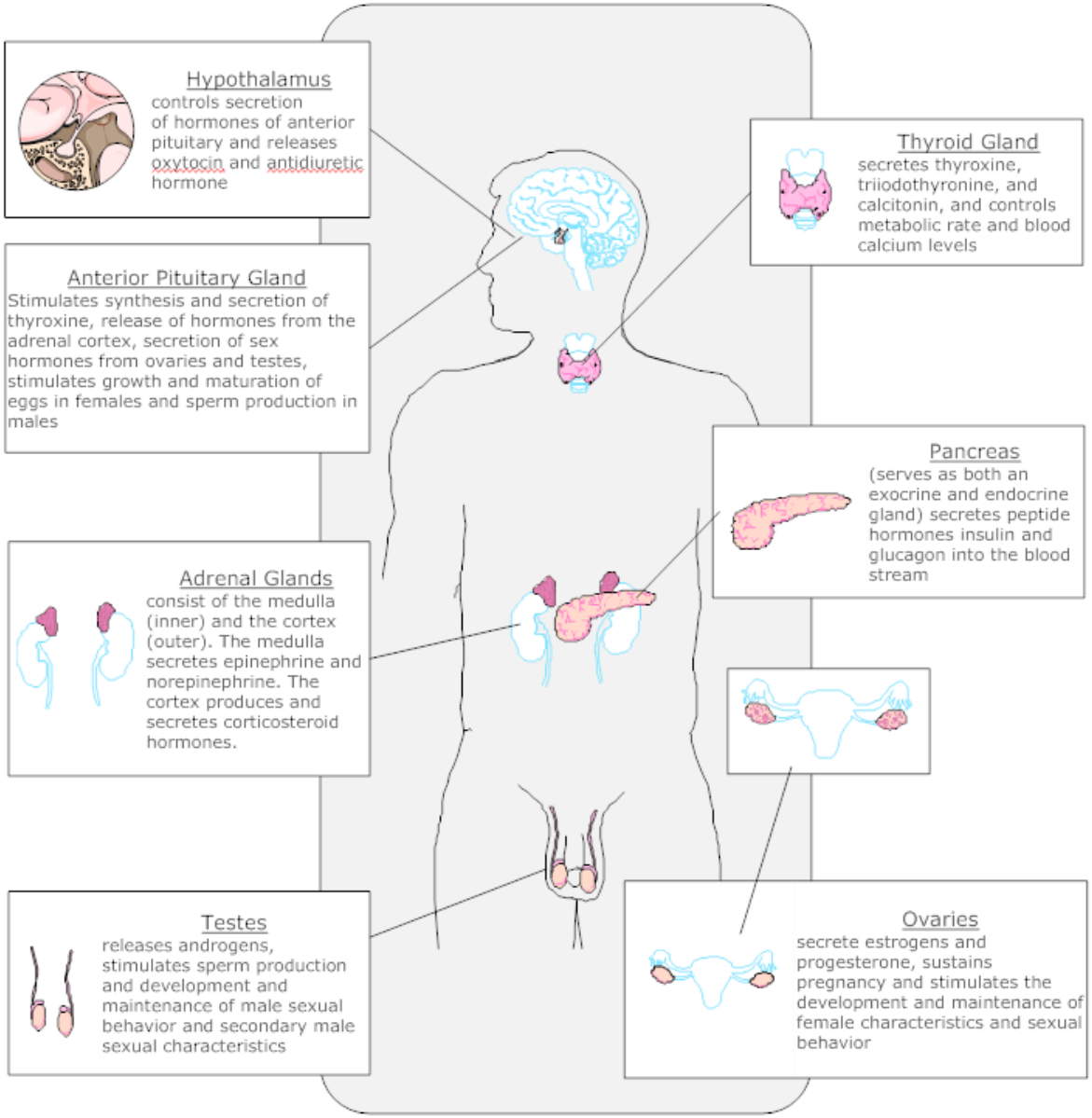
The Endocrine System

The Nutshell Version

Hormone Action

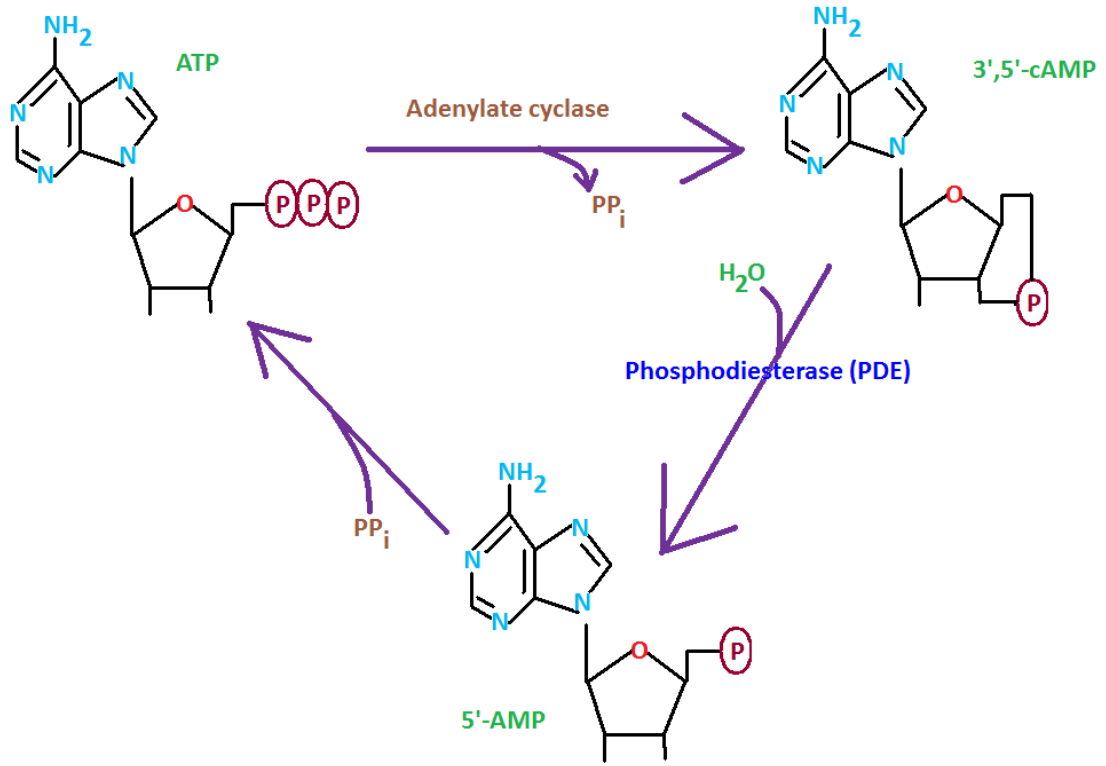


Some Definitions

- Hormone ≡ a chemical messenger which is carried from the organ where they are produced to the target organ which they effect by means of the bloodstream
- Exocrine ≡ glands that secrete their products through a duct
- Endocrine ≡ glands whose products are secreted into the interstitial compartment and are “absorbed” by the blood; are ductless

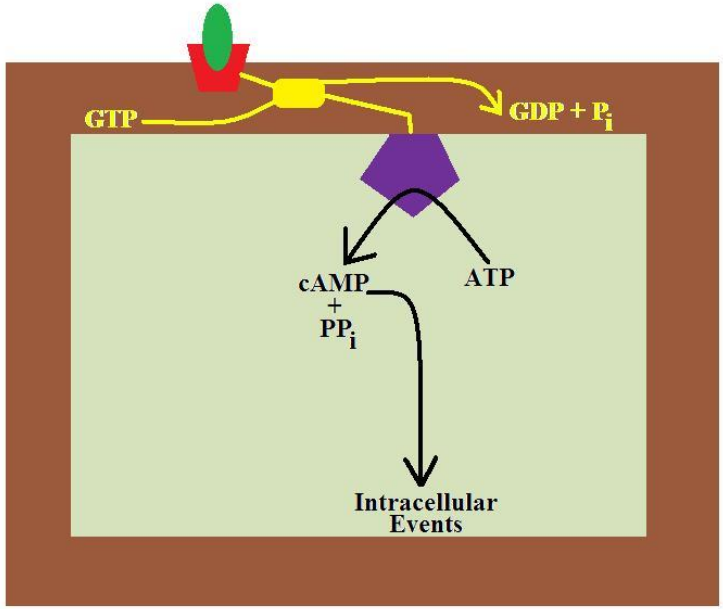
Second Messengers

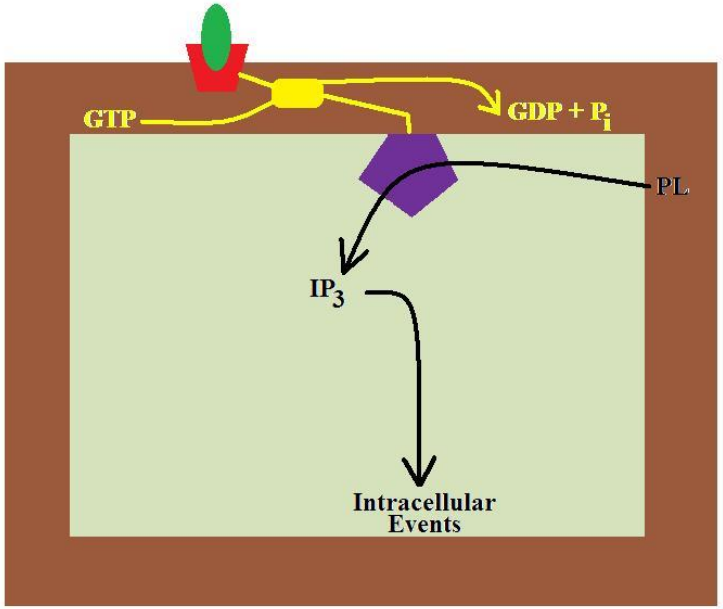
cAMP – Second Messenger

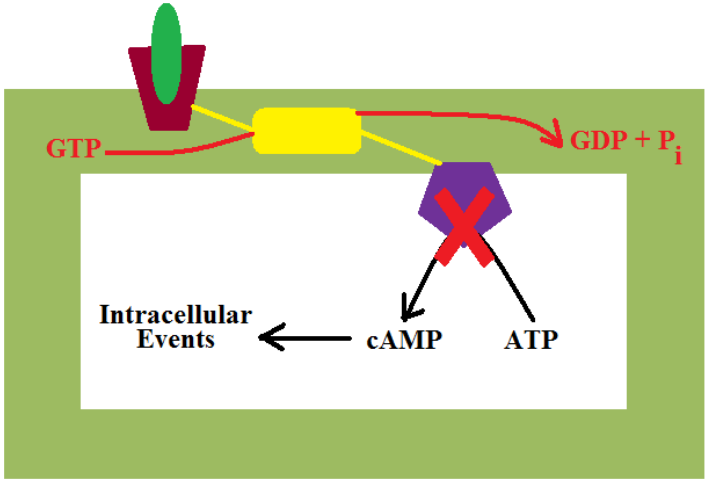


- Elevated levels of cAMP drive protein synthesis, enzyme cascades and changes in membrane permeability

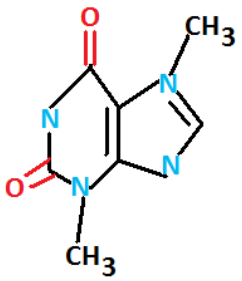
G Proteins


GTP
GDP + P_i
cAMP
+
PP_i
ATP
Intracellular
Events

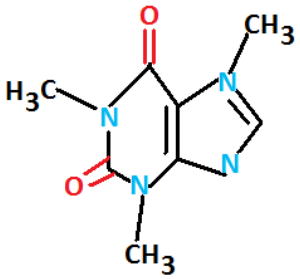

GTP
GDP + P_i
PL
IP_3
Intracellular
Events


GTP
GDP + P_i
Intracellular
Events
cAMP
ATP

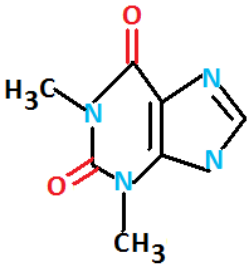
Adenylate Cyclase Inhibitors



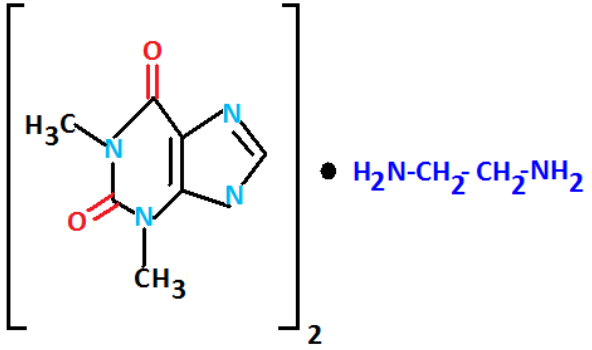
Theobromine



Caffeine



Theophylline

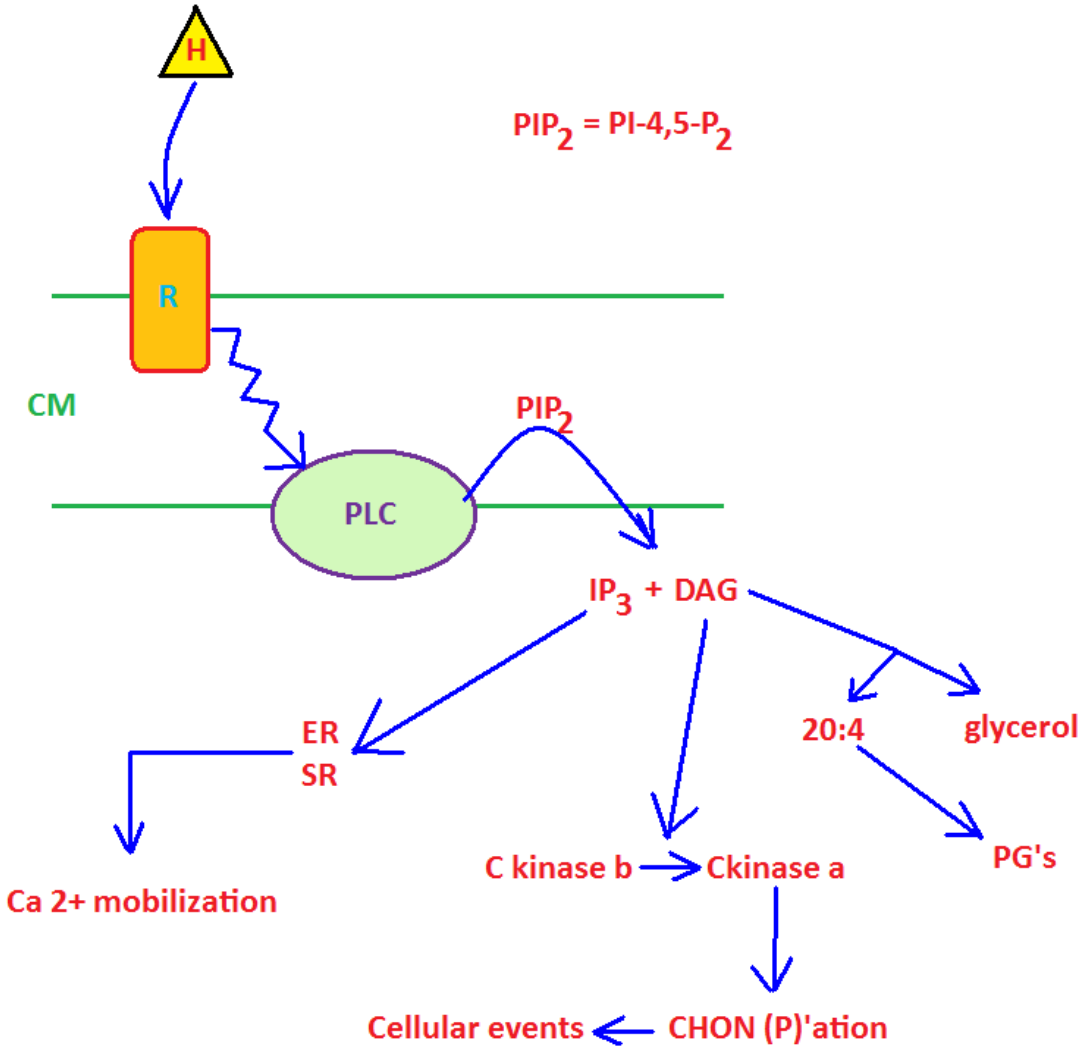


Aminophylline

- Phosphodiesterase (PDE) inhibited by:
  - Theophylline
  - Caffeine
  - Theobromine

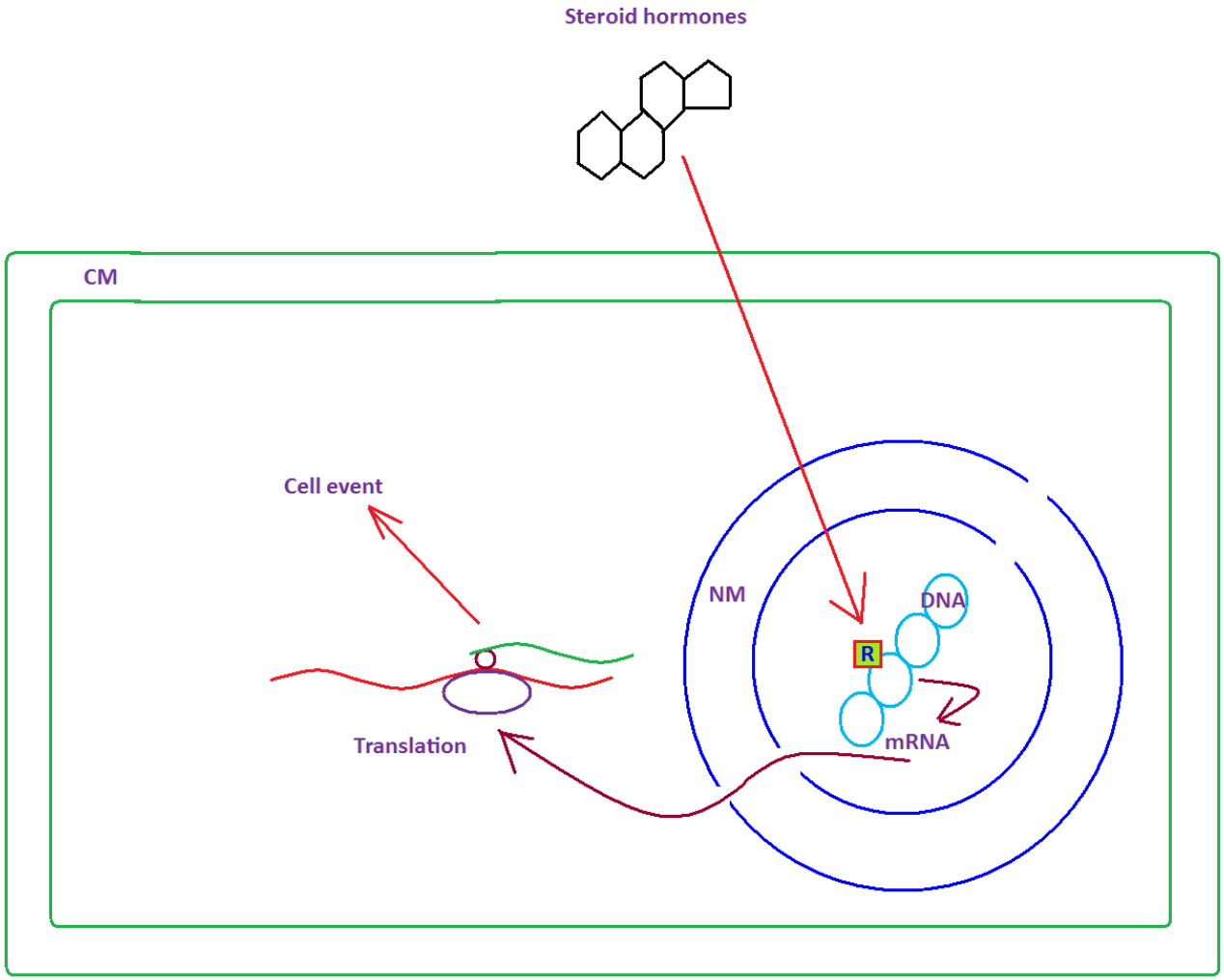
- These compounds are called xanthines.
- When PDE is inactivated, cAMP levels build up, making it easier for patients to breathe. Is this true or false???

Second Messenger: IP_3



IP_3 drives changes in:
Ca^{2+} concentration
Ca^{2+} mobilization
GABA, AVP, ANG,
TSH utilize IP_3

Steroid Hormones



- Steroids drive translation
- Functionally: increased activity
- Structurally: Bulking up

NO Second Messengers!!

Overview of Hormones With Second Messengers

Amino Acid Hormones

1. T_3 – triiodothyronine
2. T_4 – tetraiodothyronine – thyroxine
3. Epinephrine – Phe or Tyr

Peptide/Protein Hormones

1. GnRH
2. CRF
3. CRF
4. PIF?
5. PRF
6. GHIH
7. GH
8. PRL
9. LH
10. FSH
11. ACTH
12. MSH?
13. TSH
14. Insulin
15. Glucagon
16. Somatostatin
17. Gastrin
18. Secretin
19. CCK-PZ
20. PTH
21. CT
22. Renin
23. Angiotensin

AA/Protein/Peptide Hormones

All work thru 2^{d} messengers:

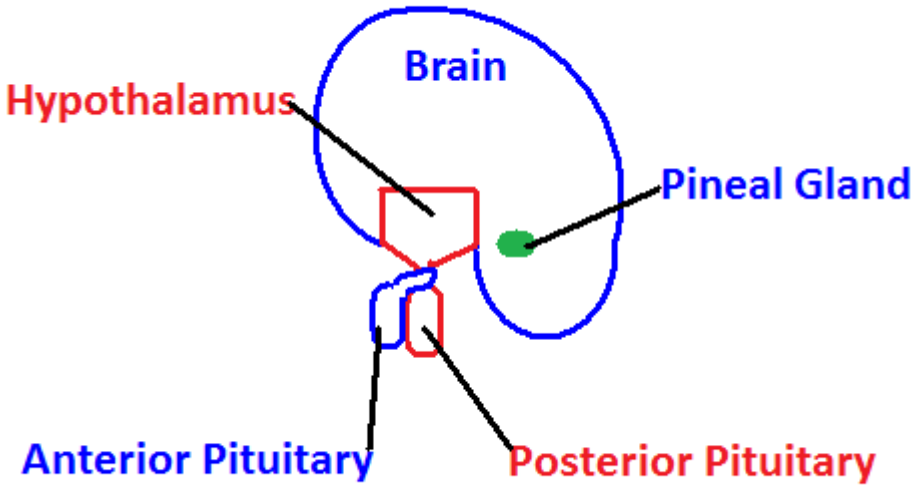
1. cAMP
2. IP_3
3. Or BOTH depending on function, e.g., AVP and cAMP in kidney and IP_3 in liver

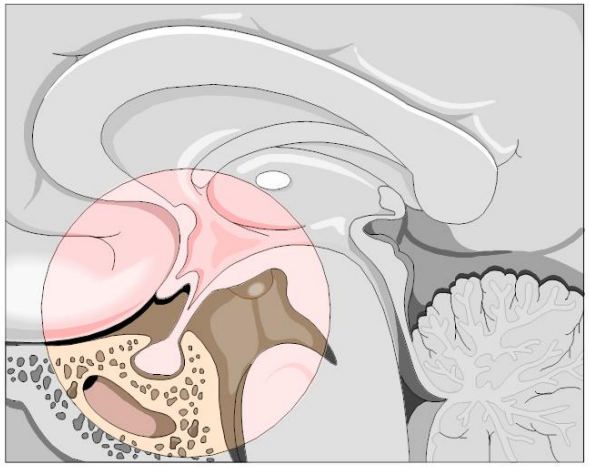
Overview of Hormones Without Second Messengers

1. Testosterone
2. Cortisol
3. Aldosterone
4. Estrogens
5. Progesterone
6. Vitamin D

- All work through direct gene activation via an intra-nuclear receptor.

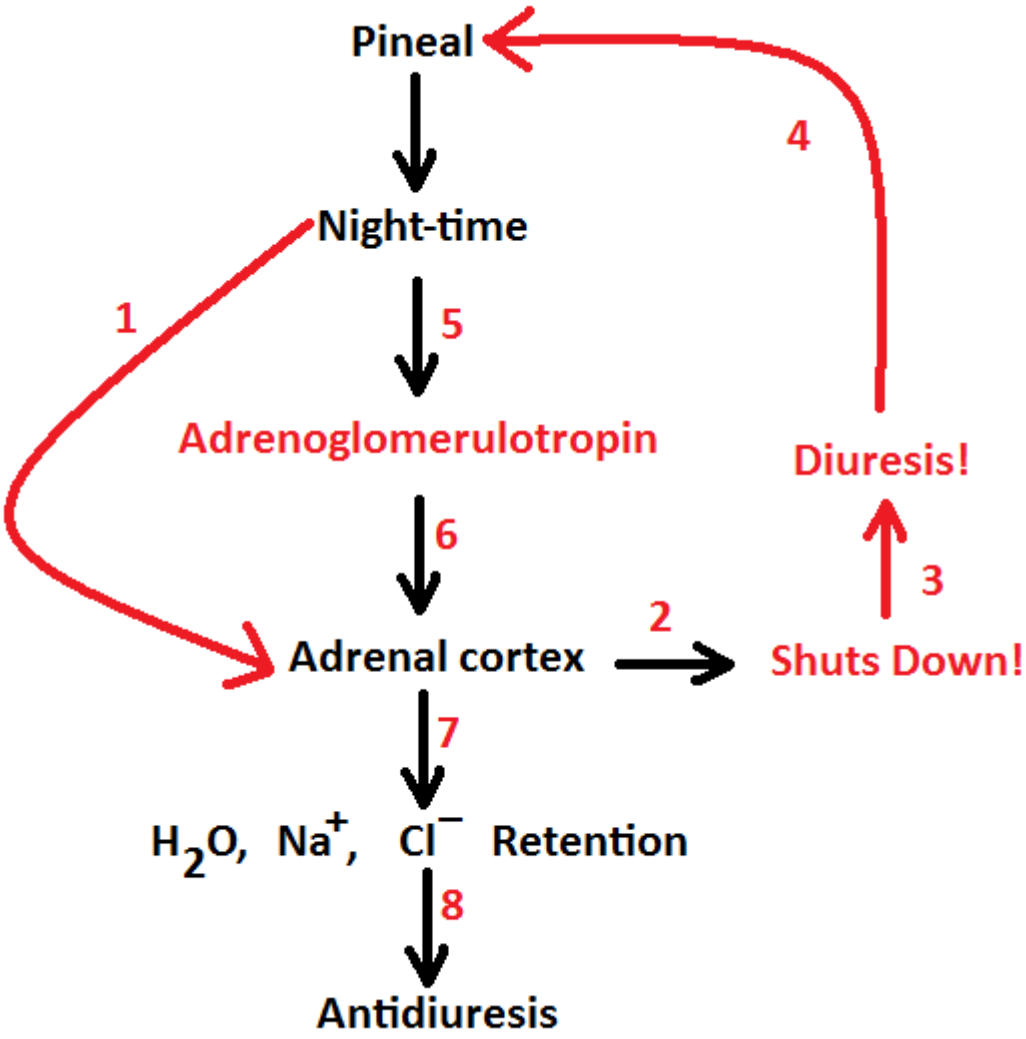
Overview



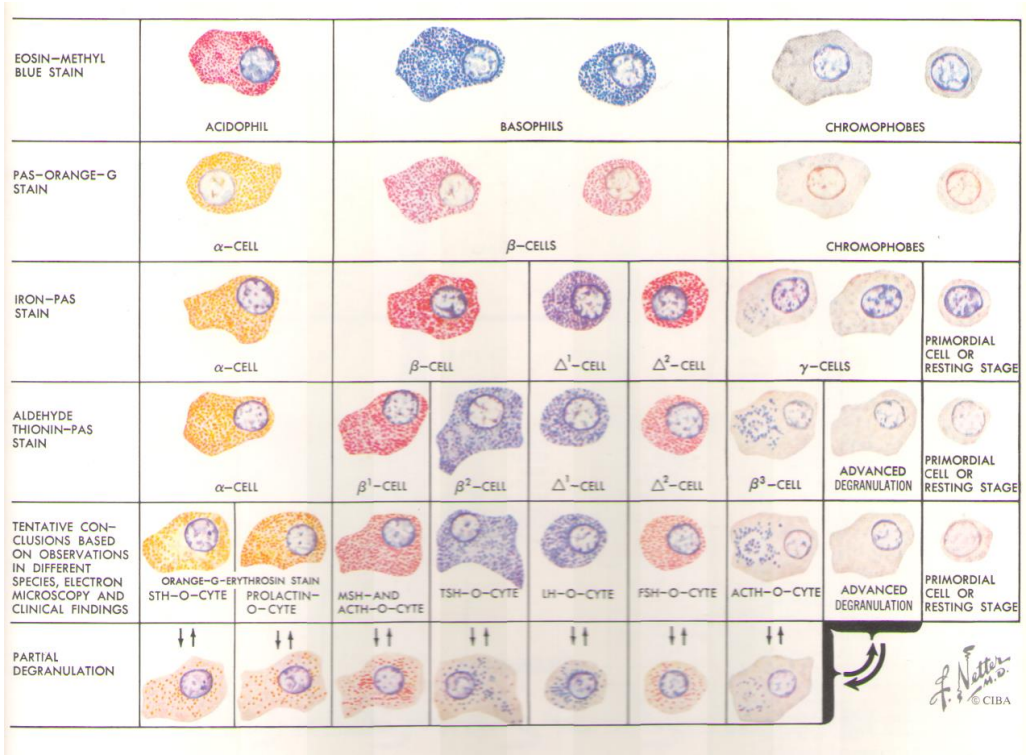


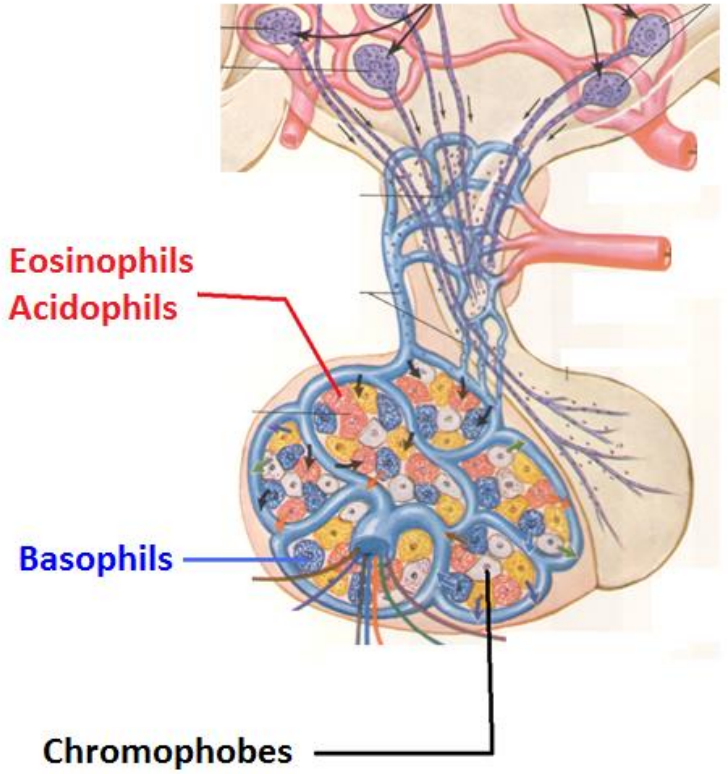
- Hypothalamus
- Releases “Releasing Factors/Hormones”
- Factors ≡ if we don’t know the structure or sequence
- Hormones ≡ if we know their sequences or structures

- Pineal Gland
- aka “Third Eye”
- Releases adrenoglomerulotropin
- Detects light


Pineal
Night-time
1
5
Adrenoglomerulotropin
6
Adrenal cortex
2
Shuts Down!
4
Diuresis!
3
7
H_2O, Na^+, Cl^- Retention
8
Antidiuresis

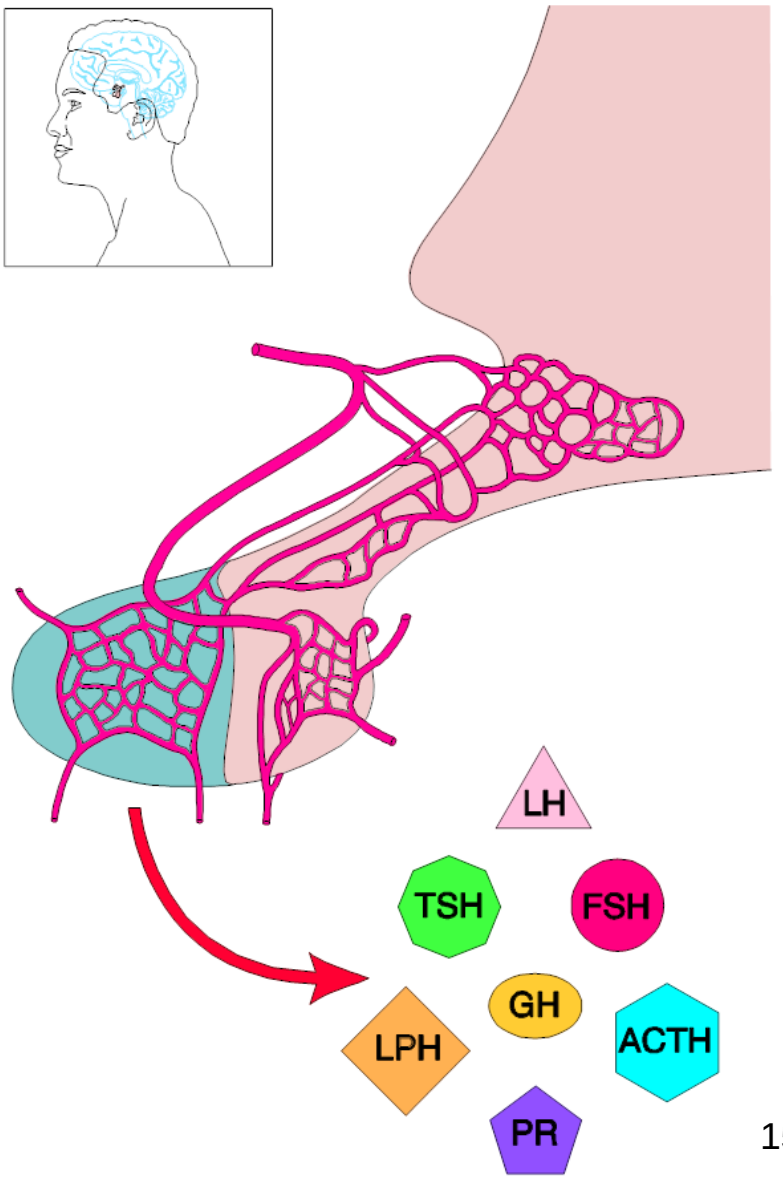
Cell Types in Anterior Pituitary





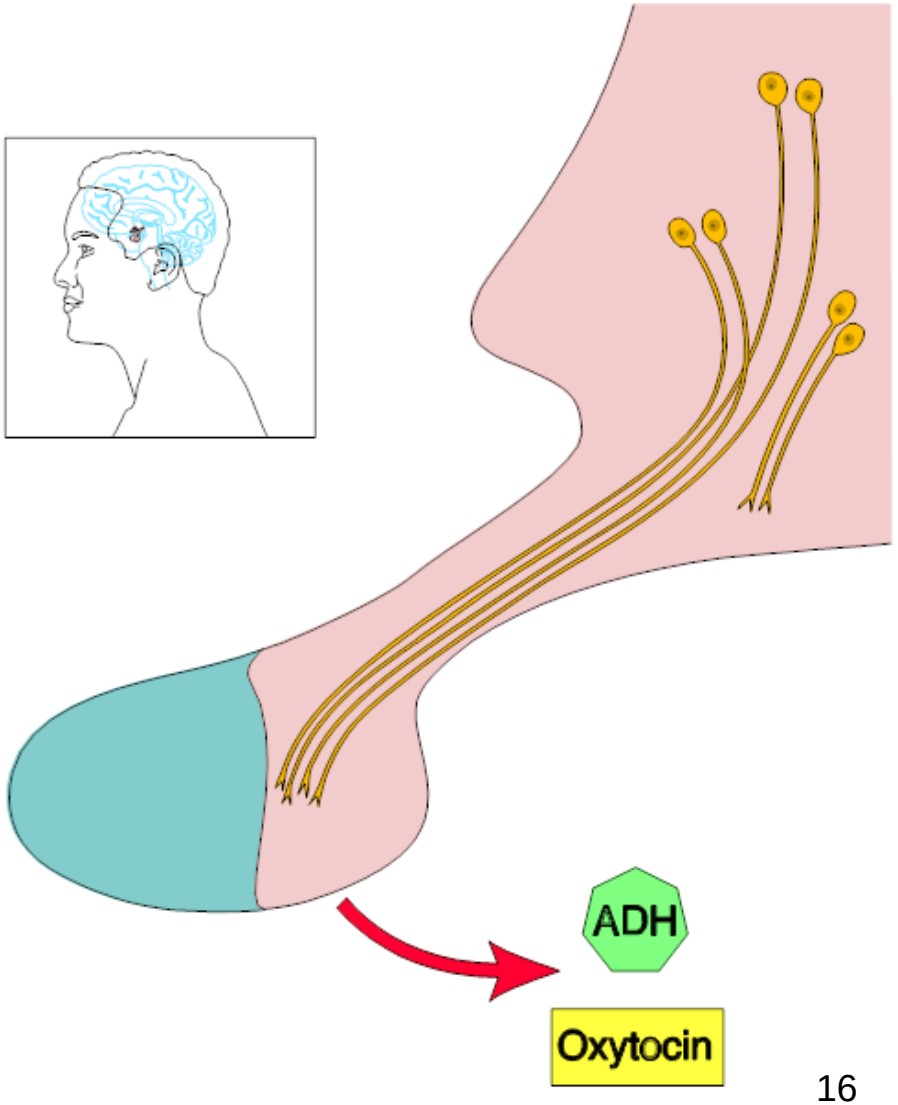
Anterior Pituitary Hormones

- Acidophilic Cell
  - GH
  - PRL
- Basophilic Cell
  - FSH
  - LH
  - TSH
- Chromophobic Cell
  - ACTH
  - LPH (lipotropin; lipid mobilizer in lipolysis and steroidogenesis)

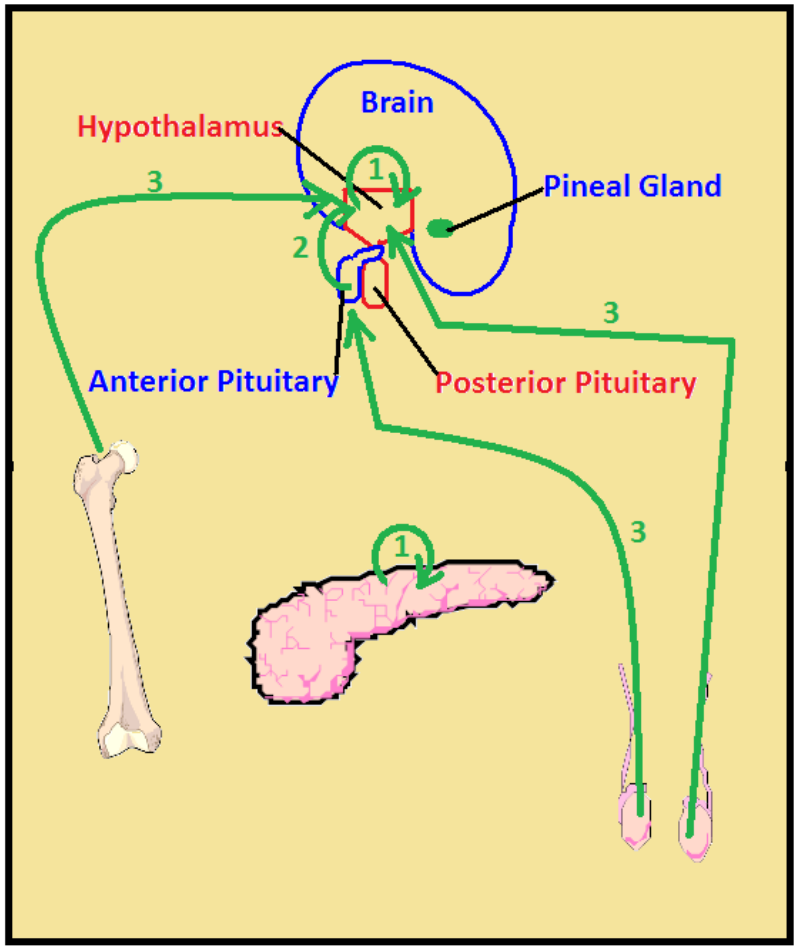


Posterior Pituitary Hormones

- ADH (AVP) (SON)
- OT (PVN)

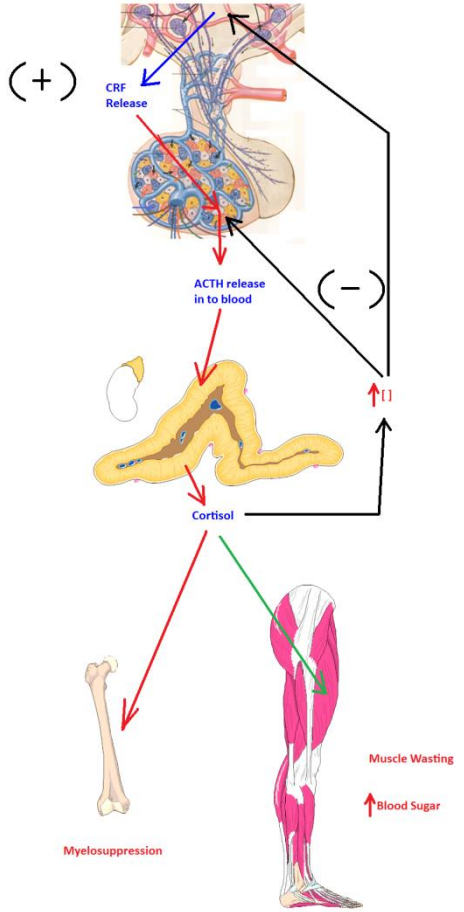


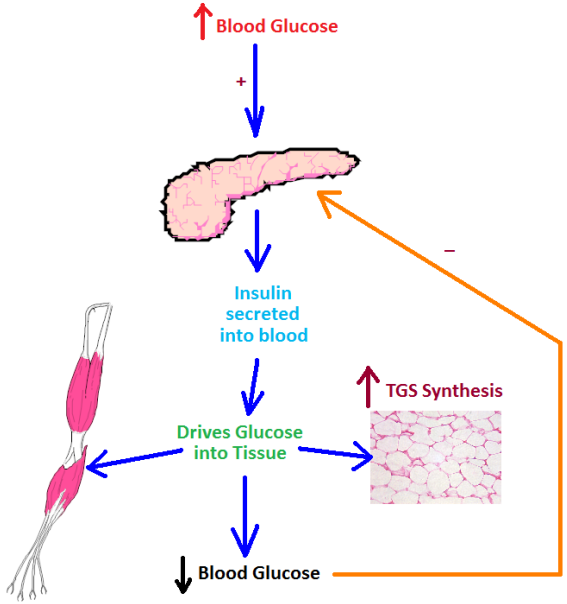
Feedback Regulation of Endocrine Function

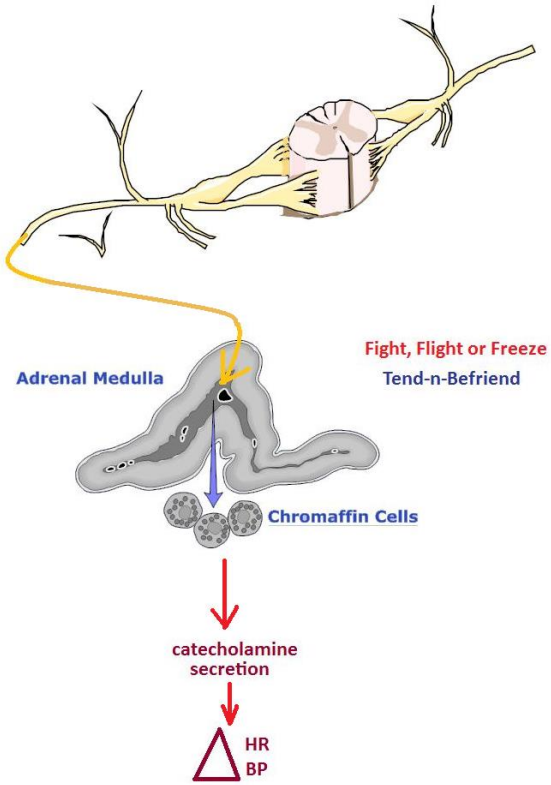


1. Self-feedback – ultra-short
2. Short
3. Long feedback

Hormonal, Humoral and Neural Stimulation of Endocrine Glands



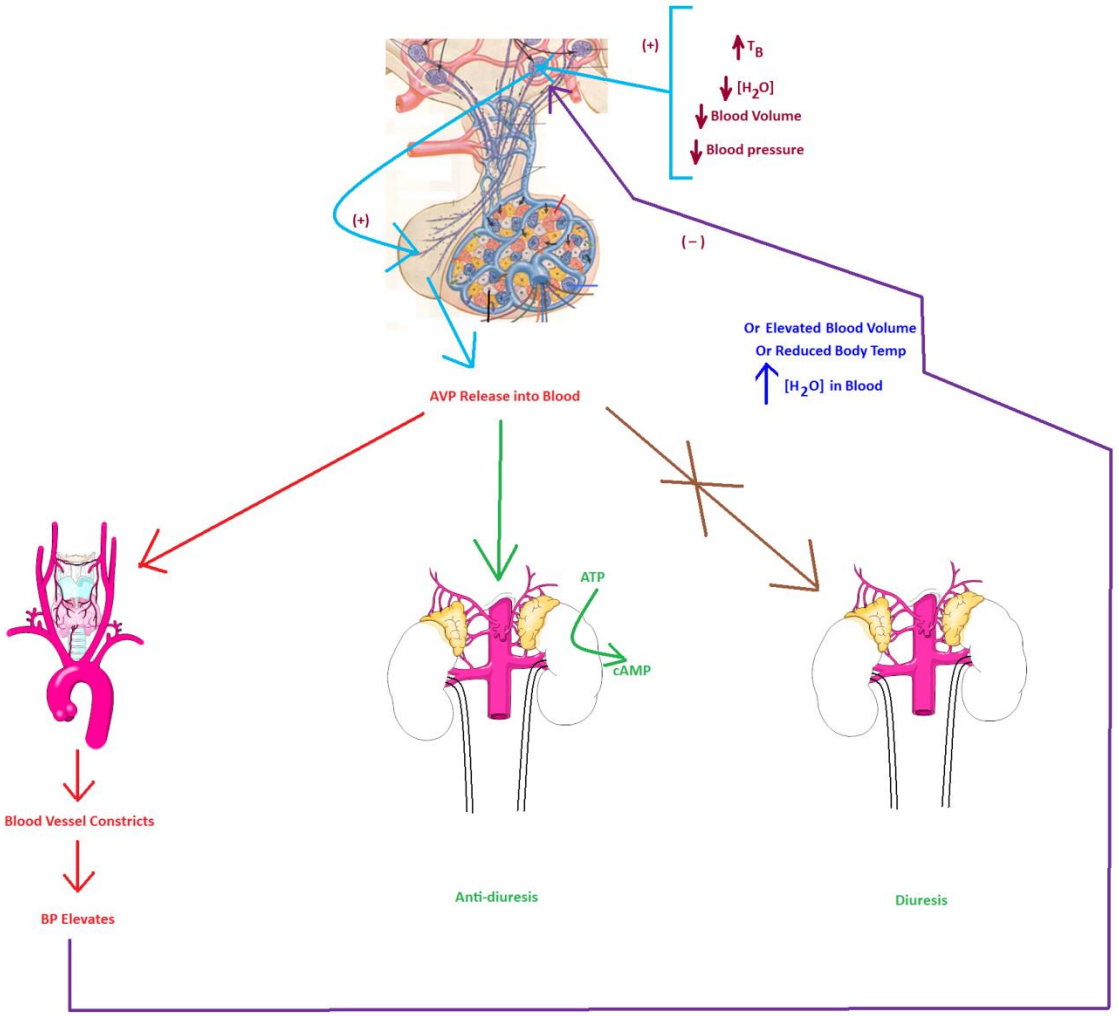




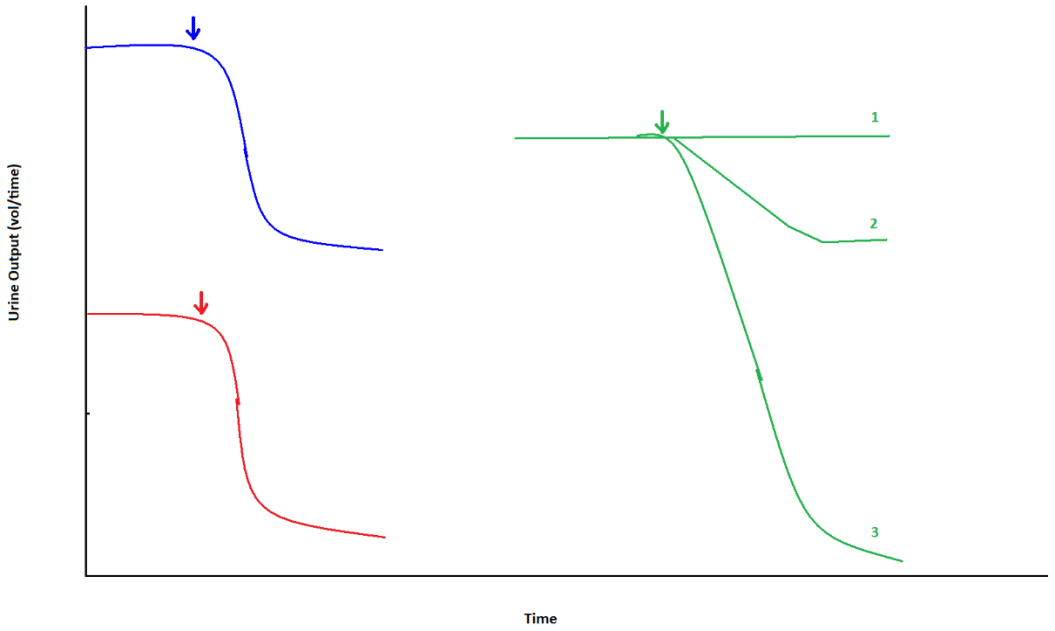
Hormone Functions

The Nuts and Bolts

Arginine Vasopressin – or Antidiuretic Hormone = AVP or ADH

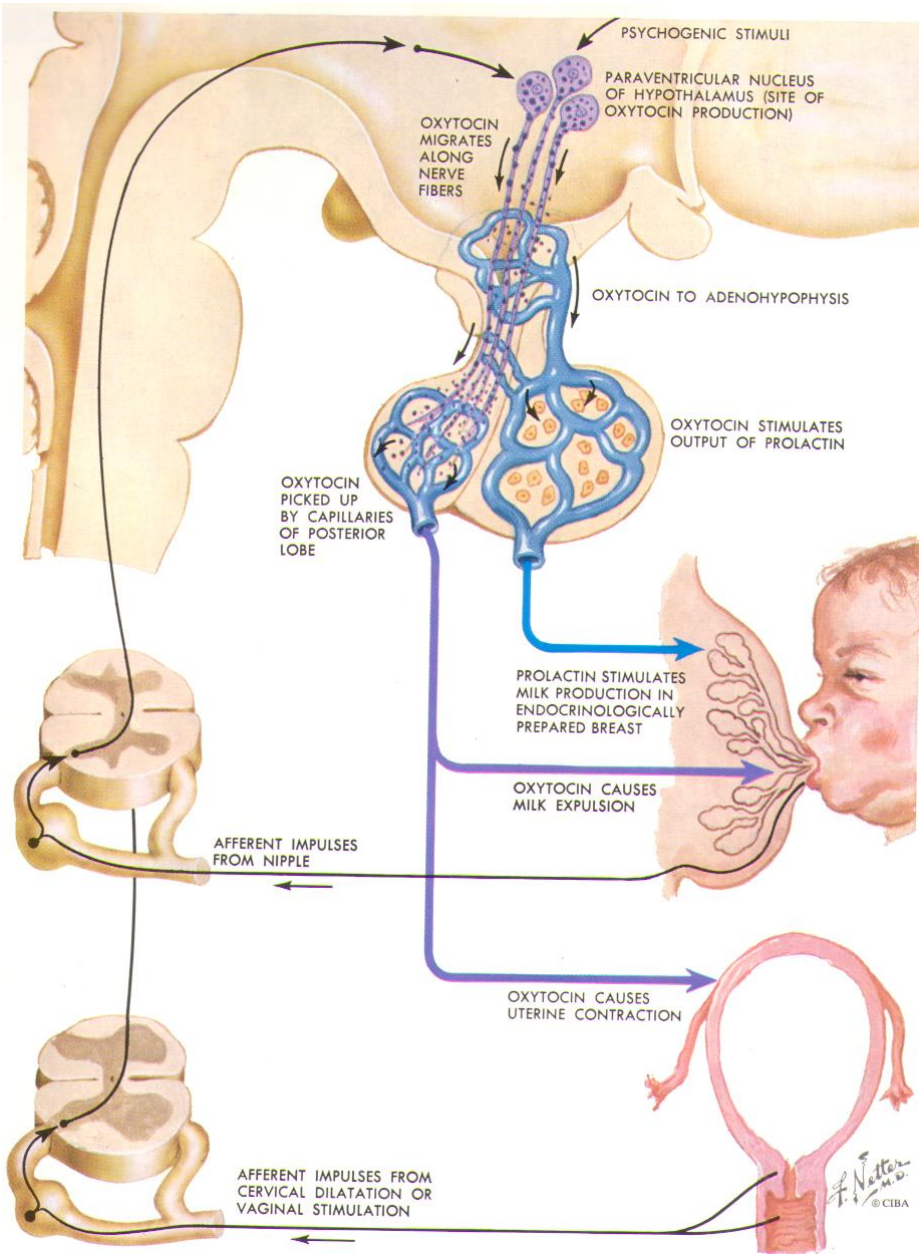


Diabetes Insipidus – an AVP Anomaly



- ↓ -- 3% saline; normal response = osmoreceptors cause AVP release
- ↓ -- Nicotine; osmoreceptor failure = nicotine causes increased secretion and synthesis of AVP
- ↓ -- ① AVP – nephrogenic Diabetes insipidus – no receptors present
- ↓ -- ② AVP – drinks excessive water
- ↓ -- ③ -- no AVP endogenously – has receptors, but posterior pituitary is not releasing AVP and SON isn't synthesizing it

Oxytocin -- OT


PSYCHOGENIC STIMULI
PARAVENTRICULAR NUCLEUS OF HYPOTHALAMUS (SITE OF OXYTOCIN PRODUCTION)
OXYTOCIN MIGRATES ALONG NERVE FIBERS
OXYTOCIN TO ADENOHYPOPHYSIS
OXYTOCIN STIMULATES OUTPUT OF PROLACTIN
OXYTOCIN PICKED UP BY CAPILLARIES OF POSTERIOR LOBE
PROLACTIN STIMULATES MILK PRODUCTION IN ENDOCRINOLOGICALLY PREPARED BREAST
OXYTOCIN CAUSES MILK EXPULSION
AFFERENT IMPULSES FROM NIPPLE
OXYTOCIN CAUSES UTERINE CONTRACTION
AFFERENT IMPULSES FROM CERVICAL DILATATION OR VAGINAL STIMULATION
F. Netter M.D.
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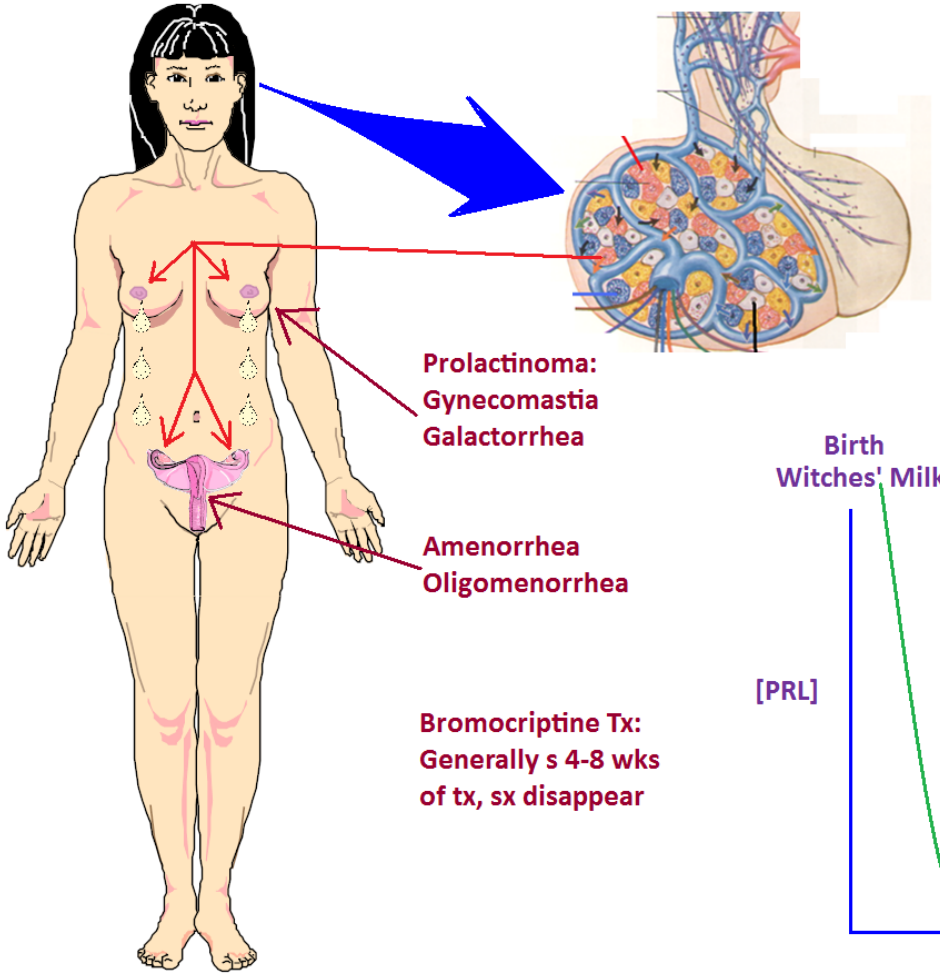
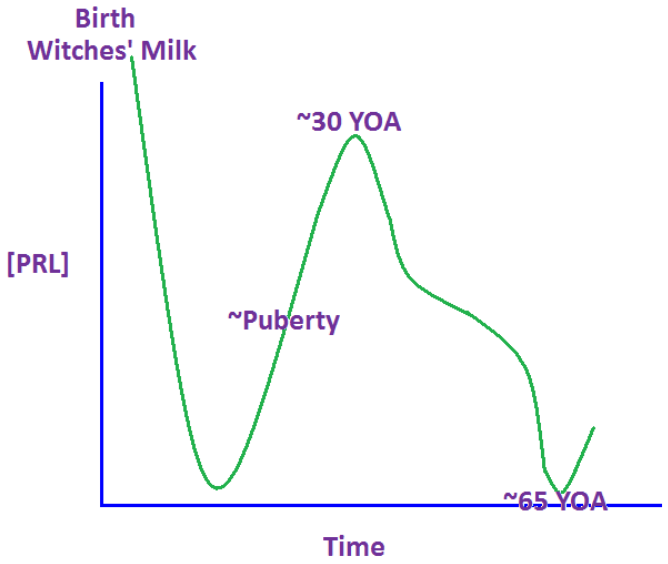
Prolactin -- PRL



Prolactinoma:
Gynecomastia
Galactorrhea

Amenorrhea
Oligomenorrhea

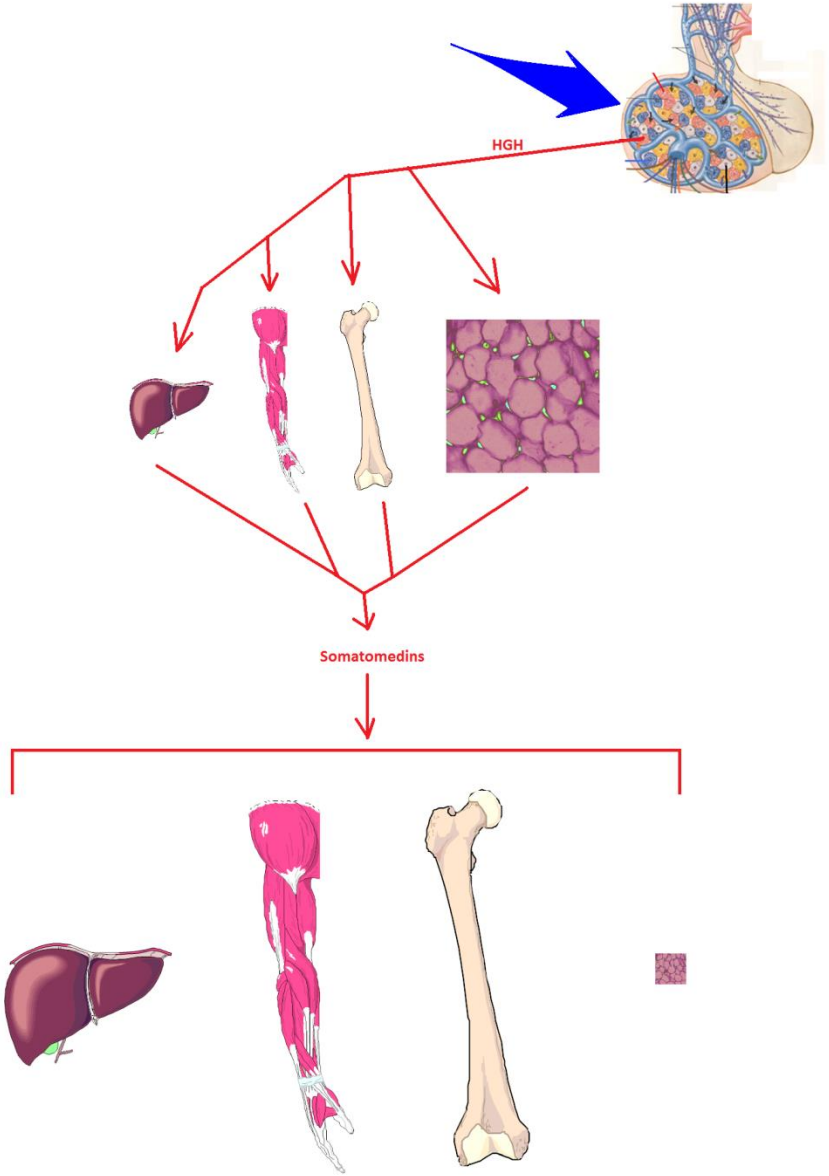
Bromocriptine Tx:
Generally s 4-8 wks
of tx, sx disappear



"Breast feeding -- Fertility -- Amenorrhea"

NOT Reliable!

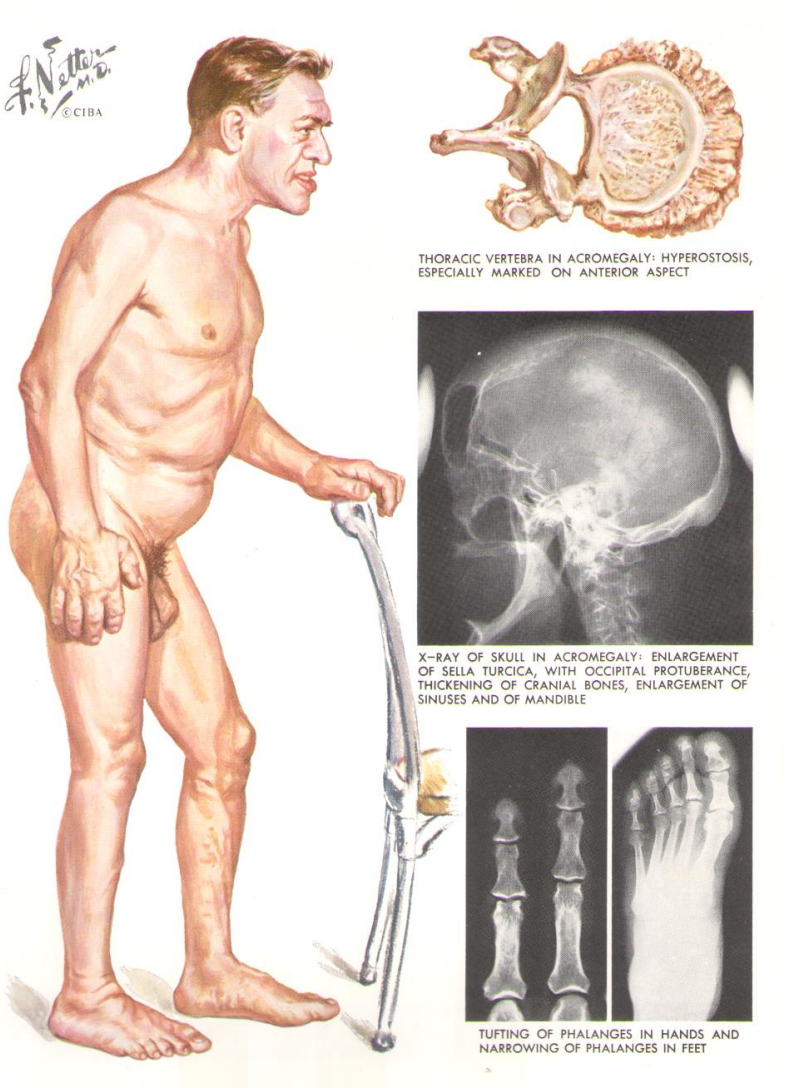
Growth Hormone -- Somatotropin

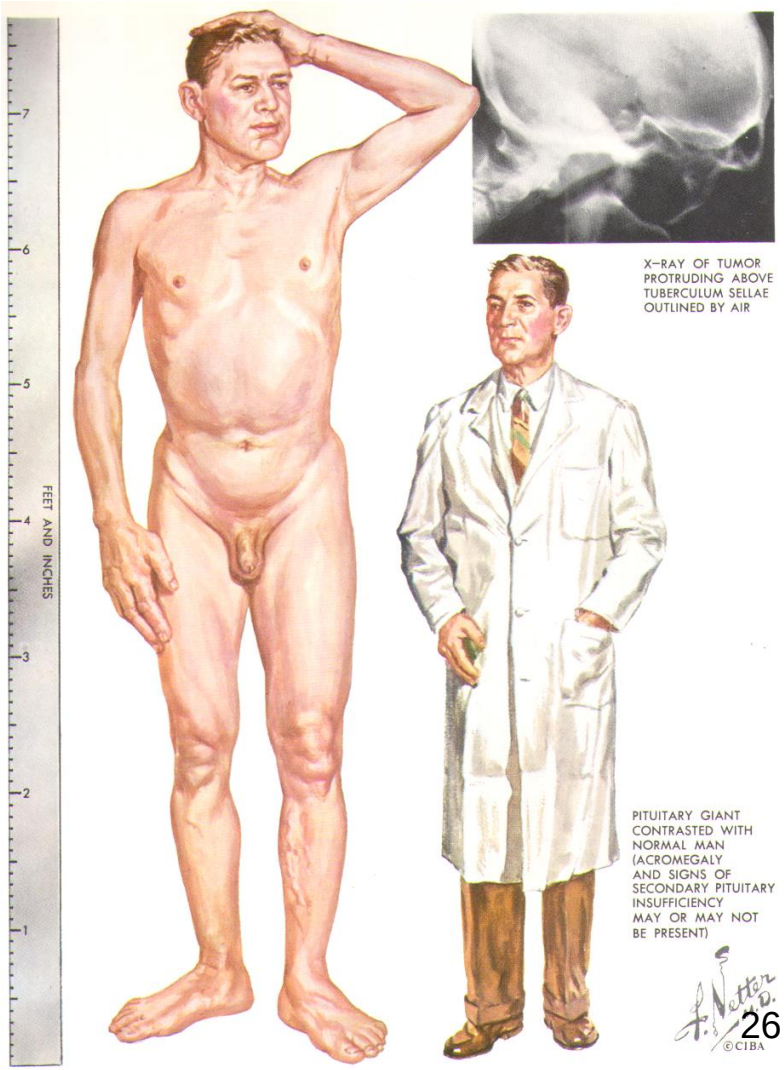


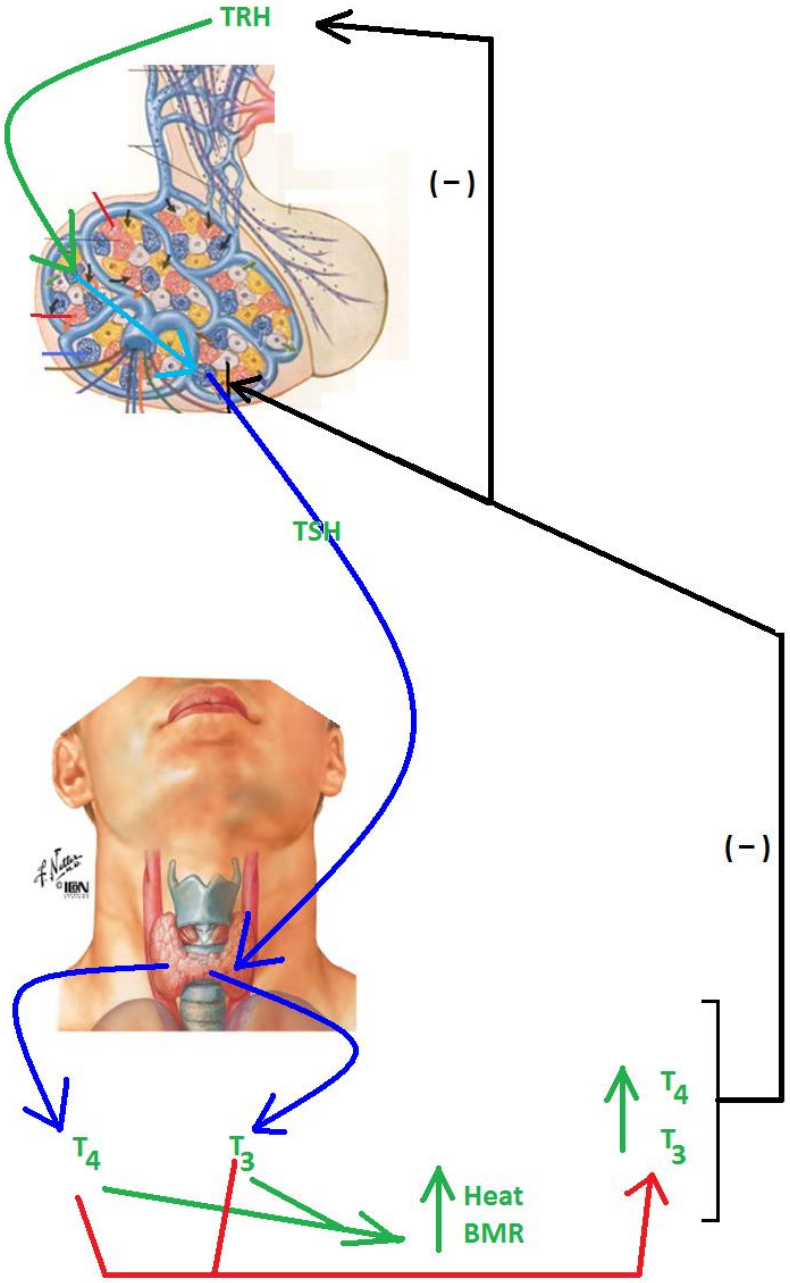
GH Anomalies

Gigantism	Acromegaly
In youth	In mature people
Epiphyseal plates still growing	Epiphyseal plates sealed
Linear growth	“splaying” growth
Tall	Organomegaly
May OR may not have acromegalic features	Hyperostosis – vertebra, phalangeal tufts, skull
May OR may not have signs of secondary pituitary insufficiency	

Acromegaly v Giantism



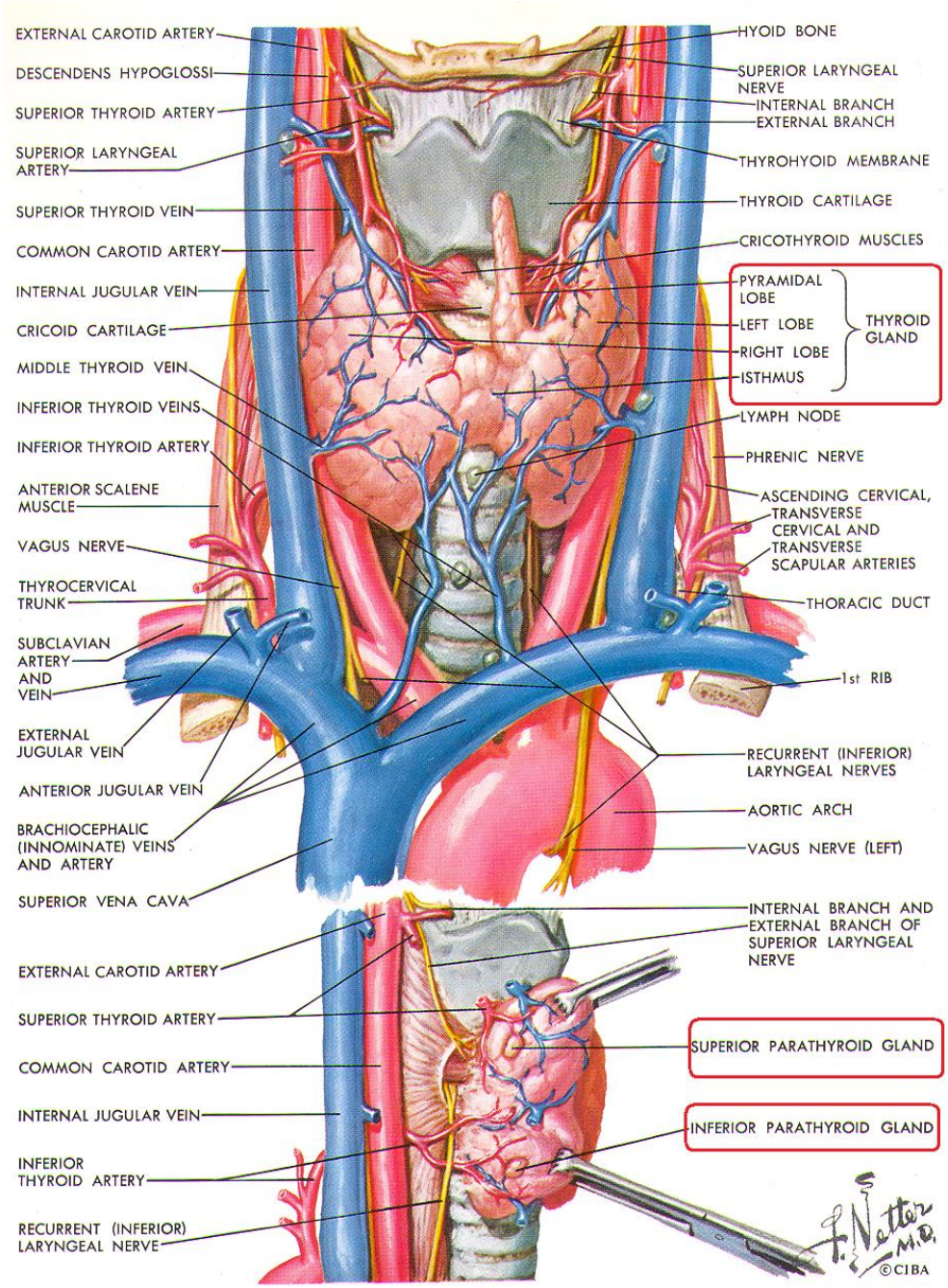




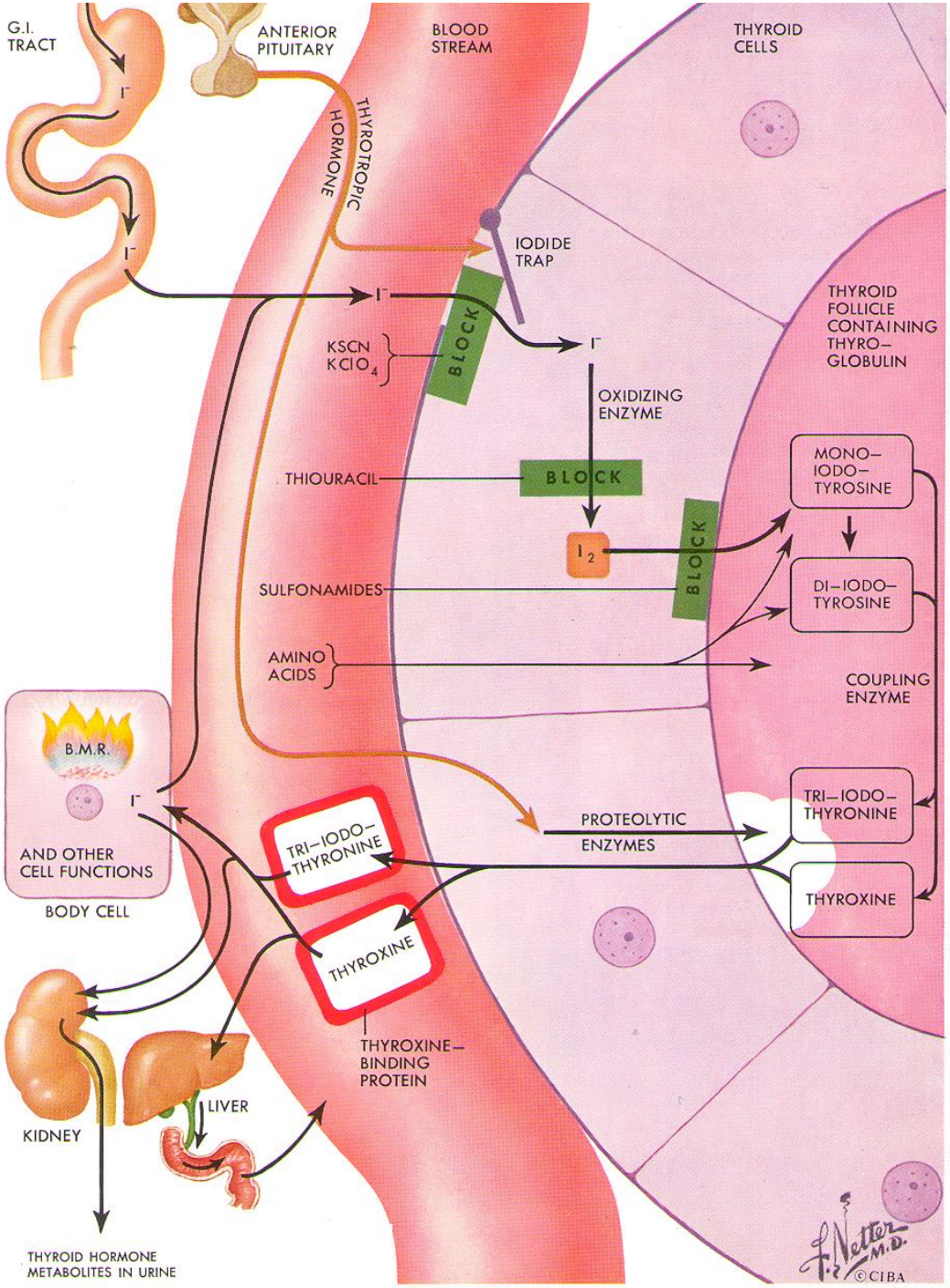
Thyrotropin Releasing Hormone -- TRH

- T_3 has 100X the activity of T_4
- T_4 activates > 180 ATP-requiring enzymes

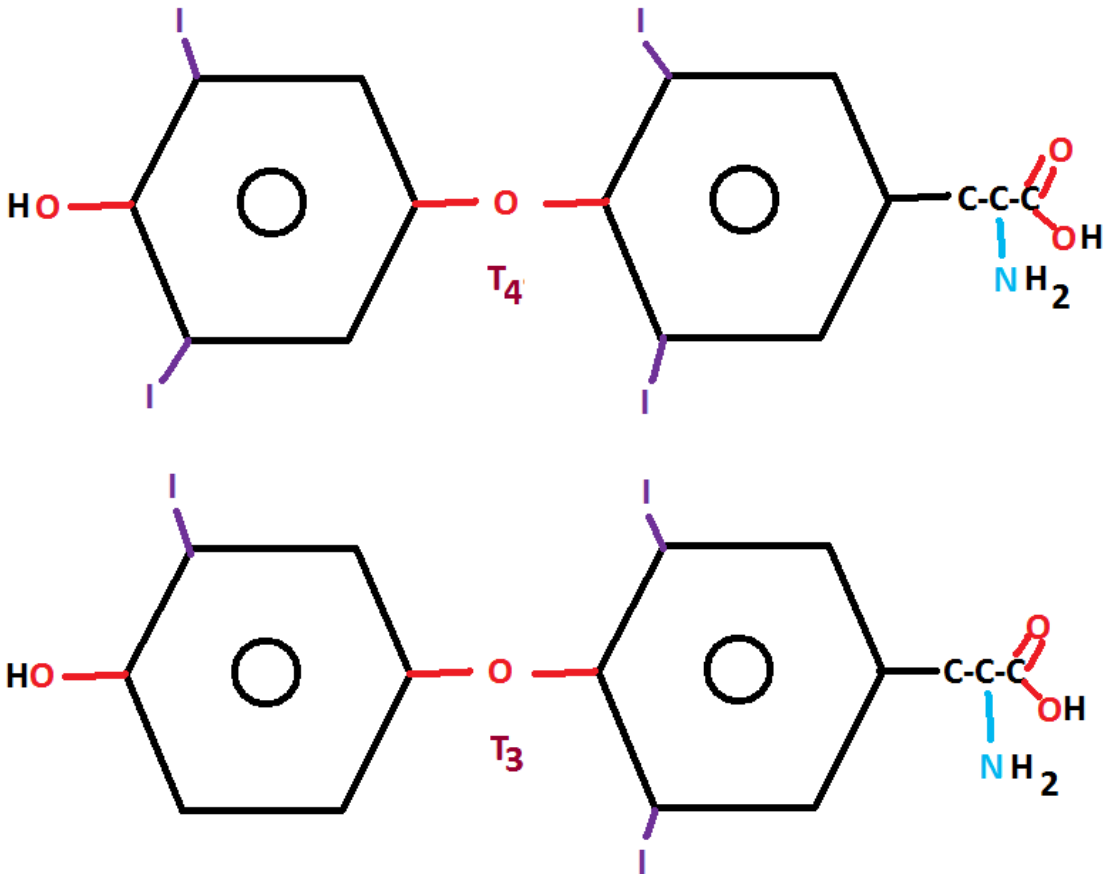
Thyroid Gland – Superficial Anatomy



T_3 and T_4 Biosynthesis



Biochemistry of T_3 and T_4



- Are aromatic ethers, hence, require binding proteins for transport in blood

T_4 Needs are Temperature Dependent

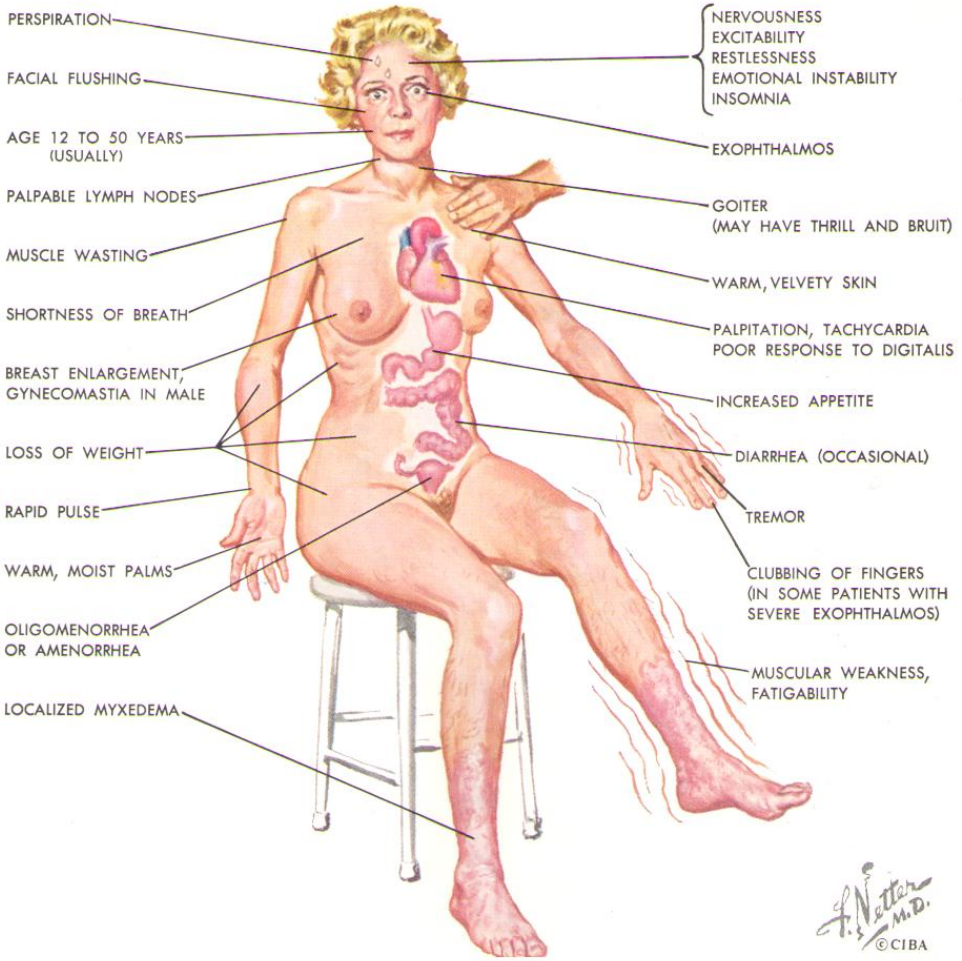
1. At 35°C, need 1.7 μg per day
2. At 25°C, need 5.2 μg per day
3. At 1°C, need 9.5 μg per day

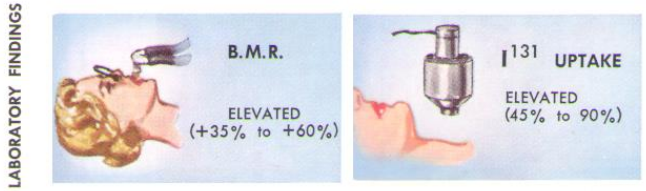
Cold is stimulating to the pituitary to release TSH to increase T_4 output.

This is data from 1943 – and remains undisputed.

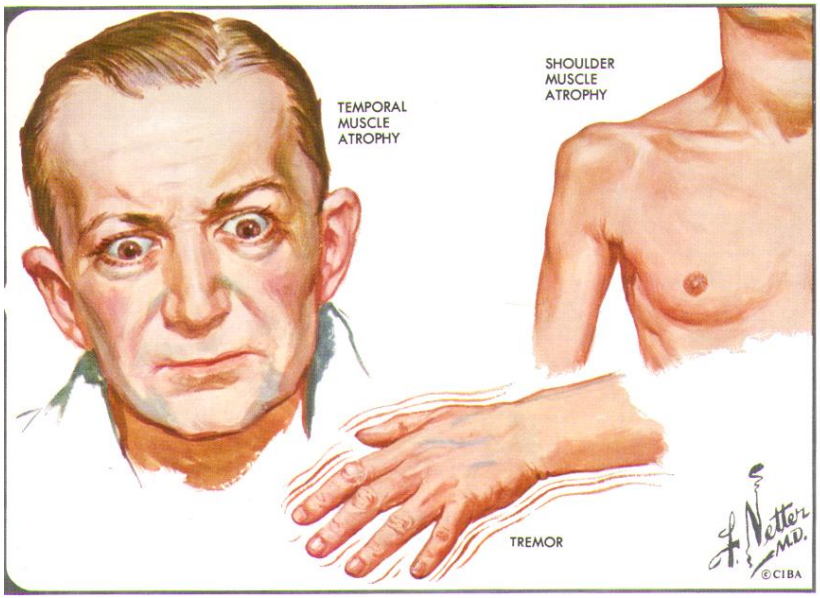
Thyroid Abnormalities

Graves' Disease -- 1



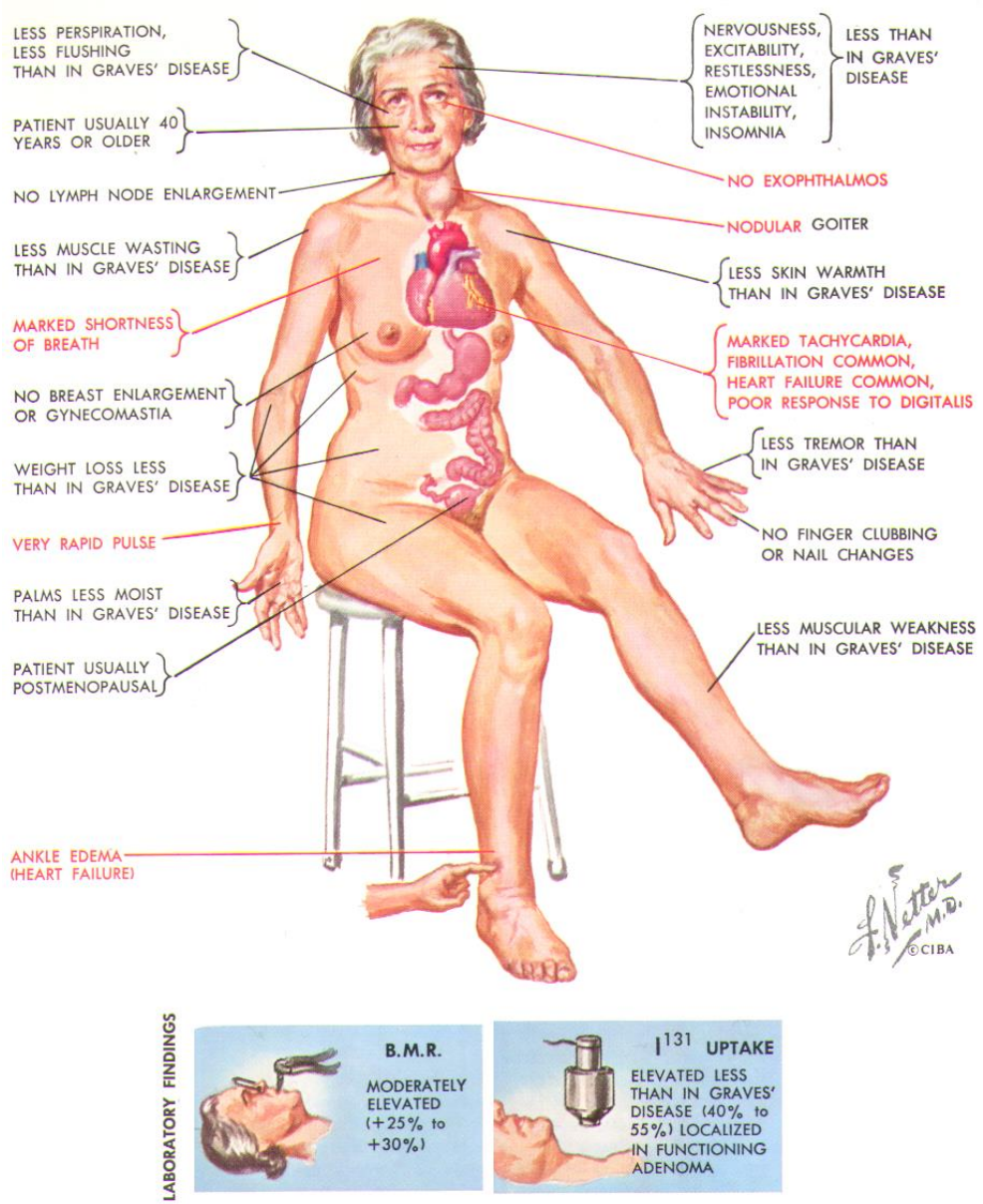


Graves' Disease -- 2



Sometimes the tremor is so "fine" that a piece of paper is needed to detect the tremor.

Hyperthyroidism: Thyroid Adenoma

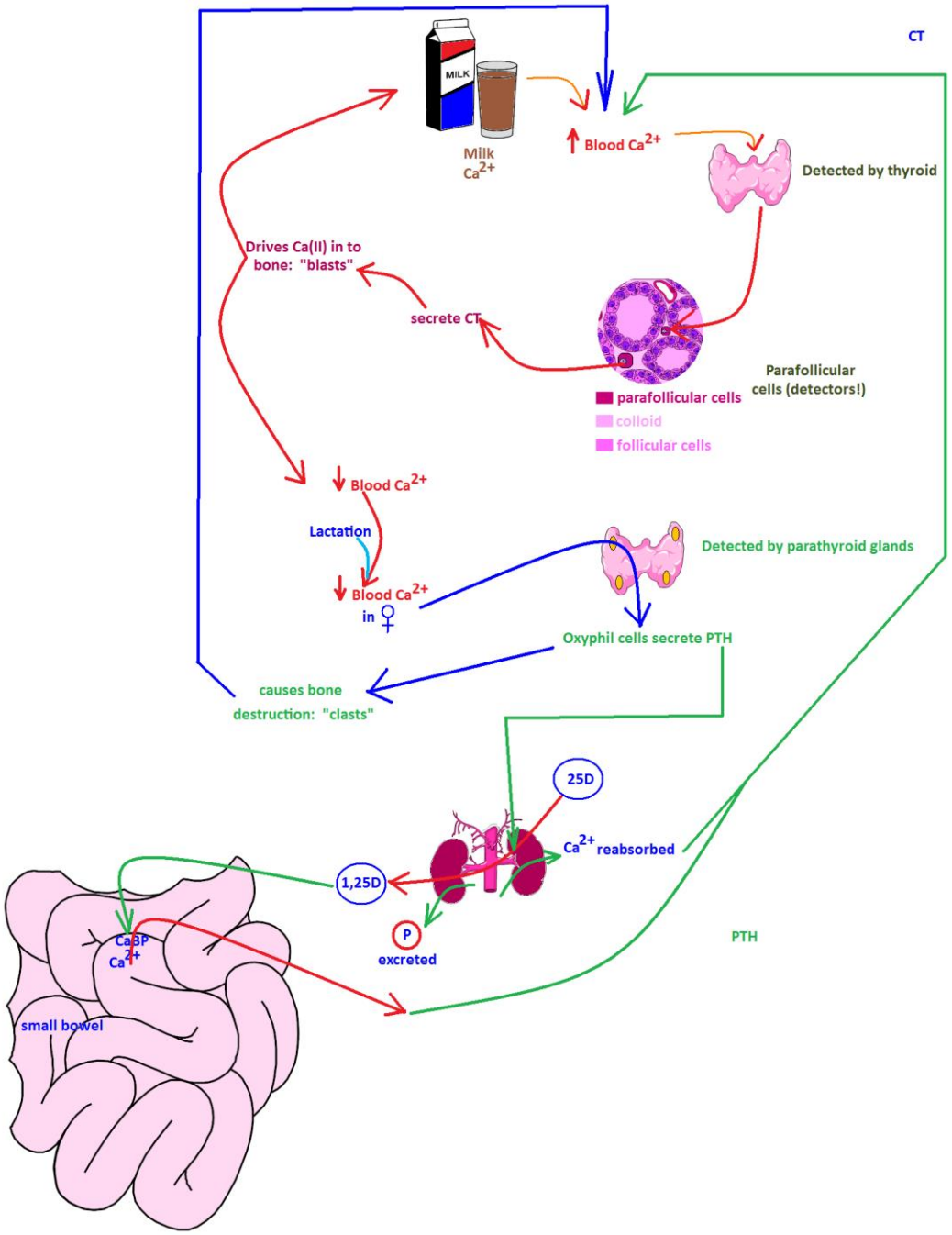


HypOthyroidism -- Cretinism

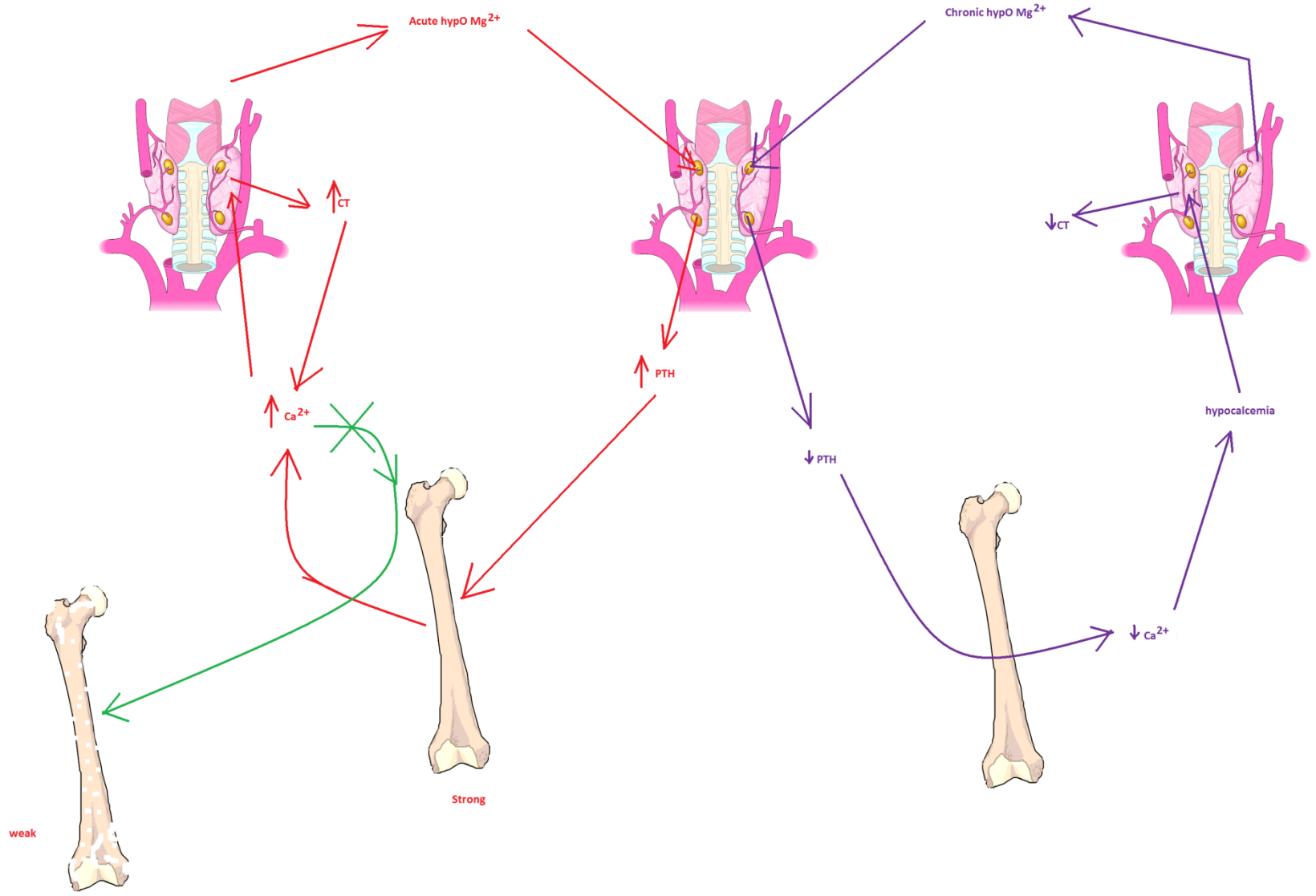
Myxedema

1. Thickening and puffiness of the skin and SQ, particularly of the face and extremities. Skin is dry and coarse. Characteristic expressionless or mask-like facies.
2. Came from an earlier belief that it was 2° mucus accumulation in tissues.
3. DOES contain mucin, a mucopolysaccharide that is highly ionized with huge osmotic activity that drags water into the tissues.
4. May be athyrotic; may be goitrous
5. Round face; extruded tongue; heavy set; short stature

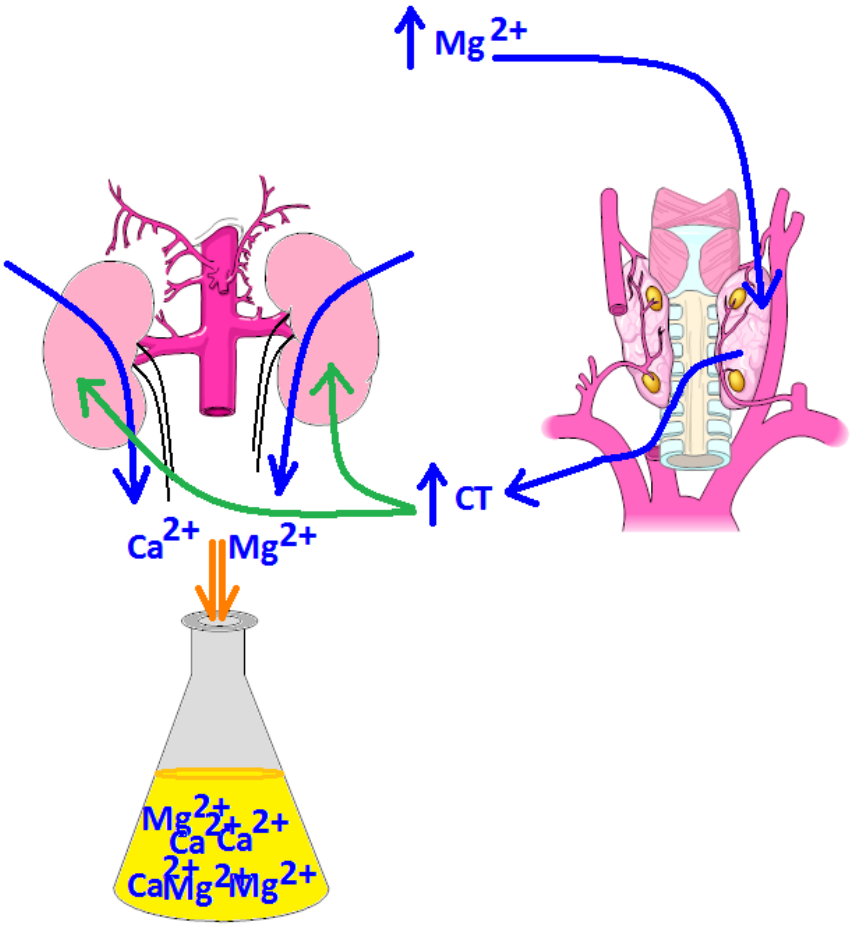
Calcitonin (CT) and Parathormone (PTH)



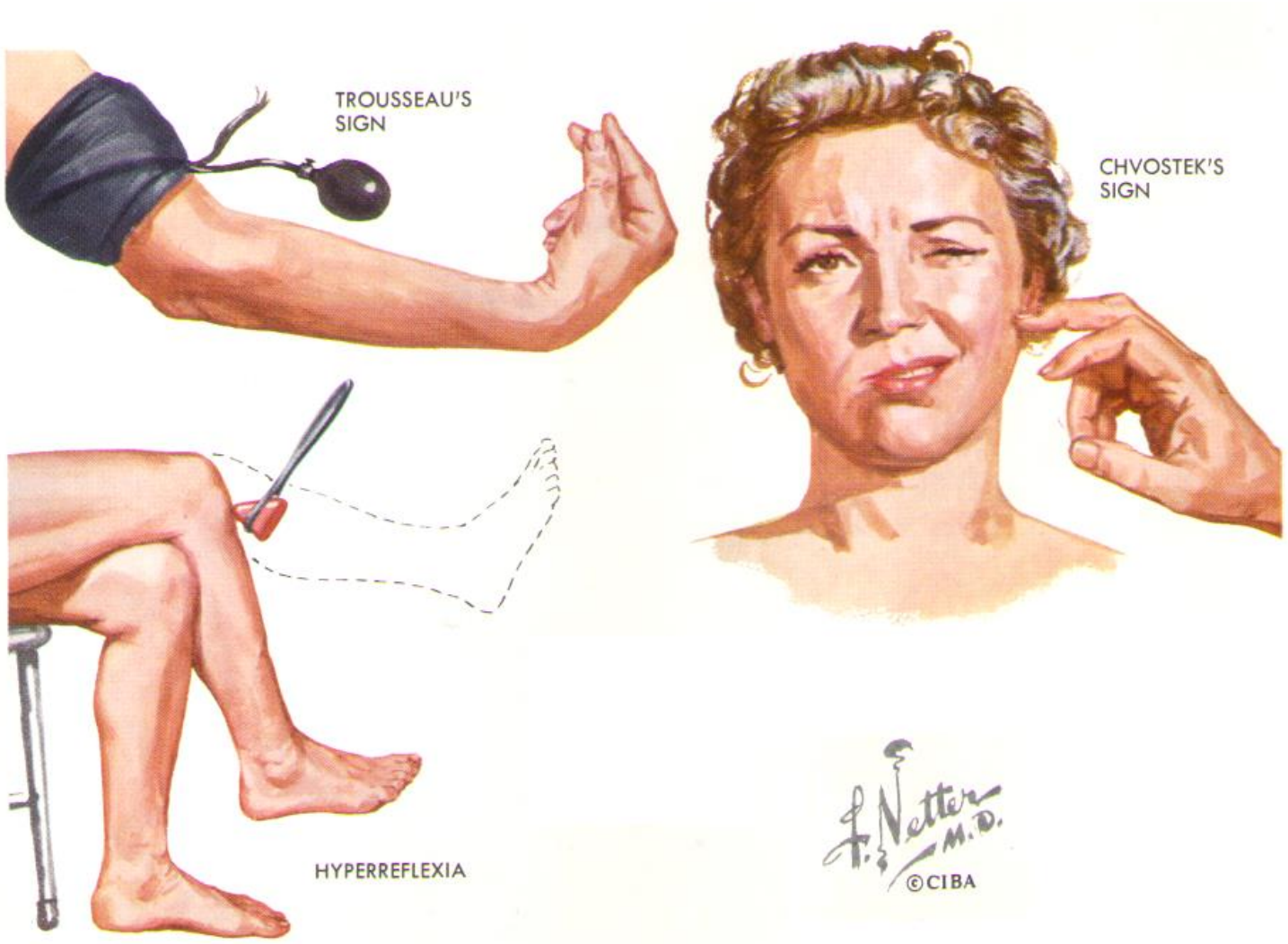
HypOmagnesemia



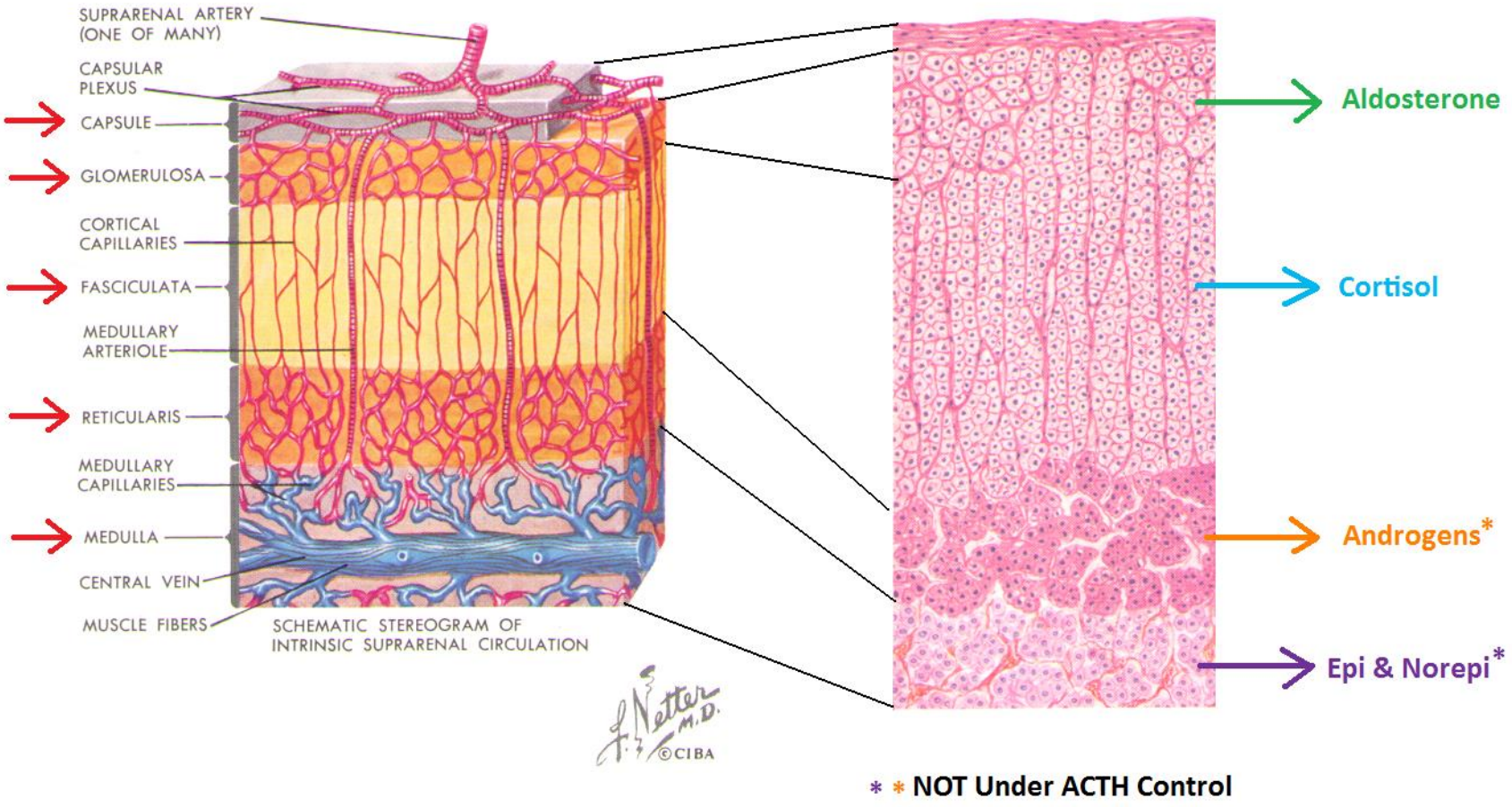
HypERmagnesemia



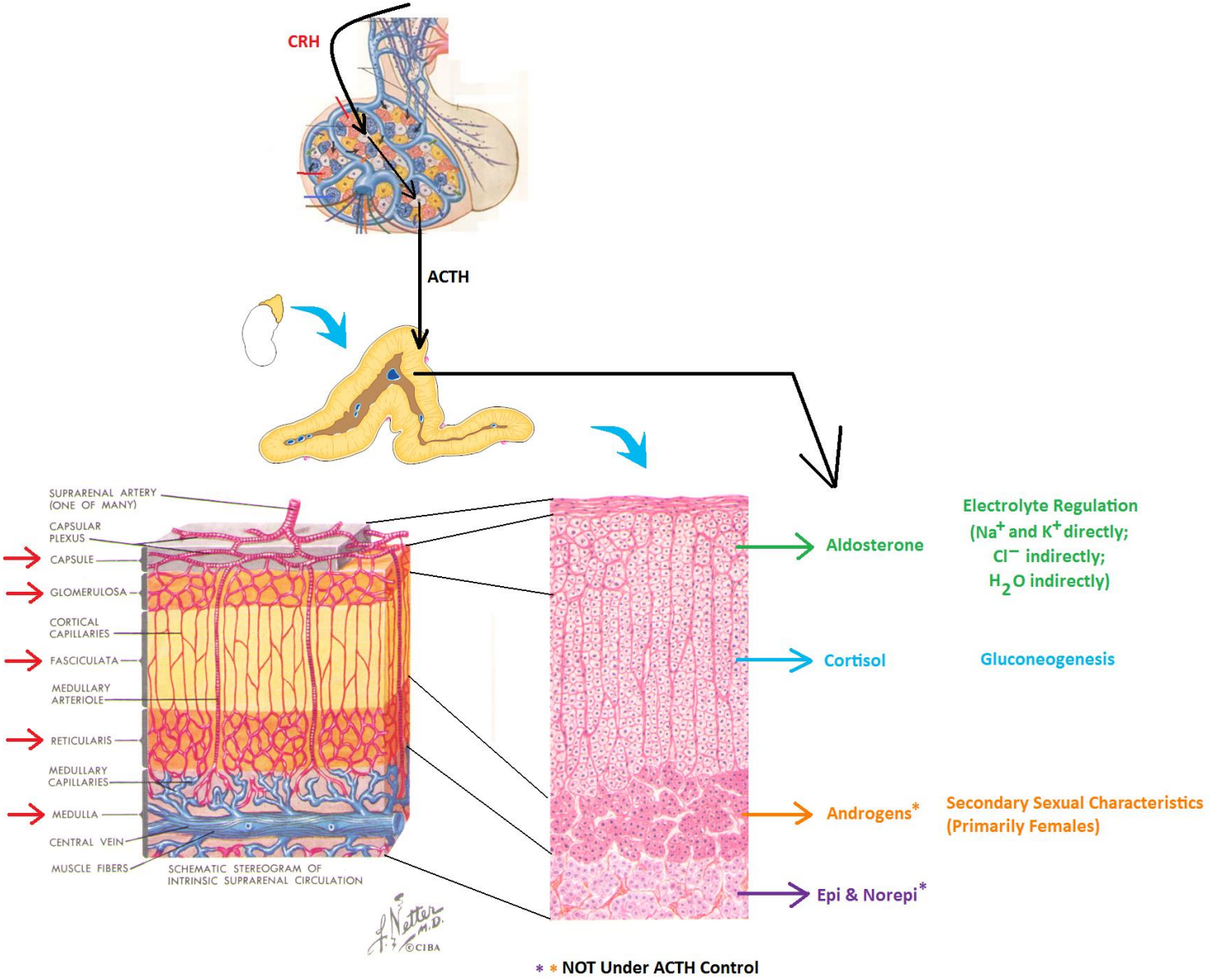
Acute HypOcalcemia



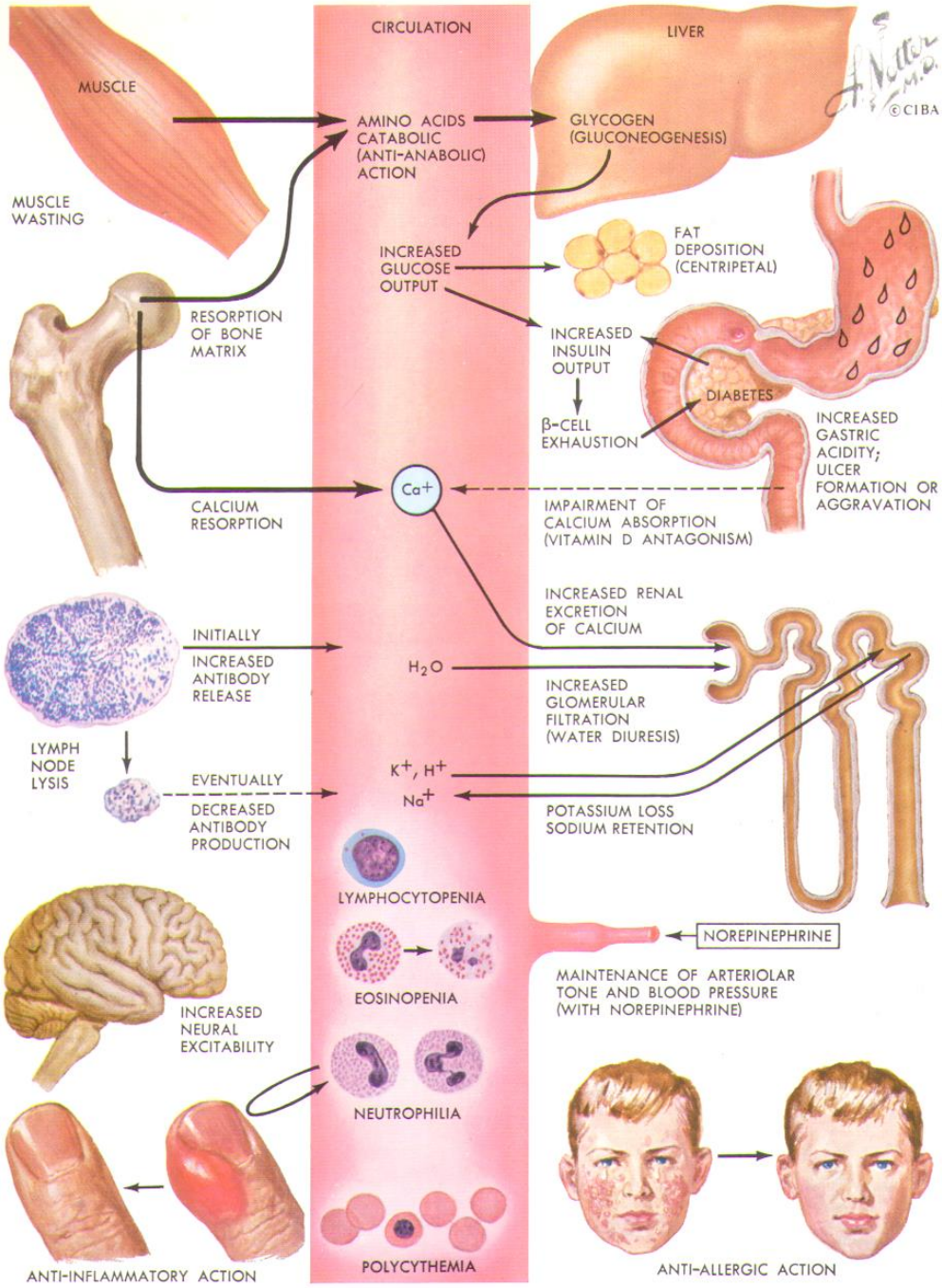
Adrenal Cortex



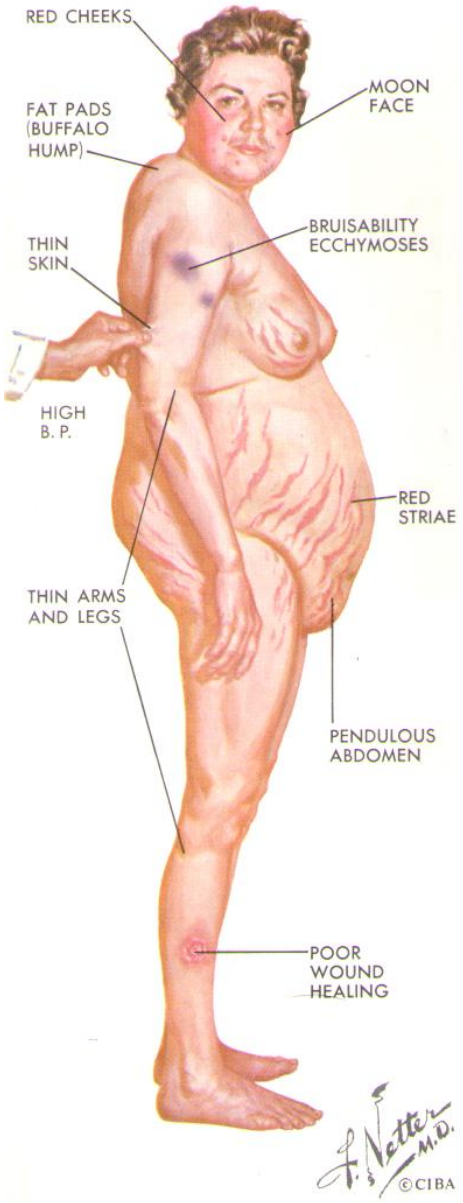
Adrenocorticotropic Hormone (ACTH)



Cortisol


CIRCULATION
LIVER
MUSCLE
AMINO ACIDS
CATABOLIC
(ANTI-ANABOLIC)
ACTION
GLYCOGEN
(GLUCONEOGENESIS)
©CIBA
MUSCLE
WASTING
INCREASED
GLUCOSE
OUTPUT
FAT
DEPOSITION
(CENTRIPETAL)
RESORPTION
OF BONE
MATRIX
INCREASED
INSULIN
OUTPUT
DIABETES
β-CELL
EXHAUSTION
INCREASED
GASTRIC
ACIDITY;
ULCER
FORMATION OR
AGGRAVATION
Ca+
CALCIUM
RESORPTION
IMPAIRMENT OF
CALCIUM ABSORPTION
(VITAMIN D ANTAGONISM)
INCREASED RENAL
EXCRETION
OF CALCIUM
INITIALLY
INCREASED
ANTIBODY
RELEASE
H2O
INCREASED
GLOMERULAR
FILTRATION
(WATER DIURESIS)
LYMPH
NODE
LYSIS
EVENTUALLY
DECREASED
ANTIBODY
PRODUCTION
K+, H+
Na+
POTASSIUM LOSS
SODIUM RETENTION
LYMPHOCYTOPENIA
NOREPINEPHRINE
EOSINOPENIA
MAINTENANCE OF ARTERIOLAR
TONE AND BLOOD PRESSURE
(WITH NOREPINEPHRINE)
INCREASED
NEURAL
EXCITABILITY
NEUTROPHILIA
POLYCYTHEMIA
ANTI-INFLAMMATORY ACTION
ANTI-ALLERGIC ACTION

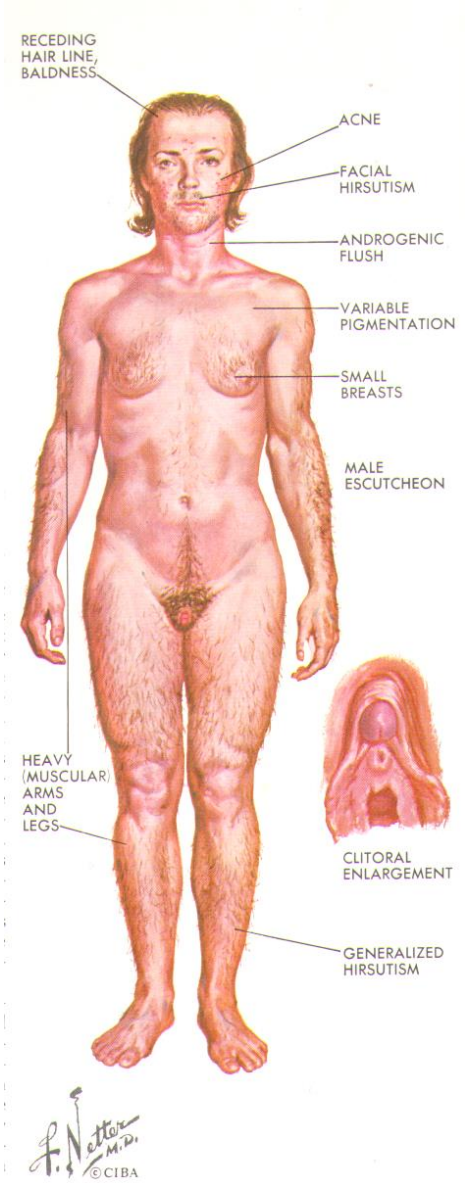
Cushing's Syndrome



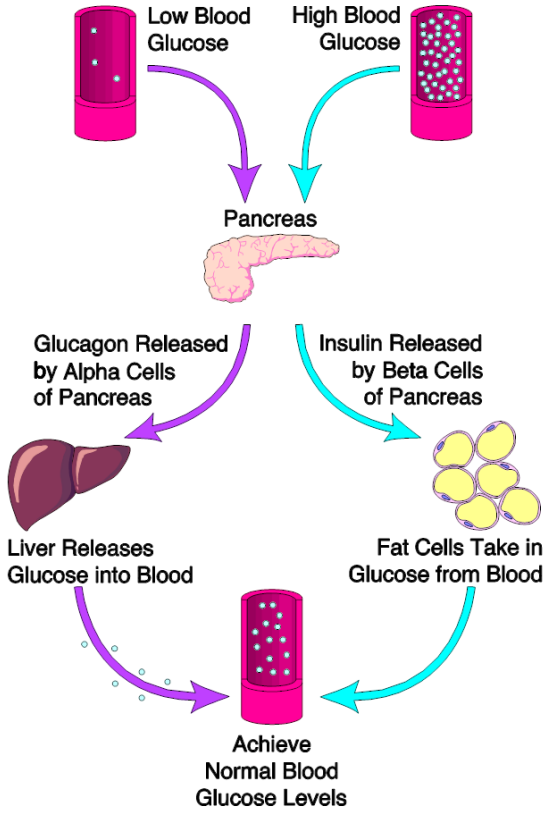
- Depression/psychoses
- Mood alterations
- Cataracts
- Moon-face
- Hirsutism
- Hypertension with secondary cardiomegaly
- Elevated glucose
- Muscle weakness
- Osteoporosis/necrosis
- Peptic ulcer

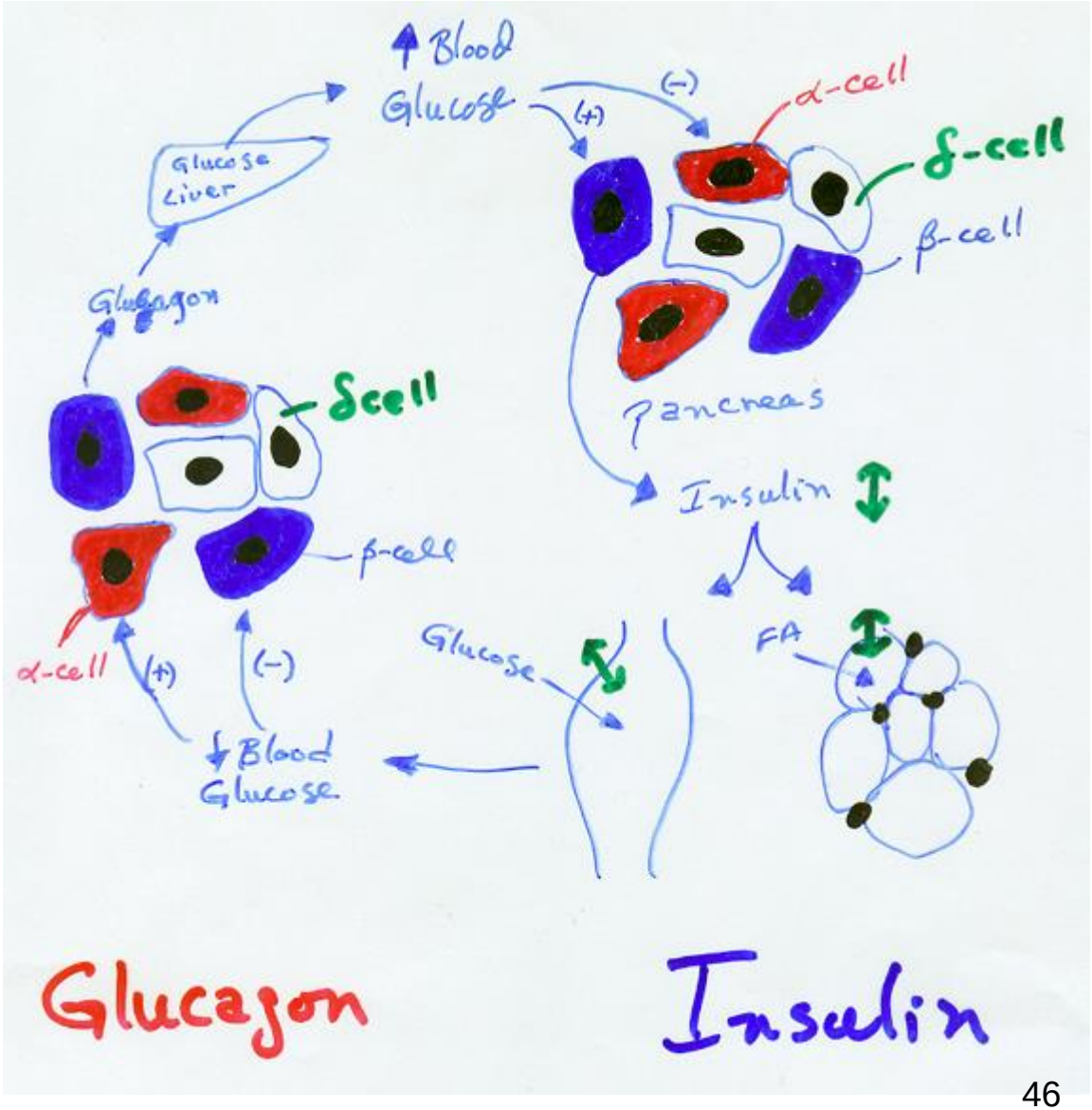
Adult Adrenogenital Syndrome

- Detected in the lab by measuring urinary levels of 17-ketosteroids.
- 17-ketosteroids are metabolites (break-down products) of androgens and other steroid hormones that are secreted from the adrenal cortex.
- Excess levels of 17-ketosteroids may be present due to ↑ACTH levels or hyperplastic adrenal or overactive cortices or due to a cortical tumor.

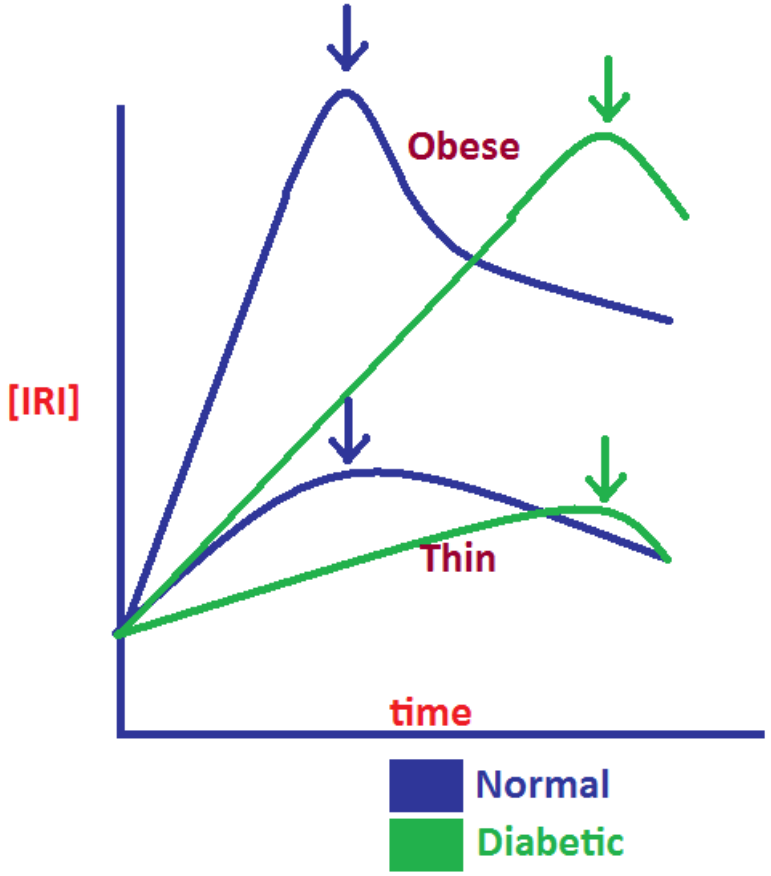


Glucagon, Insulin – A Cortisol Connection

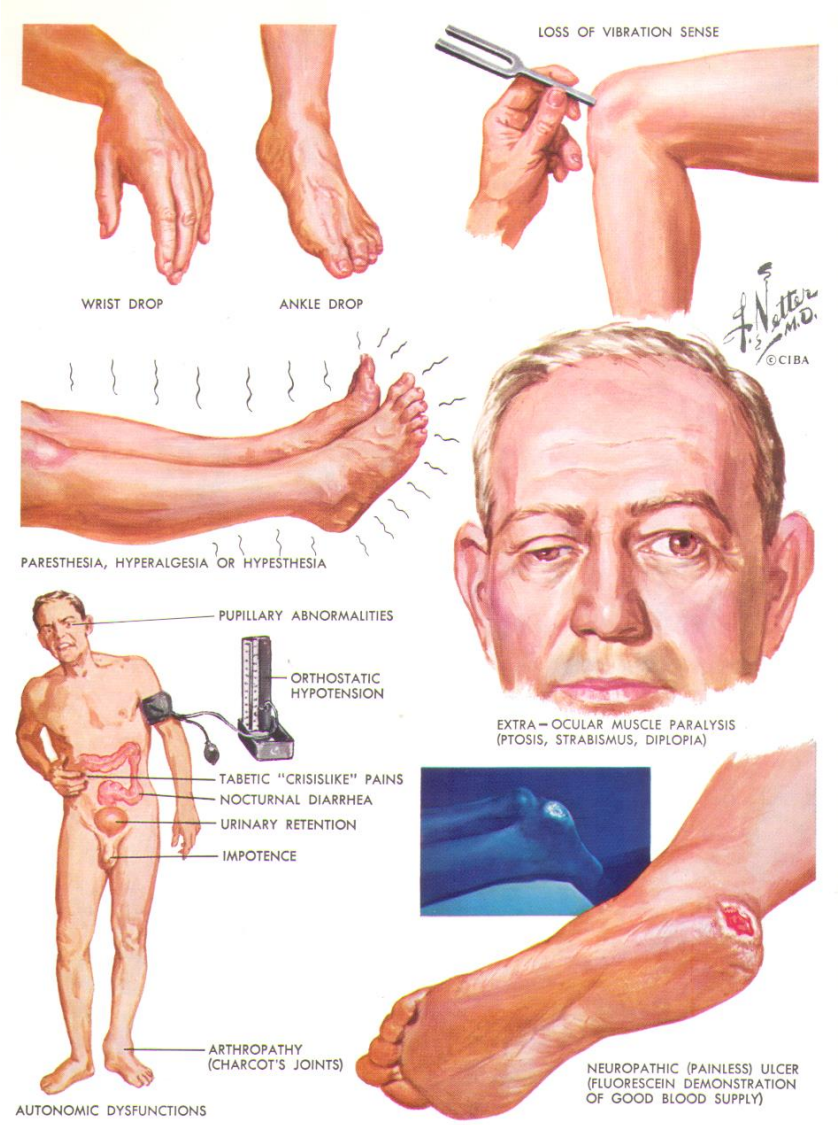


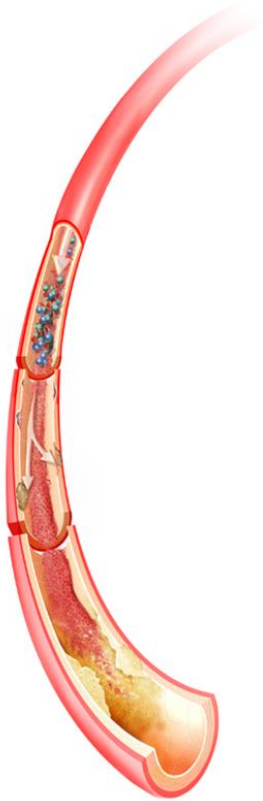


Insulin – Normal and Diabetic Responses to Glucose Load



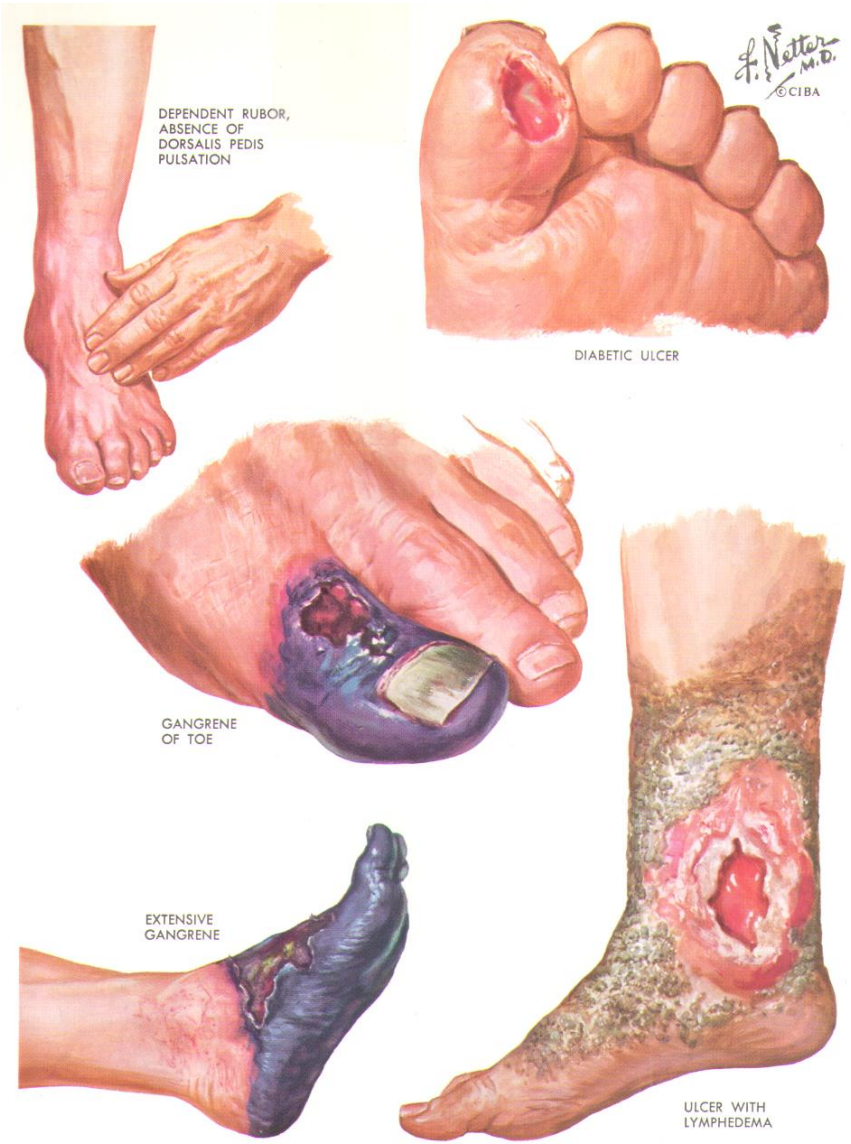
Pathologies of Diabetes Mellitus - 1





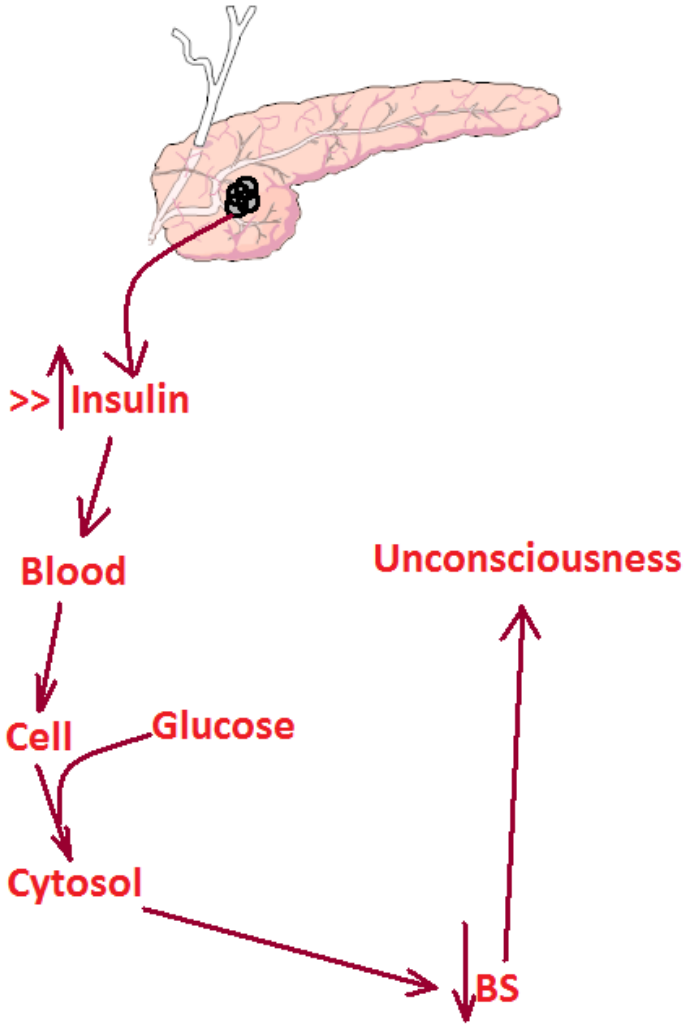
Artery with High Blood Glucose, High Blood Pressure and Fibrous Plaque (atherosclerosi)

Pathologies of Diabetes Mellitus - 2



- The dorsalis pedis pulse is located just lateral to the extensor tendon of the big toe, which can be identified by asking the patient to flex their toe while you provide resistance to this movement. Gently place the tips of your 2nd, 3rd and 4th fingers adjacent to the tendon and try to feel the pulse. If you can't feel it, try moving your hand either proximally/distally or more laterally and repeat.
- Common pitfalls include pushing too hard and/or mistaking your own pulse for that of the patient.

Hypoglycemia

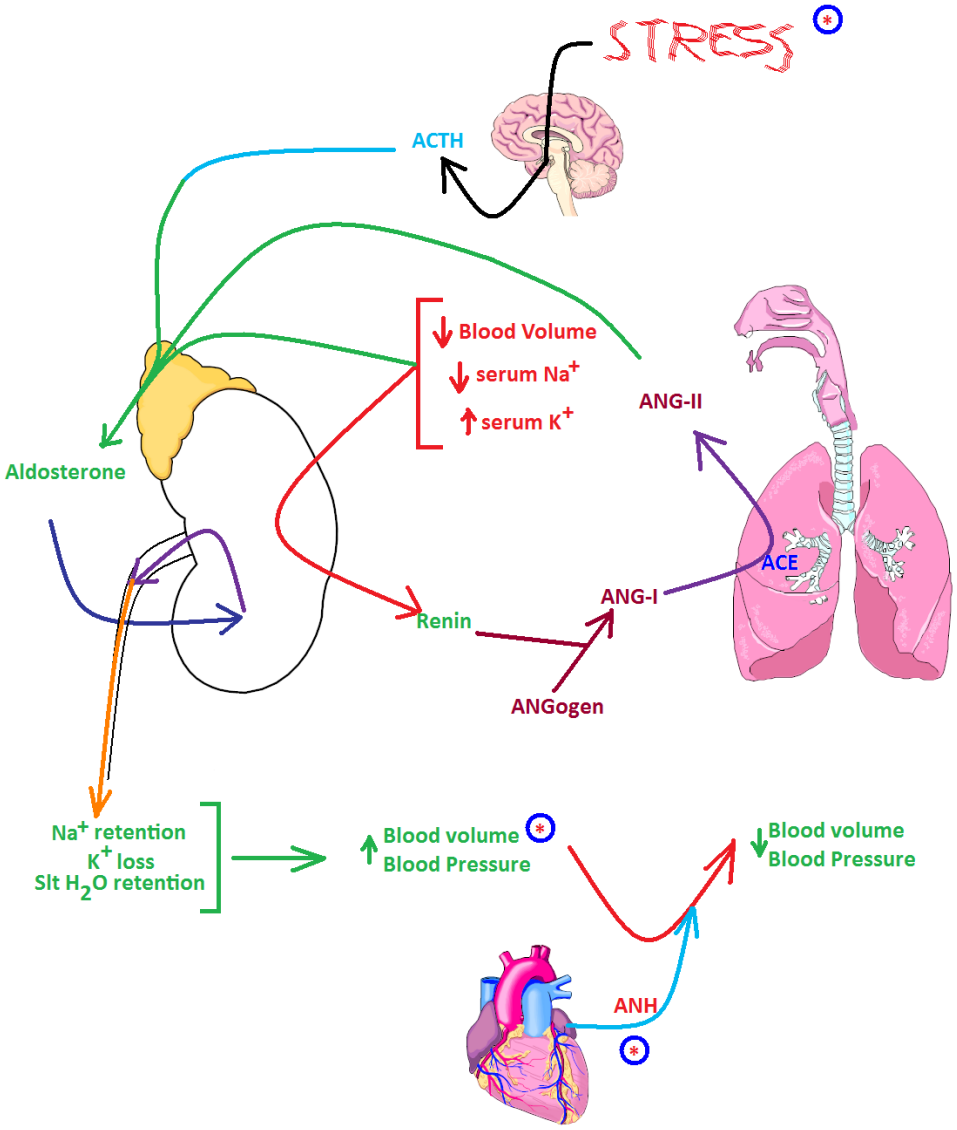


- Pancreatic membrane is very “fine”.
- Makes it hard to suture.
- Causes adhesions because of the proteases released.

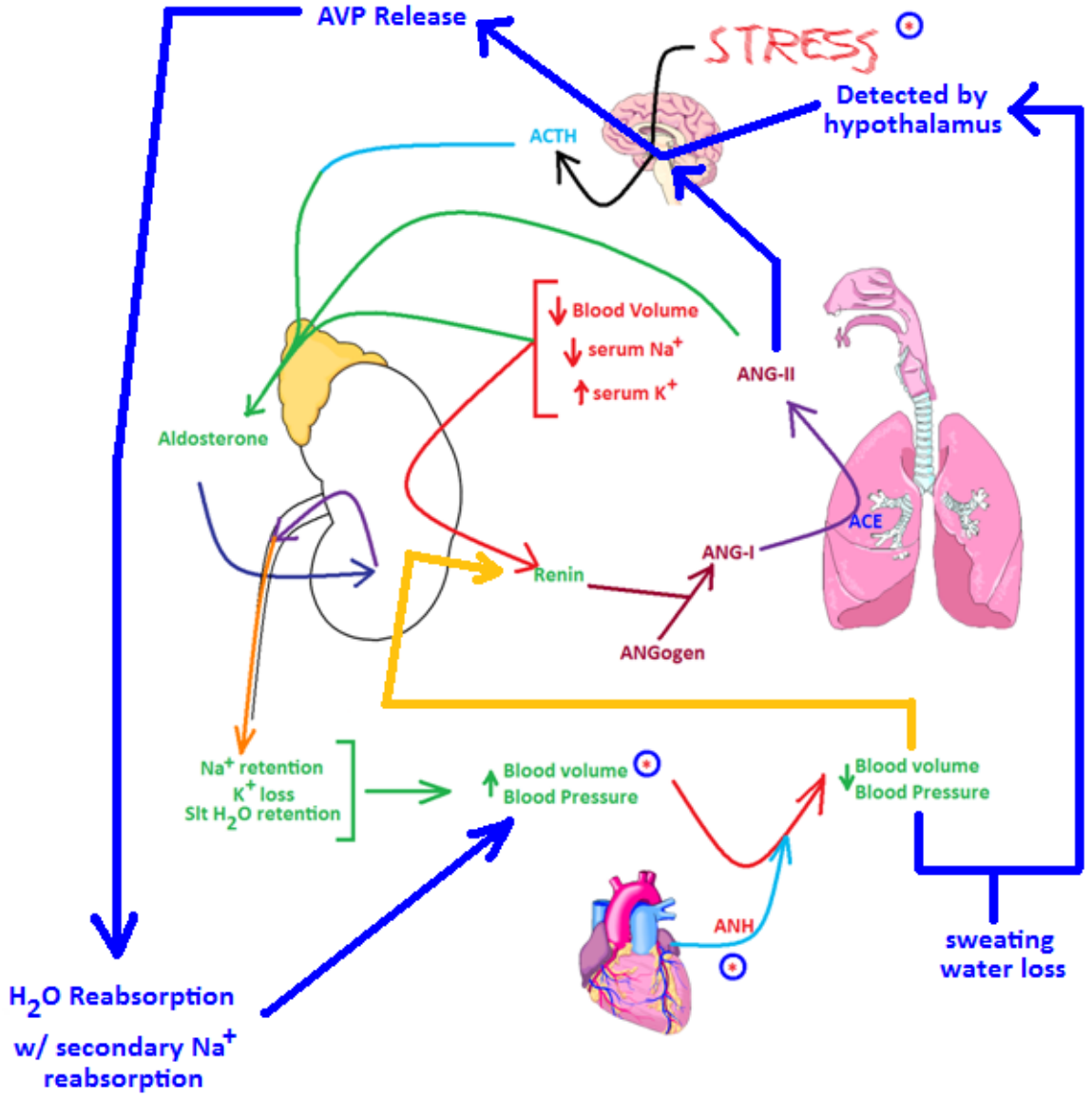
C-protein (C-peptide)

- From endogenous Insulin
- Not from exogenous Insulin
- Used to detect “High Serum Porcelain Levels”
- And Munchausen’s/by Proxy

Renin-Angiotensin-Aldosterone Axis



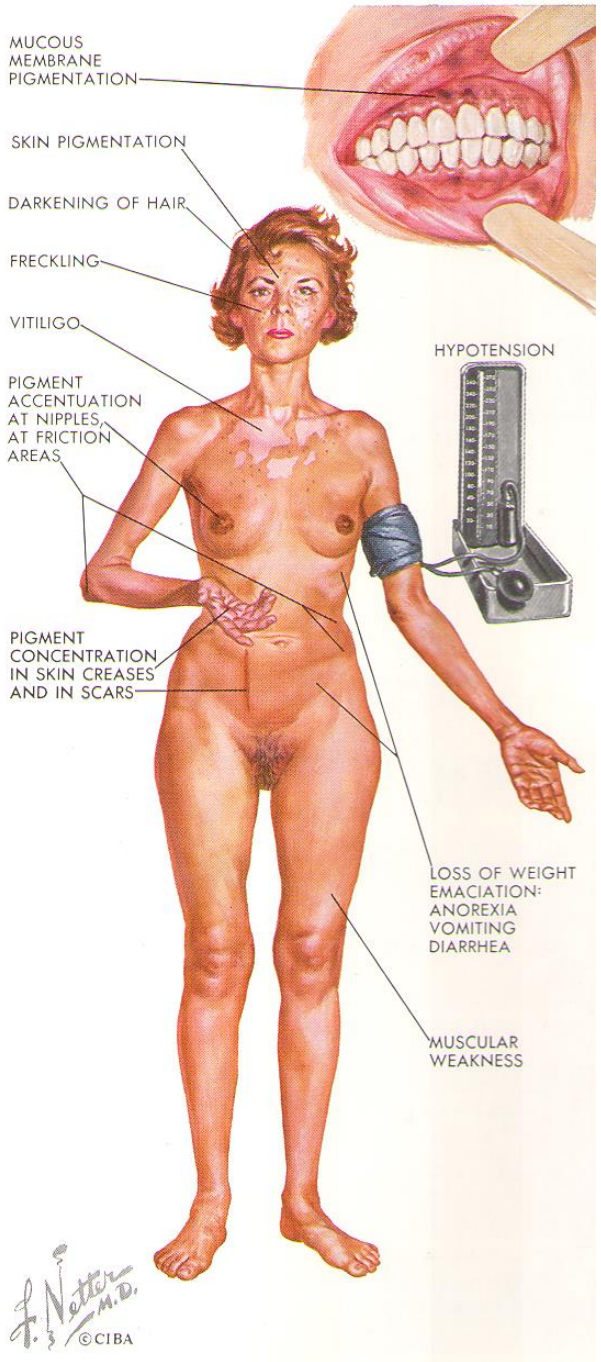
AVP and Aldosterone are Synergistic



Primary HypERaldosteronism

- Positive Chvostek's -- grimace
- Positive Trousseau's -- carpospasm

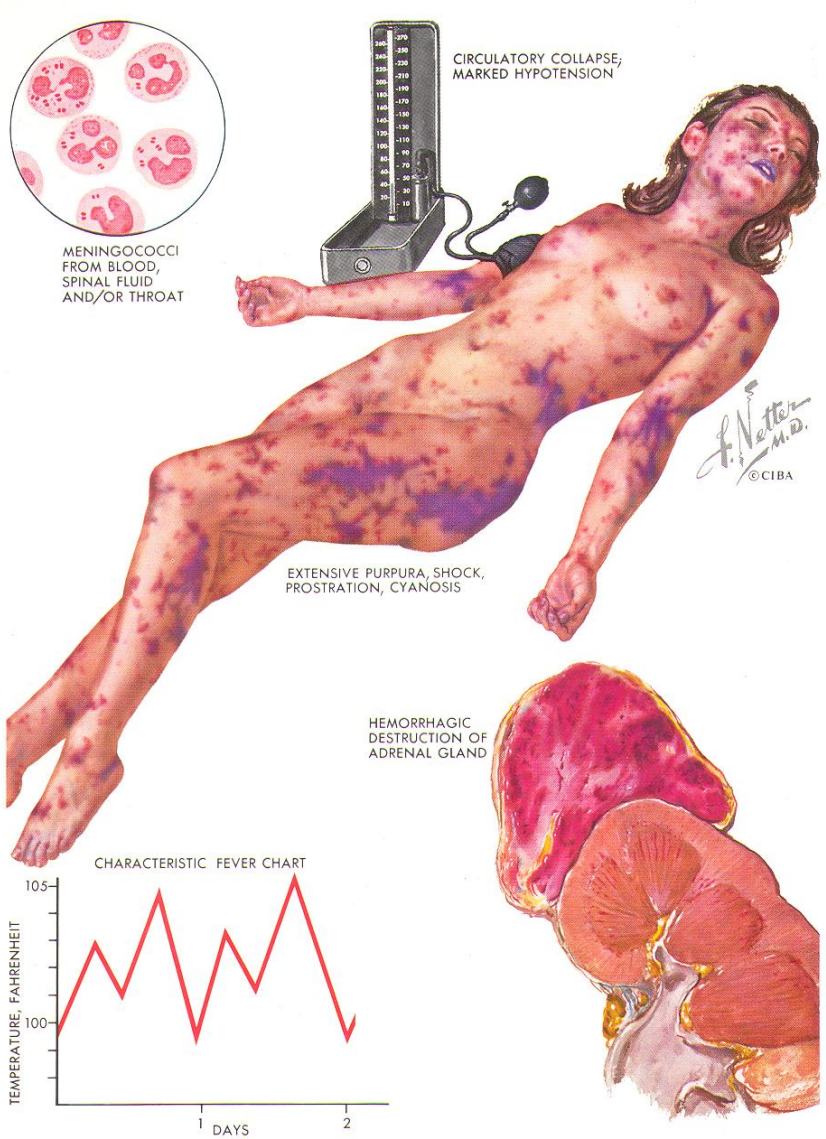
1. ↑ ECF
2. ↑ Body Na^+
3. ↓ Body K^+
4. ↑ fecal K^+
5. Polydipsia
6. Polyuria with ↑ urinary aldosterone
7. ↑ Blood Pressure
8. ↑ pH (↓ $[H^+]$ and ↓ $[K^+]$)



Addison's Disease

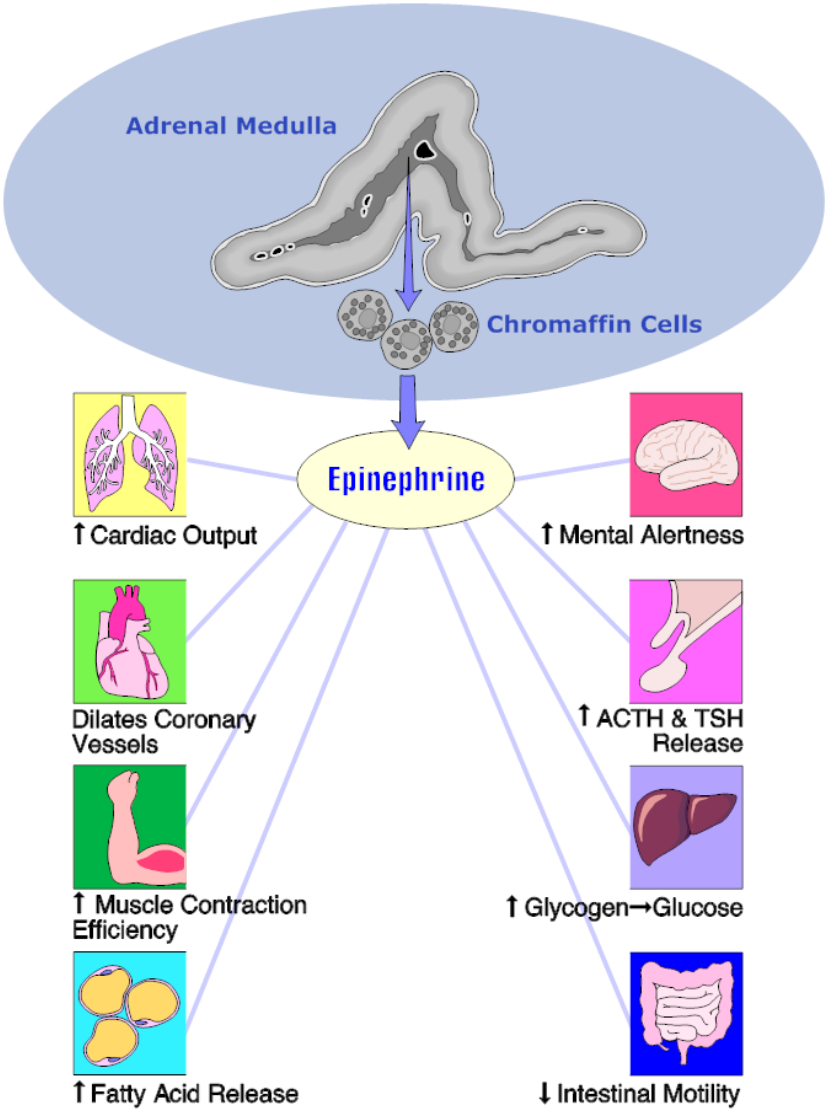
- Cortical atrophy, CA and/or trauma all lead to reduced levels of circulating aldosterone

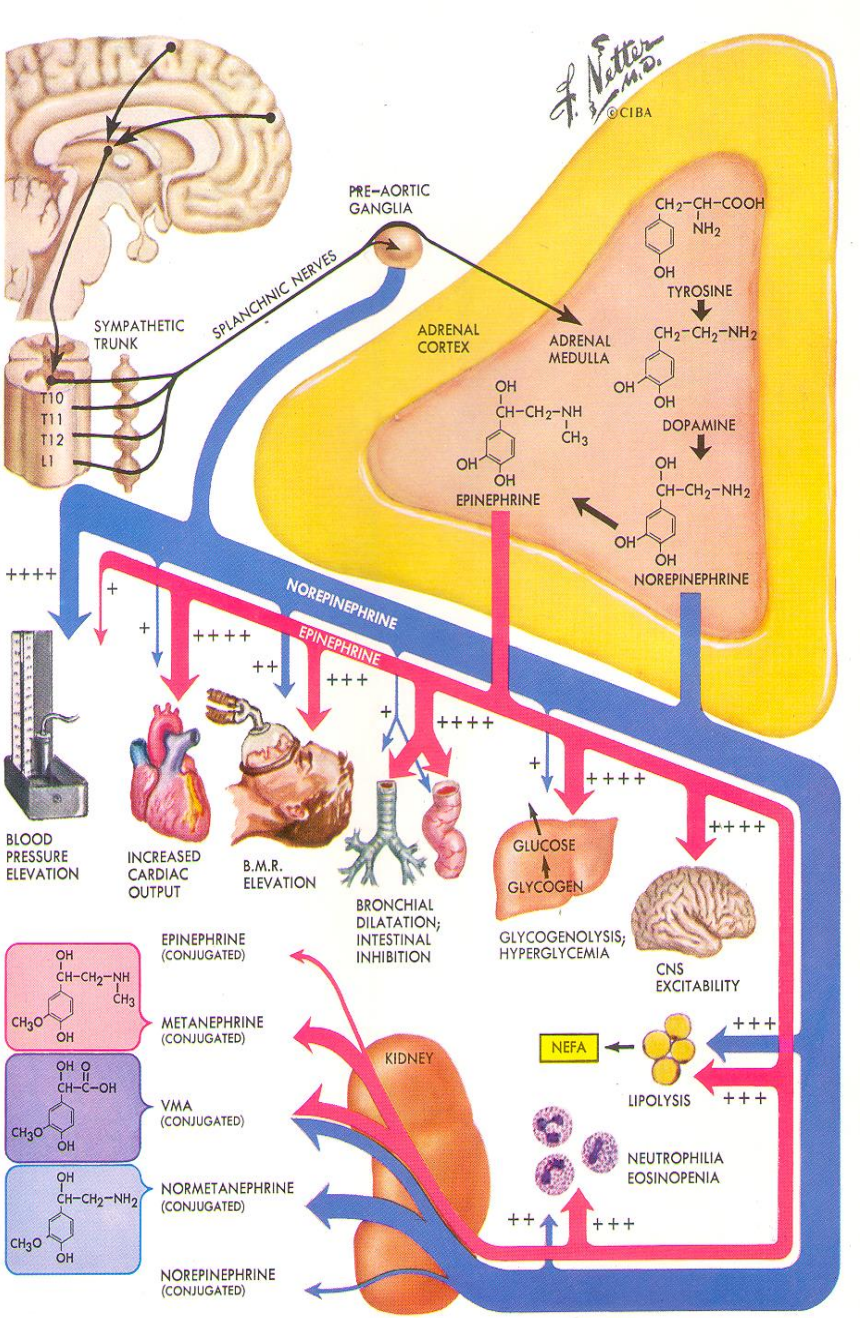
Acute Adrenal Cortical Insufficiency (Waterhouse-Friderichsen Syndrome)



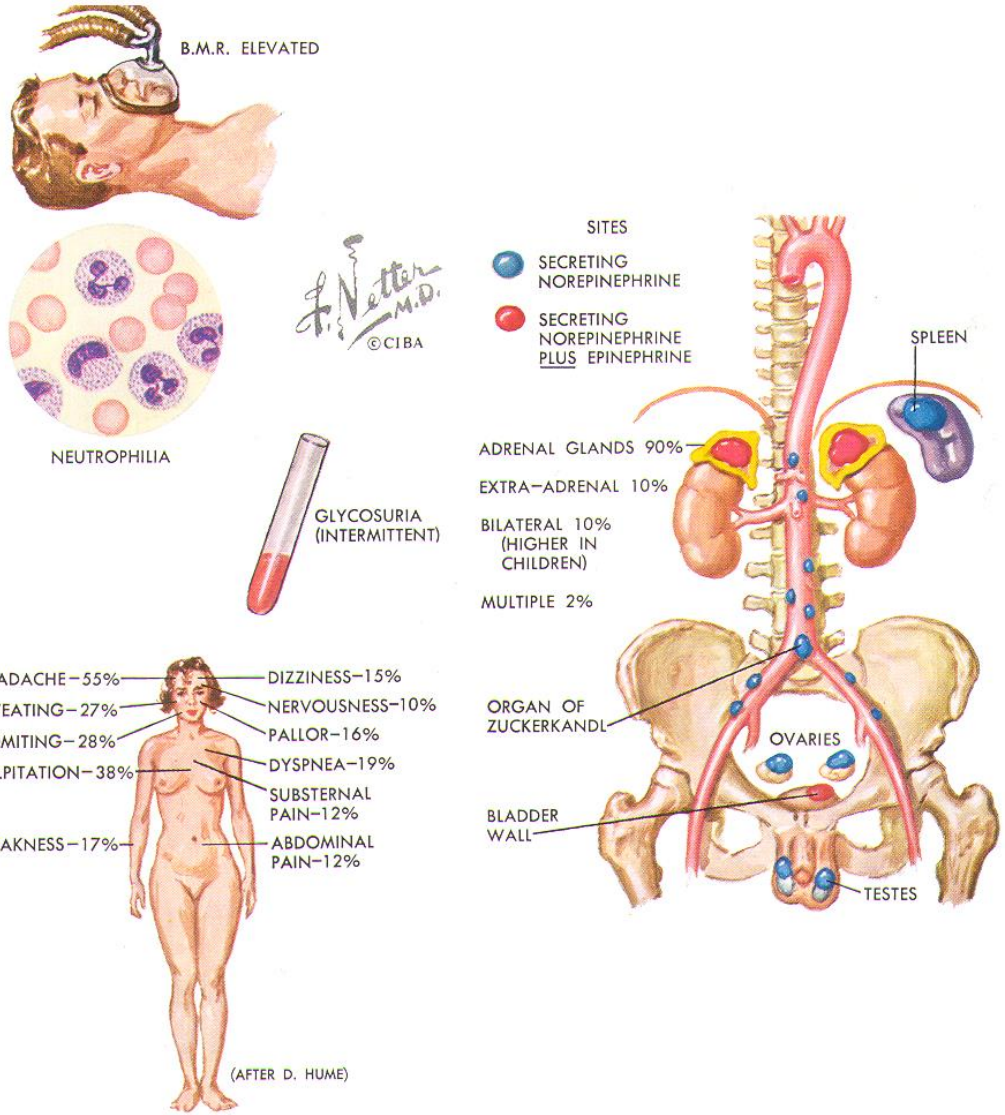
- Prevalent in camps and where young people congregate
- Common during times of high incidence of meningococcal meningitis
- May be confused with individuals seeking drugs
  - NV Case

Catecholamines: Adrenal Medulla



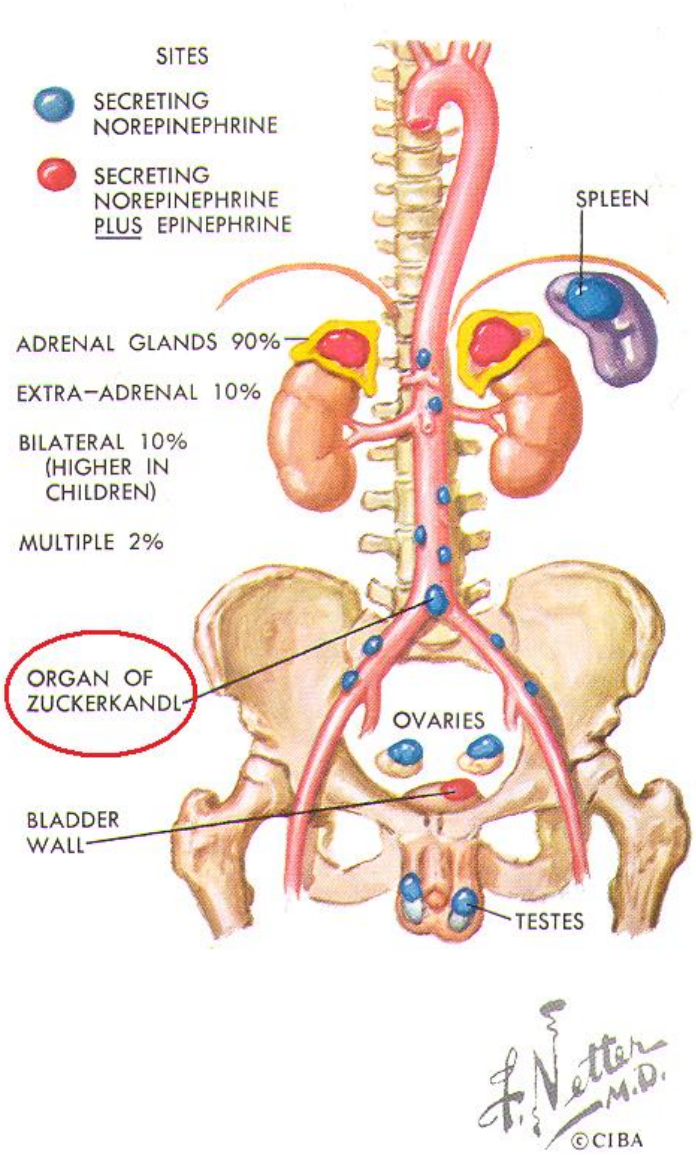


Pheochromocytoma – Aggressive!



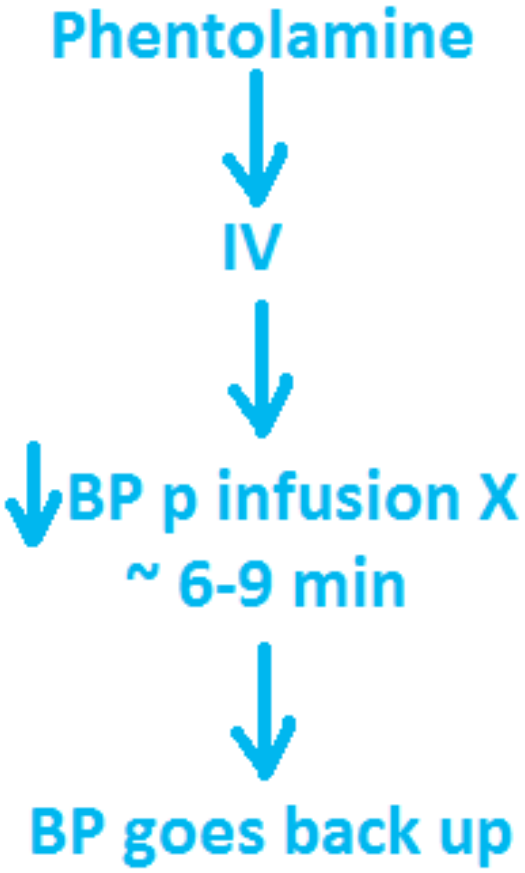
1. Adrenals are primary site. BUT metastasis is common.
2. Hypertension may be intermittent and/or sustained.
3. Headache, sweating, N/V, dizzy, SOB, cardiac palpitations
4. ↑ BMR
5. VMA in urine

Organ of Zuckerkandl



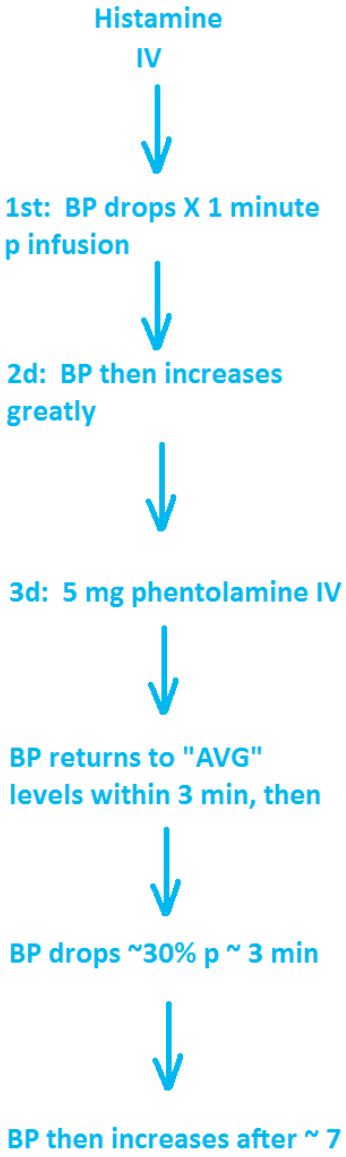
- A small mass of chromaffin cells derived from neural crest located along the aorta, beginning cranial to the renal arteries and extending to the level of the aortic bifurcation or just beyond.
- Its physiological role is thought to be of greatest importance during the early gestational period as a homeostatic regulator of blood pressure, secreting catecholamines into the fetal circulation. The organ regresses in the end of gestation and following birth to form the aortico-sympathetic group of the adult paraganglia.
- The organs of Zuckerkandl are not often visualized radiologically unless they are involved by a pathologic process, e.g. pheochromocytoma.
- http://radiopaedia.org/articles/organ-of-zuckerkandl

Testing for Pheochromocytoma - 1



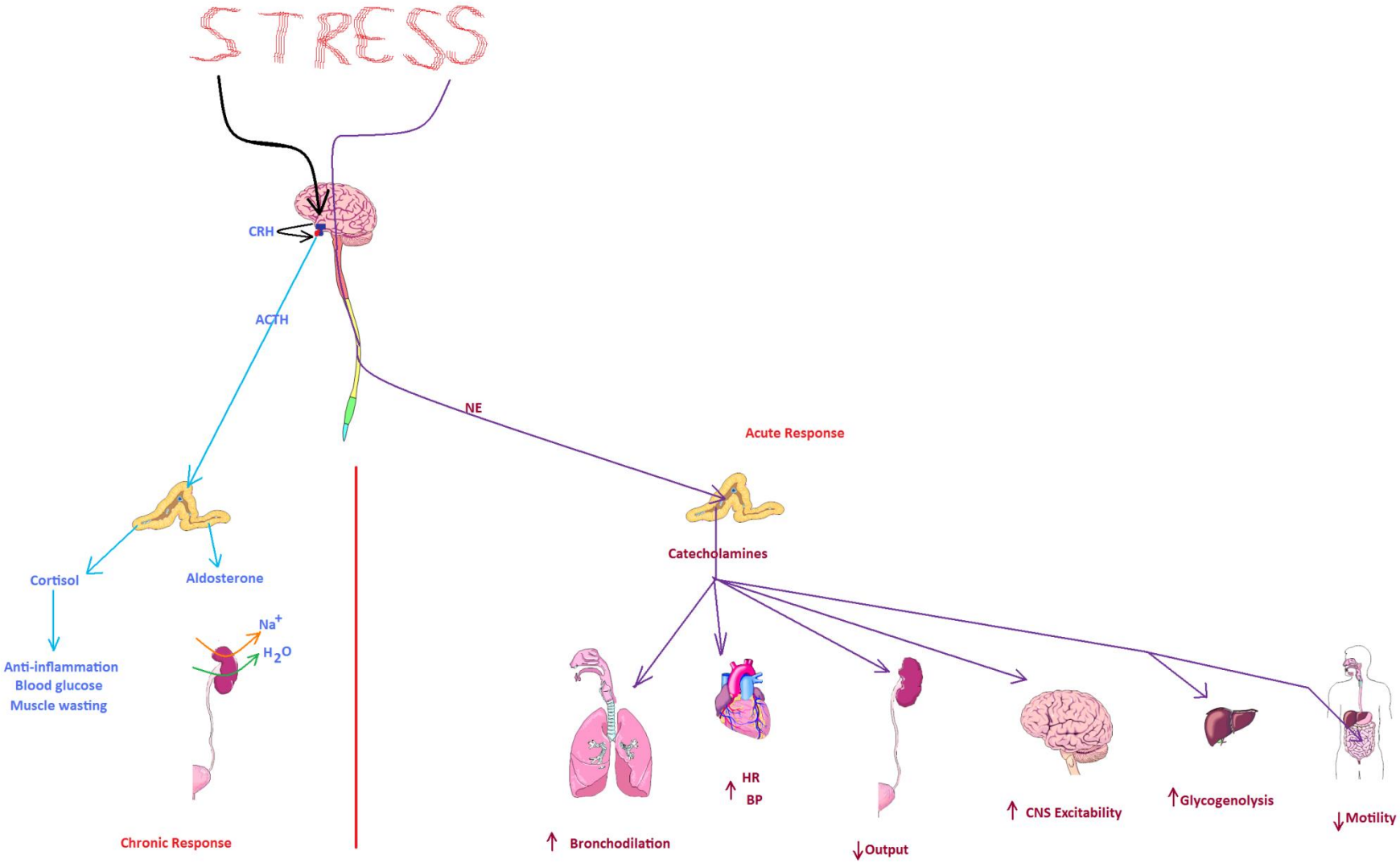
- Phentolamine injection causes a drop of BP > 35/25 mm Hg within 2 min.

Testing for Pheochromocytoma - 2

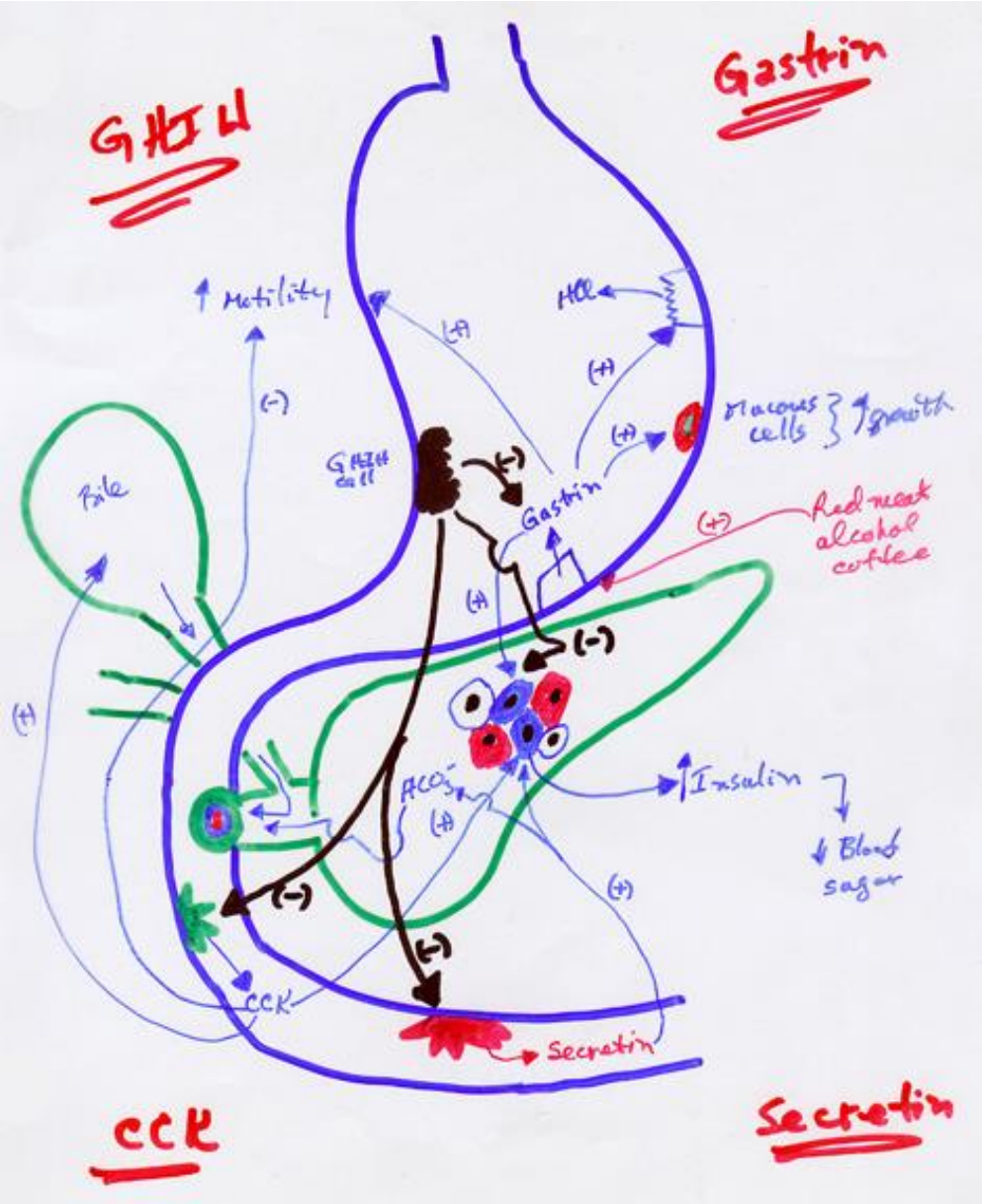


- **Provocative tests** with histamine or tyramine *are <u>hazardous and should not be used</u>.*
- Surgical removal of the tumor is the treatment of choice. The operation can usually be delayed until the patient is restored to optimal physical condition by the use of a combination of α- and β -blockers (phenoxybenzamine, 40 to 160 mg/day, and propranolol, 30 to 60 mg/day, respectively, po in divided doses).

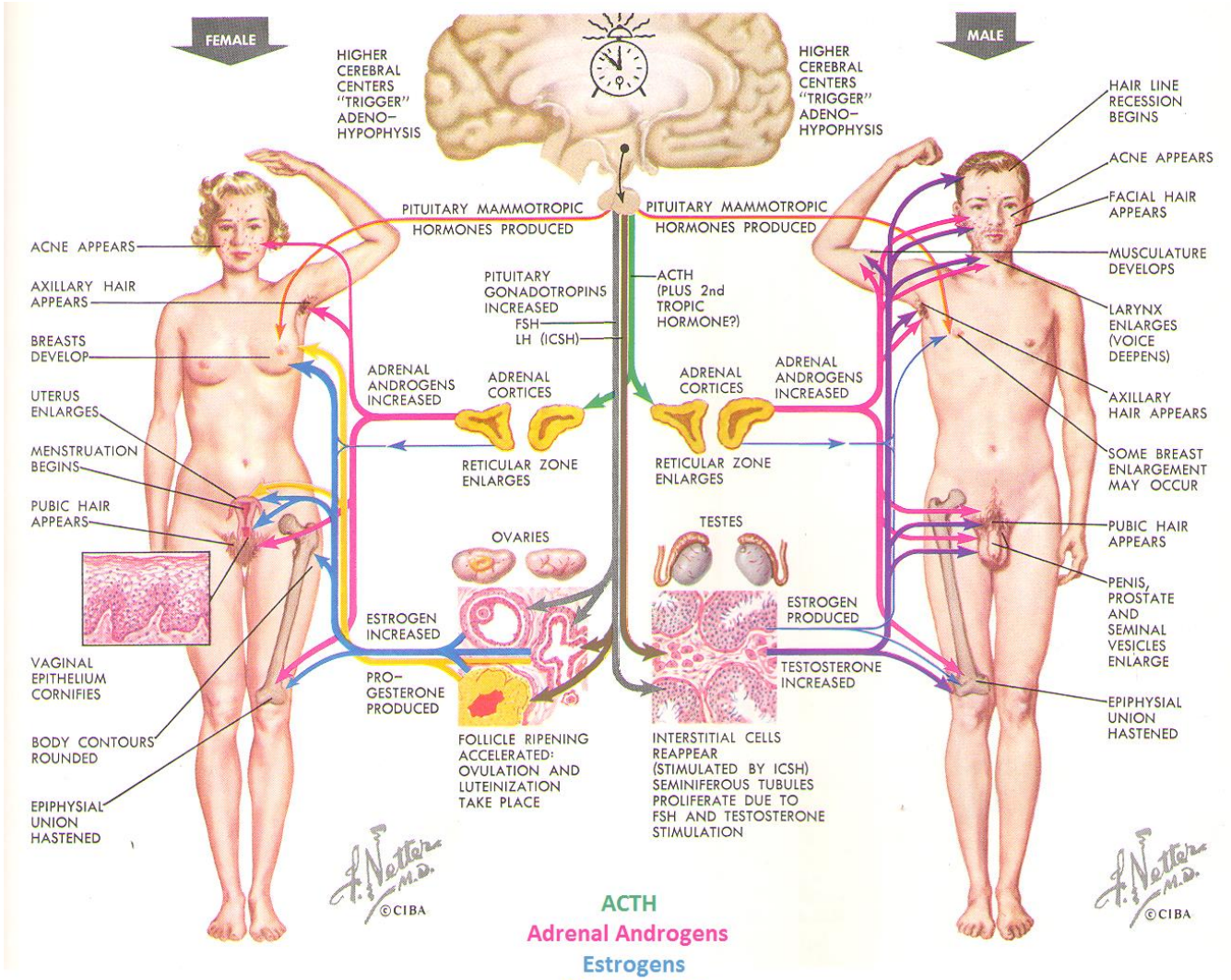
Body's Stress Response



The Stomach As an Endocrine Organ



Sex Hormones



ACTH

Adrenal Androgens

Estrogens

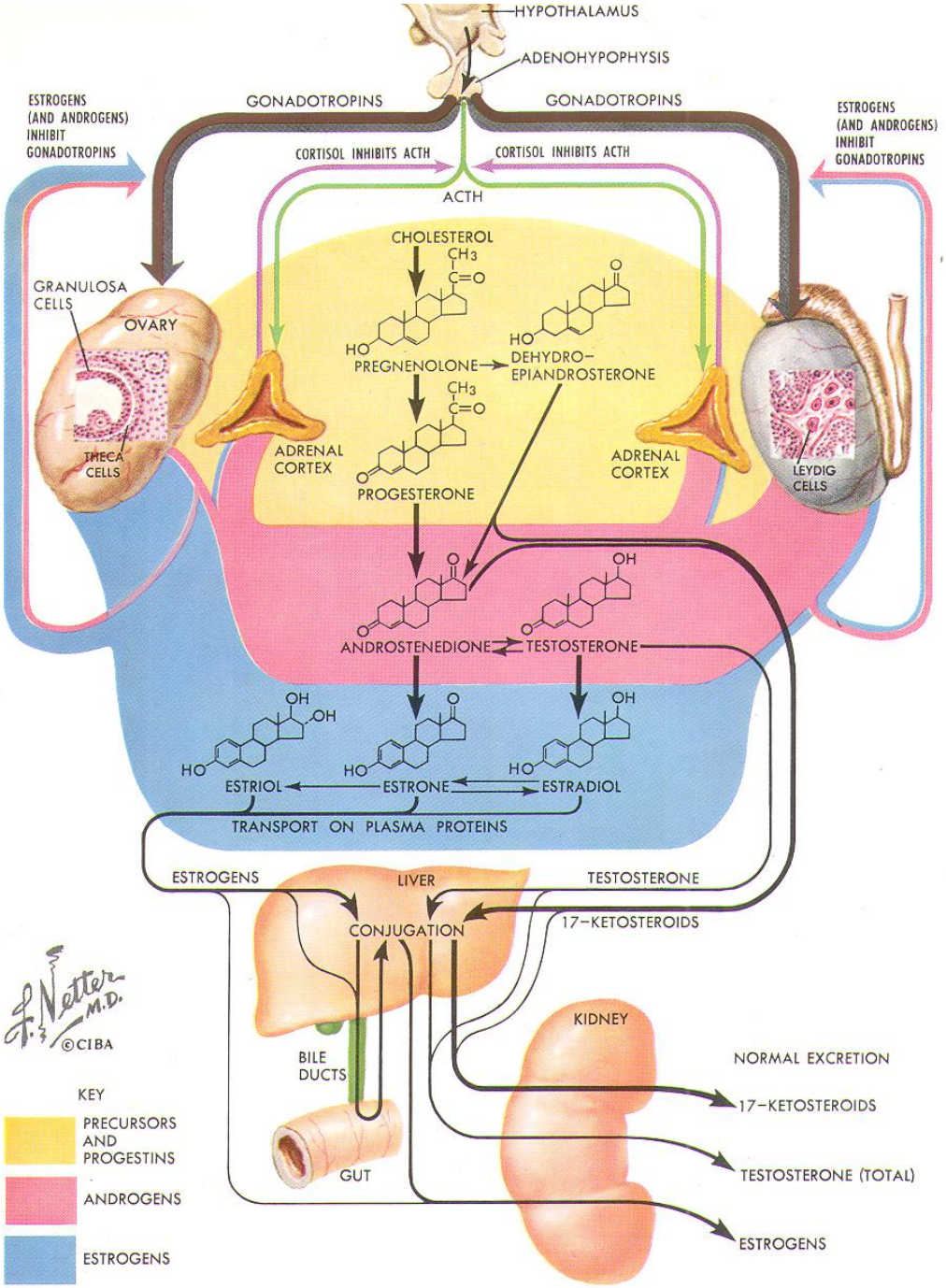
Progesterone

LH (ICSH)

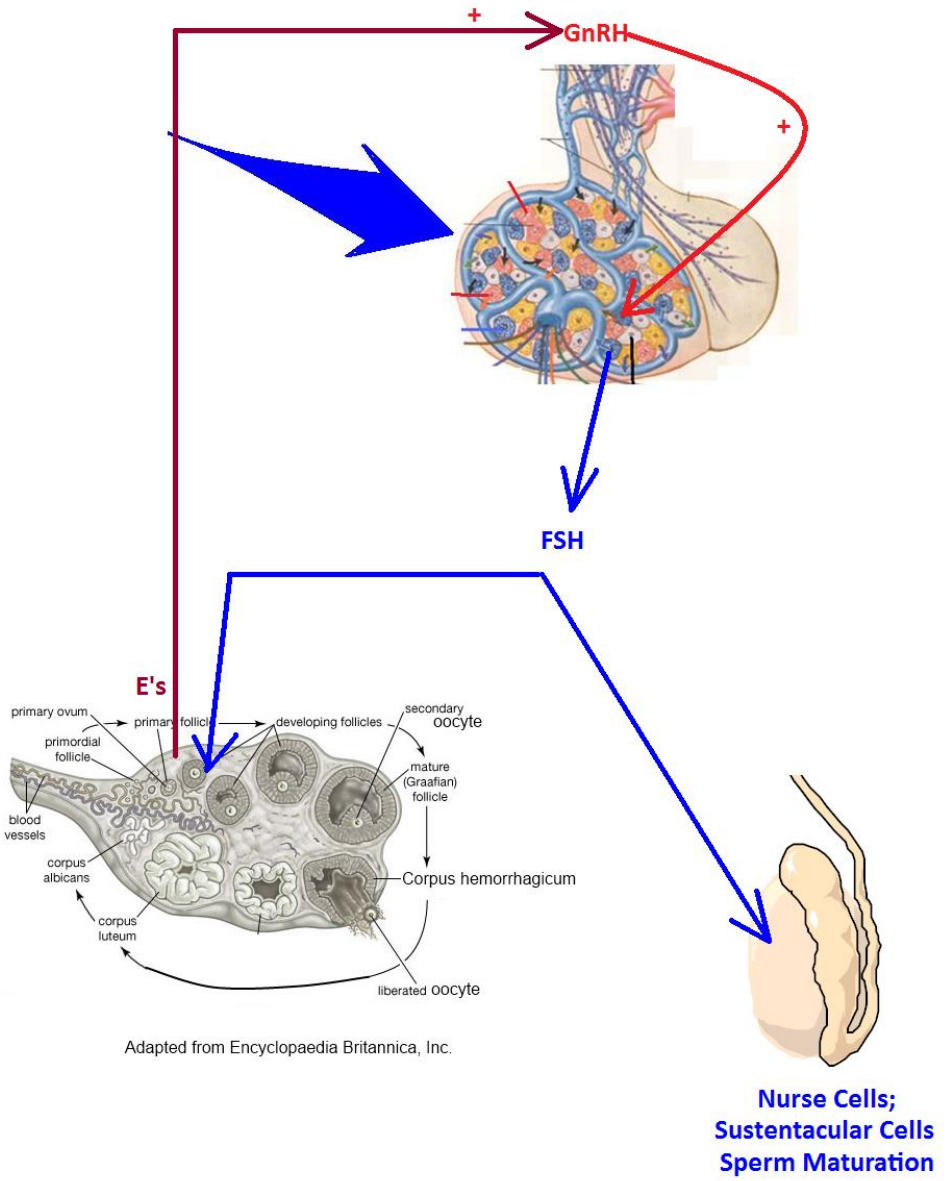
FSH

Testosterone

Sex Hormones

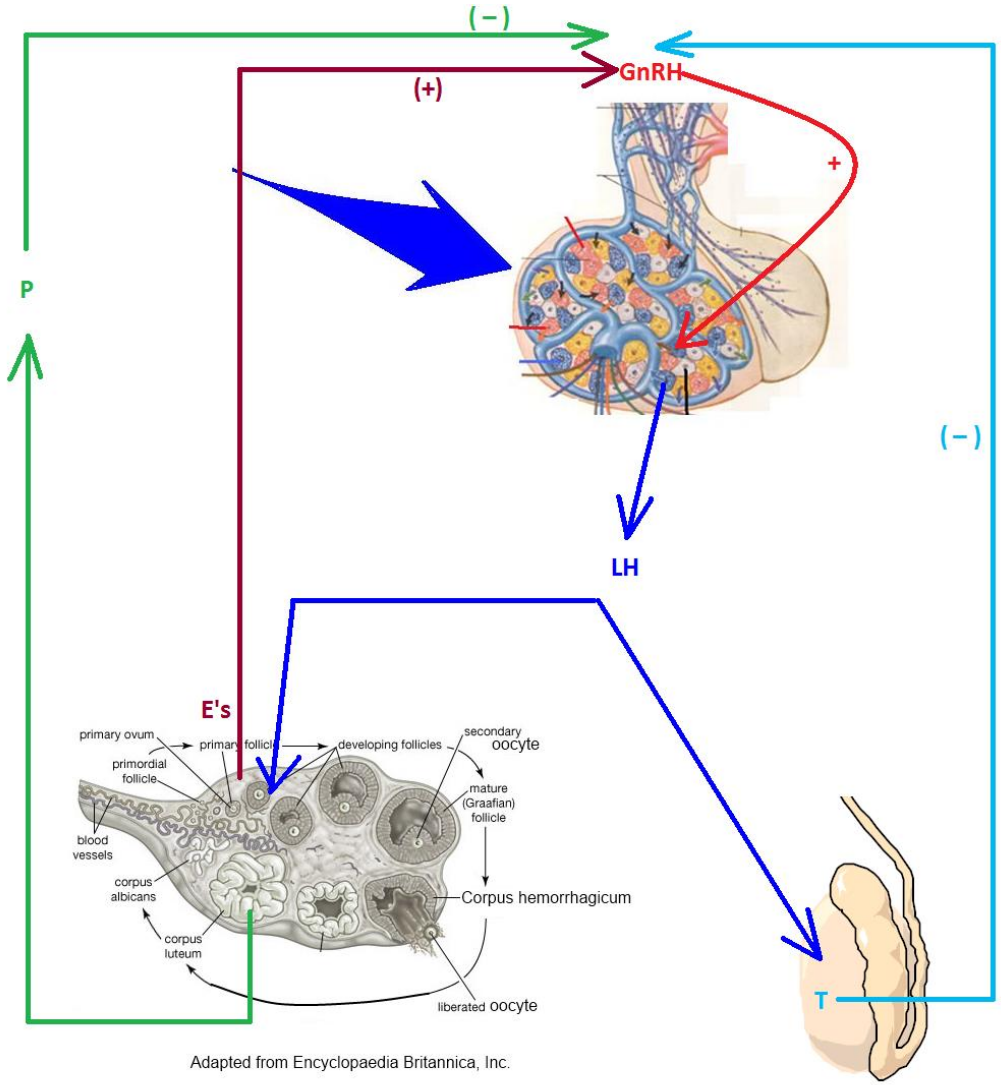


Follicle Stimulating Hormone -- FSH



- Elevated estrogens' levels eventually inhibit FSH release and drive ovulation
- FSH supports Nurse cells in testis for sperm maturation
- FSH supports growth of follicle in ovary
- Increases E's and (+) GnRH release

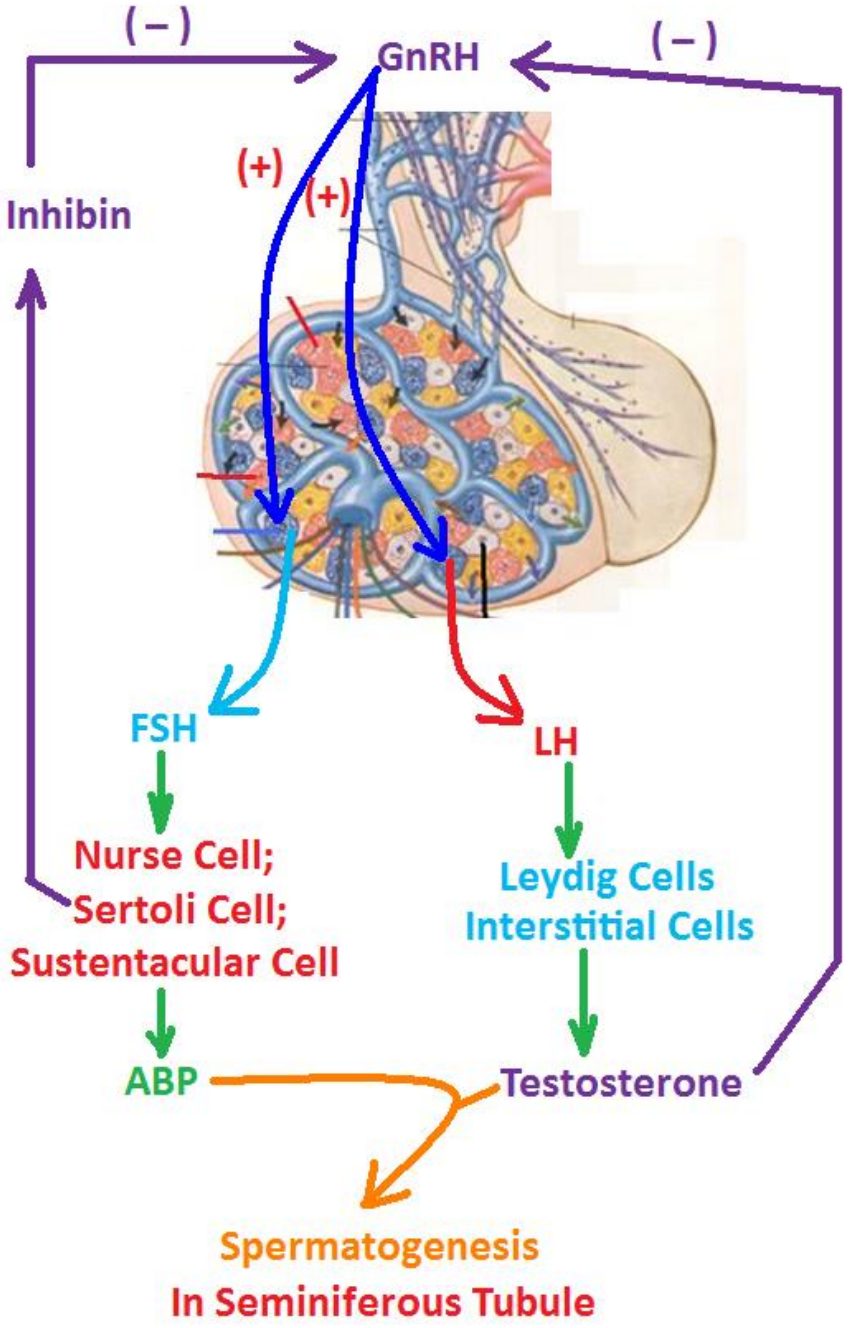
Leutinizing Hormone -- LH



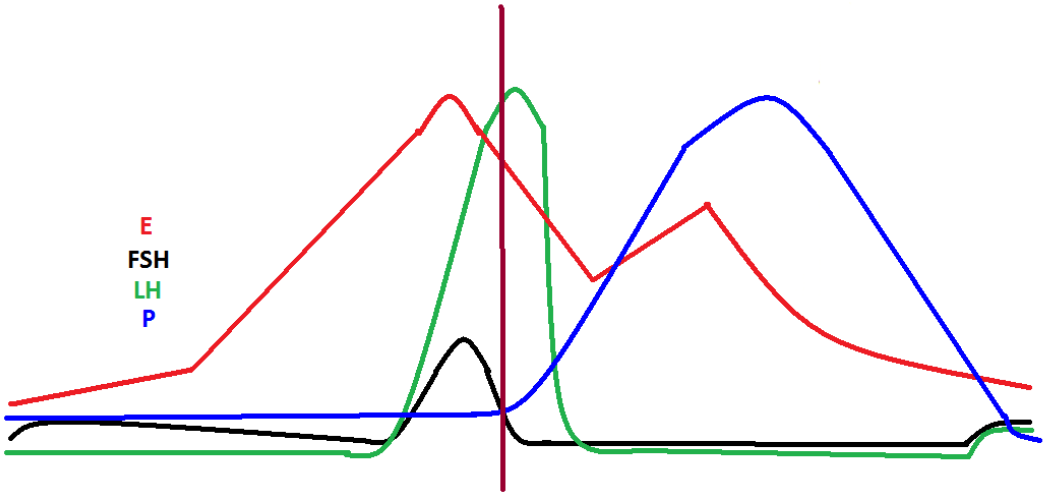
Adapted from Encyclopaedia Britannica, Inc.

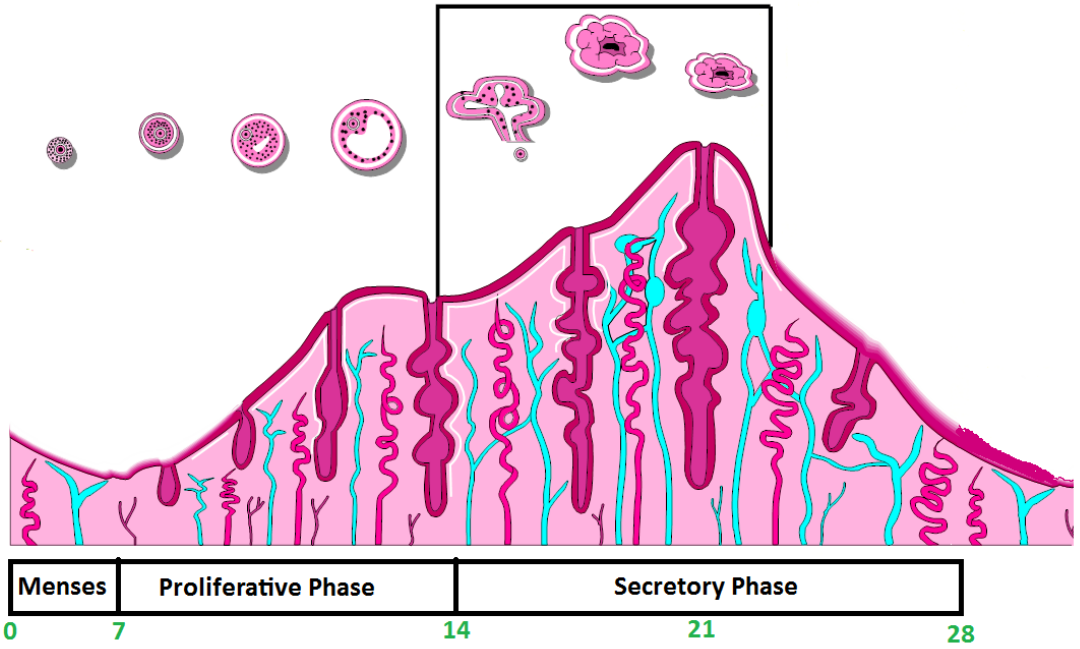
- Causes ovulation and formation of corpus luteum (CL)
  - CL secretes primarily P with a bit of E, both of which contribute to secondary sexual characteristics
  - CL "preps" uterus for pregnancy
- Causes T synthesis in Leydig cells
  - For sperm synthesis
  - For anabolic processes
  - For secondary sexual characteristics
- High P and High T inhibit LH release

Male Endocrinology

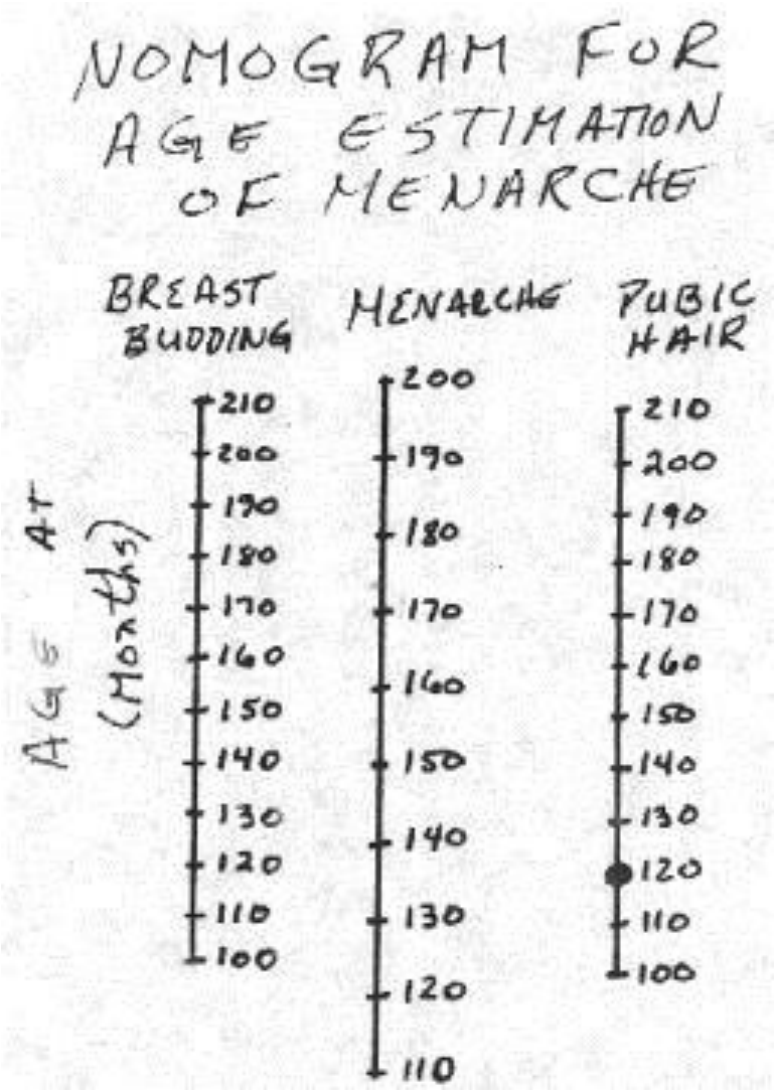


Female Endocrinology



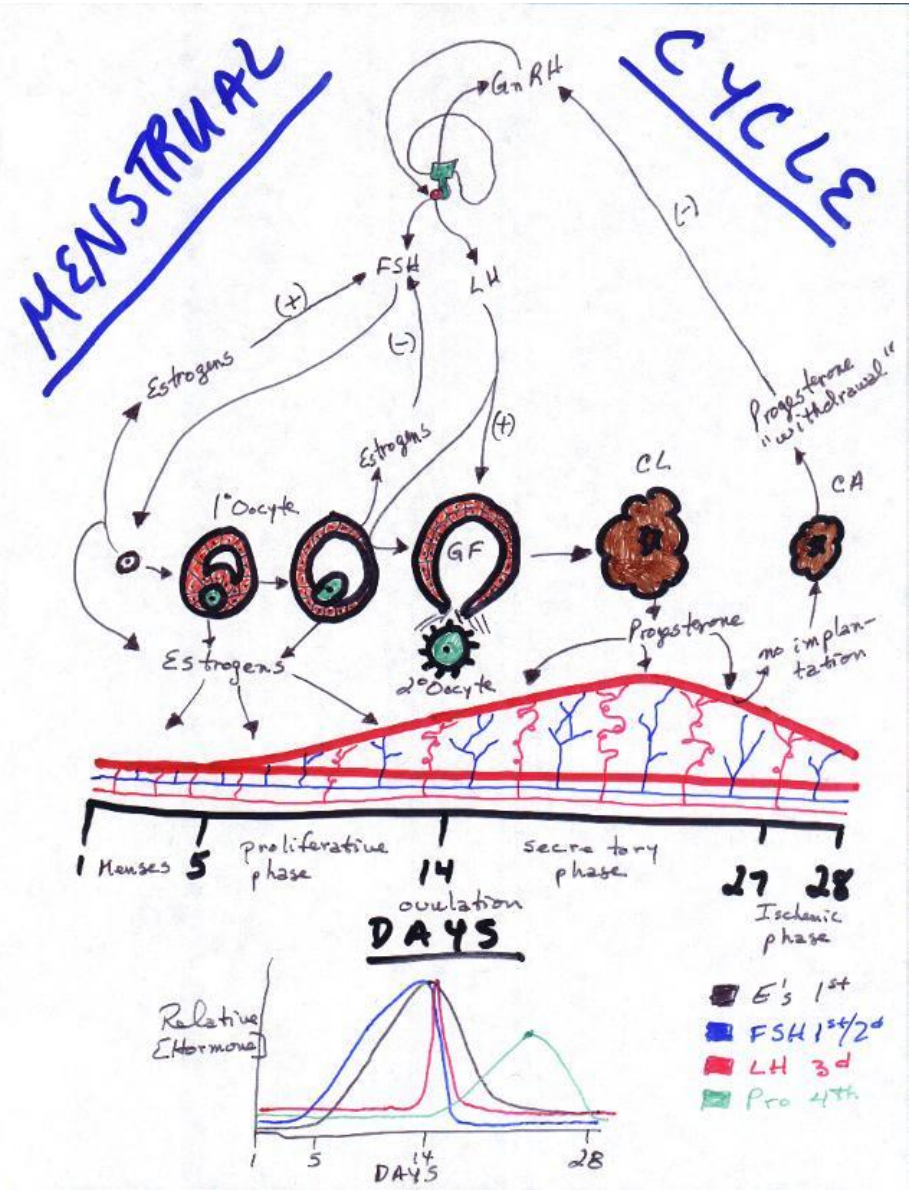


Menarche Nomogram



- The nomogram may be used to approximate the onset of menarche in pubescent girls
- In general, if you know
  - the age that a young girl's breasts began to bud and
  - when she first exhibited pubic hair (in months of age),
- you can draw a line through those two points on the nomogram and get a rough idea of when she'll have her first menstrual period.

Menstrual Cycle



Intro Female Endocrinology -- 2

A. Pre-pubertal: ↓E's; ↓ P

B. Pubertal: ↑E's; ↑P

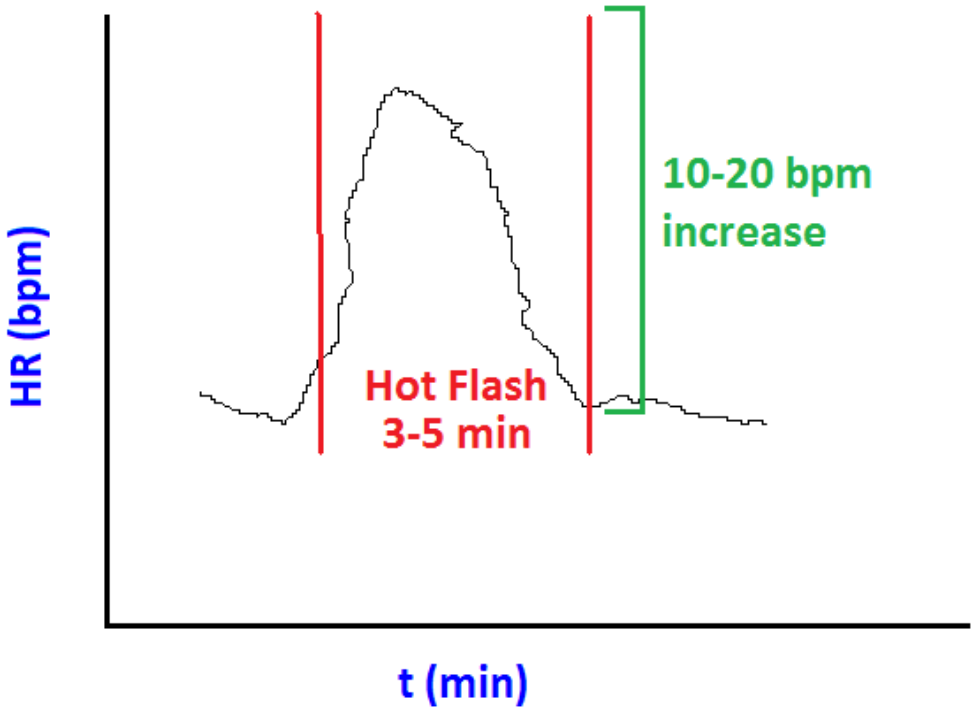
C. Reproductive: ↑E's; ↑P

D. Menopause: 0 E's; 0 P

E. 0 E's and 0 P cause cardiovascular effects called hot flashes.

F. Hot flashes may be alleviated greatly with progestins.

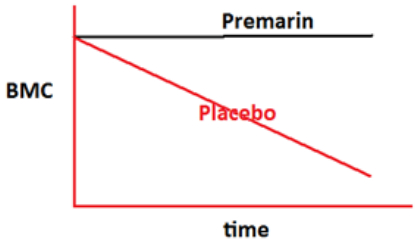
G. Hot flashes may be alleviated reasonably well with conjugated estrogens.

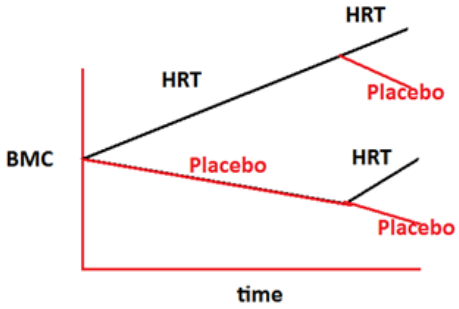


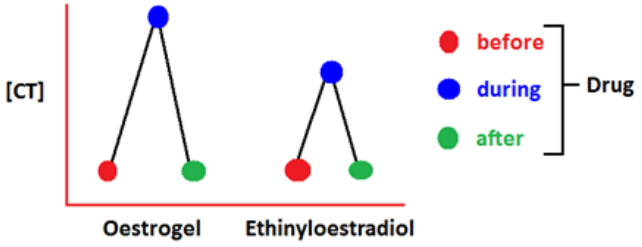
Predisposing Factors to Osteoporosis

- Reduced calcium intake
- Calcium ion absorption problems
- Reduced E/P ratio
- Race: Caucasian and Asian
- Physical inactivity
- Cigarettes and alcohol
- Age

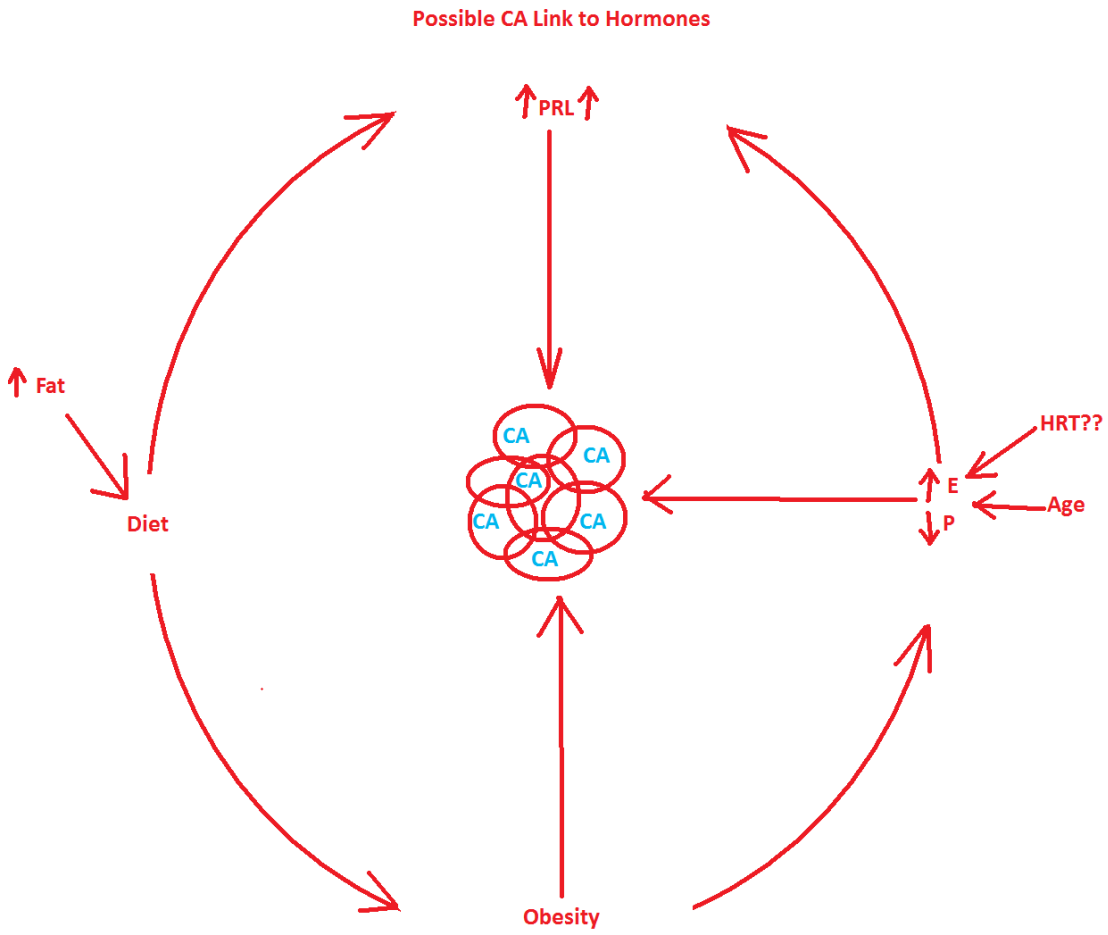
Bone Mineral Content







The Confusion Surrounding Hormones and Cancer



Sheehan's Syndrome – aka Post-Partum Anterior Pituitary Necrosis