

Lecture 14&15
18&20 Feb 2008

Vertebrate Physiology
ECOL 437 (MCB/VetSci 437)
Univ. of Arizona, spring 2008

Kevin Bonine & Kevin Oh

1. Endocrine Physiology (Ch14)
2. Reproductive Physiology (Ch15)



http://eebweb.arizona.edu/eeb_course_websites.htm

	1	2
Experimental groups	Normal cock	Castrated cock
Treatment	Both testes removed	One testis replaced
Results	Comb and wattles small No interest in hens Weak crow Littles fight behavior	Comb and wattles normal Interest in hens Normal crow Aggressive fight behavior Testis larger than in controls

Housekeeping, 18 February 2008

Upcoming Readings

Today: Ch14
Wed 20 Feb: Ch14&15
LAB Wed 20 Feb: 4 readings on website
Fri 22 Feb: no lecture, work on proposal
Monday 25 Feb: Ch15, Ch17?
Wed 27 Feb: Research Question Due
Wed 27 Feb: Ch17
LAB Wed 27 Feb: muscle readings on website
Fri 29 Feb: Ch17



Lab discussion leaders: 20 Feb
1pm - Virsheena, Mathew S. Arturo
3pm - Kat, Clif, Amber

Lab discussion leaders: 27 Feb
1pm - Steve & Cassia
3pm - Kevin & Jennifer

The Edges of Life - 7pm at Centennial Hall

The Edges of Life Lecture Series

Wednesday, February 20
Life's Human Edge: Changing Perspectives on the End of Life
Michael Gill, Associate Professor, Philosophy
Nothing looms with more certainty than the final edge of one's own life. But in fact, the edge between life and death is anything but clear. This lecture will address the attempts that have been made to define the line between life and death and will explore the biological, legal, ethical, and spiritual debates that have raged around that line.

Wednesday, March 5
Life's Technological Edge: The Singularity is Near: When Humans Transcend Biology
Ray Kurzweil, via Teleport: Teleporter
Founder, Chairman and Chief Executive Officer, Kurzweil Technologies
Humanity is on the edge of a vast transformation, when what it means to be human will be both enriched and challenged. Inventor and futurist Ray Kurzweil will introduce this radically optimistic singularity, an era when we break our genetic shackles to create a nonbiological intelligence trillions of times more powerful than today. In this new world, humans will transcend biological limitations to achieve entirely new levels of progress and longevity.
This lecture co-sponsored by: UA College of Engineering and UA College of Science

These do not count as physiology lectures.



Endocrine System

9-9 Randall et al. 2002

(b) Endocrine glands

	1	2
Experimental groups	Normal cock	Castrated cock
Treatment	Both testes removed	One testis replaced
Results	Comb and wattles small No interest in hens Weak crow Littles fight behavior	Comb and wattles normal Interest in hens Normal crow Aggressive fight behavior Testis larger than in controls

9-10 Randall et al. 2002

-Hormone action often amplified by second messenger cascade

-Hormones often released in very low concentrations
Made them difficult to study!

1. cAMP
Glycogenolysis Example: (glycogen -> glucose)

-Epi (muscle)
-Glucagon (liver)

Goal is to increase blood [glucose]

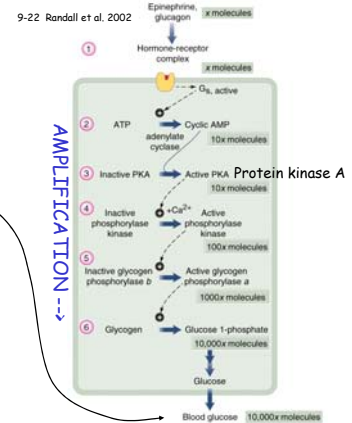


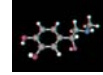
TABLE 14.2 Peptide, steroid, and amine hormones

Property	Peptides	Steroids	Amine hormones		
			Catecholamines	Thyroid hormones	Melatonin
Site of secretion	Most sites in Table 14.1, except adrenal cortex and medulla, thyroid gland, and pineal gland	Adrenal cortex, gonads, and placenta	Adrenal medulla	Thyroid gland	Pineal gland
Structure	Chains of amino acids	Derived from cholesterol	Derived from tyrosine	Derived from tyrosine and iodine	Derived from tryptophan
Solubility	Water-soluble	Lipid-soluble	Water-soluble	Lipid-soluble	Water-soluble
Synthesis and storage	Synthesized at rough ER, processed in Golgi apparatus, stored in vesicles in advance of use	Synthesized on demand in intracellular compartments; not stored	Synthesized in the cytoplasm and stored in vesicles ("chromaffin granules")	Made prior to use and stored in a colloid island within the gland	Synthesized in the cytoplasm and stored in vesicles
Secretion	Exocytosis	Simple diffusion through cell membrane	Exocytosis	Simple diffusion through cell membrane	Exocytosis
Transport	Dissolved in plasma, some bound to carrier proteins	Bound to carrier proteins	Dissolved in plasma	Bound to carrier proteins	Dissolved in plasma
Half life	Minutes	Hours	Seconds to minutes	Days	Minutes
Location of receptor molecules	Surface of target cell membrane	Cytoplasm or nucleus (some steroids bind to cell-surface receptors)	Surface of target cell membrane	Nucleus	Surface of target cell membrane
Action at target cell	Activate second-messenger systems or alter membrane channels	Alter gene expression; activate genes; initiate transcription and translation	Activate second-messenger systems	Alter gene expression; activate genes; initiate transcription and translation	Activate second-messenger systems
Response of target cell	Change activity of preexisting proteins, some of which may induce new protein synthesis	Synthesize new proteins; some may change activity of preexisting proteins	Change activity of preexisting proteins	Synthesize new proteins	Change activity of preexisting proteins

Sources: After Sherwood 2004; Silverthorn 2004; and Widmaier, Raff, and Strang 2004.

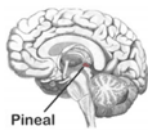
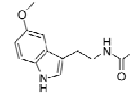
Hill et al. 2004 ANIMAL PHYSIOLOGY, Table 14.2 © 2004 Sinauer Associates, Inc.

Amines - small
(e.g., epi, norepi, thyroid)



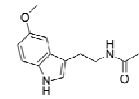
Modified Amino Acids

1. catecholamines (epi, norepi, dopamine; tyrosine)
2. thyroid (lipid soluble; tyrosine)
3. melatonin (tryptophan)



Melatonin

Pineal Gland
Retina
GI Tract



Produced at Night
Circadian Rhythms
Suprachiasmatic Nucleus (SCN) in Hypothalamus

Antioxidant
Immune System Support
Suppress libido? (LH, FSH)

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Glandular Secretion
Response to stimulus

Hormone
Neurotransmitter
Action Potential
etc. (e.g., osmolarity and ADH)



Storage before Secretion

Large molecules easily stored because can't leave readily
Small molecules often stored bound to accessory proteins
Some molecules actively/continuously taken into vesicles
Steroid hormones (lipid soluble) tend to leak out soon
Hydrophobic steroid and thyroid hormones move in blood, bound to carrier proteins

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TABLE 14.1 Summary of major blood-borne hormones in mammals (Part 1)

Endocrine tissue	Hormone	Class of molecule	Main functions
Adrenal cortex	Aldosterone (mineralocorticoid)	All steroids	Stimulates Na reabsorption and K secretion in kidney
	Androgens		Act on bone to cause growth spurt at puberty; increase sex drive in females by action on brain
	Glucocorticoids		Part of stress response; affect metabolism of many tissues to increase blood glucose and cause protein and fat catabolism
Adrenal medulla	Epinephrine and norepinephrine	Catecholamines	Part of stress response; influence cardiovascular function and organic metabolism of many tissues

Sources: After Bentley 1998; Henderson 2000; Schmidt-Nielsen 1997; Sherwood 2004; Silverthorn 2004; and Widmaier, Raff, and Strang 2004.

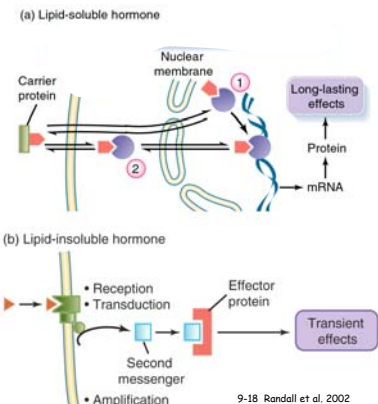
ETC...

Hill et al. 2004

ANIMAL PHYSIOLOGY, Table 14.1 (Part 1) © 2004 Sinauer Associates, Inc.

1. Lipid Soluble

2. Lipid Insoluble



9-18 Randall et al. 2002

Hormone ACTION!

Where are the receptors?

- Lipid Soluble**
 - Steroid and Thyroid Hormones (~long-lived)
 - **Through Membrane**
 - Bind **cytoplasmic receptors**, then to Nucleus
 - Directly affect **transcription** (therefore long-term)
- Lipid Insoluble**
 - Bind **cell-surface receptors**
 - Often one or more **2nd messengers**
 - Amplification
 - ~ **Rapid**, short-duration responses

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Hormone ACTION! (receptors etc.)

2. Lipid Insoluble Hormones and Intracellular Signaling

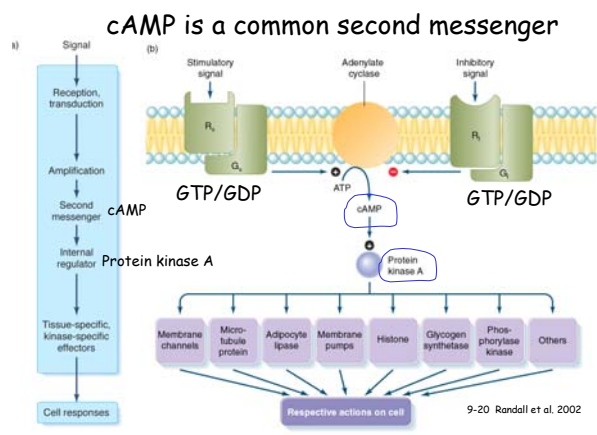
A few receptors with direct catalytic activity, but most via 2nd messengers :

Possible 2nd messengers:

1. **cAMP, cGMP** (cyclic nucleotide monophosphates)
2. **IP₃, DAG** (diacylglycerol; inositol phospholipids)
3. **Ca²⁺** ions

General Model of Hormone Binding and Intracellular Signaling:

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9-20 Randall et al. 2002

Randall et al. 2002
Table 9-6 Some hormone-induced responses mediated by the cAMP pathway

Signal	Tissue	Cellular response
Stimulatory		
Epinephrine (β -adrenoreceptors)	Skeletal muscle	Breakdown of glycogen
	Fat cells	Increased breakdown of lipids
	Heart	Increased heart rate and force of contraction
	Intestine	Fluid secretion
Thyroid-stimulating hormone (TSH)	Thyroid gland	Thyroxine secretion
ADH (vasopressin)	Kidney	Reabsorption of water
Glucagon	Liver	Breakdown of glycogen
Serotonin	Salivary gland (blowfly)	Fluid secretion
Prostaglandin I ₂	Blood platelets	Inhibition of aggregation and secretion
Inhibitory		
Epinephrine (α_2 -adrenoreceptors)	Blood platelets	Stimulation of aggregation and secretion
	Fat cells	Decreased lipid breakdown
Adenosine	Fat cells	Decreased lipid breakdown

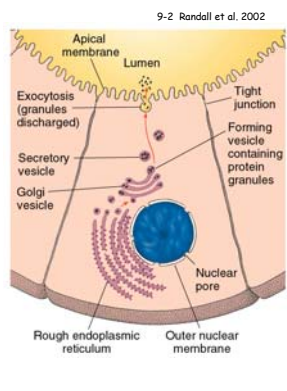
Source: Berridge, 1985.

Glandular Secretion

Secretory Vesicles

Exocytosis - common release mechanism

Regulation via Calcium - free cytosolic calcium concentration is correlated with exocytosis (including of NT, hormones, etc.)



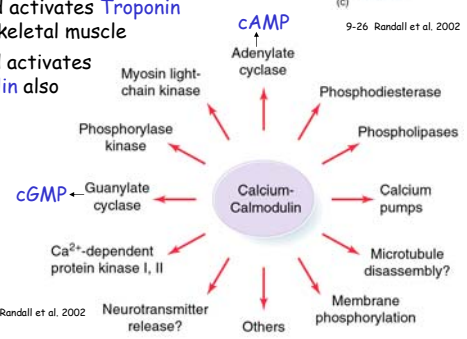
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Ca²⁺ ions

- Intracellular stores (ER)
- Influx from extracellular fluid

1- binds and activates Troponin C in skeletal muscle

2- binds and activates Calmodulin also

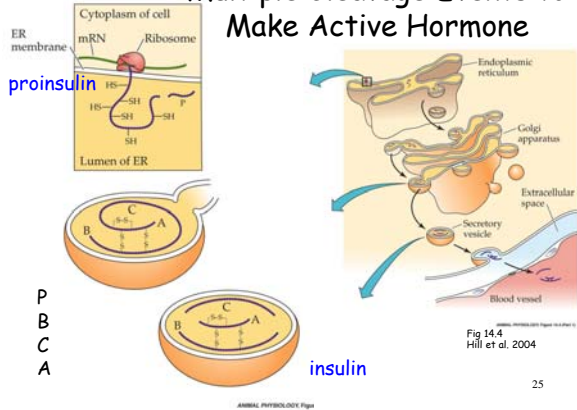


9-27 Randall et al. 2002



9-26 Randall et al. 2002

Multiple Cleavage Events to Make Active Hormone



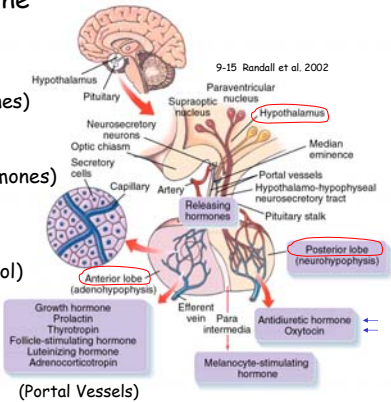
Major Endocrine Players

Hypothalamus

- (~7 neurohormones)
- mostly peptides

Pituitary (9 hormones)

1. **Anterior** (~nonneuronal)
2. **Posterior** (~neuronal control)



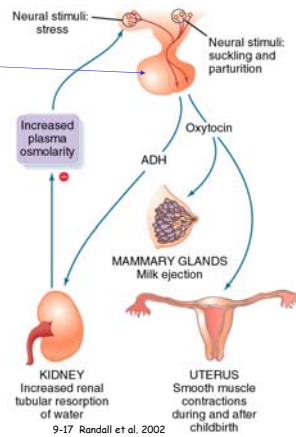
Posterior Pituitary

Oxytocin - uterine contractions, milk ejection

Antidiuretic Hormone (ADH) - water retention in kidney

Both are **peptide** hormones

Both are similar and highly **conserved**...



Posterior Pituitary

Randall et al. 2002
Table 9-4 Variant forms of neurohypophysial nonapeptide hormones

Peptide	Positions of amino acid residues*									Animal group	
	1	2	3	4	5	6	7	8	9		
Lysine vasopressin	Cys	Tyr	Ile	Gln	Asn	Cys	Pro	Lys	Gly	(NH ₂)	Pigs and relatives
Arginine vasopressin	Cys	Tyr	Ile	Gln	Asn	Cys	Pro	Arg	Gly	(NH ₂)	Mammals ADH
Oxytocin	Cys	Tyr	Ile	Gln	Asn	Cys	Pro	Leu	Gly	(NH ₂)	Mammals
Arginine vasotocin	Cys	Tyr	Ile	Gln	Asn	Cys	Pro	Arg	Gly	(NH ₂)	Reptiles, fishes, and birds
Isotocin	Cys	Tyr	Ile	Ser	Asn	Cys	Pro	Ile	Gly	(NH ₂)	Some teleosts
Mesotocin	Cys	Tyr	Ile	Gln	Asn	Cys	Pro	Ile	Gly	(NH ₂)	Reptiles, amphibians, and lungfishes
Glanitocin	Cys	Tyr	Ile	Ser	Asn	Cys	Pro	Gln	Gly	(NH ₂)	Some elasmobranchs

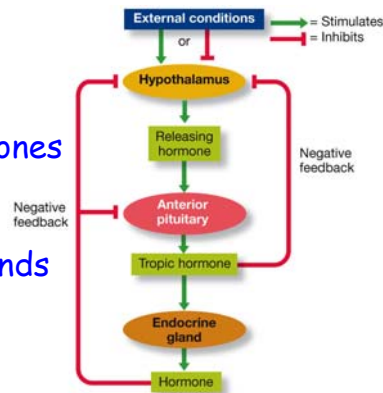
*The cysteine residues in positions 1 and 6 of each peptide are bridged by a disulfide bond. Source: Friesden and Lipner, 1971.

Similar, highly conserved peptide hormones

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Tropic Hormones

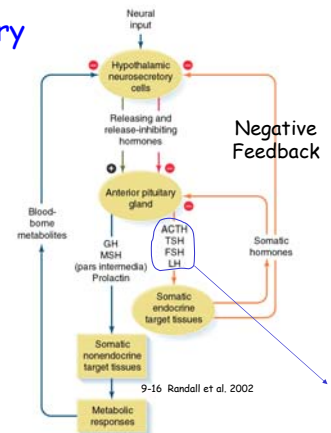
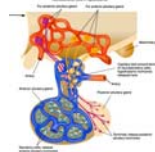
Multiple Glands



Anterior Pituitary

Tropic hormones = act on other endocrine tissues

(e.g., adrenal cortex, thyroid, gonads)



Tropic Hormones of Anterior Pituitary

Table 9-3 Tropic hormones of the anterior pituitary gland

Hormone	Structure	Target tissue	Primary action in mammals	Regulation*
ACTH Adrenocorticotropic hormone (ACTH)	Peptide	Adrenal cortex	Increases synthesis and secretion of steroid hormones by adrenal cortex	Corticotropin-releasing hormone (CRH) stimulates release; ACTH slows release of CRH
FSH Follicle-stimulating hormone (FSH)	Glycoprotein	Ovarian follicles (female); seminiferous tubules (male)	In female, stimulates maturation of ovarian follicles; in male, increases sperm production	GnRH stimulates release; inhibin and steroid sex hormones inhibit release
LH Luteinizing hormone (LH)	Glycoprotein	Ovarian interstitial cells (female); testicular interstitial cells (male)	In female, induces final maturation of ovarian follicles, estrogen secretion, ovulation, corpus luteum formation, and progesterone secretion; in male, increases synthesis and secretion of androgens	GnRH stimulates release; inhibin and steroid sex hormones inhibit release
TSH Thyroid-stimulating hormone (TSH)	Glycoprotein	Thyroid gland	Increases synthesis and secretion of thyroid hormones	TRH induces secretion; thyroid hormones and somatostatin slow release

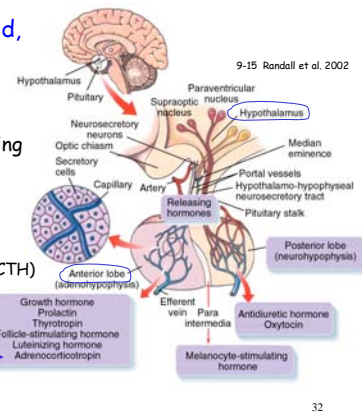
*See Table 9-2 for key to abbreviations. Randall et al. 2002

In response to cold, fright, pain etc...

Hypothalamus
-corticotropin-releasing hormone

Anterior Pituitary
-Adrenocorticotropin (ACTH)

Adrenal Cortex
(corticosterone; stress hormones)

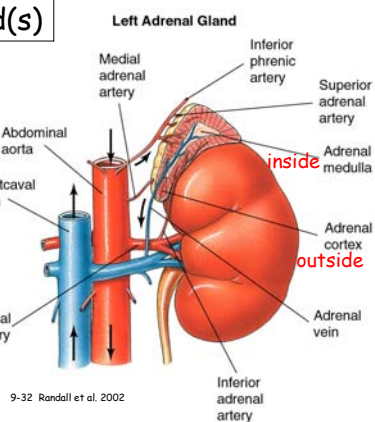


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Adrenal Gland(s)

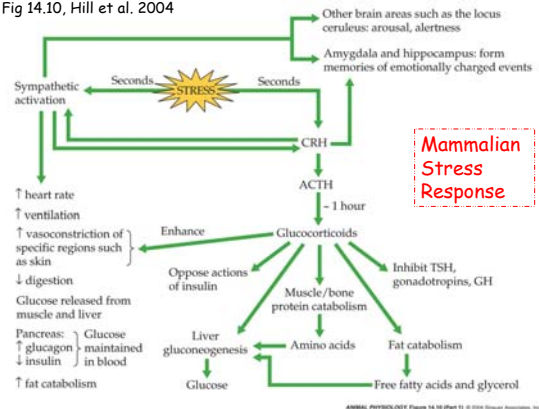
Catecholamines (from medulla)

Glucocorticoids (from cortex)



9-32 Randall et al. 2002

Fig 14.10, Hill et al. 2004



Mammalian Stress Response

ANIMAL PHYSIOLOGY: Figure 14.10 (part 1) © 2004 Sinauer Associates, Inc.

Glucocorticoids

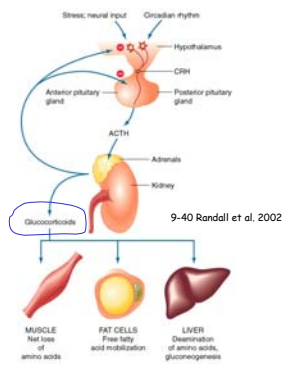
(from adrenal cortex)

Includes 'Stress Hormones'
Cortisol, cortisone, corticosterone

Released in response to ACTH (Adrenocorticotropin) from Anterior Pituitary

Steroid hormones (lipid soluble) derived from cholesterol

(mobilize a.a.s and glucose, suppress immune system etc.)



9-40 Randall et al. 2002

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Vasopressin from Anterior Pituitary

Blood loss:

↑ vasopressin → ↑ water reabsorption at kidney
↑ aldosterone → ↑ Na reabsorption at kidney

↑ fluid retention

↑ blood volume

↑ blood pressure

Negative Feedback Loop

Fig 14.10, Hill et al. 2004

More on aldosterone and other kidney hormones later

ANIMAL PHYSIOLOGY: Figure 14.10 (part 2) © 2004 Sinauer Associates, Inc.

Water and Electrolyte Balance Hormones

Randall et al. 2002
Table 9-8 Mammalian hormones involved in regulating water and electrolyte balance

Hormone	Tissue of origin	Structure	Target tissue	Primary action	Regulation
<u>Antidiuretic hormone (ADH, vasopressin)</u>	Posterior pituitary	Nonpeptide	Kidneys	Increases water reabsorption	cAMP pathway
Post. Pit., signal from Hypothal					
<u>Atrial natriuretic peptide (ANP)</u>	Heart (atrium)	Peptide	Kidneys	Reduces Na ⁺ and water reabsorption	Increased venous pressure stimulates release
<u>Calcitonin</u>	Thyroid (parafollicular cells)	Peptide	Bones, kidneys	Decreases release of Ca ²⁺ from bone; increases renal Ca ²⁺ and PO ₄ ³⁻ excretion	Increased plasma Ca ²⁺ stimulates secretion
<u>Mineralocorticoids (e.g., aldosterone)</u>	Adrenal cortex	Steroid	Distal kidney tubules	Increases reabsorption of Na ⁺ from urinary filtrate	Angiotensin II stimulates secretion
<u>Parathyroid hormone (PTH)</u>	Parathyroid gland	Peptide	Bones, kidneys, intestine	Increases release of Ca ²⁺ from bone; with calcitriol increases intestinal Ca ²⁺ absorption; decreases renal Ca ²⁺ excretion	Decreased plasma Ca ²⁺ stimulates secretion

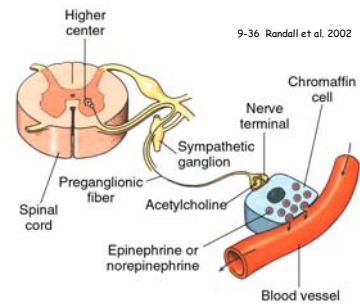
Calcitonin decrease Ca⁺⁺ in blood; PTH increase Ca⁺⁺ in blood

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Fight/flight, exertion
Catecholamines
(adrenal medulla)
- Epi, Norepi

Secretion regulated by sympathetic preganglionic cholinergic neurons

Catecholamine receptors are Alpha and Beta adrenoceptors



Alpha - smooth muscle contraction

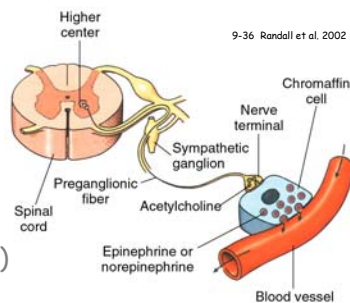
Beta1 - cardiac muscle stimulant
Beta2 - broncho/vaso dilation

Fight/Flight

Catecholamines from adrenal medulla (e.g. epinephrine)

Secretion regulated by sympathetic neurons

Response includes bronchodilation, vasodilation to major muscles, vasoconstriction to stomach and skin, increased heart rate, mobilization of resources



9-36 Randall et al. 2002

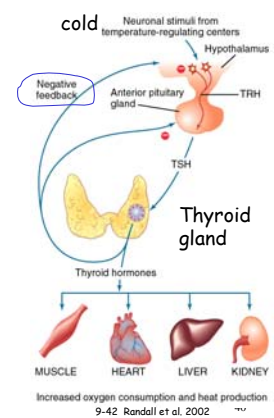
Thyroid Hormone (aka Thyroxine)

T₃ and T₄ (# of iodines)

lipid soluble

Development, maturation, protein synthesis, metabolism

Being cold can stimulate



9-42 Randall et al. 2002

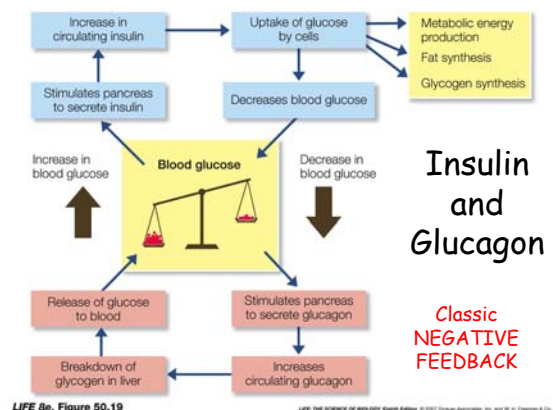
Thyroxine and Thyroid Gland

Hypothyroid Goiter
(e.g. not enough iodine in diet)

Hyperthyroid Goiter
(e.g. 1. thyroxine receptors on hypothalamus or anterior pituitary don't work, or 2. receptor for thyroid stimulating hormone is activated by autoimmune antibody)



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LIFE 6e, Figure 50.19

LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, © 2004 Sinauer Associates, Inc. and W. H. Freeman & Co.

Insulin and Glucagon Regulate blood [glucose]

- Insulin in response to high [glu]
- Glucagon in response to low [glu]

Both from pancreatic gland:
Insulin from **beta** cells
Glucagon from **alpha** cells

Leads to **glucose uptake** into tissues ETC.

Causes glycogenolysis and **glucose release** from tissues (liver, muscles)

Type 1 Diabetes
 -when beta cells **decrease insulin production**
Type 2 Diabetes
 -when insulin **receptor signal pathway defective**



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Growth Hormone

Metabolic and developmental effects

From **Anterior Pituitary**

Often has **opposite effect of insulin**

- Stimulates gluconeogenesis
- Reserves glucose for NS
- Promotes use of fatty acids as fuel

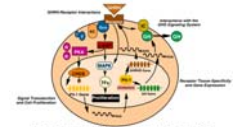


Figure 15.10: Signal Transduction in the Pituitary Somatotrophic Cell



Gigantism / Acromegaly



Works with Thyroid hormone in growth and development

abnormality



Growth Hormone

- + -Gigantism
- Acromegaly



Vertebrate Reproduction



Photography AcclaimImages.com Photography

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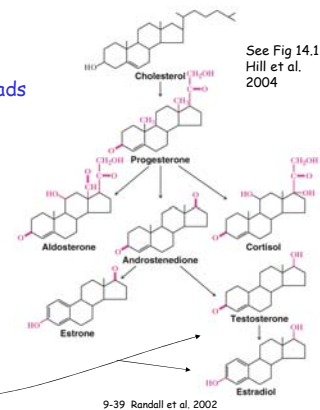
Asexual Parthenogenetic Whiptail Lizards

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Reproductive Hormones

Steroid Hormones from Adrenal cortex and Gonads

Hypothalamus
 ↓
GnRH
 ↓
 Anterior Pituitary
 ↓
FSH, LH
 ↓
 Gonads, Adrenal Cortex



See Fig 14.1, Hill et al. 2004

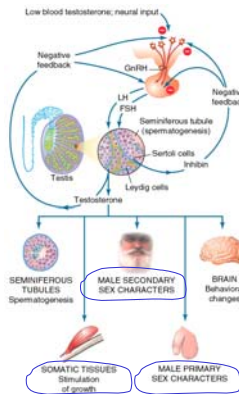
9-39 Randall et al. 2002

Male Sex Hormones

Testosterone and other **androgens**

Released from **Leydig Cells** in response to LH, FSH

FSH binding to **Sertoli cells** stimulates **spermatogenesis**



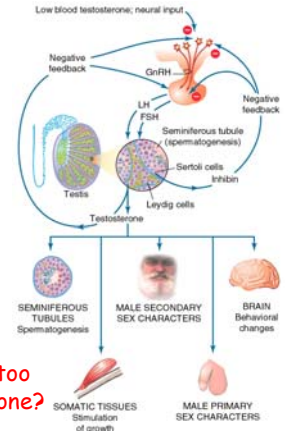
9-46 Randall et al. 2002

Steroid Abuse

Homeostasis & Negative Feedback



What happens if you take too much exogenous testosterone?



Female Sex Hormones

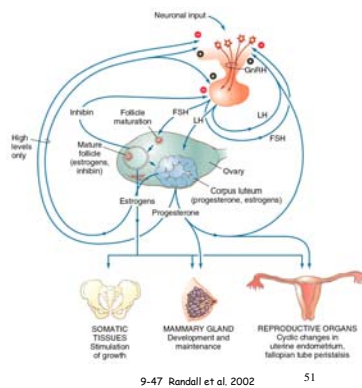
Estrogens

Ova created and stored before birth (mammals and birds)

Repro cycle in 2 phases:

Follicular and Luteal

FSH stimulates beginning of follicular phase → development of ovarian follicles



9-47 Randall et al. 2002

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Follicular Phase

1- FSH ↑
Causing follicular maturation

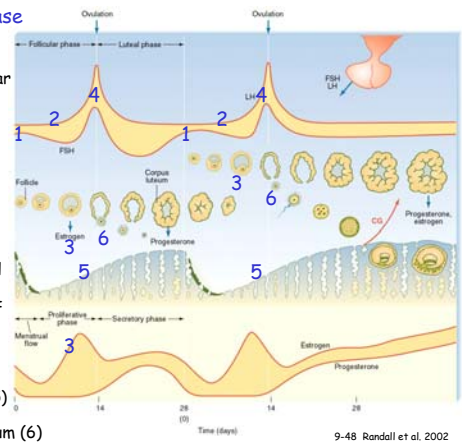
2- LH ↑

FSH and LH help generate Estrogen (3)

This Estrogen causes hypothal and ant. pit. to release spike of LH and FSH leading to ovulation (4)

(endometrium 5)

= release of ovum (6)



9-48 Randall et al. 2002

Luteal Phase

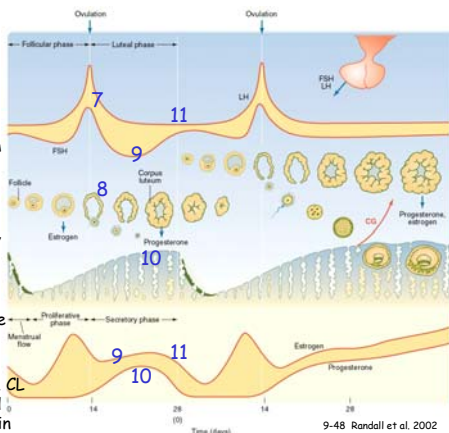
7- FSH, LH ↓
Estrogen ↓

8- LH changes ruptured follicle into corpus luteum

9- corpus luteum secretes estrogen and progesterone which inhibit FSH, LH release from anterior pituitary by slowing GnRH

10- progesterone leads to richer endometrium

11- without fert. CL degenerates and cycle begins again

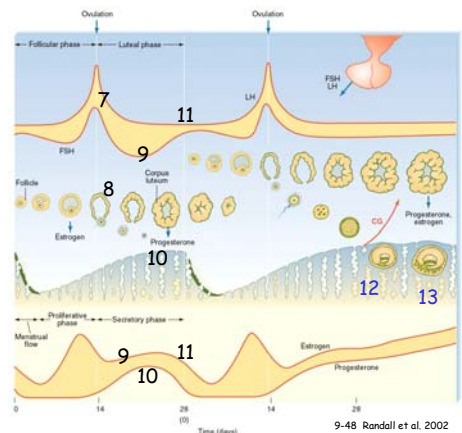


9-48 Randall et al. 2002

Luteal Phase

12- with fert. Chorionic gonadotropin maintains CL, maintaining high levels of estrogen and progesterone; maintaining endometrium; follicular development inhibited

13- Placenta takes over hormone production



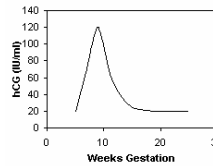
9-48 Randall et al. 2002

Dear Cecil:

I just hit 40 and still have an unanswered question from my teens that has always bothered me. **Aerosmith** in "Sweet Emotion" sings about being accused of impregnating a girl. At the end of the verse they sing, "can't catch me 'cause the rabbit done died," referring to a pregnancy test. Arguments start over just what this test entails. Most say the bunny will die, but can't agree as to why. Some say the rabbit will always die because they kill it before they take its blood (which seems pretty dumb). Some say they inject it with some fluid taken from the woman and it dies a horrible, convulsive death. And some say they have to dissect the rabbit after it has been injected. This was before those home test kits, but wasn't there a better way? --Joe Shredl, Colonial Heights, Virginia

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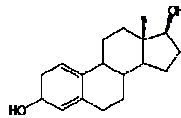
Chorionic gonadotropin
hCG
eCG



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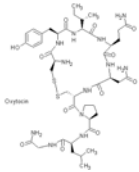
Birth Control Pills?

Progesterone and Estradiol - mimic early pregnancy and inhibit ovulation



Parturition (Birth)

Oxytocin released in response to cervical stretch
Oxytocin causes uterine smooth muscle contractions



Positive Feedback Loop

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Lactation

Decreased progesterone levels and presence of prolactin (milk production) and oxytocin (milk ejection) and other hormones

Antibodies
Vitamins

Mechanosensory feedback

Dopamine inhibits prolactin secretion



joey



marsupial

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Randall et al. 2002
Table 9-9 Important mammalian reproductive hormones

Hormone	Tissue of origin	Structure	Target tissue	Primary action	Regulation
Primary sex hormones					
Estradiol-17β (estrogen)	Ovarian follicle, corpus luteum, adrenal cortex	Steroid	Most tissues	Promotes development and maintenance of female characteristics and behavior, oocyte maturation, and uterine proliferation	Increased FSH and LH levels stimulate secretion
Progesterone	Corpus luteum, adrenal cortex	Steroid	Uterus, mammary glands	Maintains uterine secretion; stimulates mammary duct formation	Increased LH and prolactin levels stimulate secretion
Testosterone (androgen)	Testes (Leydig cells), adrenal cortex	Steroid	Most tissues	Promotes development and maintenance of male characteristics and behavior and spermatogenesis	Increased LH level stimulates secretion
Other Hormones					
Oxytocin	Posterior pituitary	Nonpeptide	Uterus, mammary glands	Promotes smooth muscle contraction and milk ejection	Cervical distention and suckling stimulate release; high progesterone inhibits release
Prolactin (PL)	Anterior pituitary	Peptide	Mammary glands (alveolar cells)	Increases synthesis of milk proteins and growth of mammary glands, elicits maternal behavior	Continues secretion of PL-inhibiting hormone (PIH) normally blocks release; increased estrogen and decreased PIH secretion permit release

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