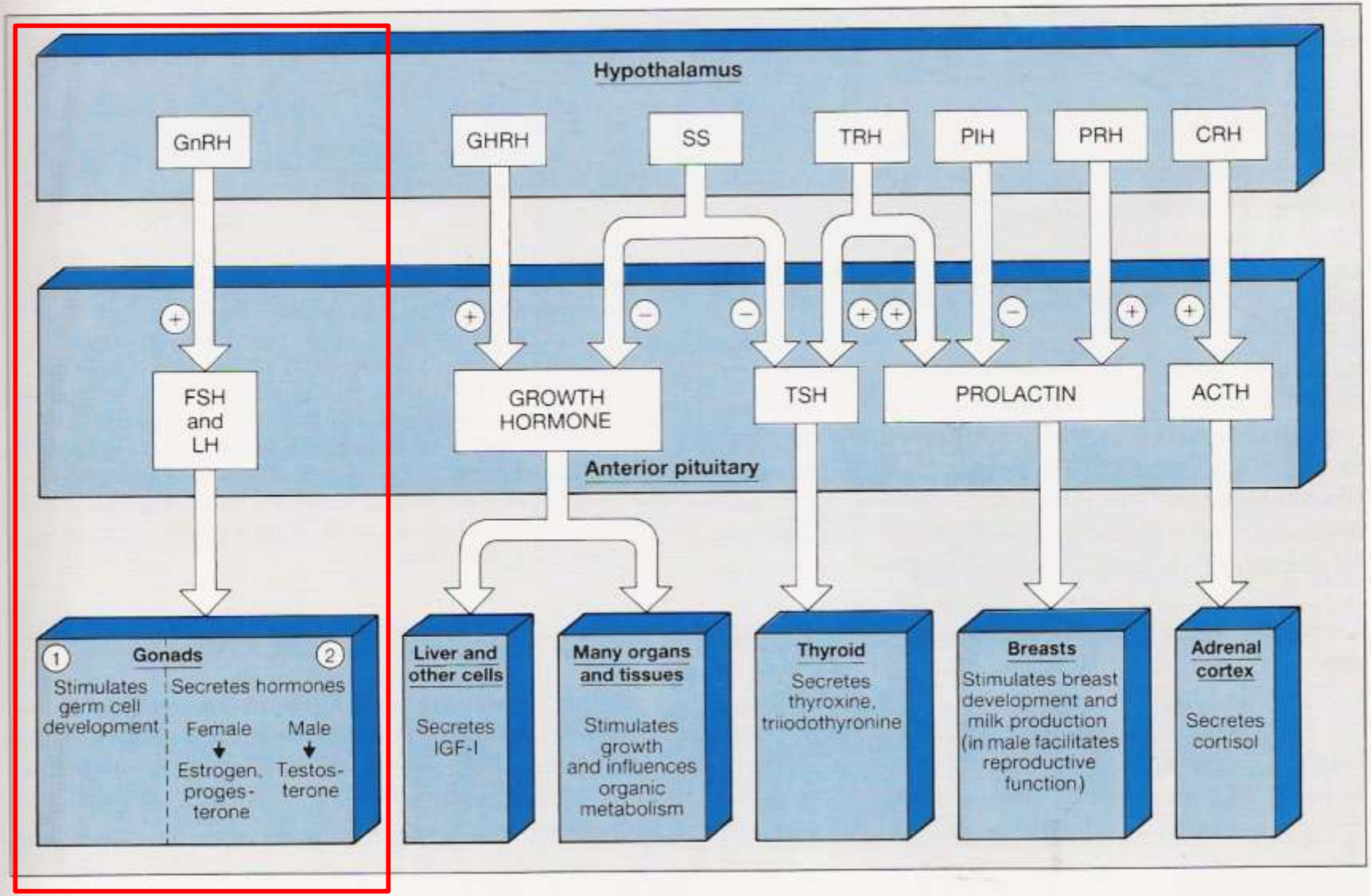
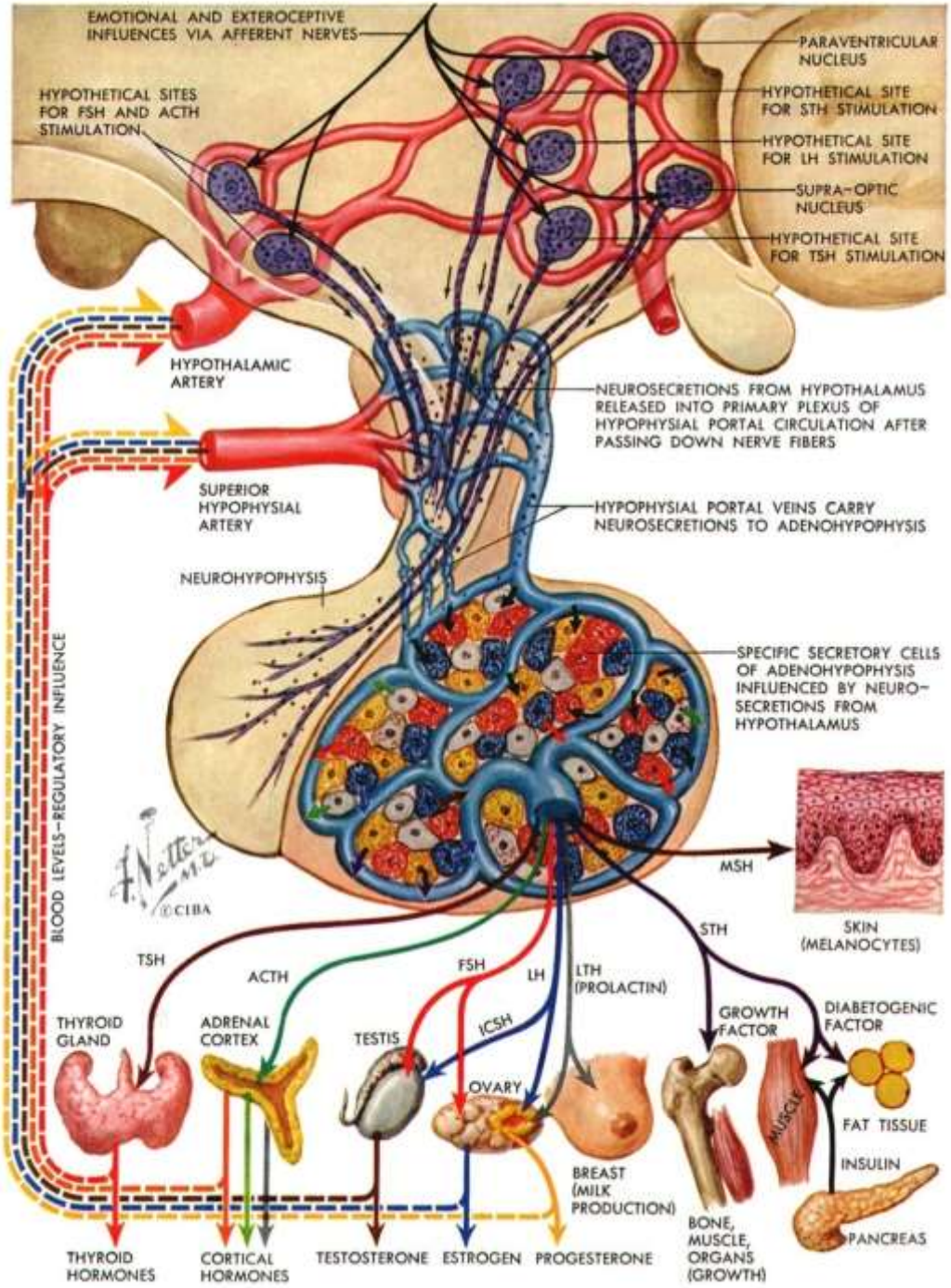


Eixo-Hipotálamo-Hipófise-Gônadas

FIGURE 10-20 A combination of Figures 10-17 and 10-19 summarizes the hypothalamic-anterior-pituitary system.

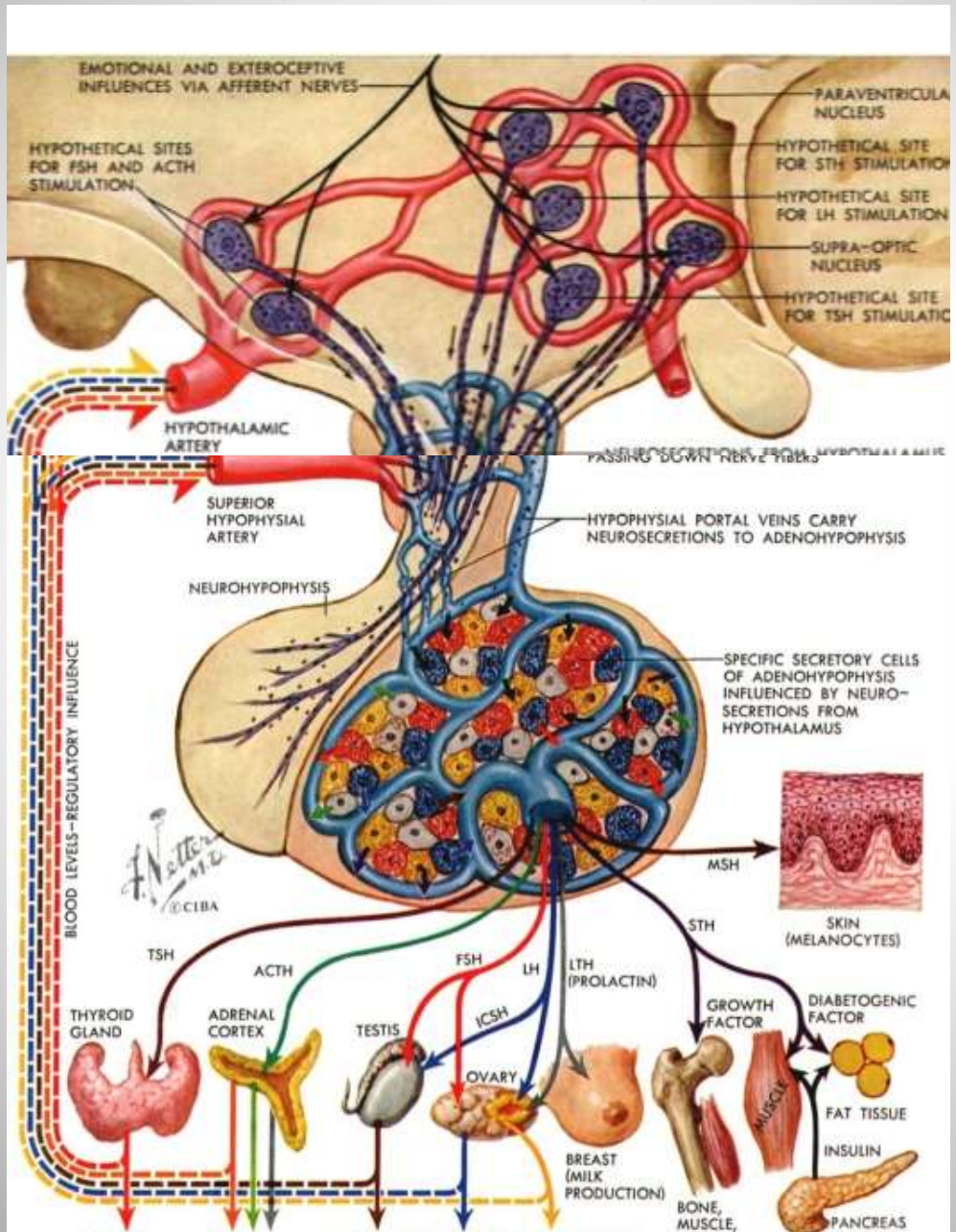



EMOTIONAL AND EXTEROCEPTIVE INFLUENCES VIA AFFERENT NERVES
PARAVENTRICULAR NUCLEUS
HYPOTHETICAL SITES FOR FSH AND ACTH STIMULATION
HYPOTHETICAL SITE FOR STH STIMULATION
HYPOTHETICAL SITE FOR LH STIMULATION
SUPRA-OPTIC NUCLEUS
HYPOTHETICAL SITE FOR TSH STIMULATION
HYPOTHALAMIC ARTERY
NEUROSECRETIONS FROM HYPOTHALAMUS RELEASED INTO PRIMARY PLEXUS OF HYPOPHYSIAL PORTAL CIRCULATION AFTER PASSING DOWN NERVE FIBERS
SUPERIOR HYPOPHYSIAL ARTERY
HYPOPHYSIAL PORTAL VEINS CARRY NEUROSECRETIONS TO ADENOHYPOPHYSIS
NEUROHYPOPHYSIS
SPECIFIC SECRETORY CELLS OF ADENOHYPOPHYSIS INFLUENCED BY NEURO-SECRETIONS FROM HYPOTHALAMUS
BLOOD LEVELS—REGULATORY INFLUENCE
©CIBA
MSH
SKIN (MELANOCYTES)
STH
TSH
ACTH
FSH
LH
ICSH
LTH (PROLACTIN)
GROWTH FACTOR
DIABETOGENIC FACTOR
THYROID GLAND
ADRENAL CORTEX
TESTIS
OVARY
FAT TISSUE
INSULIN
BREAST (MILK PRODUCTION)
BONE, MUSCLE, ORGANS (GROWTH)
PANCREAS
THYROID HORMONES
CORTICAL HORMONES
TESTOSTERONE
ESTROGEN
PROGESTERONE

CONTROLE NEUROENDÓCRINO DA REPRODUÇÃO

- **HIPOTALÂMICO**
- **HIPÓFISE**

CONTROLE HIPOTALÂMICO



Hipotálamo

GnRH - Hormônio Liberador de Gonadotropina

Mamífero	**pGlu**	**His**	**Trp**	**Ser**	**Tyr**	**Gly**	**Leu**	**Arg**	**Pro**	**Gly**
seabream	**pGlu**	**His**	**Trp**	**Ser**	**Tyr**	**Gly**	**Leu**	**Ser**	**Pro**	**Gly**
salmão	**pGlu**	**His**	**Trp**	**Ser**	**Tyr**	**Gly**	**Trp**	**Leu**	**Pro**	**Gly**
enguia I	**pGlu**	**His**	**Tyr**	**Ser**	**Leu**	**Glu**	**Trp**	**Lys**	**Pro**	**Gly**
enguia III	**pGlu**	**His**	**Trp**	**Ser**	**His**	**Asp**	**Trp**	**Lys**	**Pro**	**Gly**
dogfish	**pGlu**	**His**	**Trp**	**Ser**	**His**	**Gly**	**Trp**	**Leu**	**Pro**	**Gly**
frango I	**pGlu**	**His**	**Trp**	**Ser**	**Tyr**	**Gly**	**Leu**	**Gln**	**Pro**	**Gly**
frango II	**pGlu**	**His**	**Trp**	**Ser**	**His**	**Gly**	**Trp**	**Tyr**	**Pro**	**Gly**

Sequência de aminoácidos de formas de GnRH conhecidos em Vertebrados e Urocordados

Animal	Aminoácidos											
	1	2	3	4	5	6	7	8	9	10		
Mamífero	pGlu	His	Trp	Ser	Tyr	Gly	Leu	Arg	Pro	Gly	NH_2	
Whitefish	pGlu	His	Trp	Ser	Tyr	Gly	**Met**	**Asn**	Pro	Gly	NH_2	
Salmon	pGlu	His	Trp	Ser	Tyr	Gly	**Trp**	**Leu**	Pro	Gly	NH_2	
Sea Bream	pGlu	His	Trp	Ser	Tyr	Gly	Leu	**Ser**	Pro	Gly	NH_2	
Pejerrey	pGlu	His	Trp	Ser	**Phe**	Gly	Leu	**Ser**	Pro	Gly	NH_2	
Herring	pGlu	His	Trp	Ser	**His**	Gly	Leu	**Ser**	Pro	Gly	NH_2	
Catfish	pGlu	His	Trp	Ser	**His**	Gly	Leu	**Asn**	Pro	Gly	NH_2	
Dogfish	pGlu	His	Trp	Ser	**His**	Gly	**Trp**	**Leu**	Pro	Gly	NH_2	
Chicken-II	pGlu	His	Trp	Ser	**His**	Gly	**Trp**	**Tyr**	Pro	Gly	NH_2	
Lamprey-III	pGlu	His	Trp	Ser	**His**	**Asp**	**Trp**	**Lys**	Pro	Gly	NH_2	
Lamprey-I	pGlu	His	**Tyr**	Ser	**Leu**	**Glu**	**Trp**	**Lys**	Pro	Gly	NH_2	
Guinea Pig	pGlu	**Tyr**	Trp	Ser	Tyr	Gly	**Val**	Arg	Pro	Gly	NH_2	
Chicken-I	pGlu	His	Trp	Ser	Tyr	Gly	Leu	**Gln**	Pro	Gly	NH_2	
Frog	pGlu	His	Trp	Ser	Tyr	Gly	Leu	**Trp**	Pro	Gly	NH_2	
Tunicata-1	pGlu	His	Trp	Ser	**Asp**	**Tyr**	**Phe**	**Lys**	Pro	Gly	NH_2	
Tunicata-2	pGlu	His	Trp	Ser	**Leu**	**Cyr**	**His**	**Ala**	Pro	Gly	NH_2	
Tunicata-3	pGlu	His	Trp	Ser	Tyr	**Glu**	**Phe**	**Met**	Pro	Gly	NH_2	
Tunicata-4	pGlu	His	Trp	Ser	**Asn**	**Gln**	Leu	**Thr**	Pro	Gly	NH_2	
Tunicata-5	pGlu	His	Trp	Ser	Tyr	**Glu**	**Tyr**	**Met**	Pro	Gly	NH_2	
Tunicata-6	pGlu	His	Trp	Ser	**Lys**	Gly	**Tyr**	**Ser**	Pro	Gly	NH_2	
Tunicata-7	pGlu	His	Trp	Ser	Tyr	**Ala**	Leu	**Ser**	Pro	Gly	NH_2	
Tunicata-8	pGlu	His	Trp	Ser	**Leu**	**Ala**	Leu	**Ser**	Pro	Gly	NH_2	
Tunicata-9	pGlu	His	Trp	Ser	**Asn**	**Lys**	Leu	**Ala**	Pro	Gly	NH_2	

	1	2	3	4	5	6	7	8	9	10	11	12	
Octopus vulgaris	pGlu	Asn	Tyr	His	Phe	Ser	Asn	Gly	Trp	His	Pro	Gly	NH_2
Aplysia californica	pGlu	Asn	Tyr	His	Phe	Ser	Asn	Gly	Trp	Tyr	Ala	Gly	NH_2

Asp: ácido aspártico; Glu: ácido glutâmico; Arg: arginina; Lys: lisina; His: histidina; Asn: asparagina; Gln: glutamina; Ser: serina; Thr: treonina; Tyr: tirosina; Ala: alanina; Gly: glisina; Val: valina; Leu; leucina; Ile: isoleucina; Pro: prolina; Phe: fenilalanina; Met: metionina; Trp: triptofano; Cys: cisteína.

GnIH em vertebrados

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journal homepage: www.elsevier.com/locate/ygcen



Minireview

Evolutionary origin and divergence of GnIH and its homologous peptides

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Table 1
Amino acid sequences of GnIH and its homologous peptides (LPXRFamide peptides) in vertebrates.

Animal	Name	Sequence	Reference
Rat	RFRP-1*	SVTFQELKDWGAKKDIKMSPAPANKVPHSAANLPLRFa	Hinuma et al. (2000)
	RFRP-3	ANMEAGTMSHFPSLPQRFa	Ukena et al. (2002)
Hamster	RFRP-1*	SPAPANKVPHSAANLPLRFa	Kriegsfeld et al. (2006)
	RFRP-3*	TLSRVPSLPQRFa	Kriegsfeld et al. (2006)
Bovine	RFRP-1	SLTFEEVKDWAPKIKMNKPVVNKMPPSAANLPLRFa	Fukusumi et al. (2001)
	RFRP-3	AMAHLPLRLGKNREDSLSRWVPNLPQRFa	Yoshida et al. (2003)
Quail	GnIH	SIKPSAYLPLRFa	Tsutsui et al. (2000)
	GnIH-RP-1*	SLNFEEMKDWGSKNFMKVNTPTVNKVPNSVANLPLRFa	Satake et al. (2001)
	GnIH-RP-2	SSIQSLLNLPQRFa	Satake et al. (2001)
Sparrow	GnIH*	SIKPFSNLPLRFa	Osugi et al. (2004)
	GnIH-RP-1*	SLNFEEMEDWGSKDIIKMNPFTASKMPNSVANLPLRFa	Osugi et al. (2004)
	GnIH-RP-2*	SPLVKGSSQSLLNLPQRFa	Osugi et al. (2004)
Bullfrog	fGRP	SLKPAANLPLRFa	Koda et al. (2002)
	fGRP-RP-1	SIPNLPQRFa	Ukena et al. (2003a)
	fGRP-RP-2	YLSGKTKVQSMANLPQRFa	Ukena et al. (2003a)
	fGRP-RP-3	AQYTNHFVHSLDTLPLRFa	Ukena et al. (2003a)
Goldfish	goldfish LPXRFa-1*	PTHLHANLPLRFa	Sawada et al. (2002b)
	goldfish LPXRFa-2*	AKSNINLPQRFa	Sawada et al. (2002b)
	goldfish LPXRFa-3	SGTGLSATLPQRFa	Sawada et al. (2002b)
Hagfish	Hagfish	ALPQRFa	Osugi et al., unpublished data

GnIH

Tsutsui *et al.*, 2000 → novo peptídeo hipotalâmico que inibiu a liberação de gonadotropinas em *Coturnix japonica* (codornas japonesas).

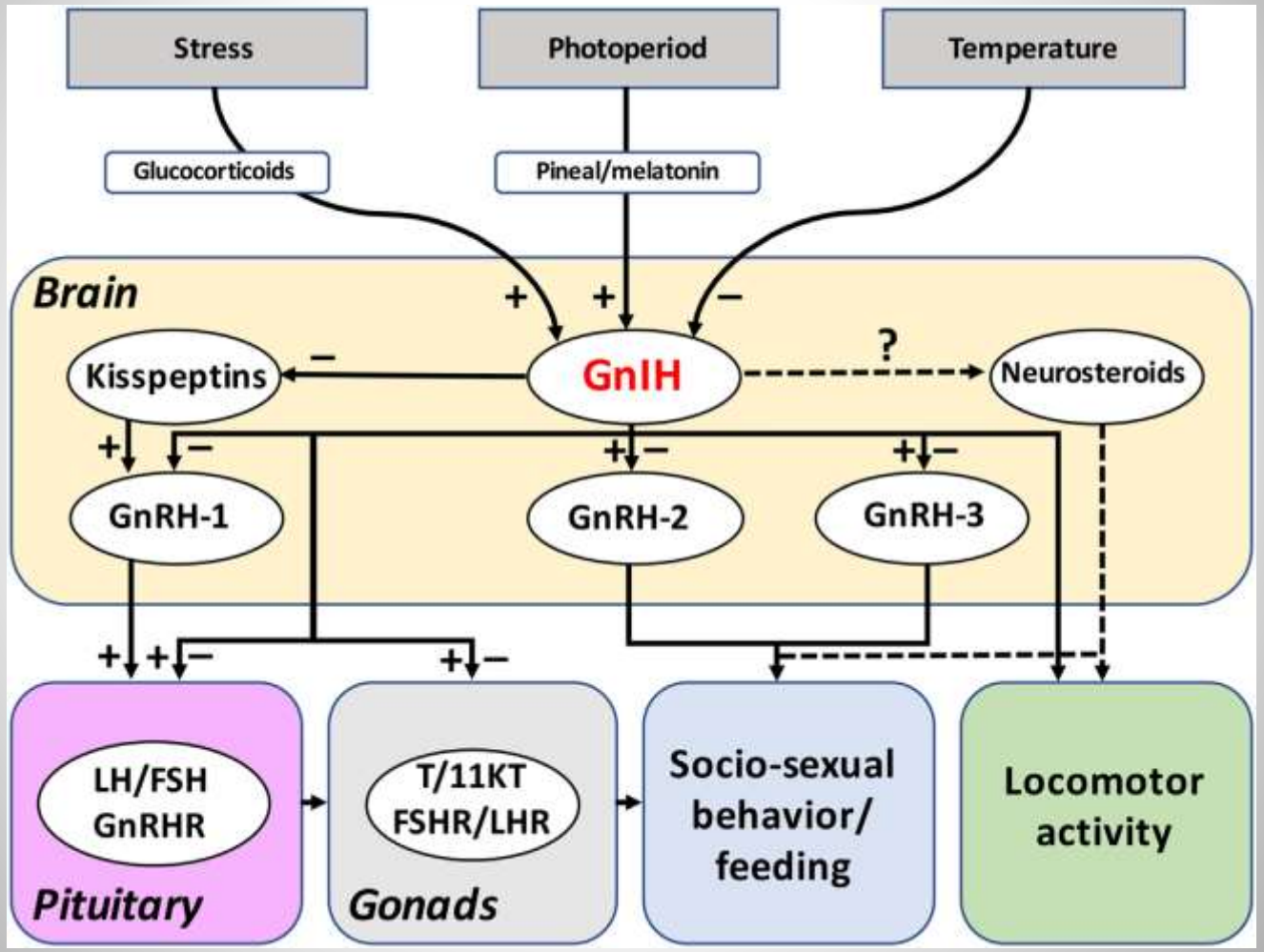


Fonte: Google imagens

Hormônio Inibidor de Gonadotropina (GnIH)

http://www.aguaonline.com.br

GnIH


Stress
Photoperiod
Temperature
Glucocorticoids
Pineal/melatonin
Brain
Kisspeptins
GnIH
Neurosteroids
GnRH-1
GnRH-2
GnRH-3
LH/FSH
GnRHR
Pituitary
T/11KT
FSHR/LHR
Gonads
Socio-sexual behavior/ feeding
Locomotor activity

GnIH

Animal	Species	GnIH types	Functions
JAWLESS FISH			
Sea lamprey	*Petromyzon marinus*	LPXRFa-2	↑ Stimulation of GnRH-III synthesis and GTHβ mRNA expression
JAWED FISH			
Goldfish	*Carassius auratus*	gfLPXRFa-1	↑ Stimulation of GTH and GH release
		gfLPXRFa-2	↑ Stimulation of GTH and GH release
			↓ Inhibition of LH and FSH synthesis
		gfLPXRFa-3	↑ Stimulation of GTH and GH release
			↓ Inhibition of LH synthesis
			↓ Inhibition of GnRH-elicited FSH synthesis
			↑ Stimulation of GTH synthesis and release in prespawning fish
			↓ Inhibition of GTH synthesis in early to later stages of gonadal recrudescence
			↓ Inhibition of GnRH-elicited GTH synthesis in early and mid gonadal recrudescence
Zebrafish	*Danio rerio*	gfLPXRFa-3	↓ Inhibition of GTH release
Grass puffer	*Takifugu niphobles*	gfLPXRFa-1	↑ Stimulation of GTH synthesis
Nile tilapia	*Oreochromis niloticus*	LPXRFa-2	↑ Stimulation of LH and FSH release (*in vivo* and *in vitro*)

Fonte: Ogawa e Parhar, 2014

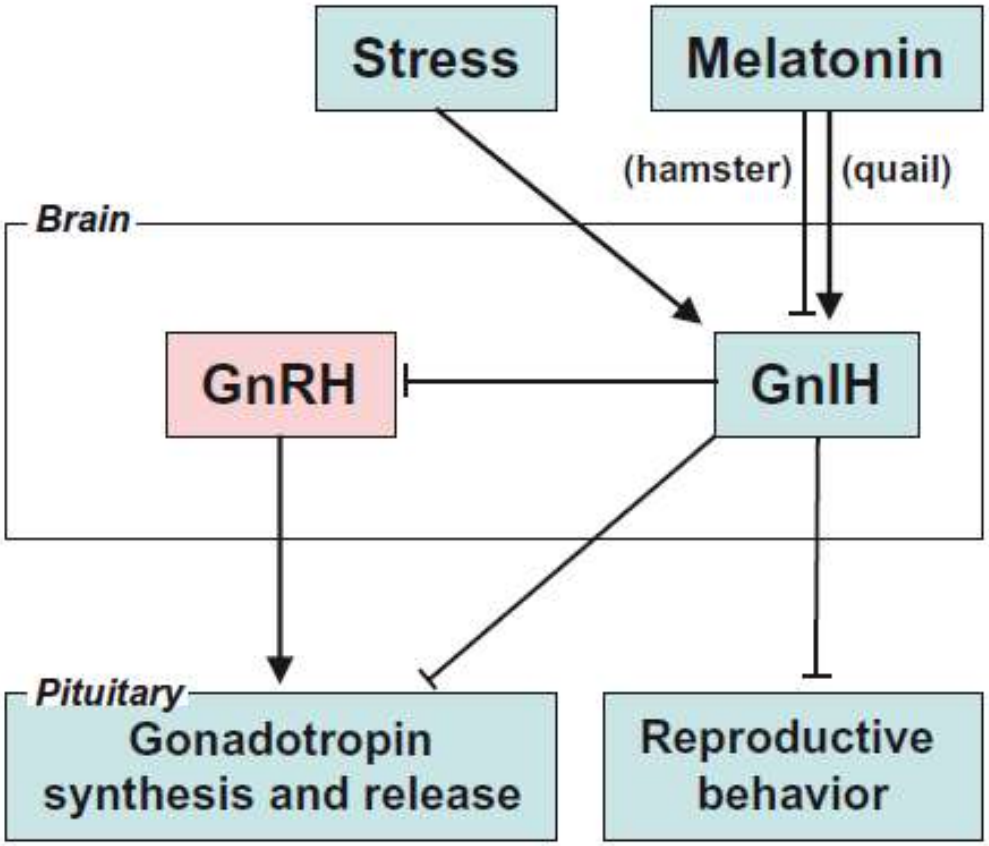
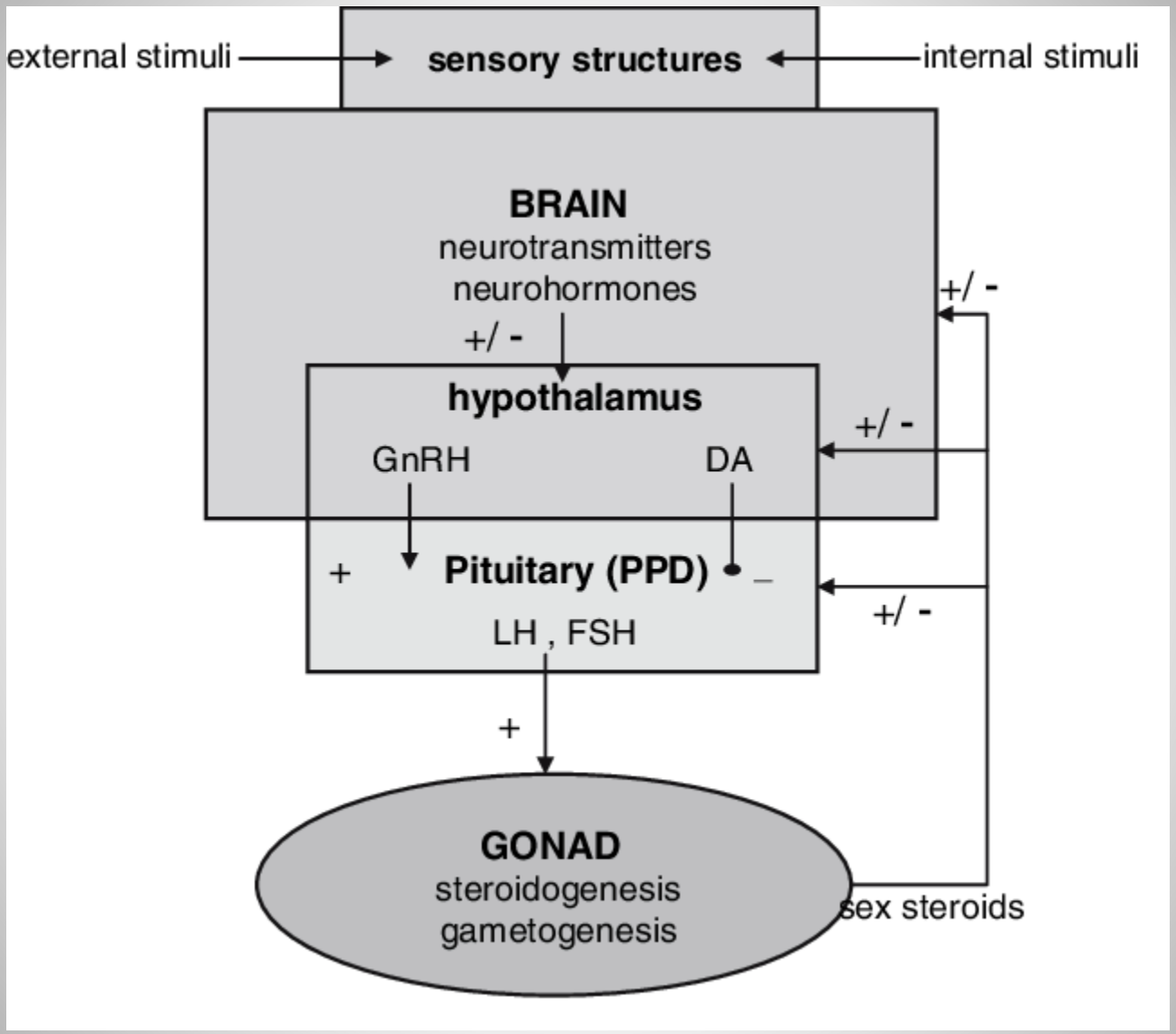
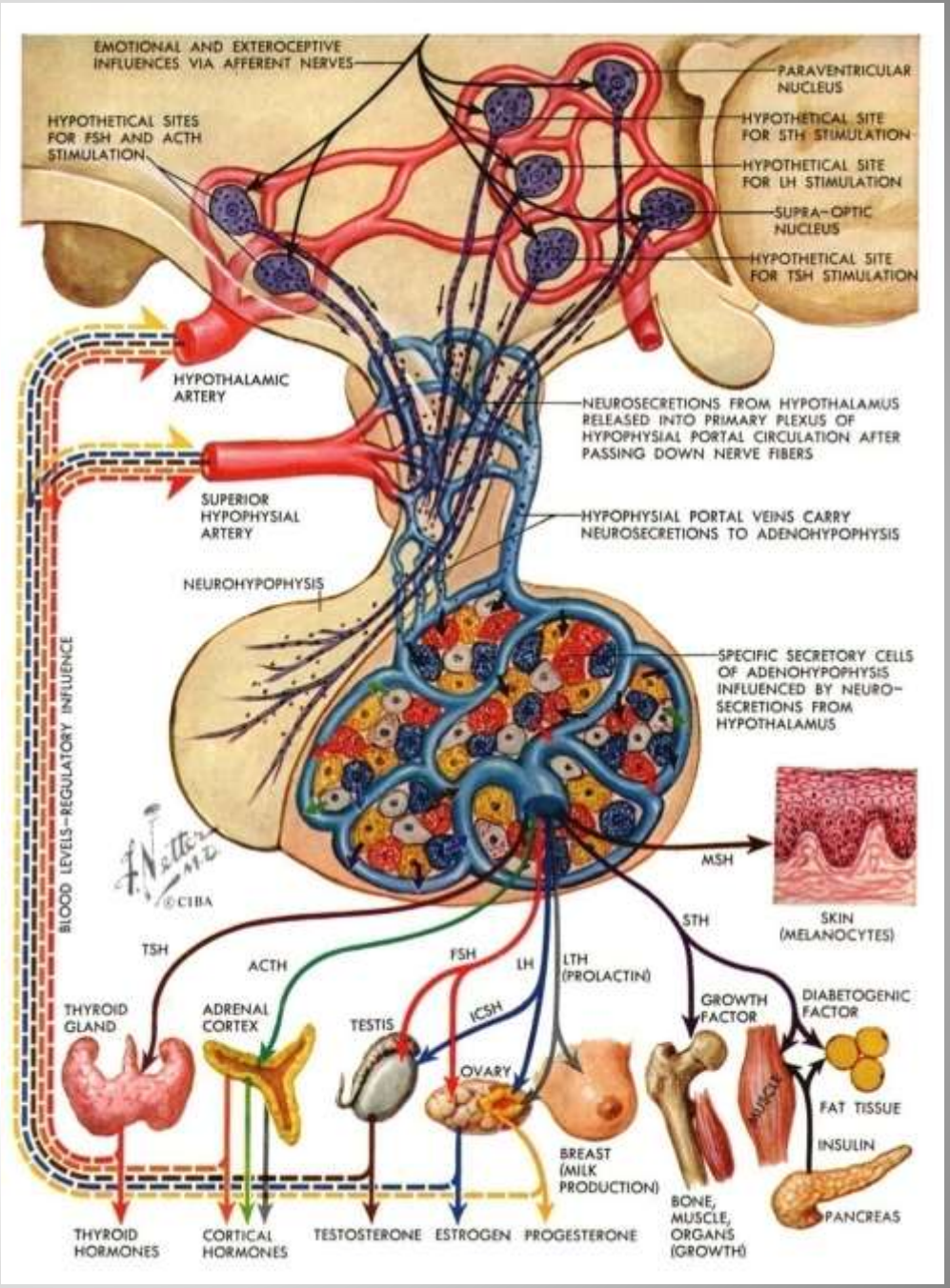


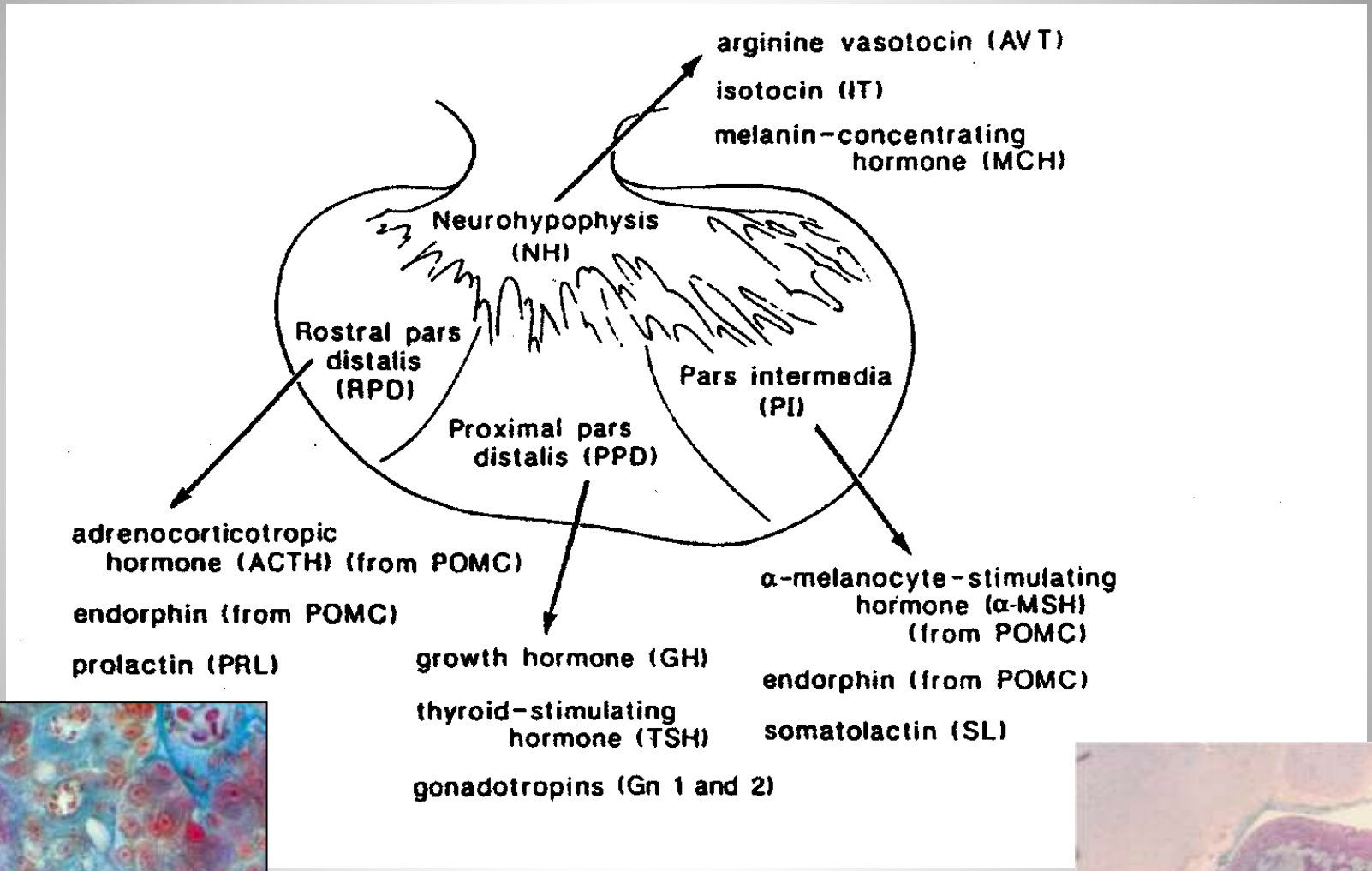
Fig. 1. GnIH actions within the brain and pituitary. GnIH inhibits gonadotropin synthesis and release by directly acting on the pituitary or by inhibiting the activity of GnRH neurons. GnIH can also inhibit reproductive behavior by possibly acting within the brain. Stress induces the expression of GnIH in birds and mammals. Melatonin induces the expression of GnIH in quail, whereas melatonin inhibits the expression of GnIH in hamsters.

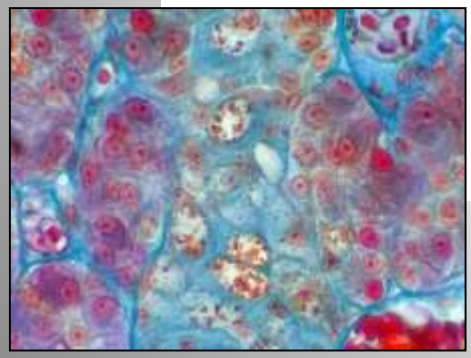

external stimuli
sensory structures
internal stimuli
BRAIN
neurotransmitters
neurohormones
+/ -
+/ -
hypothalamus
+/ -
GnRH
DA
+
Pituitary (PPD)
_
+/ -
LH , FSH
+
GONAD
steroidogenesis
gametogenesis
sex steroids

HIPÓFISE DE MAMÍFEROS

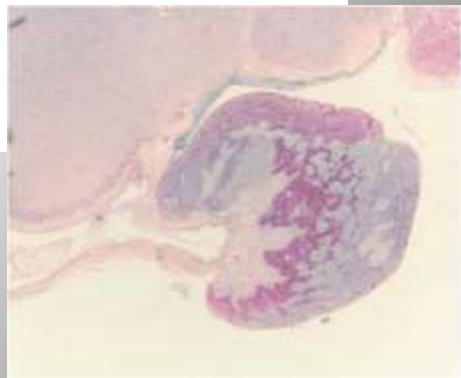


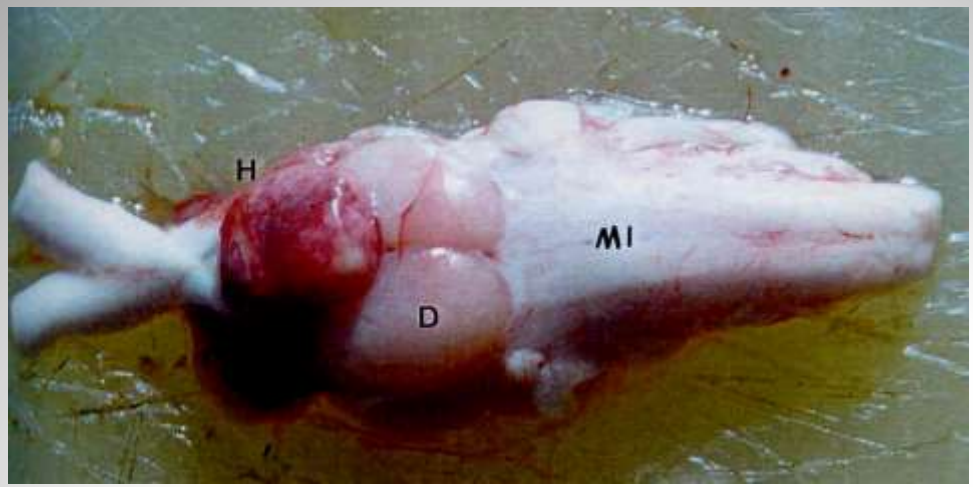
Hipófise dos teleósteos

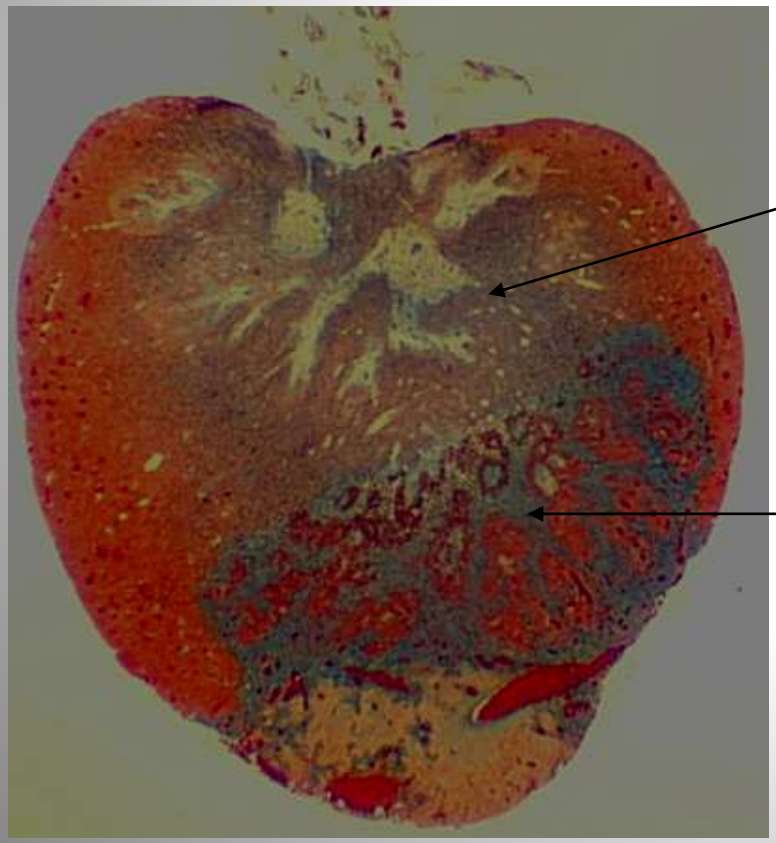




Células gonadotrópicas







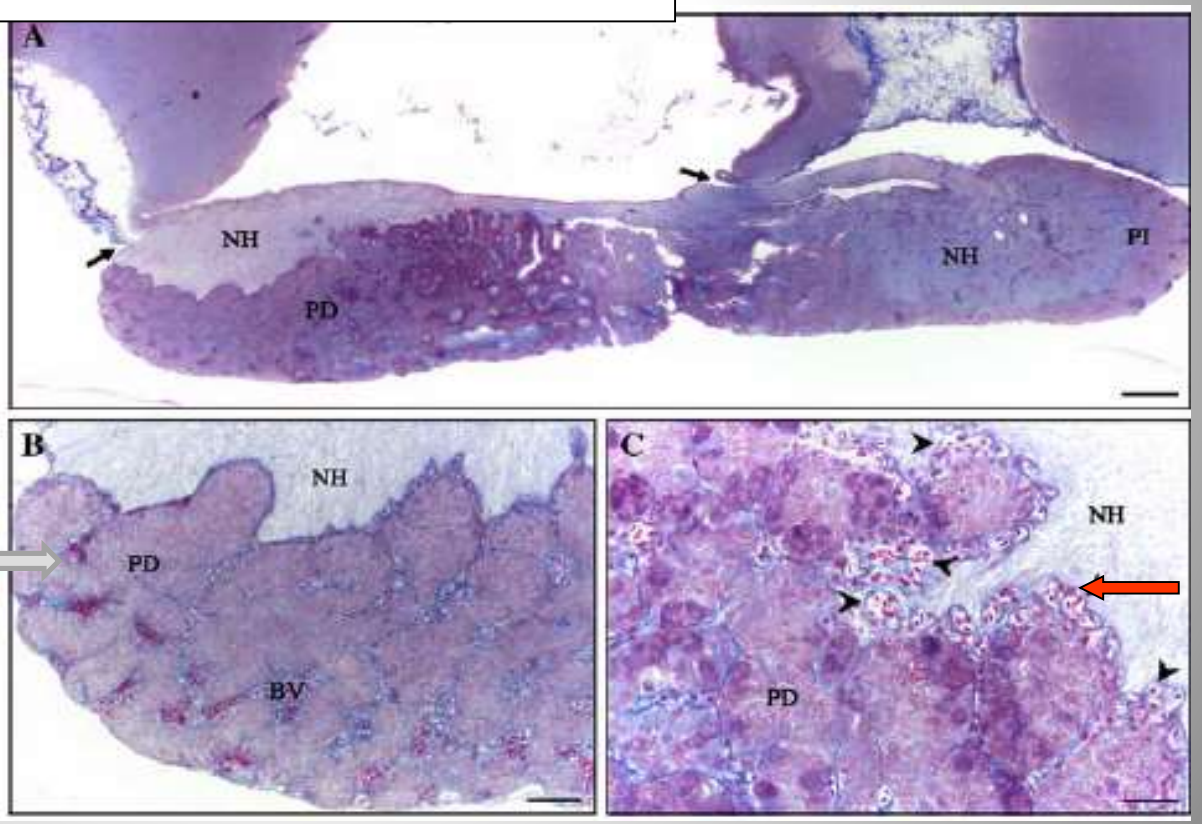
Neurohipófise

Ramos da NH

Fish Physiol Biochem
DOI 10.1007/s10695-008-9254-x

Immunocytochemical identification of adenohypophyseal cells in the pirarucu (*Arapaima gigas*), an Amazonian basal teleost

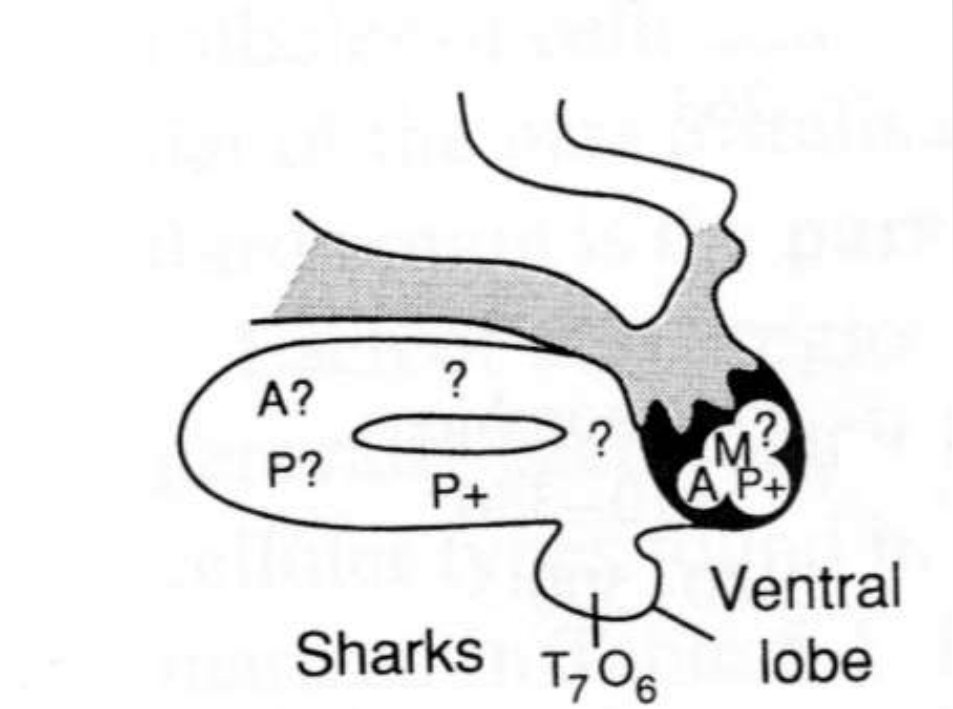
M. I. Borella · R. Venturieri · J. M. Mancera



NH não invade a hipófise

Hipófise de pirarucu – Eminência média? Sistema Porta?

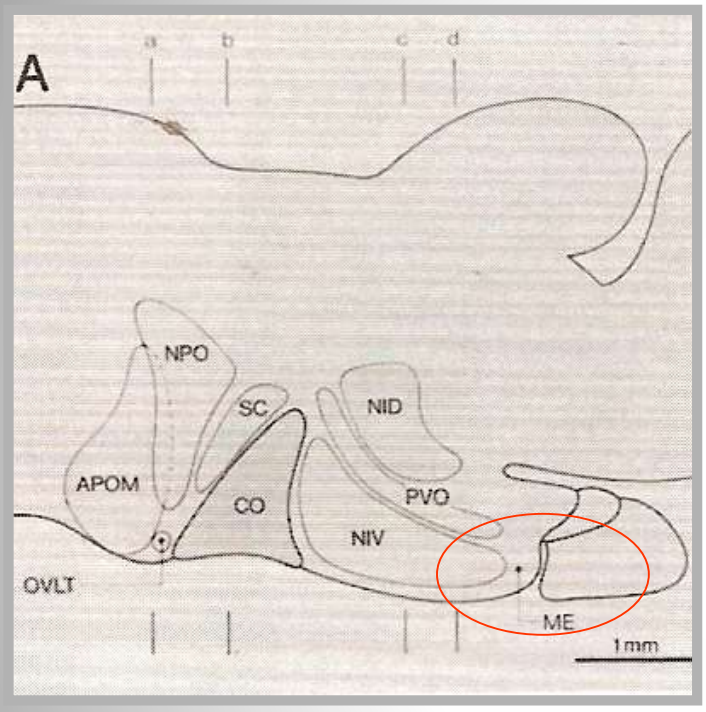
HIPÓFISE - ELASMOBRÂNQUIOS

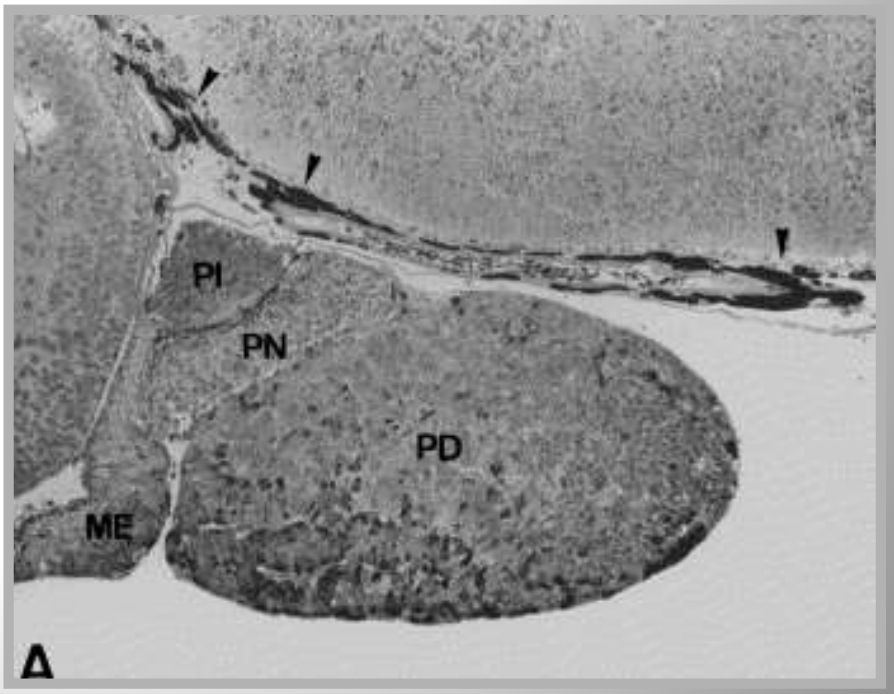


Grande desenvolvimento da **EMINÊNCIA MÉDIA**

Presença do Lobo Ventral

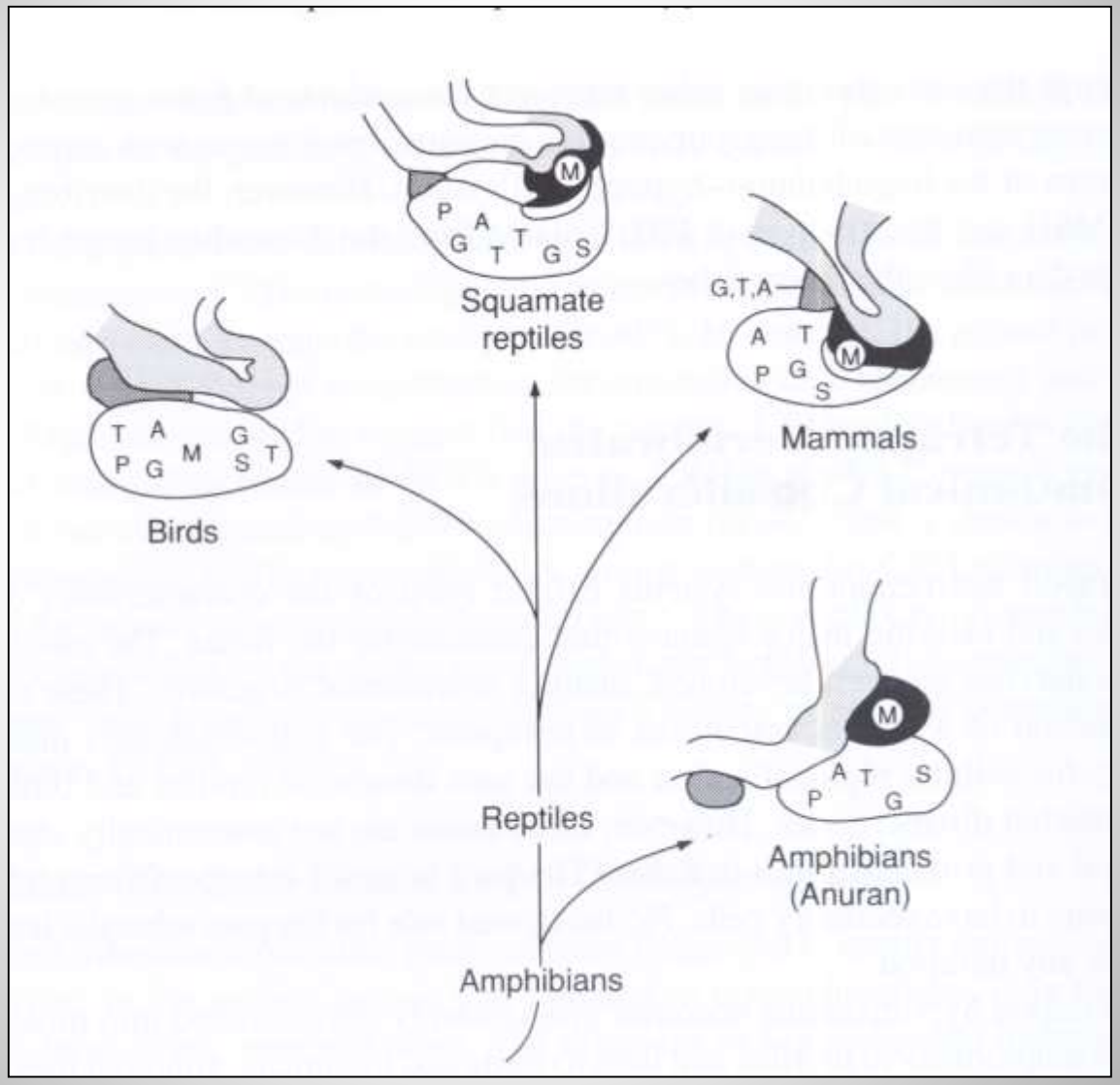
Hipófise de anfíbios



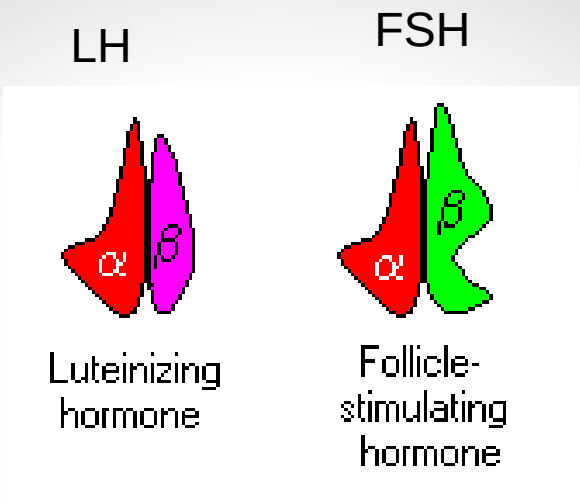


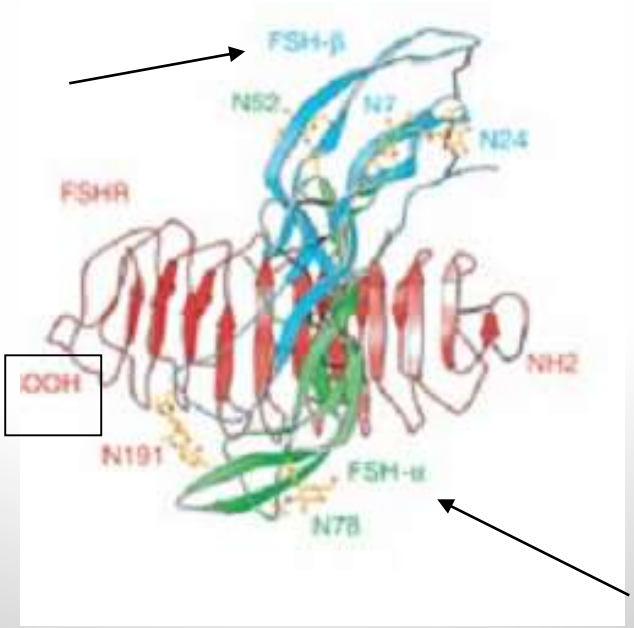
Eminência média: sistema porta desenvolvido

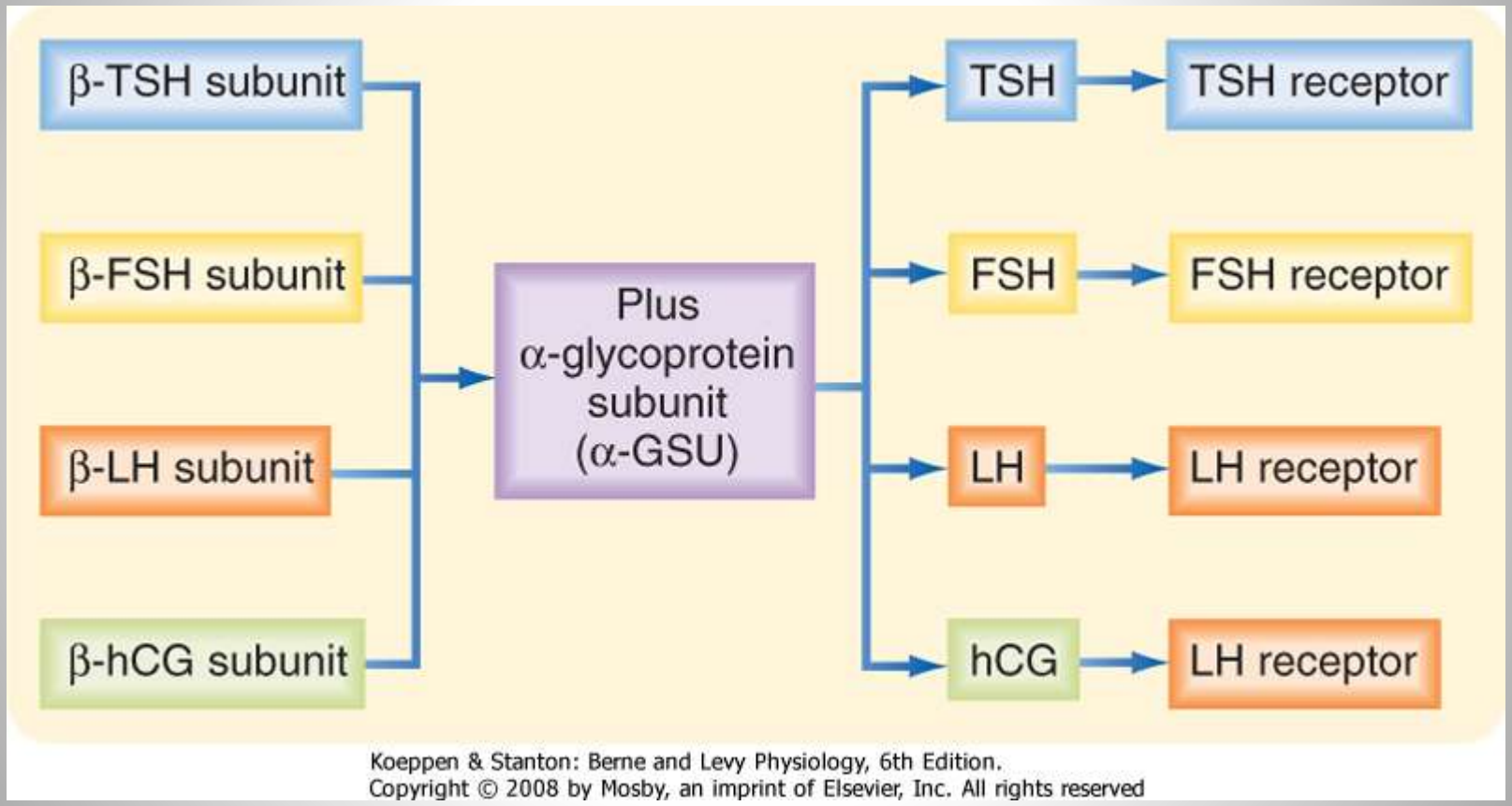
Hipófise de Tetrápoda



Gonadotropinas: glicoproteínas

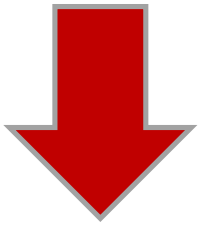






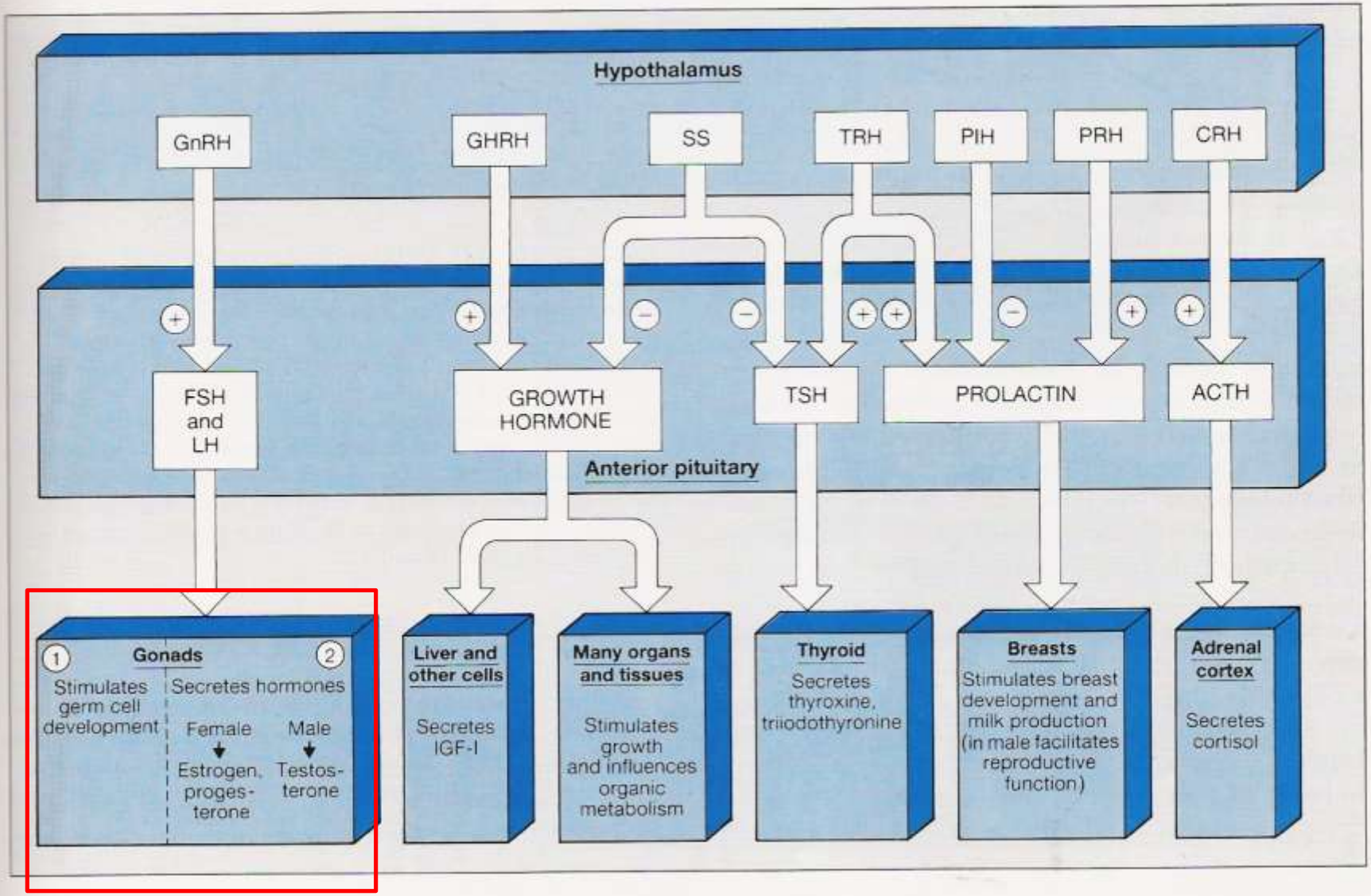
Koeppen & Stanton: Berne and Levy Physiology, 6th Edition.
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O CONTROLE DO DESENVOLVIMENTO DOS GAMETAS

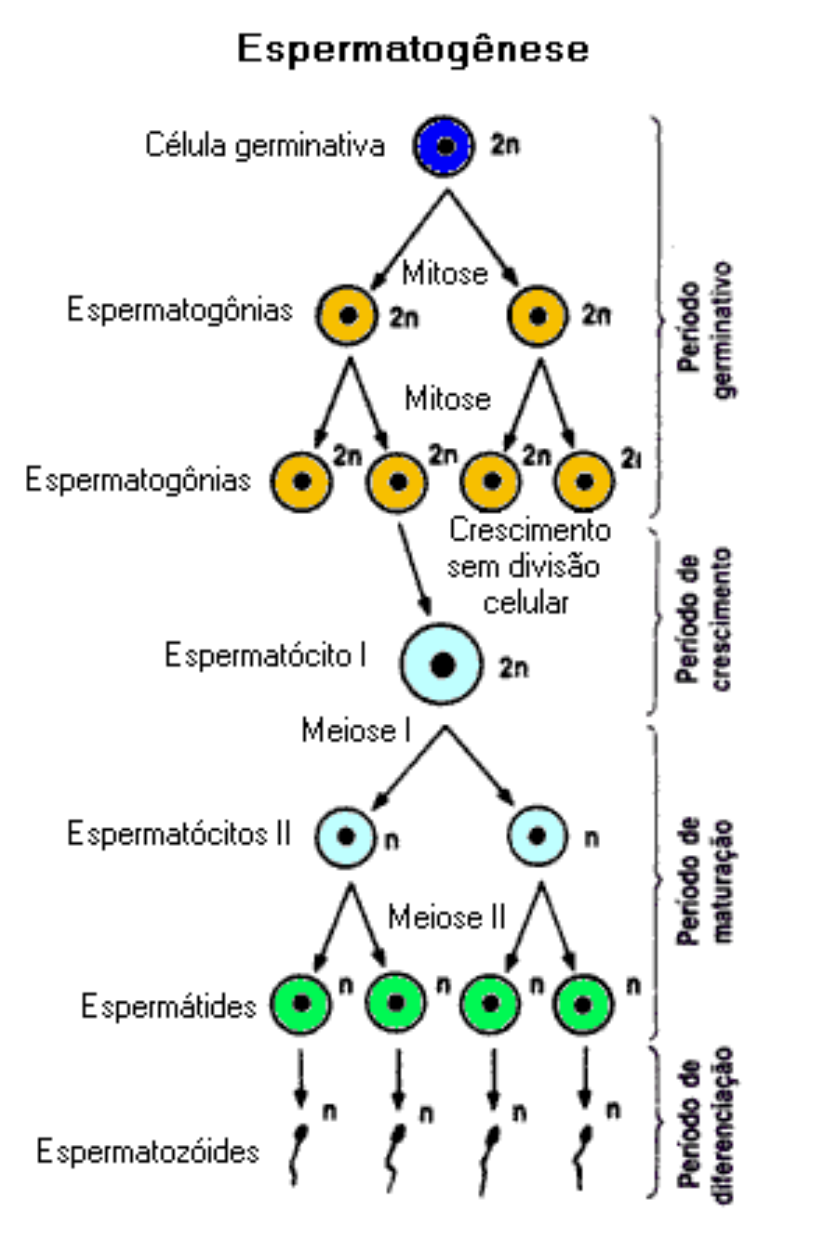


ESTEROIDES GONADAIS

FIGURE 10-20 A combination of Figures 10-17 and 10-19 summarizes the hypothalamic-anterior-pituitary system.



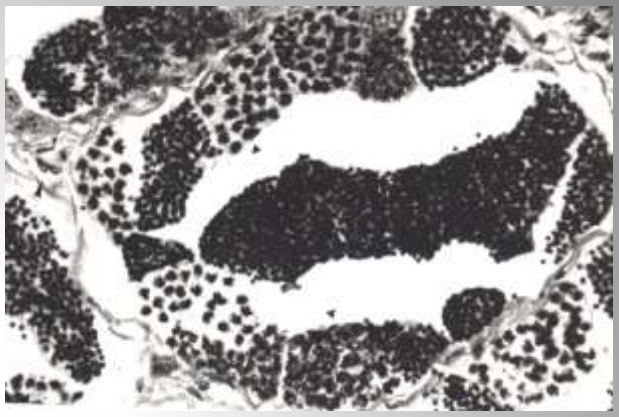
Reprodução sexuada: custo com formação de gametas



1 espermatogônia: 4 espermatozoides
(2n) (n)



Espermatogênese



Espermatogênese

- Espermatogônia
- Espermatócito Primário
- Espermatócito Secundário
- Espermátide
- Espermatozoide

Espermiogênese

ESPERMIAÇÃO

Liberação de espermatozoides para o ducto espermático

Variabilidade na estrutura do espermatozoide

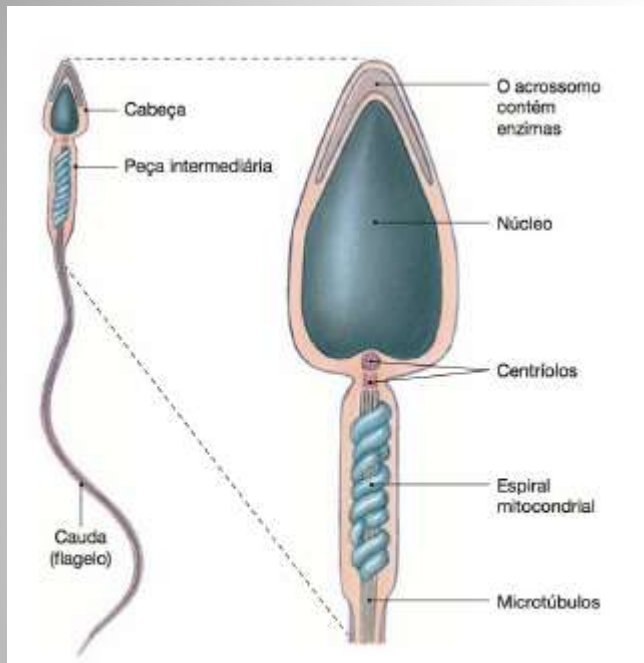
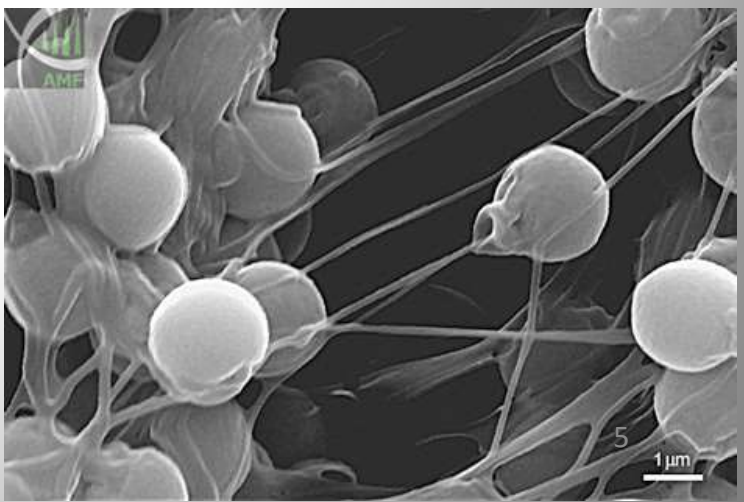


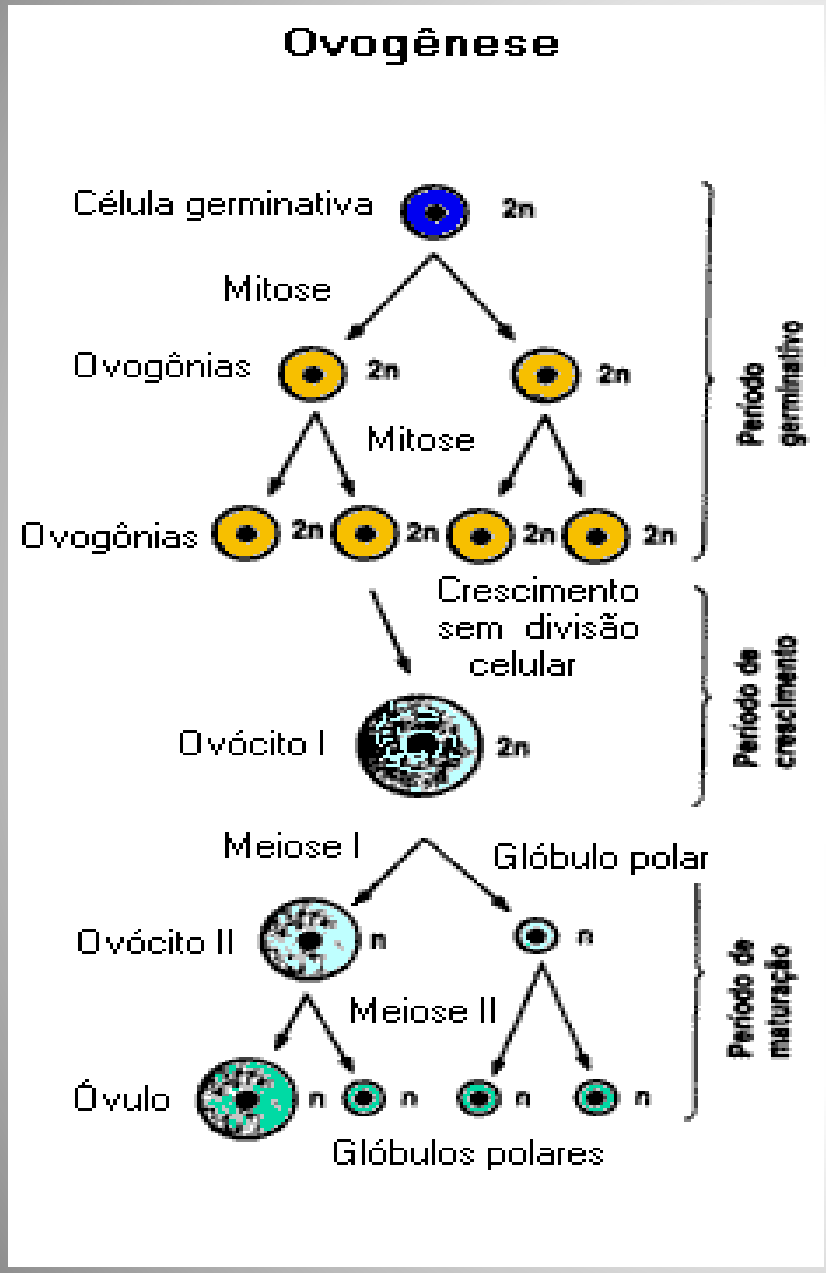
FIGURA 26-10 O espermatozoide consiste em uma cabeça com enzimas e DNA, uma cauda longa e mitocôndrias para produzir a energia usada para o movimento da cauda.

Acrossomo: enzimas



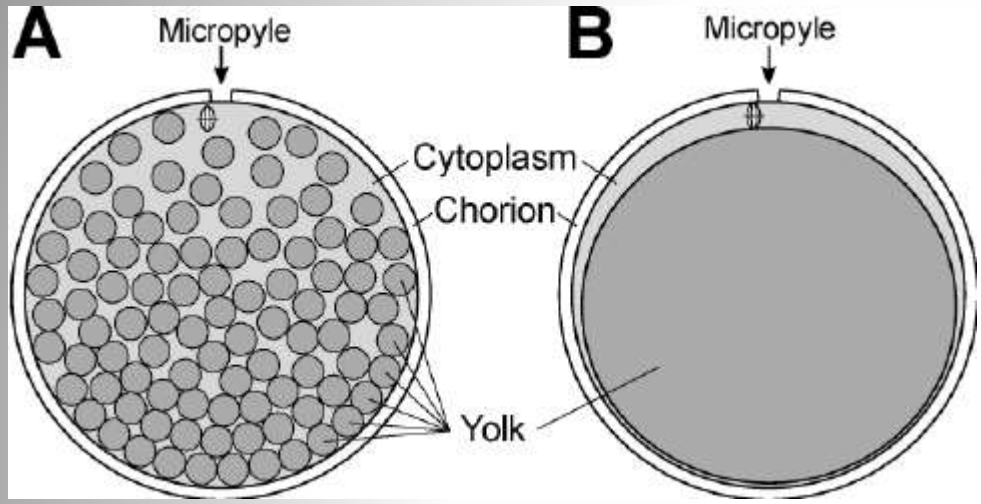
Em peixes, o espermatozoide não tem acrossomo

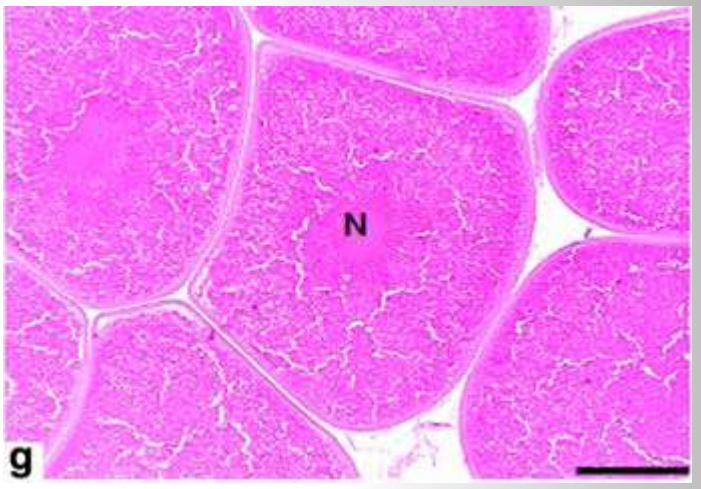
Reprodução sexuada: custo com formação de gametas



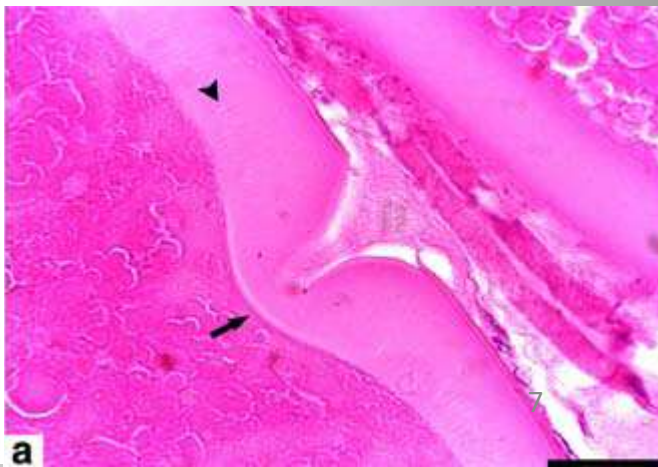
1 oogônia: 1 óvulo + 3 corpúsculos polares
(2n) (n)

Teleósteos: presença da micrópila para a fertilização





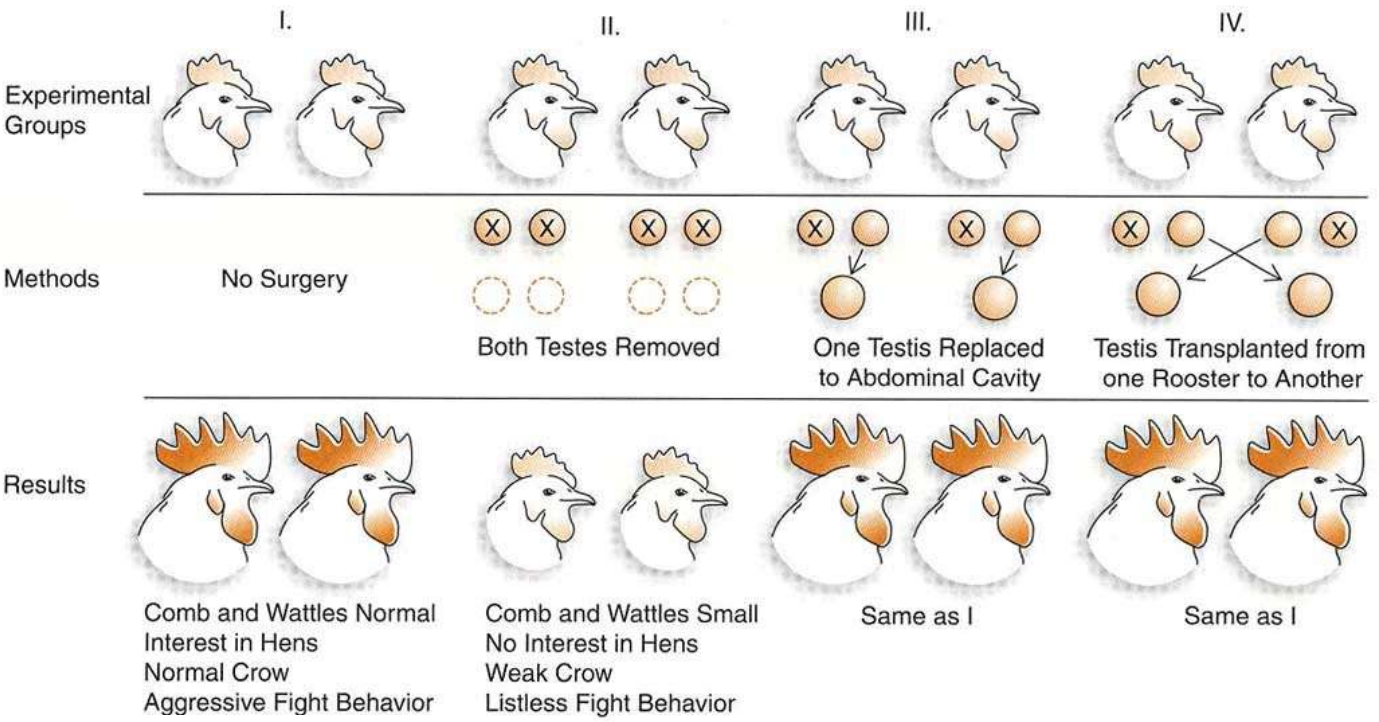






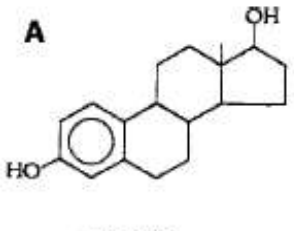
Arnold Berthold (1849) – Primeiro experimento em endocrinologia

Figure 1.1 Berthold's experiment: the first endocrine experiment.

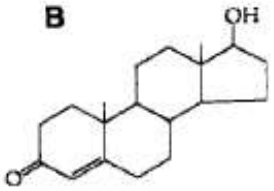


Papel dos testículos na definição das características sexuais secundárias de galos

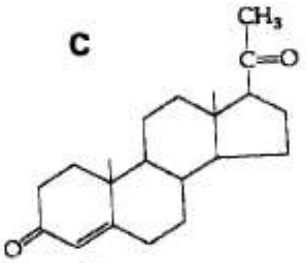
Principais esteroides gonadais



Estradiol

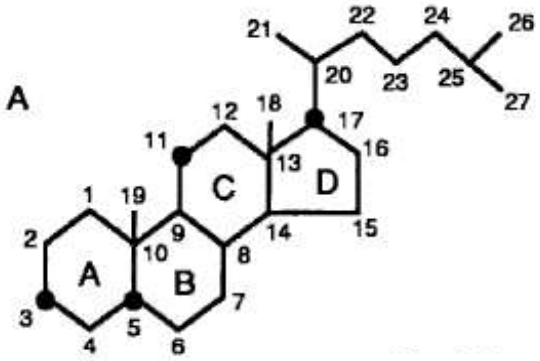


Testosterona

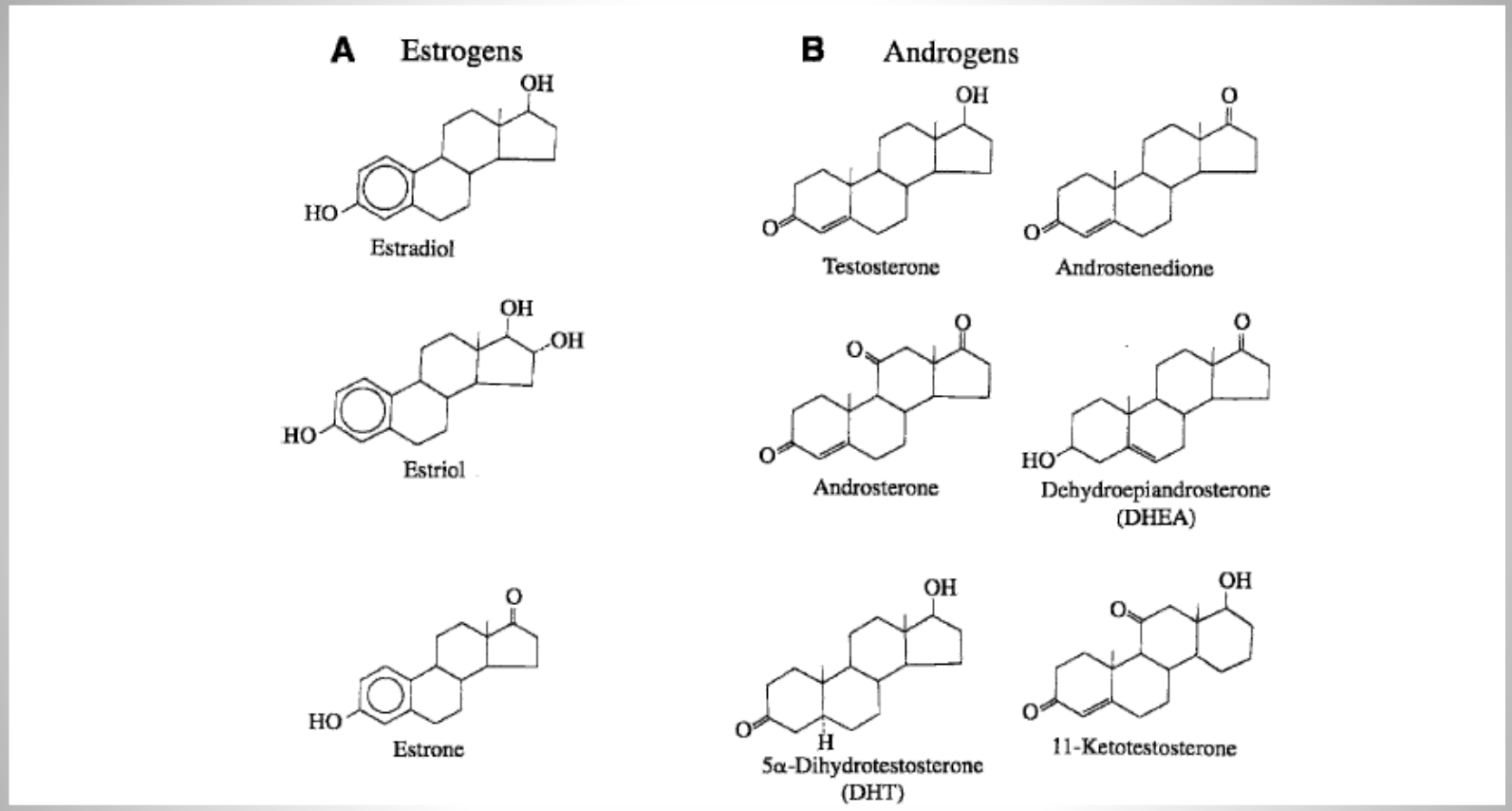


Progesterona

Estrutura do “núcleo” de um esteroide



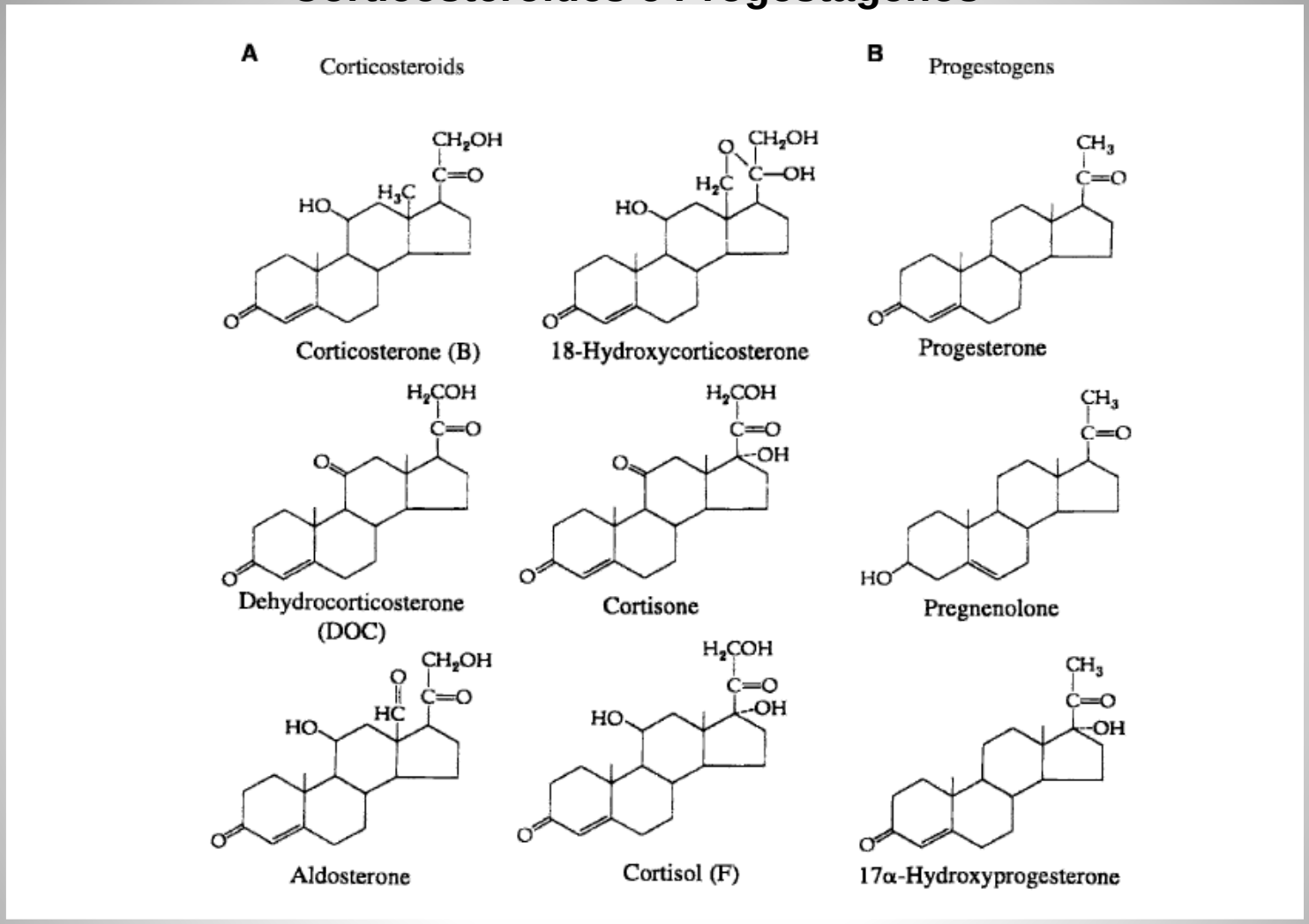
Estrógenos e andrógenos



18C

19C

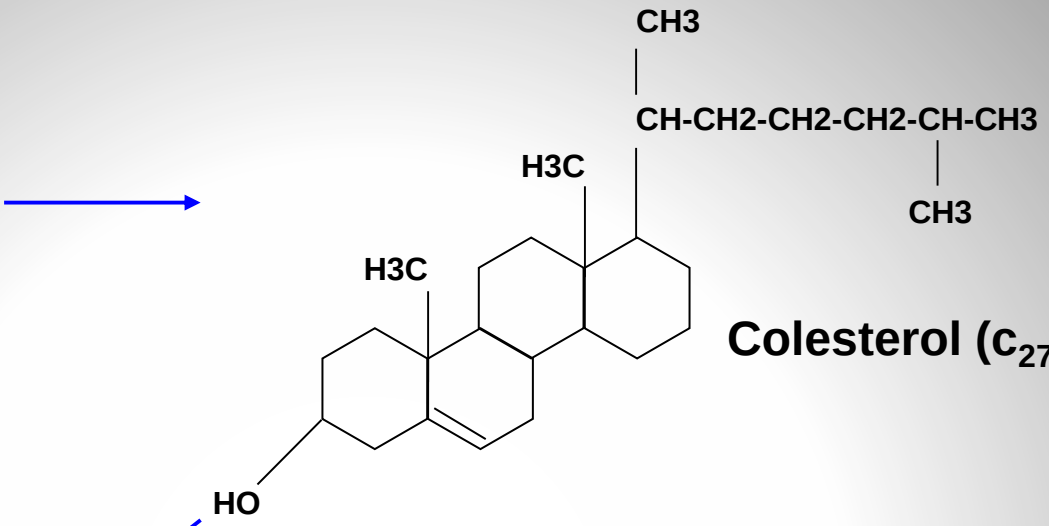
Corticosteroides e Progestágenos



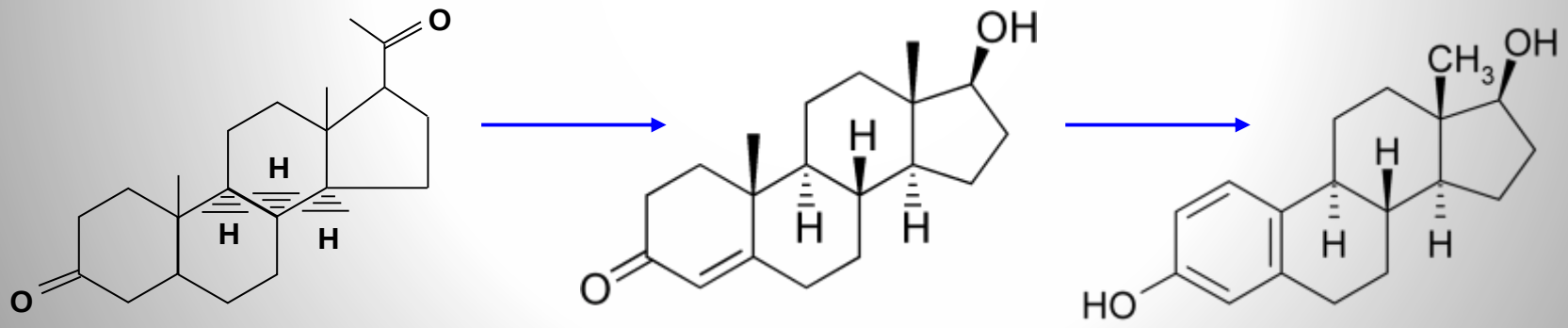
21 C

Origem: Dieta;

Síntese endógena:



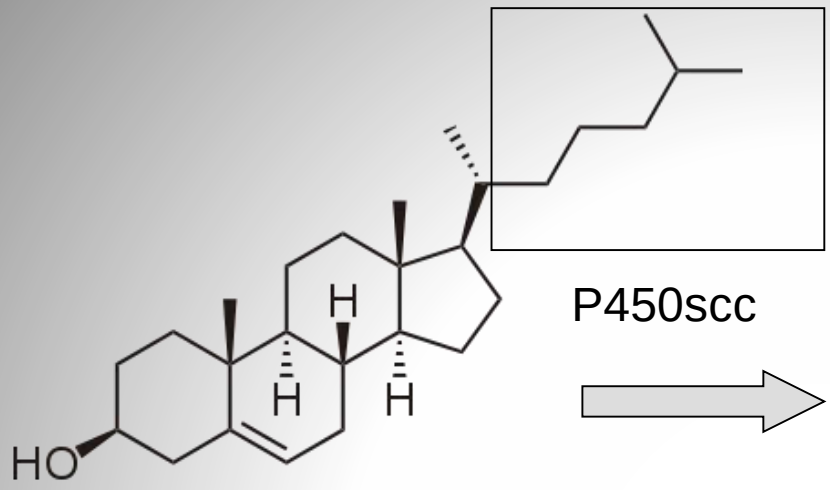
Colesterol (c_{27})



Progesterona (C_{21}) **Testosterona (C_{19})** **17βestradiol (C_{18})**

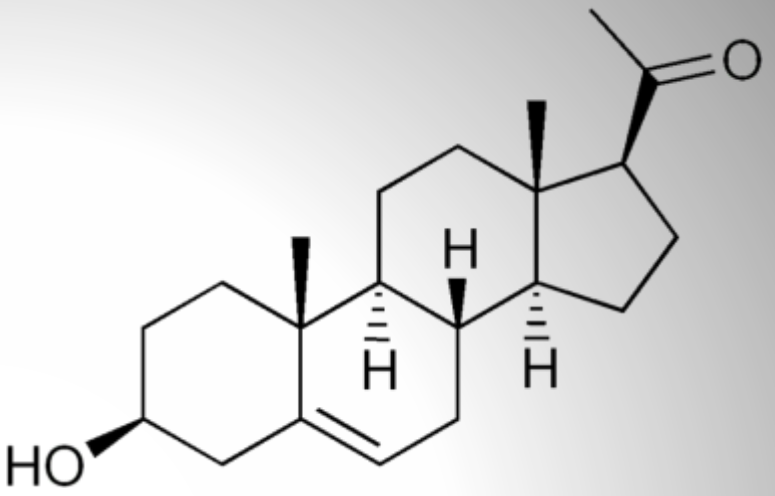
(Norris, 1997)

“corte” de 6 carbonos



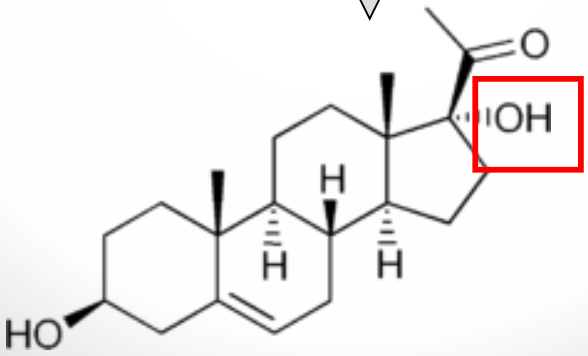
P450scc

Colesterol – 27 carbonos



Pregnenolona – 21 carbonos

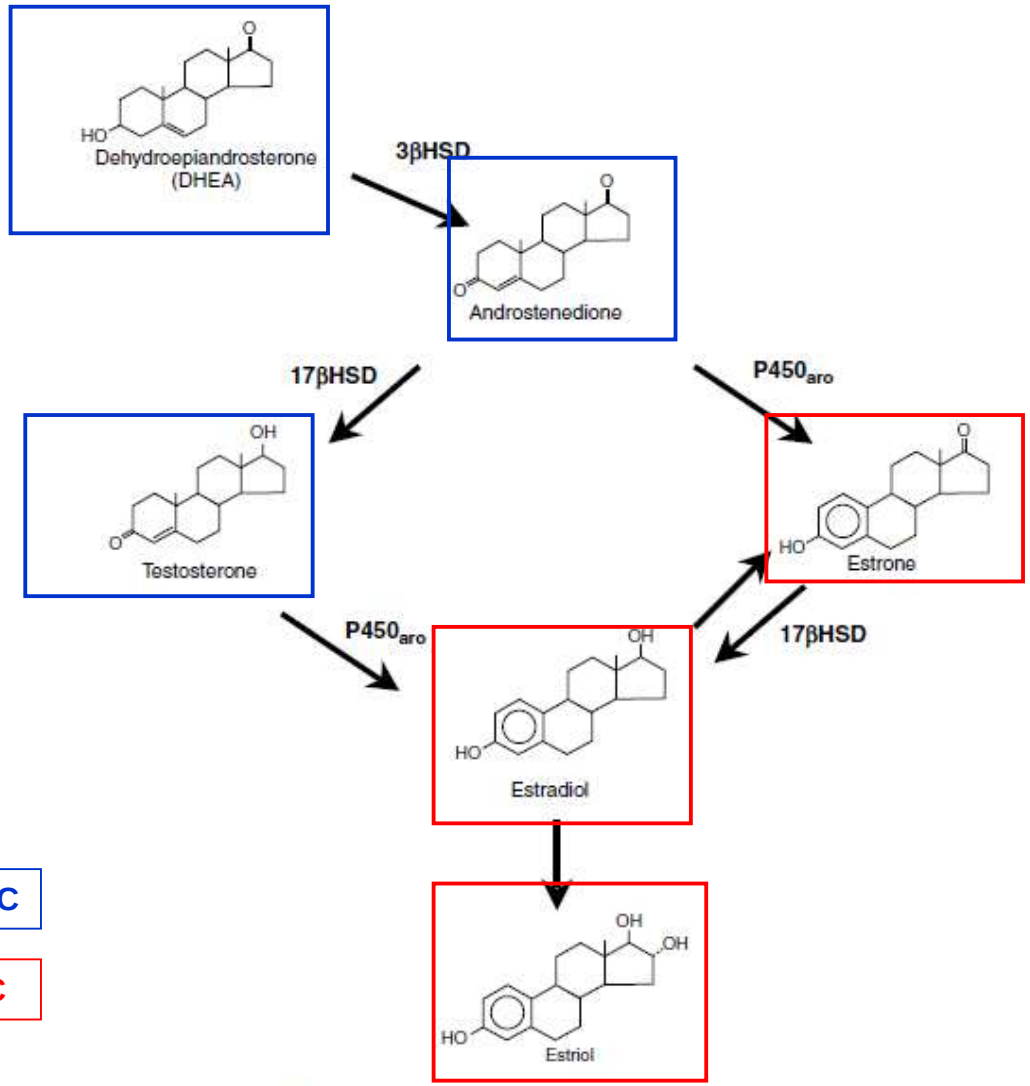
P450c17



Inserção de uma hidroxila no carbono 17

17 alfa-hidroxipregnenolona

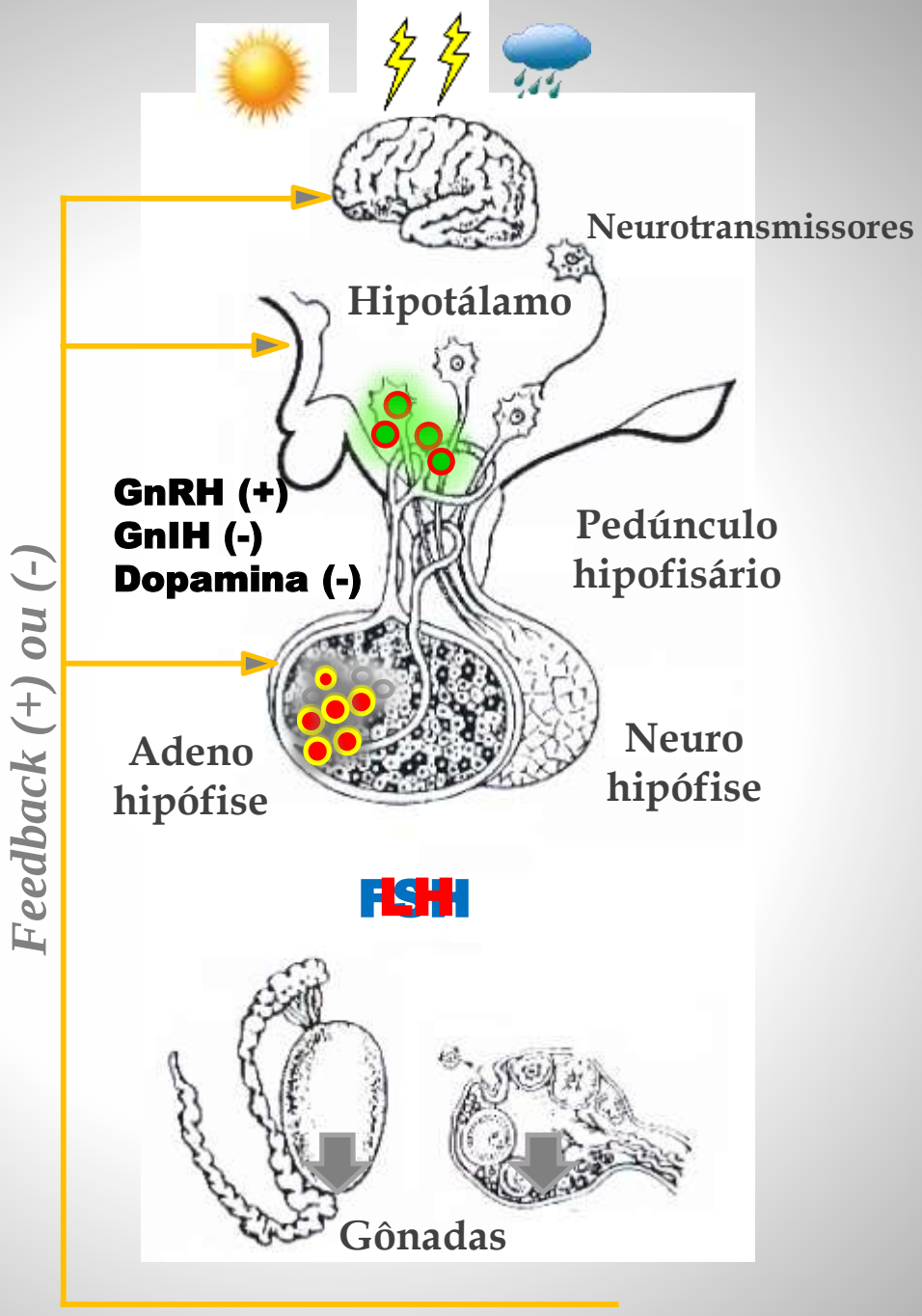
Síntese de estrógenos a partir de andrógenos



Andrógenos – 19 C

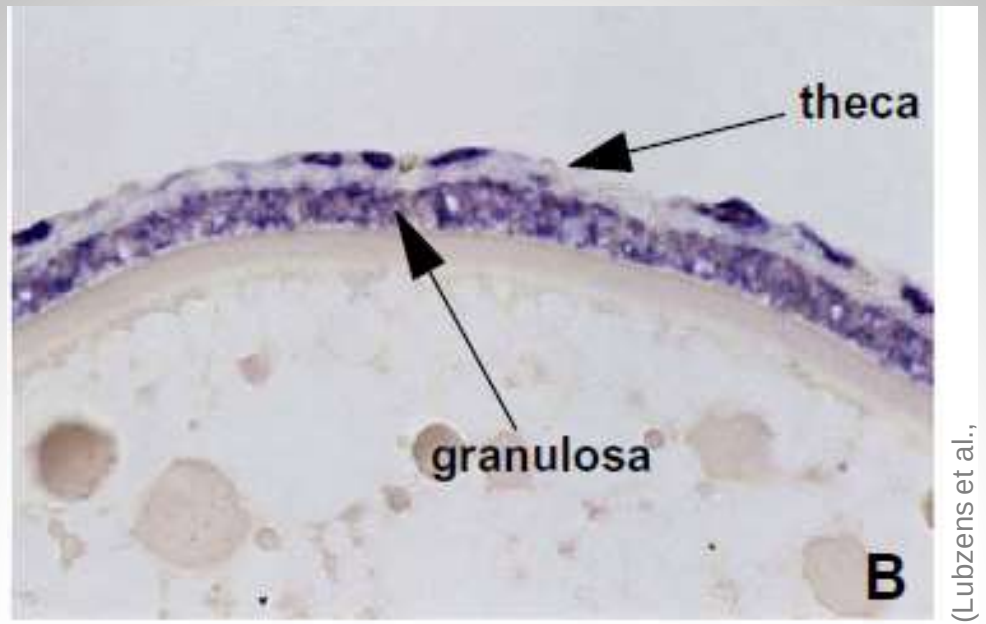
Estrógenos – 18 C

Eixo Hipotálamo-Hipófise-Gônadas no Controle da Reprodução em Vertebrados



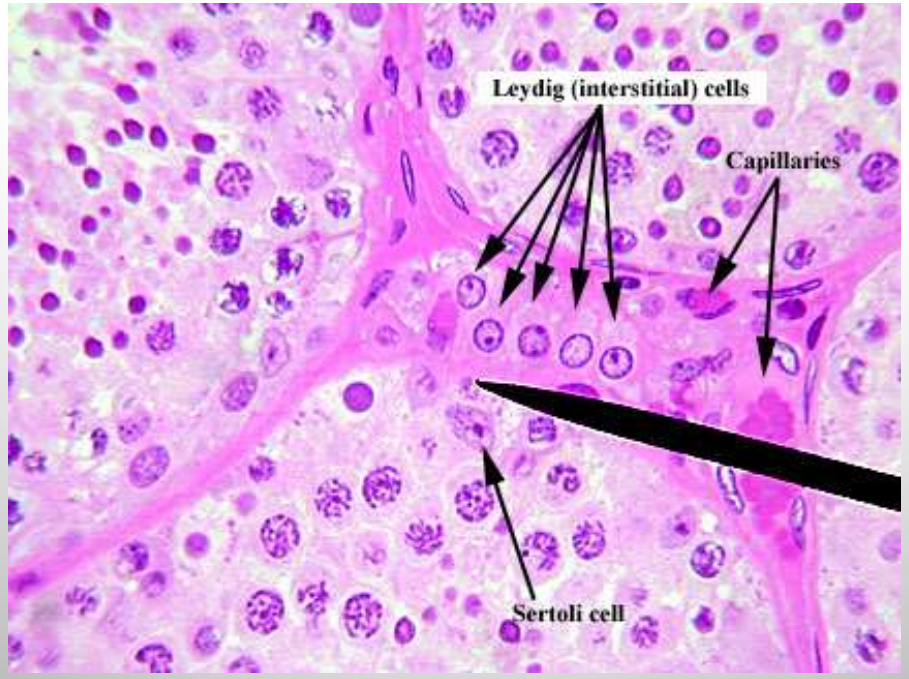
(Medrado, 2014)

Folículo ovariano



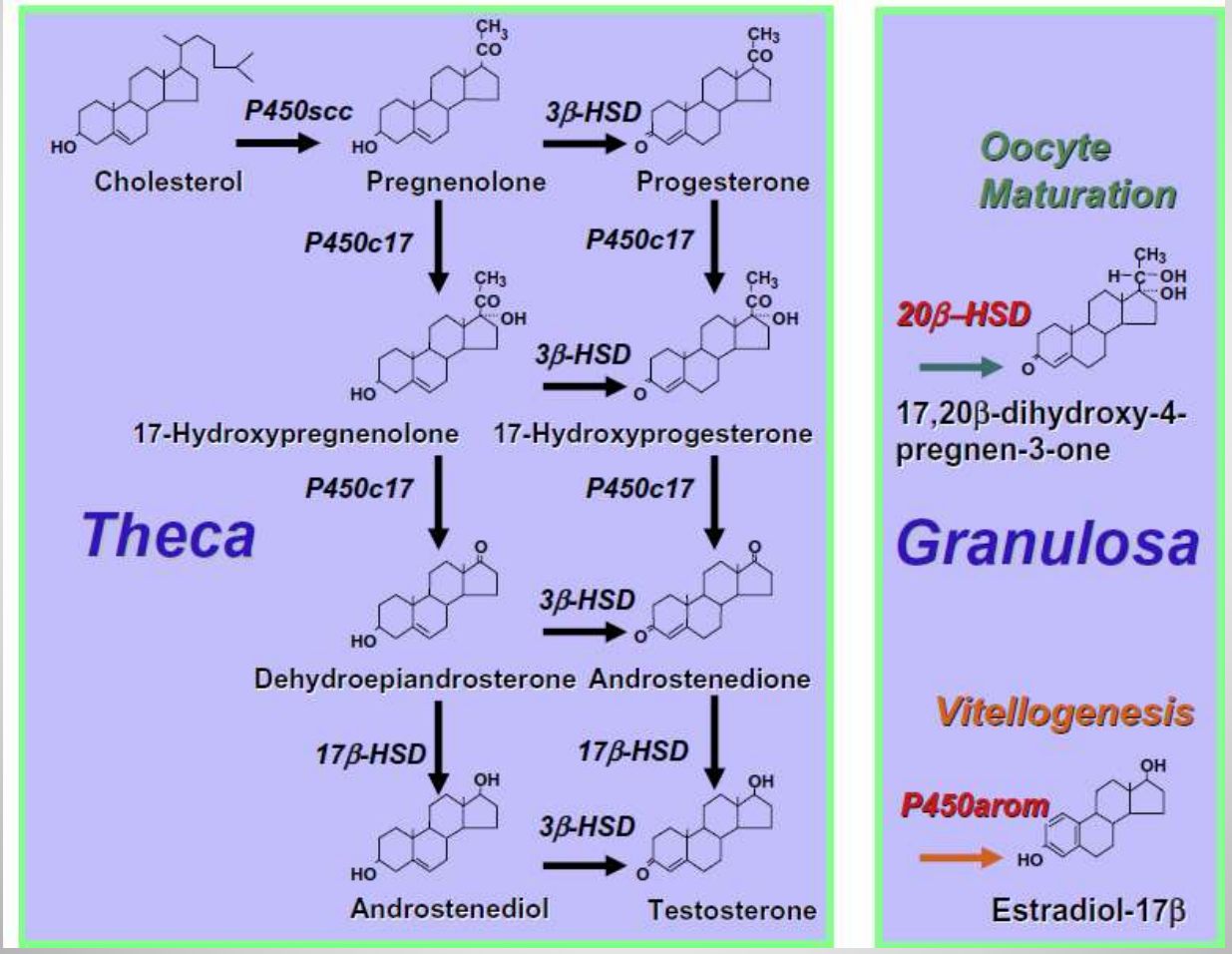
(Lubzens et al., 2010)

Testículo



(www.pixgood.com)

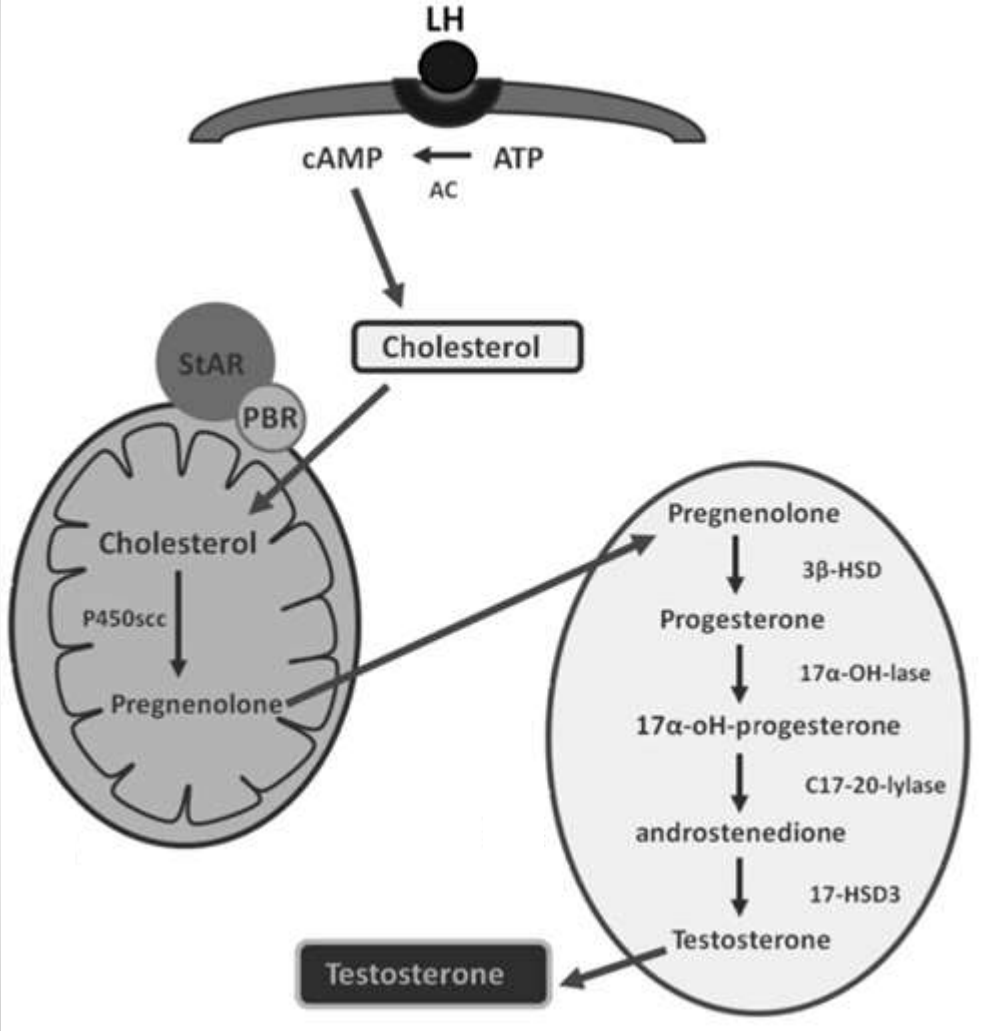
Esteroidogênese nas células foliculares



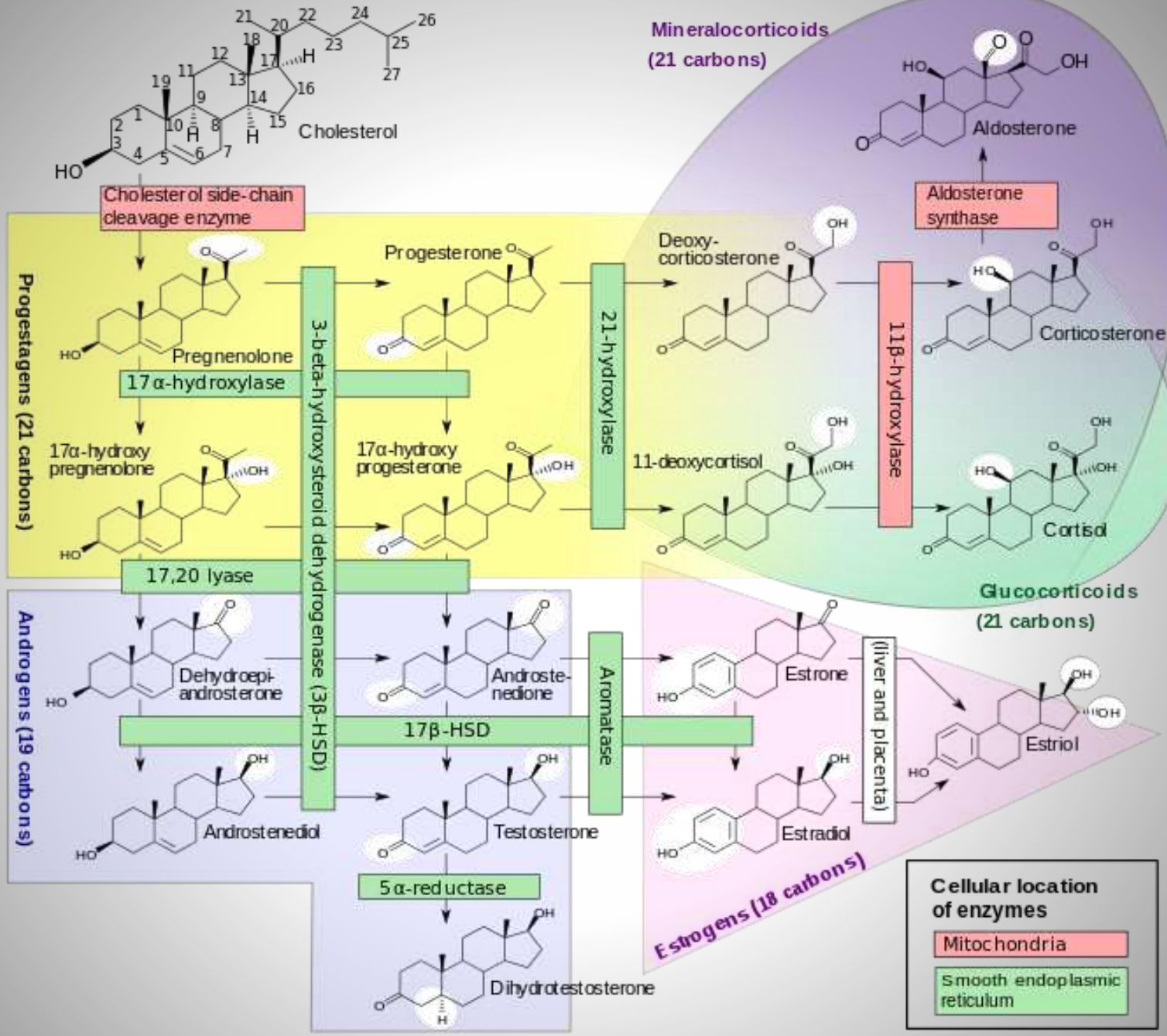
Processo conservado na escala filogenética

(Lubzens et al., 2010)

Esteroidogênese na célula de Leydig



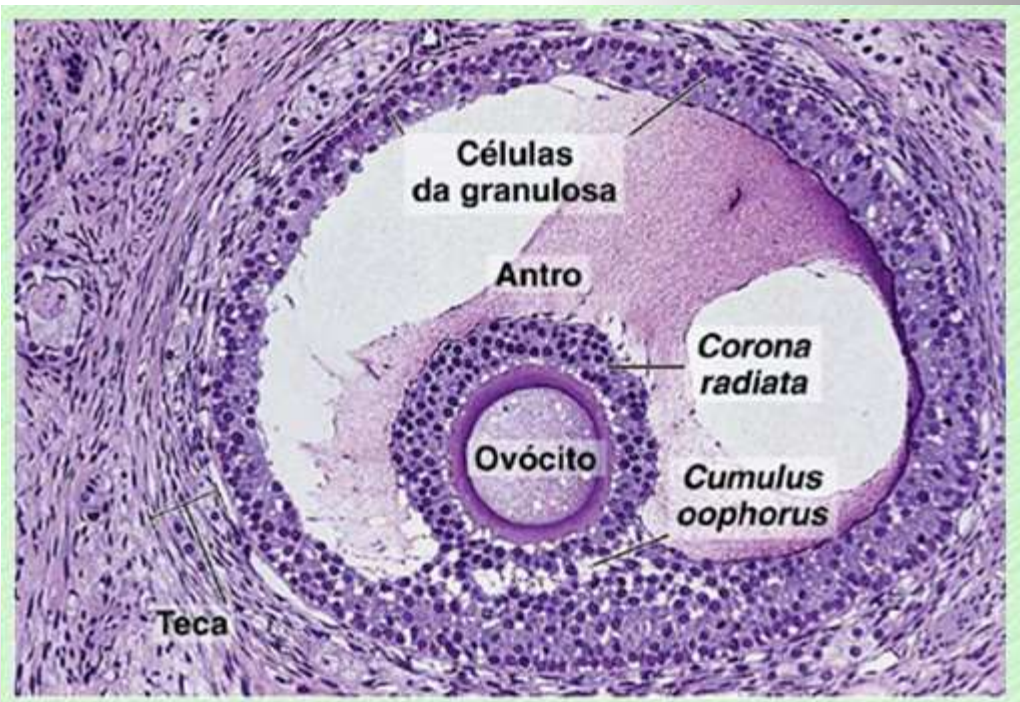
(Amaral et al., 2013)



(www.thepeproject.net)

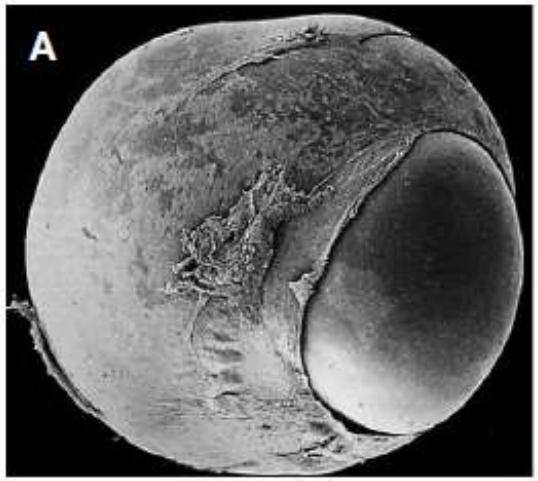


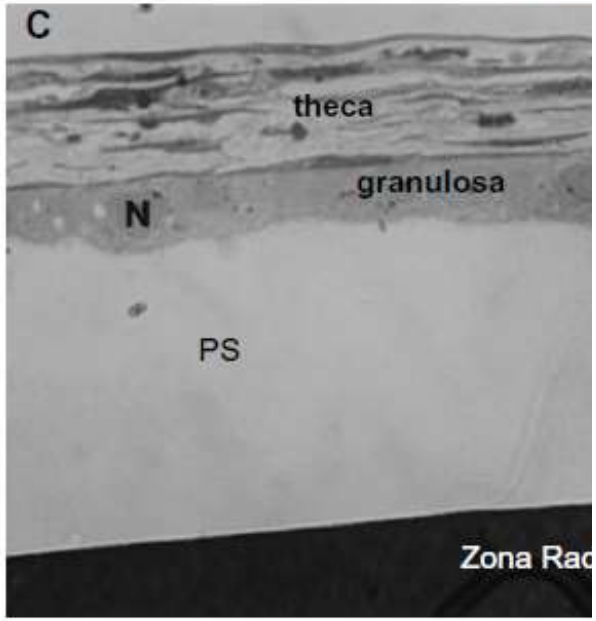
Folículo maduro
("Graaf")



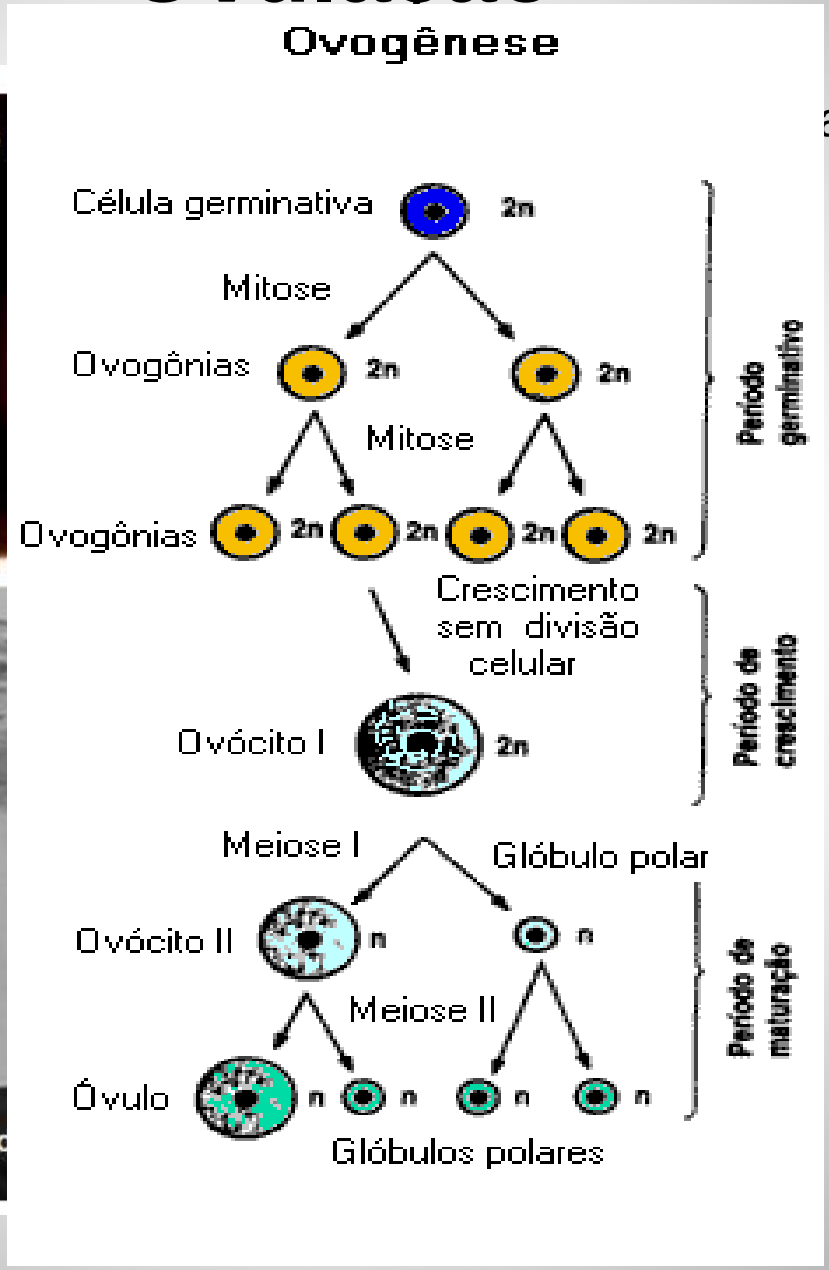
Folículo de Graaf contendo um ovócito envolvido por um conjunto de células que formam a corona radiata e apoiado nas células da granulosa que constituem o cumulus oophorus. As células restantes da granulosa formam a parede do folículo e envolvem um grande antro. O folículo é envolvido por uma teca.

Ovulacão





a Meiose



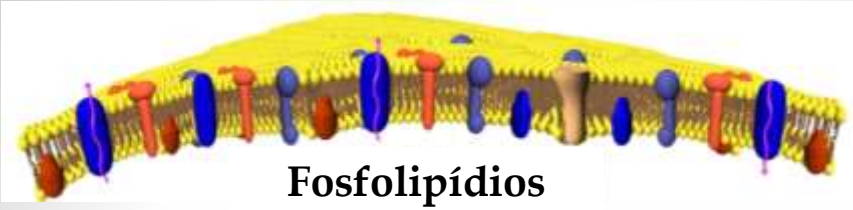
Controle da Ovulação

-Prostaglandinas;

-Proteases;

-Moléculas de adesão;

-Progestágenos



Fosfolipídios

FLA / FLC

AA EPA

COX I

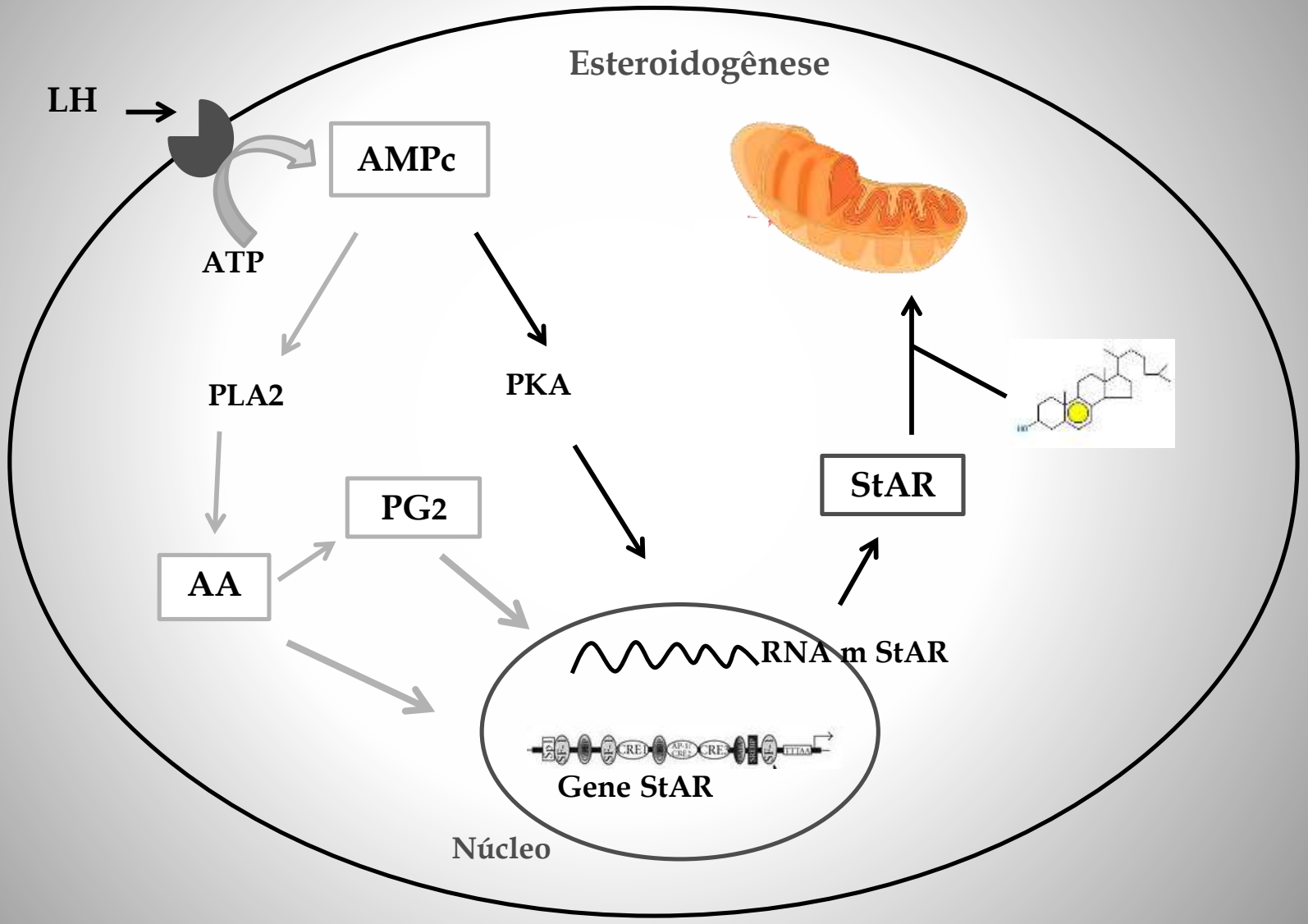
PGG2 PGG3

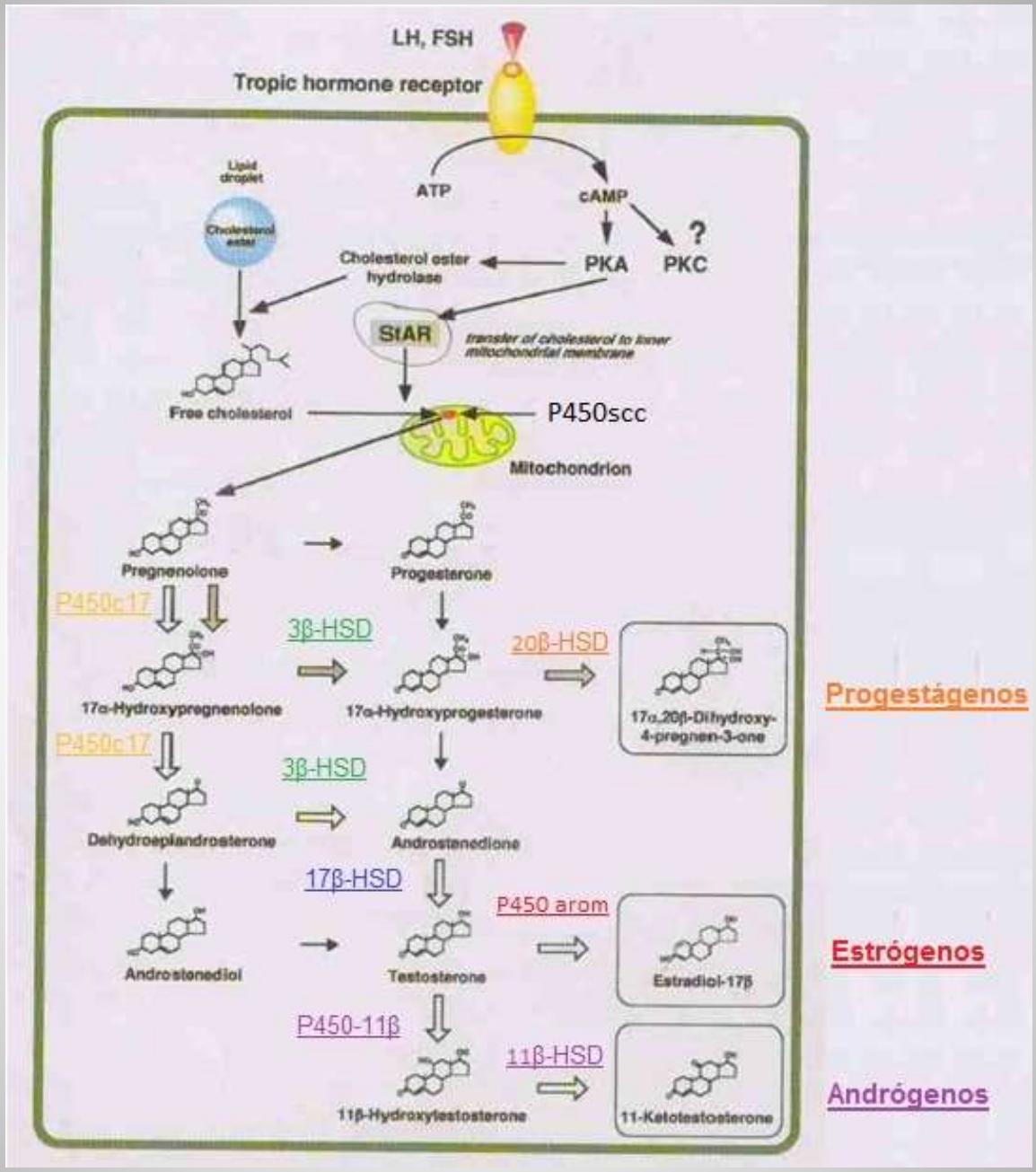
COX II

PGH2 PGH3

PG sintase

PG2 PG3


Esteroidogênese
LH
AMPc
ATP
PLA2
PKA
PG2
AA
StAR
RNA m StAR
Gene StAR
Núcleo


LH, FSH
Tropic hormone receptor
Lipid droplet
Cholesterol ester
ATP
cAMP
?
PKA
PKC
Cholesterol ester hydrolase
StAR
transfer of cholesterol to inner mitochondrial membrane
Free cholesterol
P450scc
Mitochondrion
Pregnenolone
Progesterone
P450c17
3β-HSD
20β-HSD
17α-Hydroxypregnenolone
17α-Hydroxyprogesterone
17α,20β-Dihydroxy-4-pregnen-3-one
P450c17
3β-HSD
Dehydroepiandrosterone
Androstenedione
17β-HSD
P450 arom
Androstenediol
Testosterone
Estradiol-17β
P450-11β
11β-HSD
11β-Hydroxytestosterone
11-Ketotestosterone
Progestágenos
Estrógenos
Andrógenos

Principais esteroides na gametogênese dos vertebrados:

Estrógenos

17β - Estradiol é o estrógeno mais importante em todos os grupos

Andrógenos

Teleósteos – 11 ceto-testosterona

Anuros - 5α- dihidrotestosterona

Urodelos - 11β-hidroxitestosterona

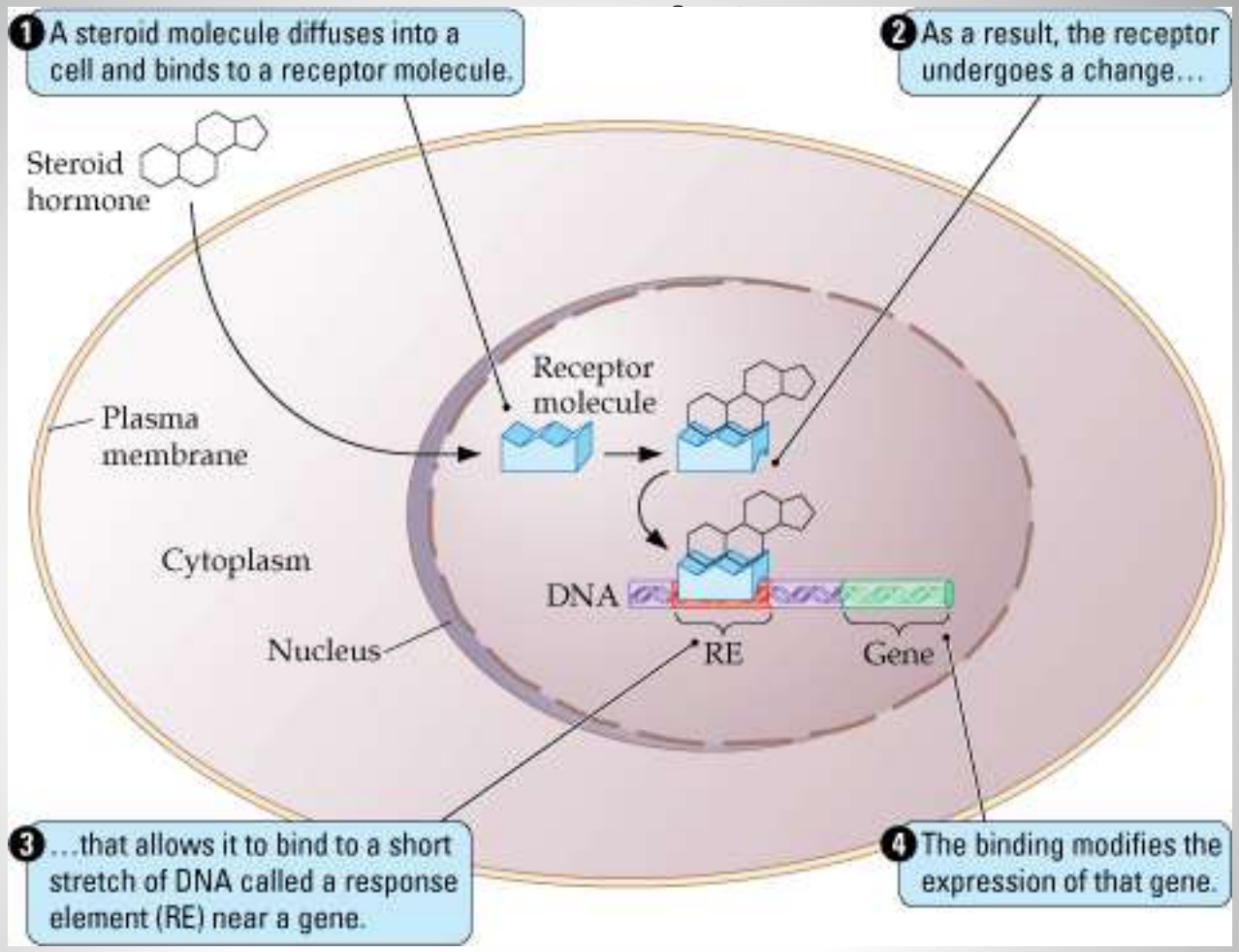
Em répteis, aves e mamíferos o andrógeno mais importante é a testosterona

Progestágenos

Teleósteos – 17 α -20 β dihidroxi-4-pregnen-3-one

Nos demais vertebrados o progestágeno mais importante é a progesterona;

Mecanismo clássico de ação dos esteroides



Hormônios esteroides formam complexos com seus receptores (no citoplasma ou no núcleo)

(www.thepeproject.net)

-Receptores intracelulares – Ashburner et al. (1974) estudando ecdisona em mosquitos (*Chironomus*) sugeriram a ação deste hormônio em genes



Paraskeva

-Ações rápidas dos esteroides foram relatadas pela primeira vez em oócitos de *Xenopus* (Godeau et al. 1978).

Proc. Natl. Acad. Sci. USA
Vol. 75, No. 5, pp. 2353–2357, May 1978
Cell Biology

Induction of maturation in *Xenopus laevis* oocytes by a steroid linked to a polymer

(mechanism of progesterone action/meiosis/plasma membrane/immobilized hormones/polyethylene oxide)

J. FRANCOIS GODEAU*, SABINE SCHORDERET-SLATKINE†, PATRICK HUBERT‡, AND ETIENNE-EMILE BAULIEU*



Tiegarten

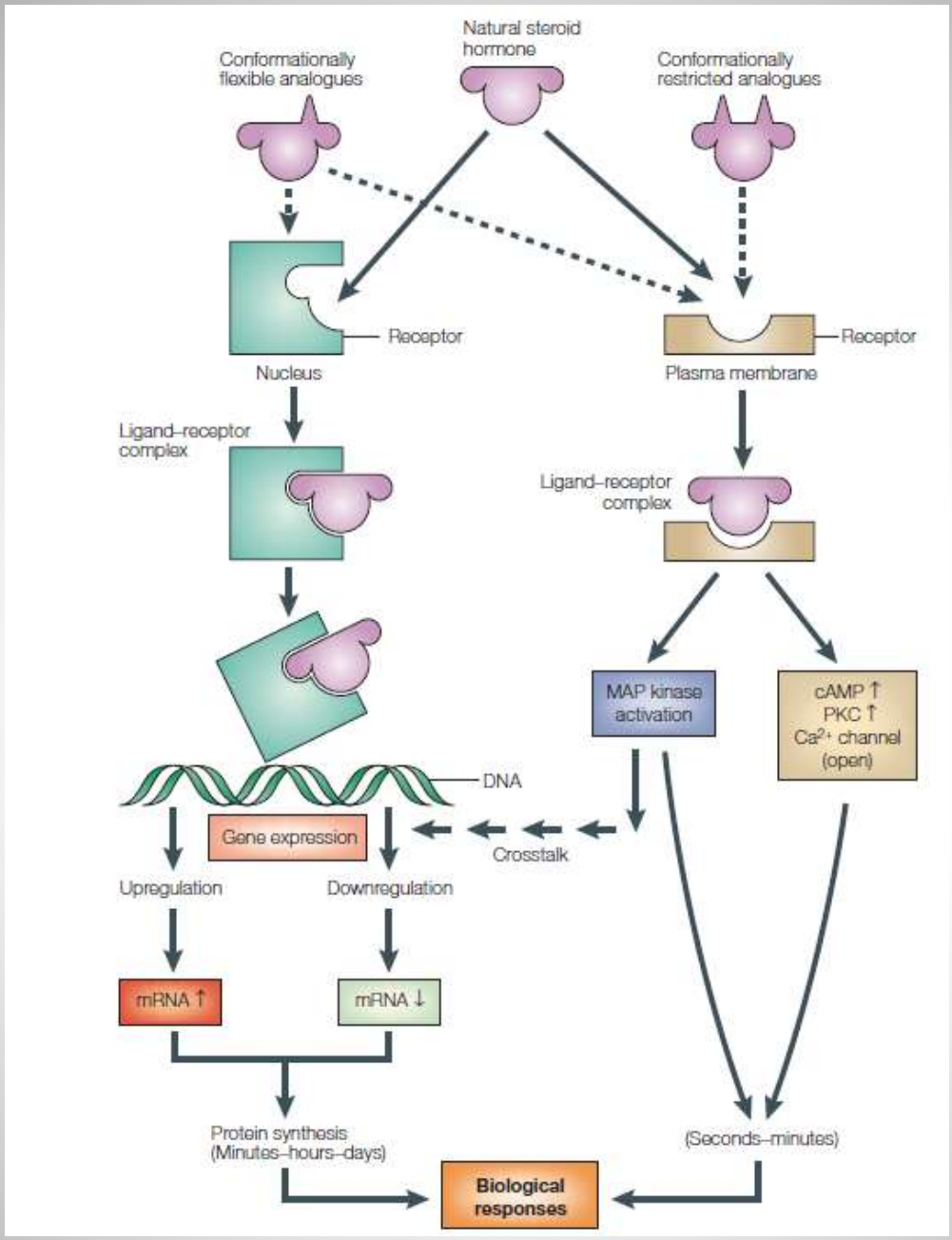
Receptores de membrana para corticosteroide sugeridos em neurônios de *Taricha granulosa* (1991)



A Corticosteroid Receptor in Neuronal Membranes

MILES ORCHINIK,* THOMAS F. MURRAY, FRANK L. MOORE

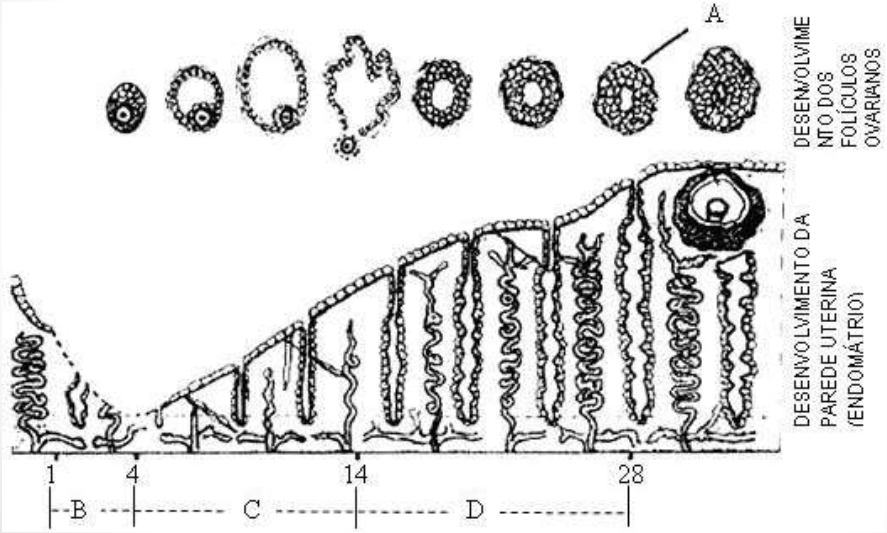
Steroids may rapidly alter neuronal function and behavior through poorly characterized, direct actions on neuronal membranes. The membrane-bound receptors mediating these behavioral responses have not been identified. [^{3}H]Corticosterone labels a population of specific, high-affinity recognition sites (dissociation constant = 0.51 nanomolar) in synaptic membranes from an amphibian brain. These binding sites were localized by receptor autoradiography in the neuropil, outside the regions of perikarya. The affinities of corticoids for this [^{3}H]corticosterone binding site were linearly related to their potencies in rapidly suppressing male reproductive behavior. Thus, it appears that brain membranes contain a corticosteroid receptor that could participate in the regulation of behavior.



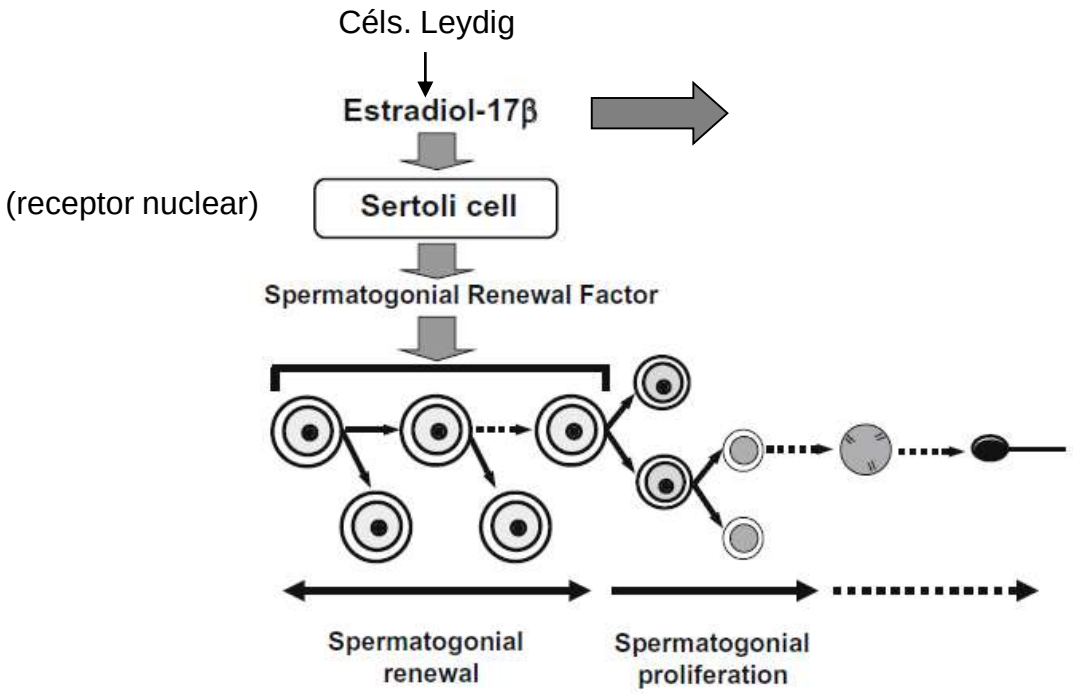
(Norman et al., 2004)

Funções dos estrógenos

- Estimula o desenvolvimento do endométrio;

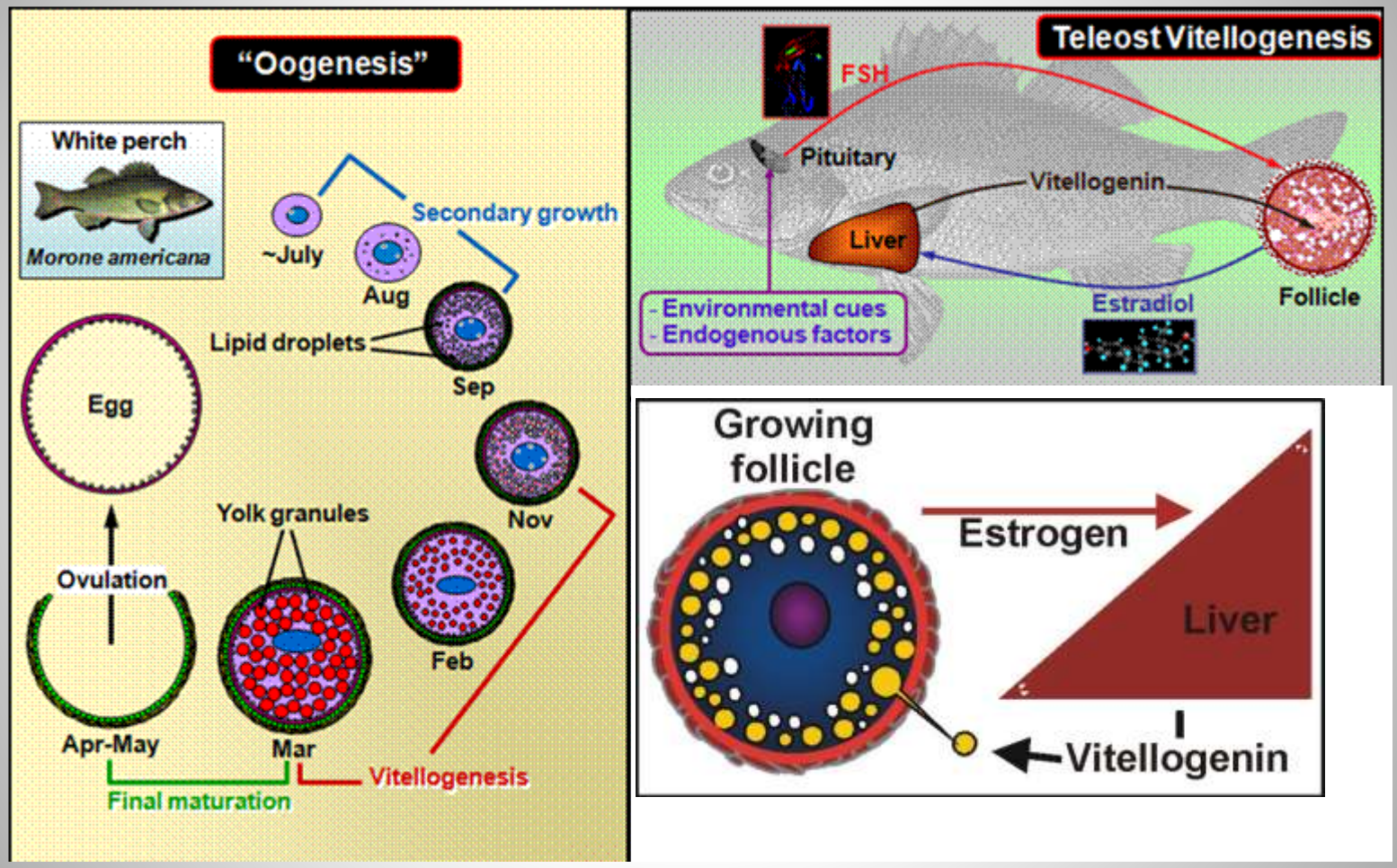


Papel dos estrógenos em machos



Schulz et al., (2010)

Estimula a síntese de vitelogenina hepática;

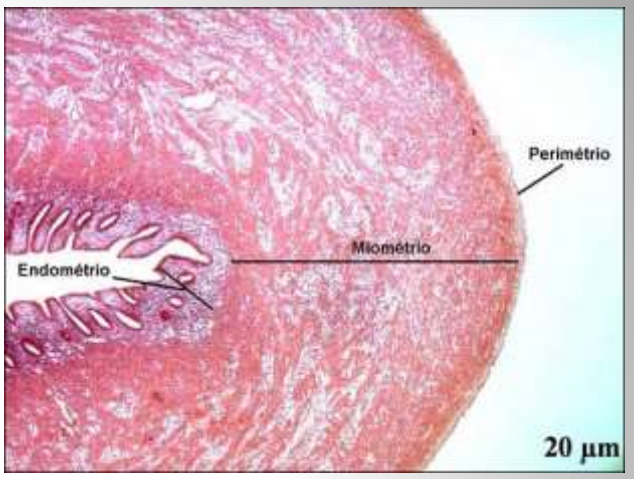


Estradiol estimula a vitelogênese em espécies ovíparas

(Jackson and Sullivan, 1995)

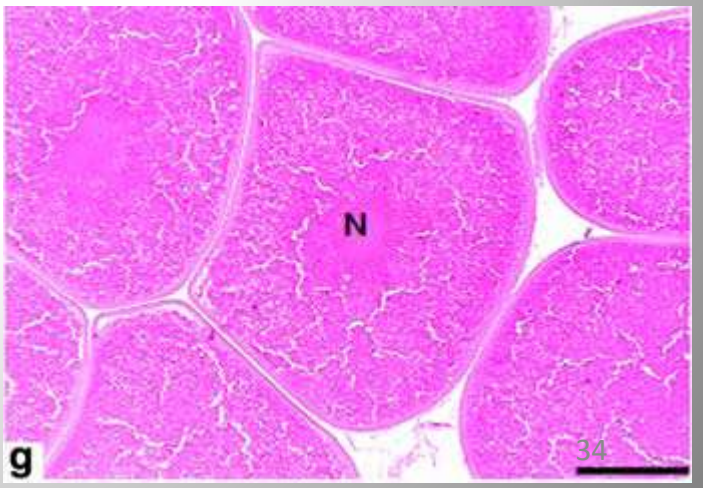
FUNÇÃO DO ESTRADIOL

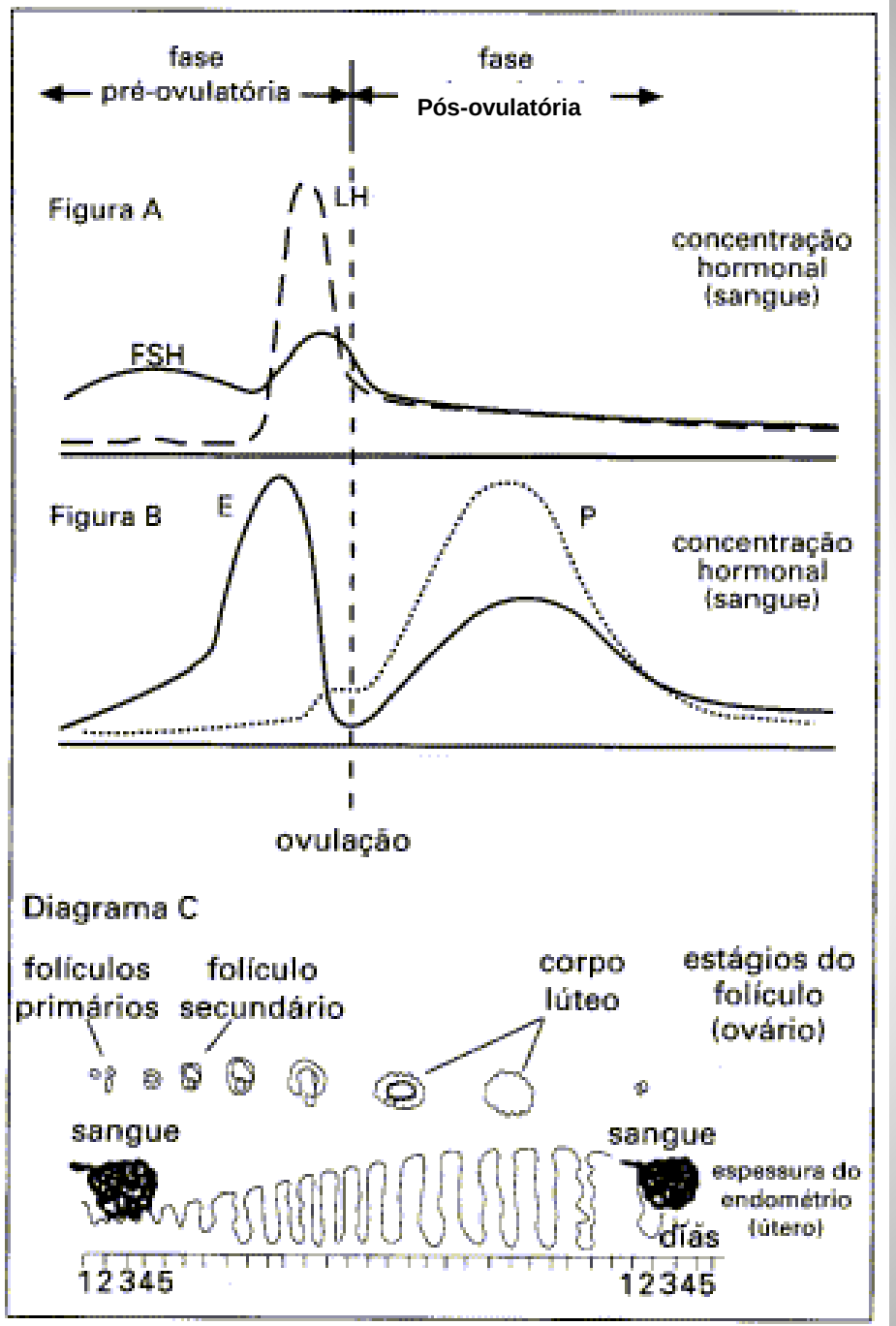
- ÚTERO DE MAMÍFEROS



X

- VERTEBRADOS OVÍPAROS??





Um folículo começa a crescer mais que os outros

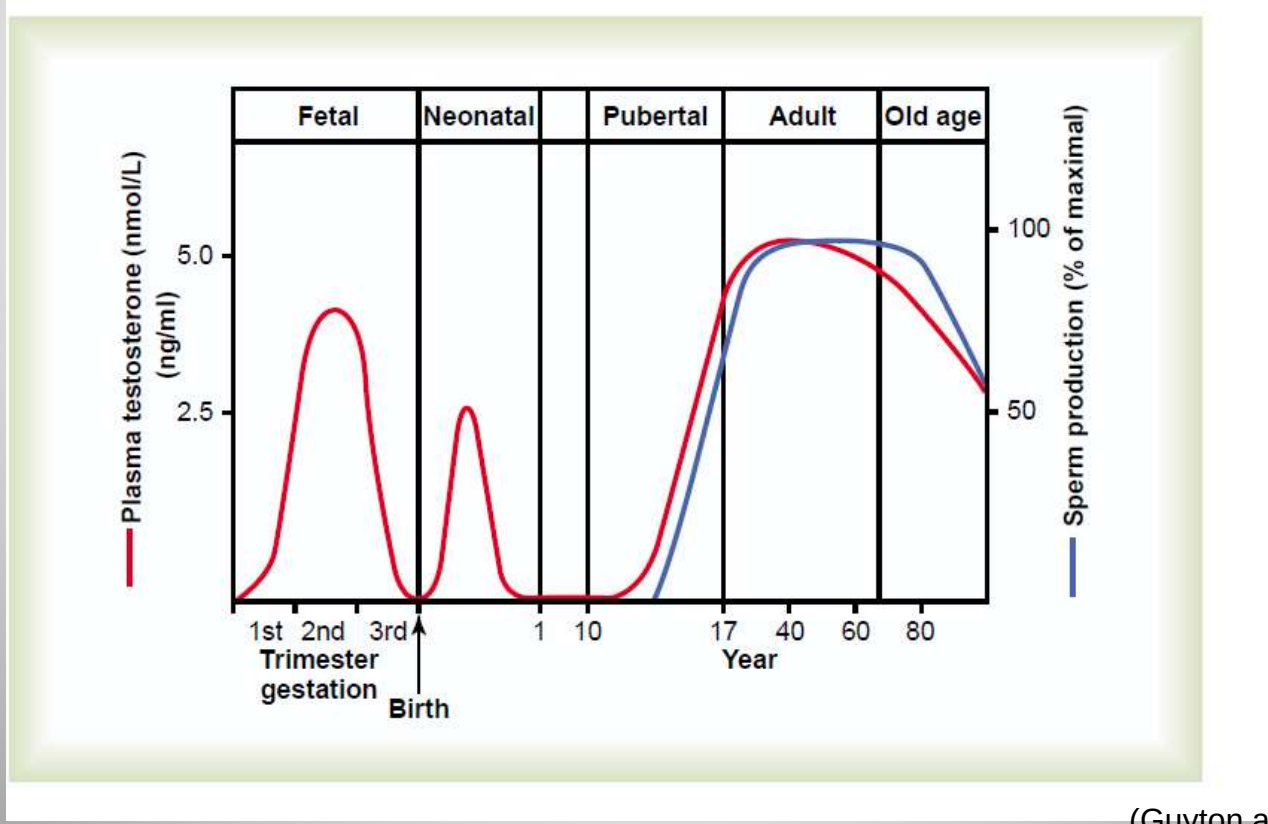
(7 dias)

Função dos andrógenos

-Espermatogênese;

-Características sexuais secundárias;

-Modula o comportamento reprodutivo em machos;



(Guyton and Hall, 2006)

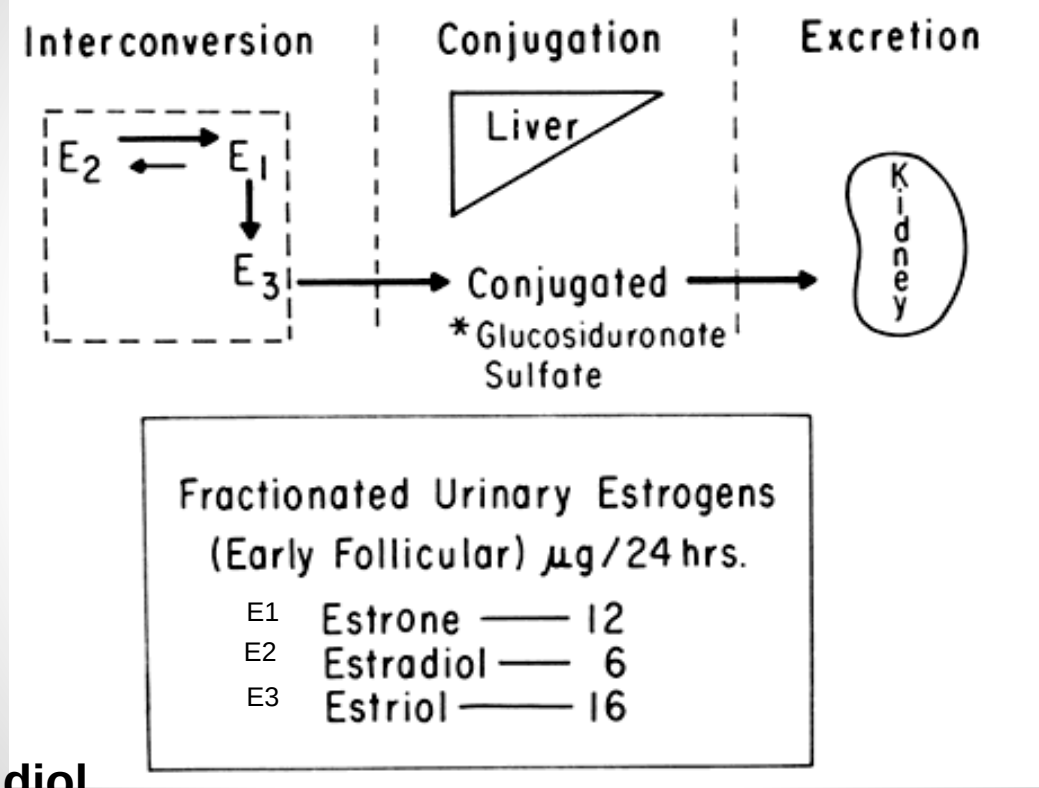
Função dos Progestágenos

- Promove as alterações secretórias no endométrio durante a fase pós-ovulatória, preparando o útero para nidação;

- Motilidade dos espermatozoides e reação acrossômica;

- Cuidado parental

Excreção dos esteroides



Ex. estradiol