Dr. Garrett next Thursday! Dr. Kaplan following Tuesday! Hooray!!...

Lecture 12

I. *Quiz 4* on CV physiology next T in class → Presentations. Q?
   For Quiz, 10 am section go to 112 WIL with Stacy just < 8:30!

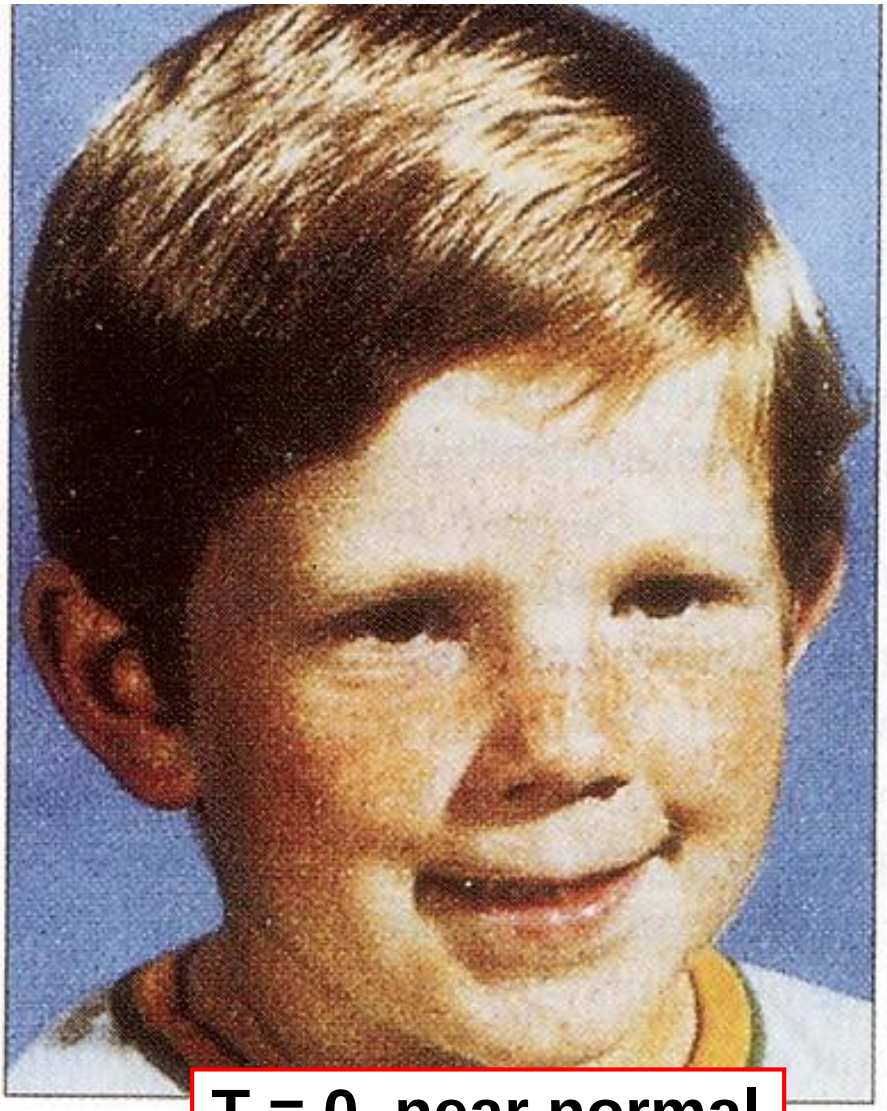
II. *Endocrinology Overview* from Lecture 10 G&H ch 75, 76

III. *Med Physiol News* Sex Allergy? Mom's eggs execute dad's mitochondria? *Science News*

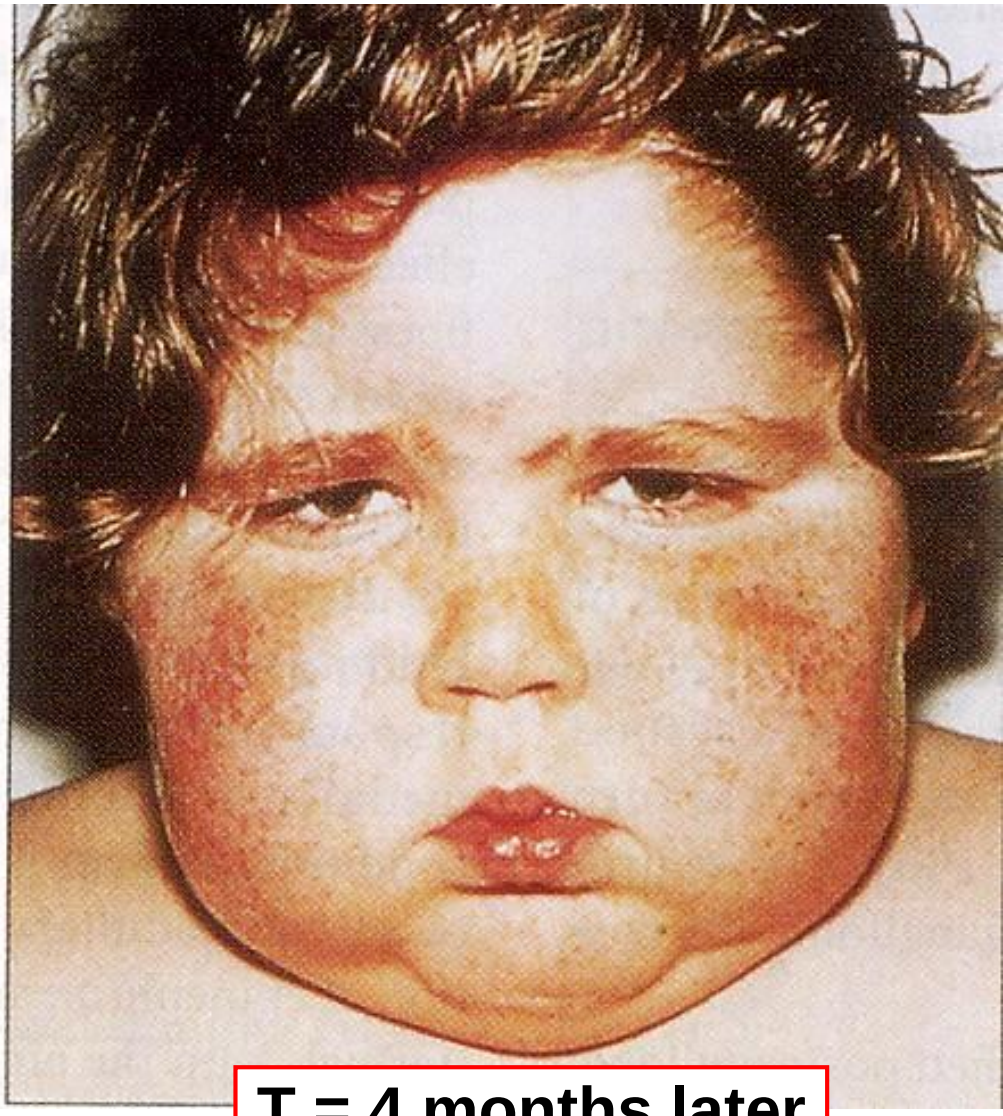
IV. *Reproductive Physiology Primer* G&H ch 82,81 +L Sherwood…

- A. Female reproductive system fig 82-1, 82-2
- B. Ovarian hormones +FB: estrogen, progesterone pp 1042-7
- C. Follicle growth & ovulation mechanism fig 82-5, 82-3
- D. Plasma gonadotropin & ovarian hormone [ ] in female sexual cycle fig 82-4
- E. Female sexual cycle, menstruation fig 82-4, 82-9
- F. Estrogen [ ] throughout lifespan, menopause fig 82-12
- G. Birth control techniques L Sherwood + G&H
- H. Male reproductive system fig 81-1 A & B
- I. Sperm & development fig 81-2, 81-7, 81-3, 81-4, 81-5
- J. Feedback regulation in males fig 81-10
- K. Plasma testosterone [ ] throughout lifespan fig 81-9

Cushing's Syndrome = Hypersecretion of Cortisol: Hypothalamic (CRH), Pituitary (ACTH), or Adrenal (Cortisol)



T = 0, near normal



T = 4 months later

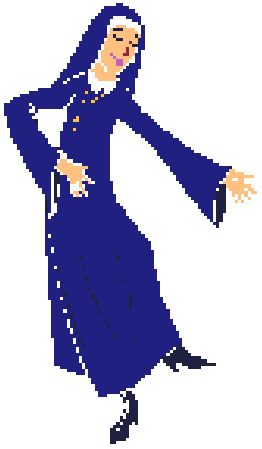
Endocrine or Hormone?

1. ***Made by gland?***
2. ***Secreted into blood?***
3. ***Acts on target?***

Endocrine or Hormone Classifications

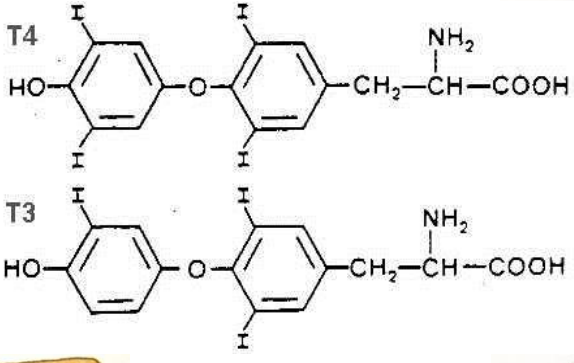
Exogenous

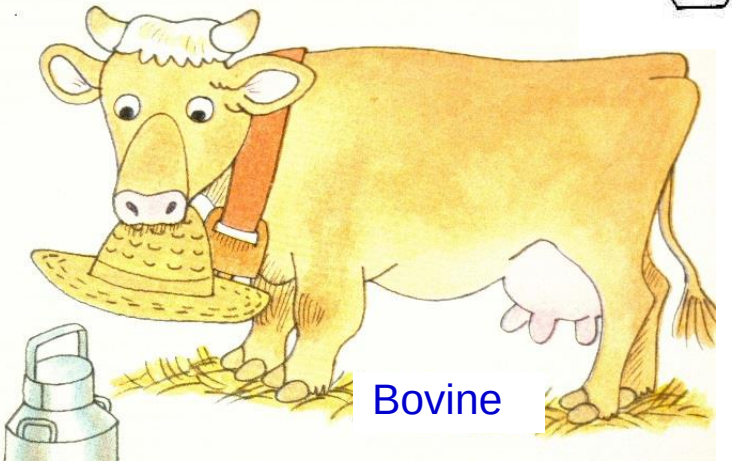
Porcine



Thyroid

Recombinant DNA

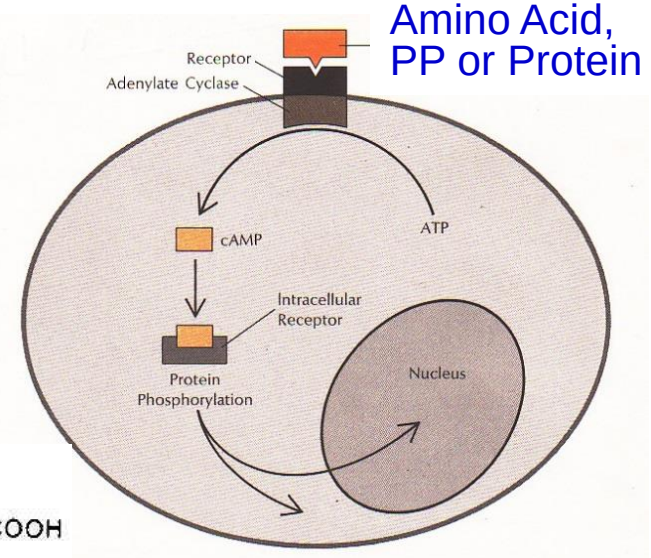




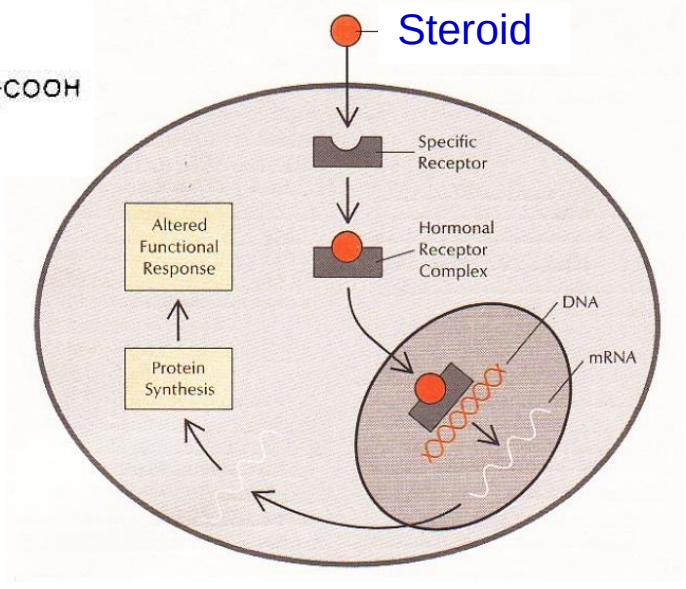
Bovine

Endogenous

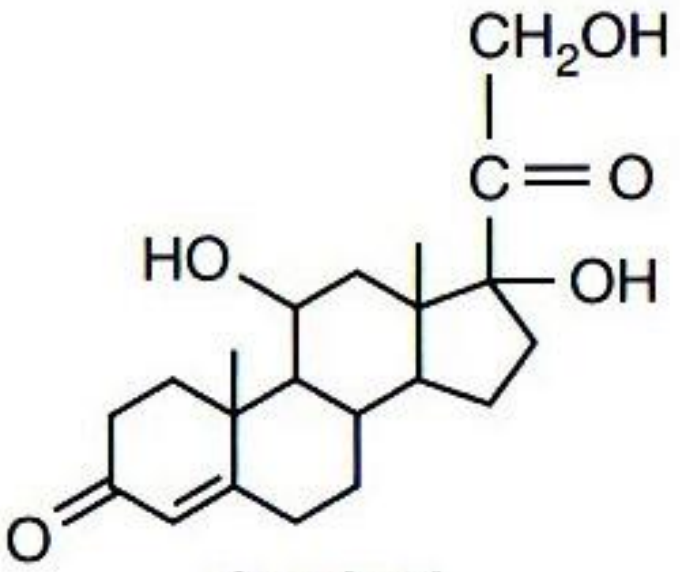
Amino Acid, PP or Protein



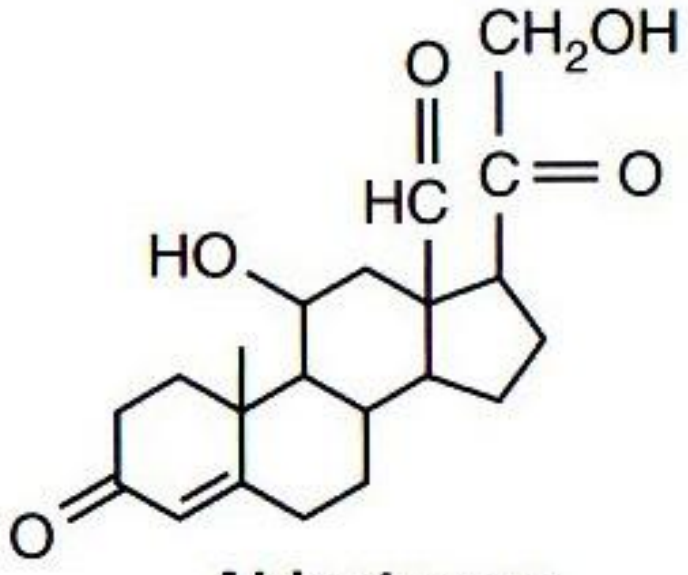
Steroid



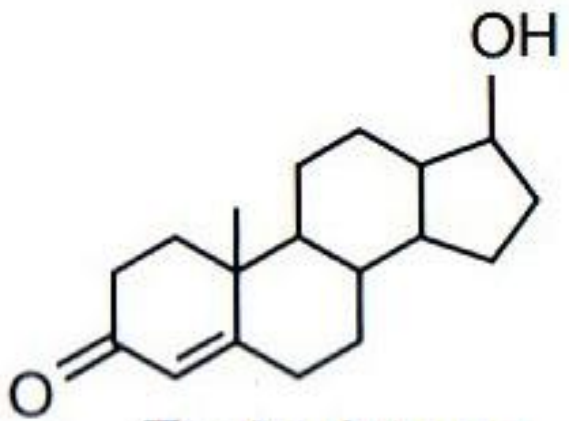
Steroid Hormone Structure: Cholesterol Backbone



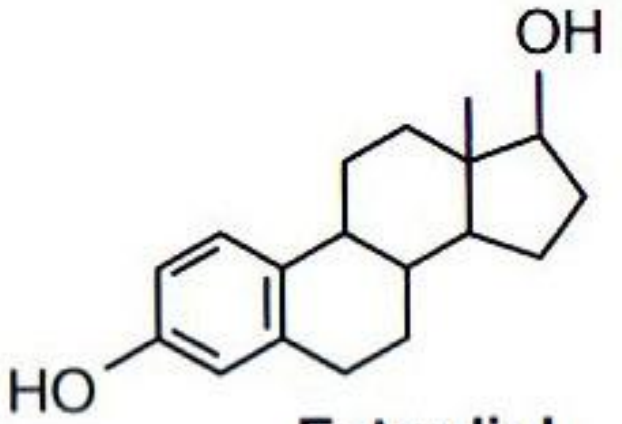
Cortisol



Aldosterone



Testosterone



Estradiol

G&H 2016 fig 75-3, G&H 2011 fig 74-3

ANP = _A_trial _N_atriuretic _P_olypeptide

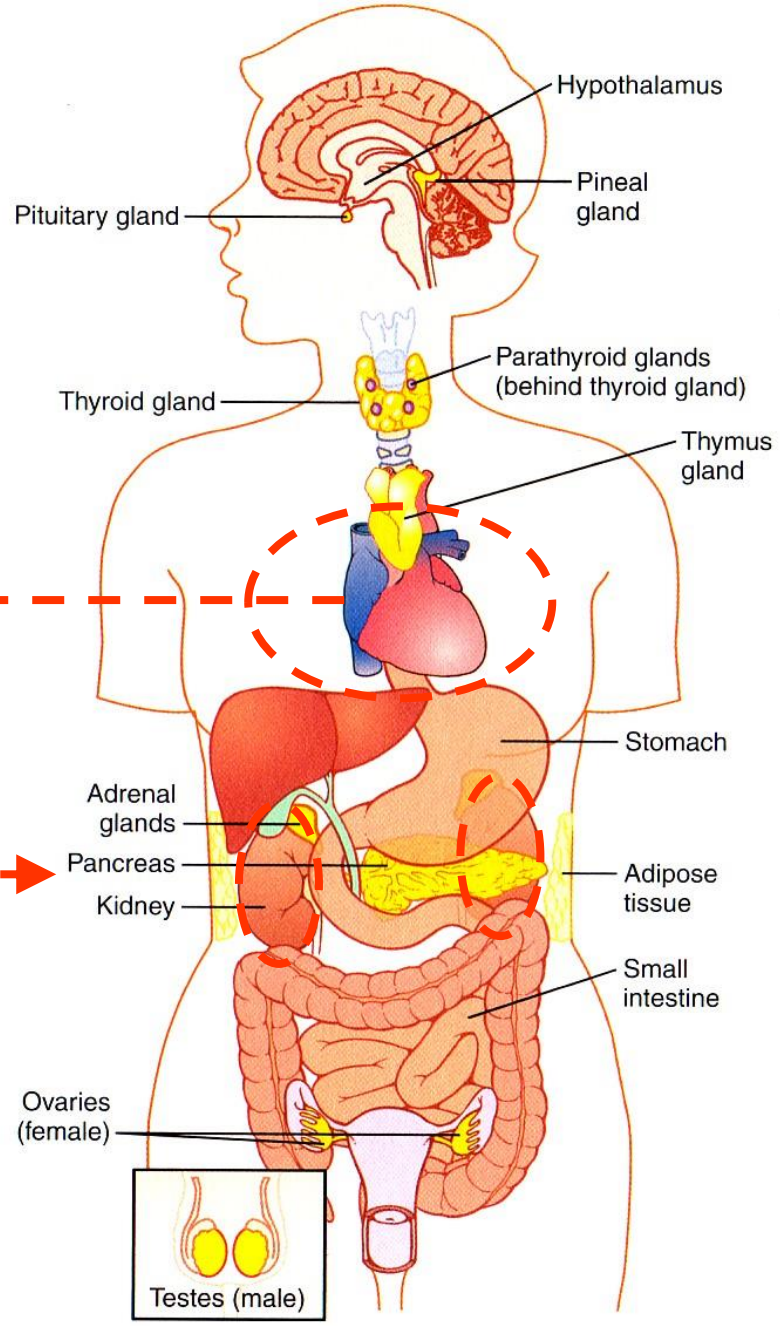
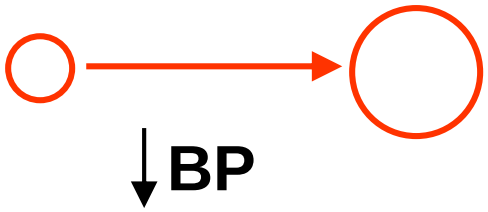


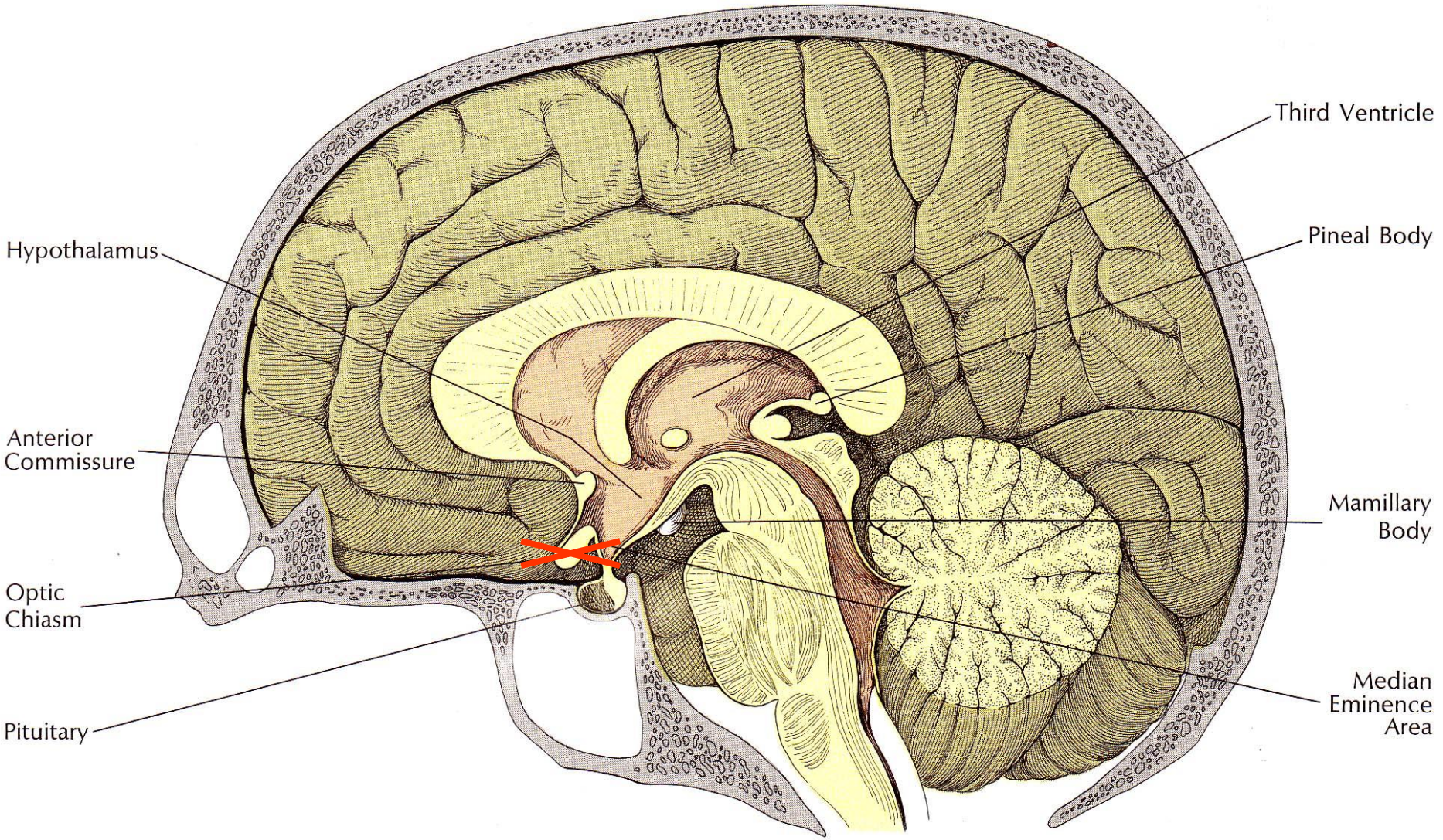
Figure 74-1 Anatomical loci of the principal endocrine glands and tissues of the body.

2 **Vasodilation**



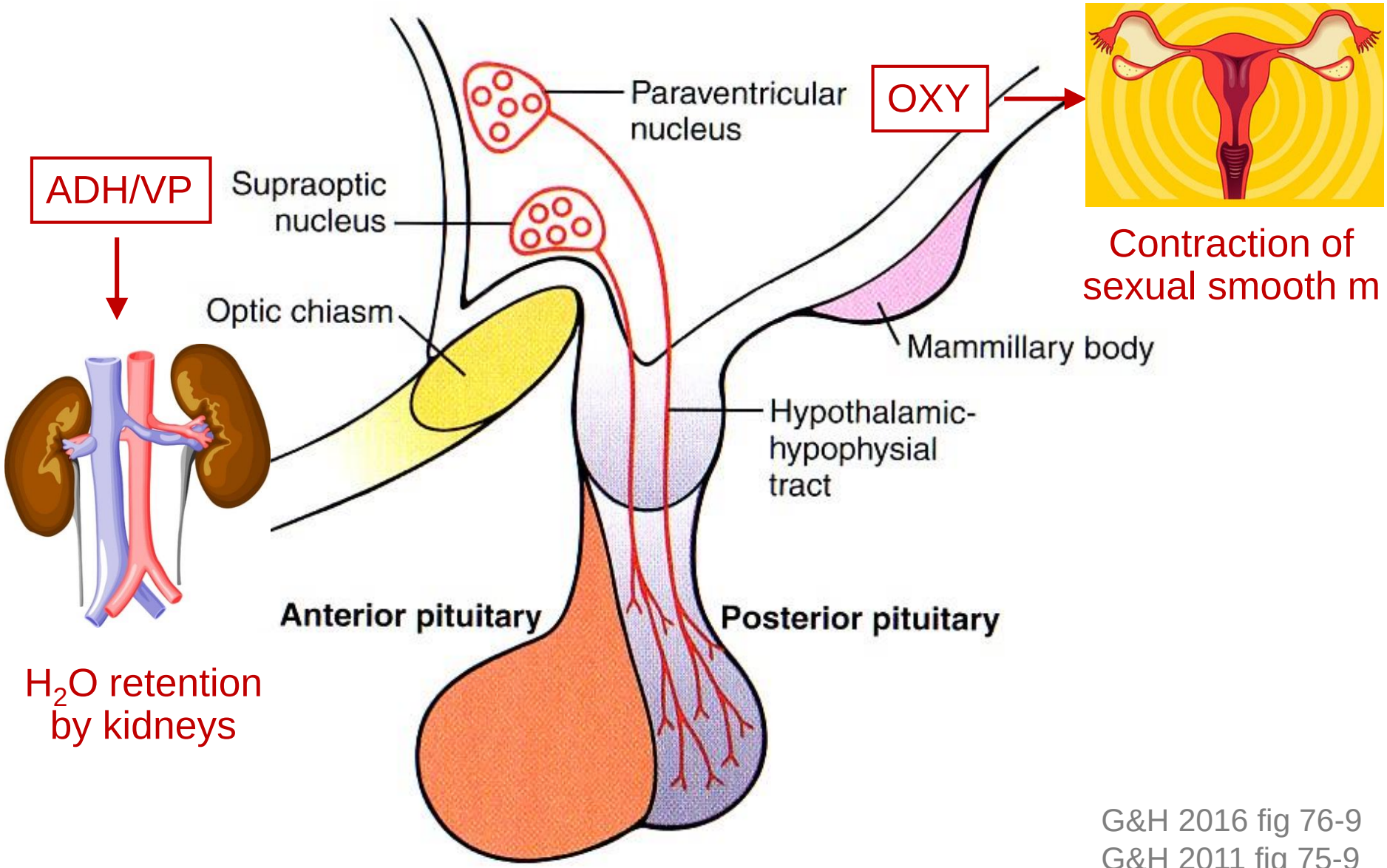
G&H 2016 fig 75-1
G&H 2011 fig 74-1

Lateral View Showing Relationship of the Pituitary Gland to the Hypothalamus



Krieger & Hughes 1980

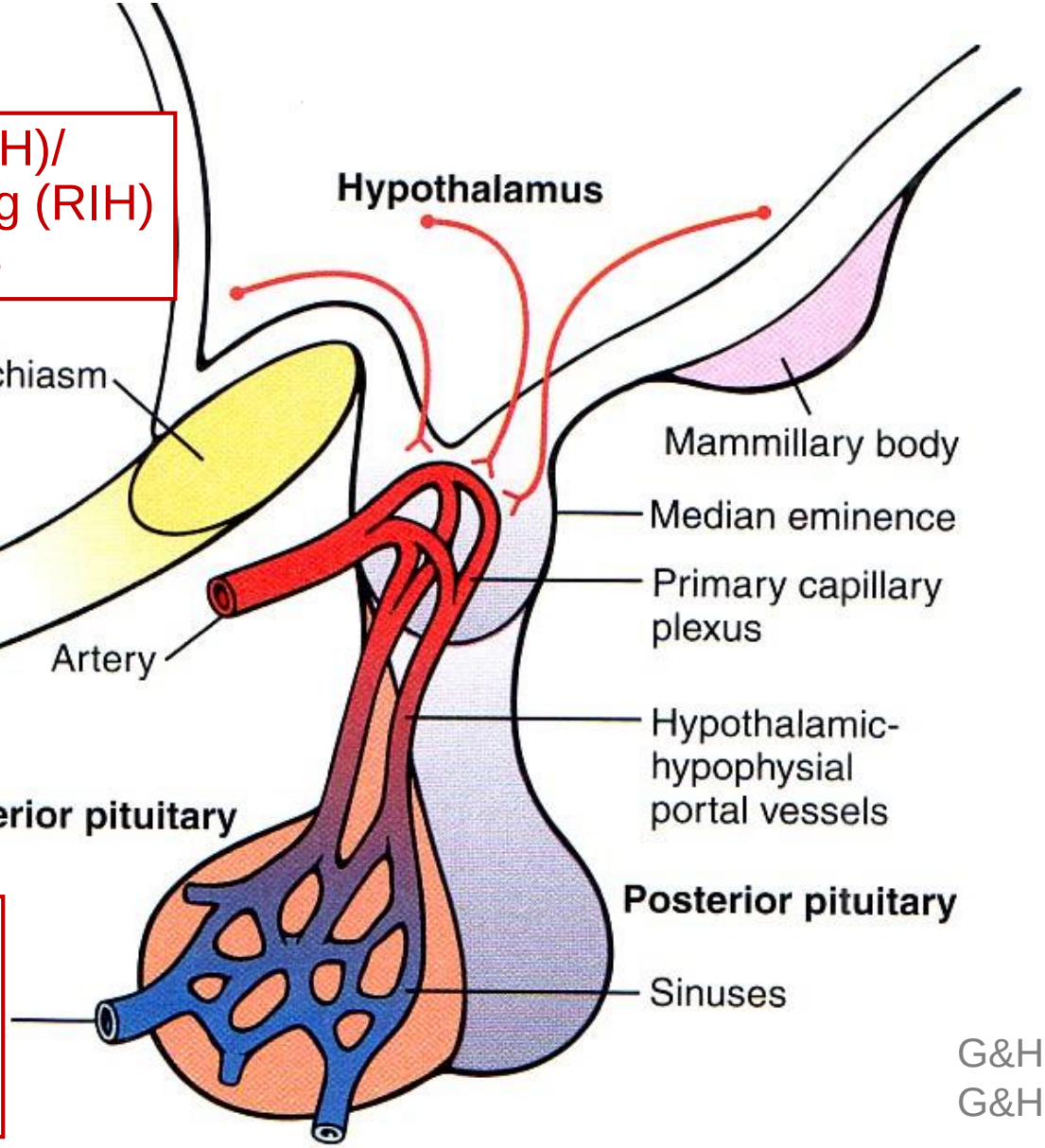
Hypothalamus – Posterior Pituitary Nervous Connection



G&H 2016 fig 76-9
G&H 2011 fig 75-9

Hypothalamus – Anterior Pituitary Vascular Connection

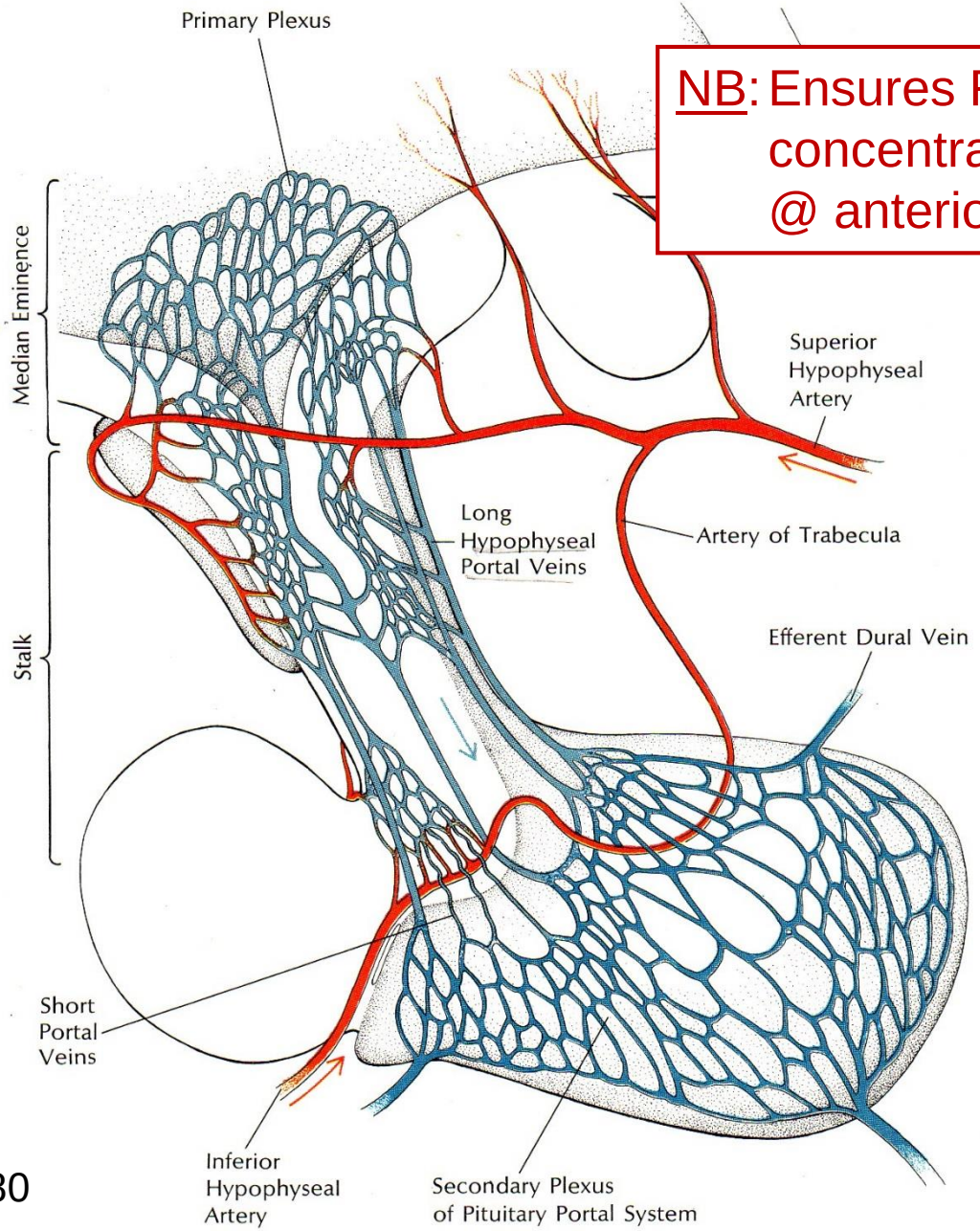
Releasing (RH)/ Release-Inhibiting (RIH) Hormones



1 of 6 Trophic/ Nourishing Hormones

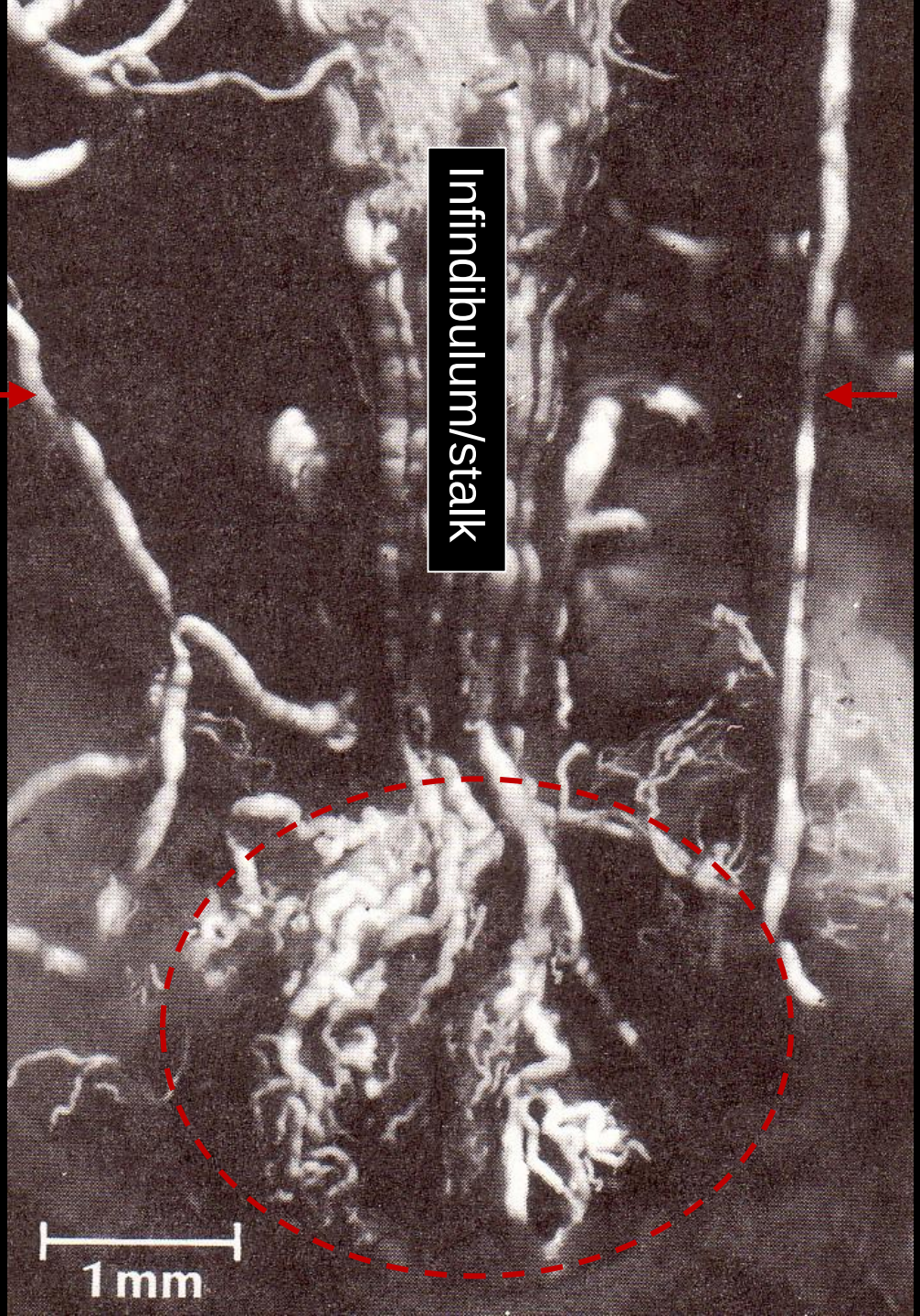
G&H 2016 fig 76-4
G&H 2011 fig 75-4

Capillary-Venule-Capillary Circulation



NB: Ensures RH/RIH super-concentrated upon arrival @ anterior pituitary!

Krieger & Hughes 1980



Long hypophyseal-portal veins

Pituitary removed!

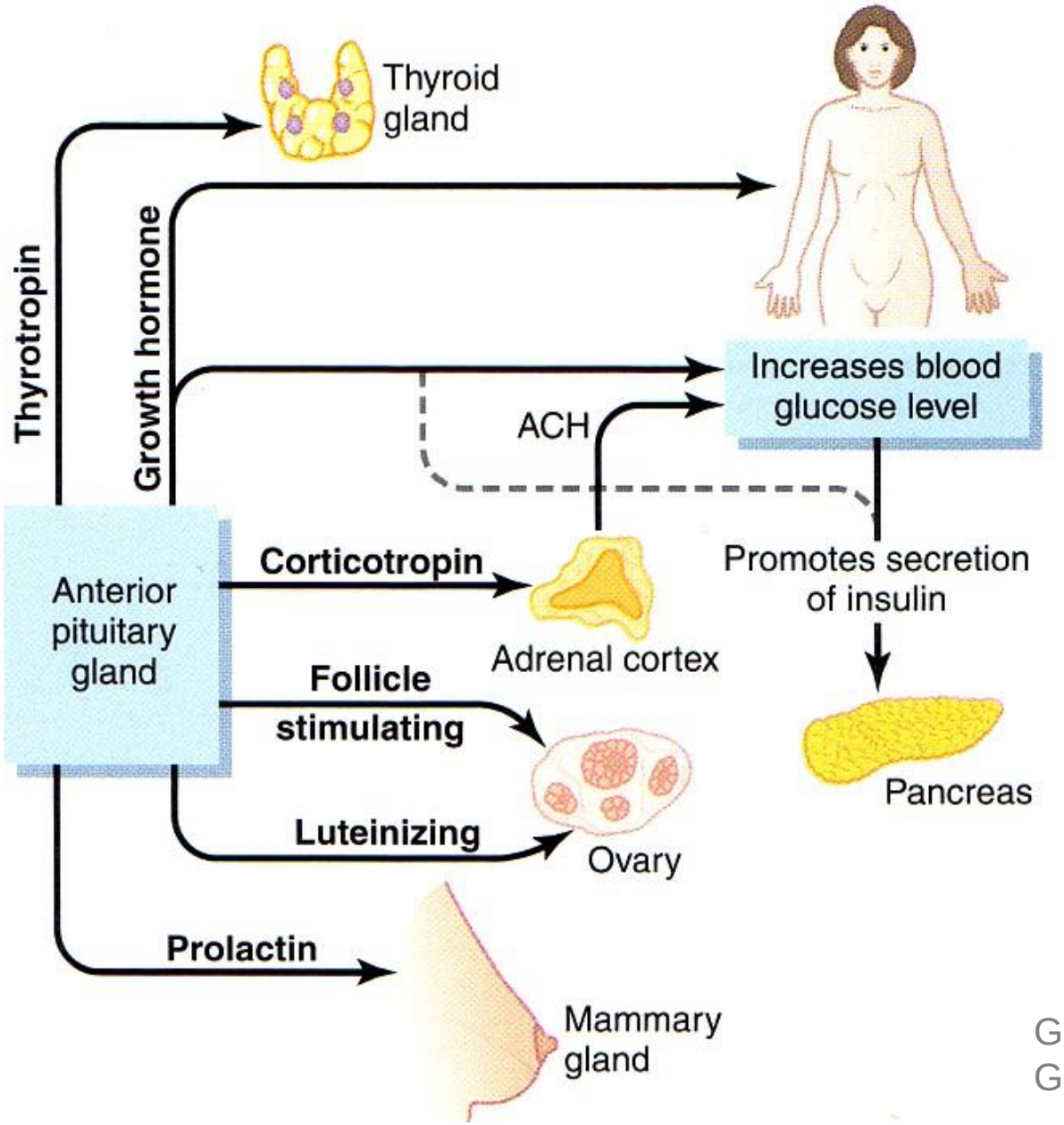
Krieger & Hughes 1980

Table 74-1 Endocrine Glands, Hormones, and Their Functions and Structure

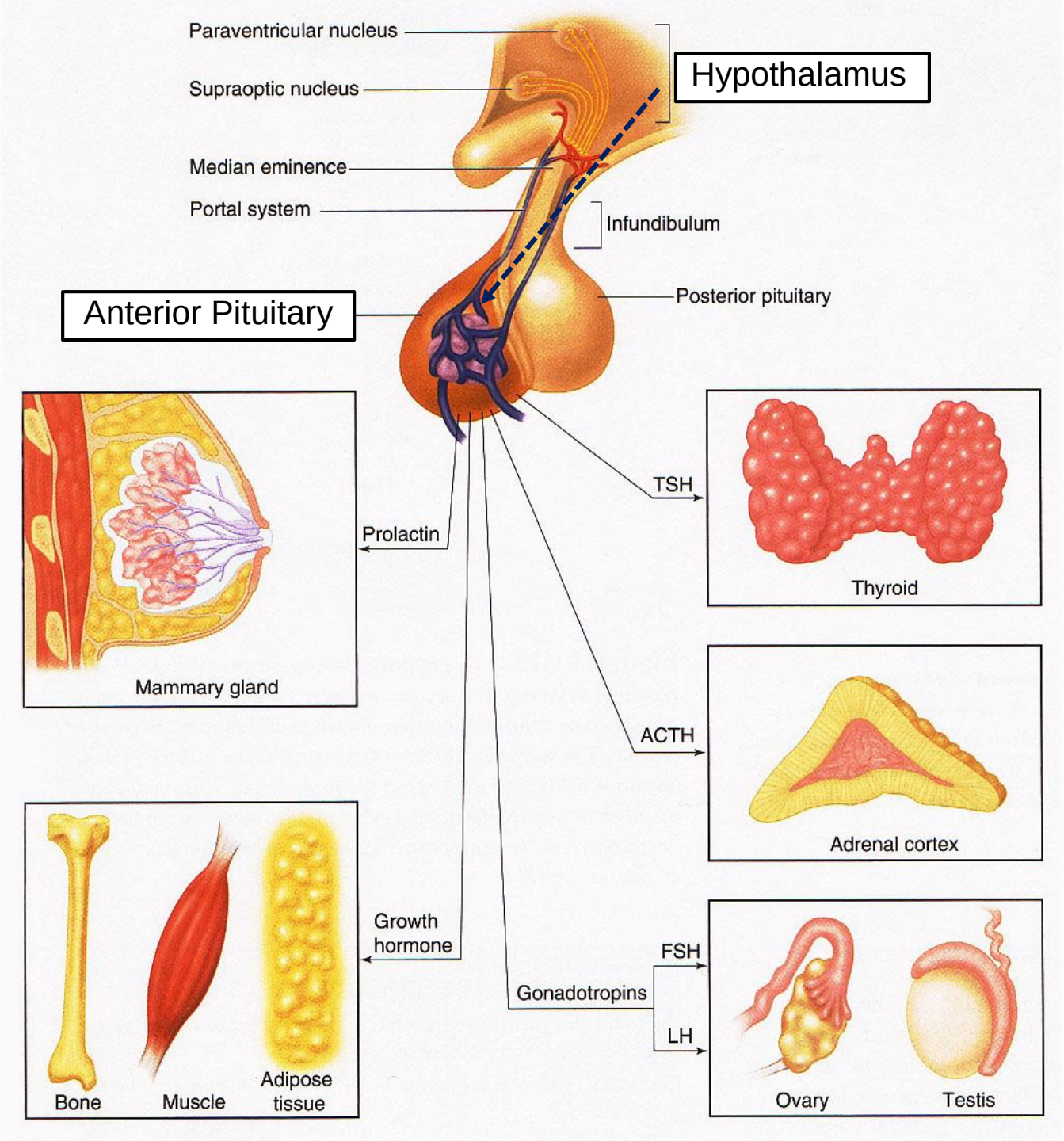
Gland/Tissue	Hormones	Major Functions	Chemical Structure
Hypothalamus (Chapter 75)	Thyrotropin-releasing hormone (TRH)	Stimulates secretion of thyroid-stimulating hormone (TSH) and prolactin	Peptide
	Corticotropin-releasing hormone (CRH)	Causes release of adrenocorticotropic hormone (ACTH)	Peptide
	Growth hormone–releasing hormone (GHRH)	Causes release of growth hormone	Peptide
	Growth hormone inhibitory hormone (GHIH) (somatostatin)	Inhibits release of growth hormone	Peptide
	Gonadotropin-releasing hormone (GnRH)	Causes release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH)	
	Dopamine or prolactin-inhibiting factor (PIF)	Inhibits release of prolactin	Amine
Anterior pituitary (Chapter 75)	Growth hormone	Stimulates protein synthesis and overall growth of most cells and tissues	Peptide
	TSH	Stimulates synthesis and secretion of thyroid hormones (thyroxine and triiodothyronine)	Peptide
	ACTH	Stimulates synthesis and secretion of adrenocortical hormones (cortisol, androgens, and aldosterone)	Peptide
	Prolactin	Promotes development of the female breasts and secretion of milk	Peptide
	FSH	Causes growth of follicles in the ovaries and sperm maturation in Sertoli cells of testes	Peptide
	LH	Stimulates testosterone synthesis in Leydig cells of testes; stimulates ovulation, formation of corpus luteum, and estrogen and progesterone synthesis in ovaries	Peptide

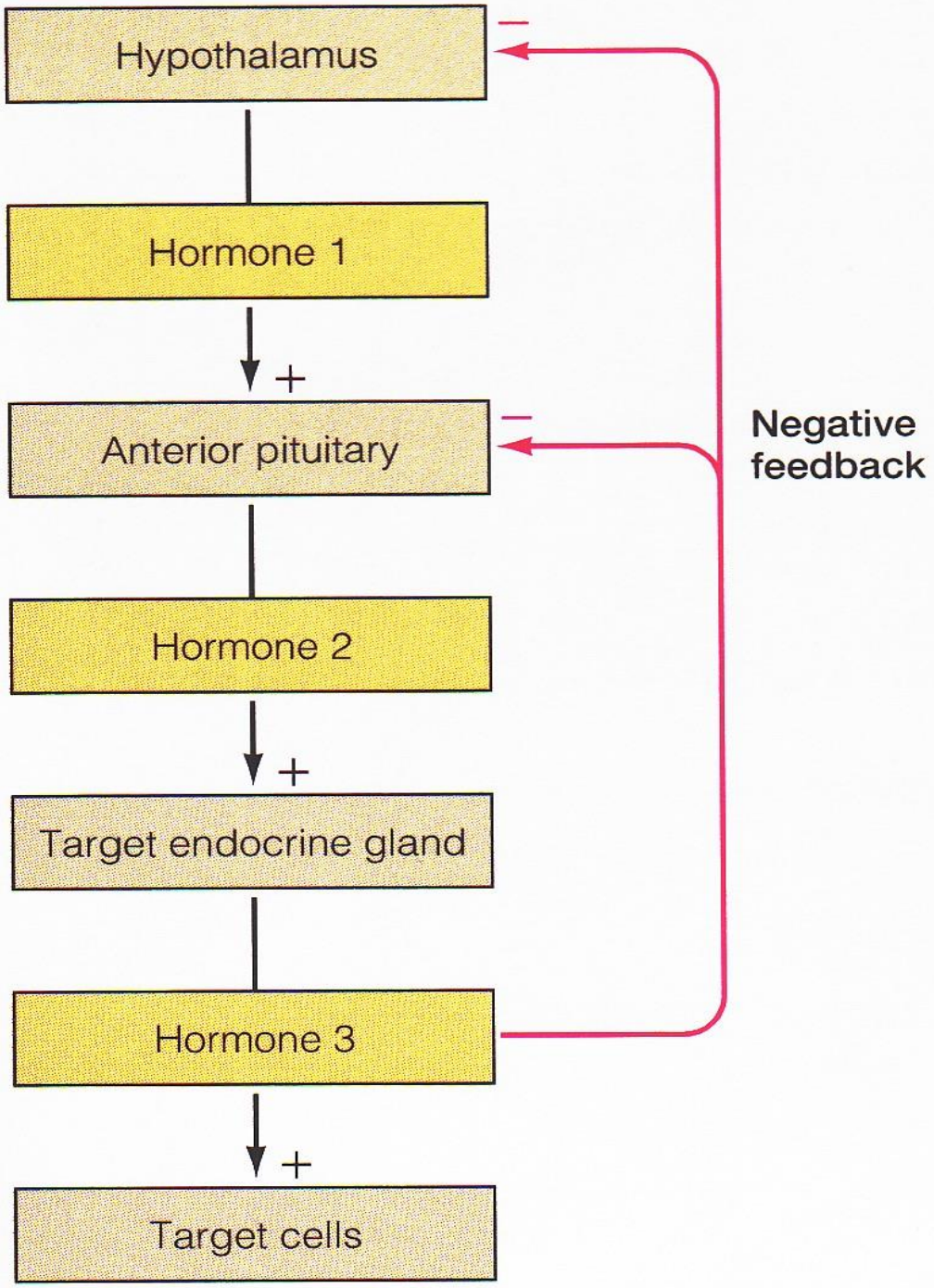
G&H 2016 tab 75-1
G&H 2011 tab 74-1

Anterior Pituitary Metabolic Functions



G&H 2016 fig 76-2
G&H 2011 fig 75-2


Paraventricular nucleus
Supraoptic nucleus
Hypothalamus
Median eminence
Portal system
Infundibulum
Anterior Pituitary
Posterior pituitary
Prolactin
TSH
Thyroid
Mammary gland
ACTH
Adrenal cortex
Growth hormone
Gonadotropins
FSH
LH
Bone
Muscle
Adipose tissue
Ovary
Testis


Hypothalamus
Hormone 1
+
Anterior pituitary
Hormone 2
+
Target endocrine gland
Hormone 3
+
Target cells
−
−
Negative feedback

LS 1991

GH, a Protein Hormone (191 AA)

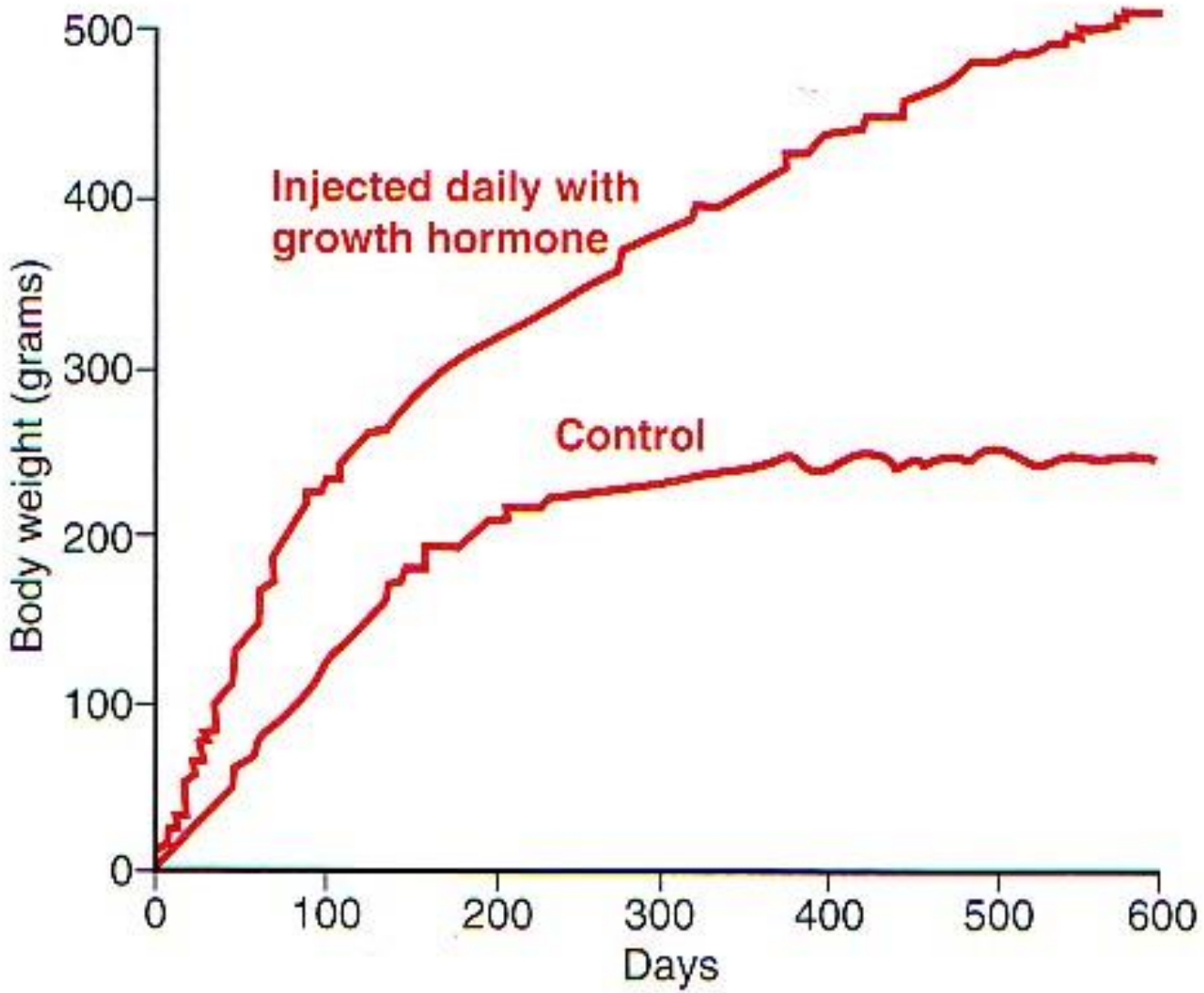


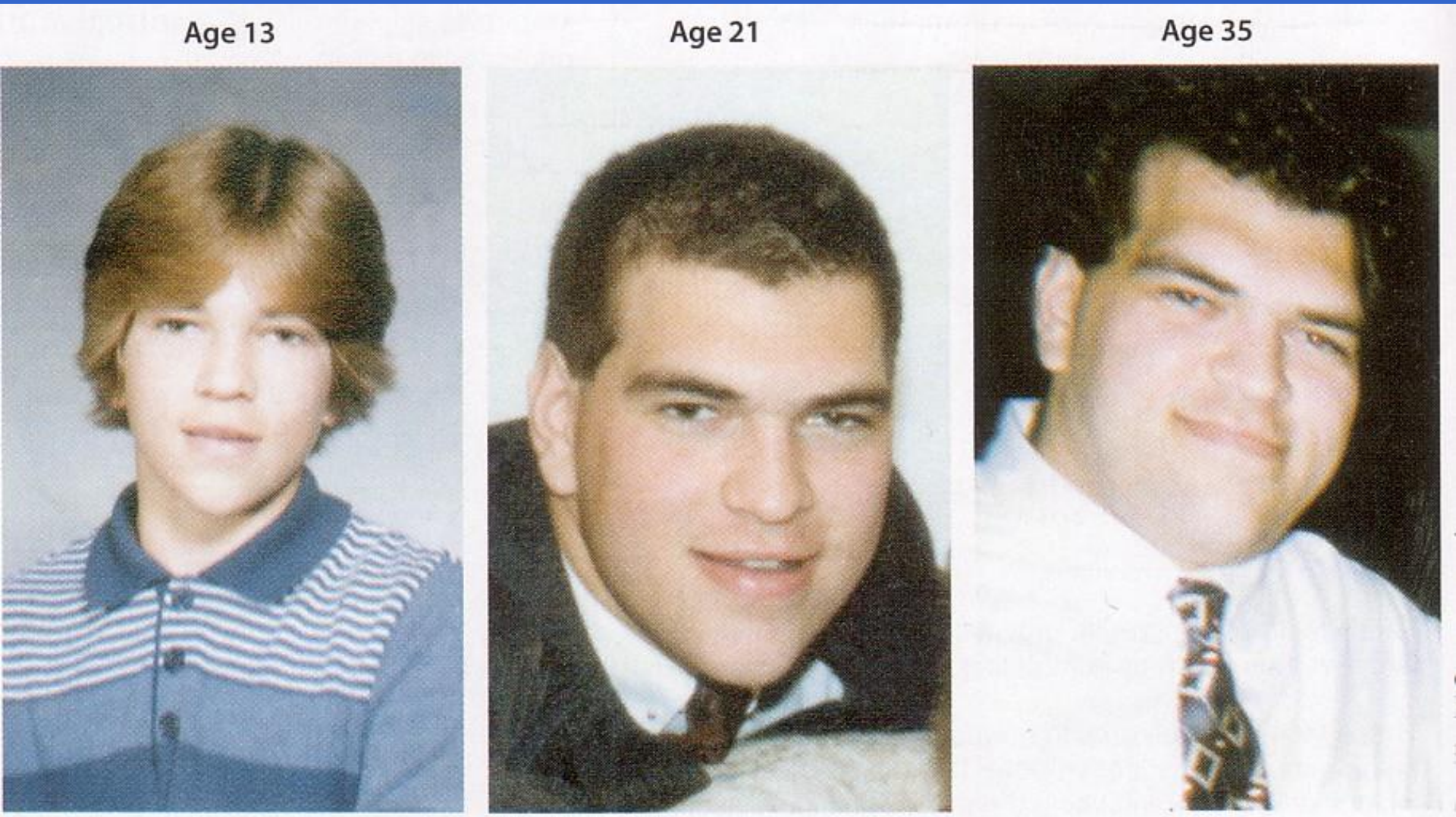
FIGURE 75–5

Comparison of weight gain of a rat injected daily with growth hormone with that of a normal littermate.

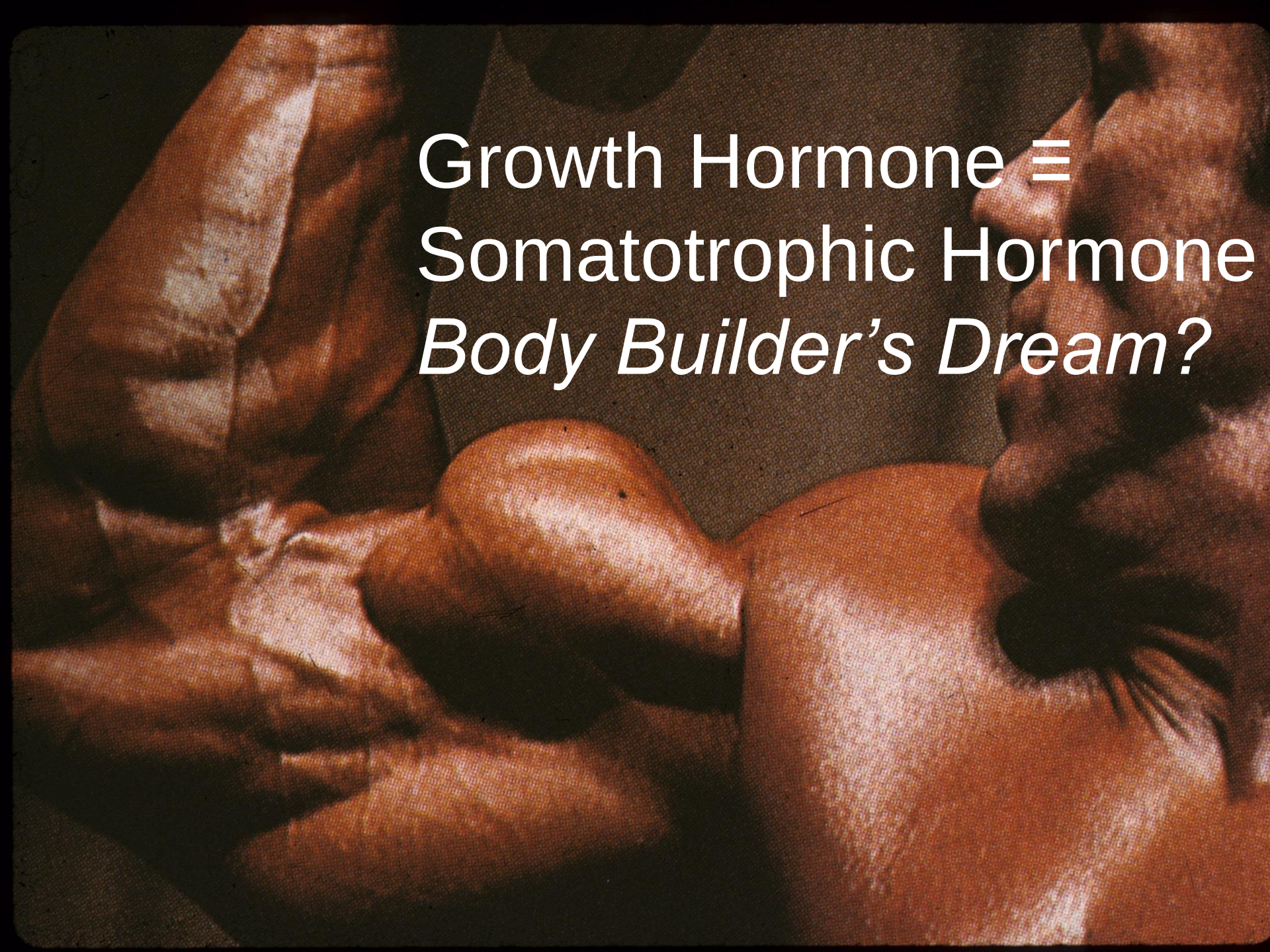
G&H 2016
fig 76-5

LS2 2006

Progression & Development of Acromegaly



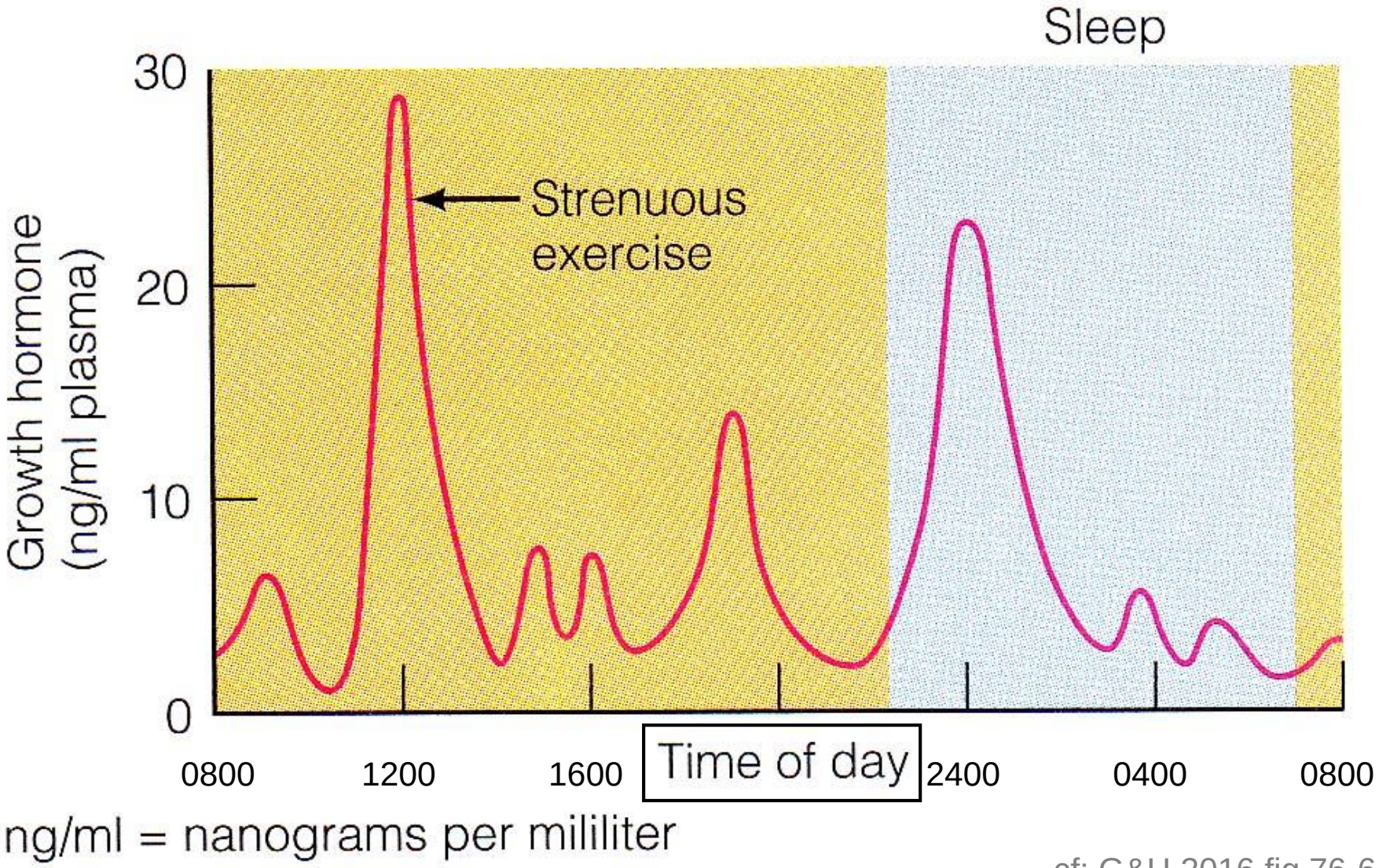
LS 2012 fig 17-11


Growth Hormone ≡
Somatotrophic Hormone
Body Builder's Dream?

GH/STH Effects: Insulin Resistance/Type II Diabetes?

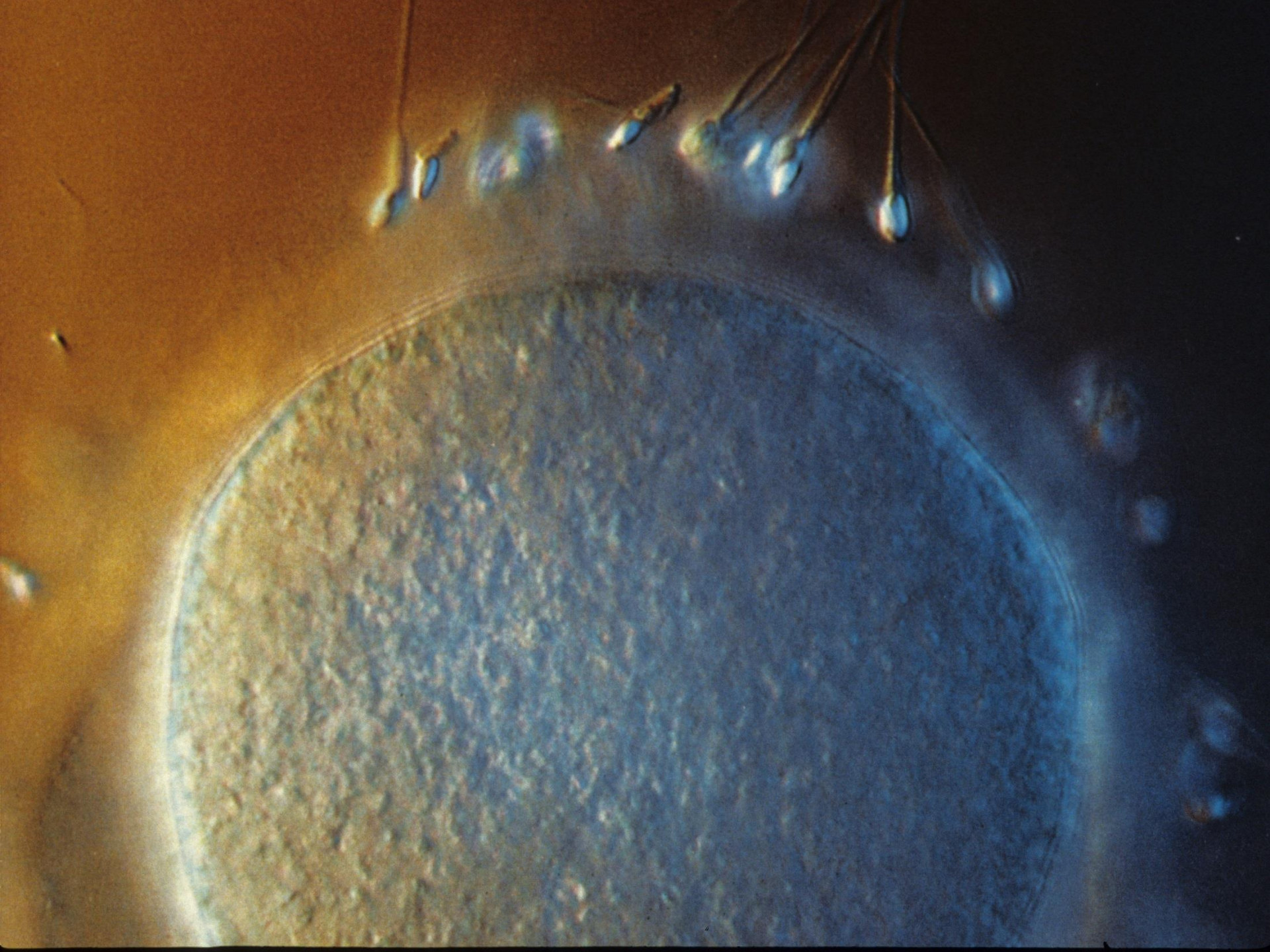
- ↑ Amino acid uptake & protein synthesis
- ↑ Lipolysis & fatty acid mobilization
- ↓ Glucose uptake
  (skeletal muscle & adipocytes)
- ↑ Glucose production
  (liver glycogenolysis)
- ↑ Insulin secretion

Increase GH naturally with exercise & sleep!!



cf: G&H 2016 fig 76-6
G&H 2011 fig 75-6

Questions + Discussion



Biomedicine

Sex allergy: No laughing matter

The phrase "Not tonight, dear" may be a deadly serious matter for women who suffer from an allergy to their husband's seminal fluid, the liquid that carries sperm. In rare cases, such an allergic response can cause death.

The first case of an allergy to human seminal fluid was documented in 1958. Since then, the disorder has been diagnosed in a small number of cases. However, allergists believe the disorder is not readily recognized by gynecologists.

Some women with this condition report a dramatic, whole-body reaction to seminal fluid. Their symptoms include wheezing, vomiting, diarrhea, unconsciousness, or complete circulatory collapse. Other women experience a localized reaction, such as vaginal burning or swelling.

Researcher Jonathan A. Bernstein of the University of Cincinnati College of Medicine and his colleagues decided to study the prevalence of the disorder. They administered a questionnaire to 1,073 women who had reported symptoms consistent with the allergy.

Bernstein's team found that 12 percent of the women they studied met the diagnostic criteria for an allergy to seminal fluid. This result indicates that the disorder is much more common than previously suspected. The team reports its findings in the January ANNALS OF ALLERGY, ASTHMA, & IMMUNOLOGY.

Allergists can treat the condition, the researchers point out. Regular injections of purified seminal proteins can prevent the relationship-stopping symptoms, says Bernstein. — *K.F.*

Semen? G&H 2016 p 1024
G&H 2011 p 976

- **~60% seminal vesicle fluid - mucoid, PGE_2, fructose, fibrinogen**
- **~30% prostatic fluid - $NaHCO_3$, clotting enzyme, Ca^{2+}, profibrinolysin**
- **~10% sperm + vas deferens fluid**

Mom's eggs execute Dad's mitochondria

In "Hamlet," Rosencrantz and Guildenstern deliver a letter to the rulers of England that carries the ill-fated duo's own death sentence. Perhaps Shakespeare knew a bit about reproductive biology.

Scientists have now found that during a sperm's creation, its mitochondria—energy-producing units that power all cells—acquire molecular tags that mark them for destruction once the sperm fertilizes an egg. This death sentence, a protein called ubiquitin, may explain why mammals inherit the DNA within mitochondria only from their mothers, a biological curiosity geneticists have used to trace human evolution (SN: 2/6/99, p. 88). The finding may also have implications

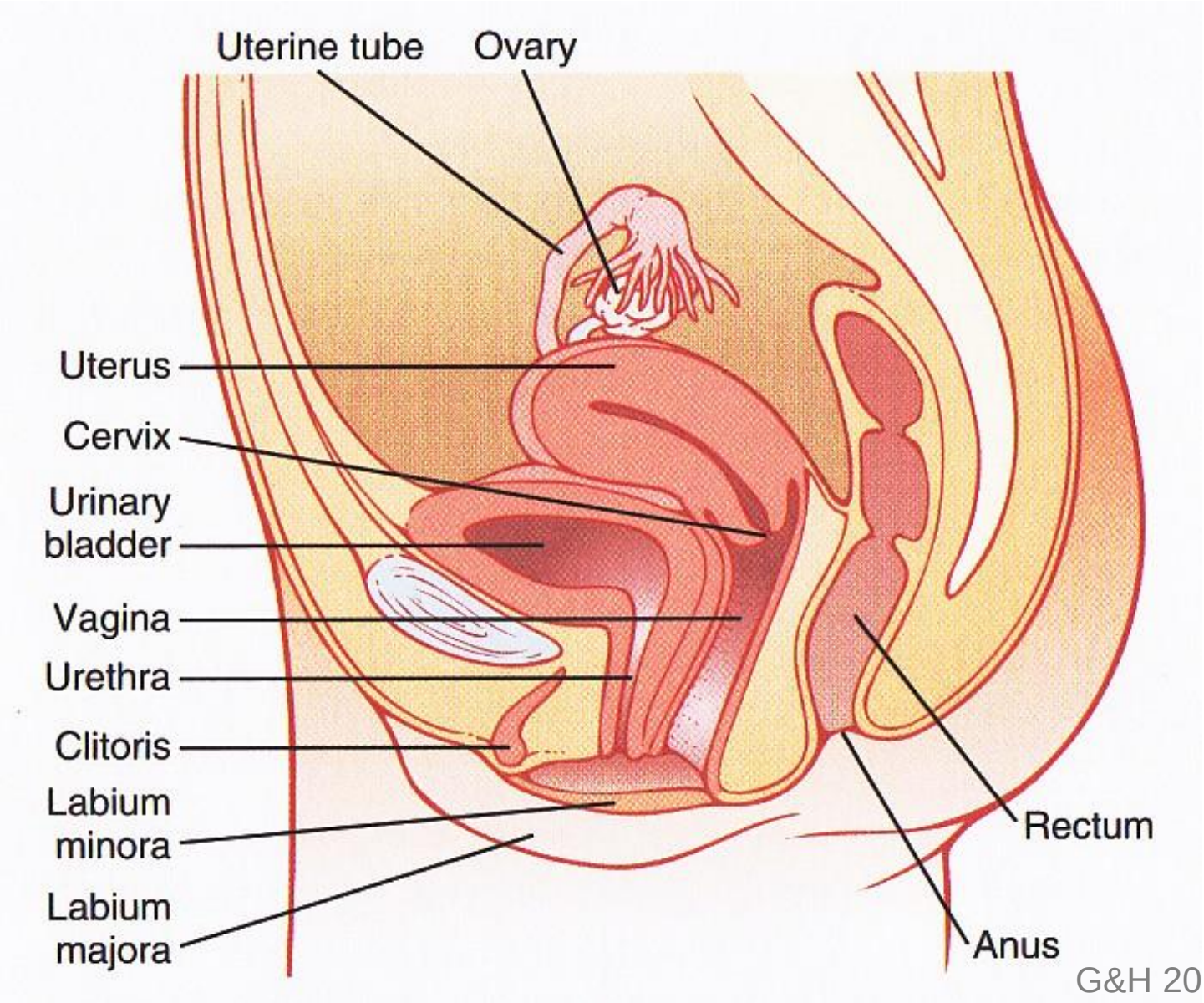
species mitochondrial inheritance. Sperm mitochondria sometimes avoid destruction when two different species of mice mate, and Schatten's team has shown this also holds true in cattle. It's hard to understand how an egg distinguishes between paternal mitochondria of closely related species, says Schon.

When paternal mitochondria escape destruction in normal mating, the resulting embryo may suffer. Schatten notes that a colleague has found sperm mitochondria in some defective embryos from infertility clinics.

The success of cloning may depend on an egg's ability to destroy foreign mitochondria. In the technique used to create

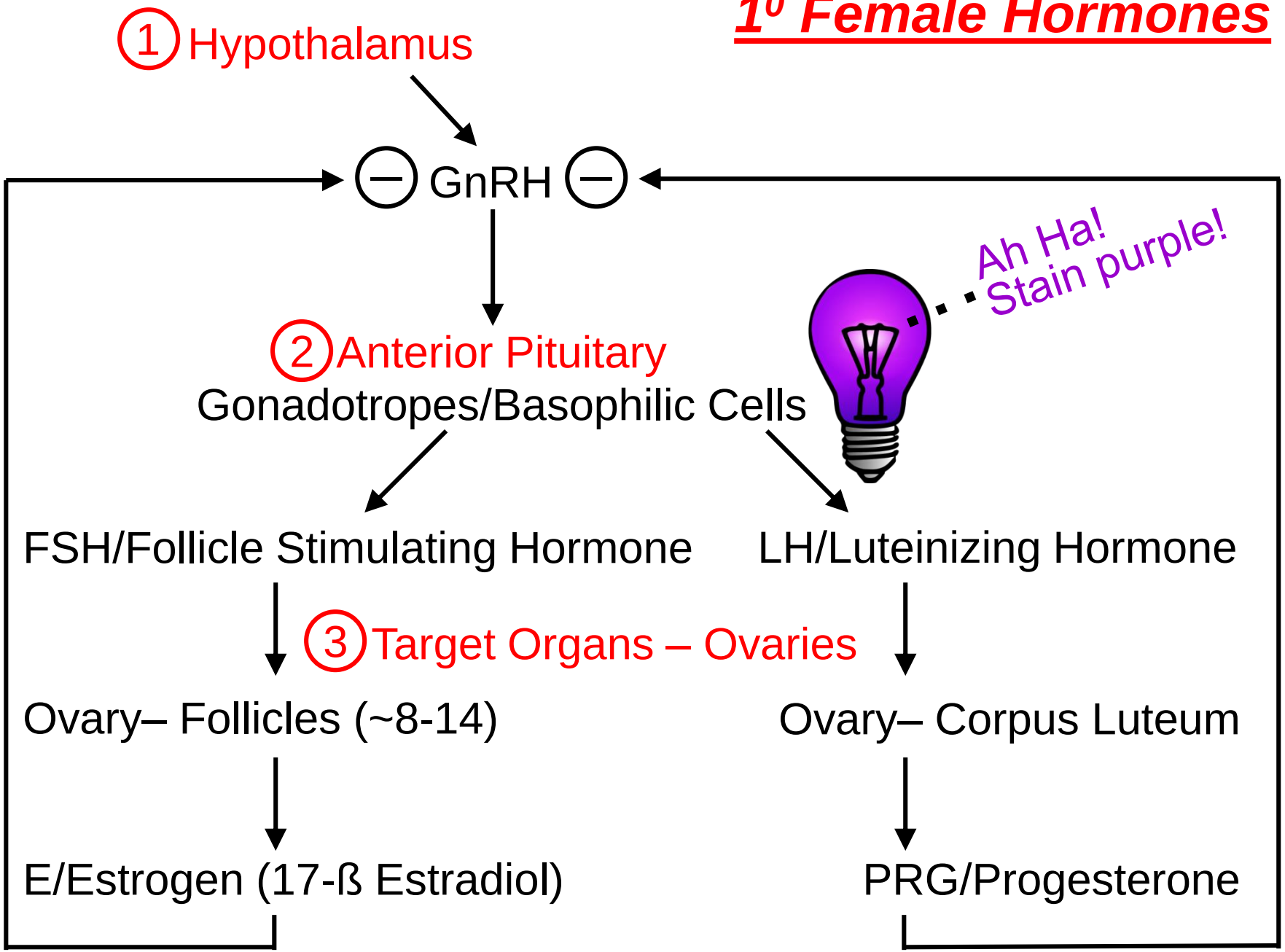
May Day! May Day! We're doomed!!

Female Reproductive System



G&H 2016 fig 82-1
G&H 2011 fig 81-1

1^0 Female Hormones

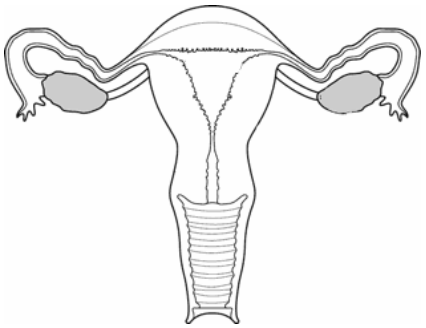


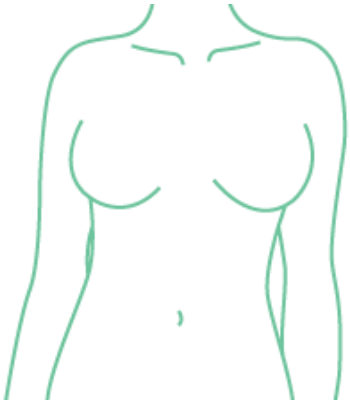
What Do Estrogen & Progesterone Do?

Estrogen – E

Growth & Development of:

1. Ovaries, fallopian tubes, uterus, vagina, external genitalia
2. Breasts stroma, ductile systems, adipocytes
3. Skeleton → osteoblastic activity



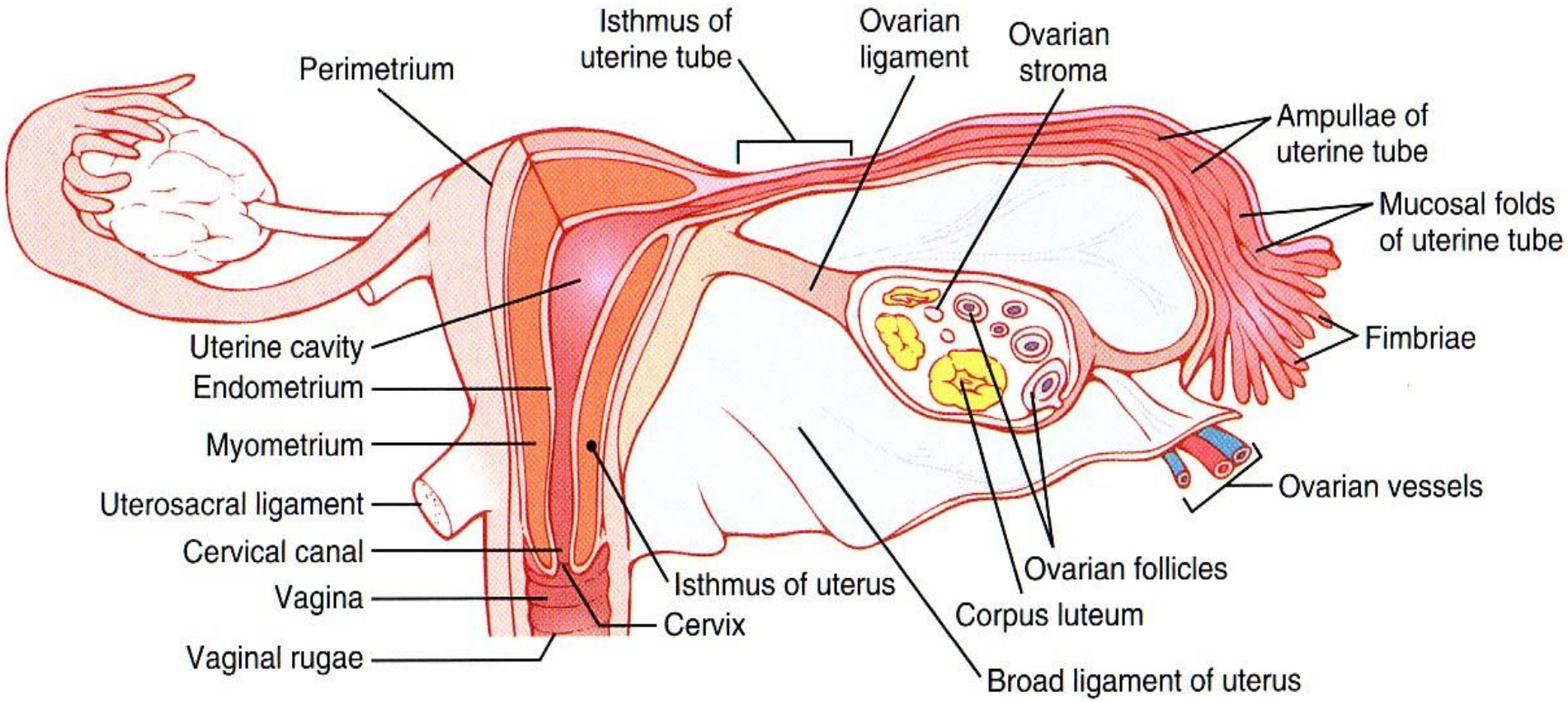


Progesterone – PRG

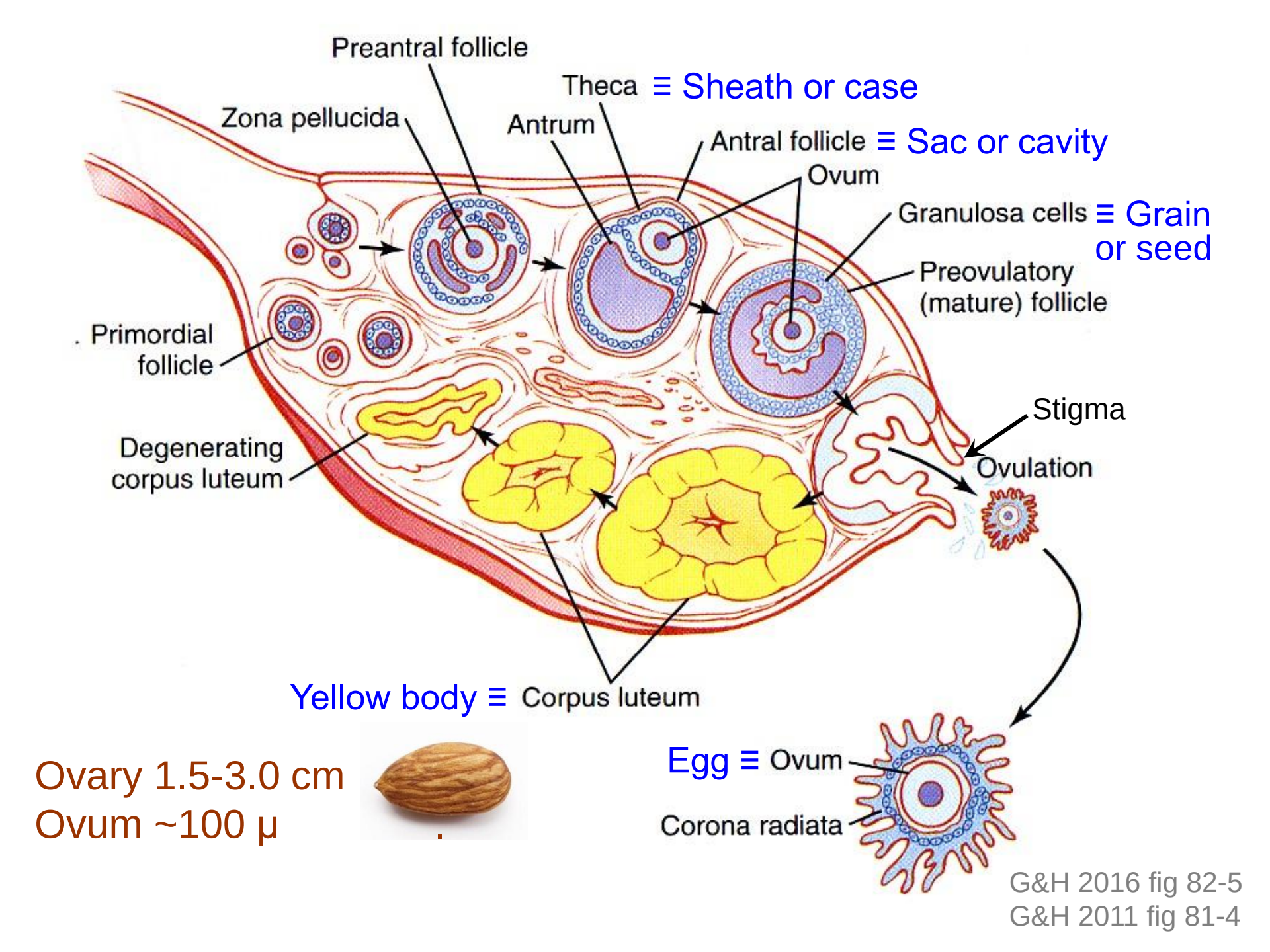
Promotes Progestation!

1. Uterus: endometrium Secretory Δ during last ½ of monthly cycle
2. Breasts: ↑ lobules & alveoli
3. Uterus: smooth muscle ↓ excitability & motility
4. Hypothalamus: ↑ body temp ~ 0.5 ^{0}F

Uterus, Ovary & Uterine/Fallopian Tube

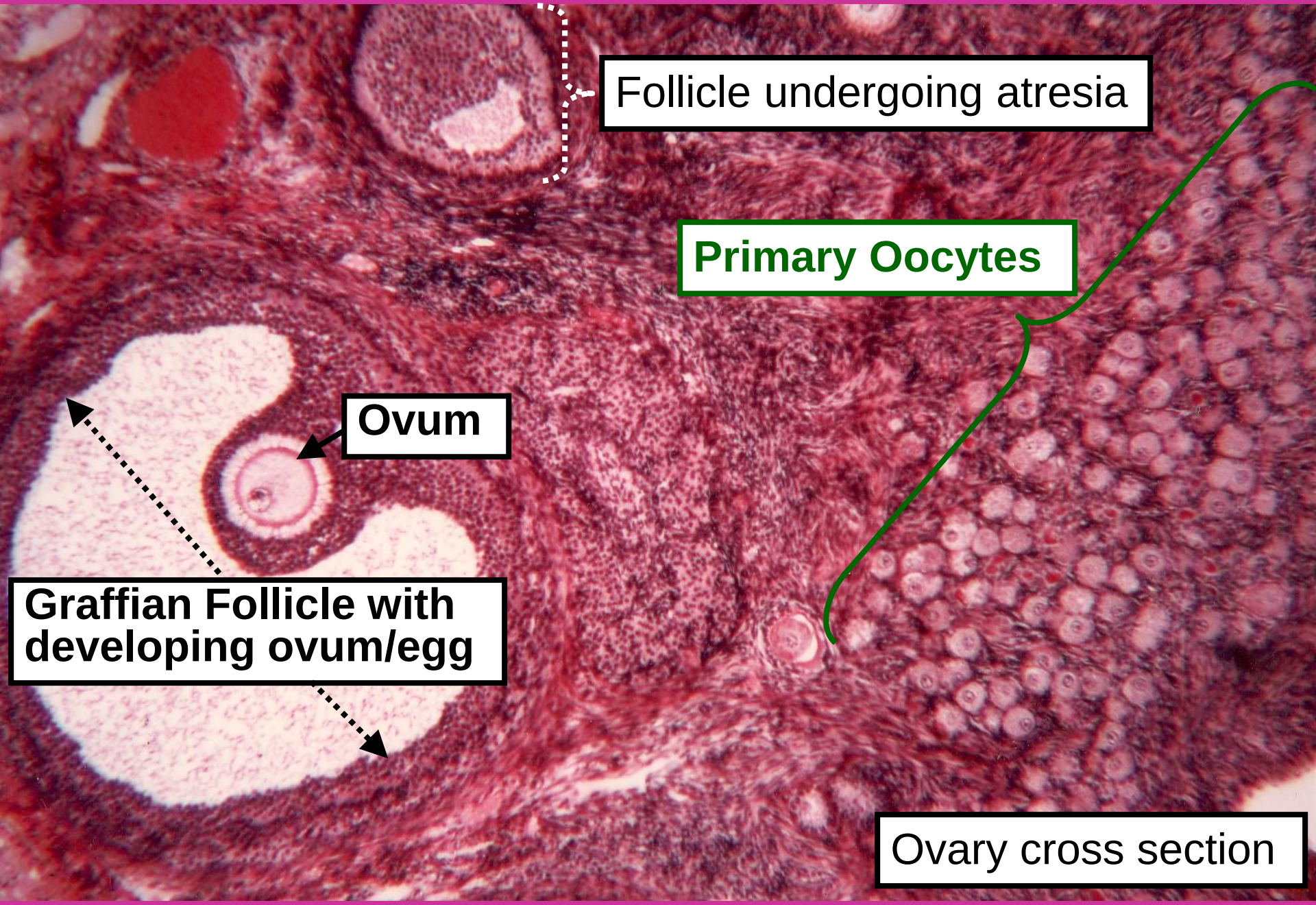


G&H 2016 fig 82-2
G&H 2011 fig 81-2



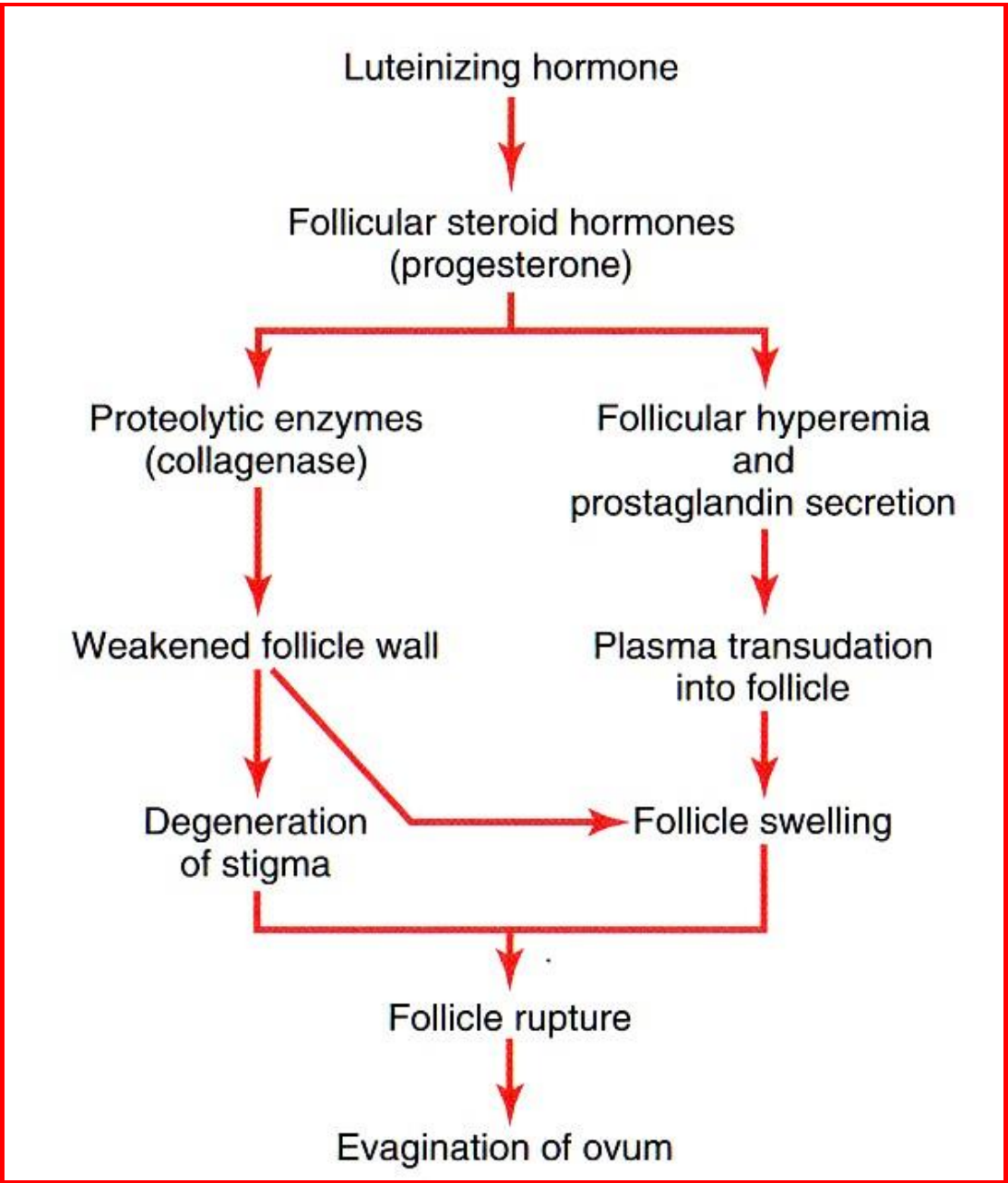
Ovary 1.5-3.0 cm
Ovum ~100 μ

G&H 2016 fig 82-5
G&H 2011 fig 81-4

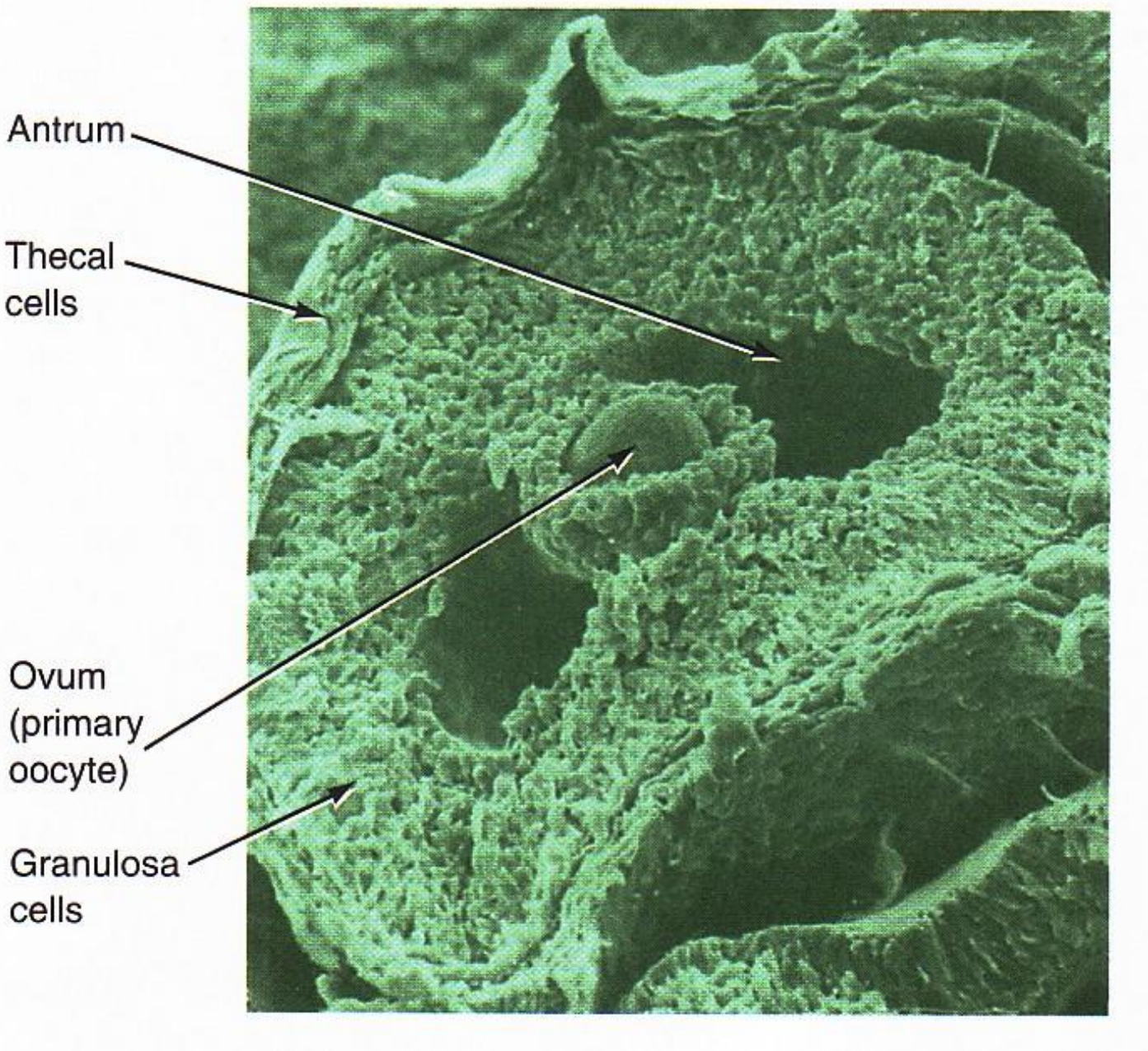


H Howard 1984

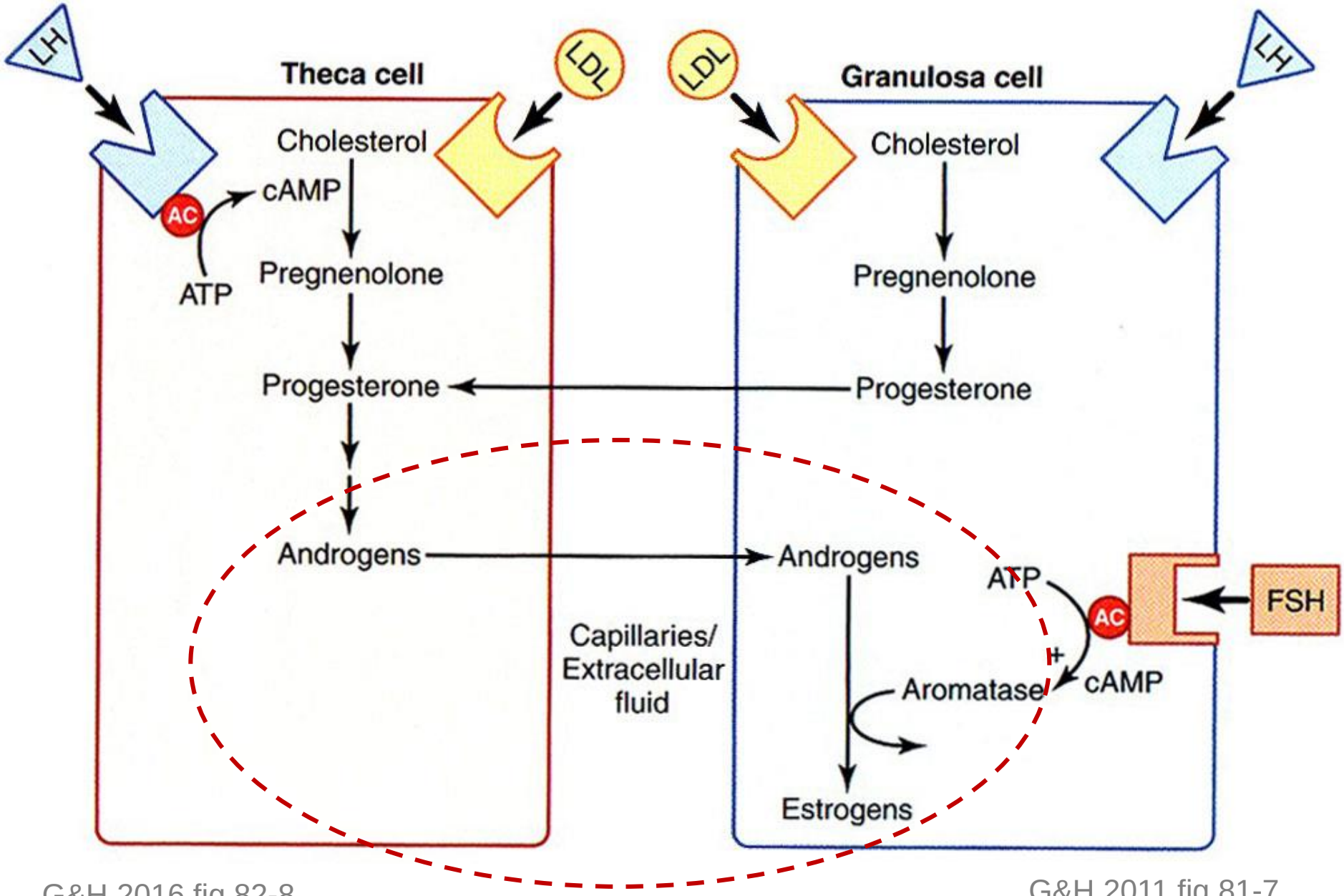
Proposed Ovulation Mechanism



G&H 2016 fig 82-6
G&H 2011 fig 81-5

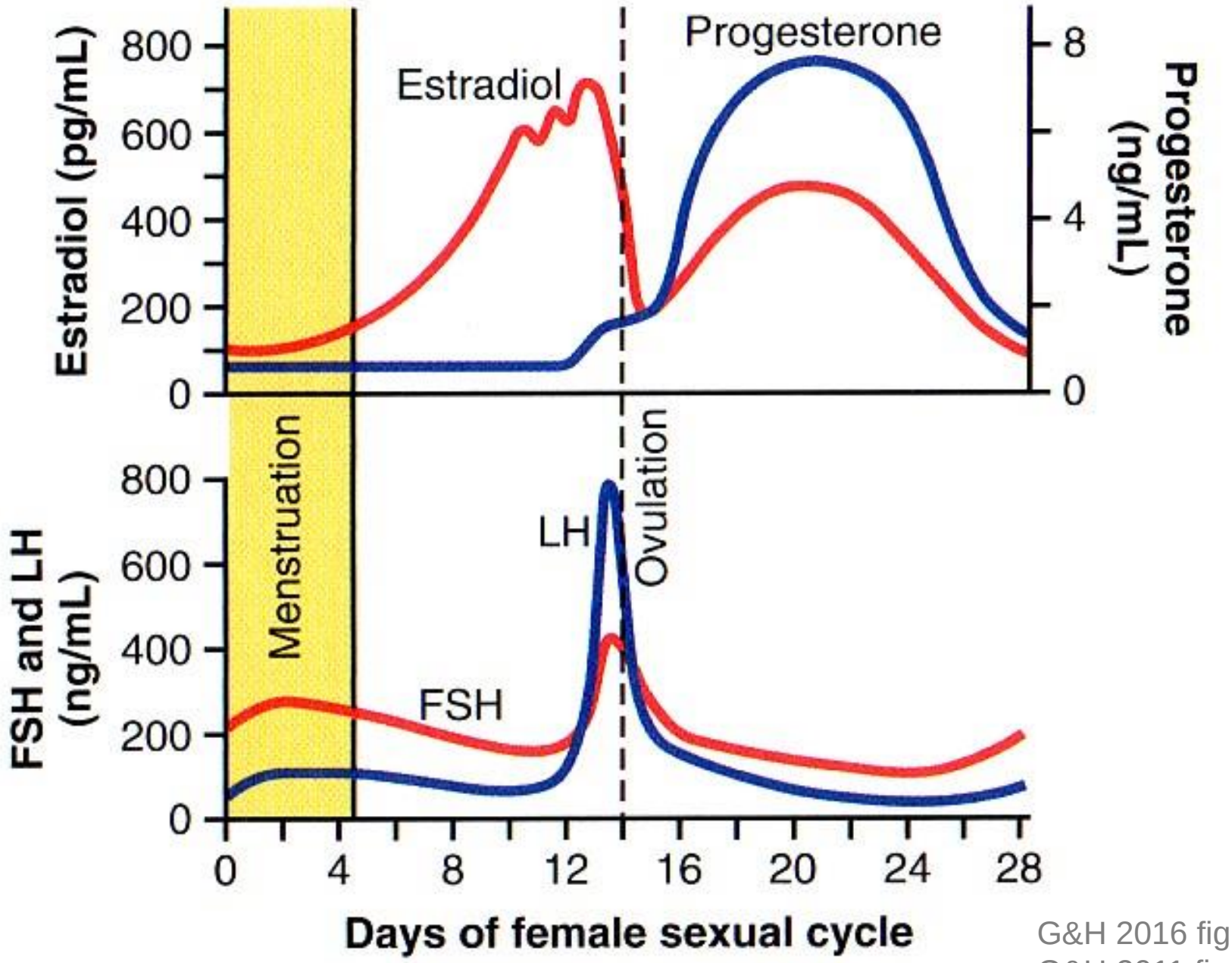

Antrum
Thecal cells
Ovum (primary oocyte)
Granulosa cells

Estrogen Production: Theca & Granulosa Cell Interaction



G&H 2016 fig 82-8

G&H 2011 fig 81-7



G&H 2016 fig 82-4
G&H 2011 fig 81-3

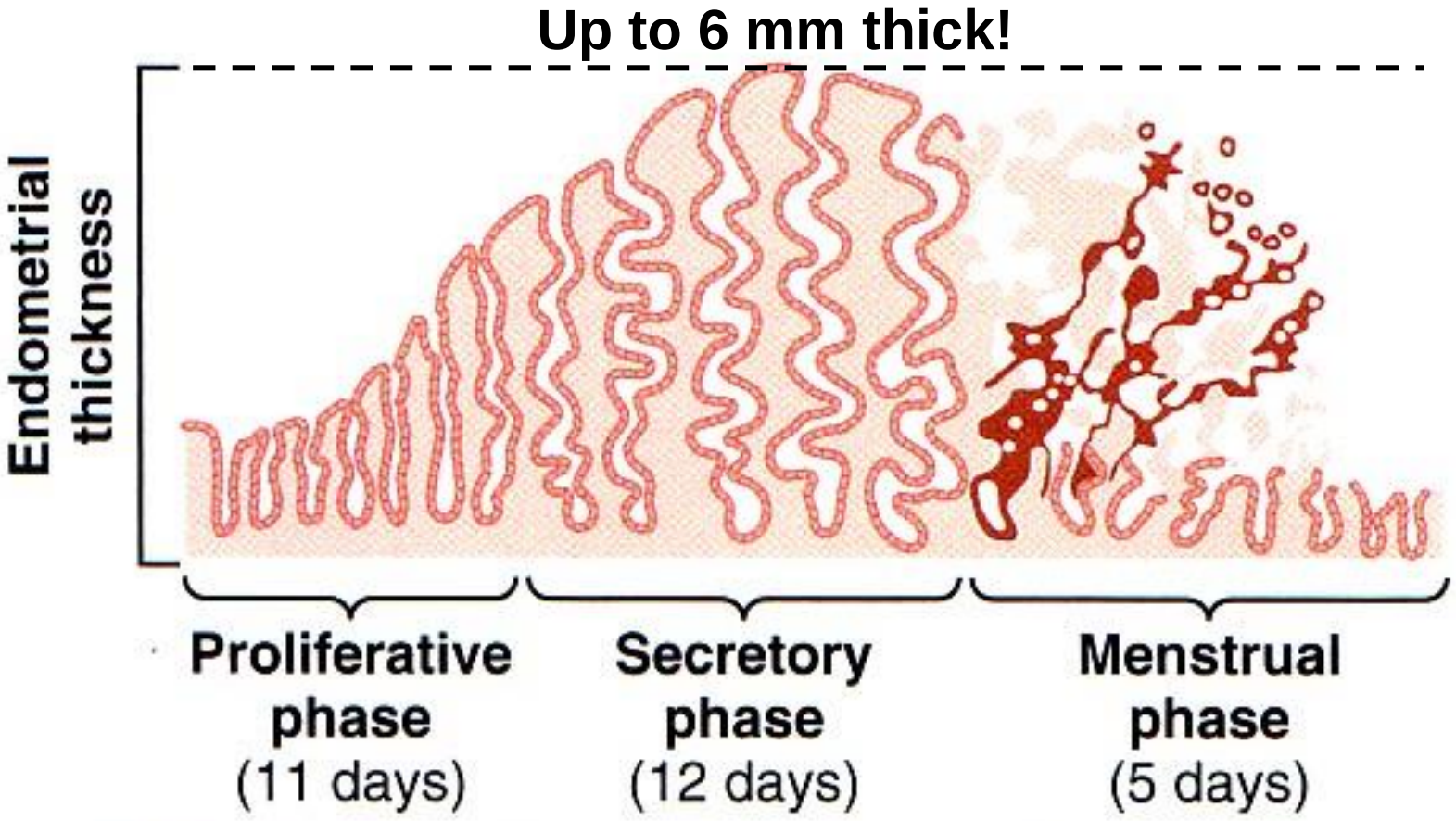
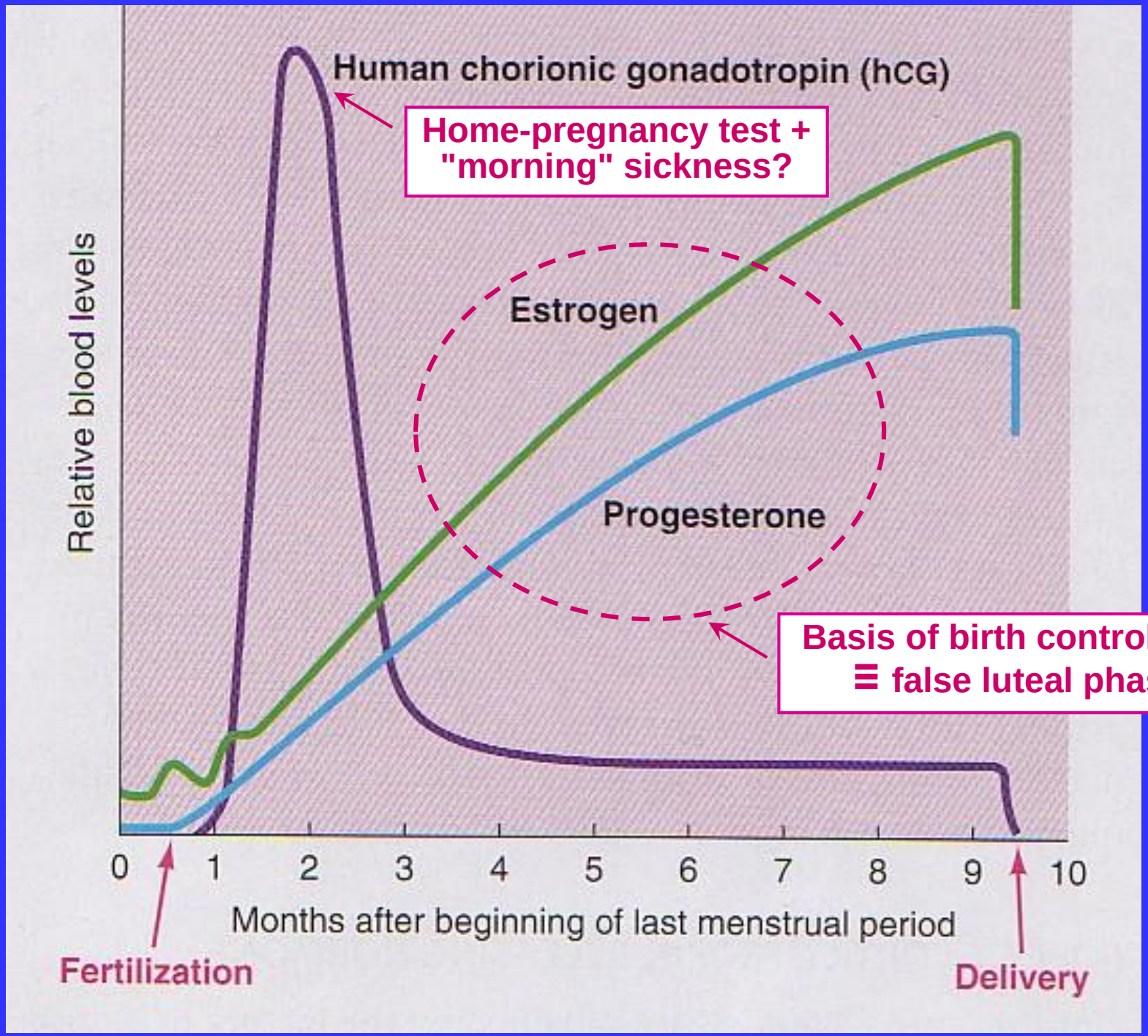
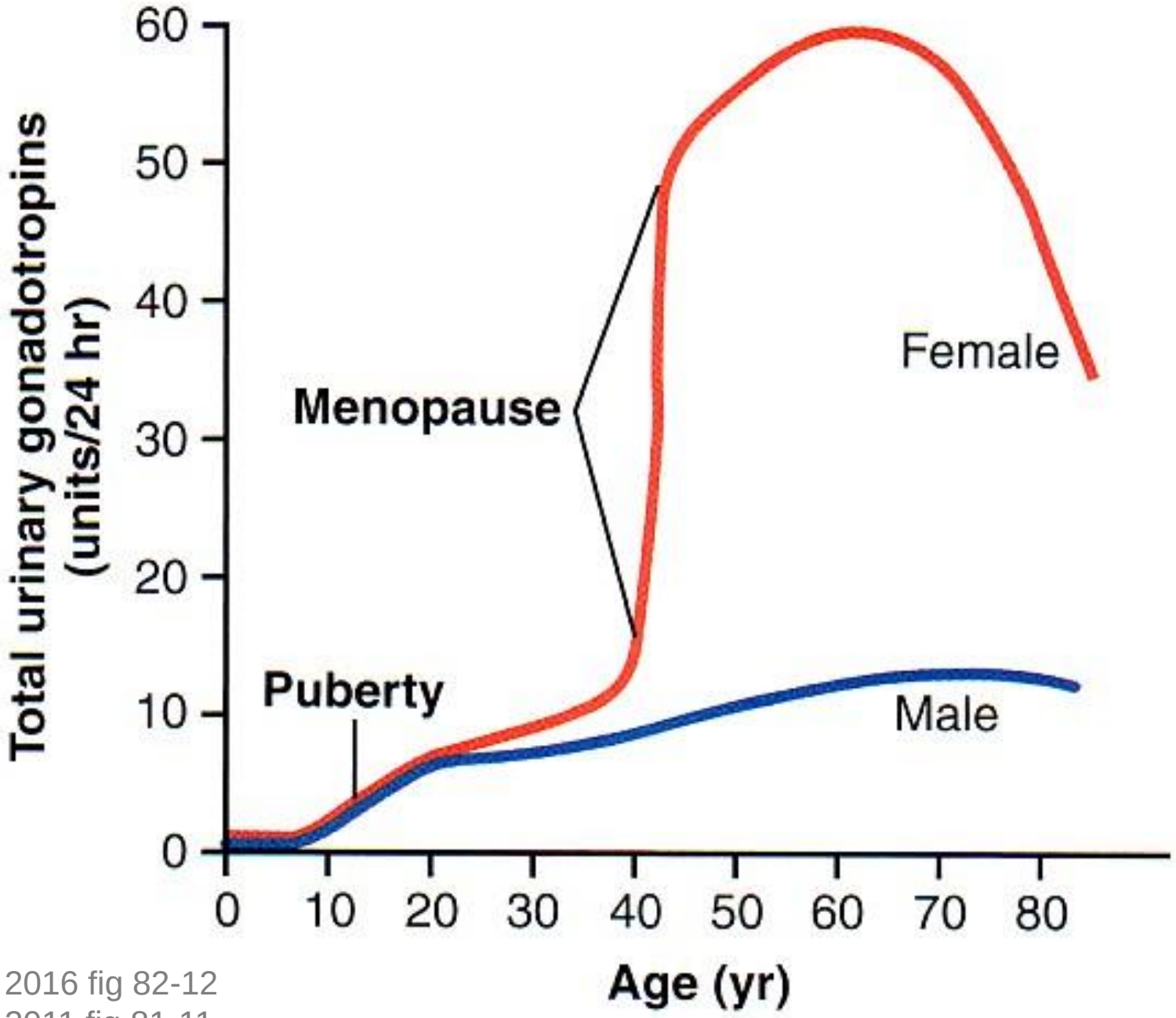


Figure 81-8 Phases of endometrial growth and menstruation during each monthly female sexual cycle.

G&H 2016 fig 82-9
G&H 2011 fig 81-8


Human chorionic gonadotropin (hCG)
Home-pregnancy test +
"morning" sickness?
Estrogen
Progesterone
Basis of birth control pills
≡ false luteal phase
Relative blood levels
0
1
2
3
4
5
6
7
8
9
10
Months after beginning of last menstrual period
Fertilization
Delivery

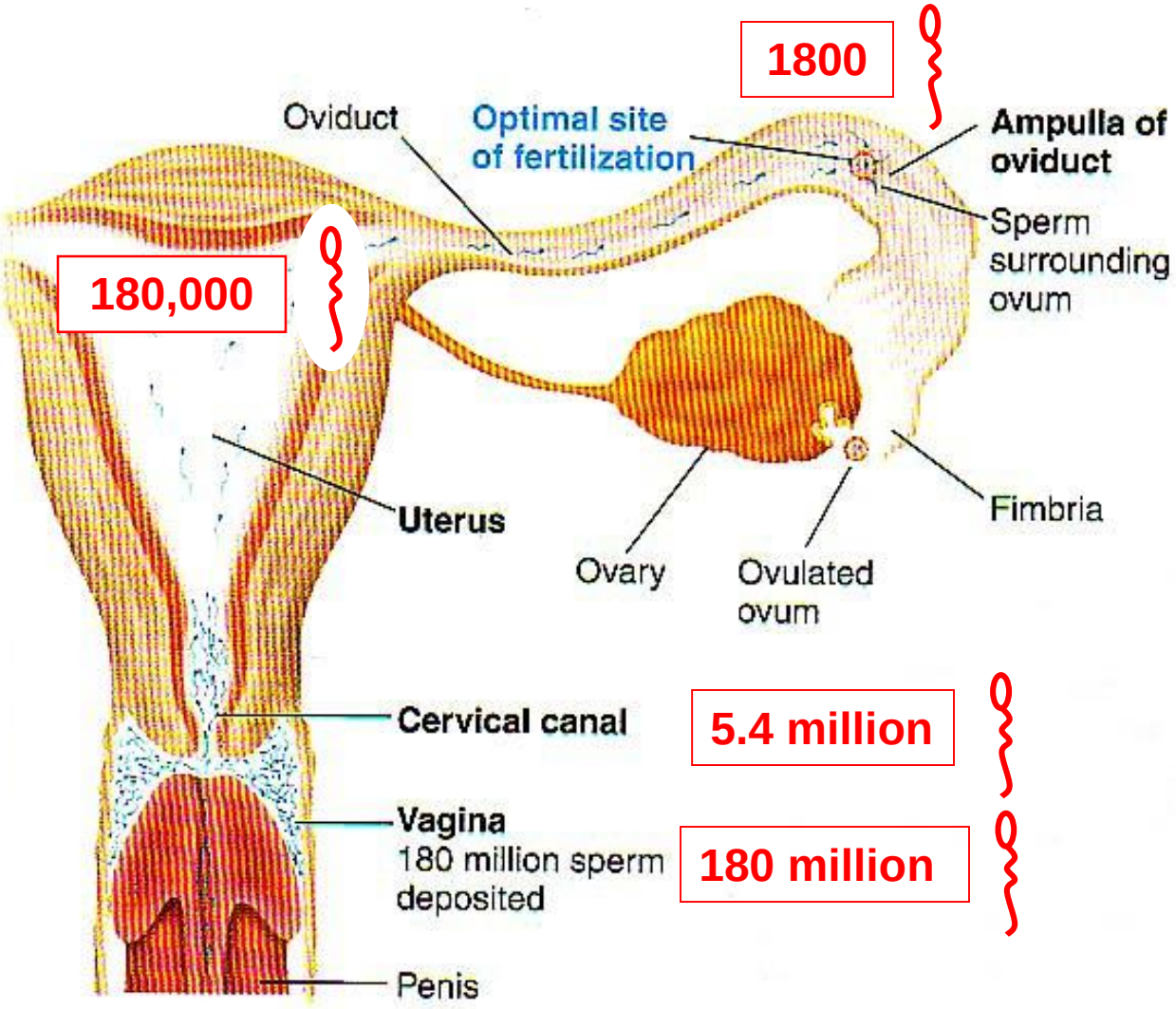
LS2
2008



G&H 2016 fig 82-12
G&H 2011 fig 81-11

Location	Time of appearance (min after ejaculation)	Percent of ejaculated sperm*
Fertilization site (upper third of oviduct)	30–60	0.001
Uterus	10–20	0.1
Cervical canal	1–3	3
Vagina	0	100

*Based on data from animals.
Sperm and ovum enlarged.

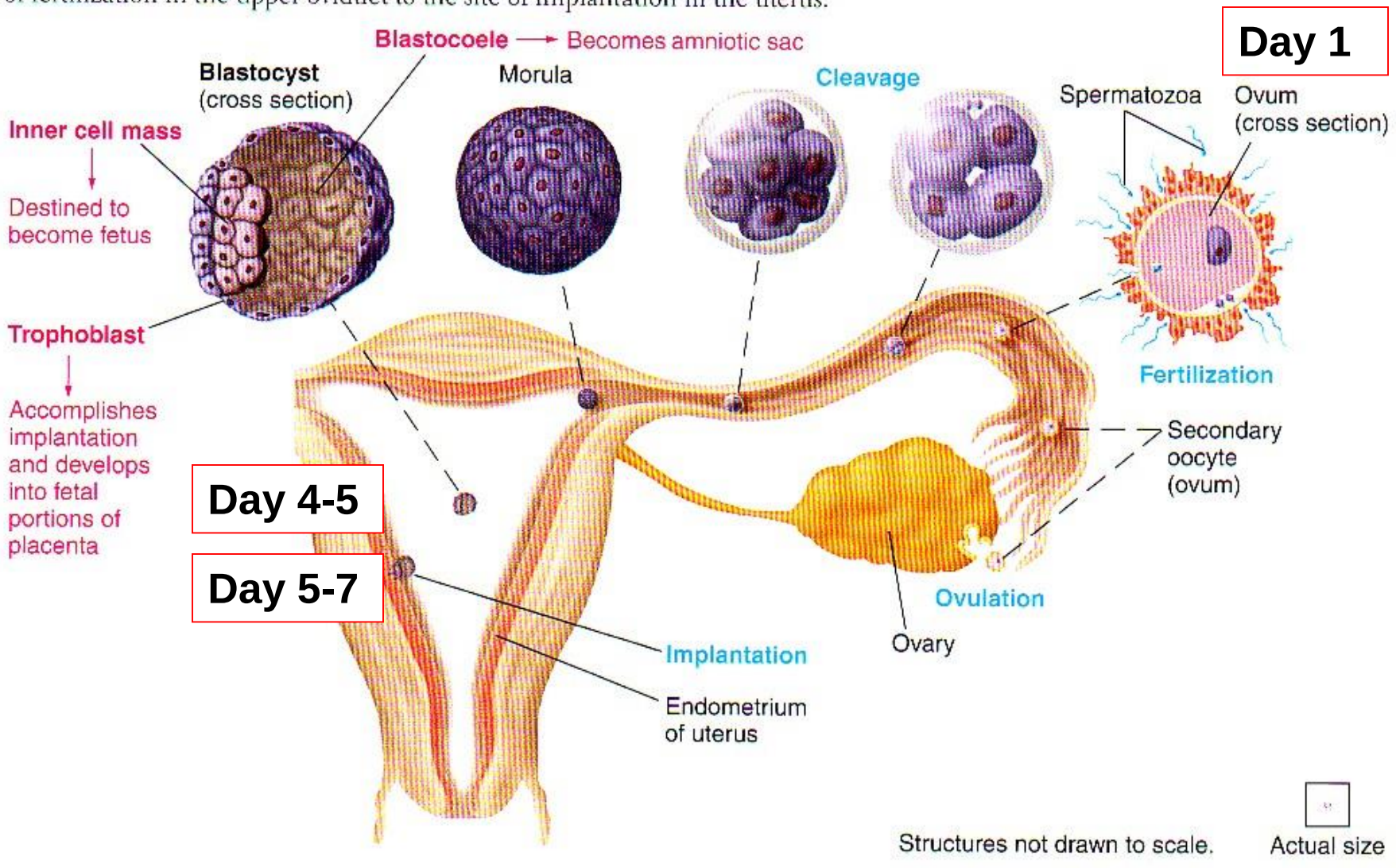


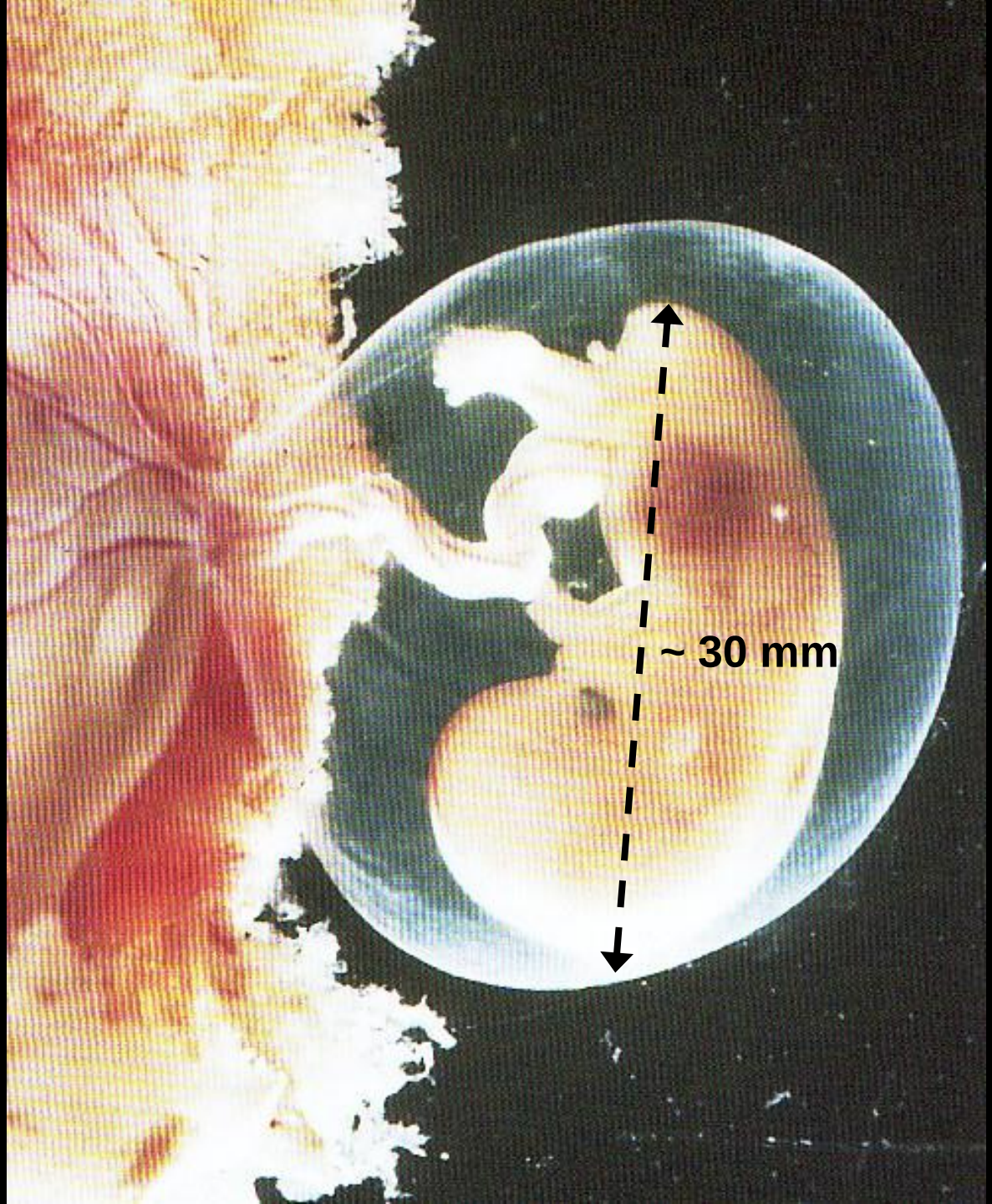
● FIGURE 20-20
Ovum and sperm transport to the site of fertilization

● FIGURE 20-23

Early stages of development from fertilization to implantation

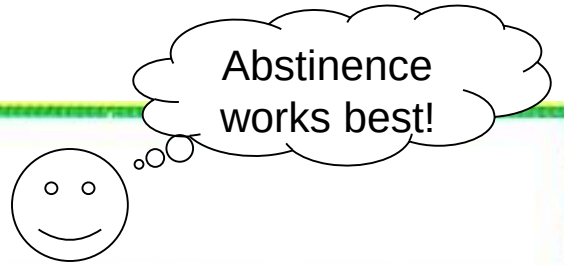
Note that the fertilized ovum progressively divides and differentiates into a blastocyst as it moves from the site of fertilization in the upper oviduct to the site of implantation in the uterus.





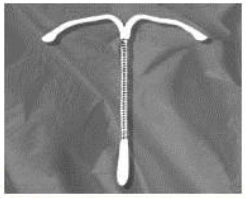
~ 56 days

LS1 2007



Average Failure Rate of Various Contraceptive Techniques

Contraceptive Method	Average Failure Rate (annual pregnancies/ 100 women)
None	90
Natural (rhythm) methods	20–30
Coitus interruptus	23
Chemical contraceptives	20
Barrier methods	10–15
Oral contraceptives	2–2.5
Implanted contraceptives	1
Intrauterine device	4

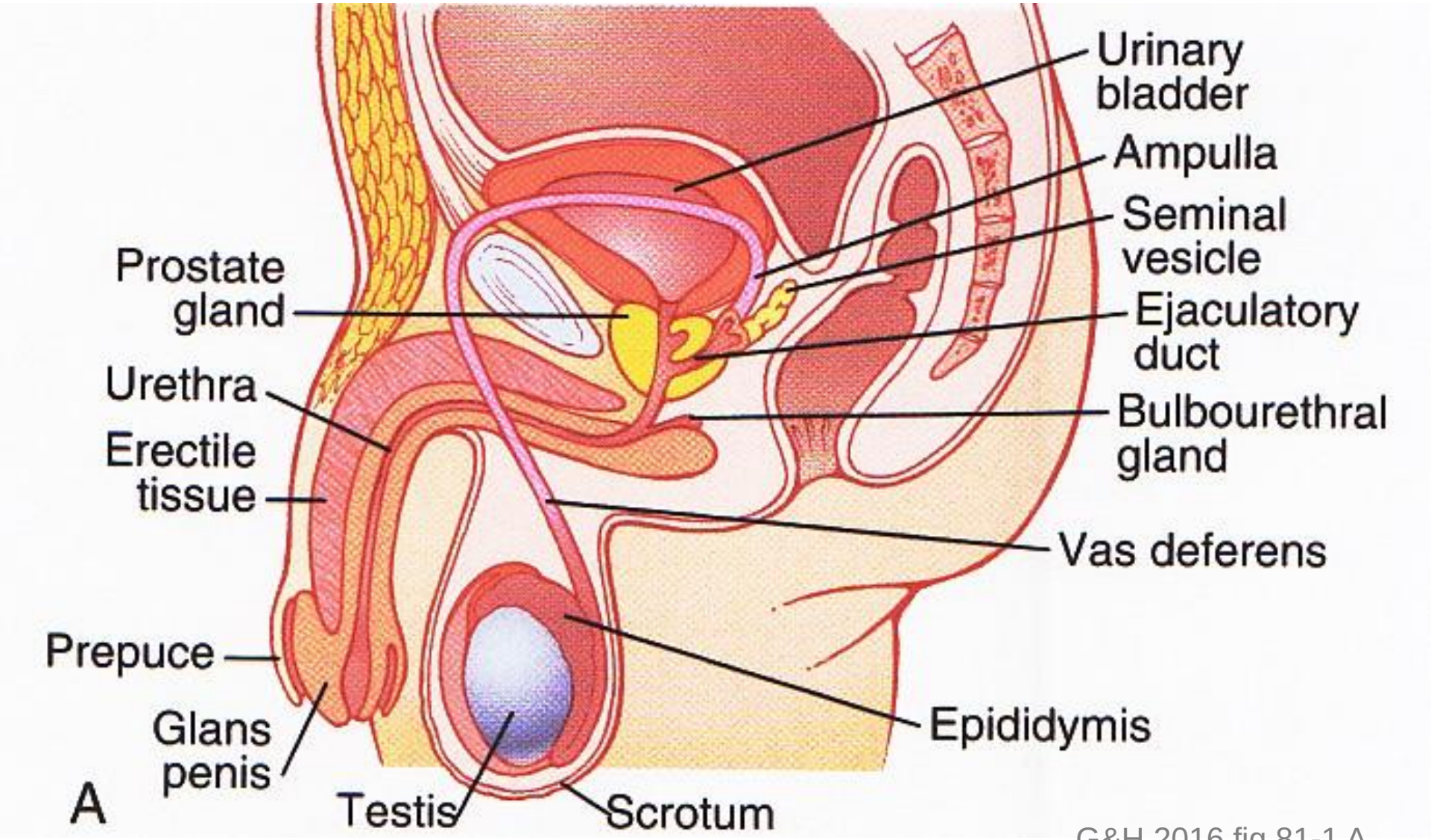


Important Facts

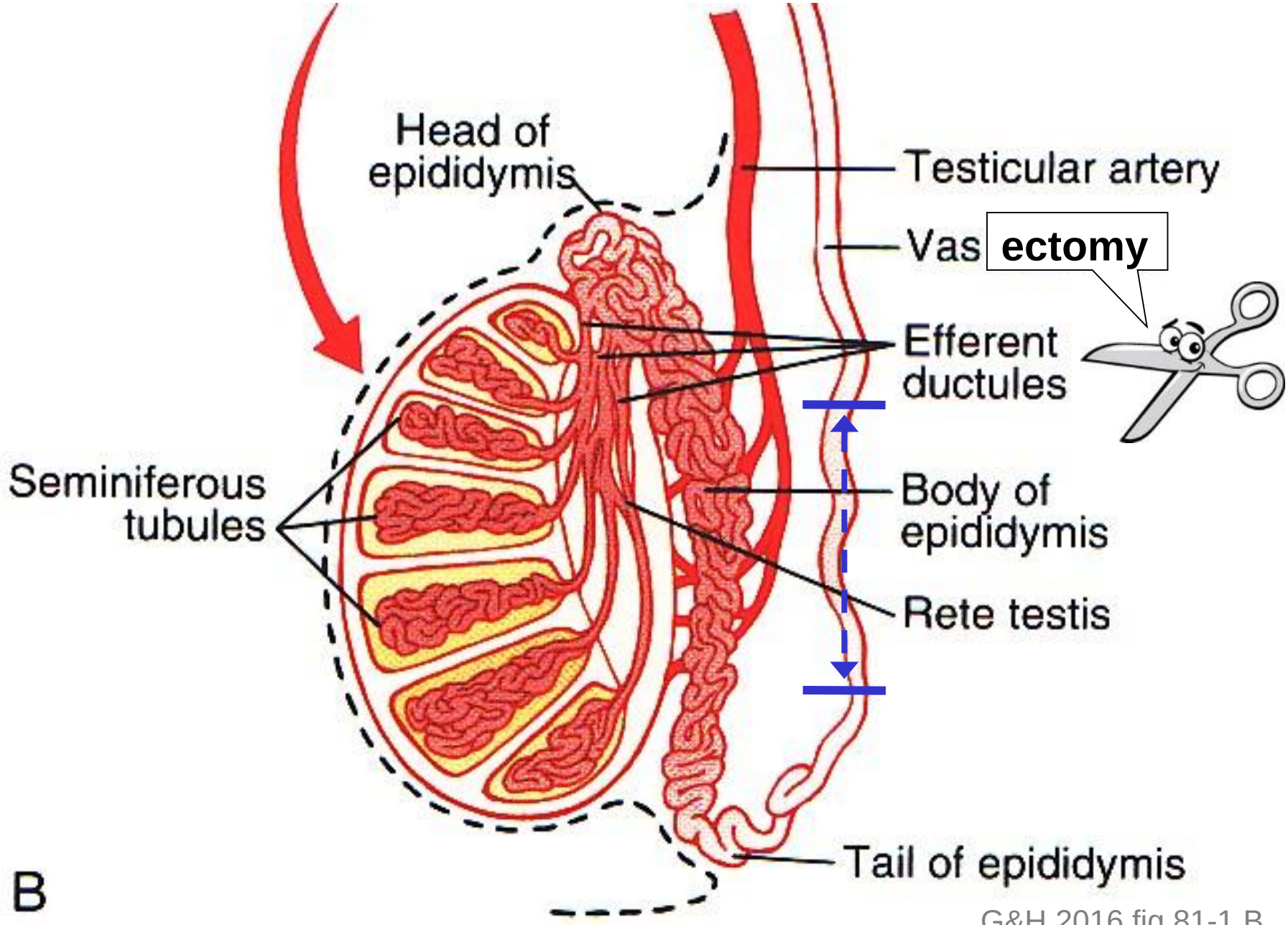
- 4 Million births in the US per yr
- 200 abortions per 1000 live births
- 664,000 legal abortions reported in 2013
- Sperm survive for 48 hr to 5 d in female reproductive tract
- Eggs start to disintegrate 12-24 hr > ovulation
- Ovulation varies & may be tough to predict…

http://www.cdc.gov/nchs/fastats/births.htm
http://www.who.int/reproductivehealth/en/
https://kinseyinstitute.org/research/index.php

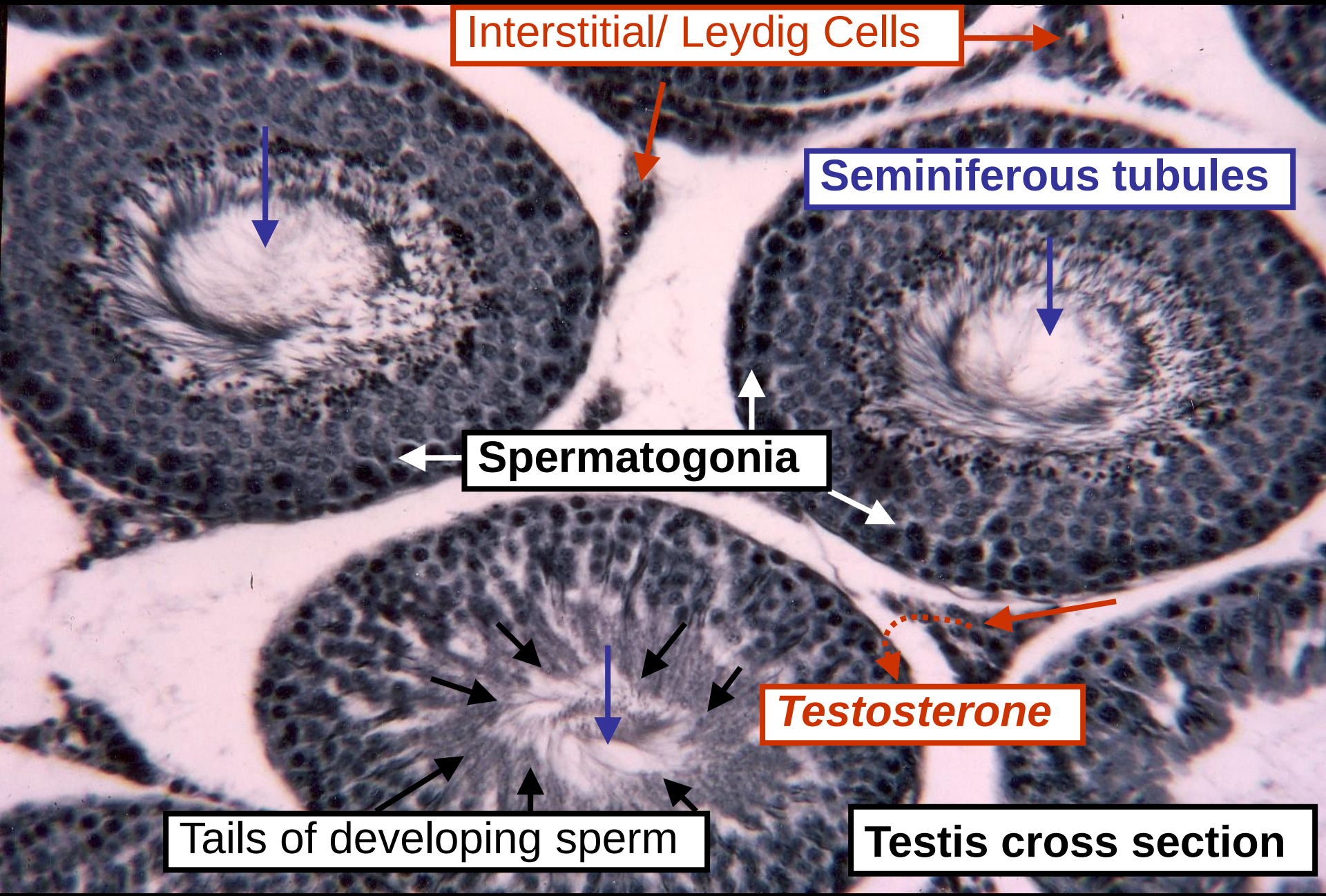
Male Reproductive System



G&H 2016 fig 81-1 A
G&H 2011 fig 80-1 A



G&H 2016 fig 81-1 B
G&H 2011 fig 80-1 B



H Howard 1984

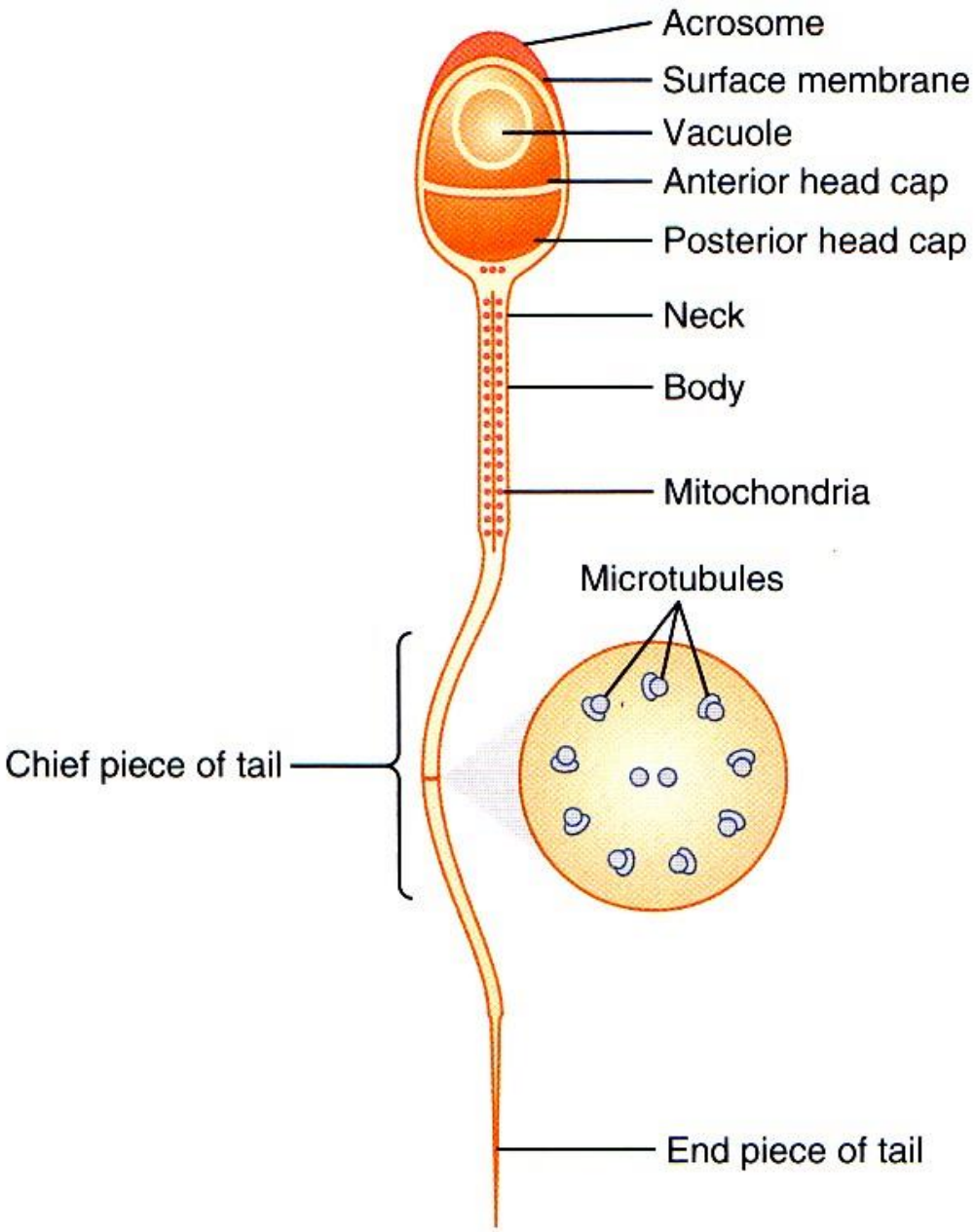


Figure 80-4 Structure of the human spermatozoon.

G&H 2016 fig 81-4
G&H 2011 fig 80-4

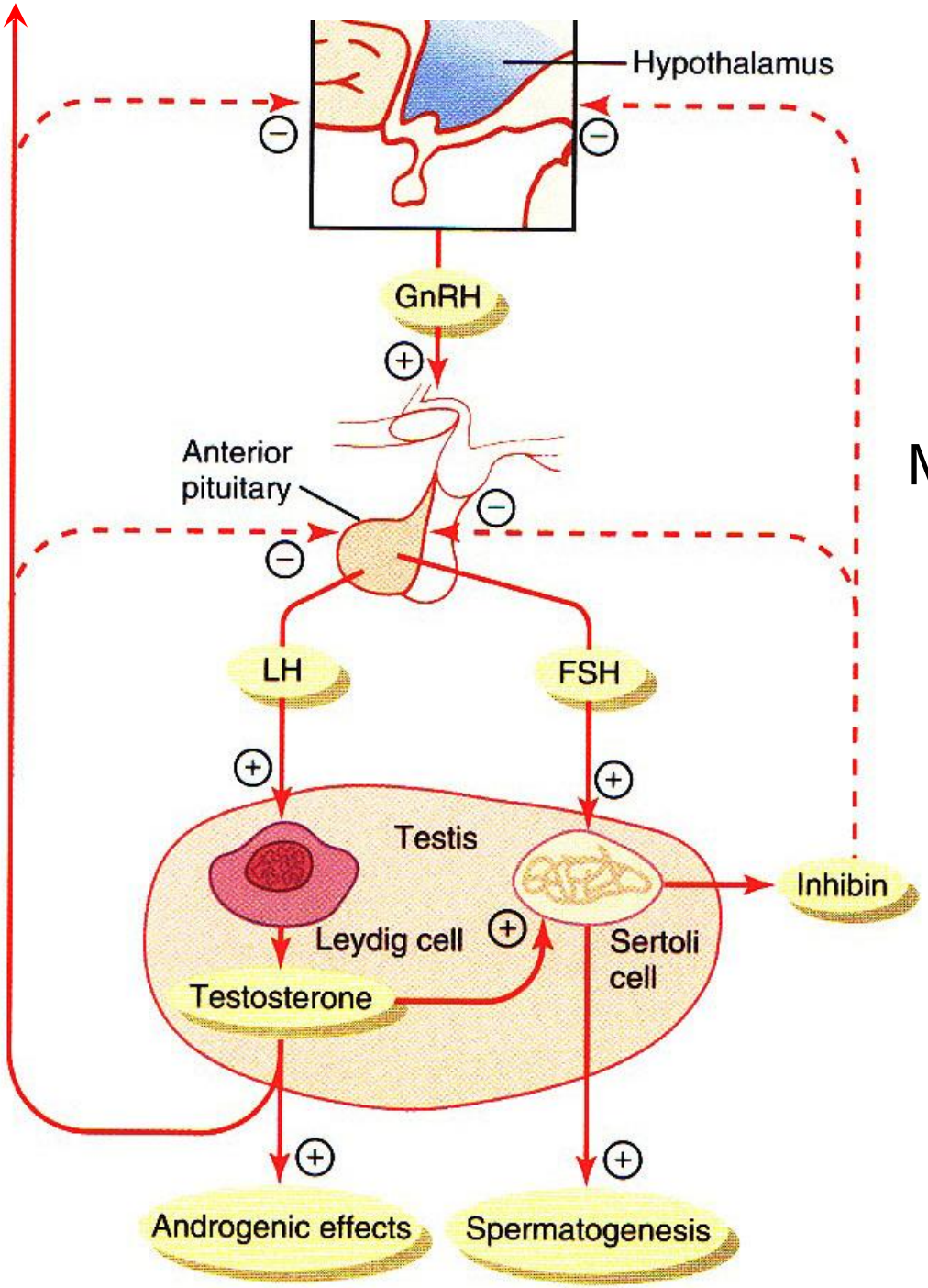
LS1 2007

LS1 2007

Figure 80-5 Abnormal infertile sperm, compared with a normal sperm on the right.

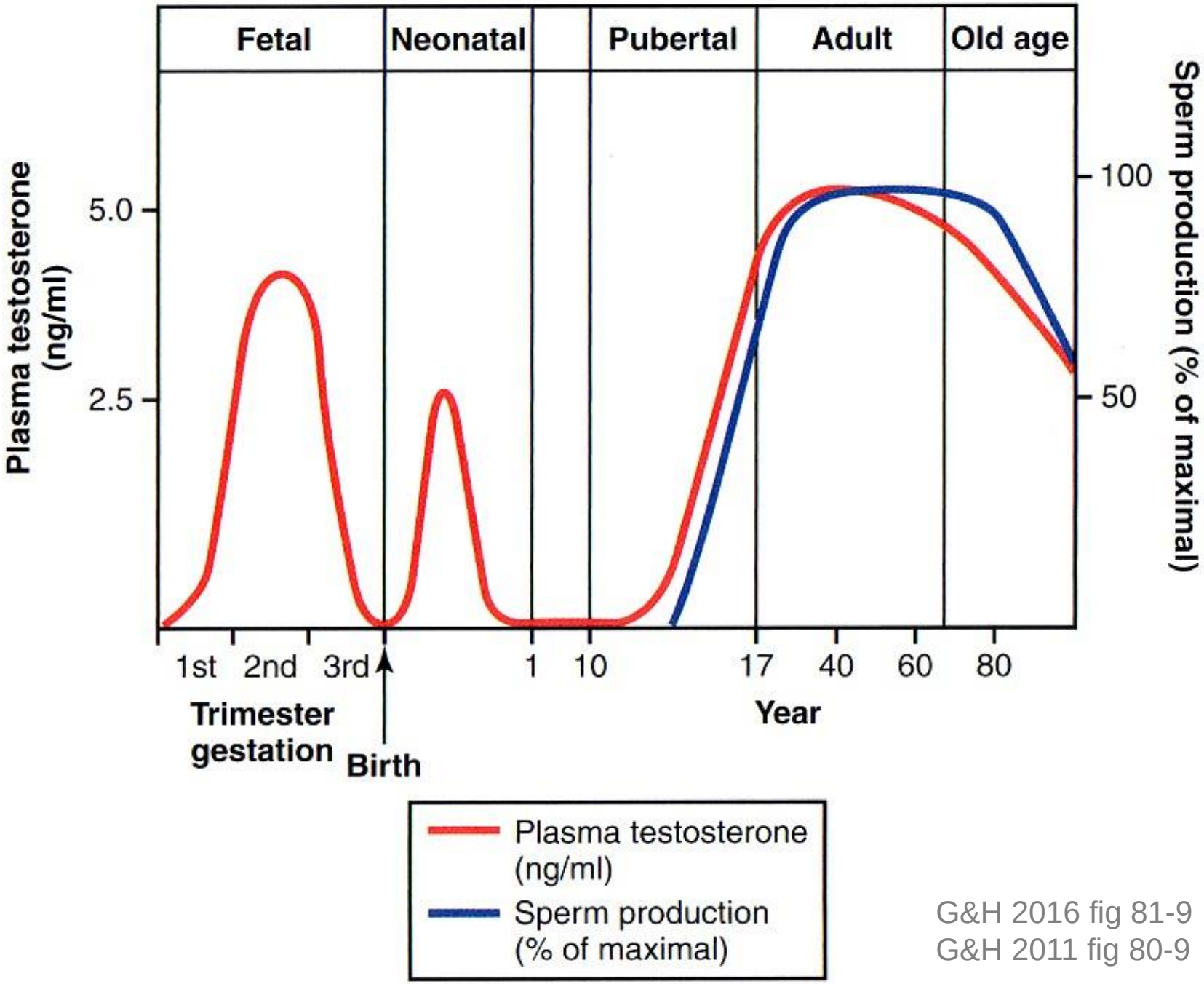
G&H 2016 fig 81-5
G&H 2011 fig 80-5

Behaviorial effects



Male Feedback Regulation

G&H 2016 fig 81-10
G&H 2011 fig 80-10



G&H 2016 fig 81-9
G&H 2011 fig 80-9