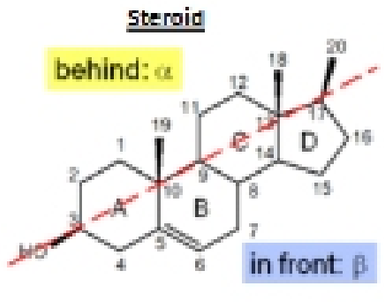
Steroid Synthesis

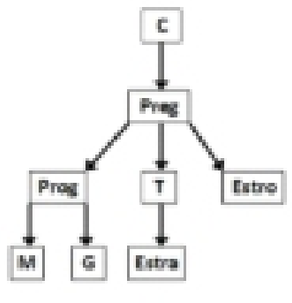
Saturday, November 22, 2014
12:06 PM

Learning Objectives:
- steroid vs. cholesterol structure
- steroid vs. peptide hormone mechanism of action
- keto steroids
- female reproductive cycle & points of pharma intervention for infertility or BC
- BP regulation & points of pharma intervention
- Vit D synth
- cause of Cushing's
- symptoms of Cushing's vs. long-term corticosteroids

Lecture Outline:
- steroids
- overview
- sex hormones (androgens, estrogens, progesterones)
- glucocorticoids
- mineralocorticoids
- Vit D

Steroid





Steroids Classification

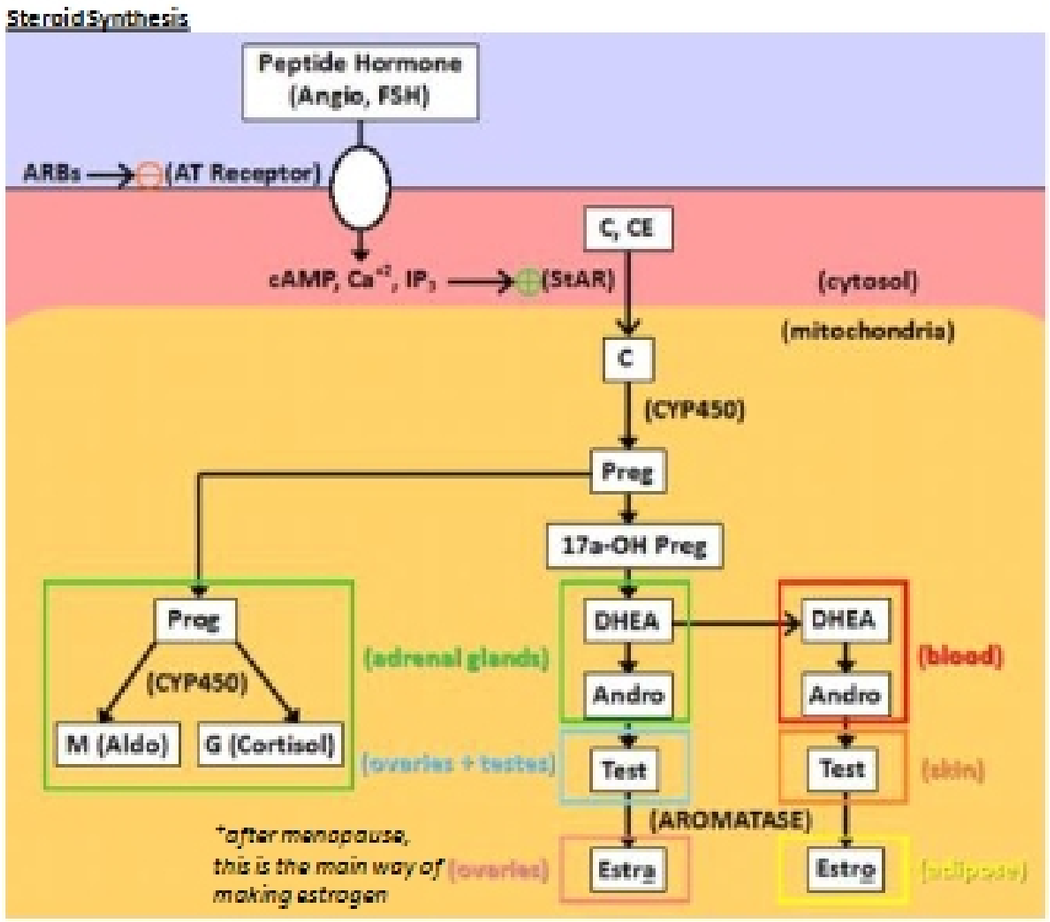
Adrenal	11-OH
Estrogens	18-C
Androgens	19-C
Progesterone & Adrenal	21-C

Steroids
- diffuse across membrane
- bind to Steroid Receptors
- Steroid:Receptor complex binds DNA & effects protein synth

Cholesterol Sources
- membranes
- CE droplets
- LDL
- de novo synth

***Steroid:Protein Binding in Blood:**
- Corticosteroid-Binding Protein (CBG)
- Sex-Hormone-Binding Protein (SHBP)
- Albumin (A)

Steroid Synthesis



Regulation of Glucocorticoid Synth

↑ Stress, ↑ CRH, ↑ ACTH, Glucocorticoids (Cortisol), Transcription

HYPOTHALAMUS	CRH (in response to stress)
PITUITARY GLAND	ACTH

Drugs
**must be tapered off*
- **CORTISONE** --> Cortisol
- **DEXAMETHASONE**
- **PREDNISONE** --> Prednisolone
- **TRIAMCINOLONE** - arthritis/skin diseases

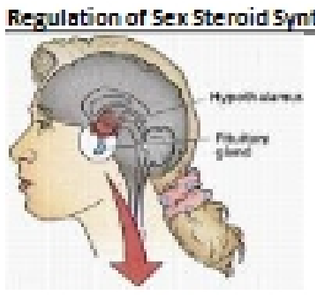
CUSHING'S - due to ↑ Cortisol; often iatrogenic; also caused by pituitary & adrenal glands tumors
1) muscle protein breakdown
2) GNG (--> Insulin Resistance)

Regulation of Mineralocorticoid Synth
ARBs - inhibit AT Receptor; prevents Cholesterol uptake into mitochondria
LISINOPRIL - ACE Inhibitor
ALDOSTERONE ANTAGONISTS - prevents water retention

Vit D Synth

Calcitriol Effects (↑ Ca^{+2}, P)
- intestine
- glomerulus
- blood

Regulation of Sex Steroid Synth (Women)

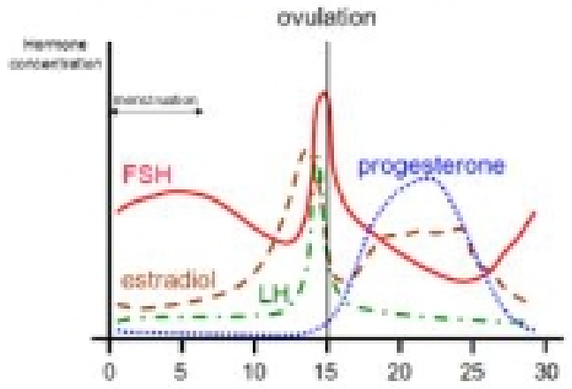


GONADOTROPINS - FSH/LH

↑ GnRH, ↑ FSH, ↑ Estra, ↓ FSH
↑ LH, ovulation

HYPOTHALAMUS	GnRH
PITUITARY GLAND	FSH & LH
OVARIAN FOLICLES	Estra
CORPUS LUTEUM/PLACENTA	Prog

PROGESTERONE - continued secretion if egg is fertilized



Selective Estrogen Receptor Modulators (SERMs):

CLOMIPHENE	infertility	↑ FSH
TAMOXIFEN	breast cancer adjuvant breast cancer prevention	inhibits Estrogen Receptors
RALOXIFENE	osteoporosis breast cancer prevention	- Bone: acts like Estrogen - Breast/Uterus/Tumors: inhibits Estrogen Receptors
TOREMIFENE	breast cancer adjuvant	inhibits Estrogen Receptors

AROMATASE INHIBITOR - ↓ Estradiol synth
CONTRACEPTIVES - Estrogen + Progesterone; ↓ FSH/LH

Regulation of Sex Steroid Synth (Men)

↑ LH, ↑ Testosterone, ↑ DihydroTestosterone

PITUITARY GLAND	LH
LEYDIG CELLS (TESTES)	Testosterone

TESTOSTERONE - low affinity for Androgen Receptor
DIHYDROTESTOSTERONE - high affinity for Androgen Receptor