Reproductive Cyclicity

"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

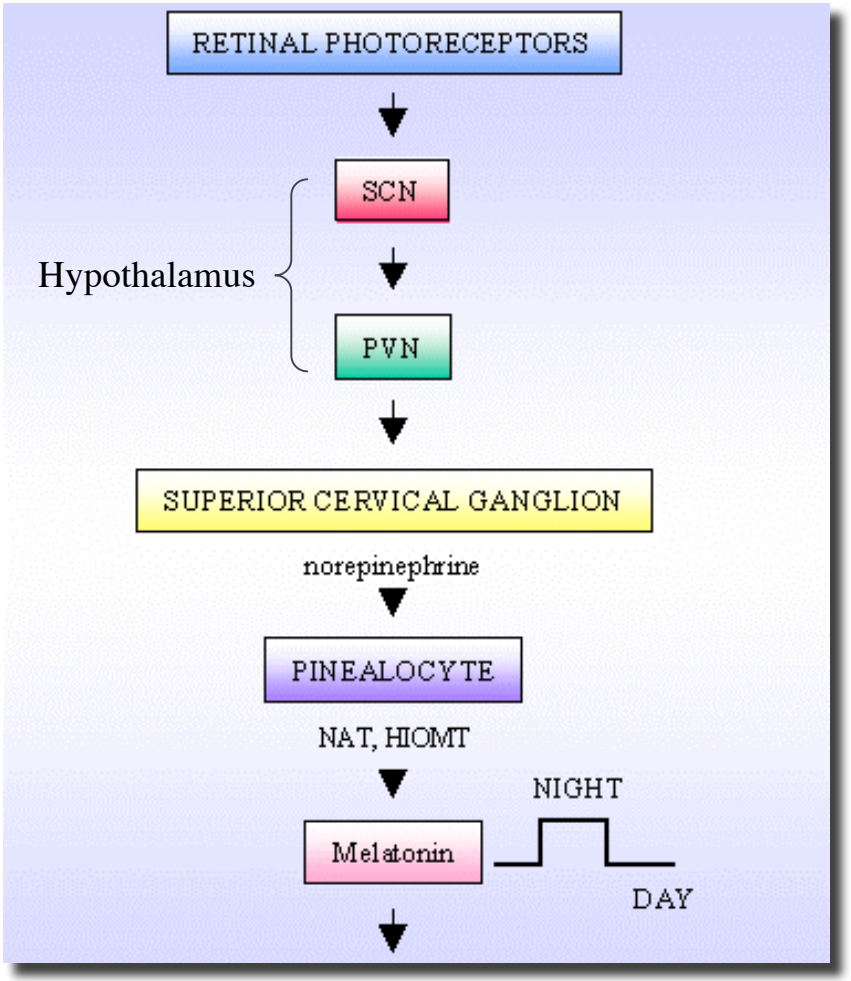
those that enhance offspring survival

- lower predation
- nutrition for offspring

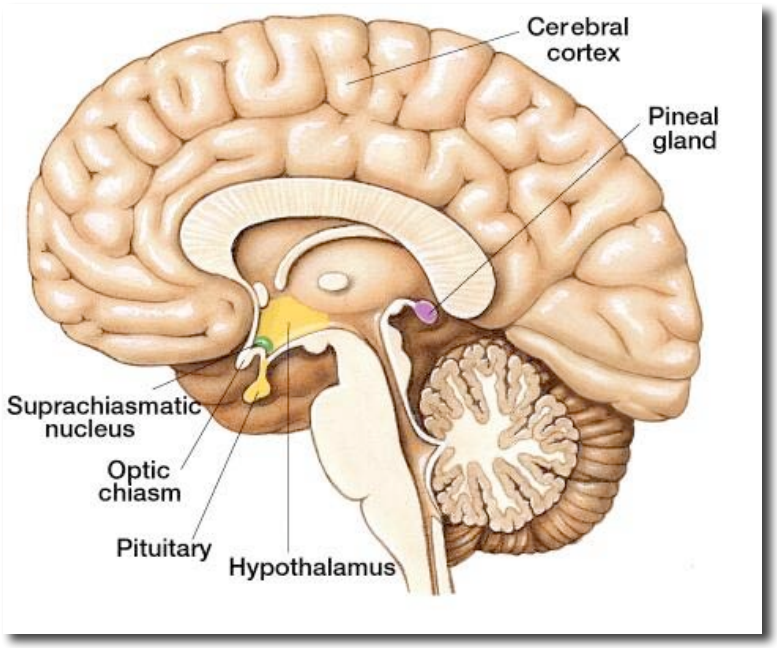
Endocrinology of Gonadal Cycles

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

Photoperiod - Melatonin



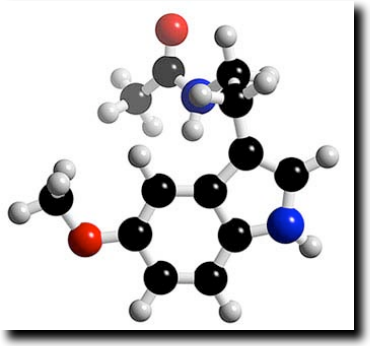
- Photoperiod detected
- transmitted to the hypothalamus
- neural signal is transduced into a hormonal response
- SCN
  - suprachiasmatic nucleus
  - is an integrative center (ie.,neural clock)
  - processes information provided by synchronizing agents (zeitgebers).



Pineal Gland

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

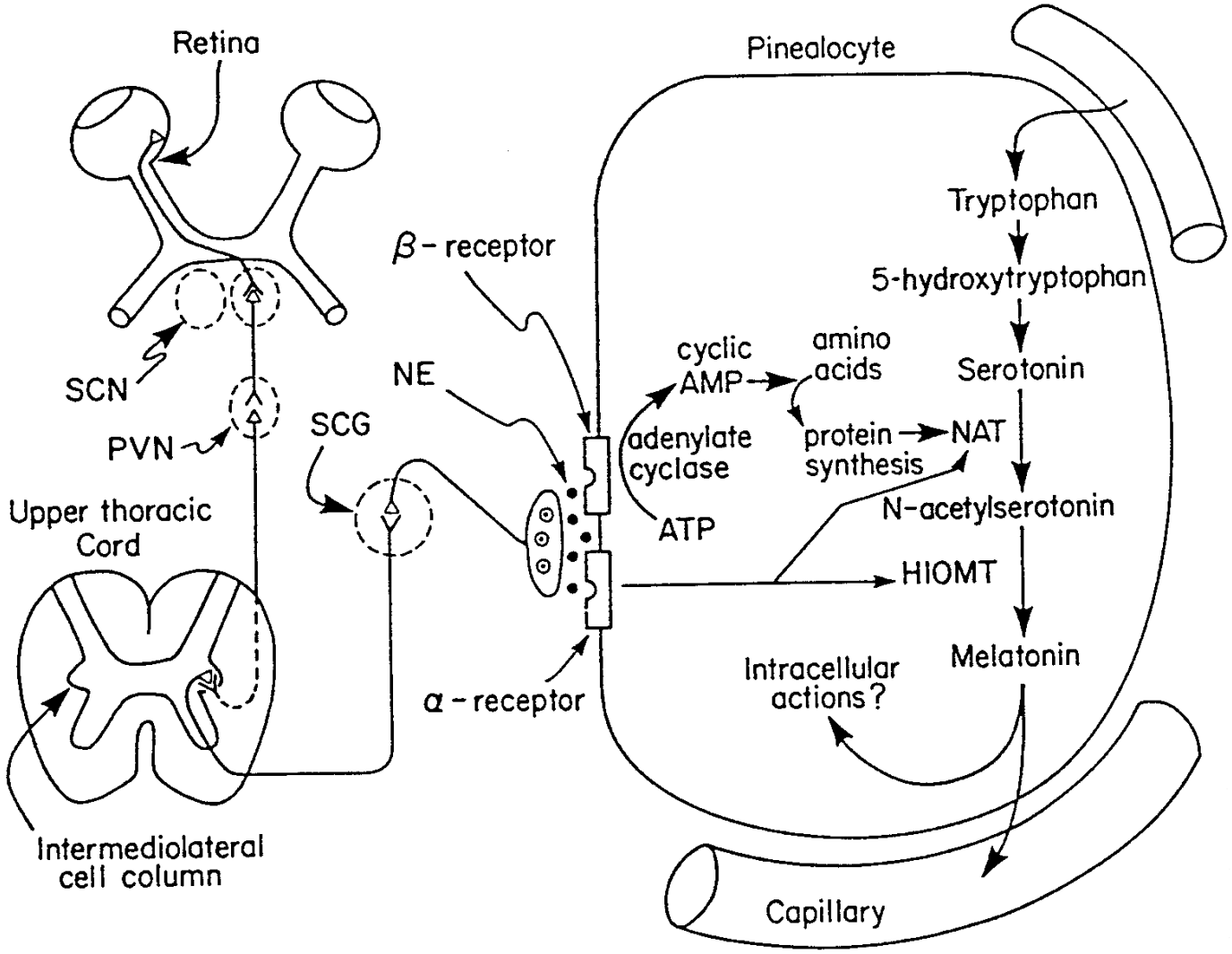
Melatonin



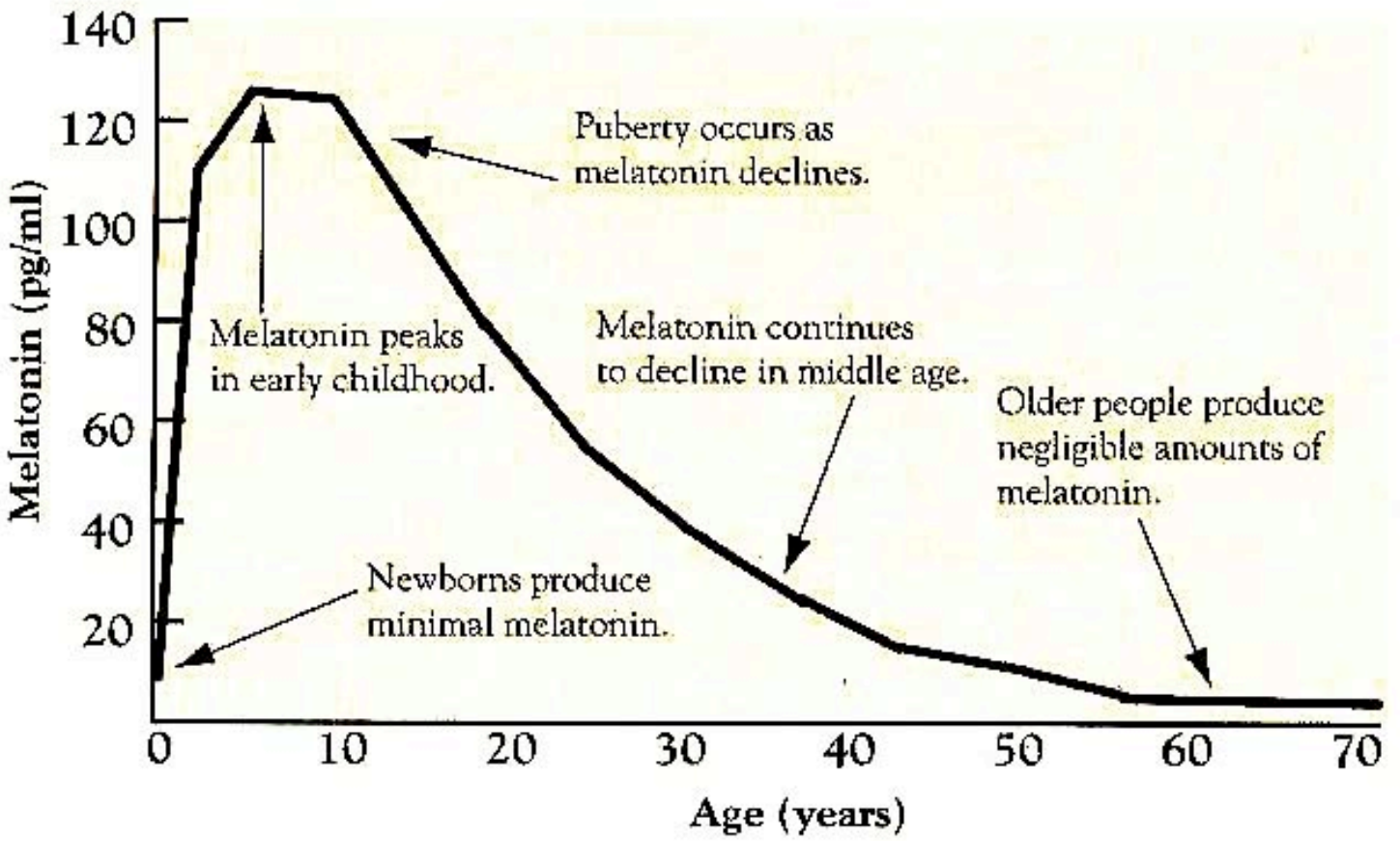
- Circadian (daily) rhythm of melatonin
  - codes the circannual cycle of seasonal reproduction
- Melatonin
  - is synthesized by the pineal gland in the darkness
  - exerts an inhibitory action on secretion of gonadotropins
    - long day -> low melatonin -> more GnRH -> reproduction
- Pinealectomy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

Can they help you sleep? Some of the melatonin products tested by CL.

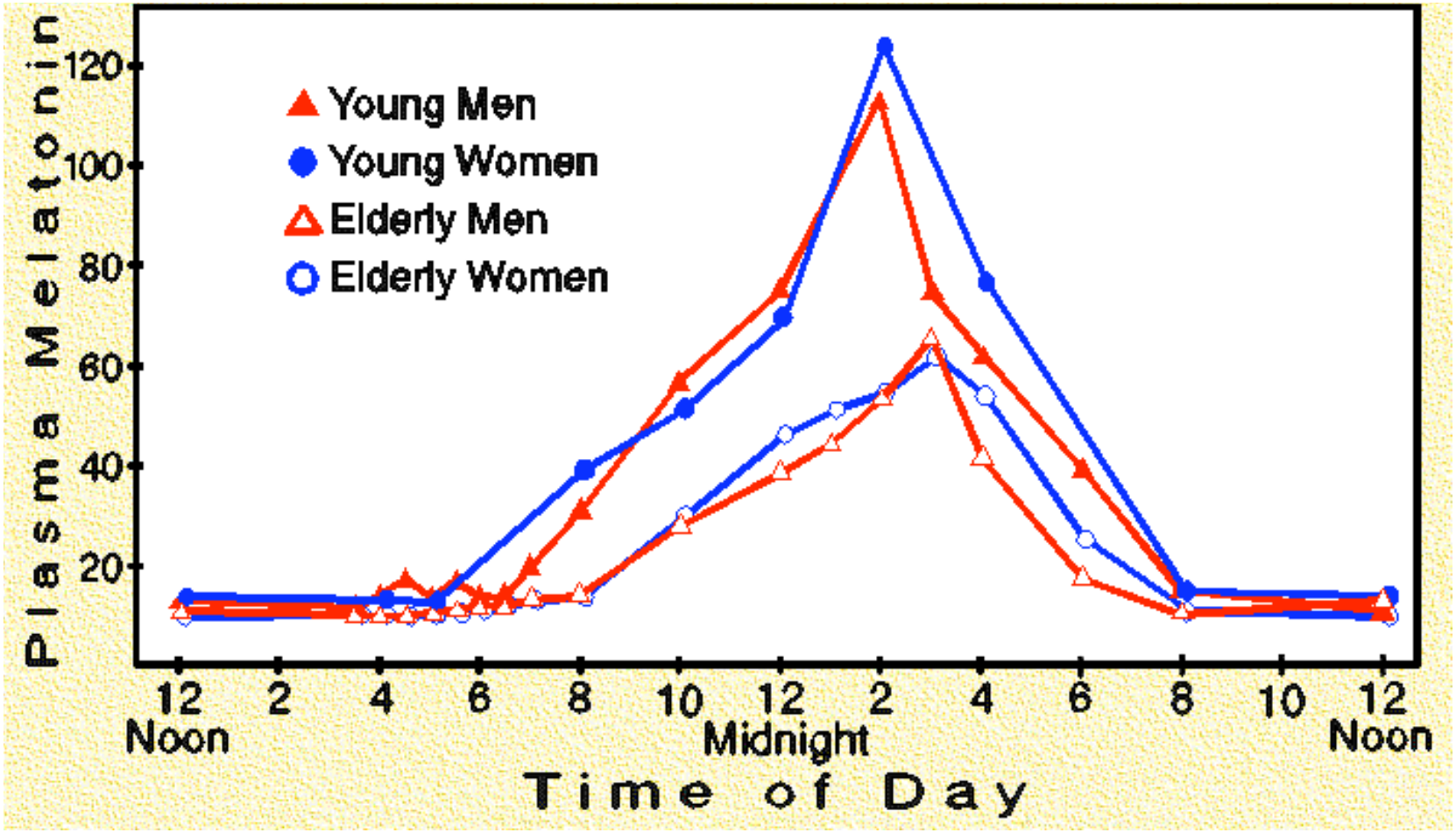
Synthesis of Melatonin



Melatonin and Age



Age and Melatonin



Ovarian Activity

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

Mammals

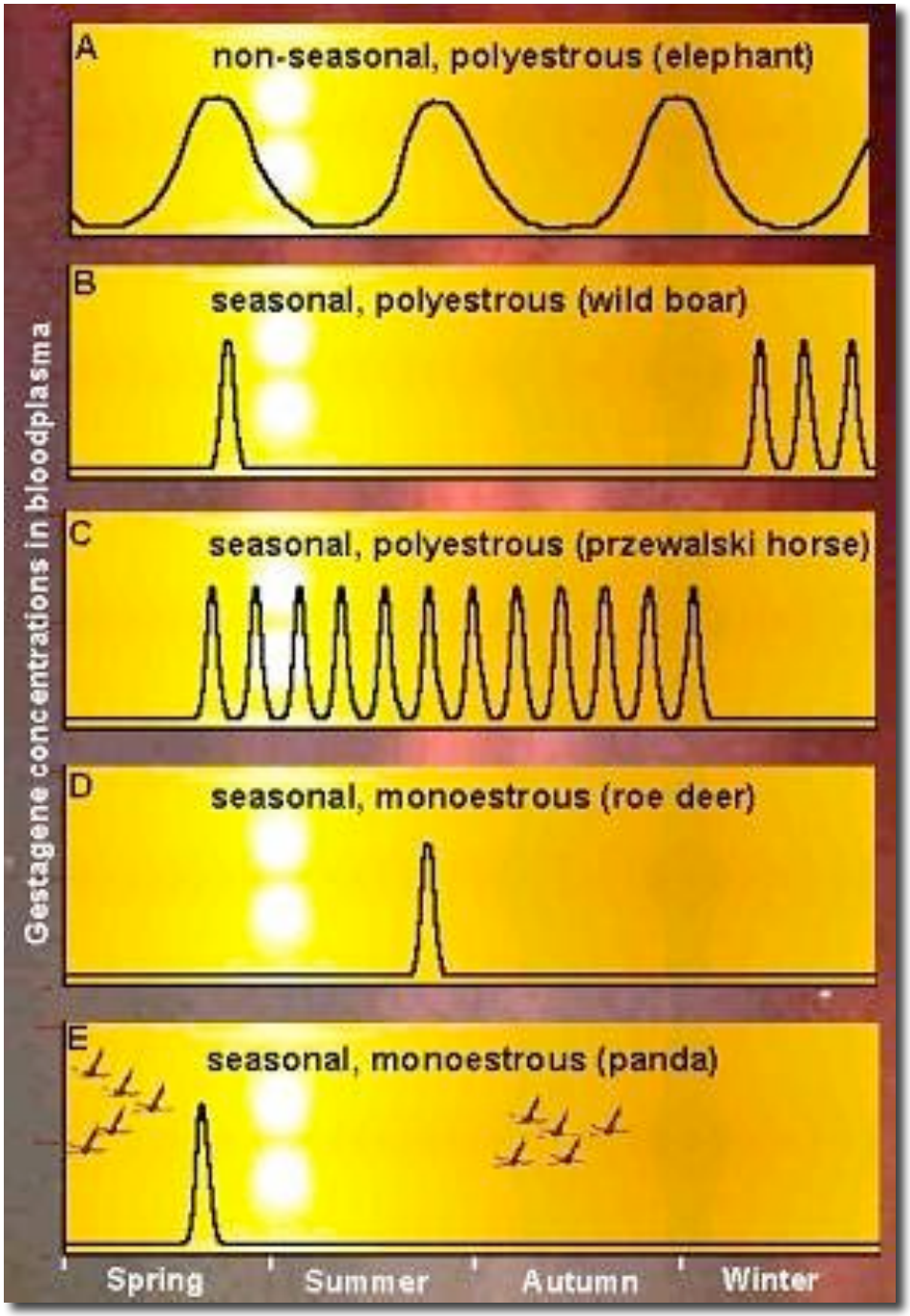
Estrous Cyclicity

- 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

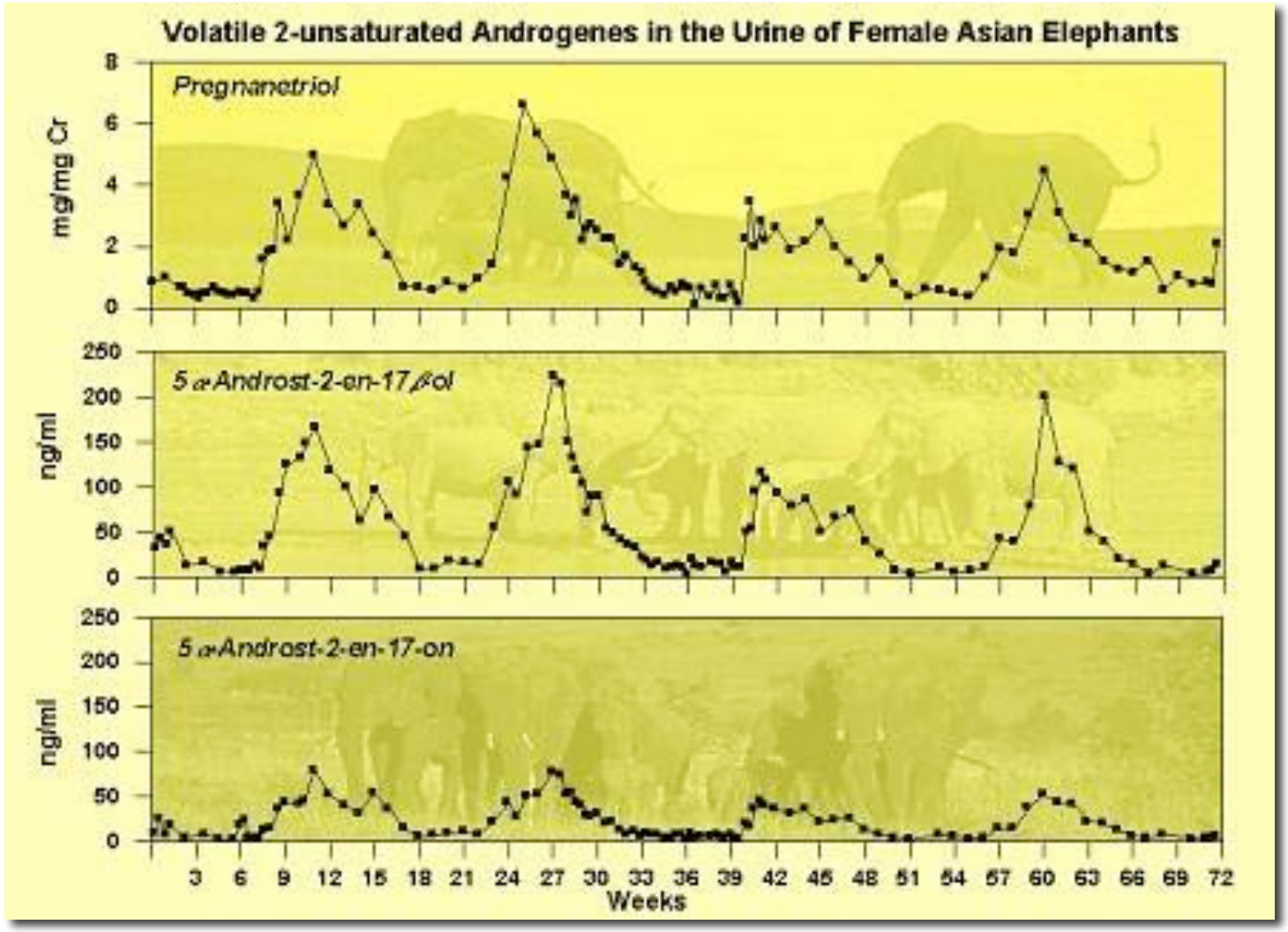
Cycle designation

- 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 cyclicity -Mammals-

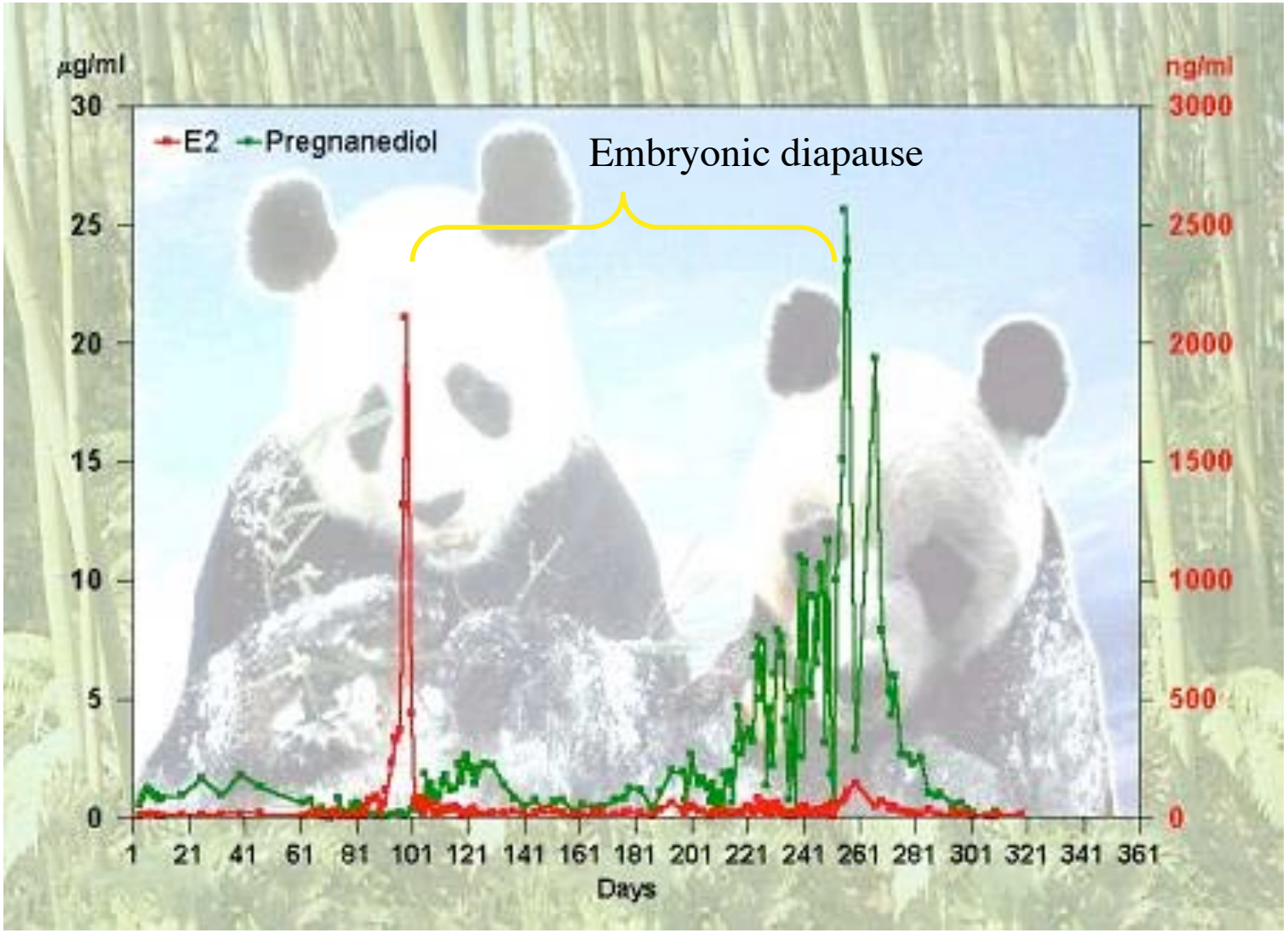


Elephant - polyestrous - 4 cycles - urinary hormones



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

Panda - monoestrous - cycle

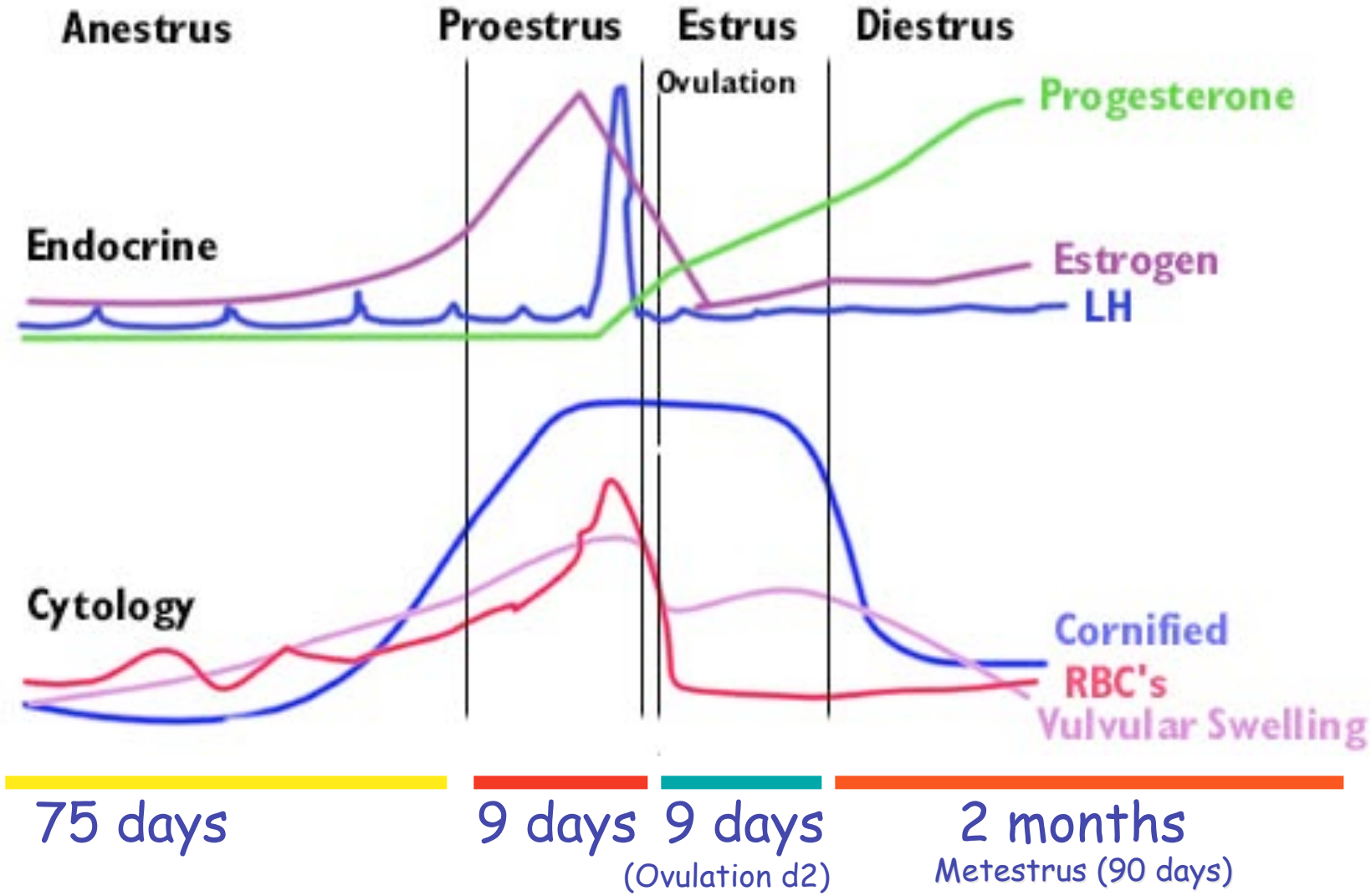


http://www.izw-berlin.de/en/research/fg4/index.html?reproduktionsmonitoring.html~rechts

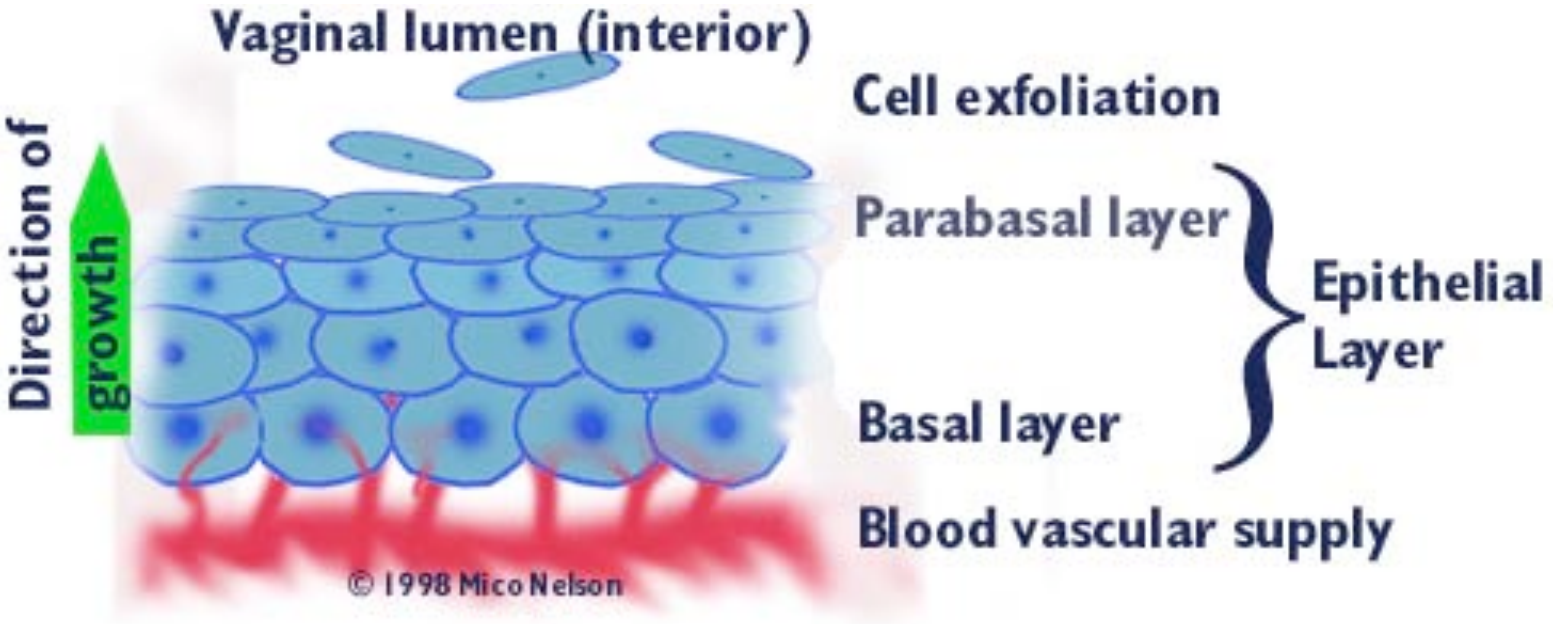
Estrous cycles - Dogs

- 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



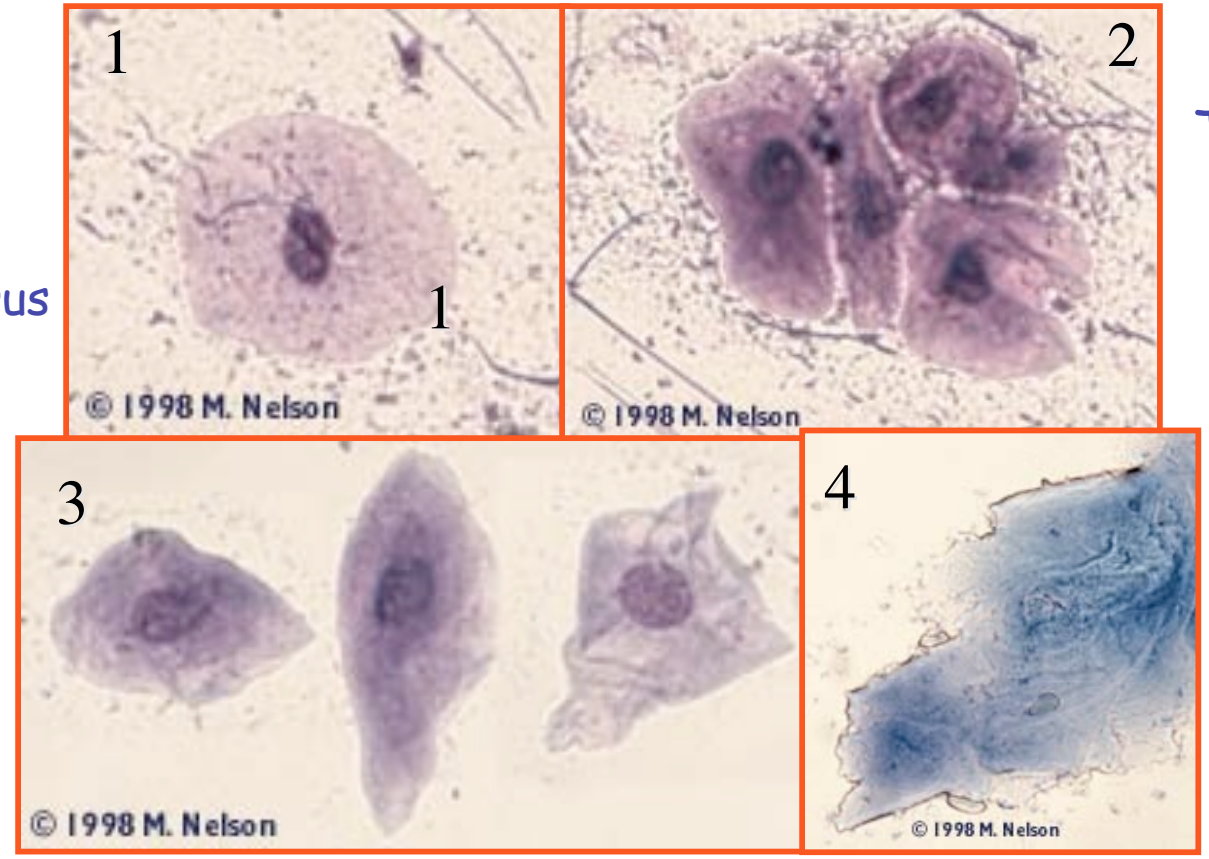
Cytological Changes - Vagina



Cytology of Estrus - Dog

Cornification/Keratinization

Parabasal
Anestrus -
early proestrus



Transitional

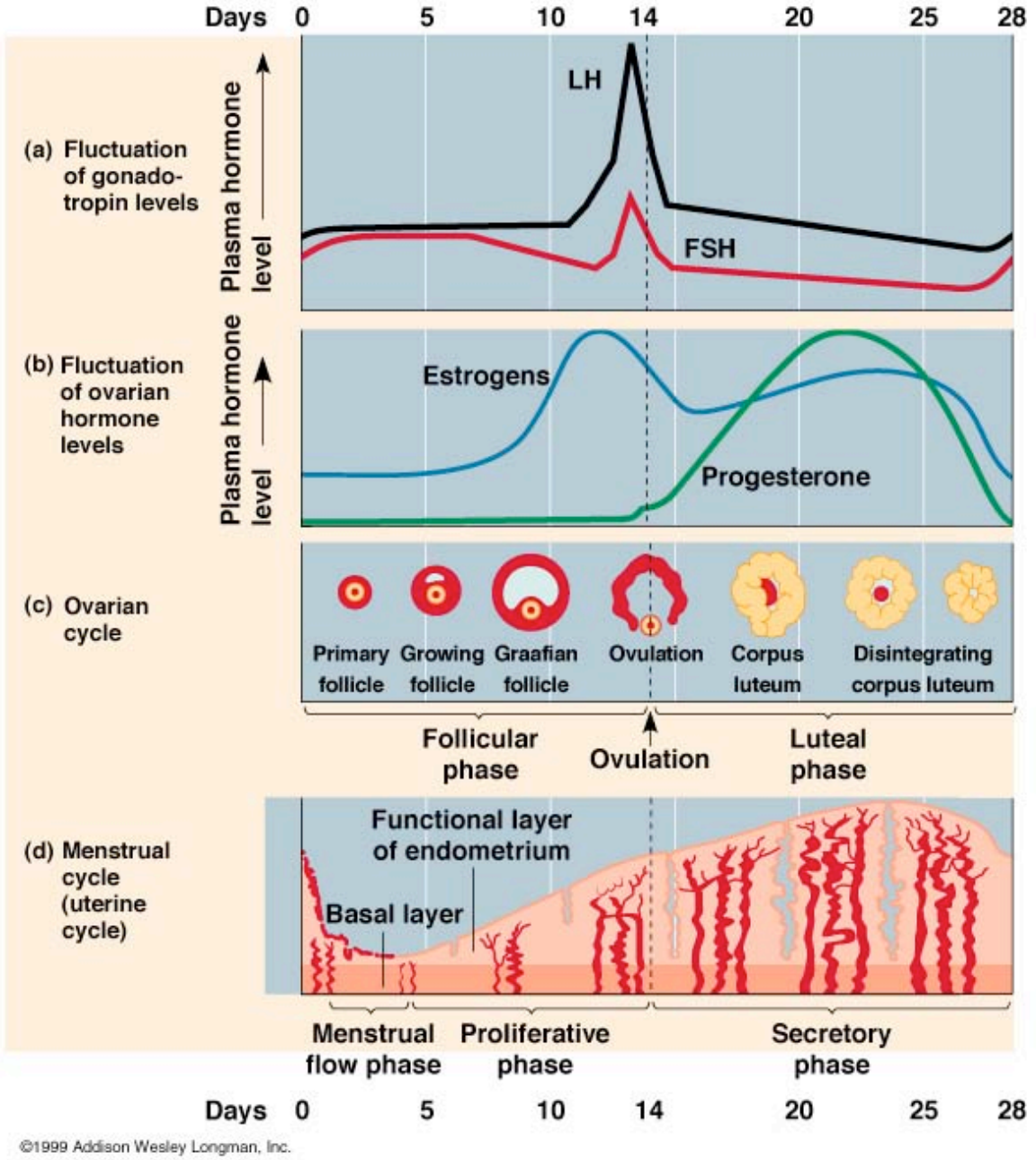
Partly Cornified
proestrus

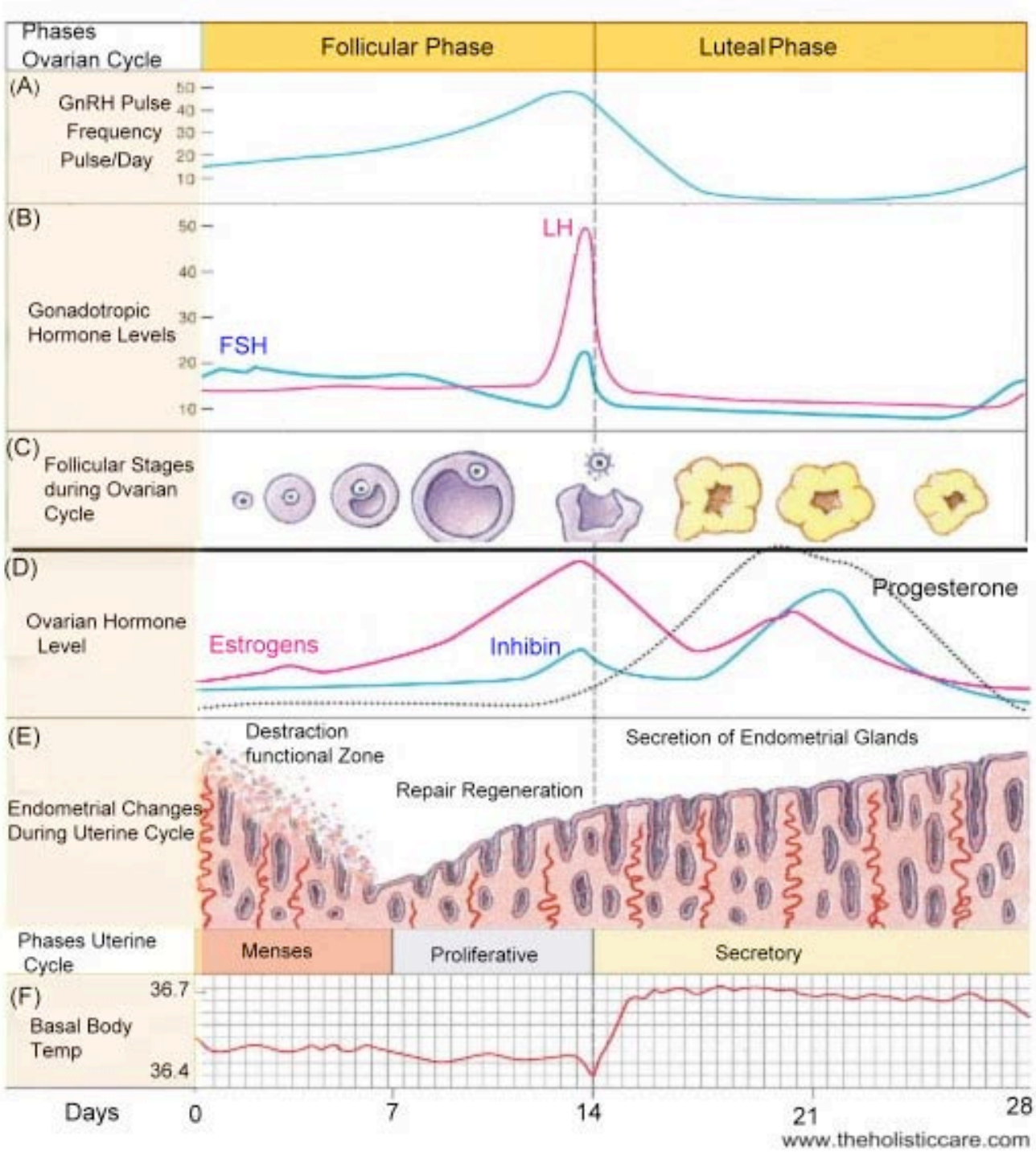
Cornified or Squamous
estrus

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
E_2
P




Phases
Ovarian Cycle
Follicular Phase
Luteal Phase
(A)
GnRH Pulse
Frequency
Pulse/Day
50
40
30
20
10
(B)
Gonadotropic
Hormone Levels
LH
FSH
50
40
30
20
10
(C)
Follicular Stages
during Ovarian
Cycle
(D)
Ovarian Hormone
Level
Estrogens
Inhibin
Progesterone
(E)
Endometrial Changes
During Uterine Cycle
Destraction
functional Zone
Repair Regeneration
Secretion of Endometrial Glands
Phases Uterine
Cycle
Menses
Proliferative
Secretory
(F)
Basal Body
Temp
36.7
36.4
Days
0
7
14
21
28
www.theholisticcare.com

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

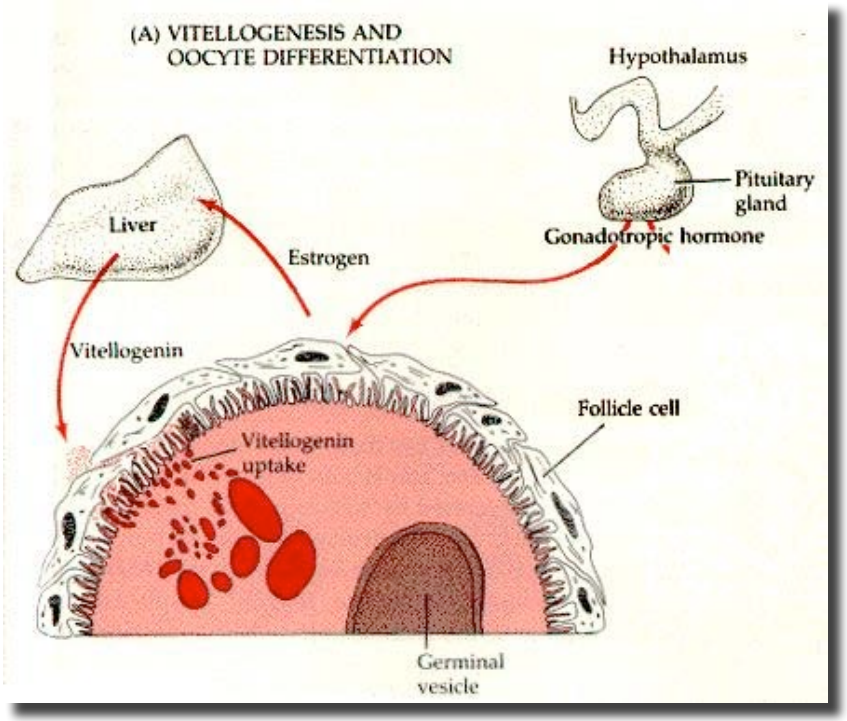
Nonmammalian Species - Reptiles

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

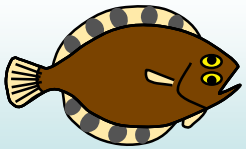
- estrogen stimulates protein synthesis in liver
  - vitellogenins (Vtgs)
  - may be more than 1
    - Most species 3



- 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"

Barfin flounder



Verasper moseri

~Jun

Aug

Secondary growt

Lipid droplets

Sep

Egg

Oct

Yolk granules

Dec

Ovulation

Apr

Mar

Vitellogenesis

Final maturation

Takahiro Matsubara and associates

Hokkaido National Fisheries Research Institute

Teleost Vitellogenesis

FSH

Pituitary

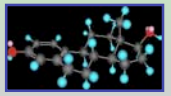
Vitellogenin

Liver

Oocyte

- Environmental cues
- Endogenous factors

Estradiol



Vitellogenin and yolk proteins

Blood

Vitellogenin

N

Lipid

Phosphate

C

Oocyte

Lipovitellin

Light-chain

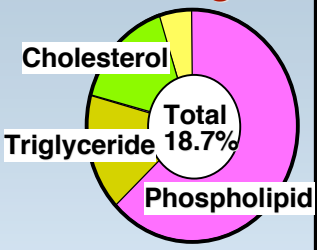
Heavy-chain

Phosvitin

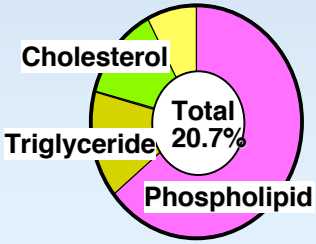
β'-component

C-terminal component

Vitellogenin

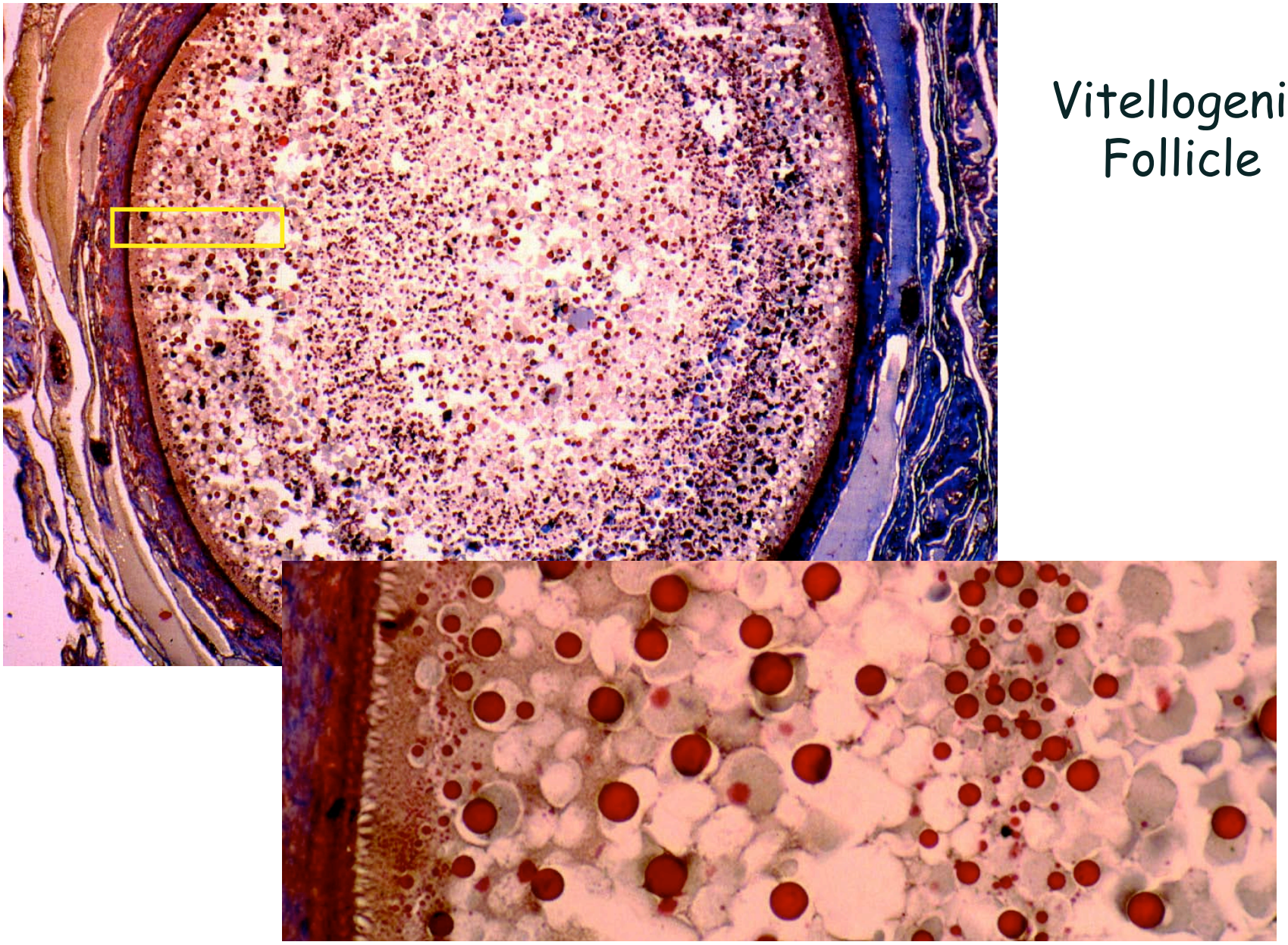


Lipovitellin



Vertebrate Yolk

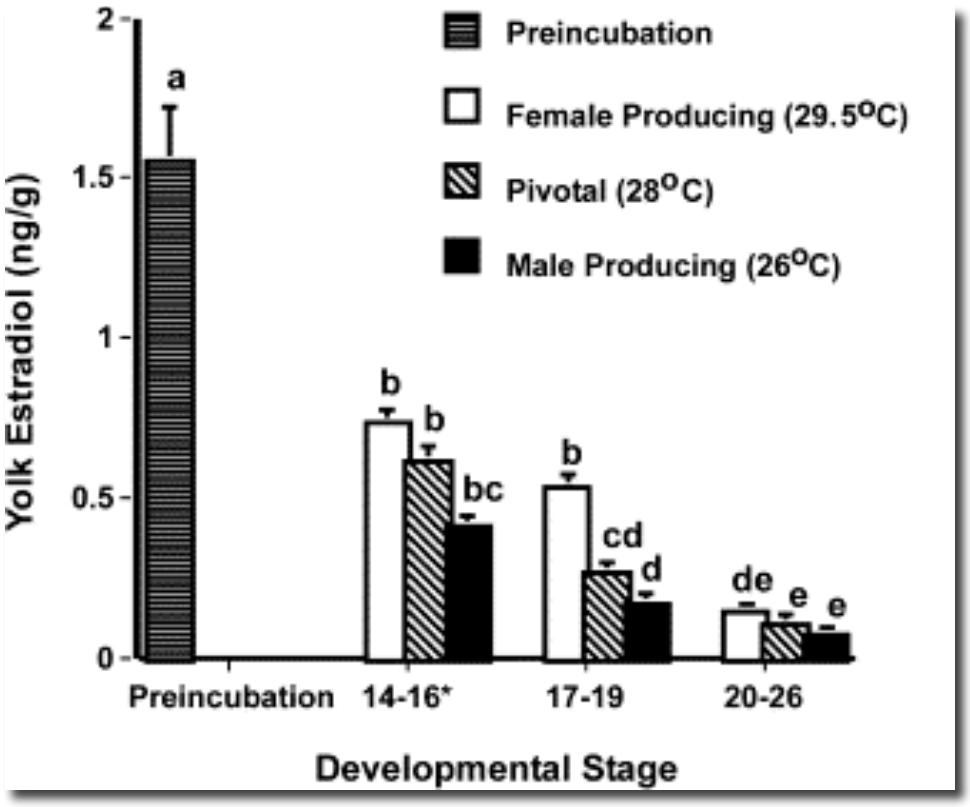
- proteins, phospholipids, neutral fats, hormones
  - Protein stored as yolk platelets or spheres
    - can be formed into yolk crystals
  - Fats stored in lipochondria
    - cytoplasmic inclusions
    - fish - fat droplets or yolk spherules present
  - Carbohydrate in form of glycogen granules
  - Hormones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



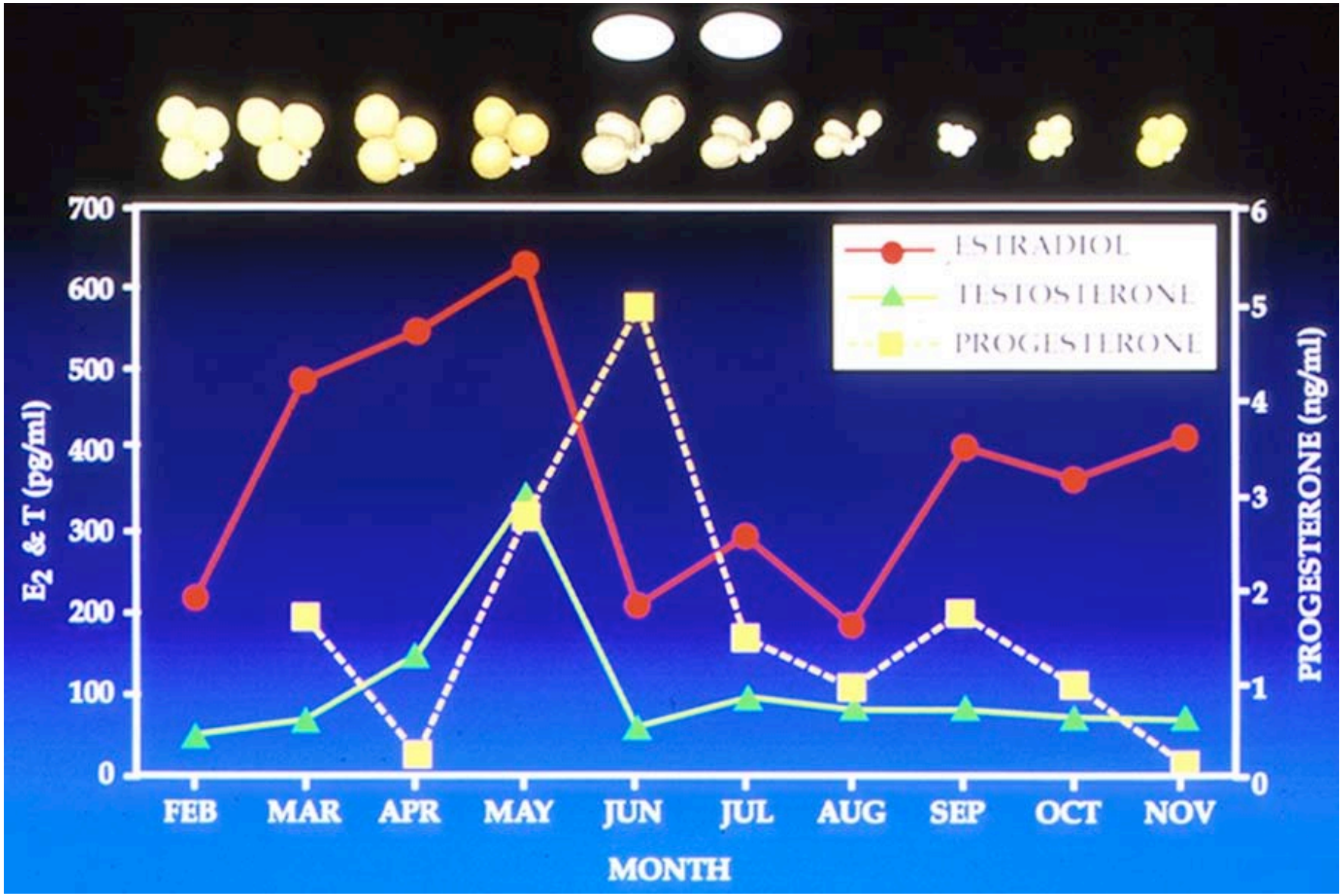
Vitellogenic Follicle

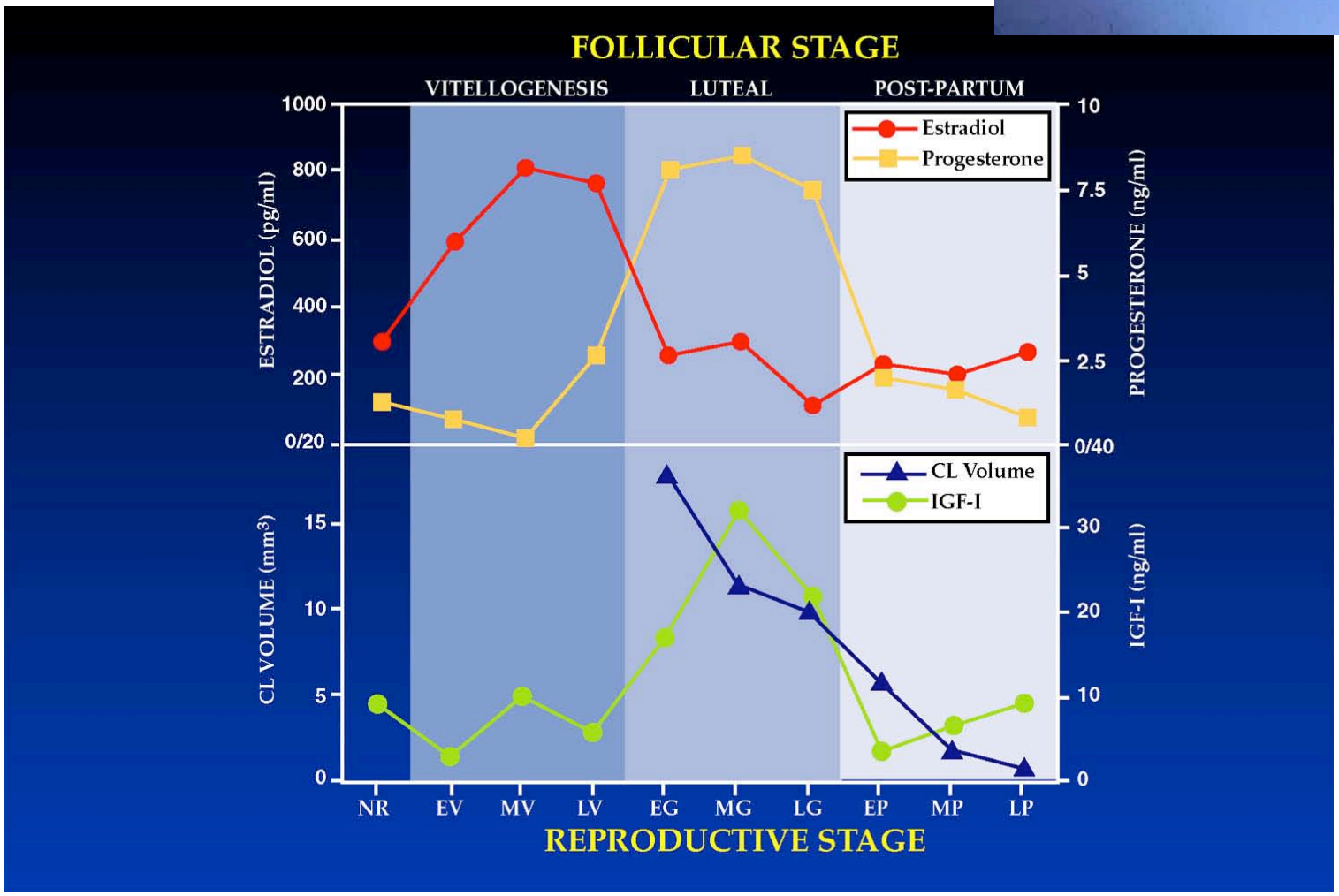
American alligator

Uribe and Guillette (2000) J. Morphol. 245: 225-240



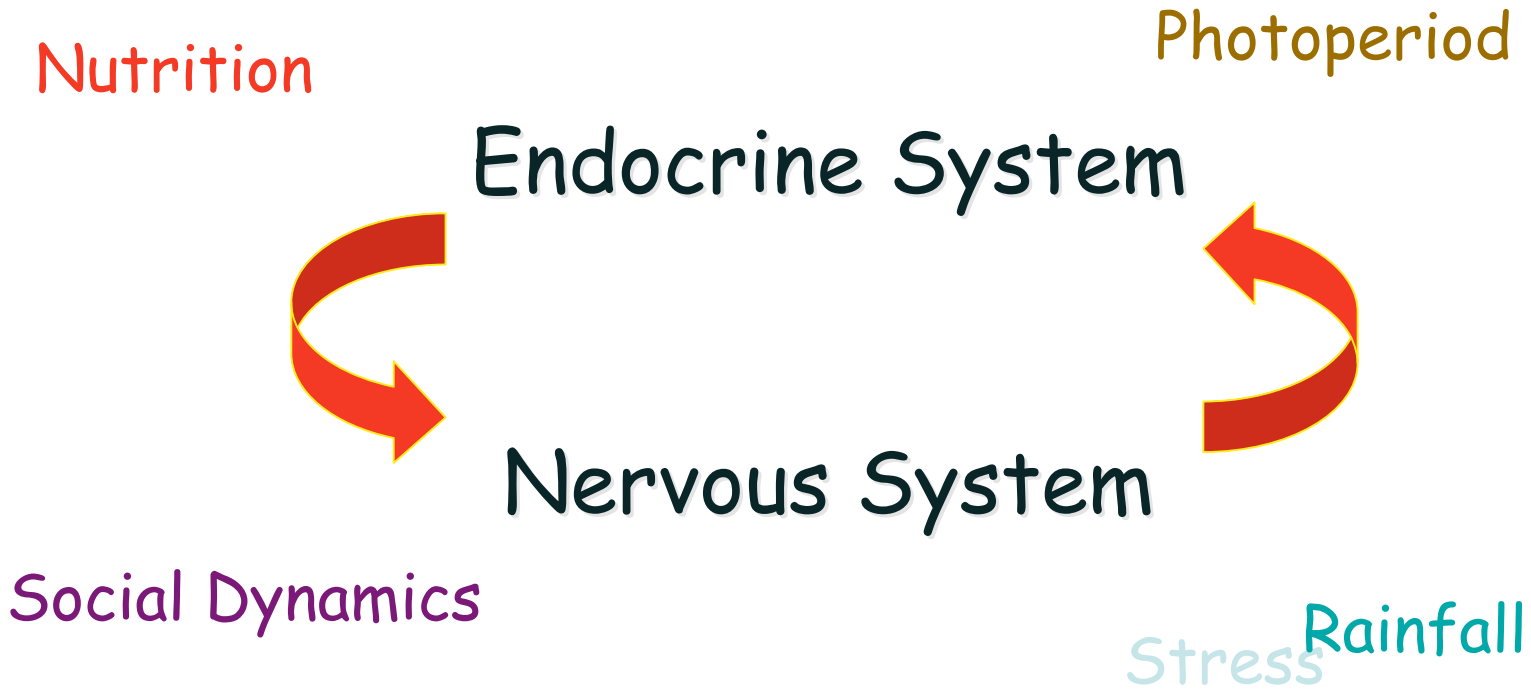
Elf, P.K., Gen. Comp. Endocrinol.132:349-355. 2003


ESTRADIOL
TESTOSTERONE
PROGESTERONE
E_2 & T (pg/ml)
PROGESTERONE (ng/ml)
700
600
500
400
300
200
100
0
6
5
4
3
2
1
0
FEB
MAR
APR
MAY
JUN
JUL
AUG
SEP
OCT
NOV
MONTH



Guillette and Milnes (2001)

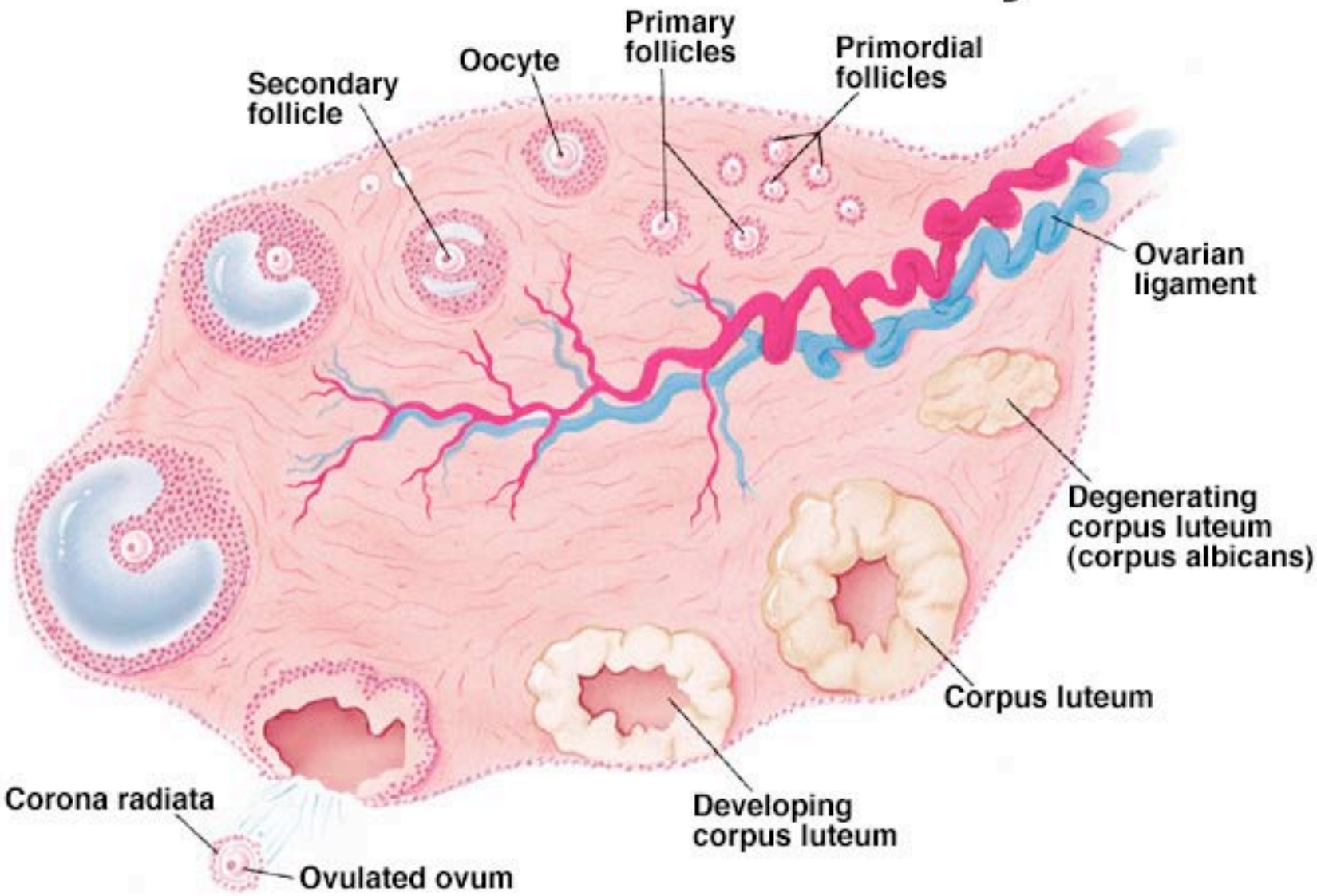
Mechanisms controlling cycles



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

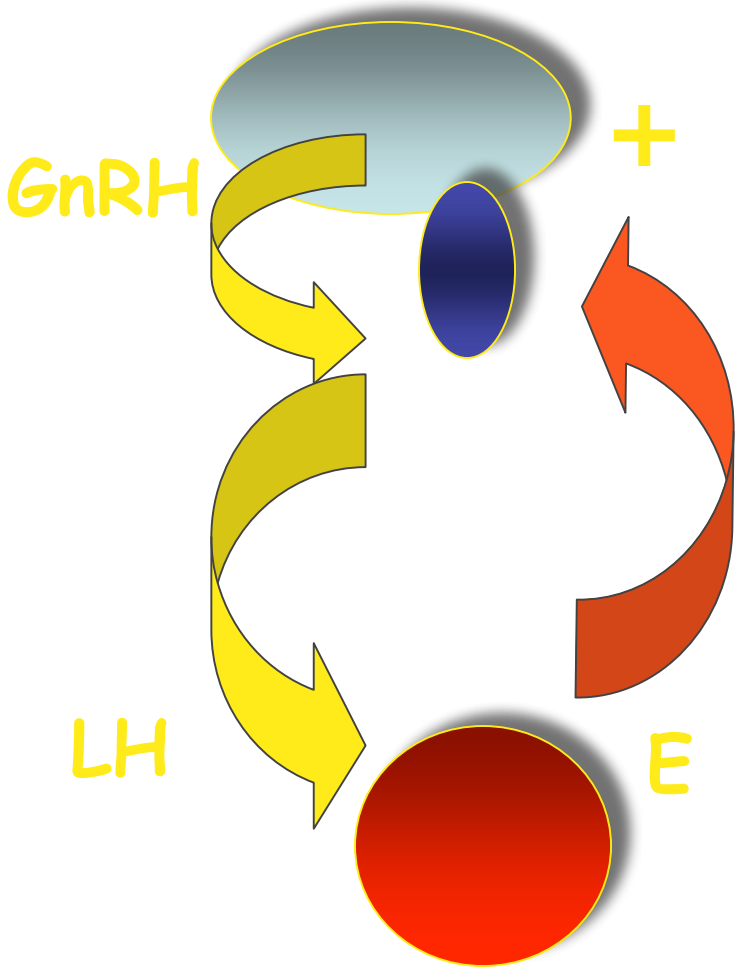


Which follicle grows?

- 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 of $PGF_{2\alpha}$ and PGE_2

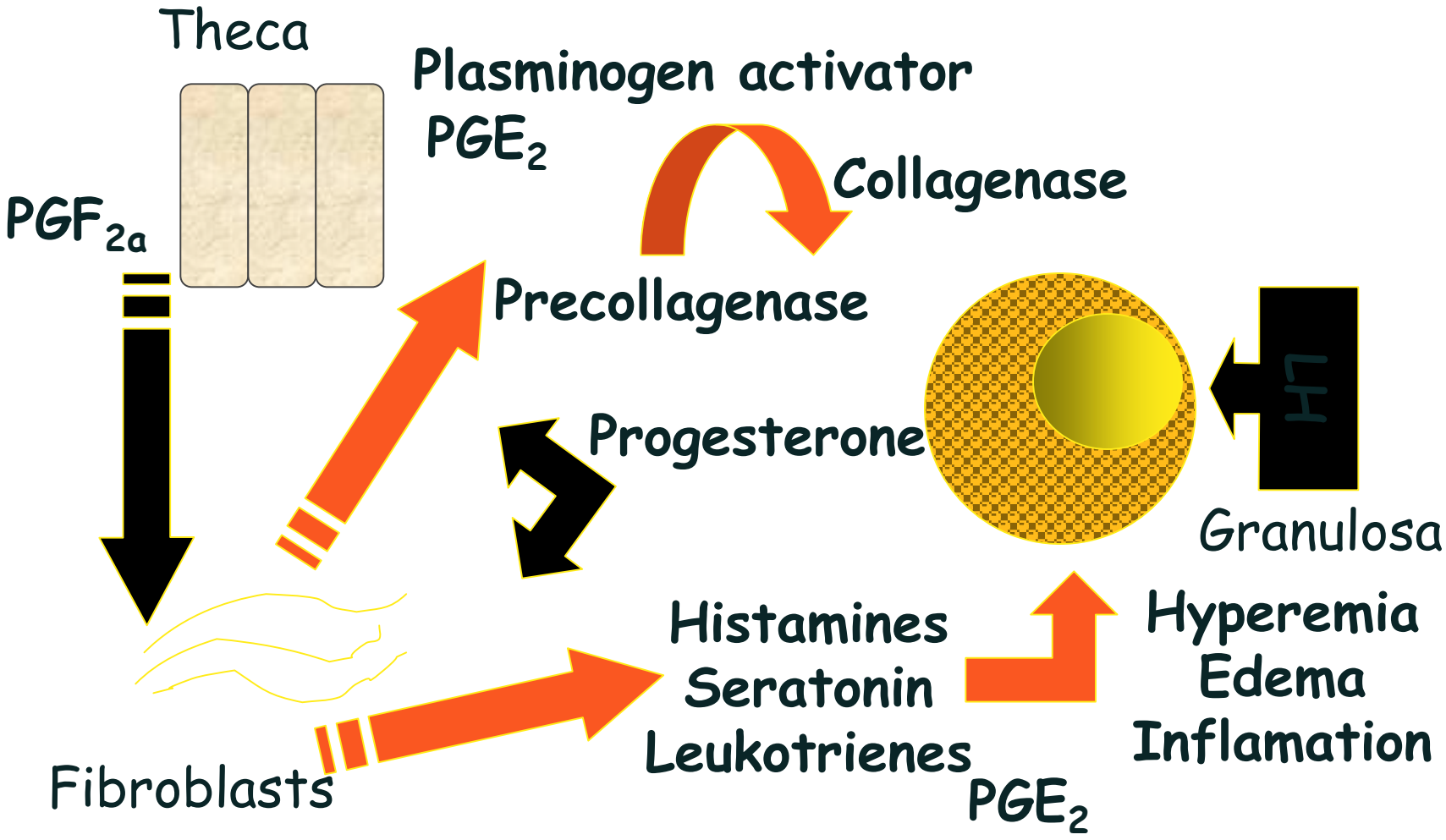
PGE_2 & $PGF_{2\alpha}$

- PGE_2
  - 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

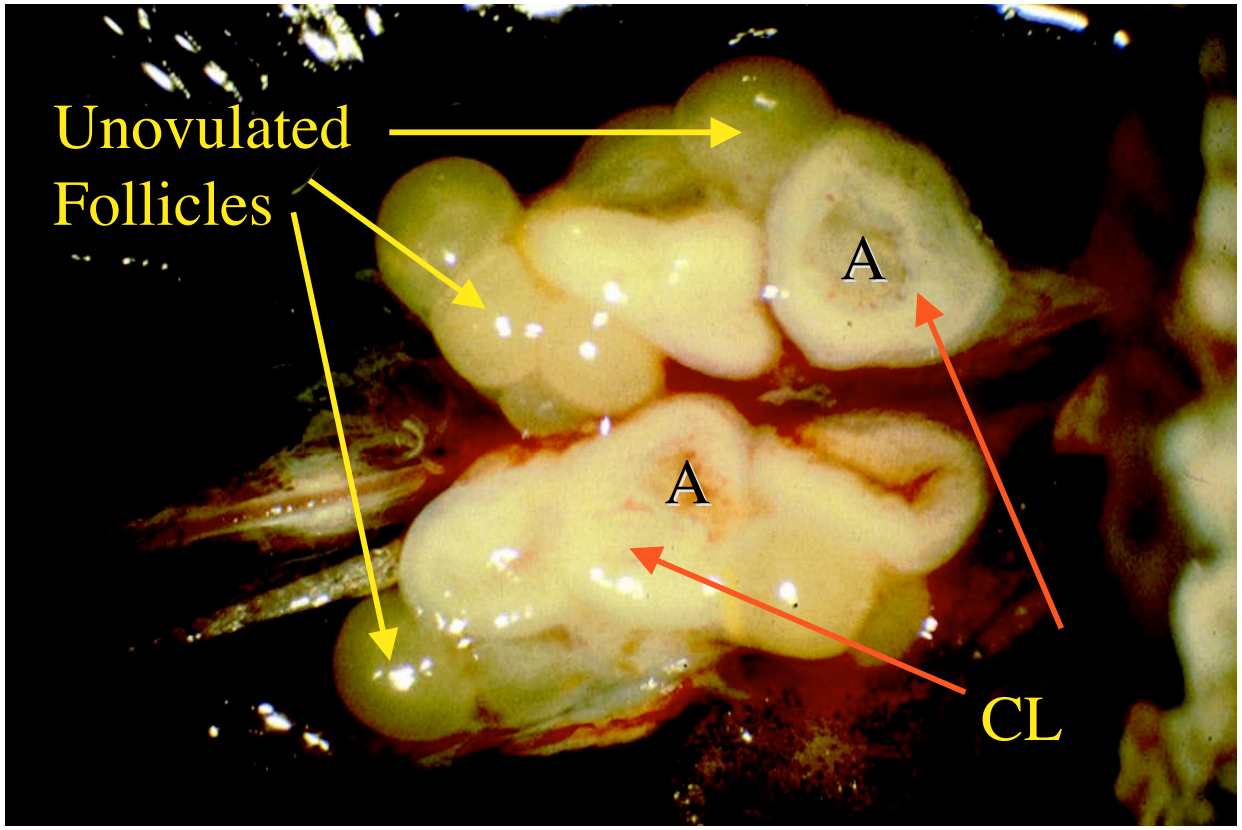

Theca
Plasminogen activator
PGE_2
PGF_{2a}
Collagenase
Precollagenase
Progesterone
LH
Granulosa
Histamines
Seratonin
Leukotrienes
PGE_2
Hyperemia
Edema
Inflamation
Fibroblasts

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

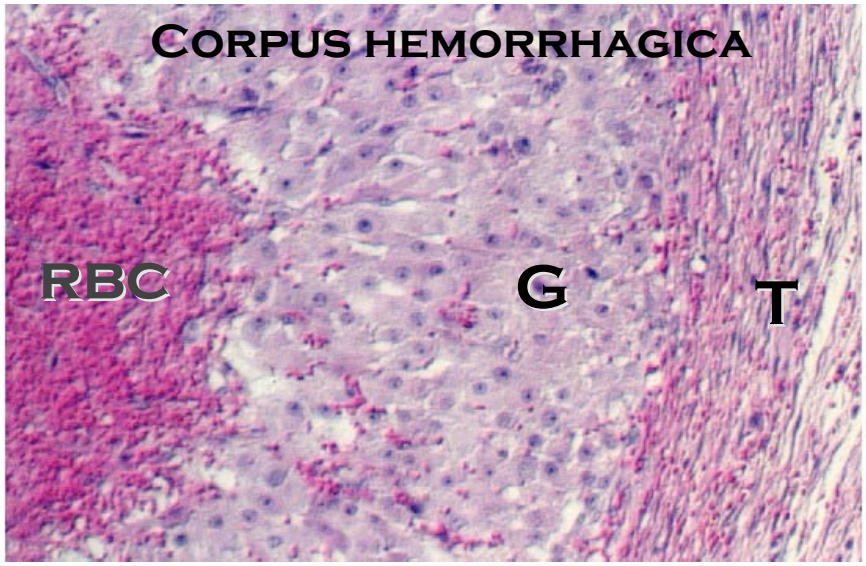


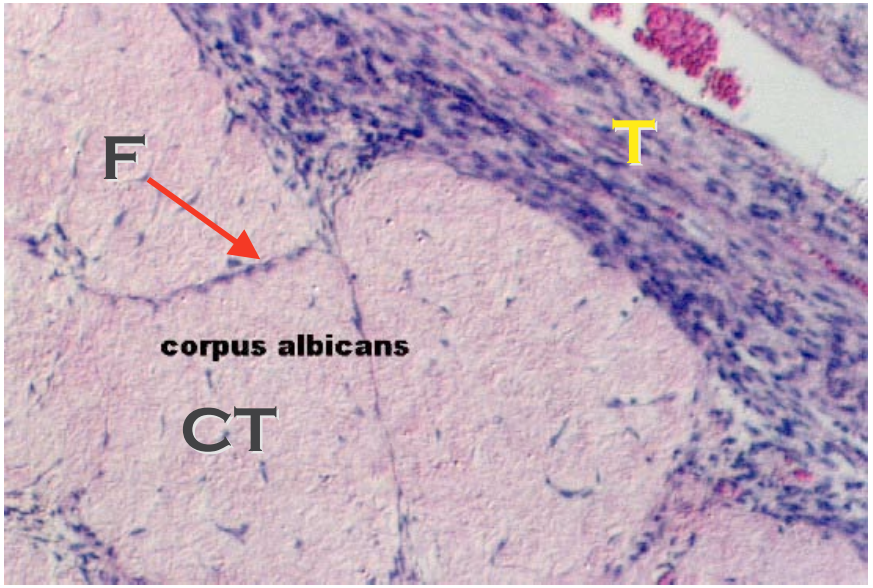
Corpus Luteum
gross anatomy

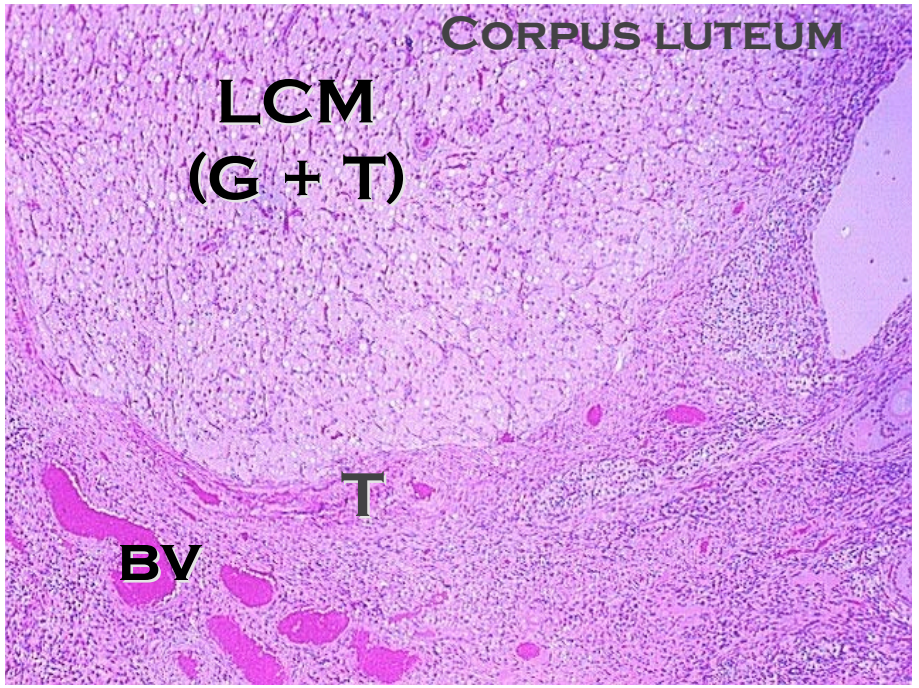
Lizard (*Sceloporus* sp.) Ovary -within hours of ovulation

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

CL histology

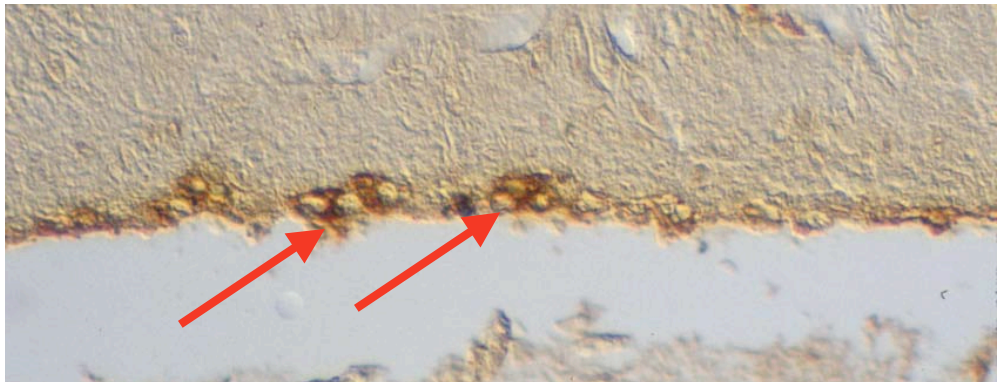


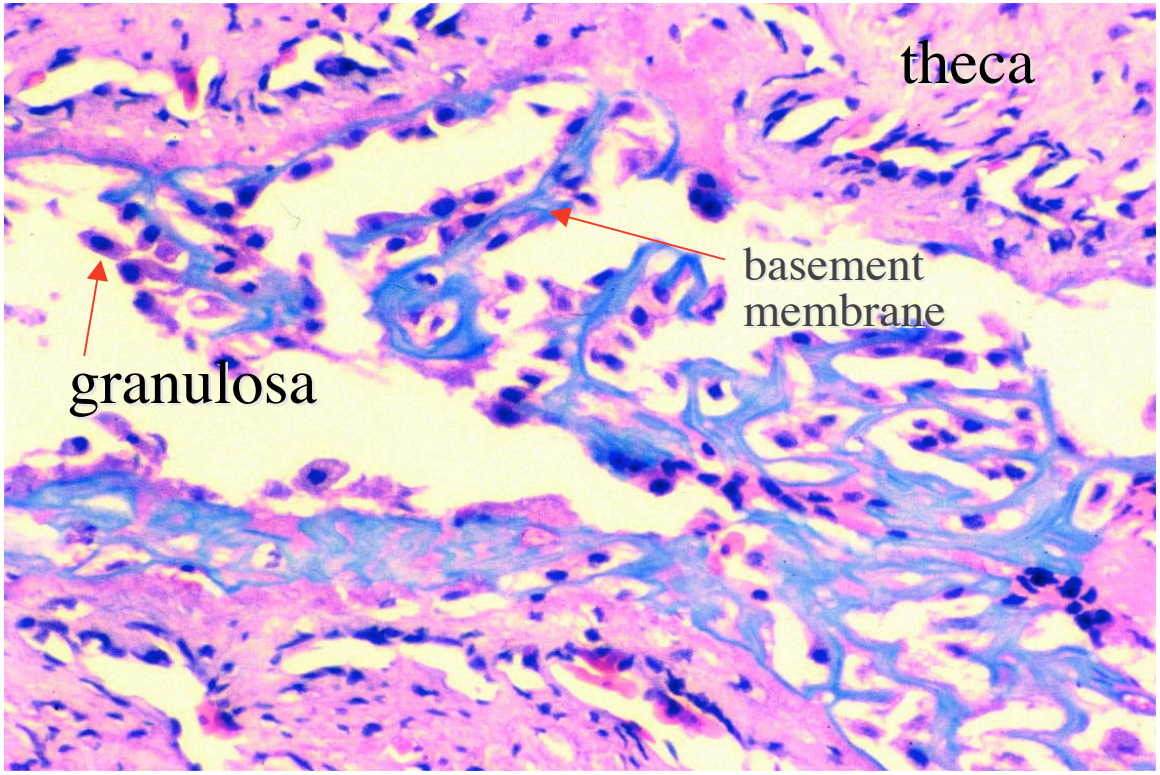


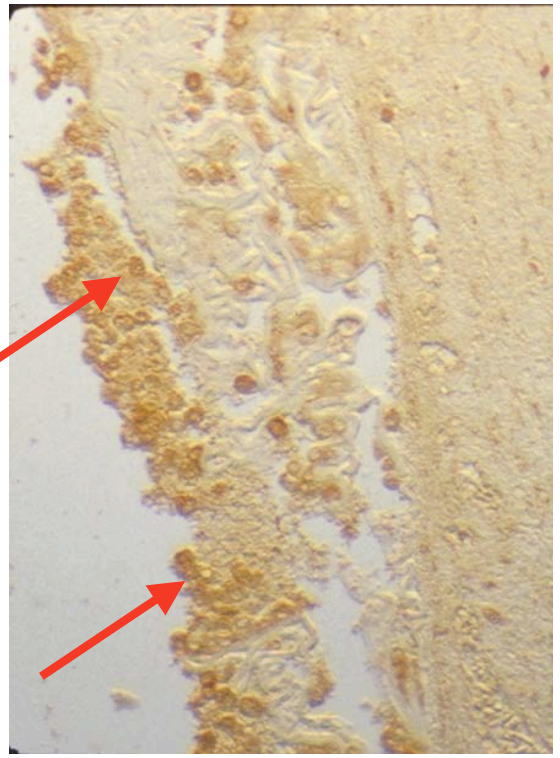


G, granulosa; T, theca; BV, blood vessels; RBC, red blood cells; F, fibroblast, CT, connective tissue

Immunocytochemistry for relaxin in alligator CL



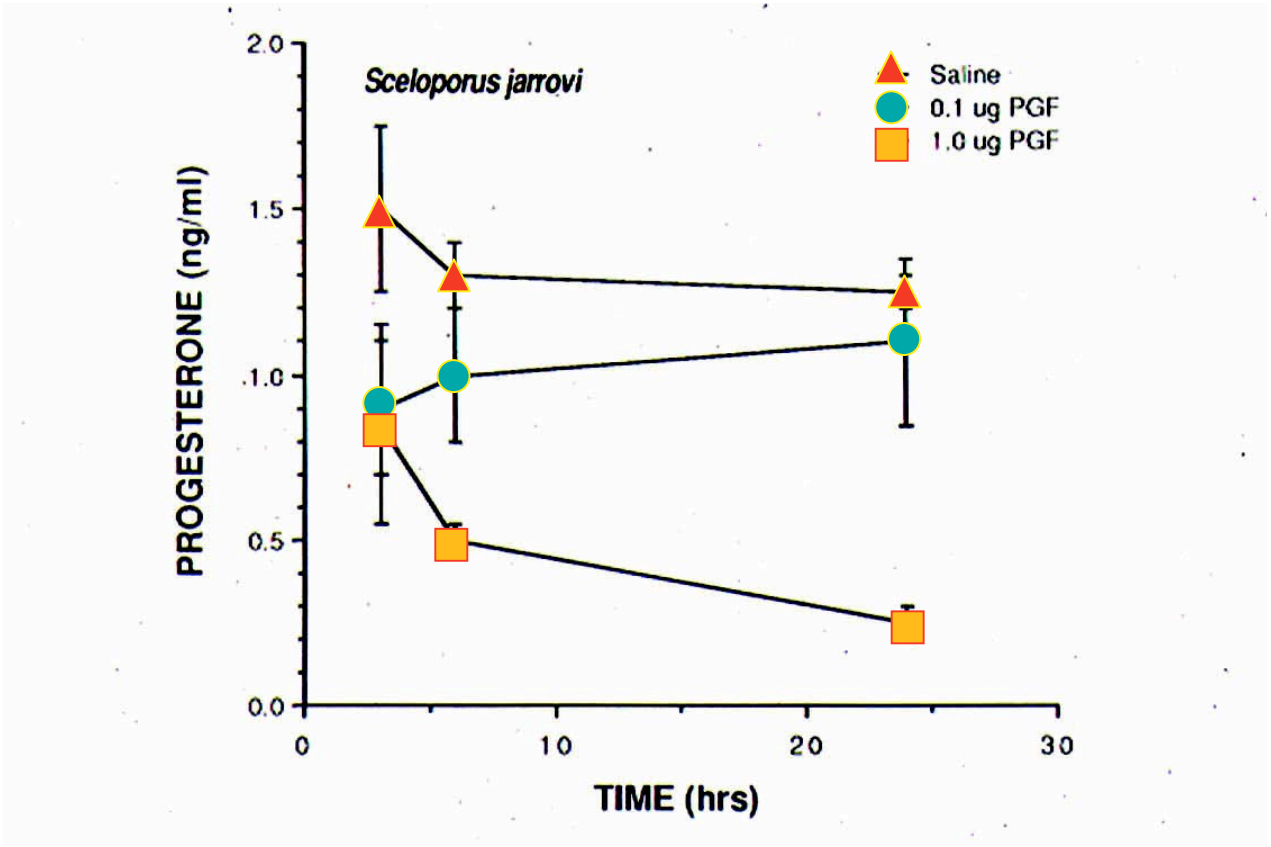




"activity" of CL

- can remain 'active' thru out pregnancy
- can degrade rapidly after ovulation
- luteotropic (stimulatory) agents include
  - FSH, LH, E, PGE_2
- luteolysis - CL death
  - induced by $PGF_{2\alpha}$ in many species
  - estrone luteolytic in primates

$PGF_{2\alpha}$-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