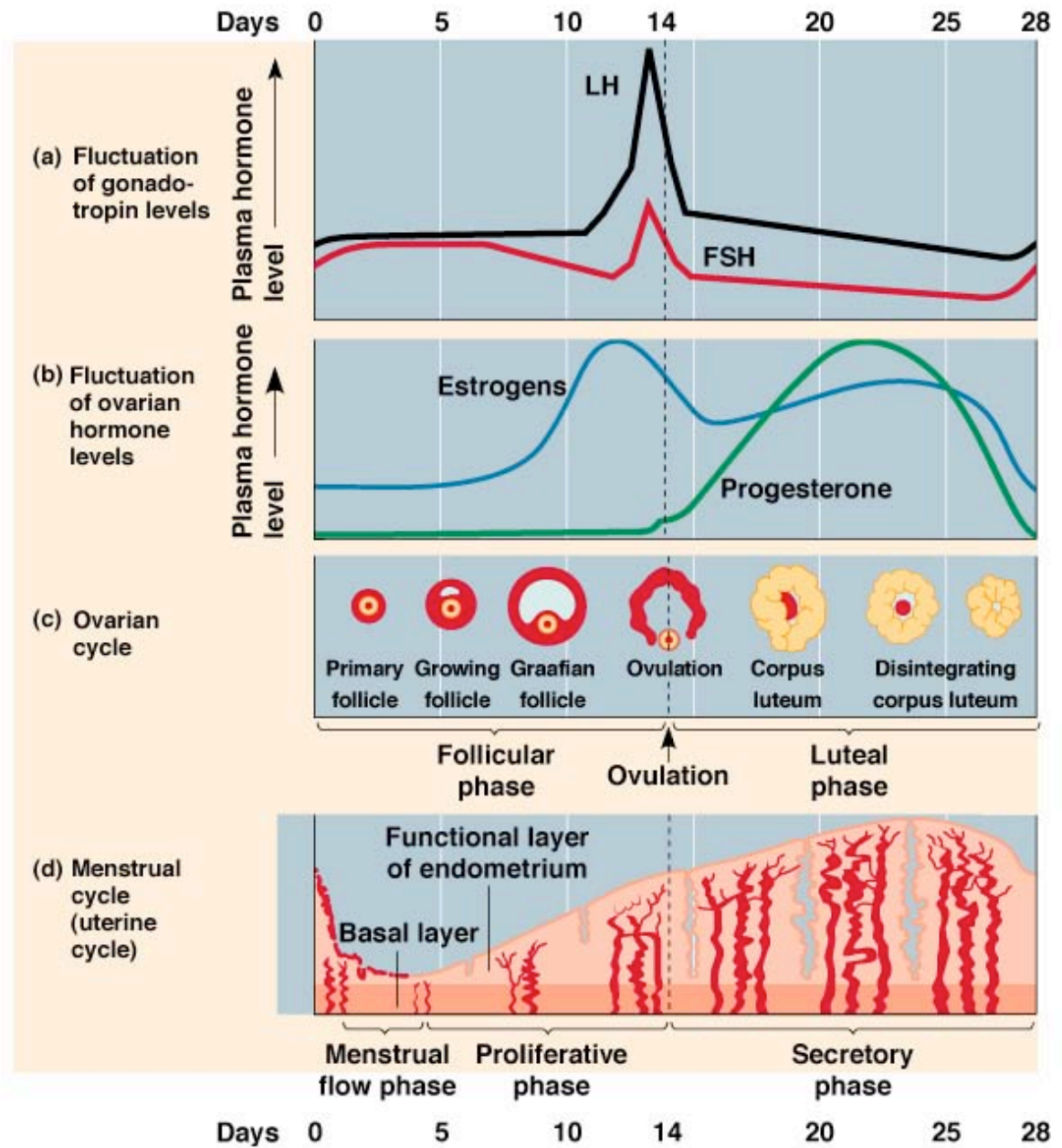


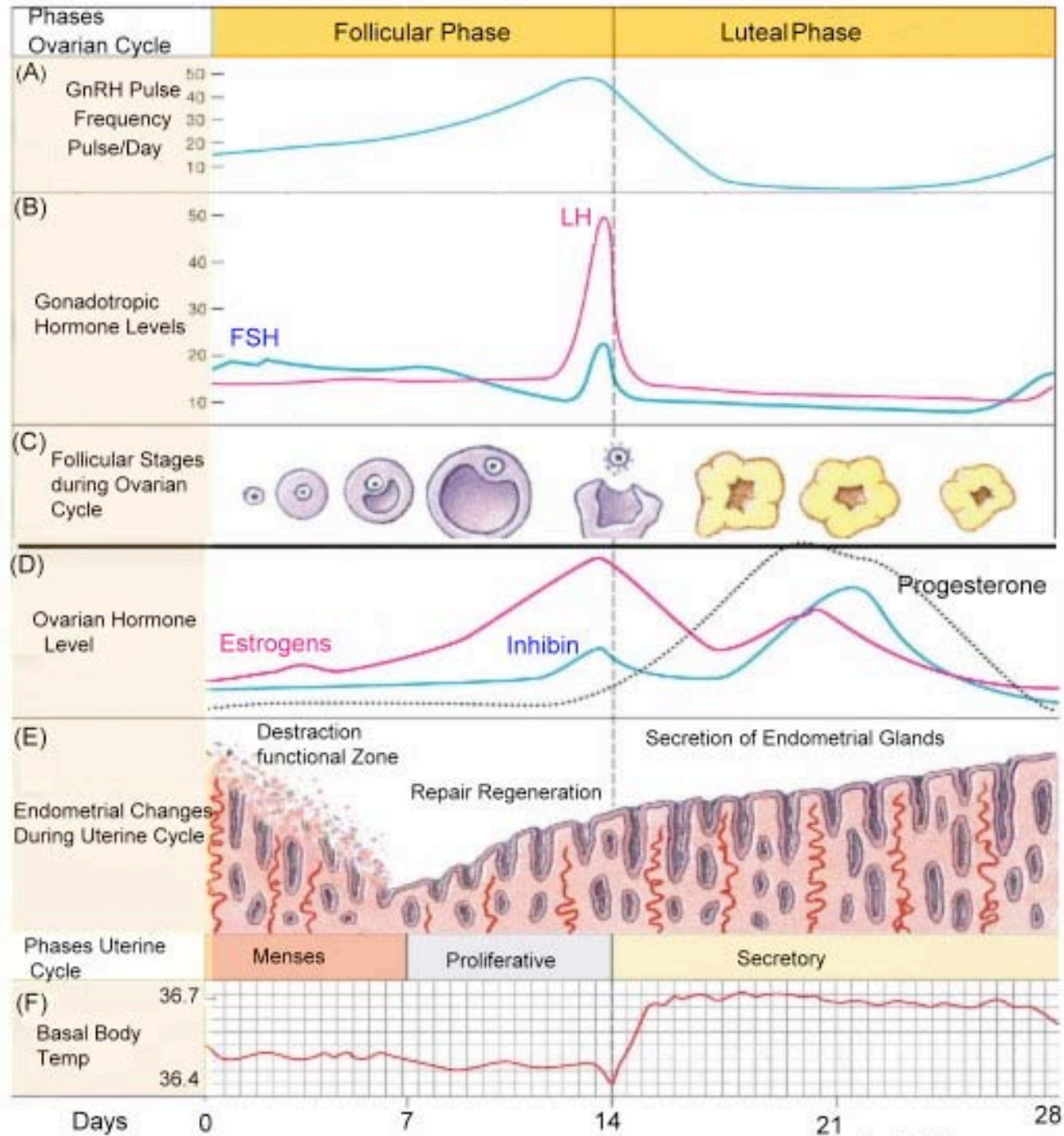
Cornified or Squamous
estrus

Menstrual Cycle

- 3 major phases
 - Follicular or proliferative
 - Luteal or secretory
 - Menstrual
- found in several primates
- 'Period'
 - sloughing of uterine lining and vaginal discharge of blood and cellular material (menstrual fluid)
 - response to hormonal withdrawal
- period of menstruation is menses

— FSH
— LH
— E₂
— P





Social Influences

- Whitten effect
 - House female rats together with male and they will synchronize estrus
- Dormitory effect
 - McClintock shown that women housed together in dorm synchronize menstrual cycle
 - College women who have coitus frequently break synchrony
 - Further, those with frequent coitus have more regular cycle than those that abstain
- Pheromones

Nonmammalian Species - Reptiles

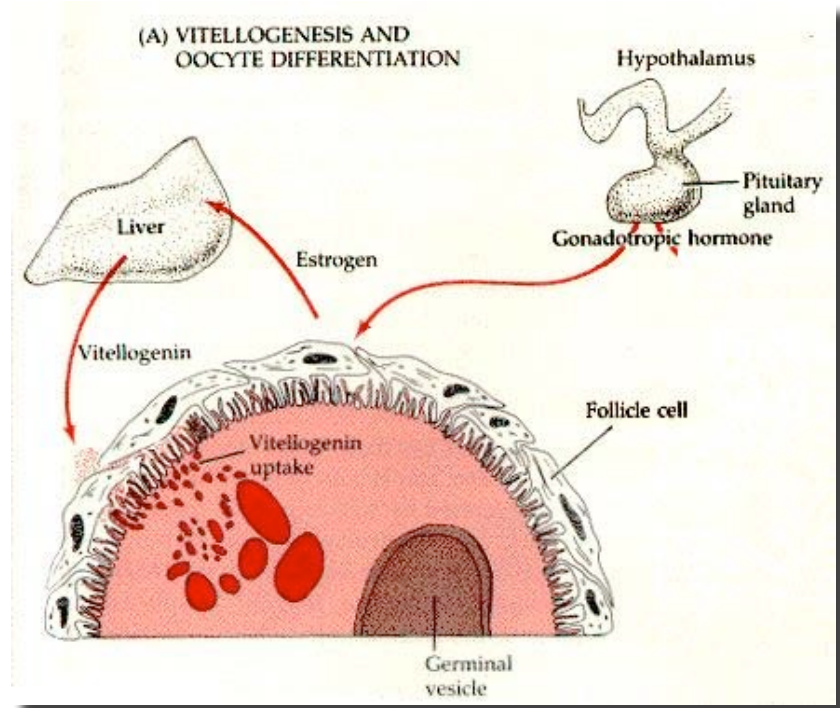


Oviparous (egg laying) species

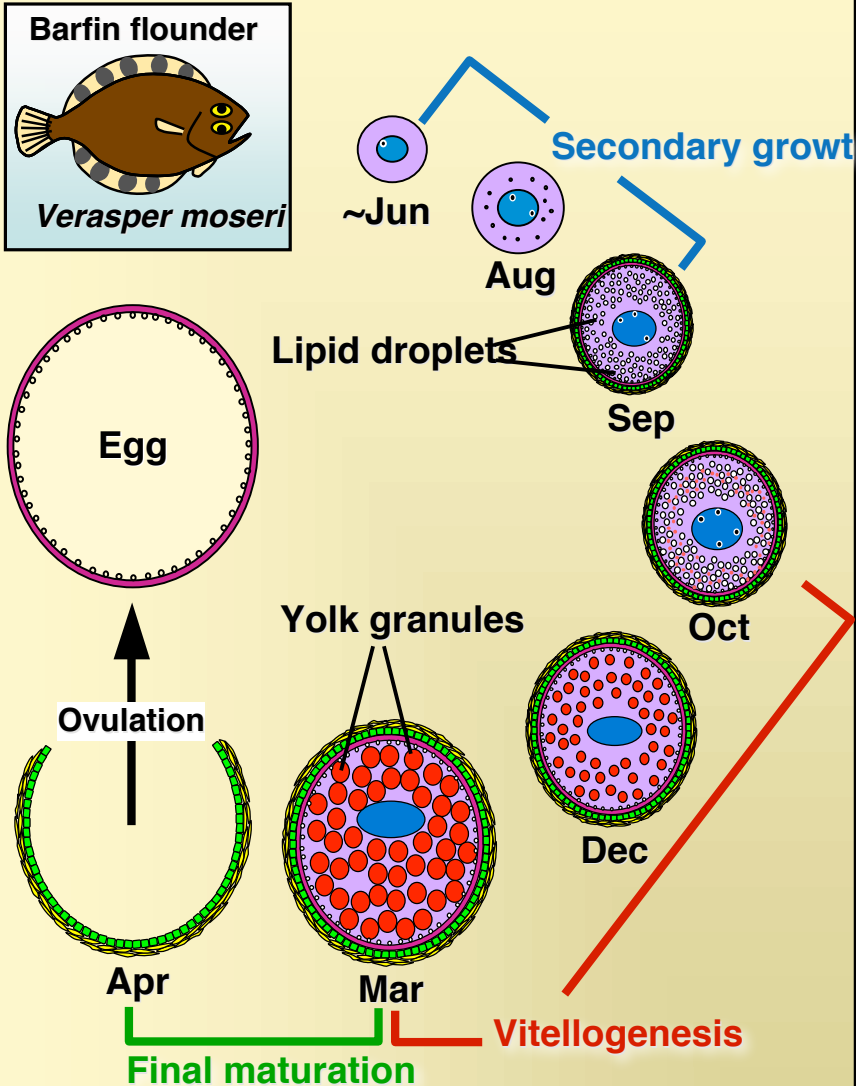
- estradiol
 - stimulates the synthesis of vitellogenin
 - egg yolk precursor protein
 - from the liver
 - known as heterosynthetic yolk synthesis
 - mobilization of fat
 - increase in phospholipids observed
 - increase in plasma calcium also seen


Vitellogenesis

- estrogen stimulates protein synthesis in liver
 - vitellogenins (Vtgs)
 - may be more than 1
 - Most species 3
- Vtg enters blood
 - travels to ovary
 - transported to perivitelline space
 - endocytosis via coated vesicles
 - specific receptors for Vtg
 - once in oocyte cytoplasm cleaved
 - phosvitin (35 kD)
 - lipovitellin I & II (400 kD)

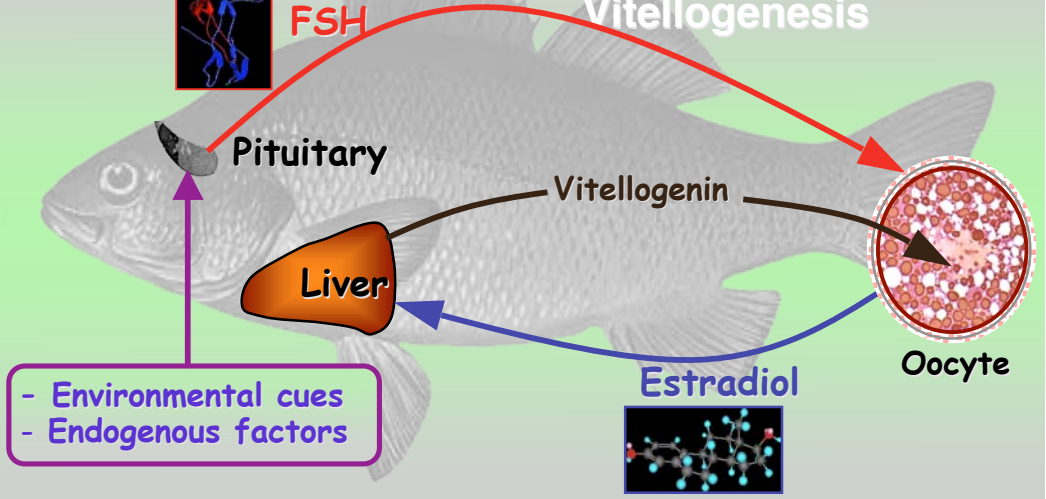


"Oogenesis"

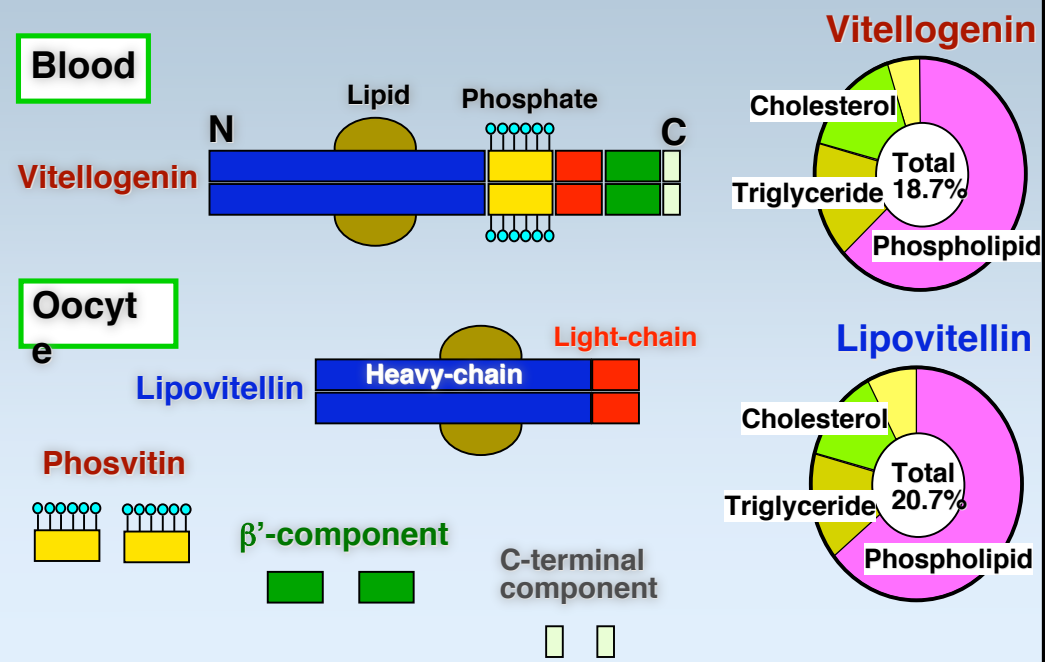


Takahiro Matsubara and associates  Hokkaido National Fisheries Research Institute

Teleost Vitellogenesis

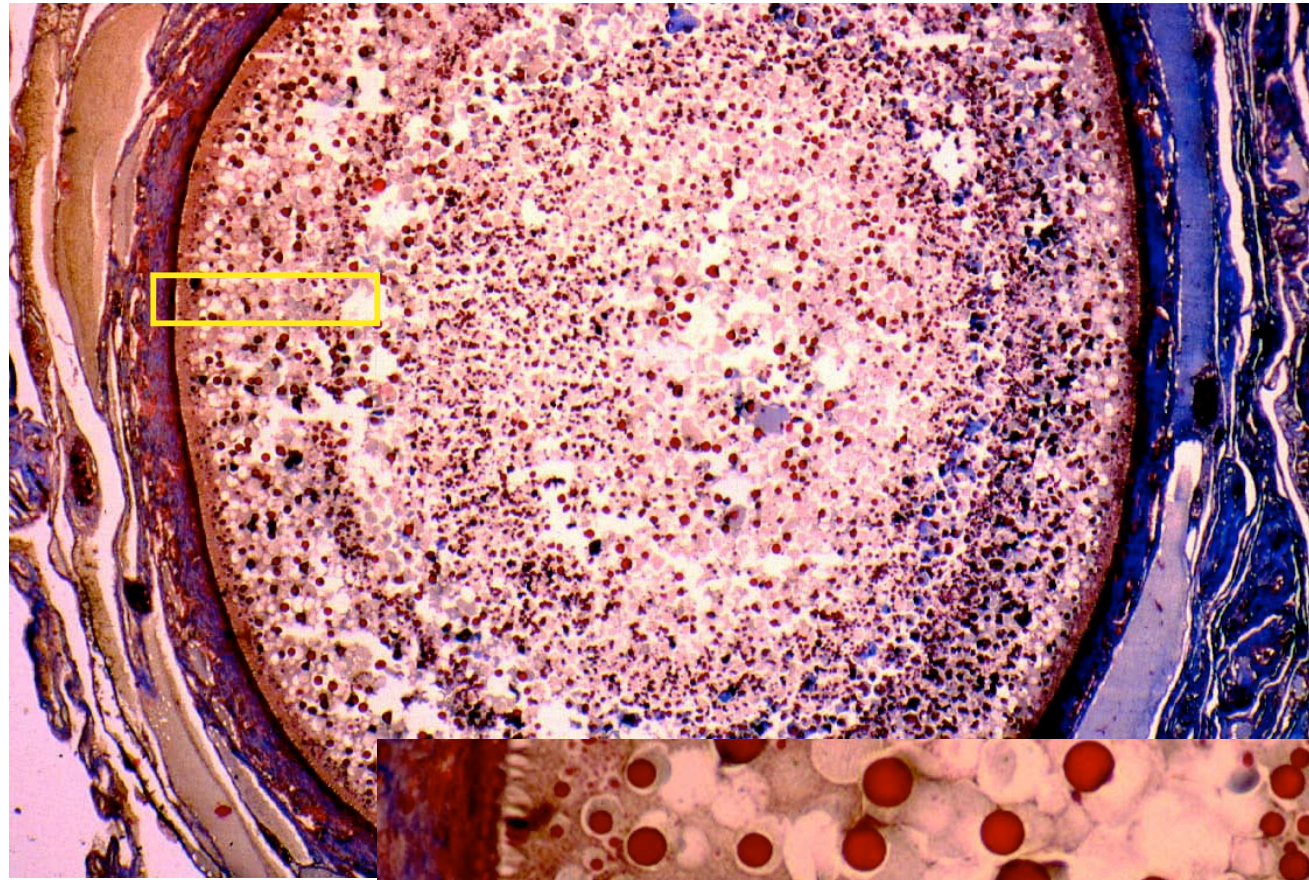


Vitellogenin and yolk proteins

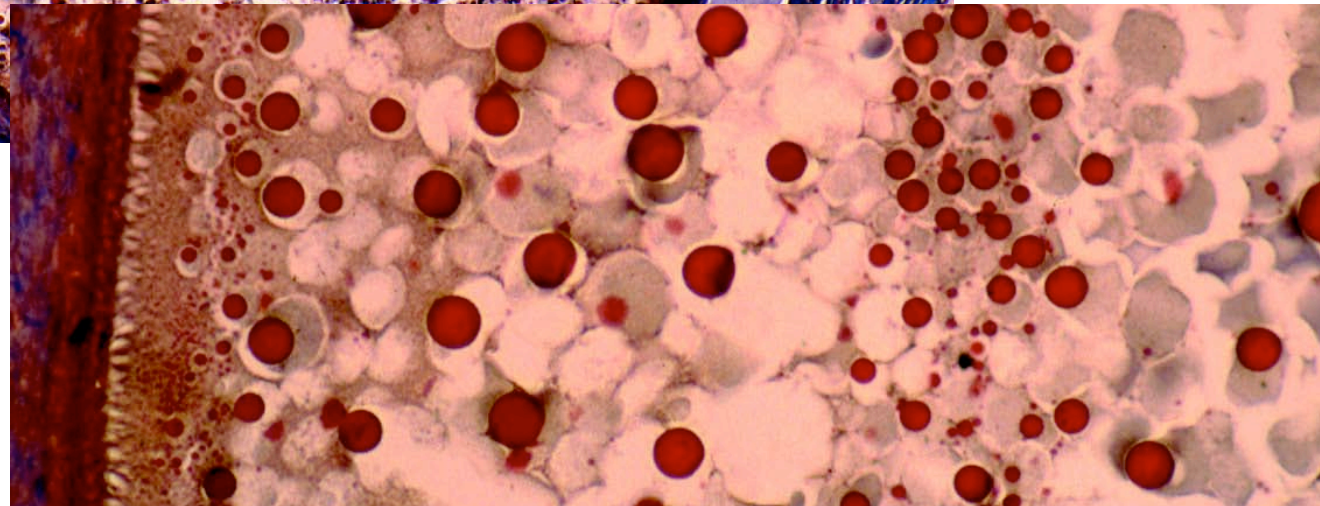


Vertebrate Yolk

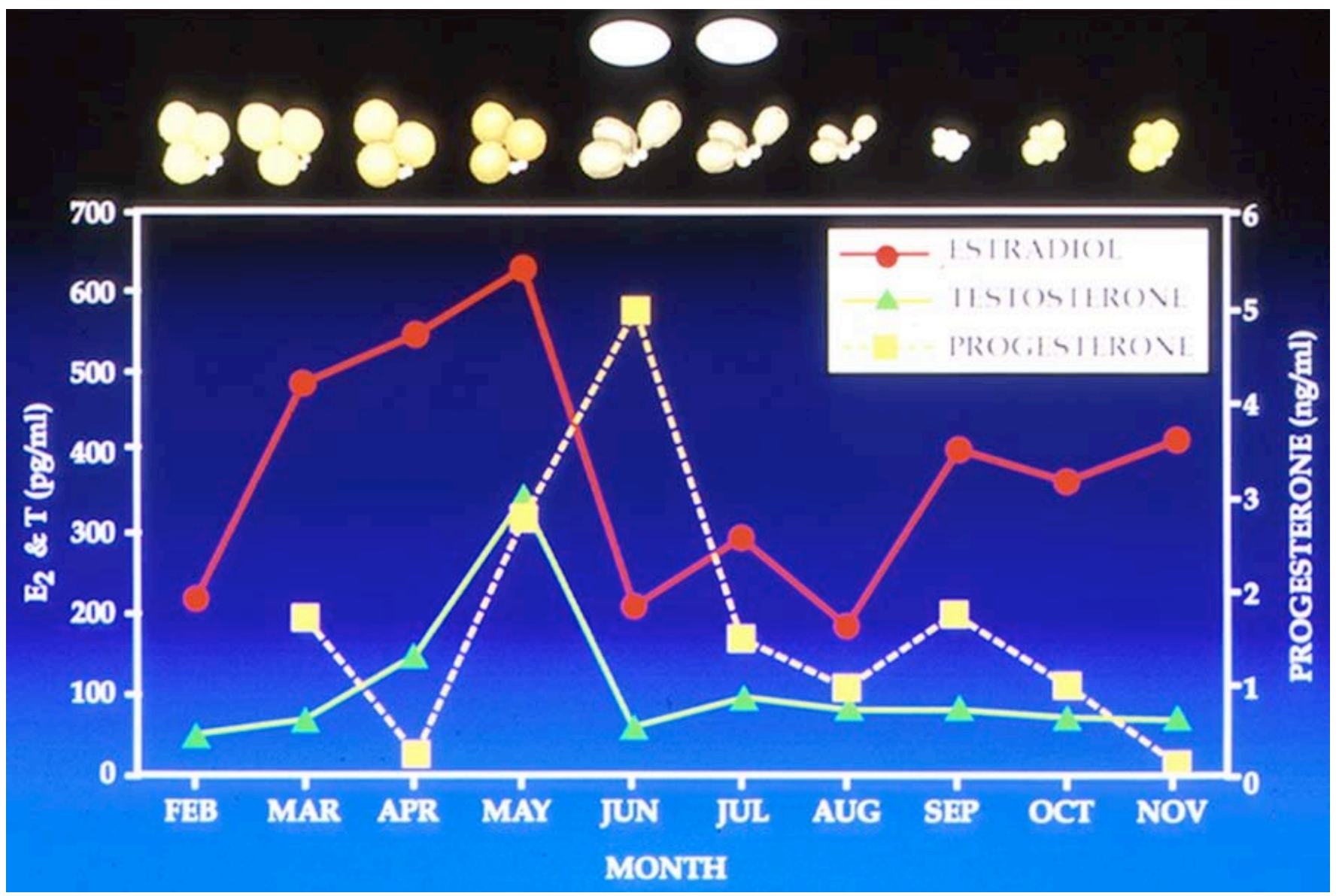
- proteins, phospholipids, neutral fats, hormones
 - Protein stored as yolk platelets or spheres
 - can be formed into yolk crystals
 - Fats stored in lipochondria
 - cytoplasmic inclusions
 - fish - fat droplets or yolk spherules present
 - Carbohydrate in form of glycogen granules
 - Hormones present
 - Ovarian hormones such as steroids
 - Thyroid hormones
 - Anything in circulation?

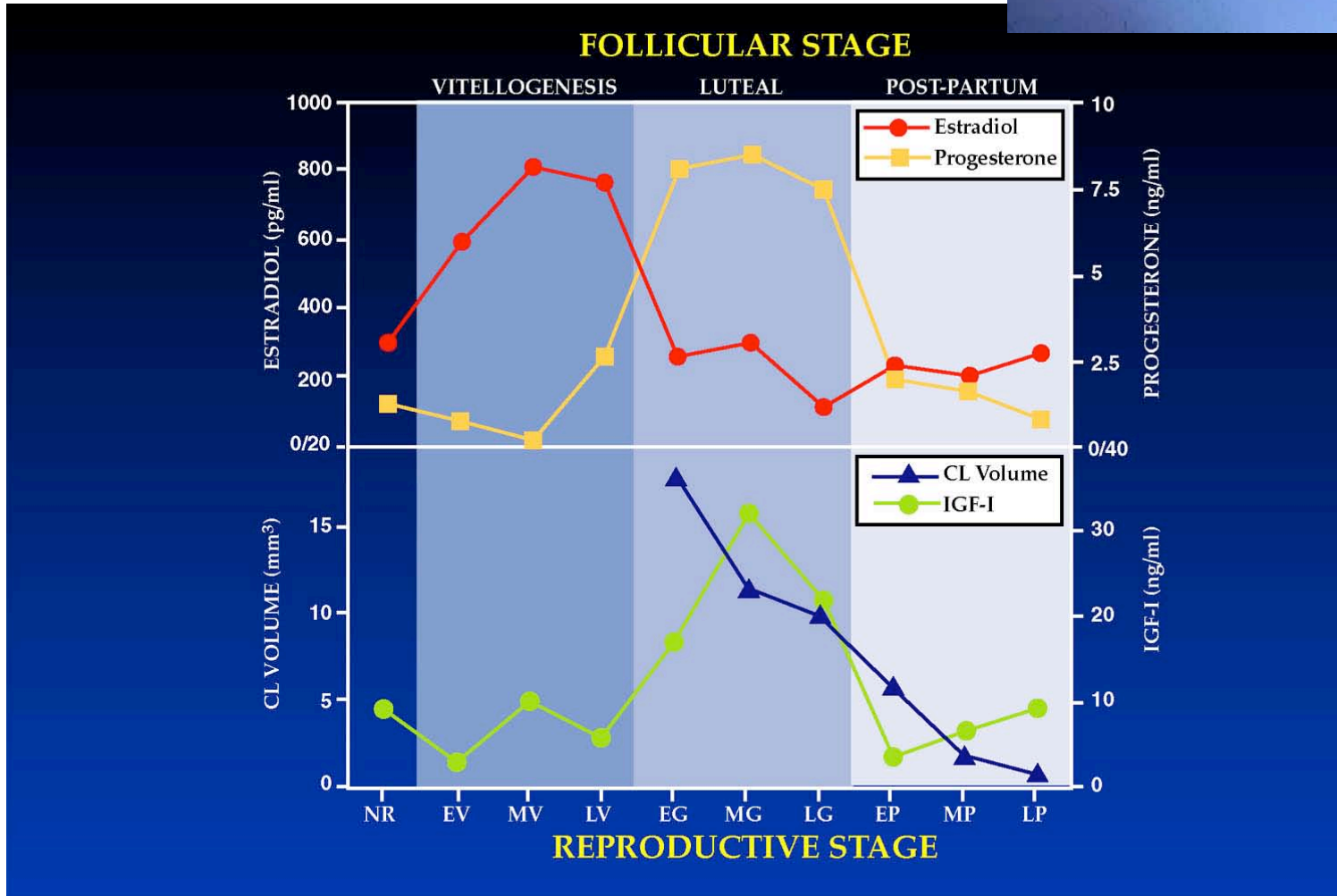


Vitellogenic
Follicle



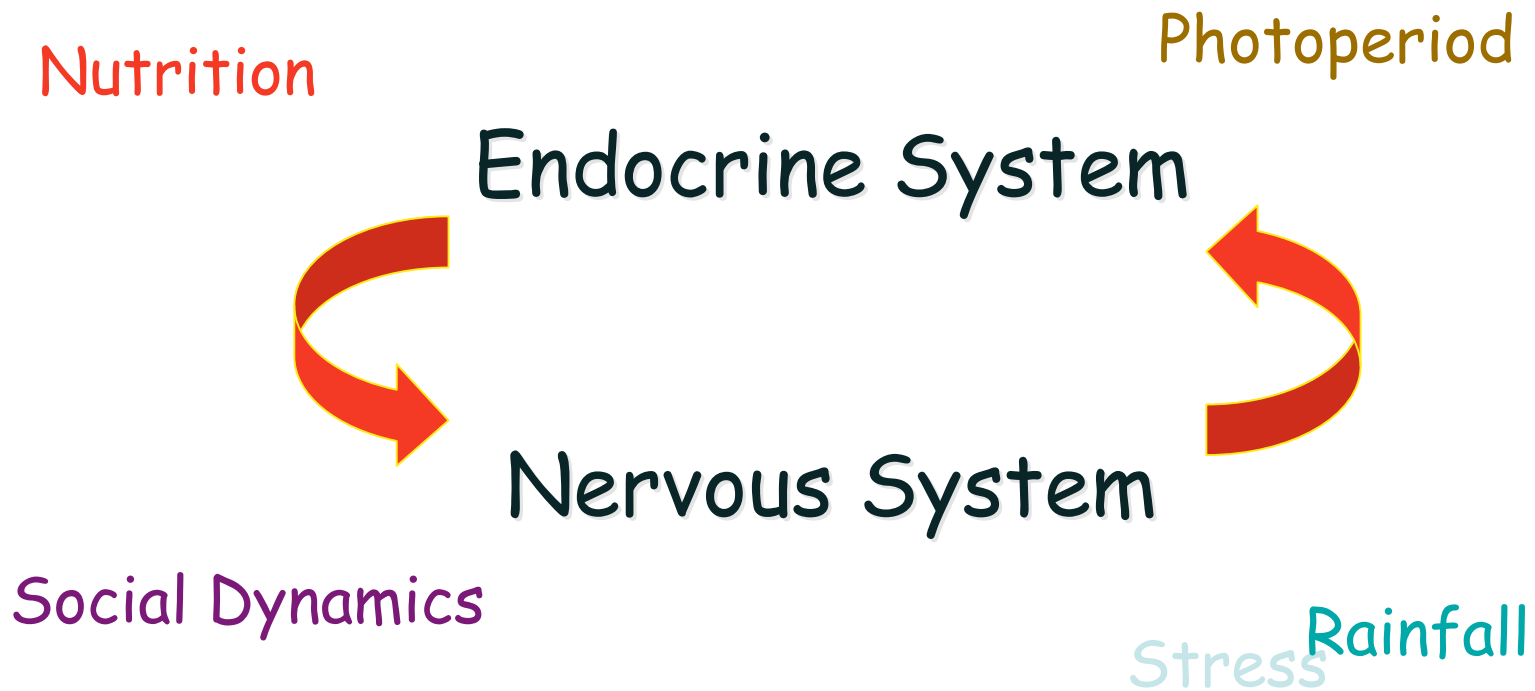
American alligator





Guillette and Milnes (2001)

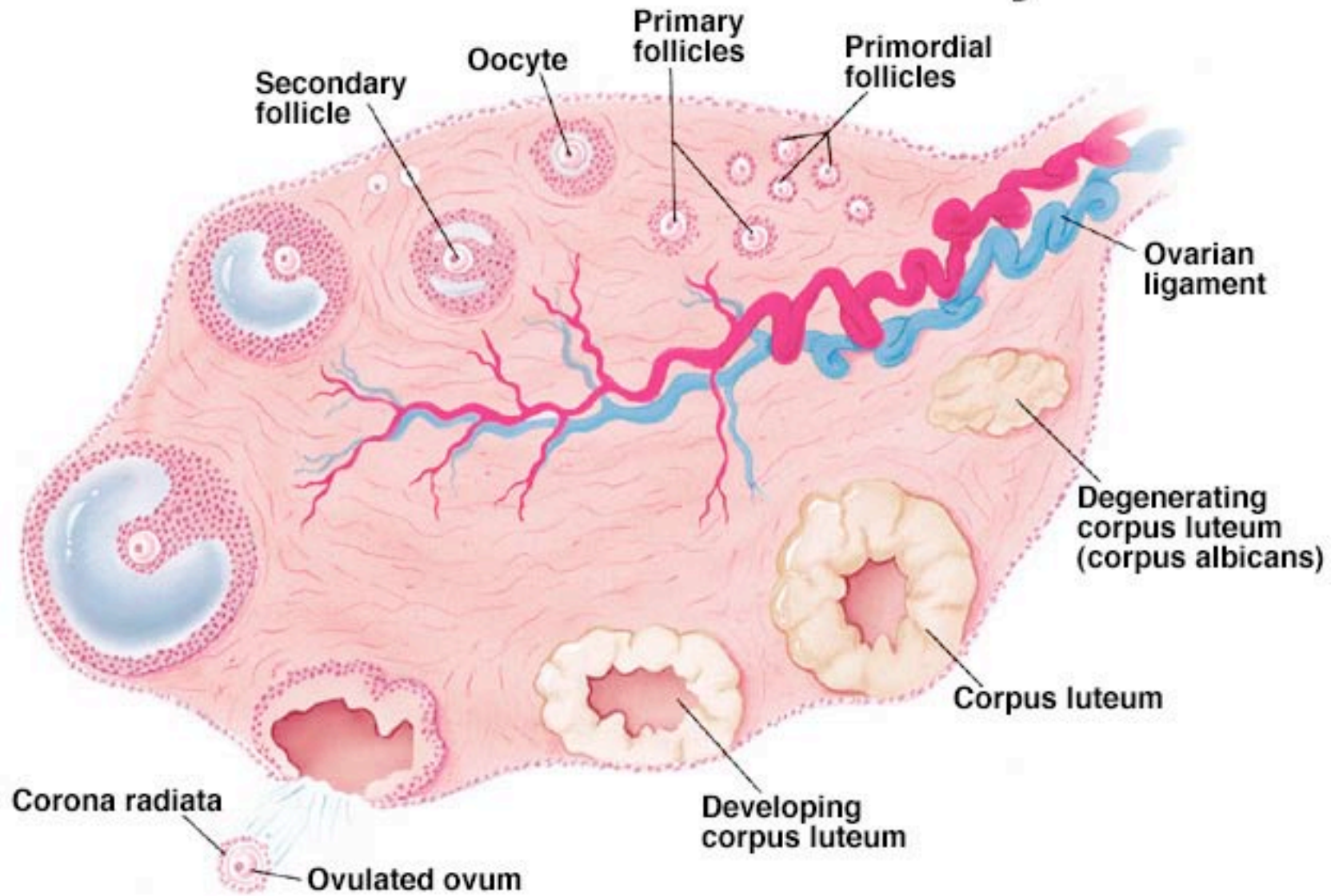
Mechanisms controlling cycles



Follicular Growth

- involves growth and differentiation
 - oocyte and surrounding ovarian follicle
- induction controlled by FSH
- mechanism by which specific follicles are selected for growth unknown

Structure of an Ovary

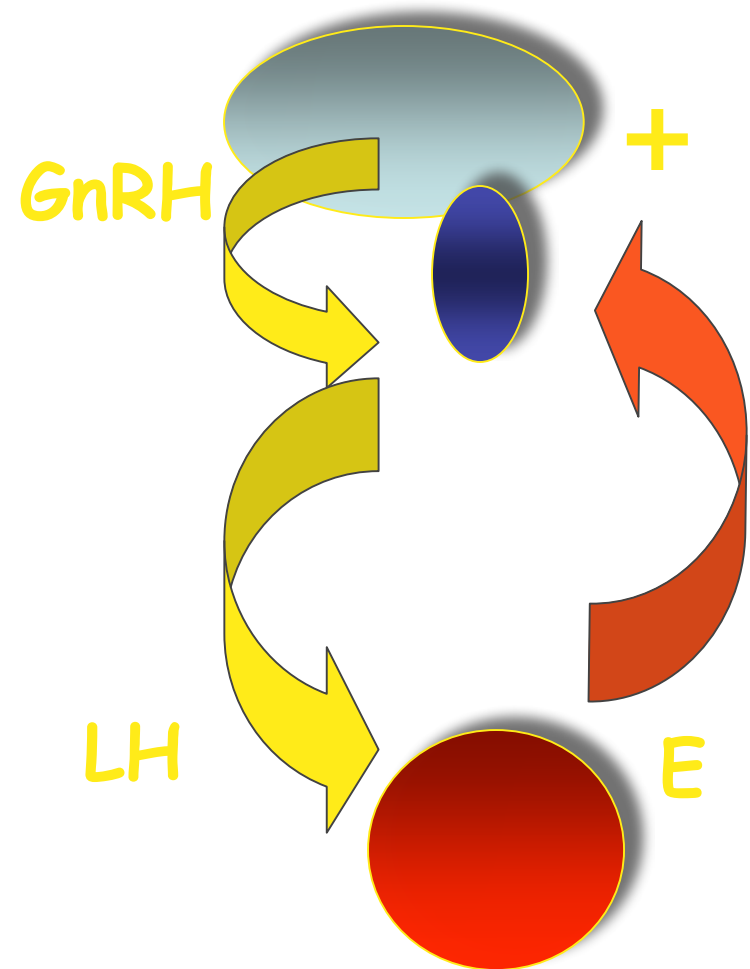


Which follicle grows?

- Hypothesis: FSH alters release of histamine from surrounding Mast cells
 - increases localized blood flow,
 - thus stimulating specific follicles to grow
 - bathed by more nutrient and hormone
- As follicle grows, granulosa and theca proliferate and LH stimulates increasing estrogen synthesis

Loss of Negative Feedback

- negative feedback of E on LH decreases
- positive feedback begins about mid cycle
- sharp increase in plasma E stimulates mid cycle gonadotropin surge - LH surge
- final oocyte maturation and ovulation



Ovulation

- in most vertebrates
 - ovulation appears to be induced by a LH surge
- in mammalian model systems
 - LH surge luteinizes the follicle
- luteinized follicle secretes progesterone

Progesterone

- induces a local inflammatory response
 - release of histamines, serotonin and leukotrienes by cells adjacent to follicle
- stimulates thecal cell release
 - $\text{PGF}_{2\alpha}$ and PGE_2

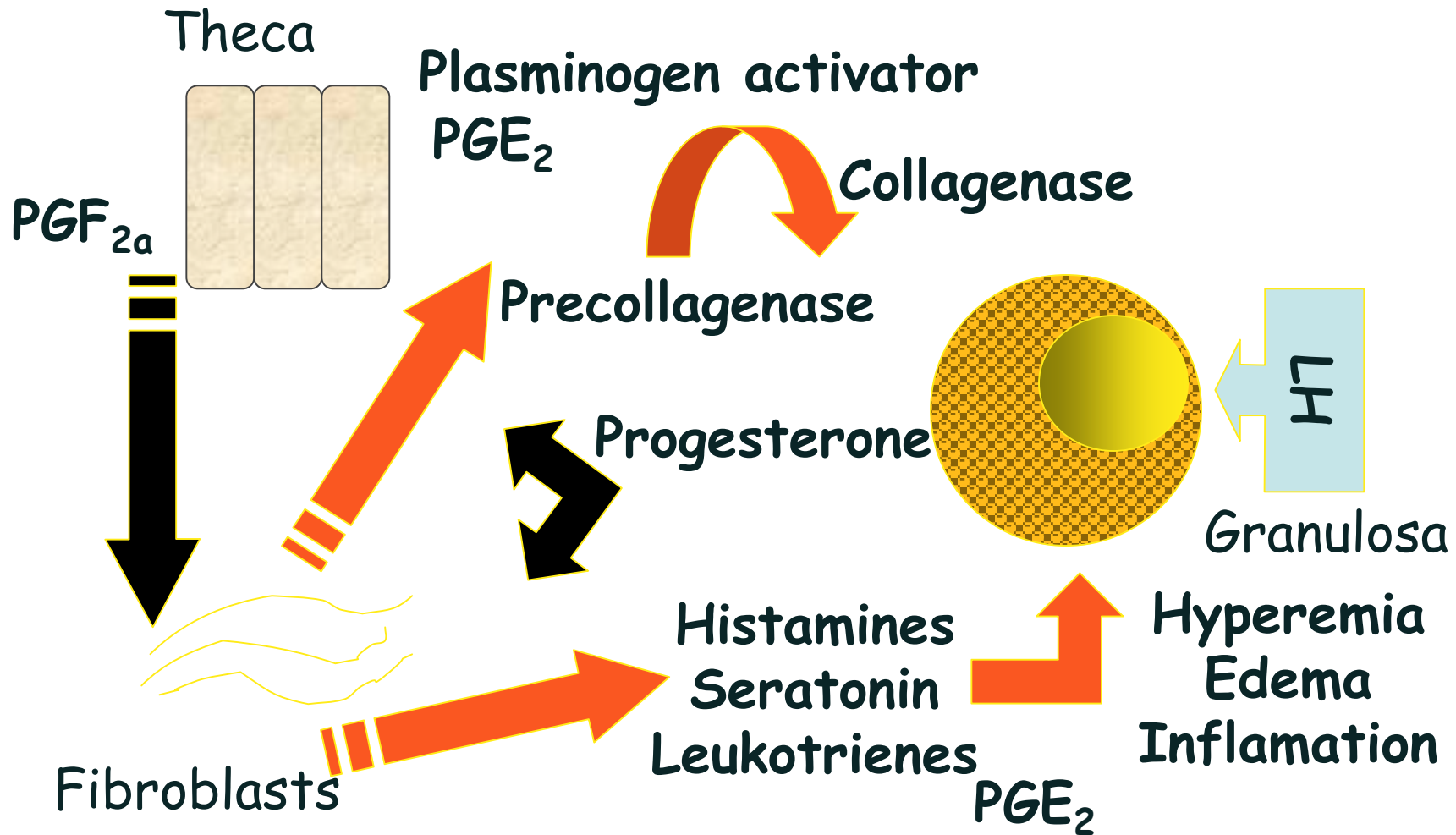
PGE₂ & PGF_{2α}

- PGE₂
 - stimulates hyperemia & edema
 - release of plasminogen activator and plasmin that convert precollagenase to collagenase
- PGF
 - stimulates fibroblasts to release precollagenase

Collagenase

- causes breakdown of tissue in area of stigma
 - localized region lacking blood vessels
 - thru which ovulated follicle will be released

Ovulation

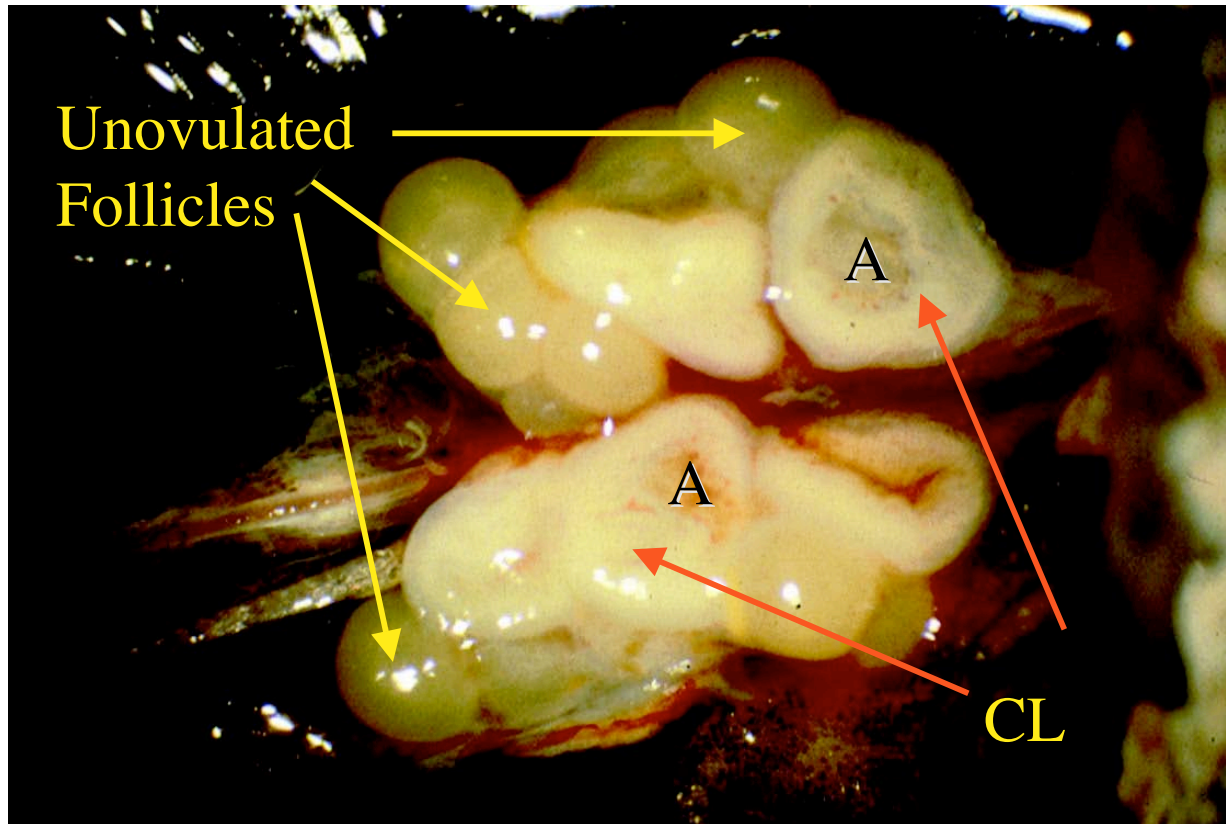


Other Factors

- role of intrafollicular pressure and follicular contraction still debated
 - some species contraction observed
 - important in birds, amphibians and reptiles

Luteal Phase

- LH surge -follicle transformed - luteinized
- Granulosa, TI and TE cells remain
 - transformed into **CORPUS LUTEUM**
- role debated
 - role in gestation maintenance
 - essential in many mammalian species but not all
- synthesizes
 - progesterone, some androgens and estrogens
 - the peptide hormone relaxin

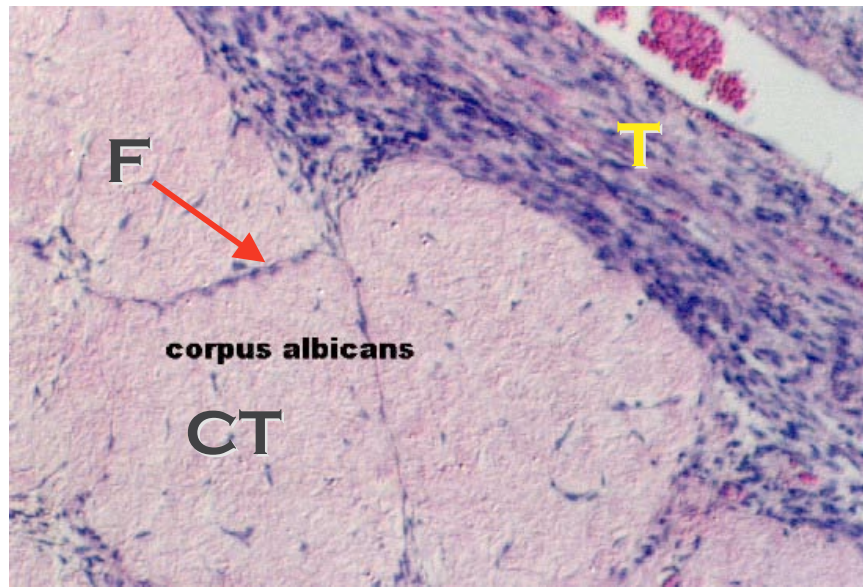
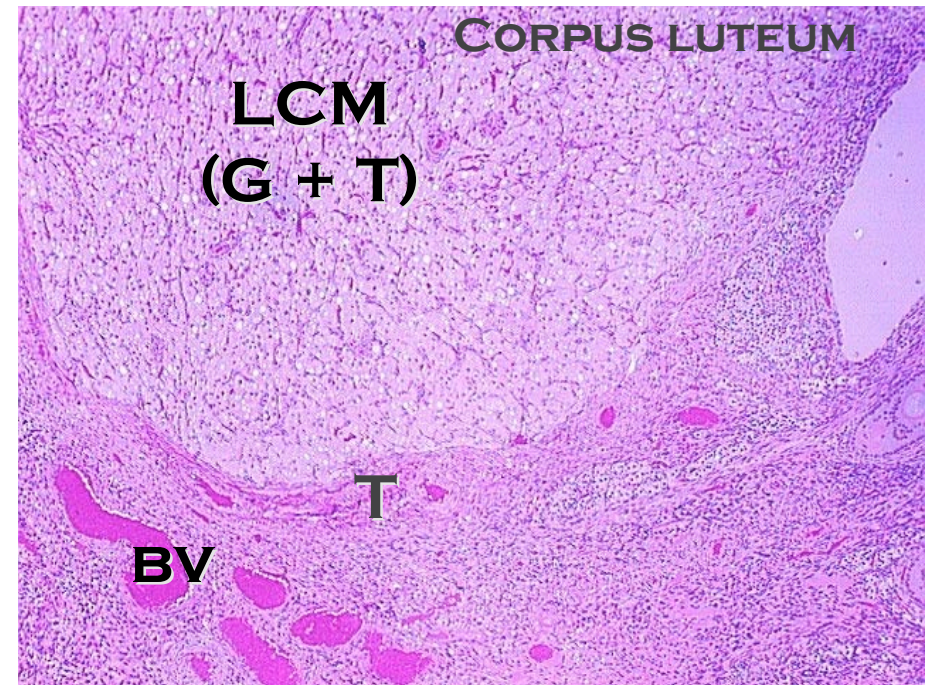
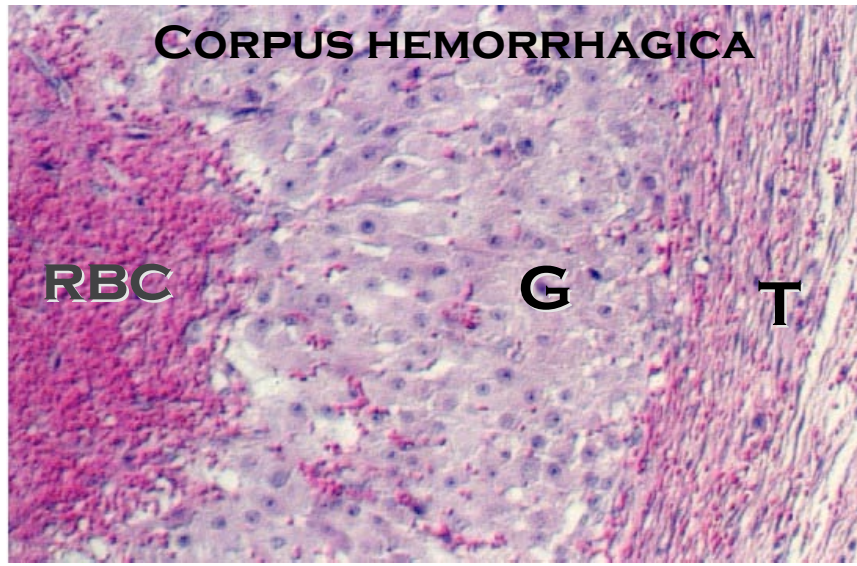


Corpus Luteum
gross anatomy

Lizard (*Sceloporus* sp.) Ovary -within hours of ovulation

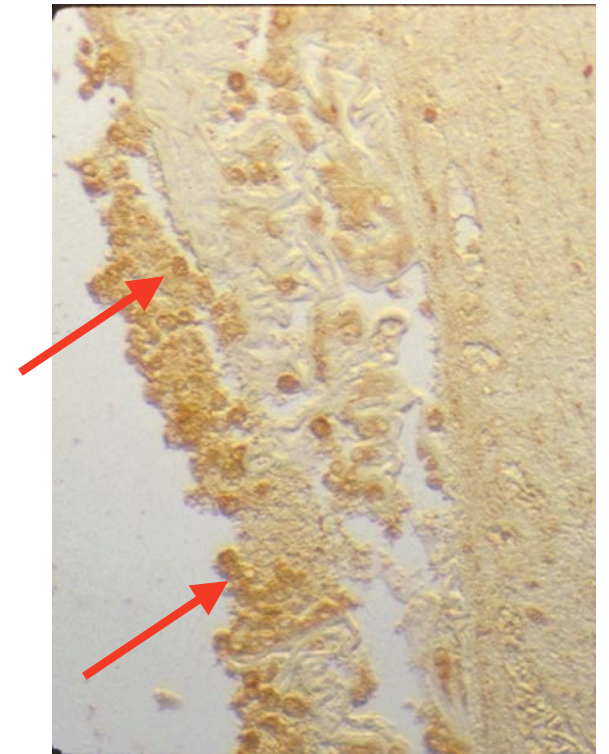
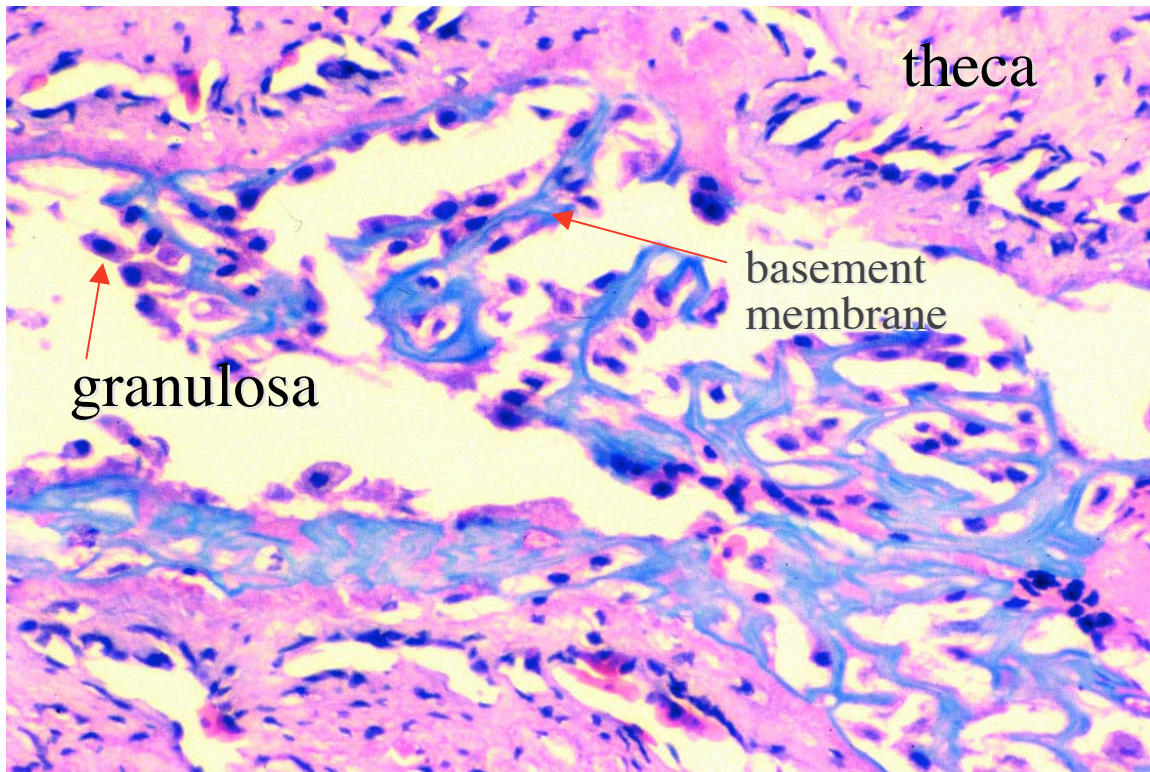
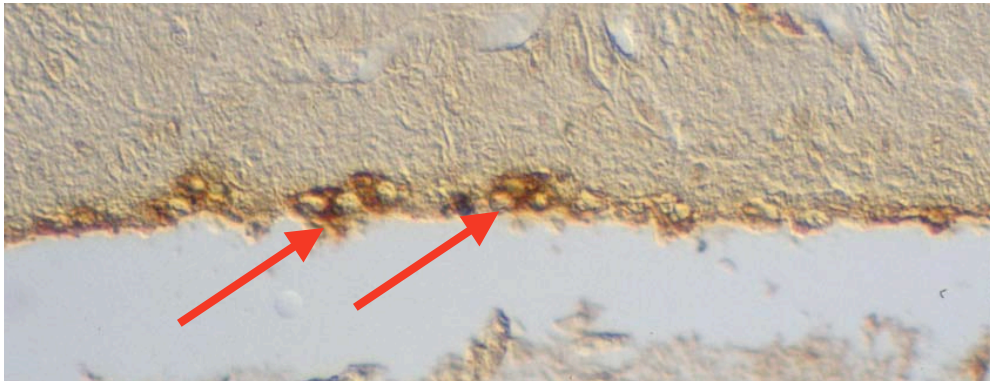
NOTE: ovulation Aperture (A) and small amount
of remaining blood

CL histology



G, granulosa; T, theca; BV, blood vessels; RBC, red blood cells; F, fibroblast, CT, connective tissue

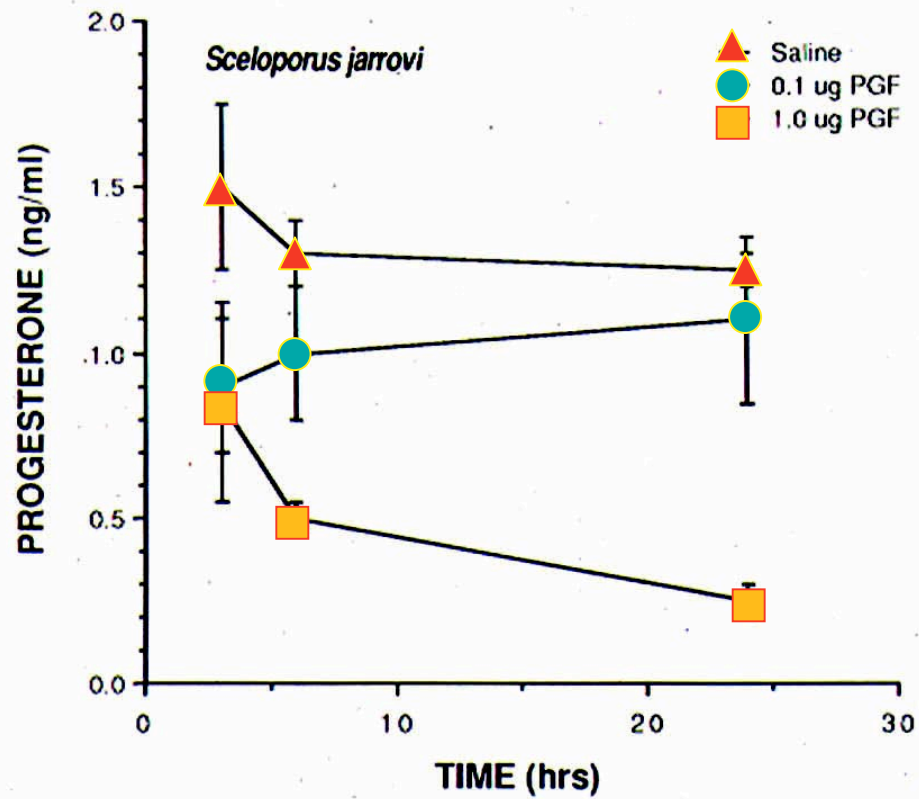
Immunocytochemistry for relaxin in alligator CL



"activity" of CL

- can remain 'active' thru out pregnancy
- can degrade rapidly after ovulation
- luteotropic (stimulatory) agents include
 - FSH, LH, E, PGE₂
- luteolysis - CL death
 - induced by PGF_{2α} in many species
 - estrone luteolytic in primates

PGF_{2α}-induced luteolysis



Guillette et al. (1984) *GCE* 56:271-277

"Maternal Recognition of Pregnancy"

- CL dies unless 'rescued' by pregnancy
 - known as "Maternal Recognition of Pregnancy"
- in humans -
 - human chorionic gonadotropin
 - embryonic origin
 - basis for home pregnancy test