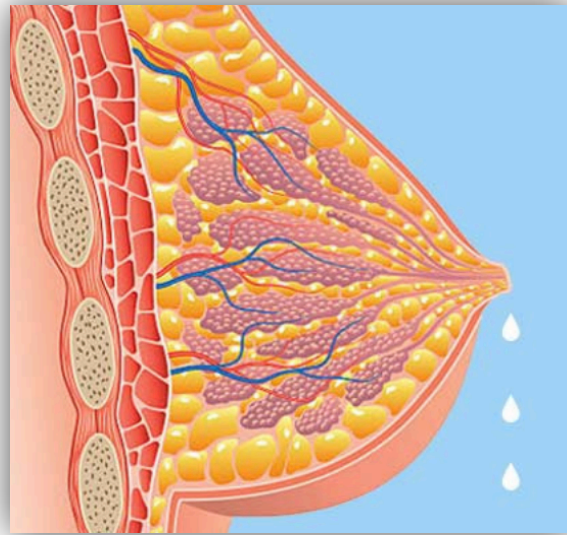


Building Prolactin Questions for the USMLE Step One Exam



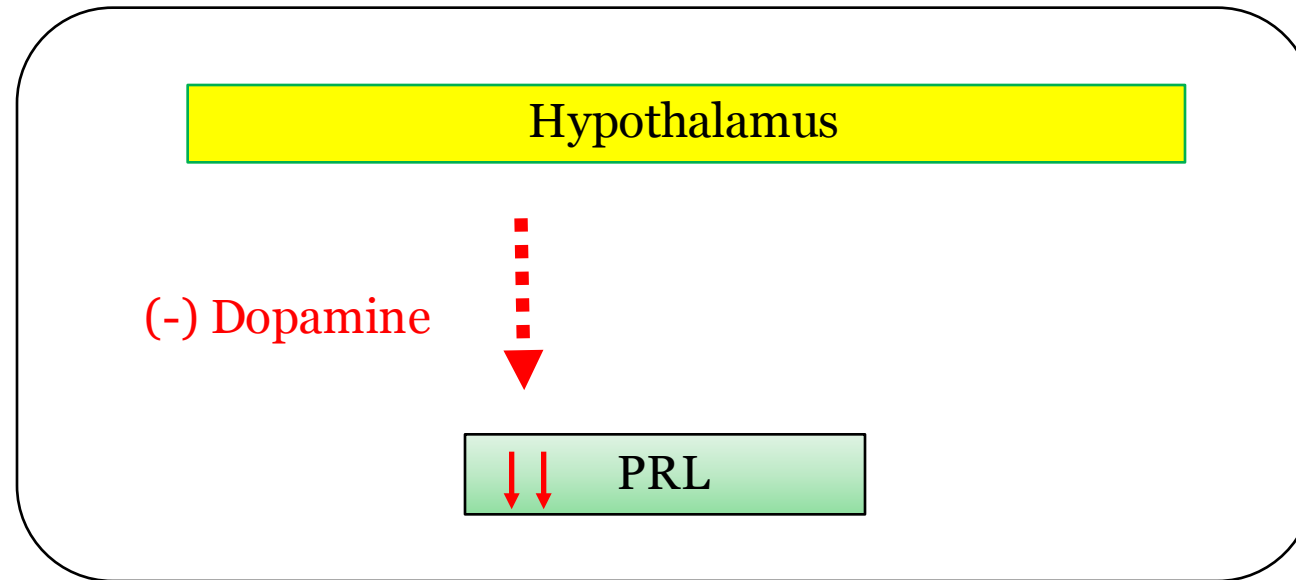
Howard J. Sachs, MD
Associate Professor of Medicine
University of Massachusetts Medical School
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E-mail: Howard@12daysinmarch.com

Building Prolactin (PRL) Derivatives for USMLE Step One

- Physiology of Prolactin
- Prolactin Dysregulation
- Prolactin Deficiency
- Hyperprolactinemia

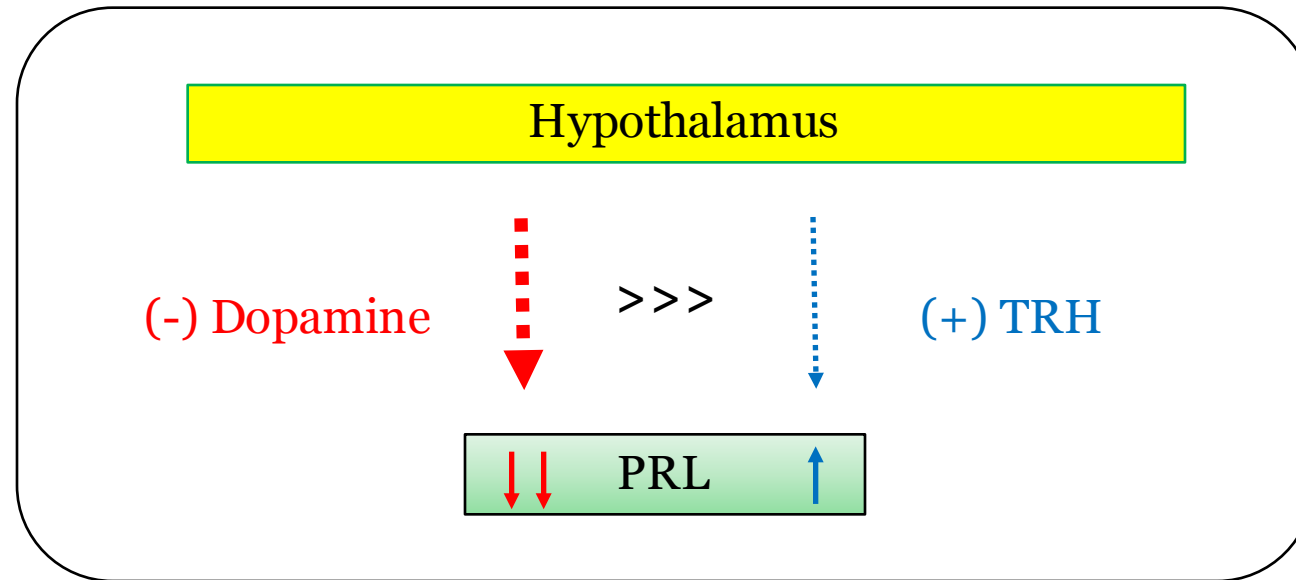
Prolactin Physiology: Regulation

- Secreted by acidophilic (*lactotrophic*) cells of anterior pituitary
- Regulated by *hypothalamic release of dopamine* (*prolactin inhibitory factor*)
 - Tonic *inhibition* (from dopaminergic neurons)
 - TRH stimulates lactotrophs



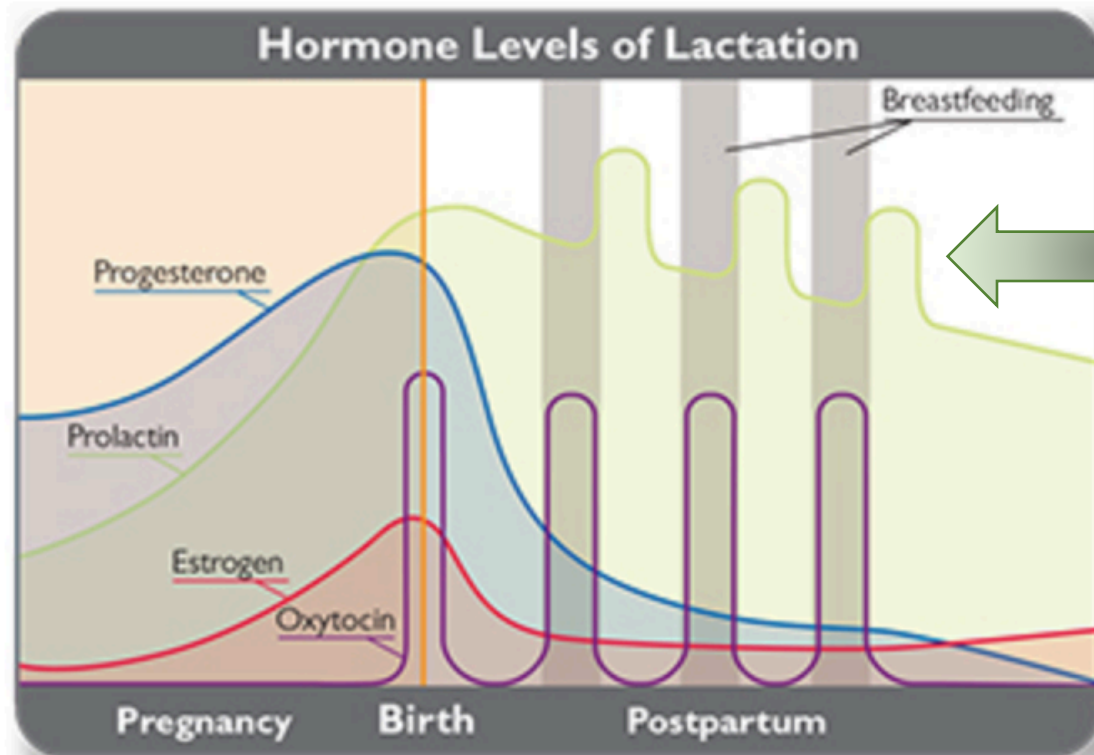
Prolactin Physiology: Regulation

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- Regulated by *hypothalamic release of dopamine (prolactin inhibitory factor)*
 - Tonic inhibition (from dopaminergic neurons)
 - **TRH** stimulates lactotrophs



Prolactin Physiology: Role

- Purpose: *milk production* and mammary gland development (*alveoli*)
 - Suckling/Nipple stimulation elevates PRL level
 - Note: *Oxytocin stimulates mammary myoepithelium* → *milk ejection*

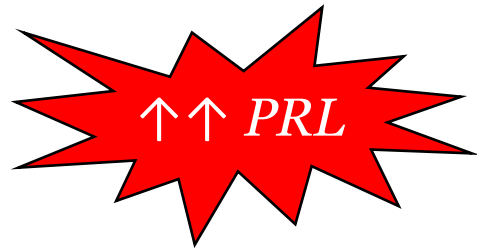


Suckling and PRL secretion

Adapted from Love, 1990

Prolactin Physiology: Role

- Purpose: *milk production* and mammary gland development (*alveoli*)

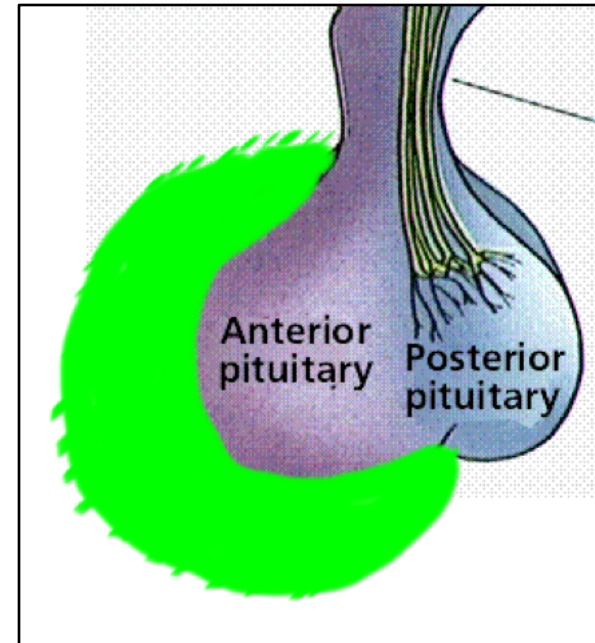


Galactorrhea

Prolactin Physiology: Pregnancy

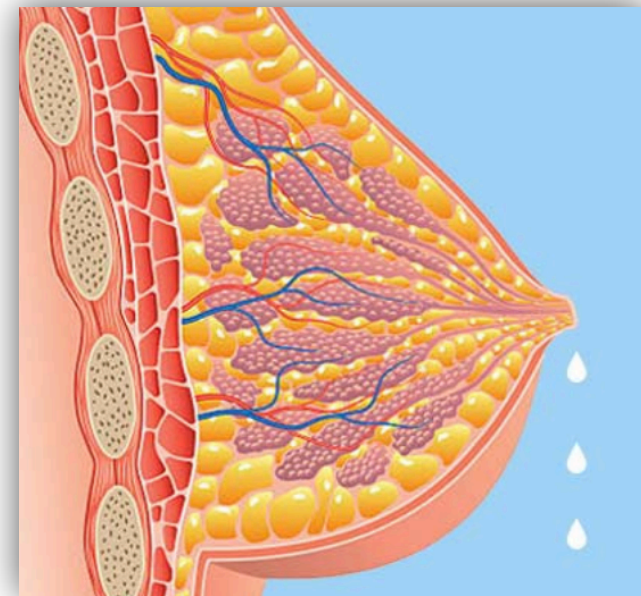
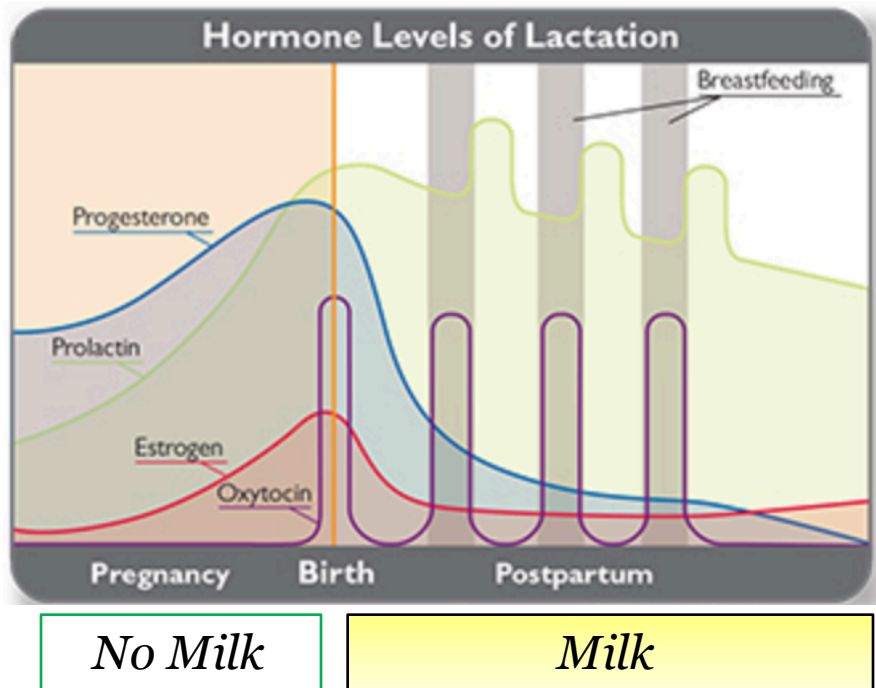
- Pregnancy
 - Estrogen stimulates PRL release (*accounts of doubling of pituitary size during pregnancy*)

Lactotroph Hypertrophy
(blood supply does not double)

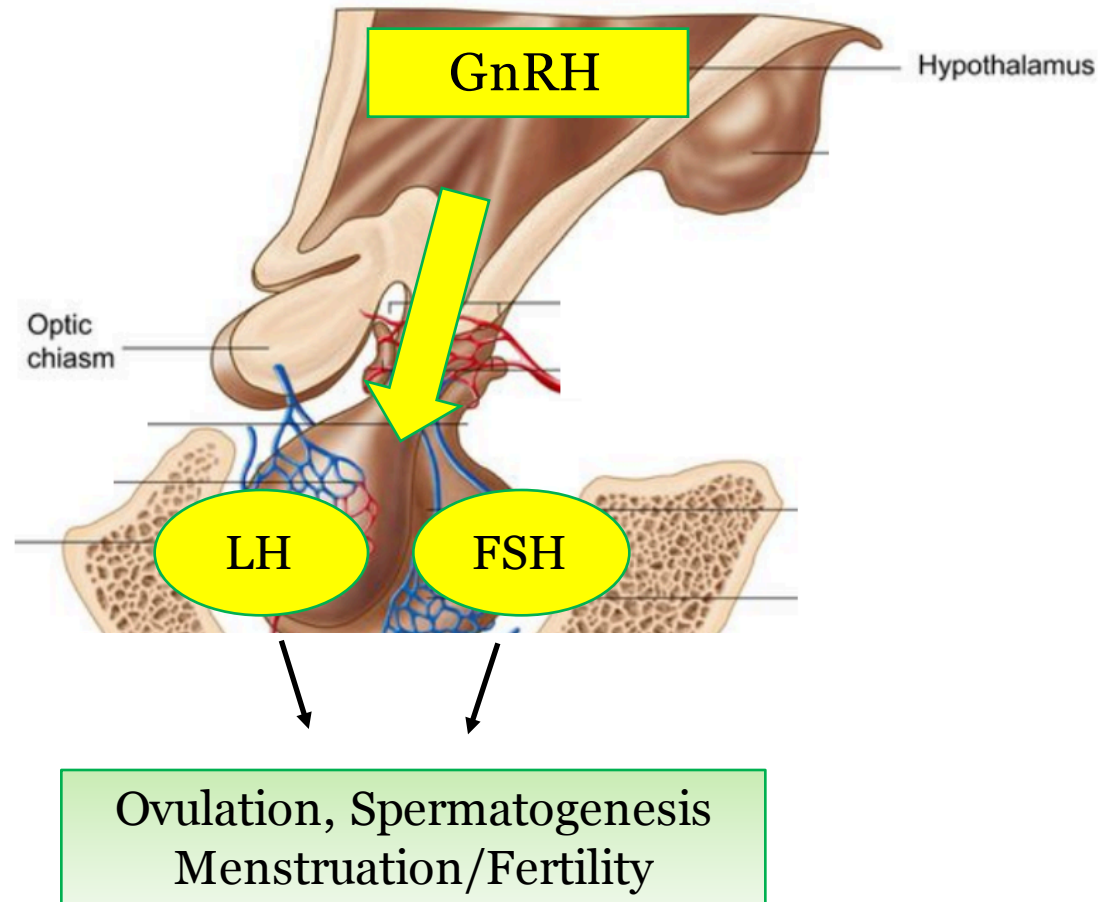


Prolactin Physiology: Pregnancy

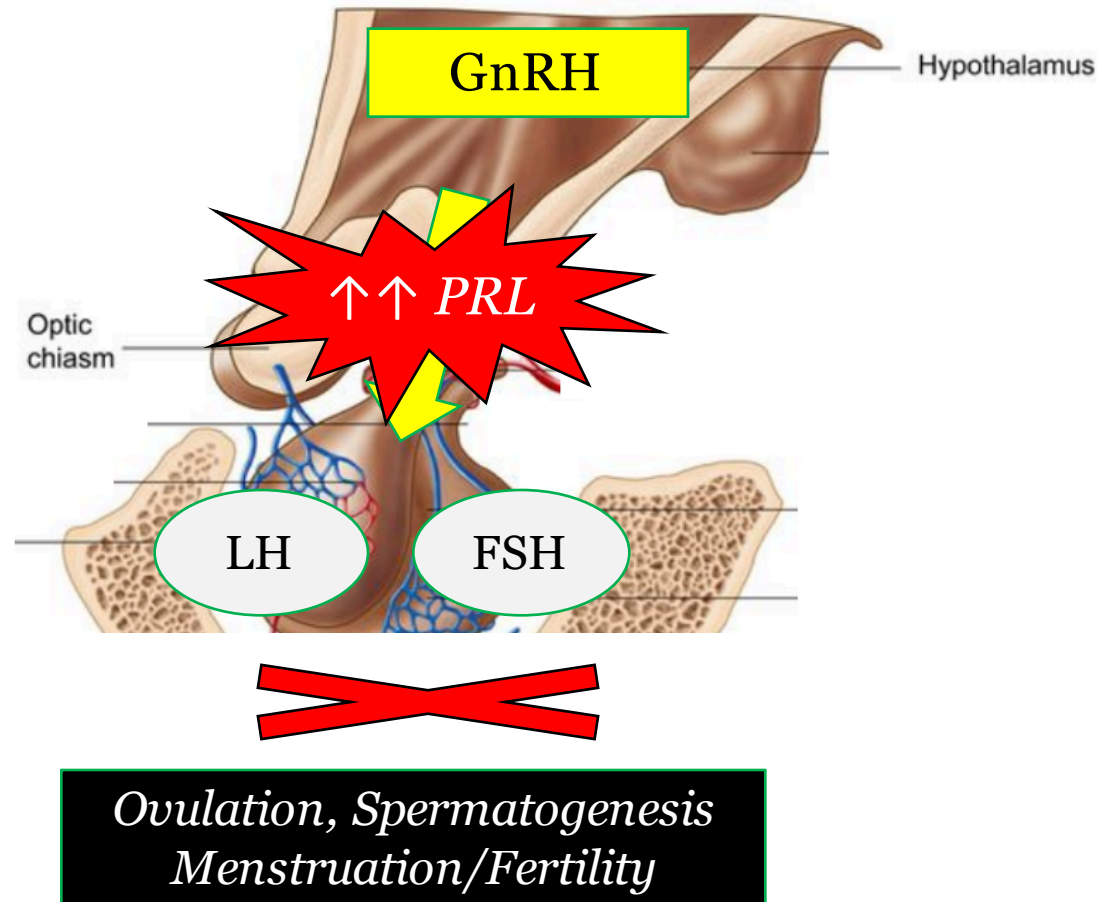
- Pregnancy
 - Estrogen/Progesterone *inhibit secretion of milk during pregnancy*
 - *Breast: E/P downregulate PRL receptors*
 - Immediately following birth, the high levels of E/P secreted by the placenta fall and the *lactogenic effects of PRL become manifest*

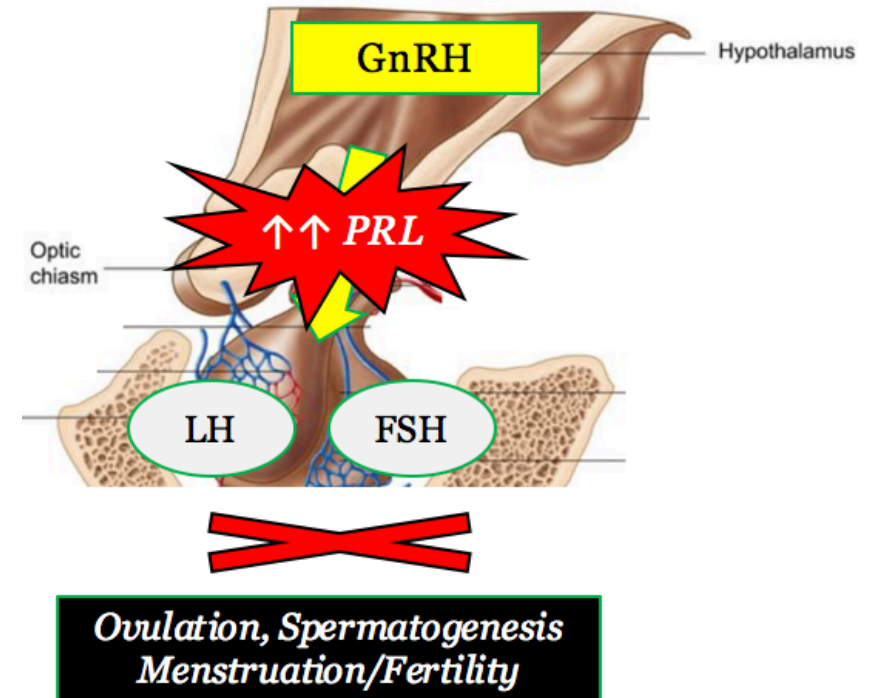
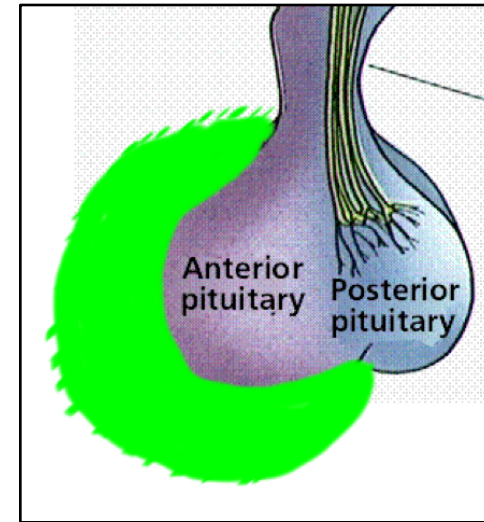
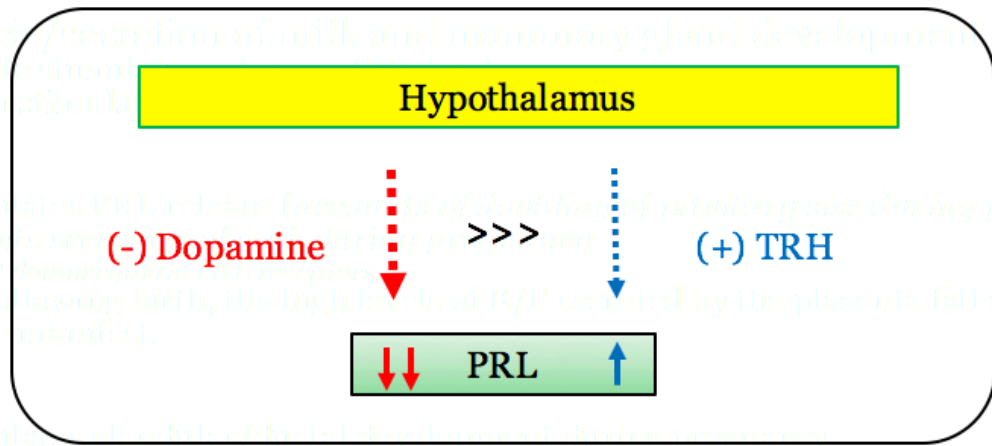


Prolactin Physiology: Inhibits GnRH



Prolactin Physiology: *Inhibits GnRH*



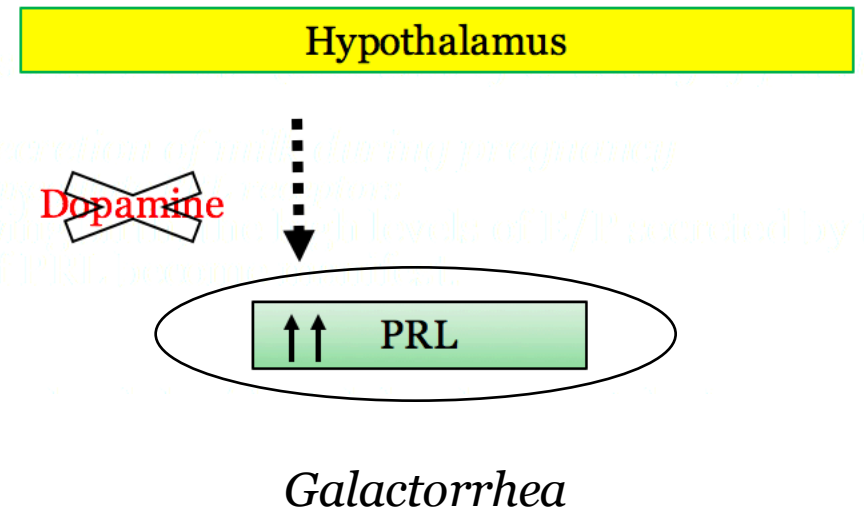
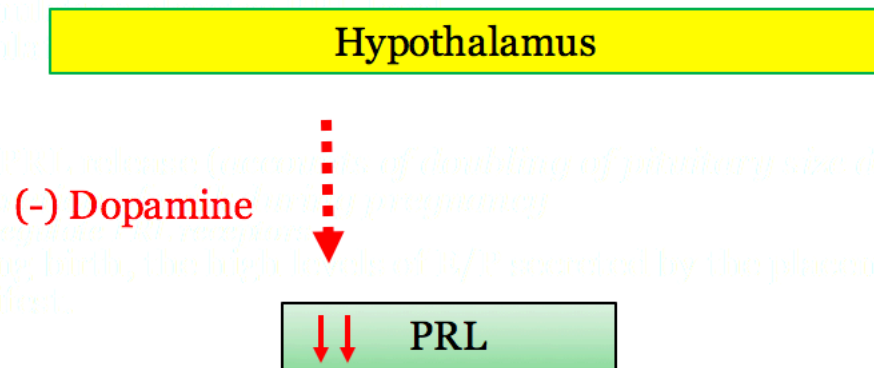


Building Prolactin Derivatives for USMLE Step One

- Physiology of Prolactin
- Prolactin Dysregulation
- Prolactin Deficiency
- Hyperprolactinemia

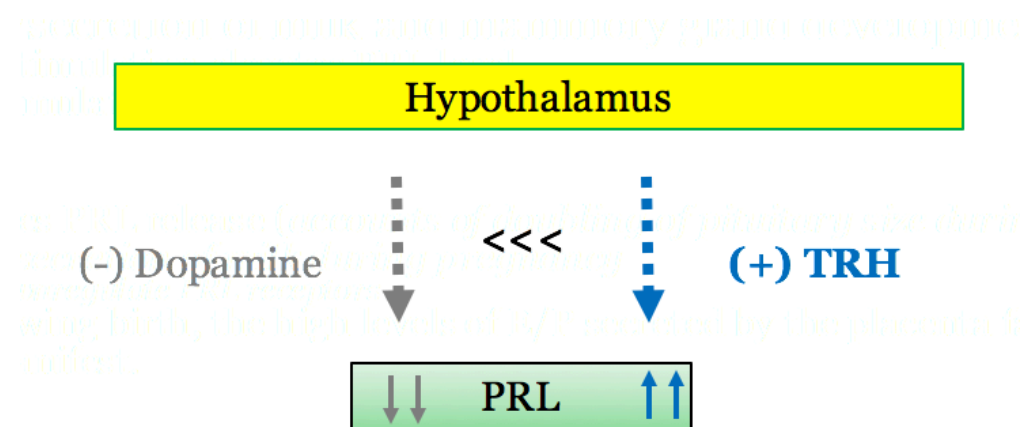
Prolactin Dysregulation: *Lactotroph Hyperplasia*

- Dopamine receptor antagonists (i.e. *medications*)
 - Metoclopramide
 - Antipsychotics (e.g. *risperidole*)



Prolactin Dysregulation: *Lactotroph Hyperplasia*

- Dopamine receptor antagonists (i.e. *medications*)
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 - Antipsychotics (e.g. *risperidole*)
- 1° Hypothyroidism → ↑ TRH → weak stimulatory effect on lactotrophs
 - Derivative: 1° hypothyroidism → hyperPRL/galactorrhea

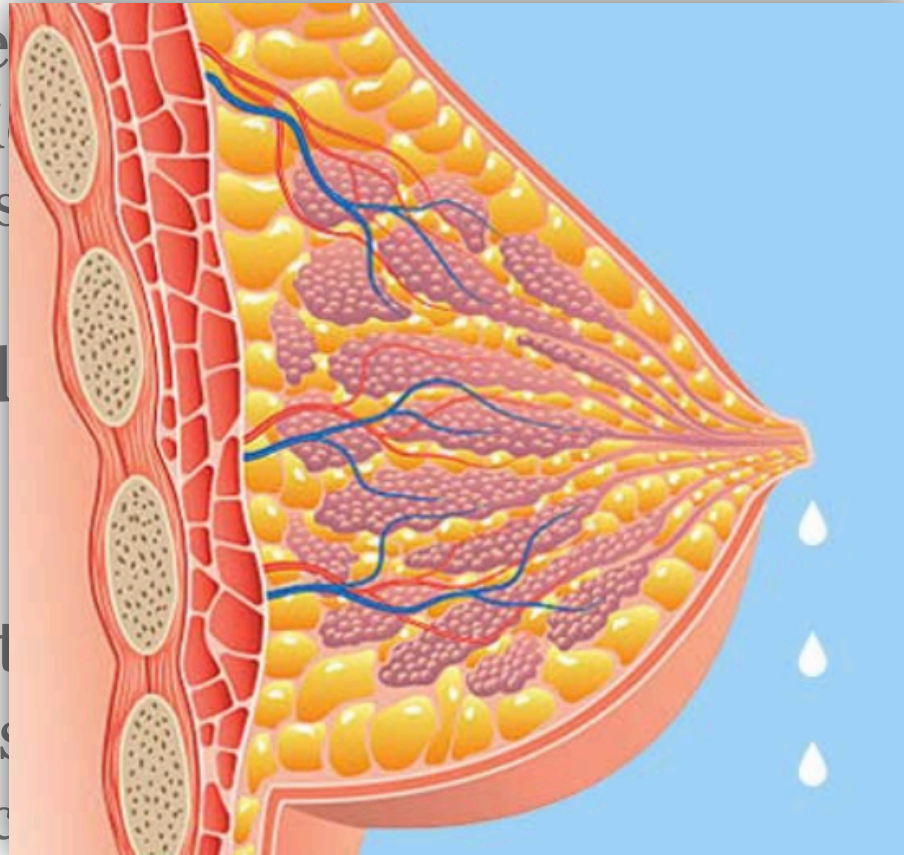


Prolactin Dysregulation: *Lactotroph Hyperplasia*

- Dopamine receptor antagonists (i.e. *medications*)
 - Metoclopramide
 - Antipsychotics (e.g. *risperidole*)
- 1° Hypothyroidism → ↑ TRH → weak stimulatory effect on lactotrophs
 - Derivative: 1° hypothyroidism → hyperPRL/galactorrhea
- Hypothalamic tumors (e.g. craniopharyngioma)/infiltrative disorders (e.g. sarcoidosis)
 - Loss of prolactin inhibitory factor

Prolactin Dysregulation: *Lactotroph Hyperplasia*

- Dopamine receptors (antagonists)
 - Metoclopramide
 - Antipsychotics
- 1° Hypothyroidism (stimulatory effect on lactotrophs)
- Hypothalamic tumors (e.g. prolactinoma)/infiltrative
 - Loss of prolactin-inhibiting factor

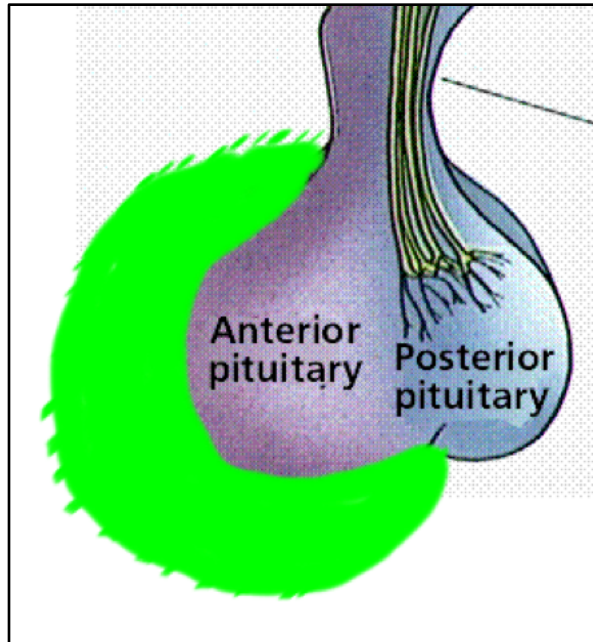


Building Prolactin Derivatives

- Physiology of Prolactin
 - Mammary development; milk production
 - Regulator: hypothalamic release of dopamine (inhibitory)
- Prolactin Dysregulation
 - Lactotroph hyperplasia: meds (receptor antagonists), ↑ TRH
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- Prolactin Deficiency
- Hyperprolactinemia

Prolactin Deficiency: Sheehan's Syndrome

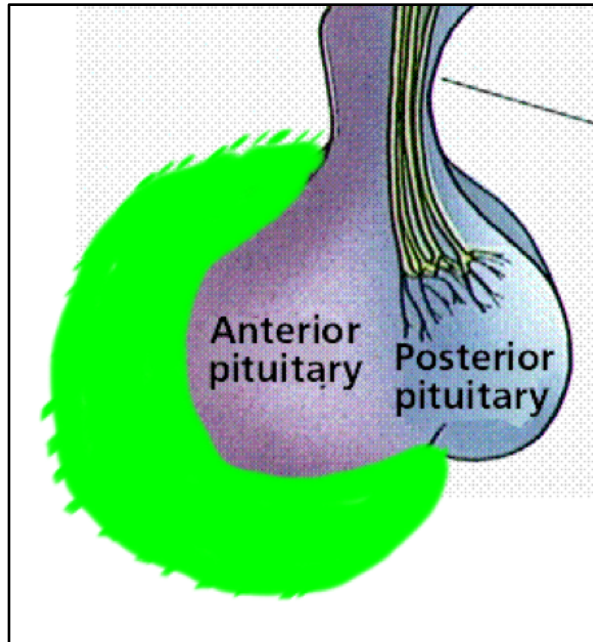
- Ischemic injury to Pituitary



Lactotroph Hypertrophy
(blood supply does not double)

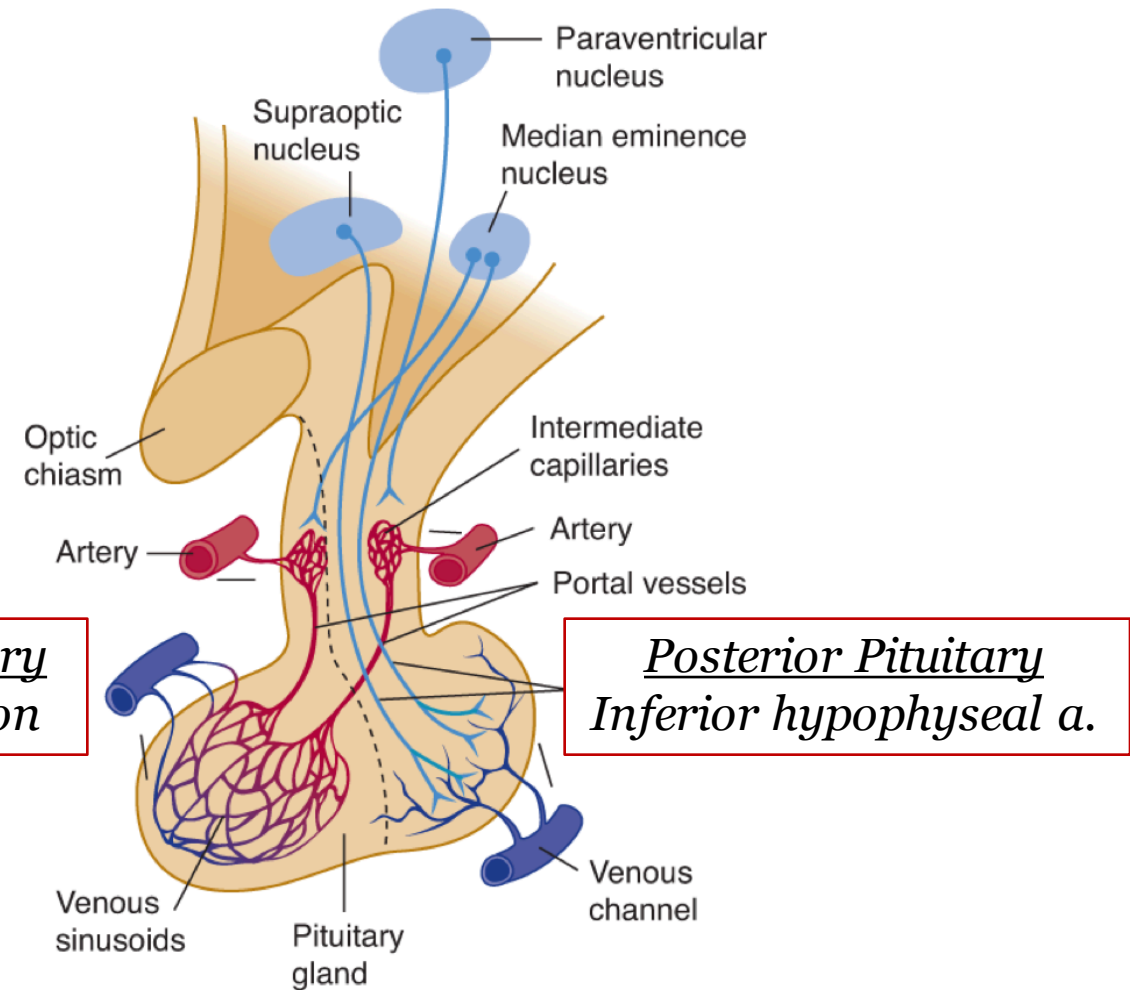
Prolactin Deficiency: Sheehan's Syndrome

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*Lactotroph Hypertrophy
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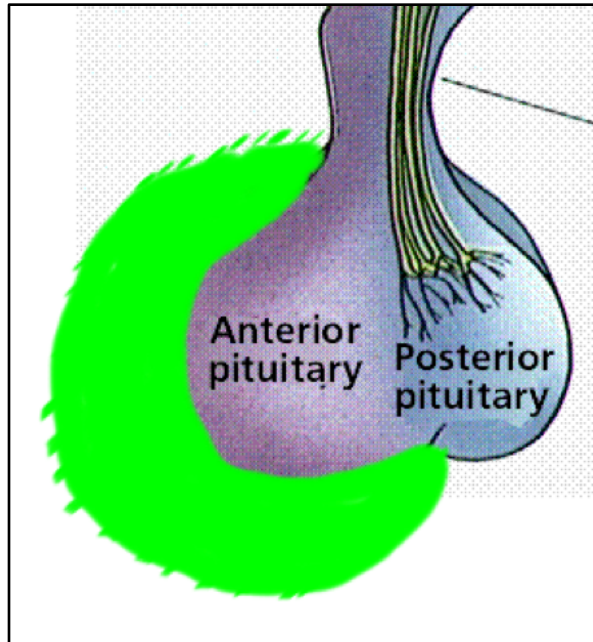
*Anterior Pituitary
Portal circulation*



*Posterior Pituitary
Inferior hypophyseal a.*

Prolactin Deficiency: Sheehan's Syndrome

- Ischemic injury to Pituitary
- Manifestations: HypoPRL

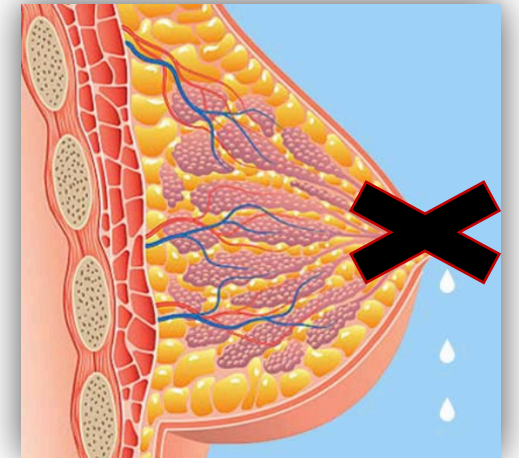


*Lactotroph Hypertrophy
(blood supply does not double)*

Prolactin Deficiency



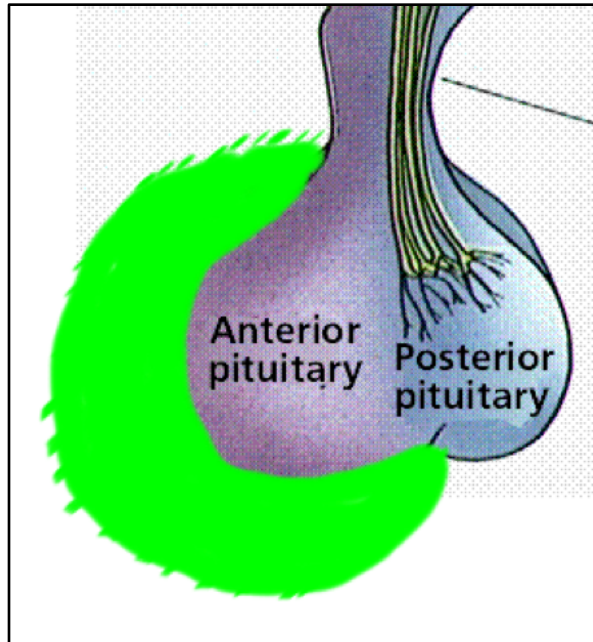
Failure of Breast Feeding



Ischemic necrosis of the pituitary in setting of hemorrhage/hypotension

Prolactin Deficiency: Sheehan's Syndrome

- Ischemic injury to Pituitary
- Manifestations: HypoPRL

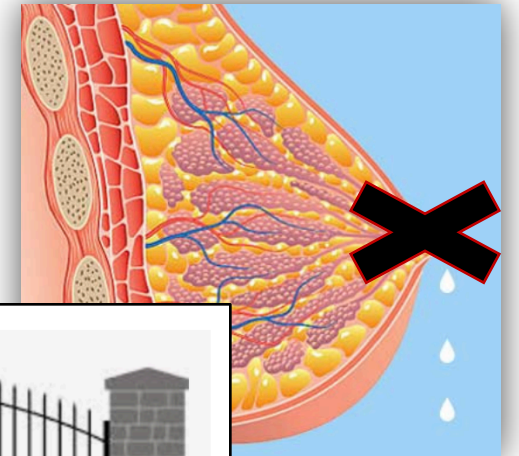


*Lactotroph Hypertrophy
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Prolactin Deficiency

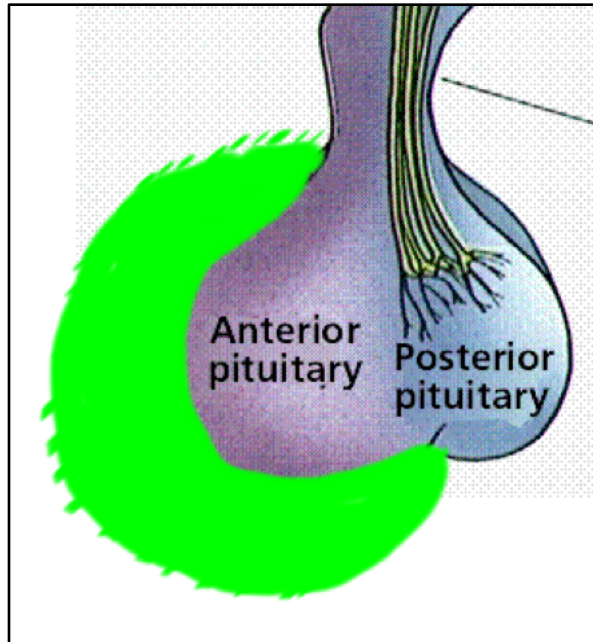


Failure of Breast Feeding

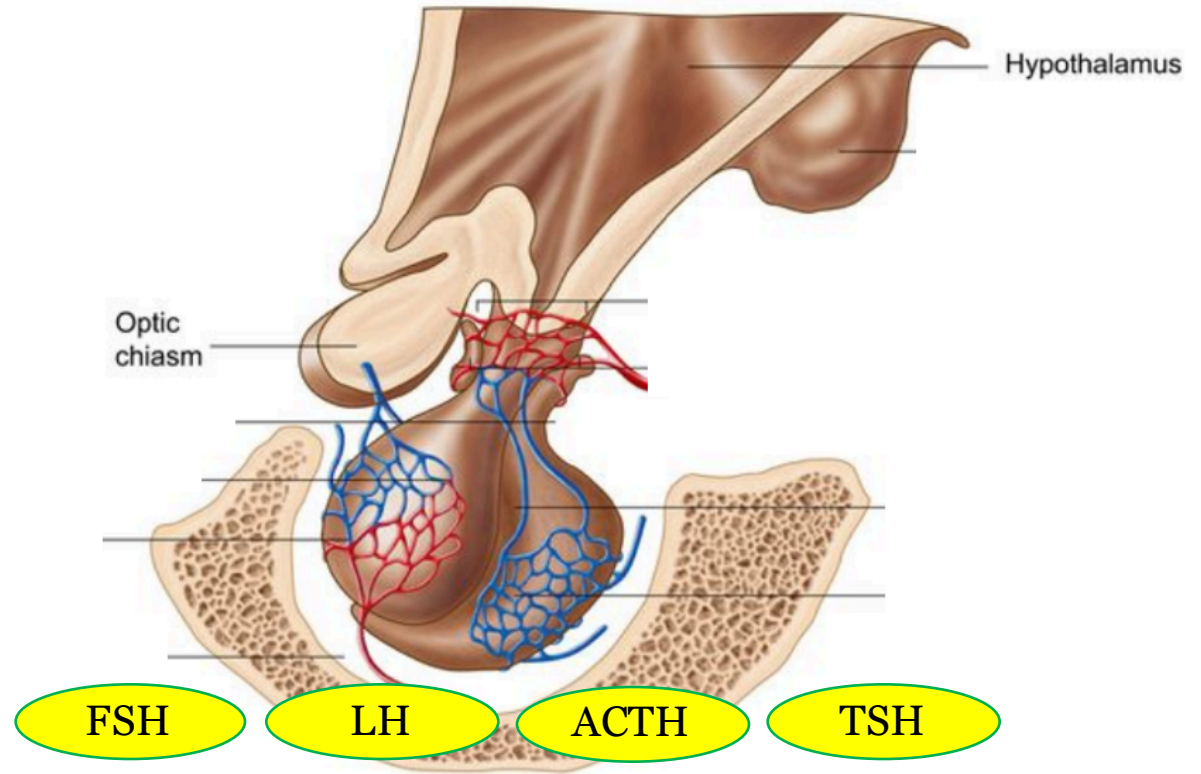


Prolactin Deficiency: Sheehan's Syndrome

- Ischemic injury to Pituitary
- Manifestations: Hypopituitarism

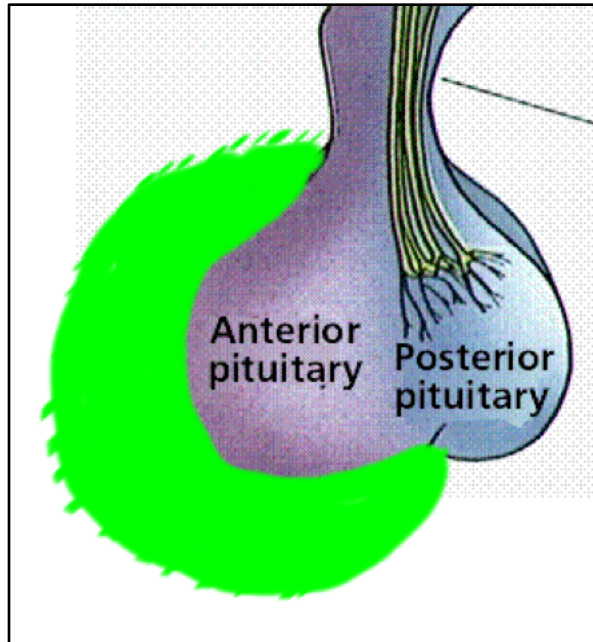


*Lactotroph Hypertrophy
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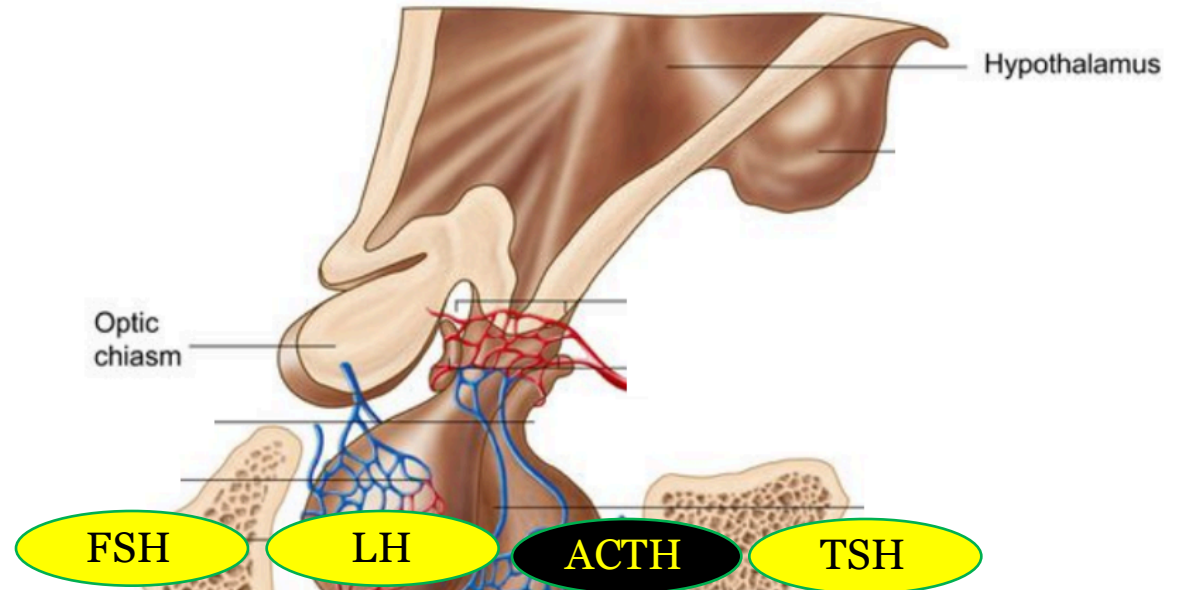


Prolactin Deficiency: Sheehan's Syndrome

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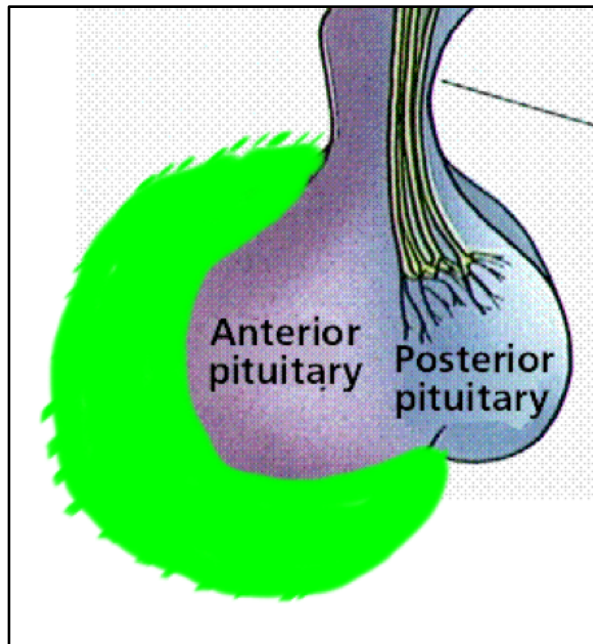
*Lactotroph Hypertrophy
(blood supply does not double)*



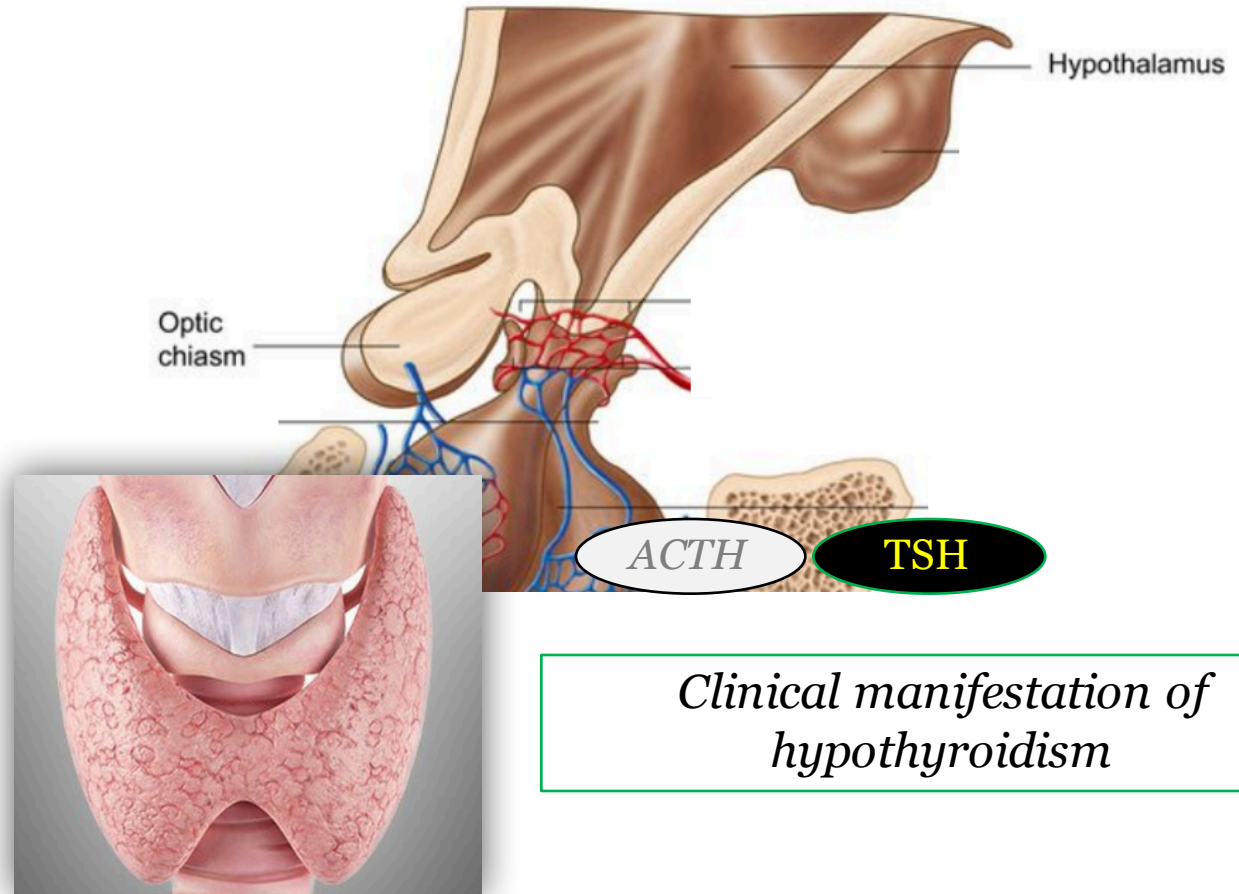
*ACTH independence and
Aldosterone production (i.e. renin)*

Prolactin Deficiency: Sheehan's Syndrome

- Ischemic injury to Pituitary
- Manifestations: Hypopituitarism



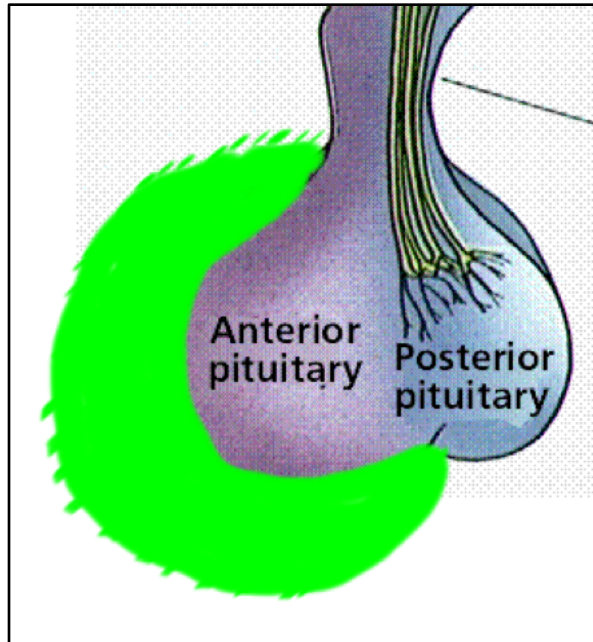
*Lactotroph Hypertrophy
(blood supply does not double)*



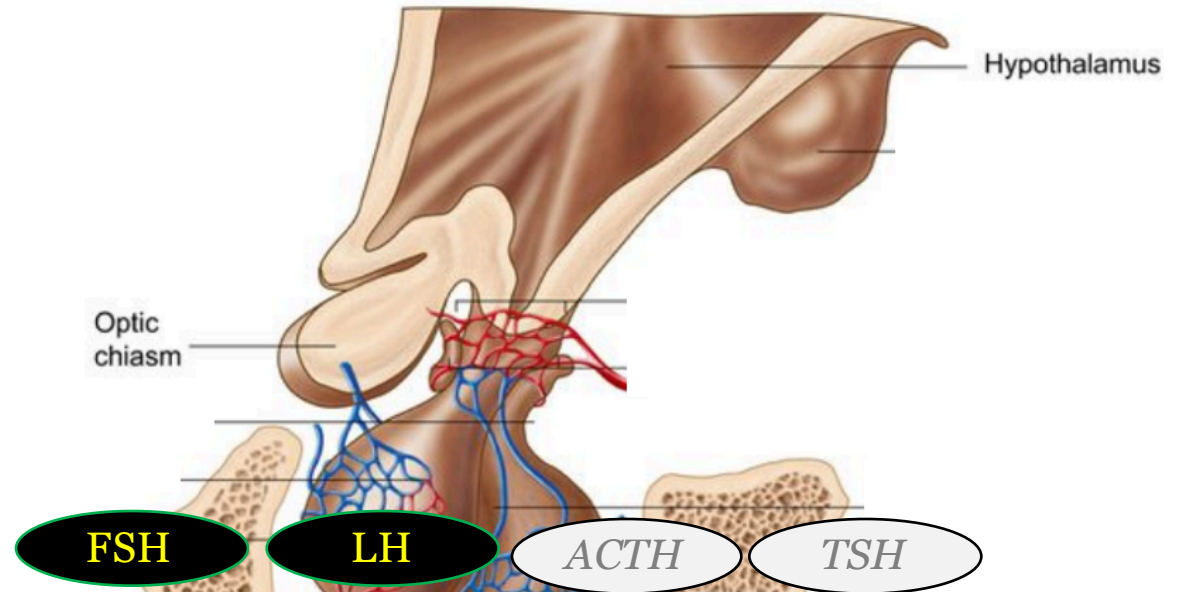
*Clinical manifestation of
hypothyroidism*

Prolactin Deficiency: Sheehan's Syndrome

- Ischemic injury to Pituitary
- Manifestations: Hypopituitarism



*Lactotroph Hypertrophy
(blood supply does not double)*

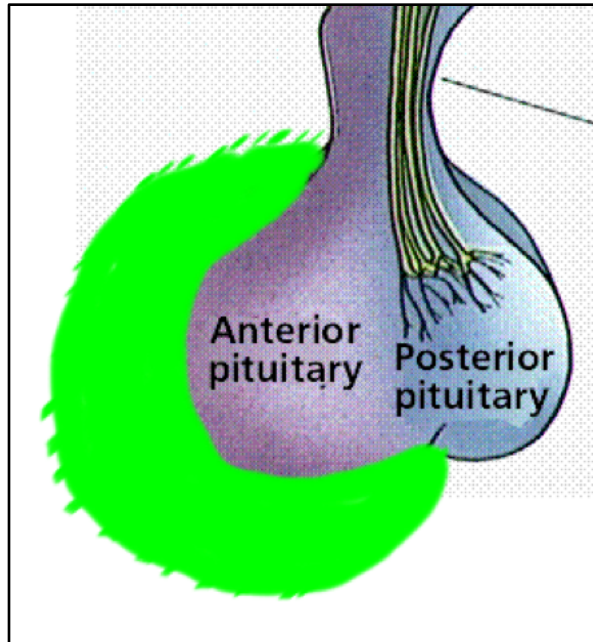


*Amenorrhea/Infertility →
Long term consequences: OP*

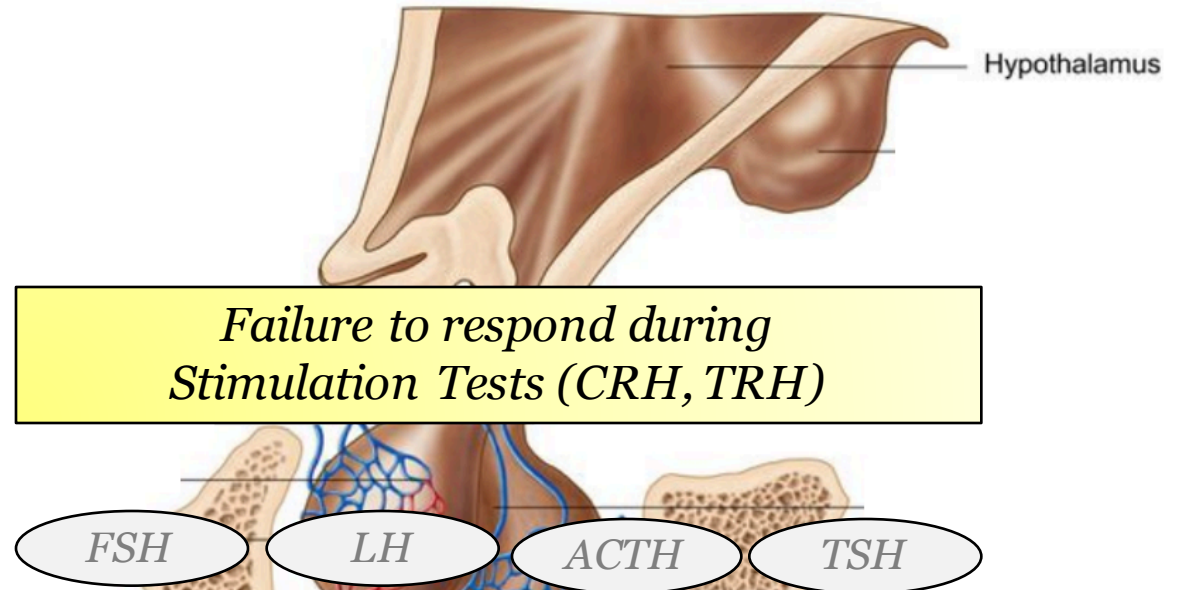


Prolactin Deficiency: Sheehan's Syndrome

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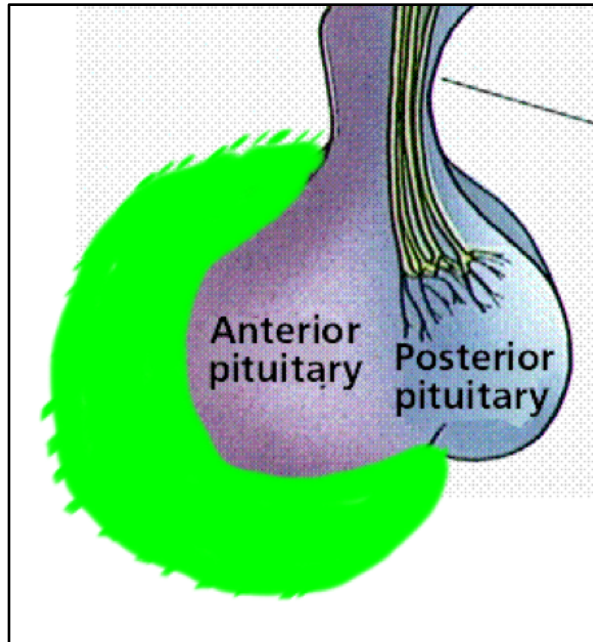


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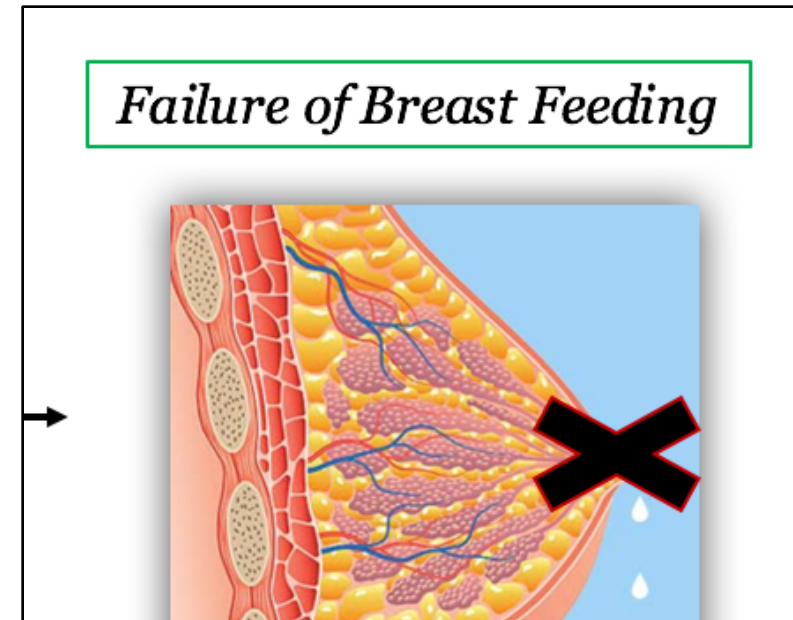


Prolactin Deficiency: Sheehan's Syndrome

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- Manifestations: Hypopituitarism



*Lactotroph Hypertrophy
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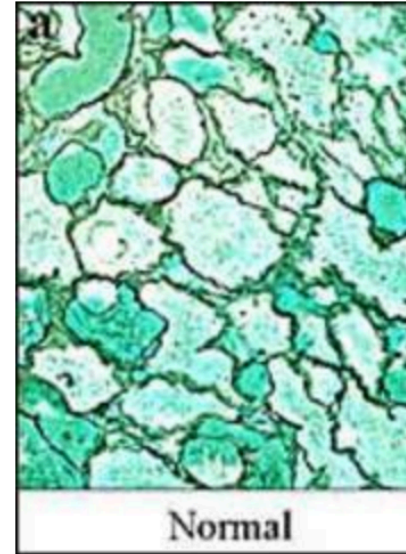
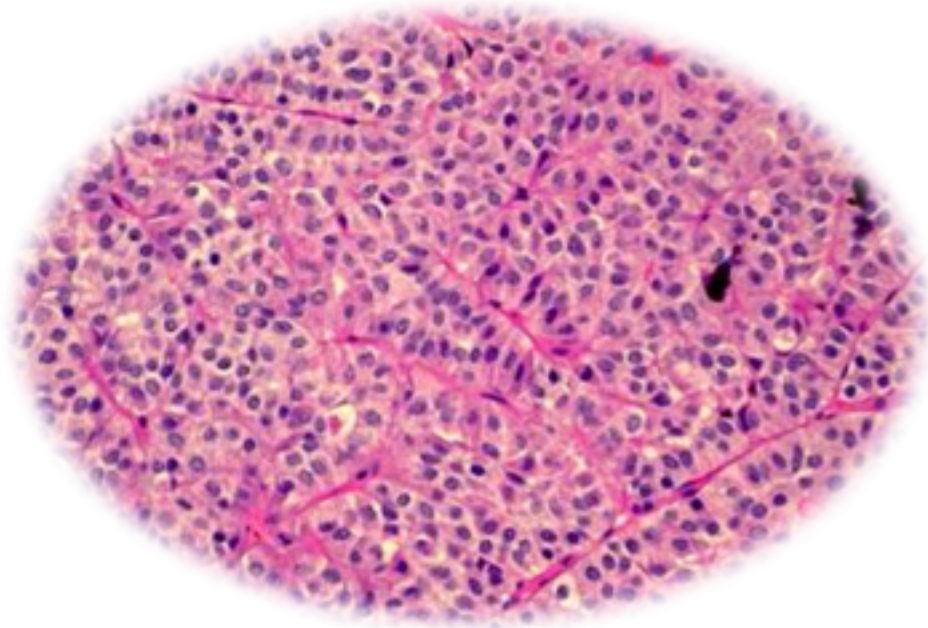


Prolactin Deficiency

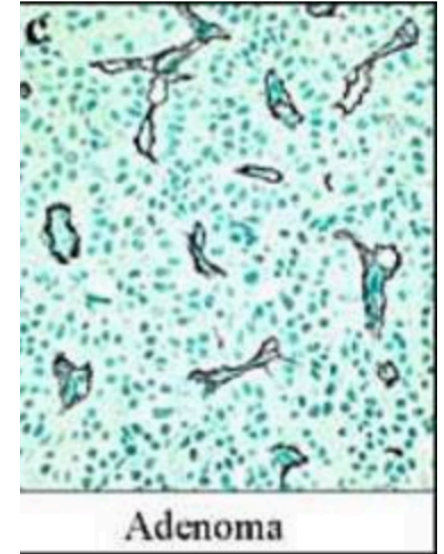
Building Prolactin Derivatives

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 - Sheehan's/Hypopituitarism
- Hyperprolactinemia (Pituitary Adenoma)

HyperPRL: *Adenoma* Pathology

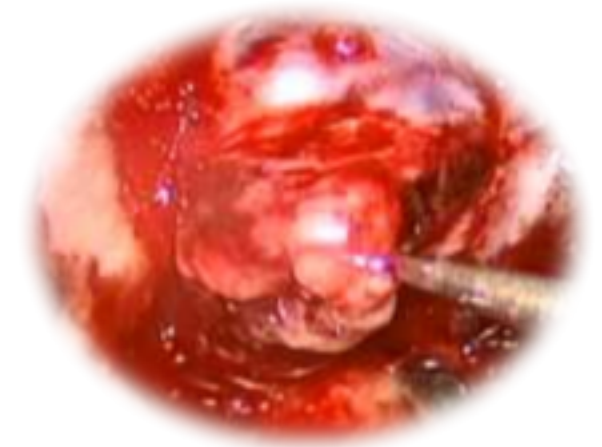


Lacks
→
Reticulin

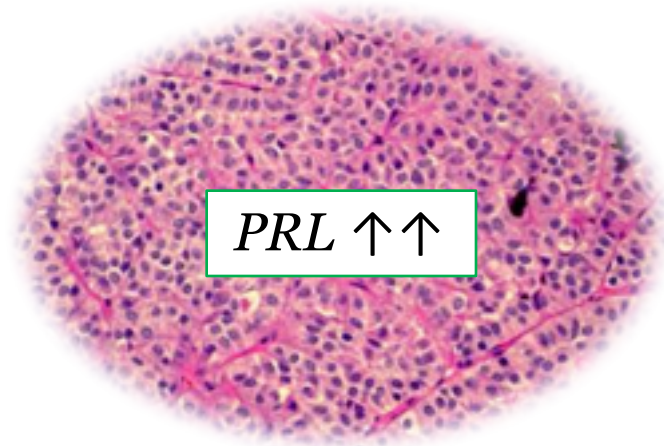


Sheets/Cords of uniform (monomorphic) cells
Capsule absent, 30%

Lack of reticulin network (sparse connective tissue) gelatinous appearance



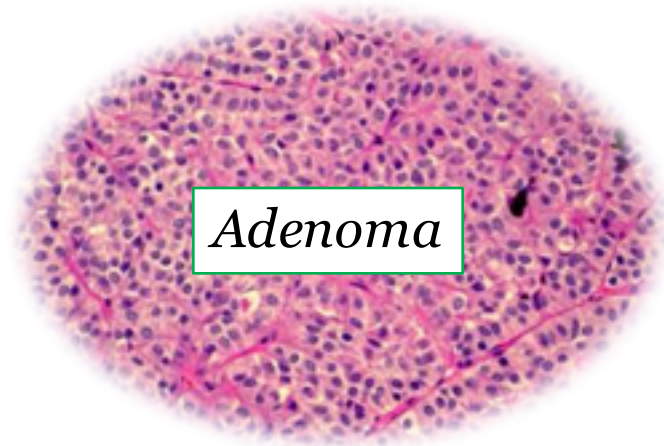
HyperPRL: Clinical Manifestations



Mass Effects

Endocrine

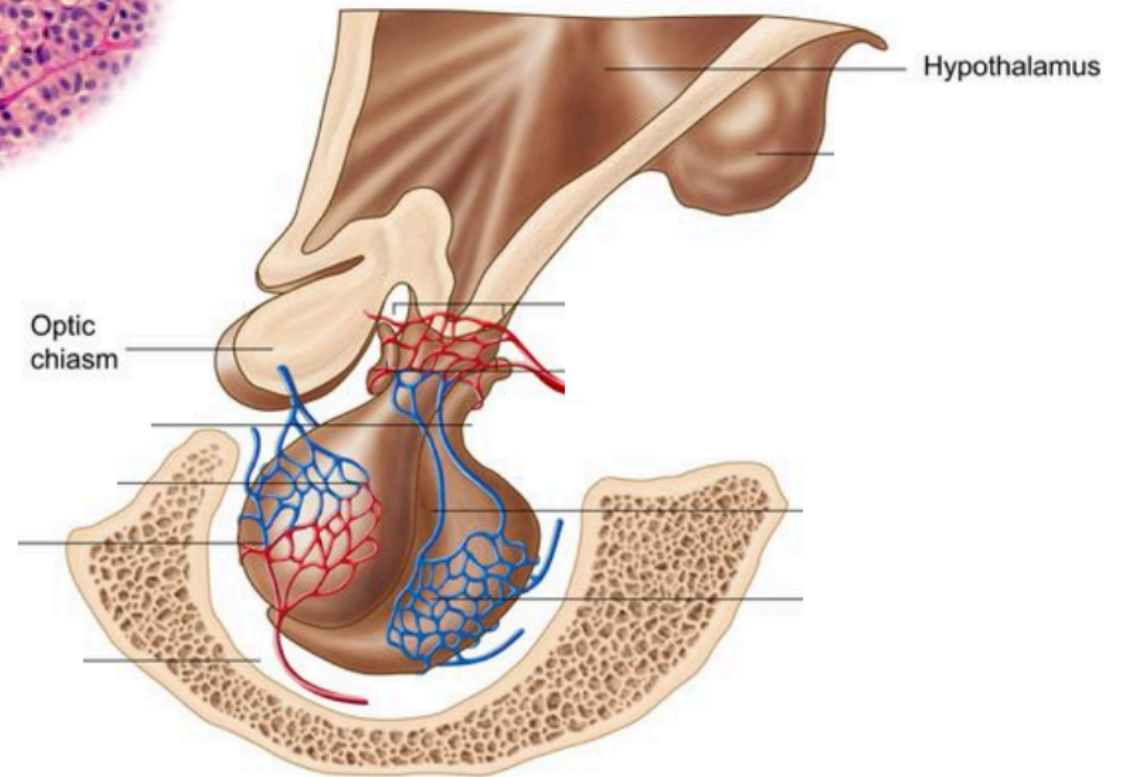
Adenoma: Mass Effects



Mass Effects

*Bitemporal
Hemianopsia*

*Patient with MVA as he didn't see
the car **coming from his side...***



Adenoma: Mass Effects

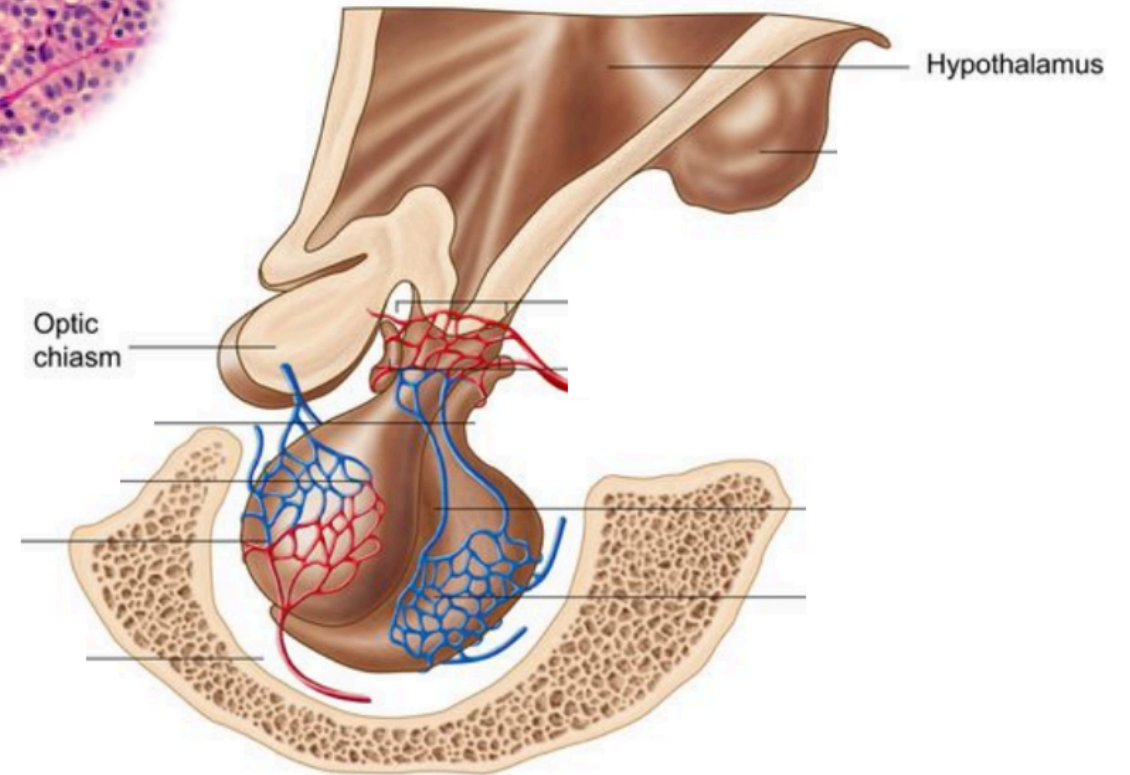


Mass Effects:

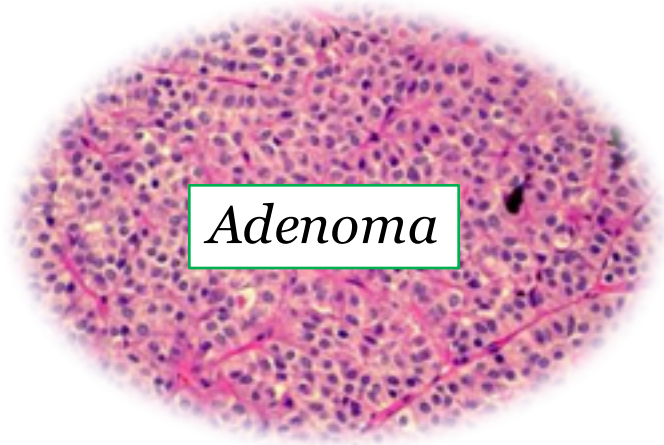
Visual field defect
Headache

Null Cell Tumor more likely
to present with mass effect

Bitemporal
Hemianopsia

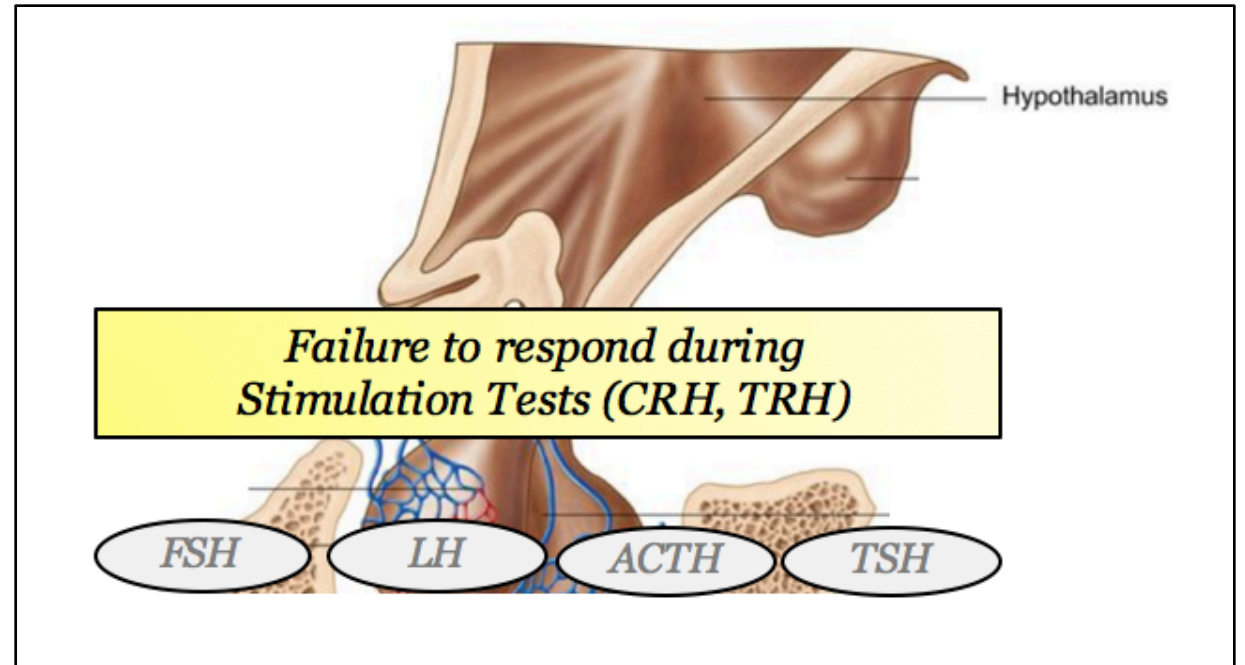


Adenoma: Mass Effects

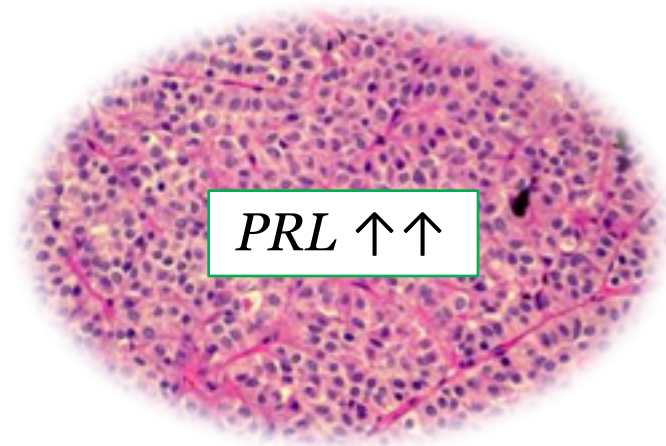


Mass Effects:

Visual field defect
Headache
Hypopituitarism



HyperPRL: Endocrine Manifestations



Endocrine



Gals

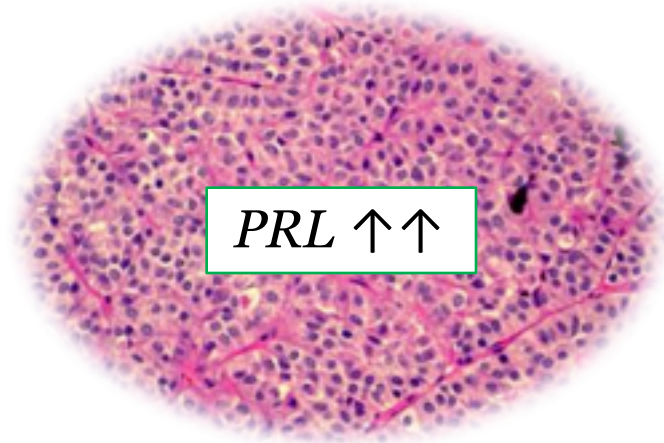


Boys

HyperPRL: Endocrine Manifestations



Gals



PRL ↑↑



Gals

PRL: Galactorrhea

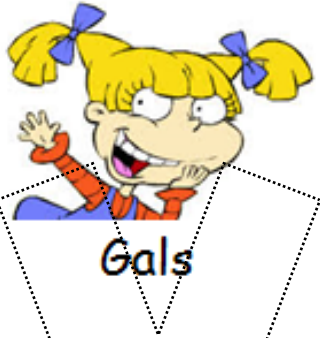
Endocrine

↓ GnRH



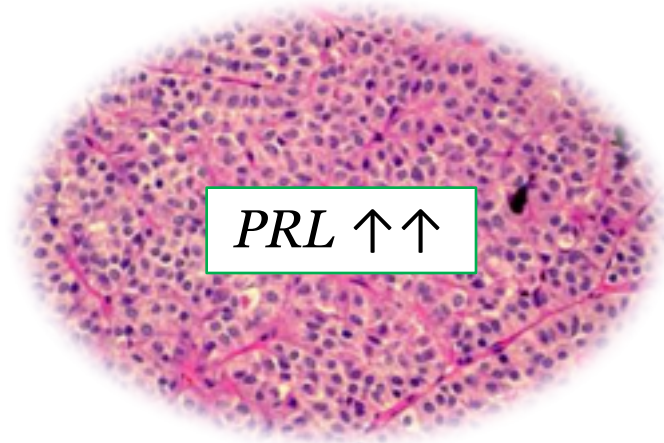
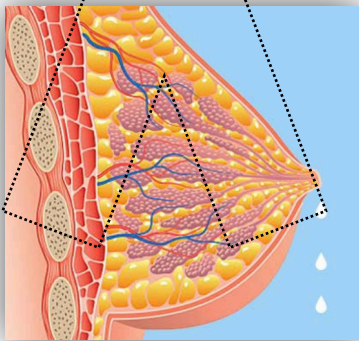
Amenorrhea
Infertility

HyperPRL: Endocrine Manifestations



Gals

PRL: Galactorrhea



PRL ↑↑

Endocrine



Boys

↓ GnRH

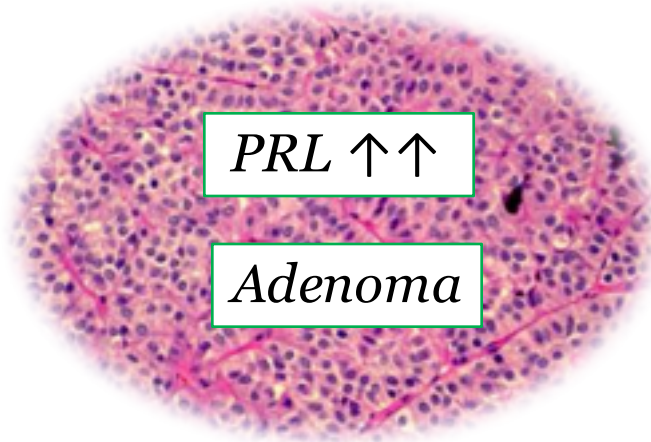
Erectile dysfunction
Loss of libido
Infertility

HyperPRL: Mass/Endocrine Manifestations



Gals

PRL: Galactorrhea



PRL ↑↑

Adenoma

Endocrine

Mass effects



Gateway Condition



Boys

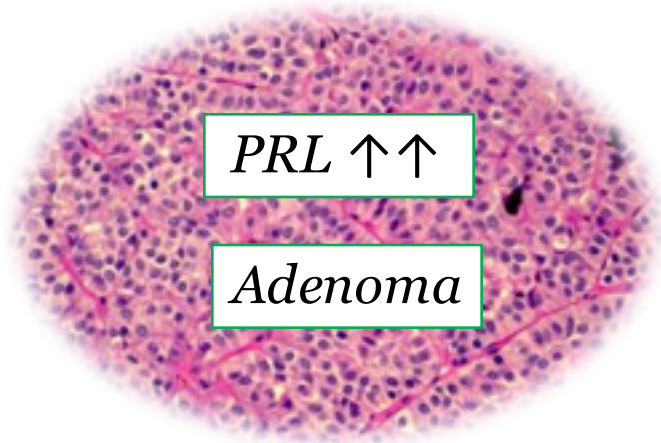
↓ GnRH

Erectile dysfunction
Loss of libido
Infertility

HyperPRL: Mass/Endocrine Manifestations



Gals



PRL ↑↑

Adenoma



Boys

PRL: Galactorrhea



Endocrine

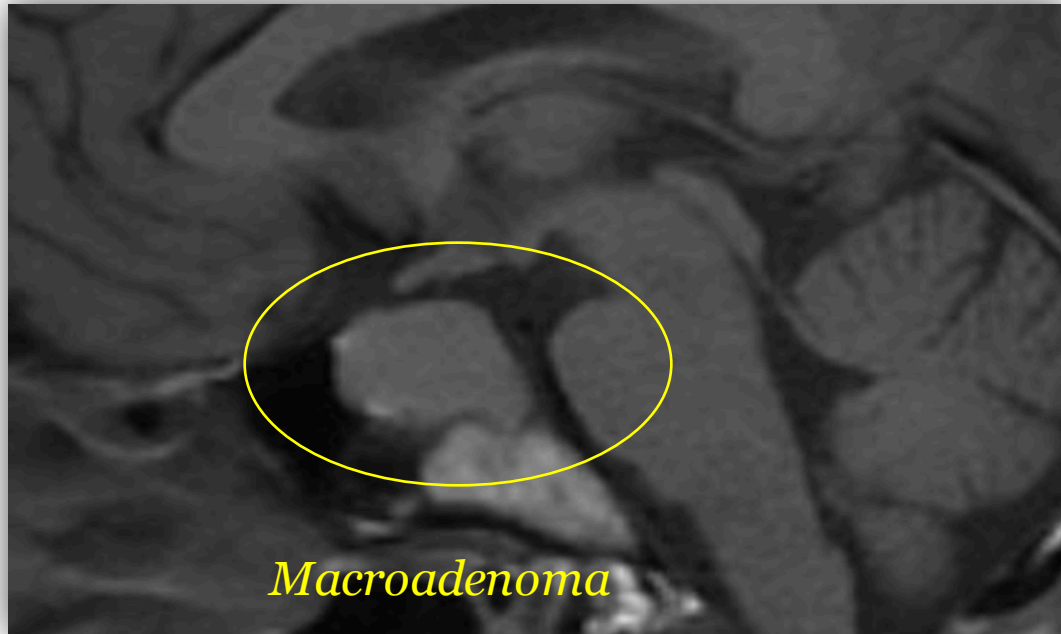
Mass effects

↓ GnRH

Erectile dysfunction
Loss of libido
Infertility

- MEN 1:**
- Pituitary
 - Parathyroid (hyperCa/phosphaturia)
 - Pancreas (neuroendocrine tumor)

Loose Ends



Prolactinoma: most common pituitary adenoma

Hypothalamus

(-) Dopamine



↓↓ PRL

Treatments

PharmacRx: *Dopamine Agonists*
Cabergoline, Bromocriptine

Surgery: Transphenoidal hypophysectomy

Building Prolactin Derivatives

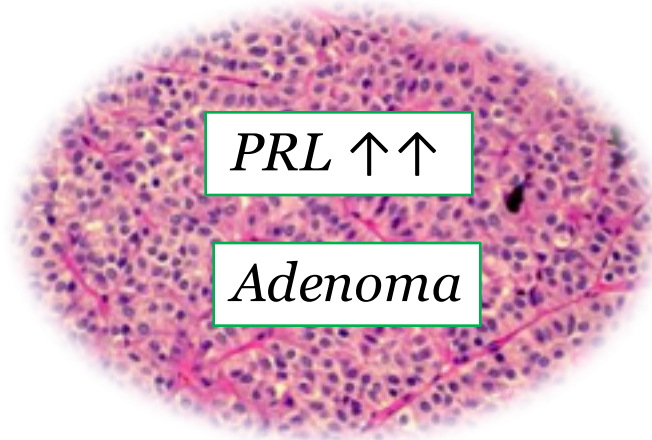


- Physiology of Prolactin
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 - Lactotroph hyperplasia: meds (receptor antagonists), \uparrow TRH
 - Hypothalamic disorders (decrease dopamine)
- Prolactin Deficiency: failure of lactation
 - Sheehan's/Hypopituitarism
- Hyperprolactinemia (Pituitary Adenoma)
 - Mass effect: visual field defect, HA, hypopituitarism
 - Endocrine: galactorrhea/amenorrhea (female), libido/erection (male)
 - Gateway Condition: MEN1 Syndrome
 - Treatment: Dopamine agonists, Transphenoidal resection

Building Prolactin Questions for the USMLE Step One Exam



Gals



Boys

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University of Massachusetts Medical School
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