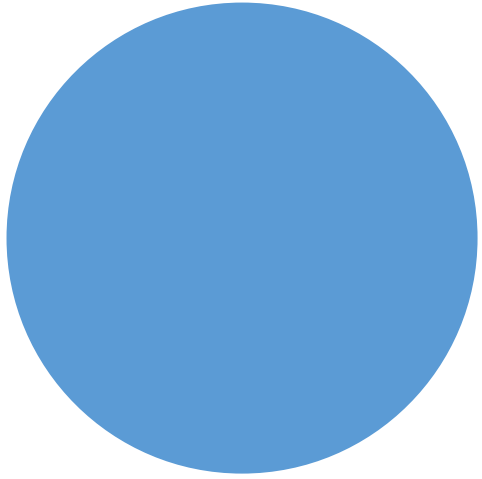
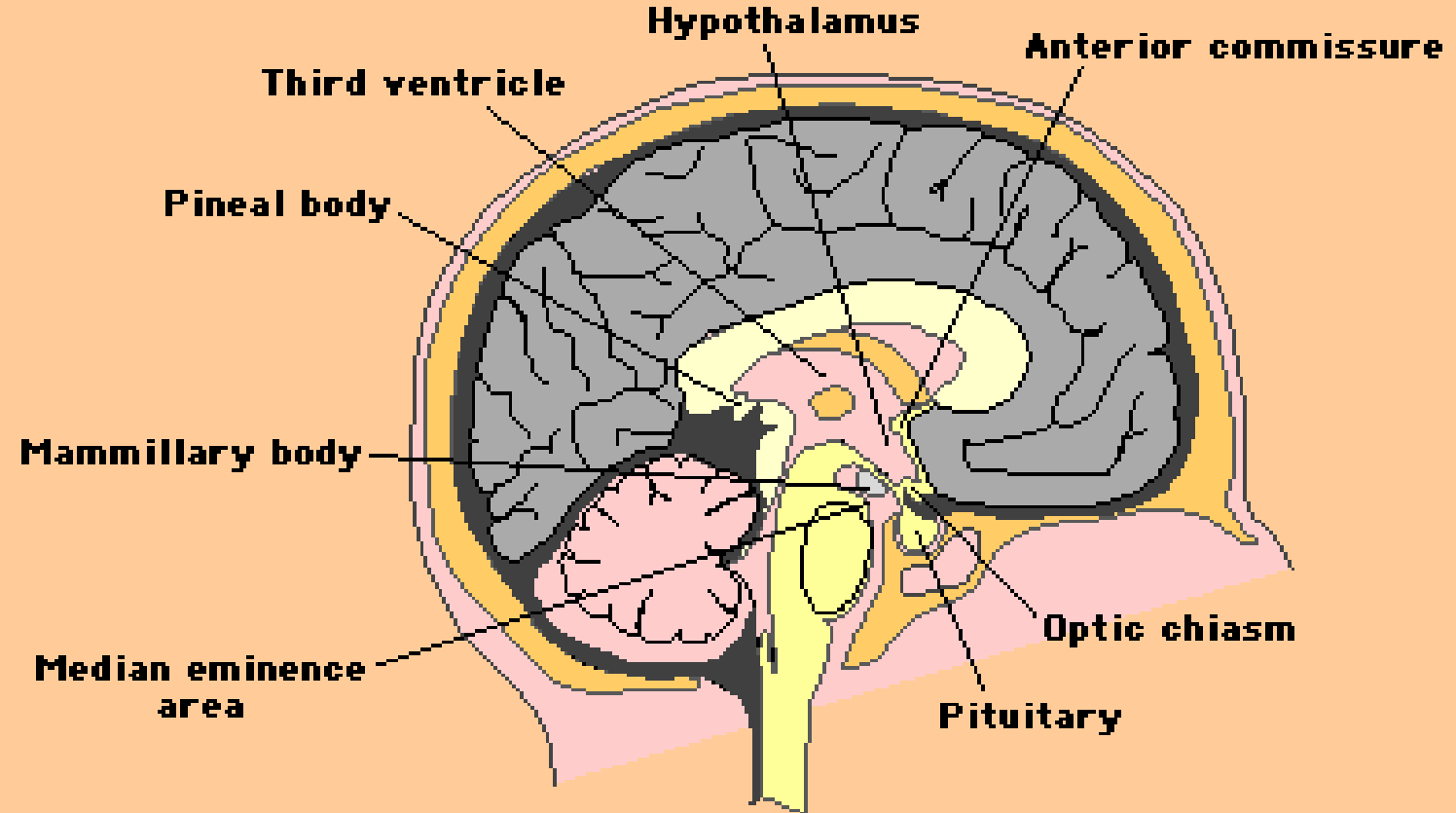


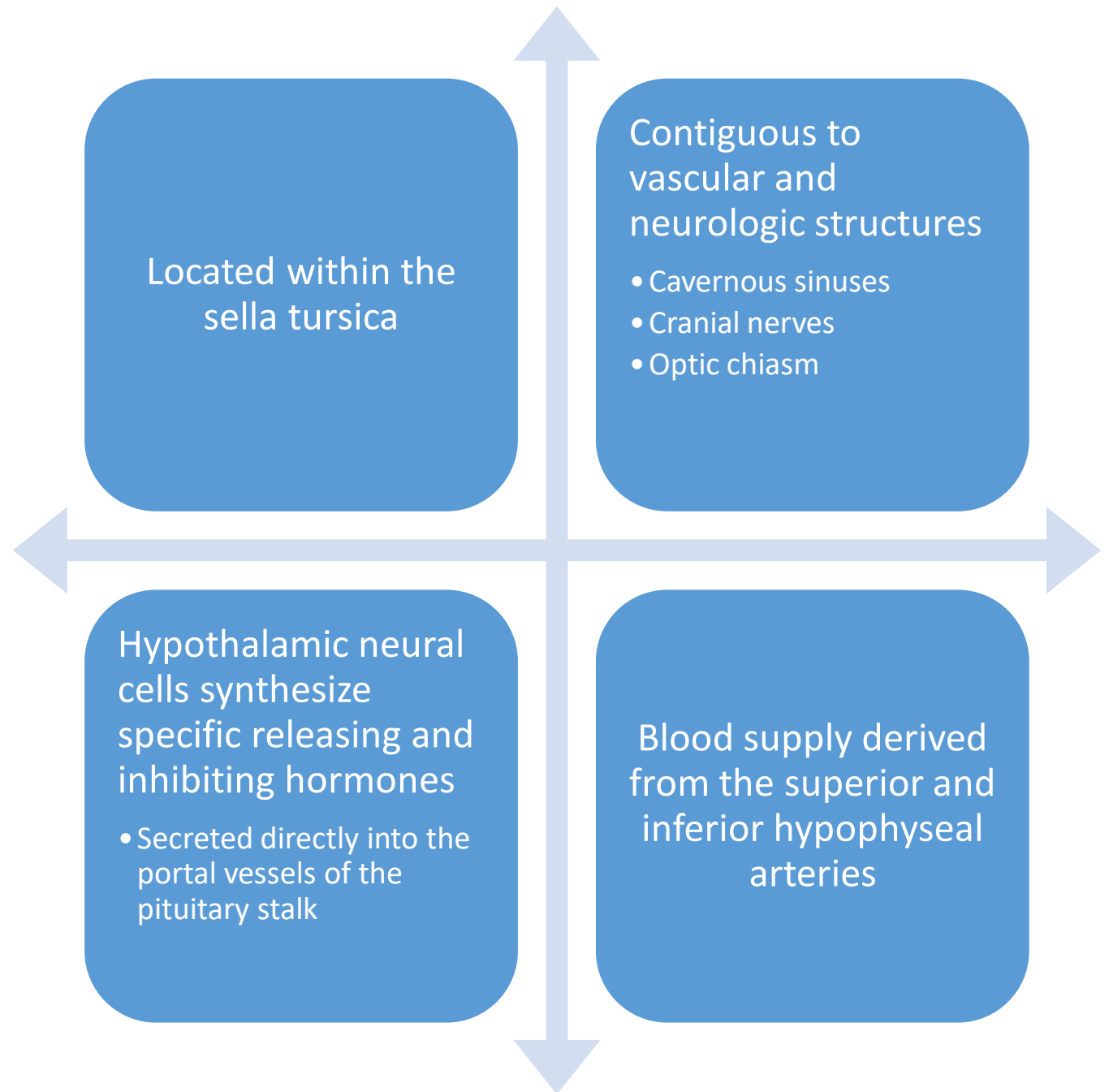
Anterior Pituitary Diseases

Anatomy of the pituitary gland



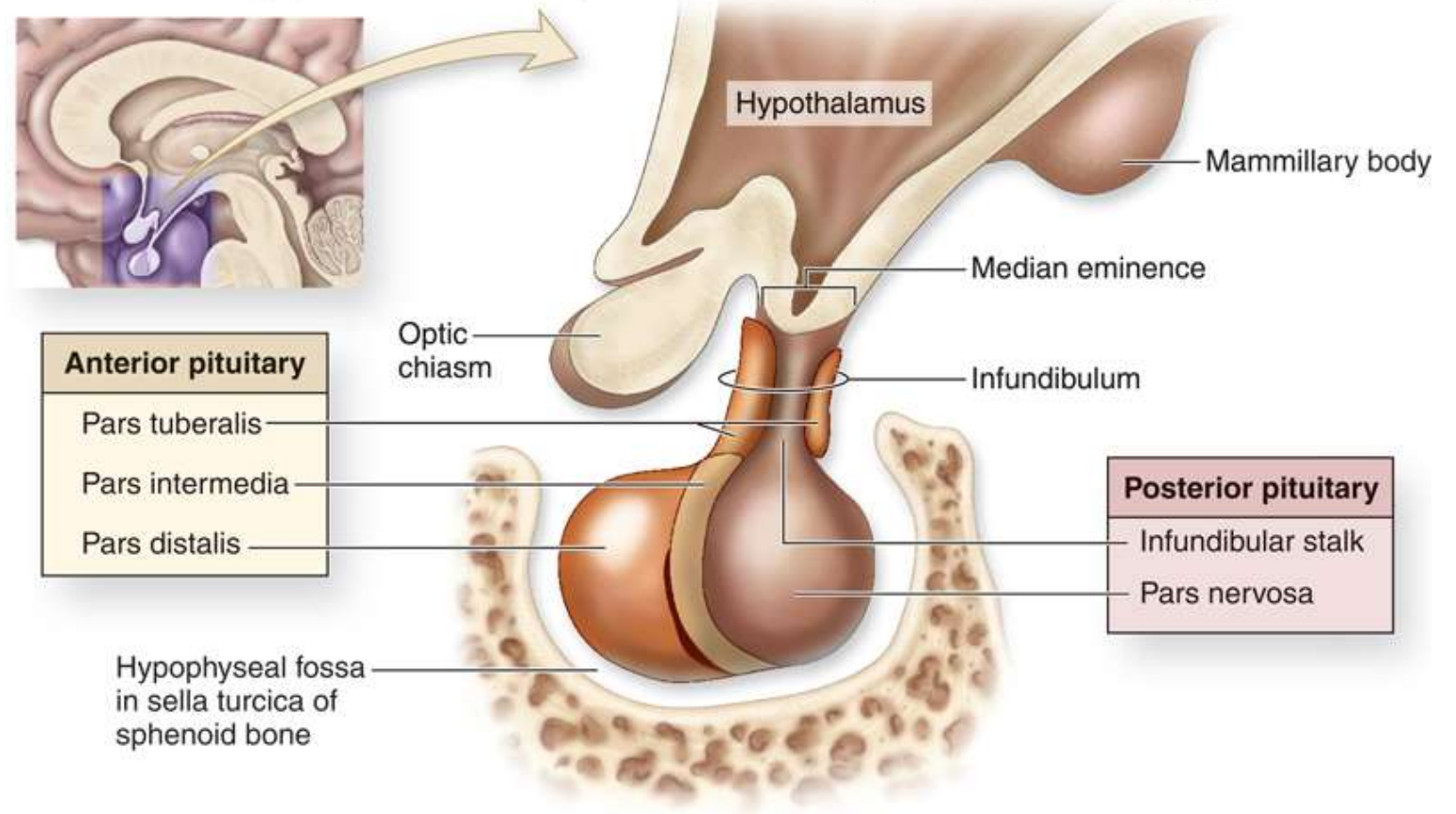
Anatomy of the hypothalamic-pituitary axis Lateral view of the brain showing the relationship of the hypothalamus to the median eminence and the pituitary gland. (Adapted from Krieger, DT, in: Neuroendocrinology, Krieger, DT, Hughes, JC (Eds), Sinauer Associates, Sunderland, MA, 1980, p. 4.)

Pituitary Gland

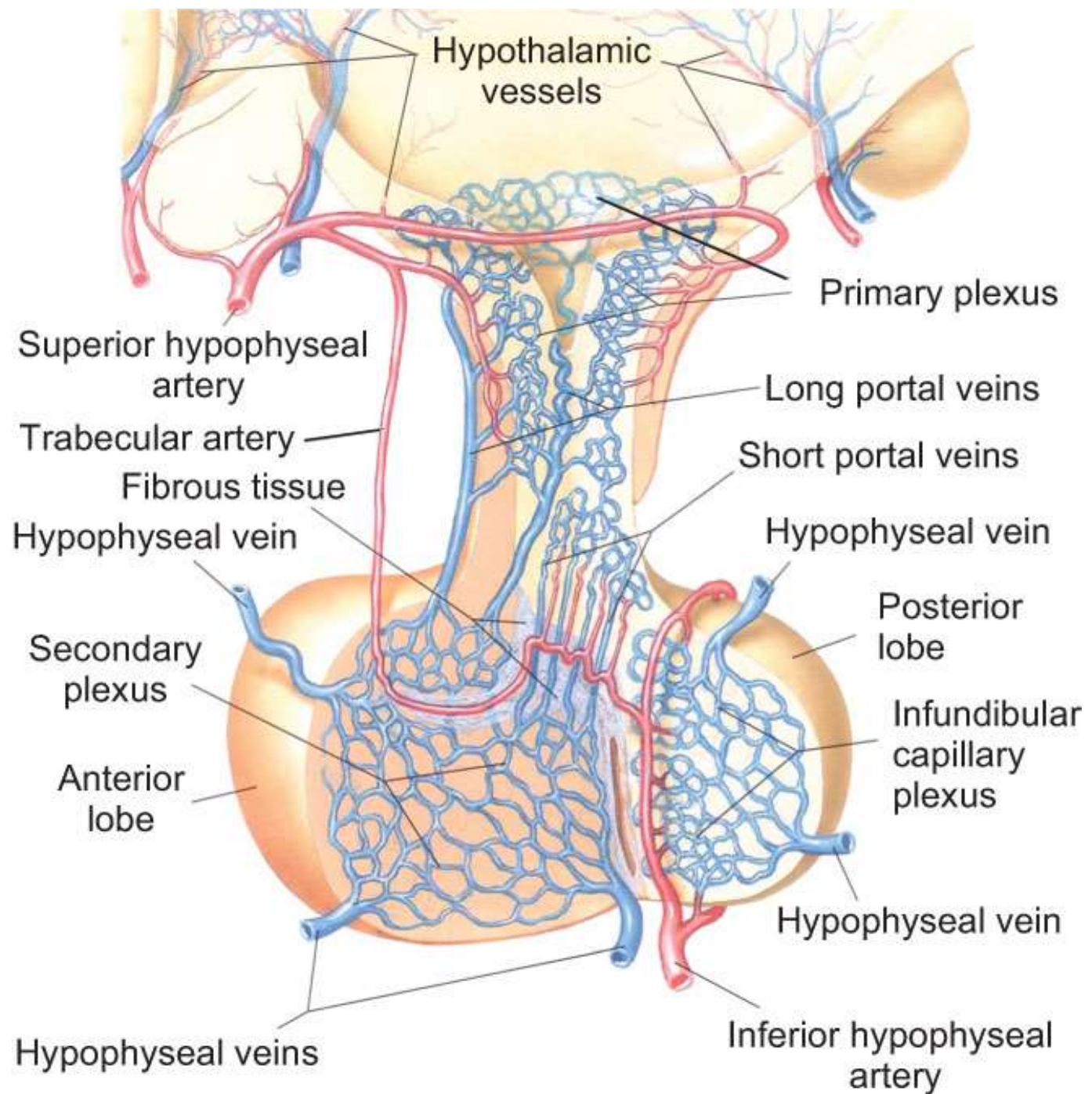


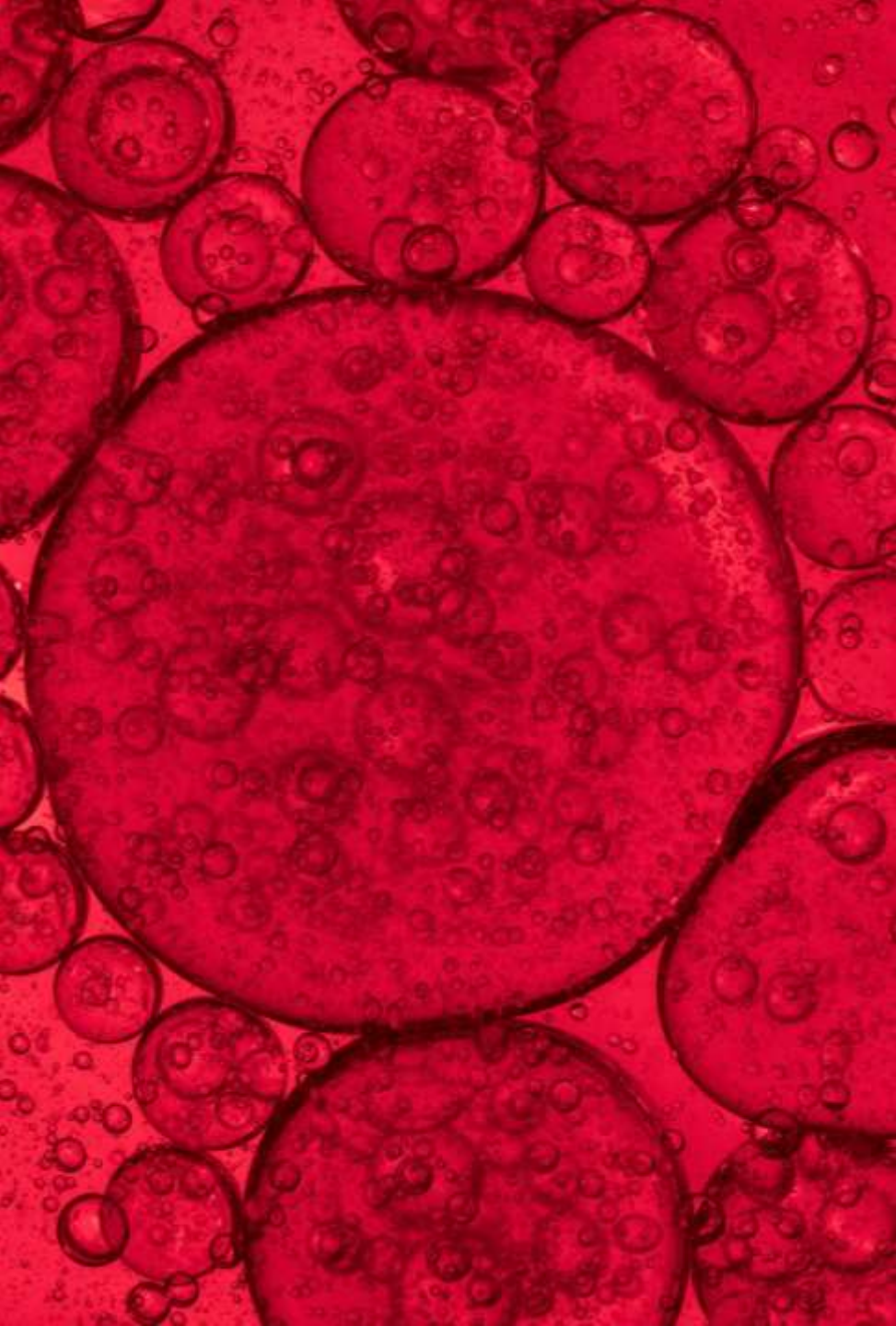
Anatomy

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



Anatomy

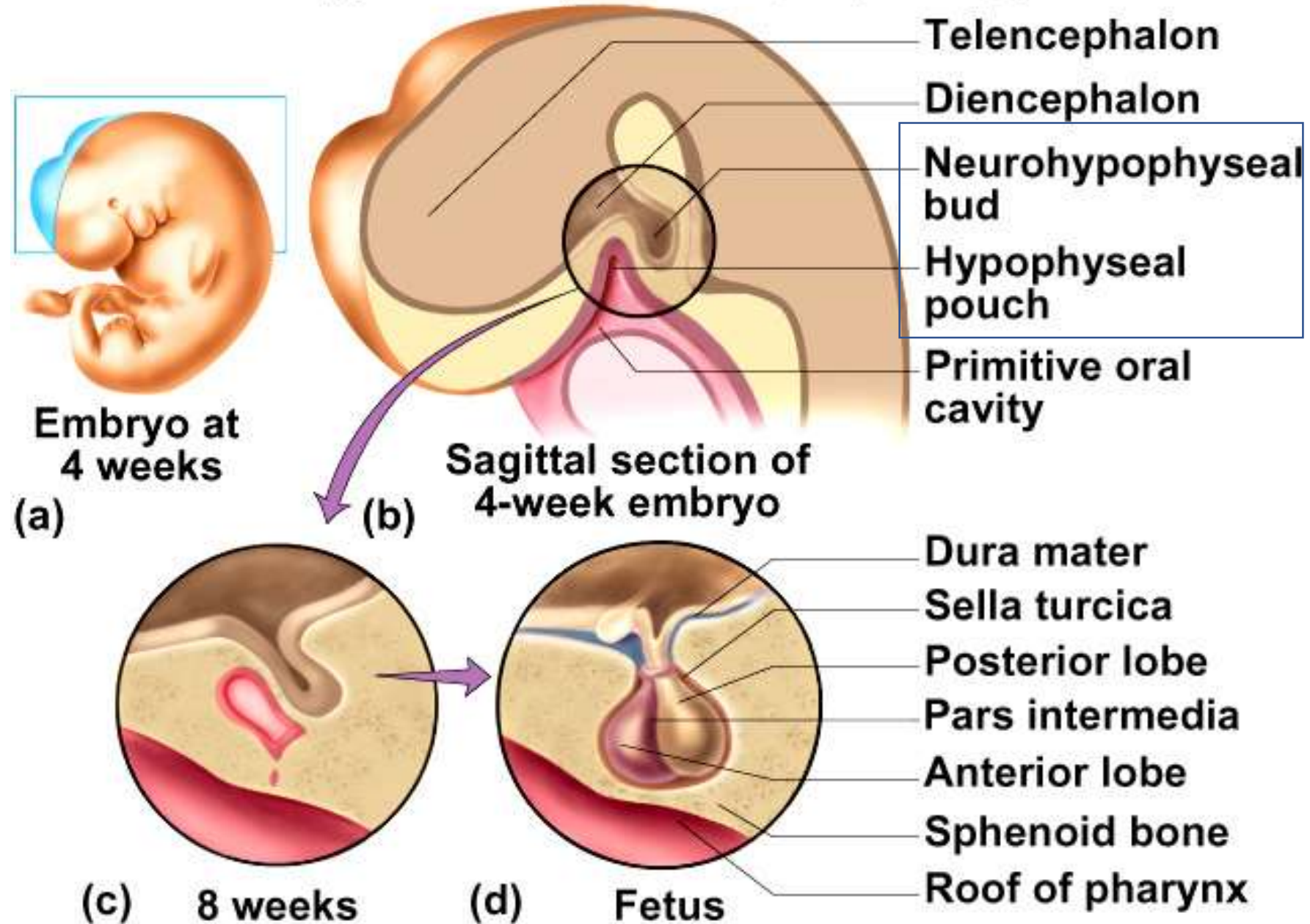


A microscopic view of red blood cells, showing numerous circular cells with a darker central area (nucleus) and a lighter outer ring, all set against a dark red background.

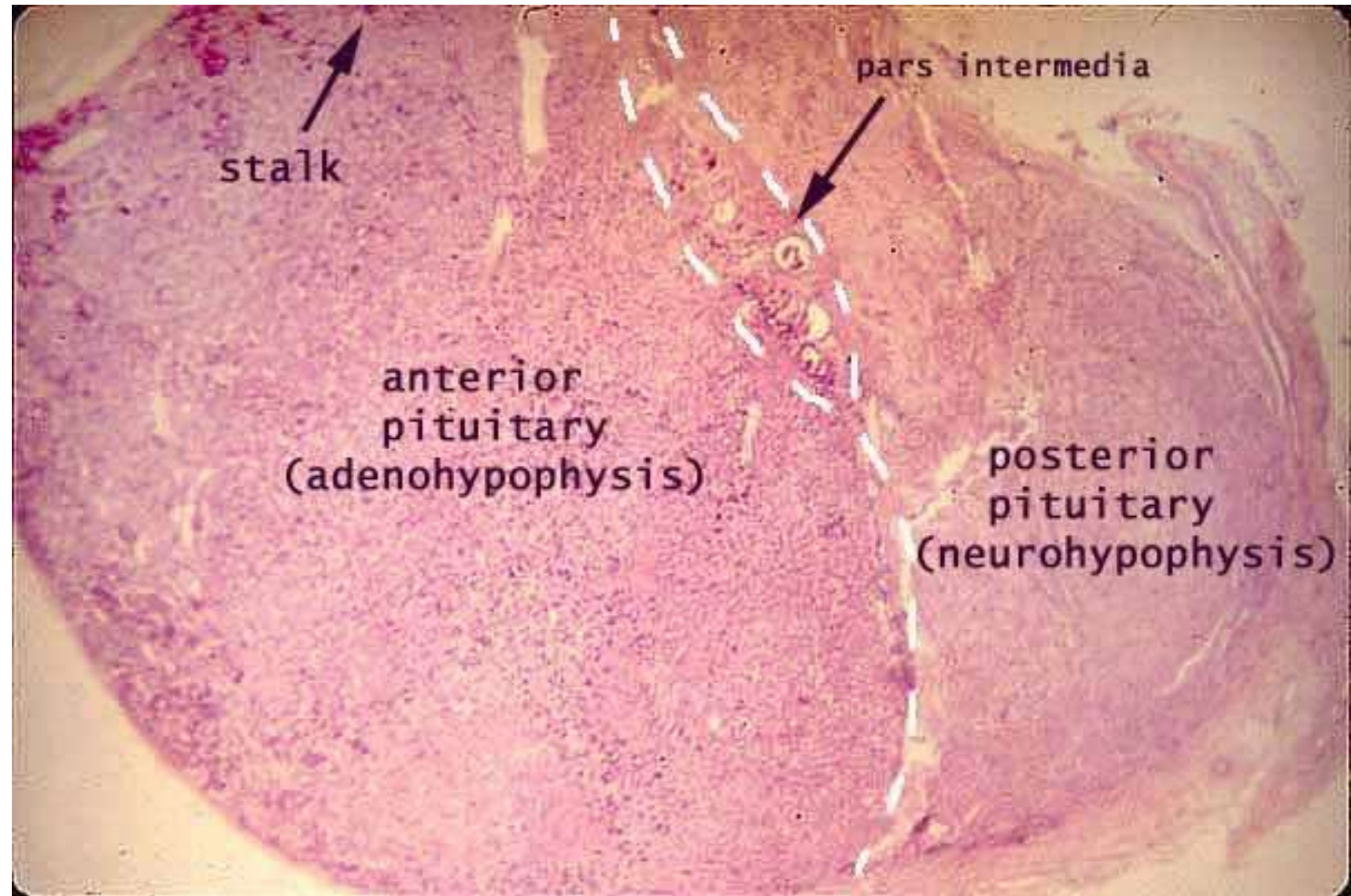
Blood supply

- Major blood source: hypothalamic-pituitary portal plexus:
 - -Allows transmission of hypothalamic peptide pulses without significant systemic dilution
 - -Consequently, pituitary cells are exposed to sharp spikes of releasing factors and in turn release their hormones as discrete pulses

Embryological Development



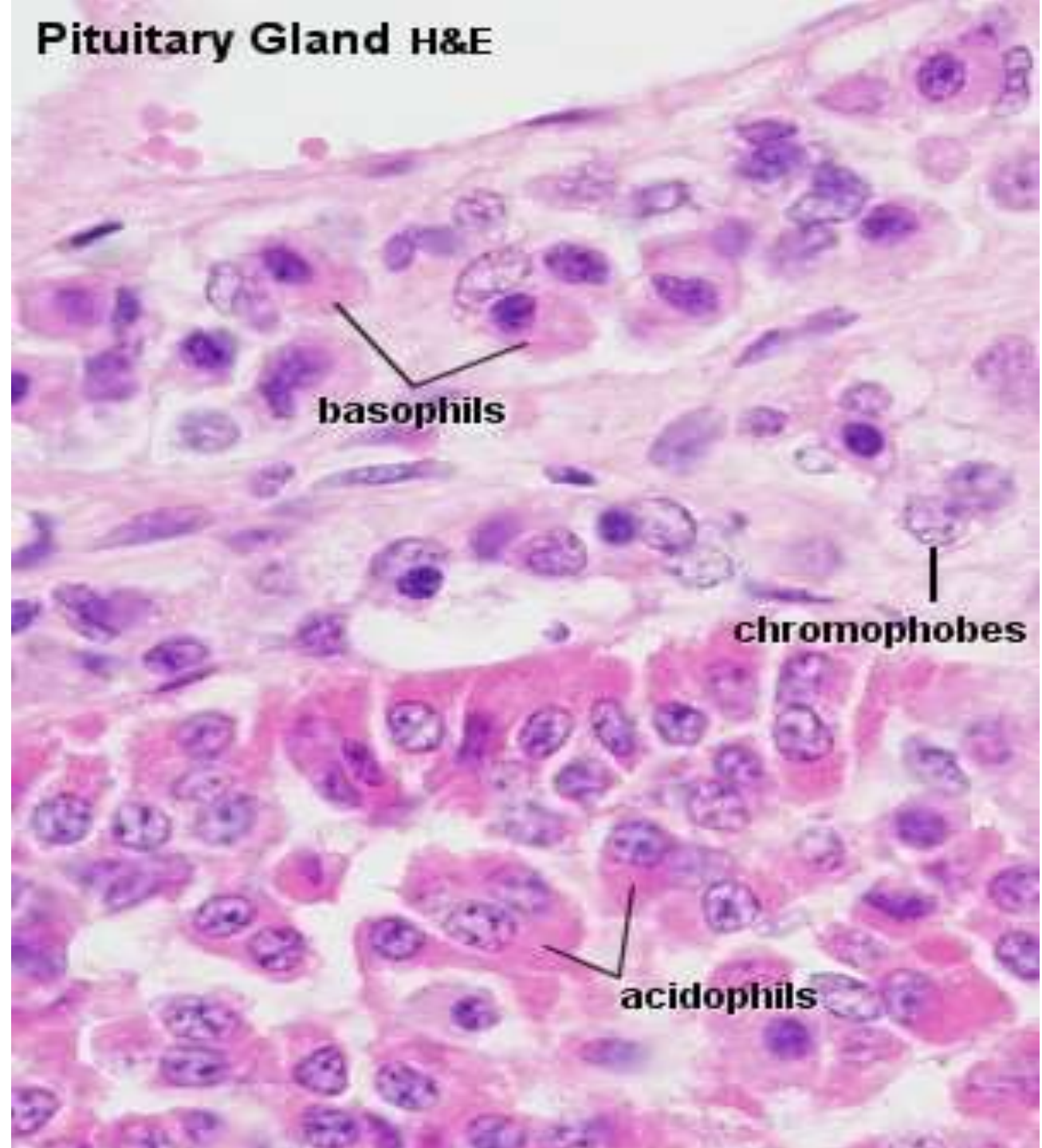
Histology

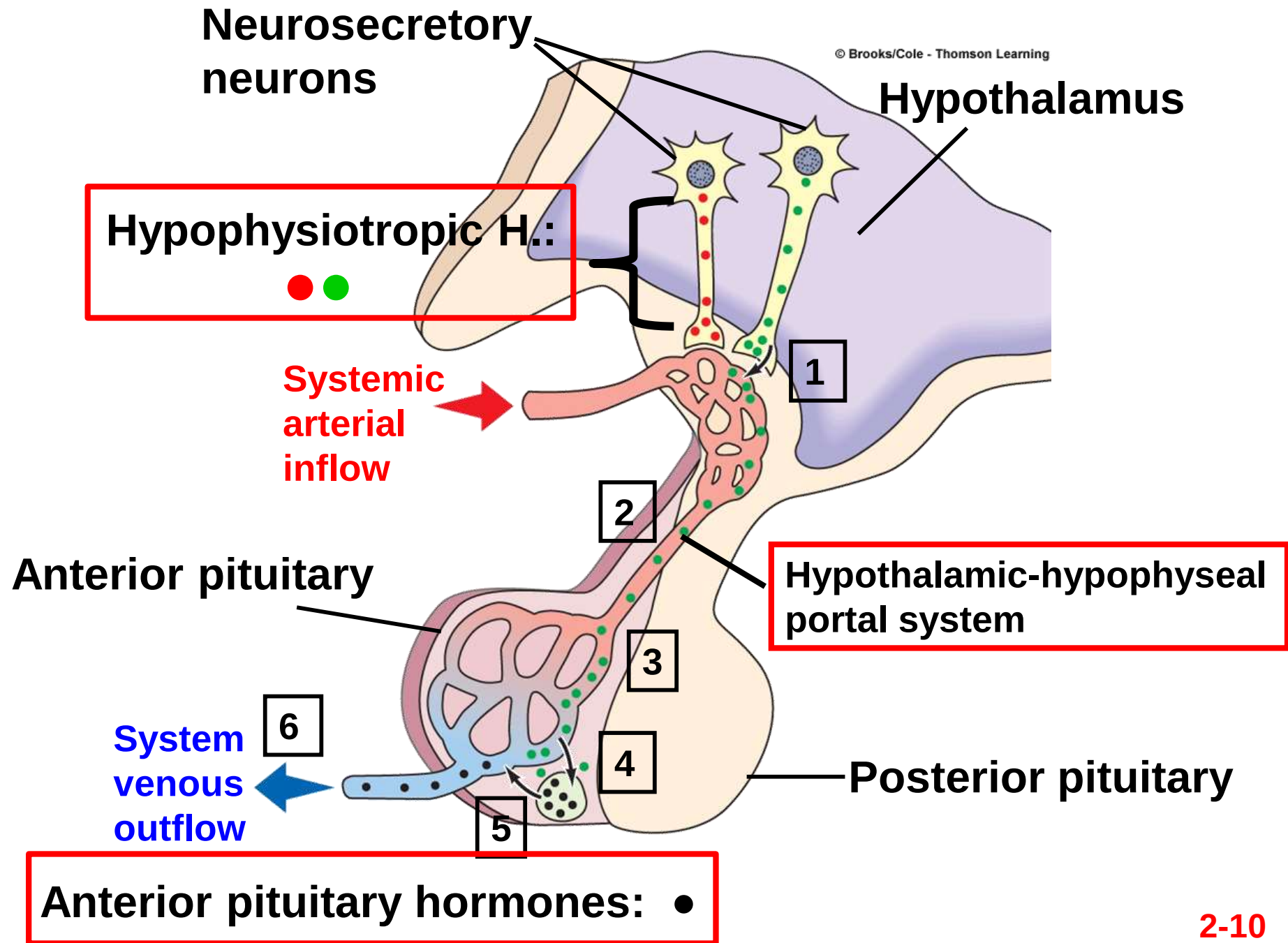


Histology

- Adenohypophysis
- Neurohypophysis
- Chromophobes
- Chromophiles

Pituitary Gland H&E





Hormones secreted by anterior pituitary

FSH (follicle
stimulating hormone)

LH (luteinizing
hormone)

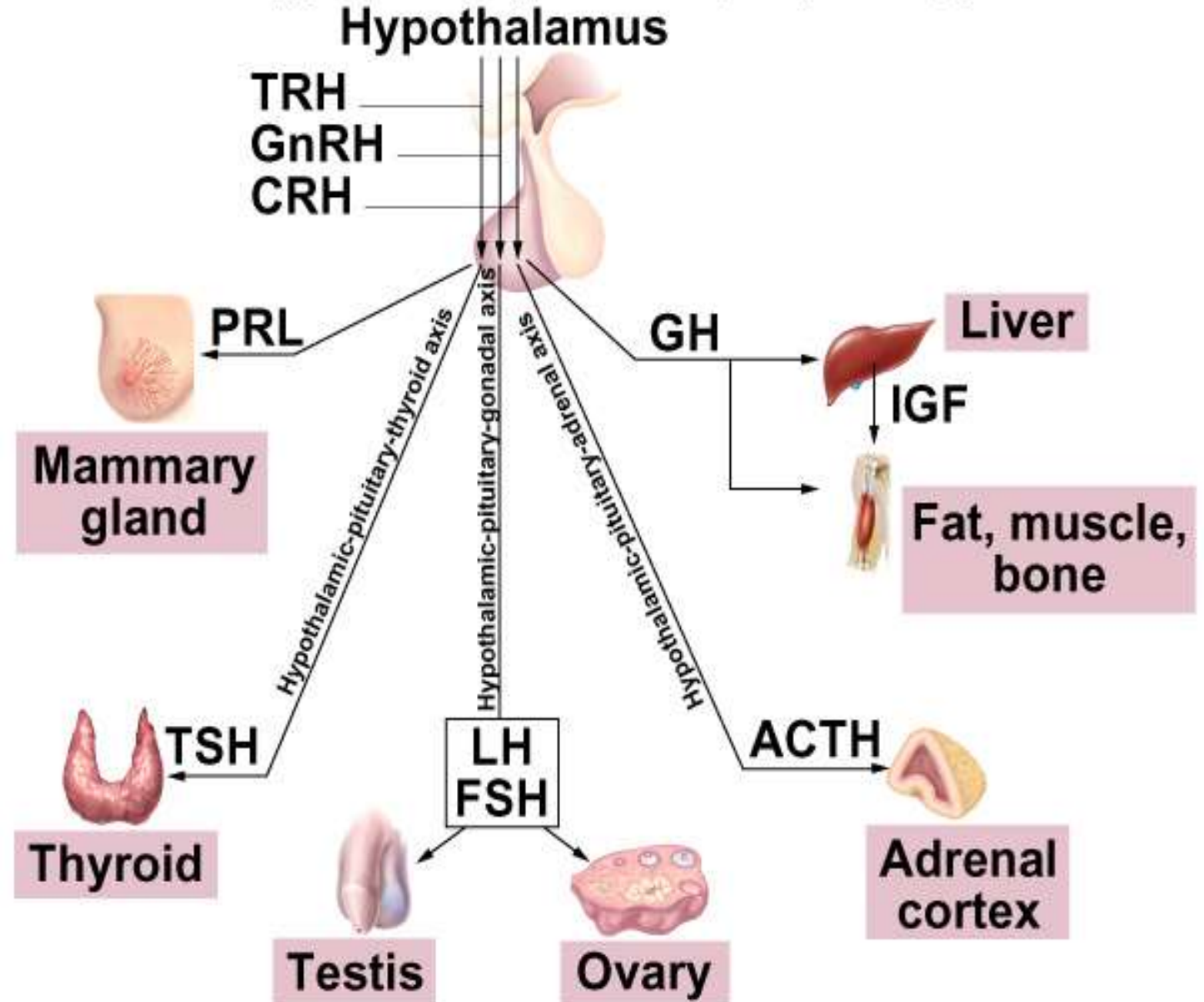
TSH (thyroid
stimulating hormone,
thyrotropin)

ACTH
(adrenocorticotrophic
hormone)

GH (growth hormone;
somatotropin or
somatotrophic
hormone)

PRL (prolactin)

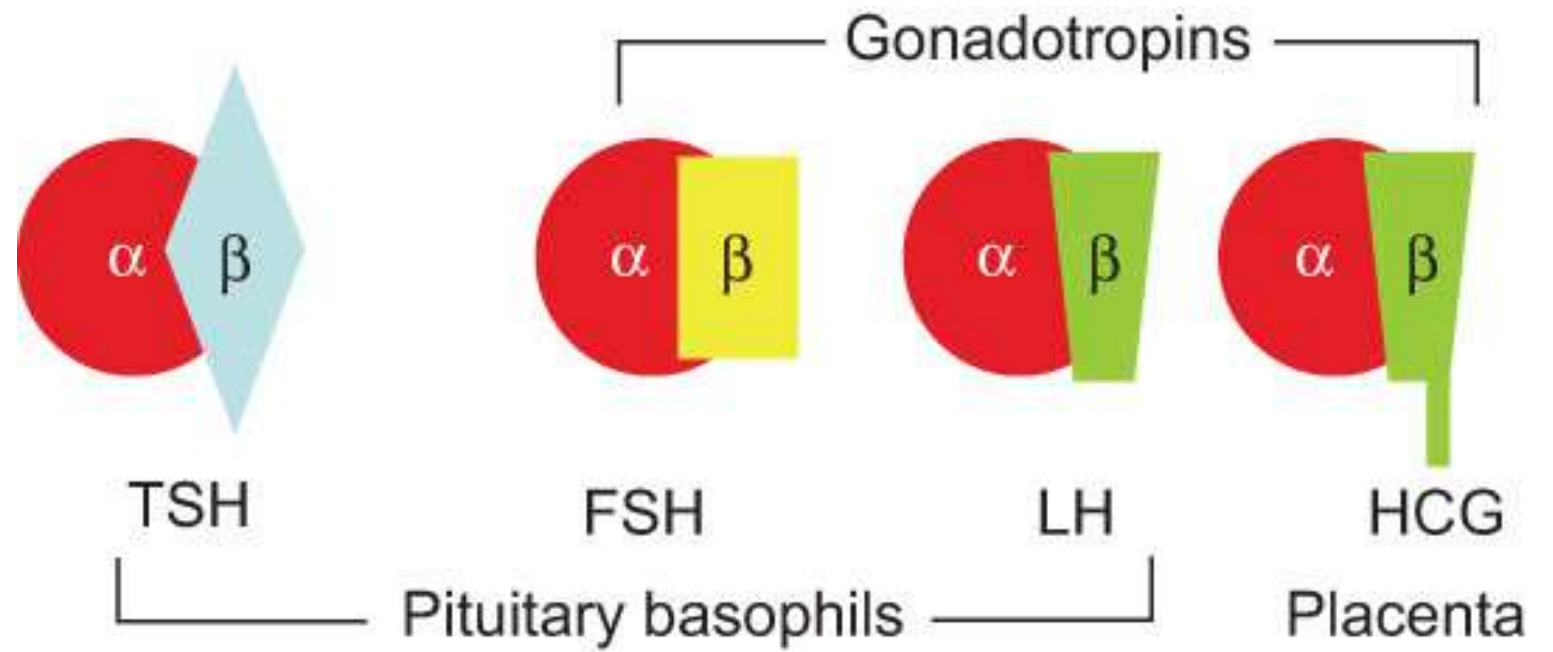
Targets of
ant. Pituitary
hormones



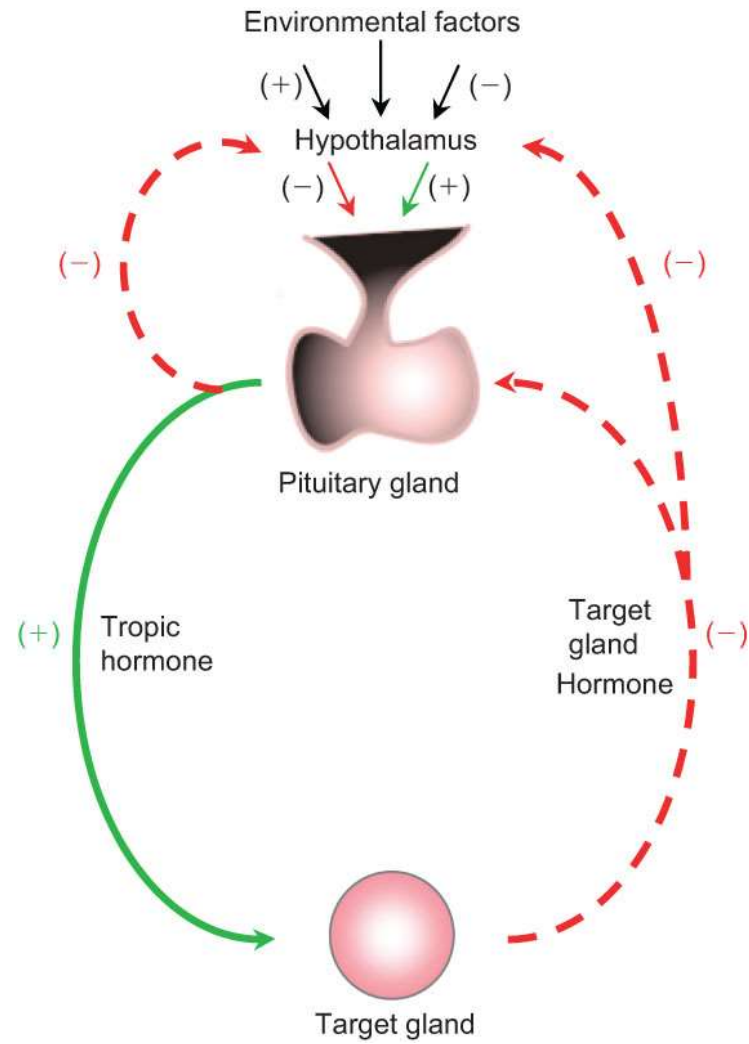
Anterior Lobe Hormone: Functions

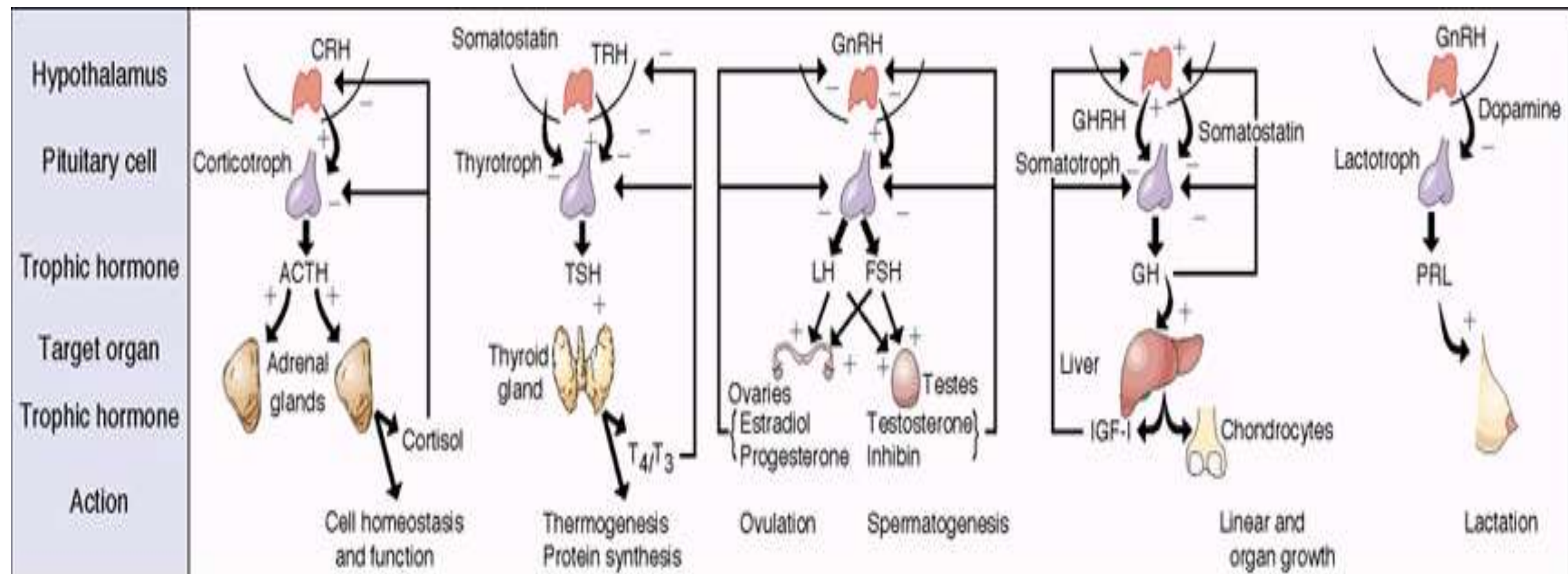
- **Growth Hormone (GH):**
 - Effects growth of skeletal muscles and long bones.
 - Causes amino acids to be built into proteins and stimulates target cells to grow and divide.
 - Causes fat to be broken down and used for energy.
 - Helps to maintain blood sugar homeostasis.
 - **Prolactin (PRL):**
 - Stimulates and maintains milk production by the mother's breasts after childbirth.
 - **Adrenocorticotrophic Hormone (ACTH):**
 - Regulates endocrine activity of adrenal cortex.
 - **Thyroid Stimulating Hormone (AKA thyrotropic hormone) (TH):**
 - Influences growth and activity of thyroid gland.
-
- **Gonadotropic Hormones:**
 - Regulate the hormonal activity of the gonads (ovaries and testes).
 - **Follicle Stimulating Hormone (FSH):**
 - Stimulates follicle development in ovaries in women. As they mature, they produce estrogen.
 - Stimulates sperm development by the testes in men.
 - **Luteinizing Hormone (LH):**
 - Triggers ovulation of an egg from the ovary in women.
 - Stimulates testosterone production by the interstitial cells of testes in men.

Glycopeptid e Hormones



Control of ant. Pituitary function





```
graph LR; A((Types of endocrine diseases)) --> B[Hormone excess]; A --> C[Hormone deficiency]; A --> D[Hormone resistance];
```

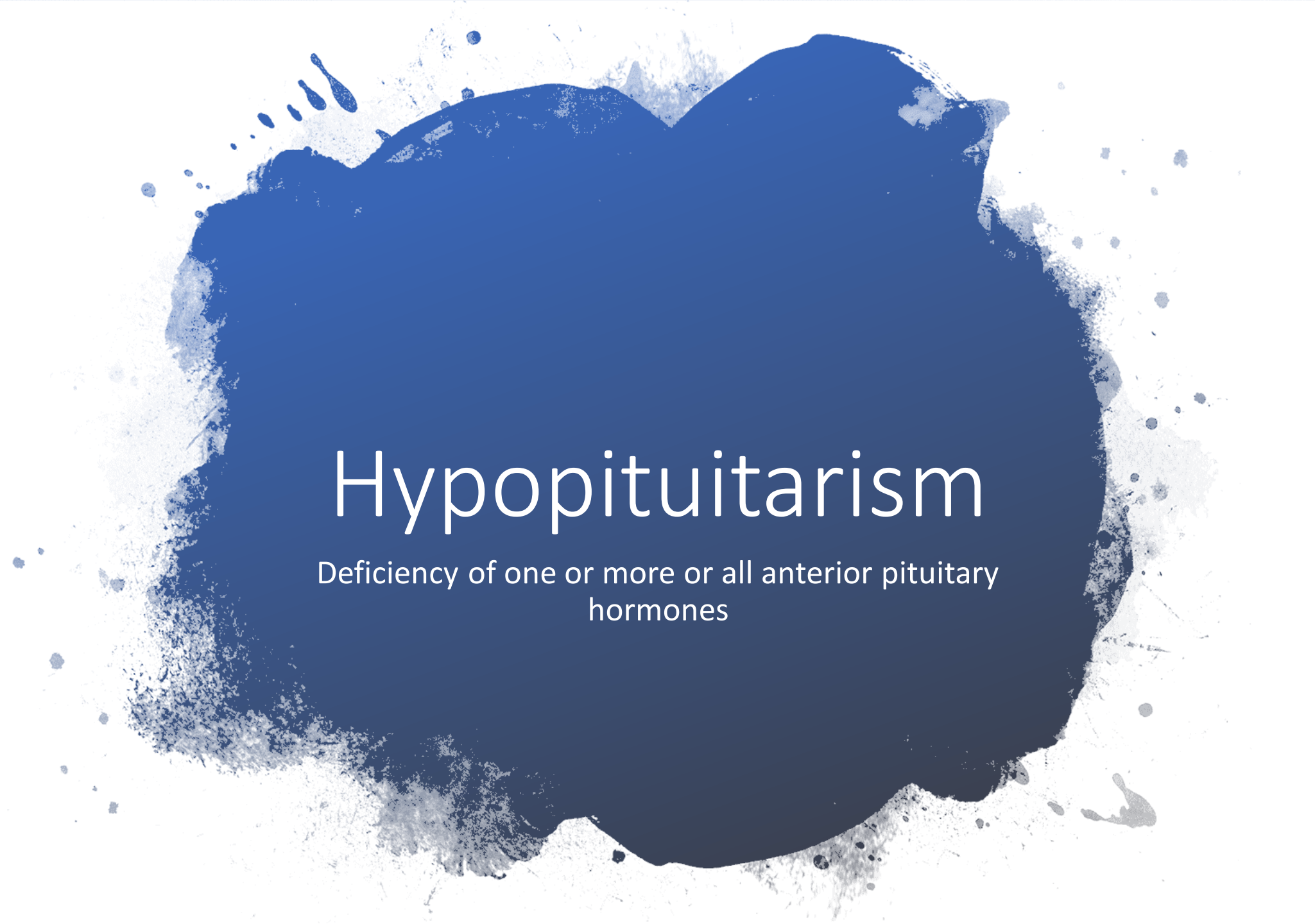
Types of
endocrine
diseases

Hormone excess



Hormone deficiency

Hormone resistance



Hypopituitarism

Deficiency of one or more or all anterior pituitary hormones

DOES YOUR EYESIGHT
EVER GIVE YOU
HEADACHES?

ONLY WHEN I LOOK
AT MY BOSS, MY
MOTHER IN LAW,
MY MONTHLY BILLS,
THE PRICE OF GAS...

A
COFZXS
DPEWQBLJR
GIJLWMUAFZTJ'
KSNTPTZOQSM



@ 2000 by Randy Glasbergen.

GLASBERGEN

Gonadotropin Deficiency

Women

- Oligomenorrhea or amenorrhea
- Loss of libido
- Vaginal dryness or dyspareunia
- Loss of secondary sex characteristics (estrogen deficiency)

Men

- Loss of libido
- Erectile dysfunction
- Infertility
- Loss of secondary sex characteristics (testosterone deficiency)
- Atrophy of the testes
- Gynecomastia (testosterone deficiency)

ACTH Deficiency

Results in hypocortisolism

- Malaise
- Anorexia
- Weight-loss
- Gastrointestinal disturbances
- Hyponatremia

Pale complexion

- Unable to tan or maintain a tan

No features of mineralocorticoid deficiency

- Aldosterone secretion unaffected

```
graph LR; A((TSH Deficiency)) --> B[Hypothyroidism]; B --> C[Atrophic thyroid gland];
```

TSH
Deficiency

Hypothyroidism

Atrophic thyroid
gland

```
graph LR; A((Prolactin Deficiency)) --> B[Inability to lactate postpartum]; B --> C[Often 1st manifestation of Sheehan syndrome];
```

Prolactin
Deficiency

Inability to lactate
postpartum

Often 1st
manifestation of
Sheehan syndrome



Growth Hormone Deficiency

Adults

- Often asymptomatic
- May complain of
- Fatigue
- Decreased exercise tolerance
- Abdominal obesity
- Loss of muscle mass

Children

- GH Deficiency
- Constitutional growth delay

Hypopituitarism

- Primary pituitary disease
 - Tumors
 - Pituitary surgery
 - Radiation treatment
- Hypothalamic disease
 - Functional suppression of axis
 - Exogenous steroid use
 - Extreme weight loss
 - Exercise
 - Systemic illness
- Interruption of the pituitary stalk
- Extrasellar disorders
 - Craniopharyngioma
 - Rathke pouch

Hypopituitarism

Major Causes of Hypopituitarism

Pituitary diseases

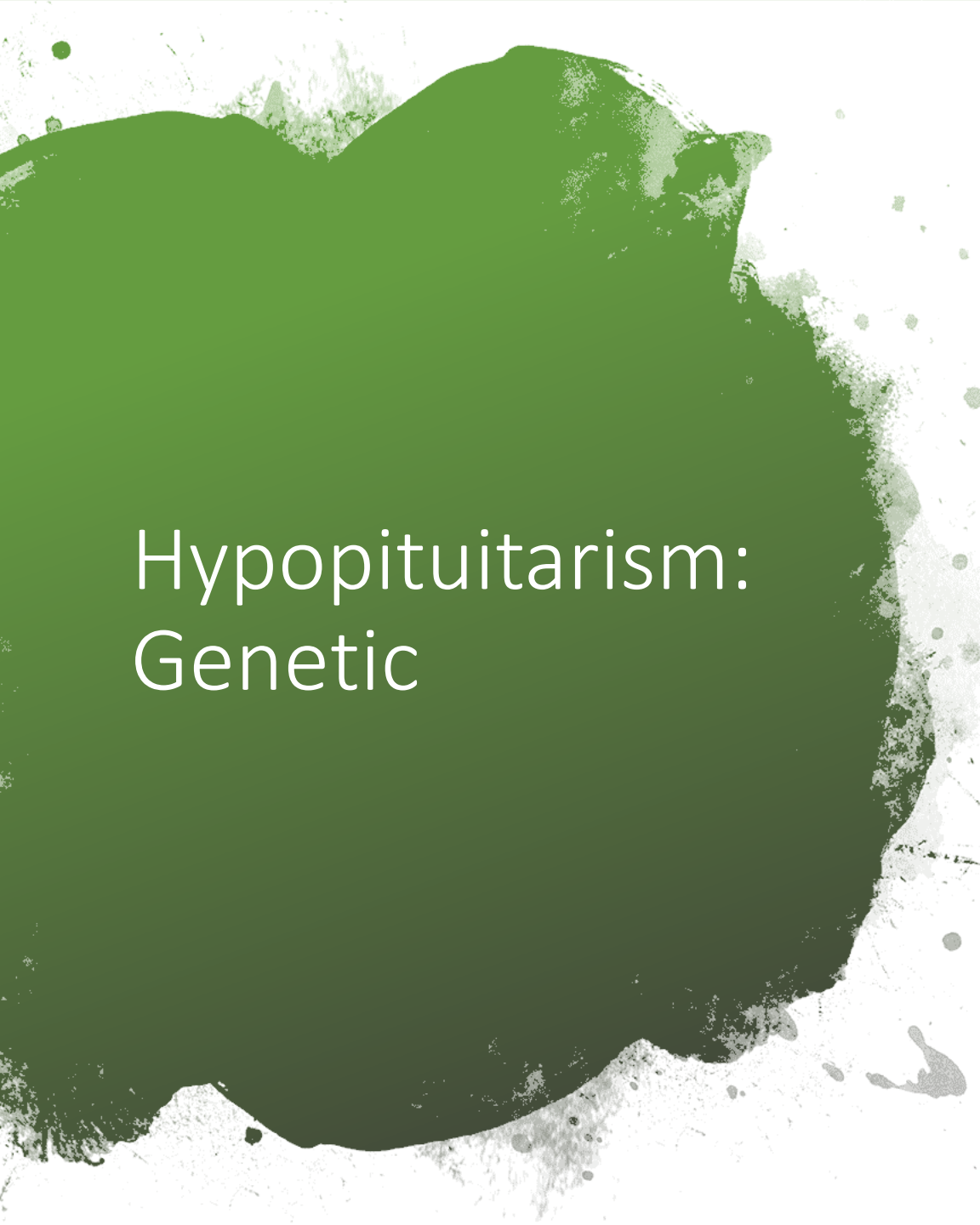
- Mass lesions – pituitary adenomas, other benign tumors, cysts
- Pituitary surgery
- Pituitary radiation
- Infiltrative lesions – lymphocytic hypophysitis, hemochromatosis
- Infarction – Sheehan syndrome
- Apoplexy
- Genetic diseases – pit-1 mutation
- Empty sella syndrome

Hypothalamic diseases

- Mass lesions – benign (craniopharyngiomas) and malignant tumors (metastatic from lung, breast, etc.)
- Radiation – for CNS and nasopharyngeal malignancies
- Infiltrative lesions – sarcoidosis, Langerhans cell histiocytosis
- Trauma – fracture of skull base
- Infections – tuberculous meningitis

Hypopituitarism

- Developmental and genetic causes
 - Dysplasia
 - Septo-Optic dysplasia
 - Developmental hypothalamic dysfunction
 - Kallman Syndrome
 - Laurence-Moon-Bardet-Biedl Syndrome
 - Frohlich Syndrome (Adipose Genital Dystrophy)
- Acquired causes:
 - Infiltrative disorders
 - Cranial irradiation
 - Lymphocytic hypophysitis
 - Pituitary Apoplexy
 - Empty Sella syndrome



Hypopituitarism: Genetic

- Septo-Optic dysplasia

- Hypothalamic dysfunction and hypopituitarism
 - may result from dysgenesis of the septum pellucidum or corpus callosum
- Affected children have mutations in the *HESX1* gene
 - involved in early development of the ventral prosencephalon
- These children exhibit variable combinations of:
 - cleft palate
 - syndactyly
 - ear deformities
 - hypertelorism
 - optic atrophy
 - micropenis
 - anosmia
- Pituitary dysfunction
 - Diabetes insipidus
 - GH deficiency and short stature
 - Occasionally TSH deficiency



Hypopituitarism: Developmental

- Kallman Syndrome
 - Defective hypothalamic gonadotropin-releasing hormone (GnRH) synthesis
 - Associated with anosmia or hyposmia due to olfactory bulb agenesis or hypoplasia
 - May also be associated with: color blindness, optic atrophy, nerve deafness, cleft palate, renal abnormalities, cryptorchidism, and neurologic abnormalities such as mirror movements
 - GnRH deficiency ***prevents progression through puberty***
 - characterized by
 - low LH and FSH levels
 - low concentrations of sex steroids

Hypopituitarism: Developmental

- Kallman Syndrome
 - Males patients
 - Delayed puberty and hypogonadism, including micropenis
 - result of low testosterone levels during infancy
 - Long-term treatment:
 - human chorionic gonadotropin (hCG) or testosterone
 - Female patients
 - Primary amenorrhea and failure of secondary sexual development
 - Long-term treatment:
 - cyclic estrogen and progestin
 - Diagnosis of exclusion
 - Repetitive GnRH administration restores normal pituitary
 - Fertility may also be restored by the administration of gonadotropins or by using a portable infusion pump to deliver subcutaneous, pulsatile GnRH

A diagram illustrating the acquired causes of hypopituitarism. On the left, a dark grey circle with a white border contains the text 'Hypopituitarism' and 'Acquired causes'. To the right of this circle, five colored rectangular boxes are arranged in two rows. The top row contains three boxes: 'Infiltrative disorders' (orange), 'Cranial irradiation' (dark orange), and 'Lymphocytic hypophysitis' (brownish-orange). The bottom row contains two boxes: 'Pituitary Apoplexy' (brownish-grey) and 'Empty Sella syndrome' (grey). All boxes have white text.

Hypopituitarism
Acquired causes

Infiltrative
disorders

Cranial
irradiation

Lymphocytic
hypophysitis

Pituitary
Apoplexy

Empty Sella
syndrome

Hypopituitarism: Lymphocytic Hypophysitis

Etiology

- Presumed to be autoimmune

Clinical Presentation

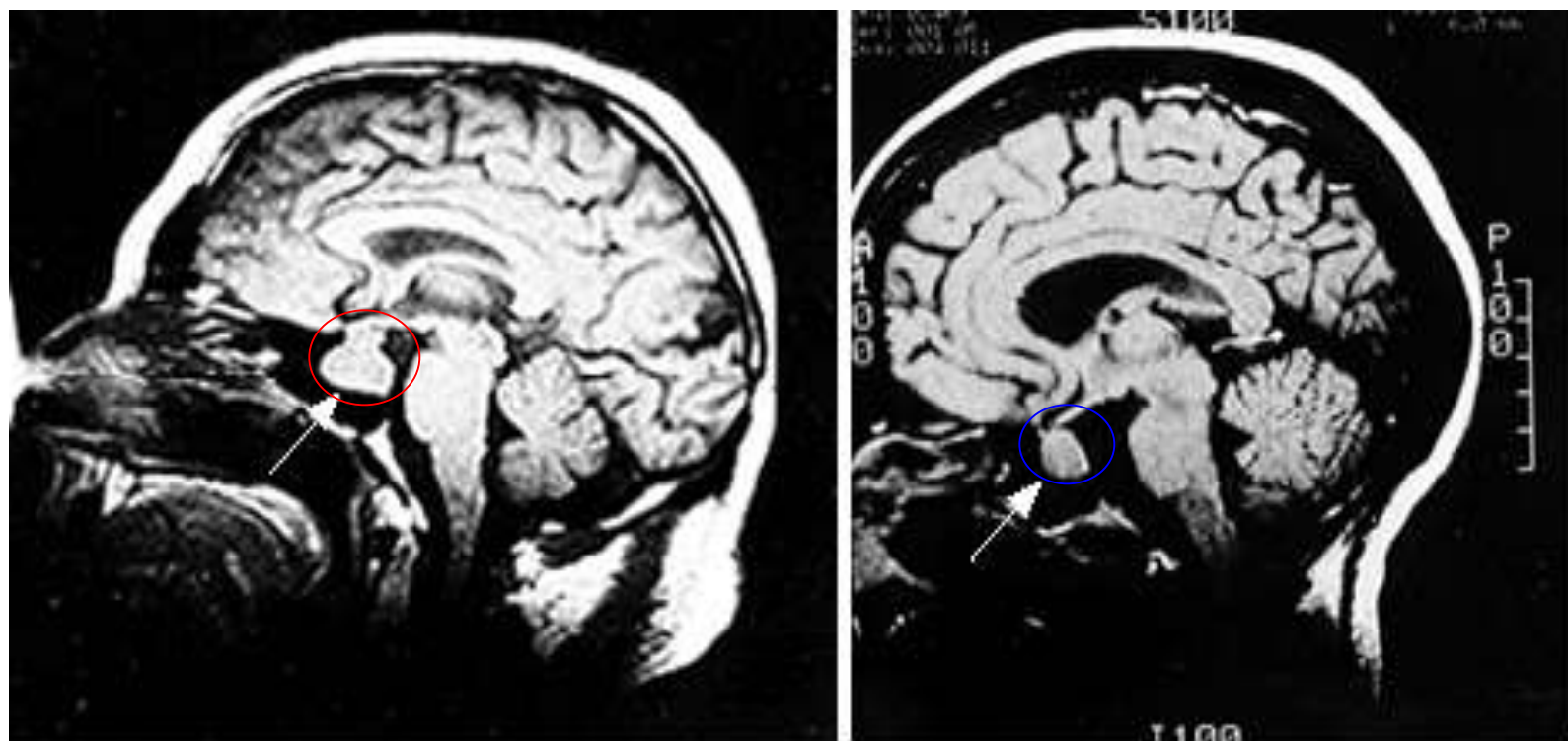
- Women, during postpartum period
- Mass effect (sellar mass)
- Deficiency of one or more anterior pituitary hormones
 - ACTH deficiency is the most common

Diagnosis

- MRI - may be indistinguishable from pituitary adenoma

Treatment

- Corticosteroids – often not effective
- Hormone replacement



Sellar masses The unenhanced MRI on the left shows in sagittal view a clinically nonfunctioning pituitary adenoma that is extending just above the sella (arrow). The unenhanced MRI on the right shows a sellar mass of similar size (arrow), which is interpreted radiologically as a pituitary adenoma, but pathologically was found to be lymphocytic hypophysitis. Courtesy of Peter J Snyder, MD.

Hypopituitarism:
Pituitary
Apoplexy

Hemorrhagic infarction of a pituitary adenoma/tumor

Considered a neurosurgical emergency

Presentation:

- Variable onset of severe headache
- Nausea and vomiting
- Meningismus
- Vertigo
- +/- Visual defects
- +/- Altered consciousness

Symptoms may occur immediately or may develop over 1-2 days

Hypopituitarism: Pituitary Apoplexy

Risk factors:

- Diabetes
- Radiation treatment
- Warfarin use

Usually resolve completely

Transient or permanent hypopituitarism is possible

- undiagnosed acute adrenal insufficiency

Diagnose with CT/MRI

Differentiate from leaking aneurysm

Treatment:

- Surgical - Transsphenoid decompression
 - Visual defects and altered consciousness

Medical therapy – if symptoms are mild

- Corticosteroids

Hypopituitarism:
Empty Sella
Syndrome

Often an incidental MRI finding

Usually have normal pituitary function

- Implying that the surrounding rim of pituitary tissue is fully functional

Hypopituitarism may develop insidiously

Pituitary masses may undergo clinically silent infarction with development of a partial or totally empty sella by cerebrospinal fluid (CSF) filling the dural herniation.

Rarely, functional pituitary adenomas may arise within the rim of pituitary tissue, and these are not always visible on MRI



Hypopituitarism

Can present with features of deficiency of one or more anterior pituitary hormones

Clinical presentation depends on:

- Age at onset
- Hormone effected, extent
- Speed of onset
- Duration of the deficiency

Hypopituitarism: Diagnosis

Biochemical diagnosis of pituitary insufficiency

Demonstrating low levels of trophic hormones in the setting of low target hormone levels



Provocative tests may be required to assess pituitary reserve

Hypopituitarism:
Treatment

Hormone replacement
therapy

- usually free of complications

Treatment regimens
that mimic physiologic
hormone production

- allow for maintenance of satisfactory clinical homeostasis

Hormone Replacement

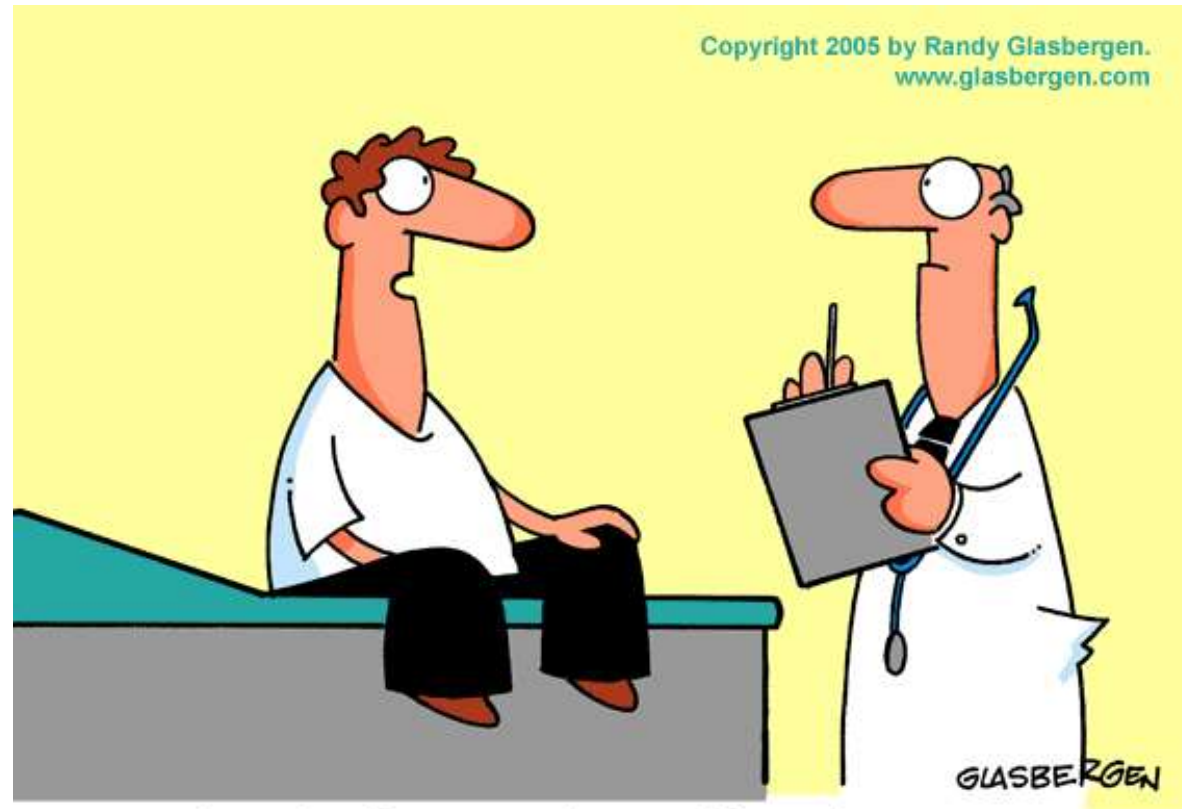
Trophic Hormone Deficit	Hormone Replacement
ACTH	Hydrocortisone (10-20 mg A.M.; 10 mg P.M.) Cortisone acetate (25 mg A.M.; 12.5 mg P.M.) Prednisone (5 mg A.M.; 2.5 mg P.M.)
TSH	L-Thyroxine (0.075-0.15 mg daily)
FSH/LH	Males Testosterone enanthate (200 mg IM every 2 wks) Testosterone skin patch (5 mg/d) Females Conjugated estrogen (0.65-1.25 mg qd for 25days) Progesterone (5-10 mg qd) on days 16-25 Estradiol skin patch (0.5 mg, every other day) For fertility: Menopausal gonadotropins, human chorionic gonadotropins
GH	Adults: Somatotropin (0.3-1.0 mg SC qd) Children: Somatotropin [0.02-0.05 (mg/kg per day)]
Vasopressin	Intranasal desmopressin (5-20 ug twice daily) Oral 300-600 ug qd



Take home points:

- Remember that the cause may be functional
 - Treatment should be aimed at the underlying cause
- Hypopituitarism may present
 - Acutely with cortisol deficiency
 - After withdrawal of prolonged glucocorticoid therapy that has caused suppression of the HPA axis.
 - Post surgical procedure
 - Post trauma
 - Hemorrhage
- Exacerbation of cortisol deficiency in a patient with unrecognized ACTH deficiency
 - Medical/surgical illness
 - Thyroid hormone replacement therapy

Pituitary Tumors



**“I already diagnosed myself on the Internet.
I’m only here for a second opinion.”**

Causes of Sellar Masses

Benign tumors

- Pituitary adenoma (most common sellar mass)
- Craniopharyngioma
- Meningiomas

Pituitary hyperplasia

- Lactotroph hyperplasia (during pregnancy)
- Thyrotroph and gonadotroph hyperplasia
- Somatotroph hyperplasia due to ectopic GHRH

Malignant tumors

- Primary
 - Germ cell tumor (ectopic pinealoma)
 - Sarcoma
 - Chordoma
 - Pituitary carcinoma (rare)
- Metastatic
 - Lung
 - Breast

Cysts

- Rathke's cleft
- Arachnoid
- Dermoid

Pituitary abscess

Lymphocytic hypophysitis

Carotid arteriovenous fistula

Pituitary
Tumors

Microadenoma < 1 cm

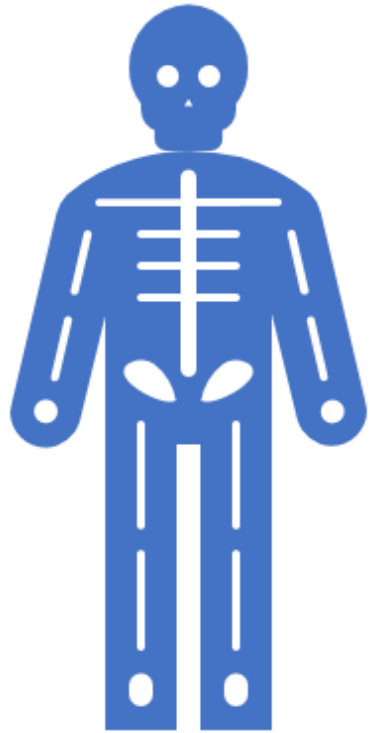
Macroadenoma > 1 cm

Is the tumor causing local mass effect?

Is hypopituitarism present?

Is there evidence of hormone excess?

Pituitary tumors: Clinical presentation



- Mass effect
 - Superior extension
 - May compromise optic pathways – leading to impaired visual acuity and visual field defects
 - May produce hypothalamic syndrome – disturbed thirst, satiety, sleep, and temperature regulation
 - Lateral extension
 - May compress cranial nerves III, IV, V, and VI – leading to diplopia
 - Inferior extension
 - May lead to cerebrospinal fluid rhinorrhea

Pituitary Tumors: Diagnosis and treatment



Diagnosis

Check levels of all hormones produced

Check levels of target organ products



Treatment

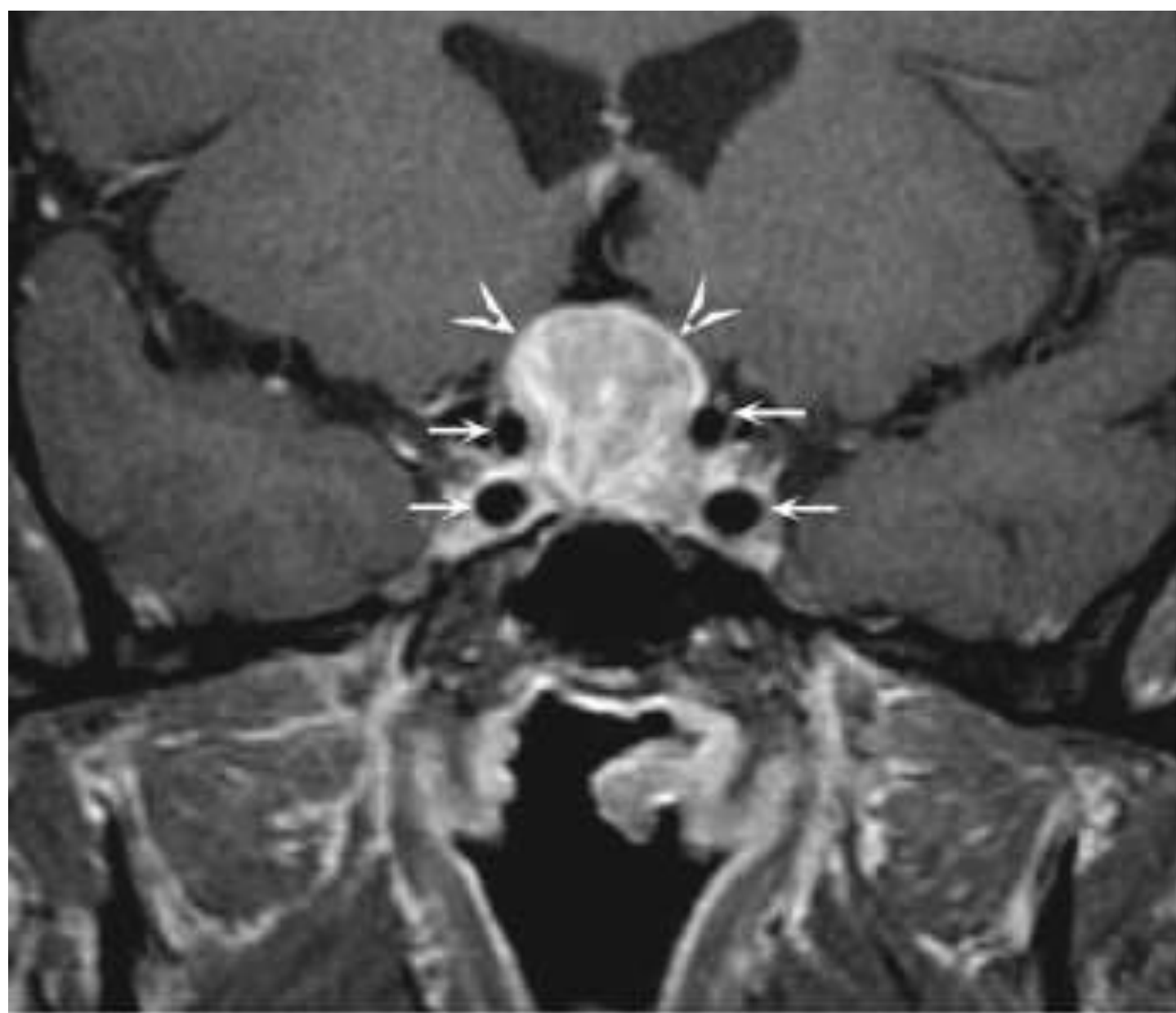
Surgical excision, radiation, or medical therapy

Generally, first-line treatment surgical excision

Drug therapy available for some functional tumors

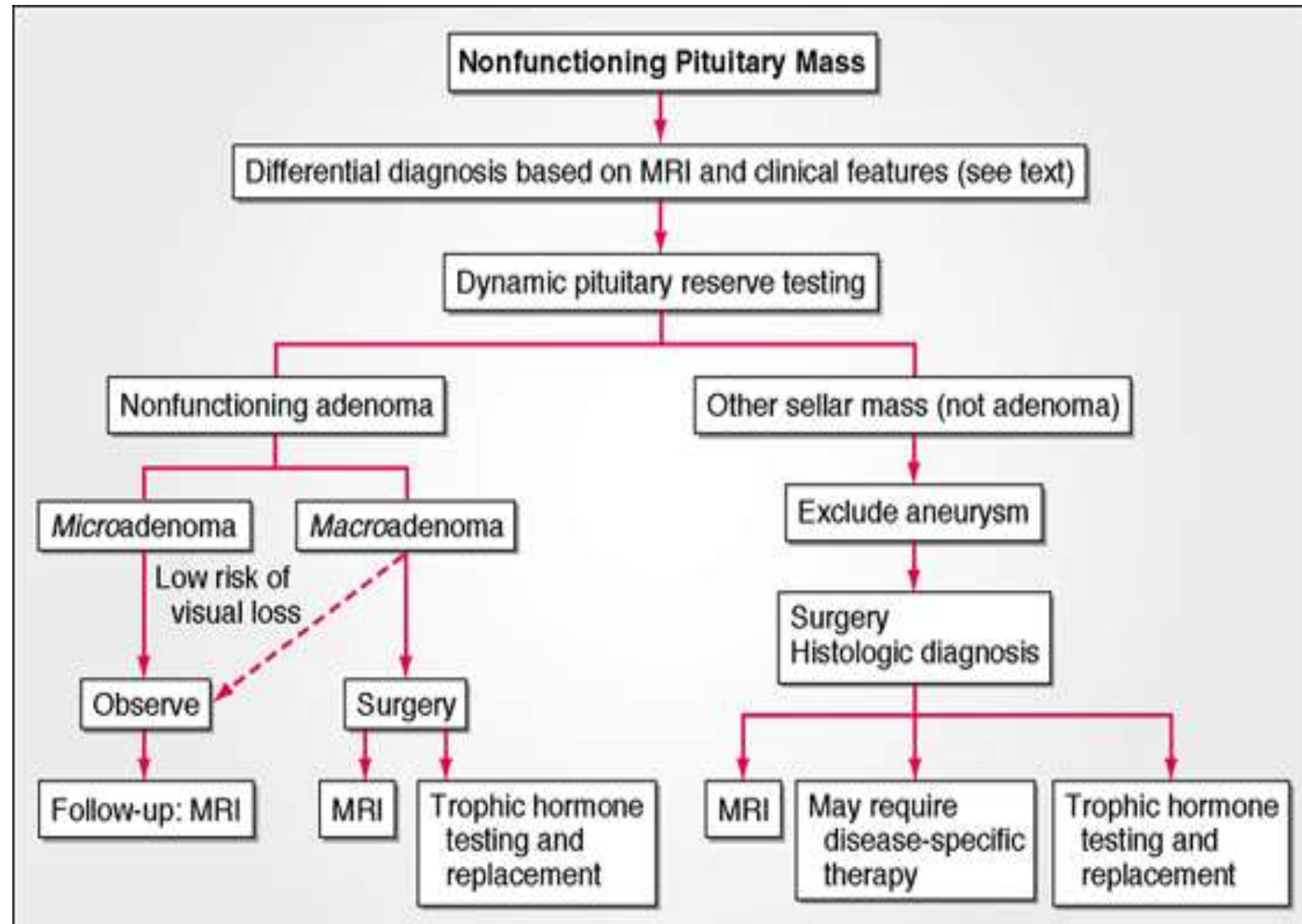
Simple observation

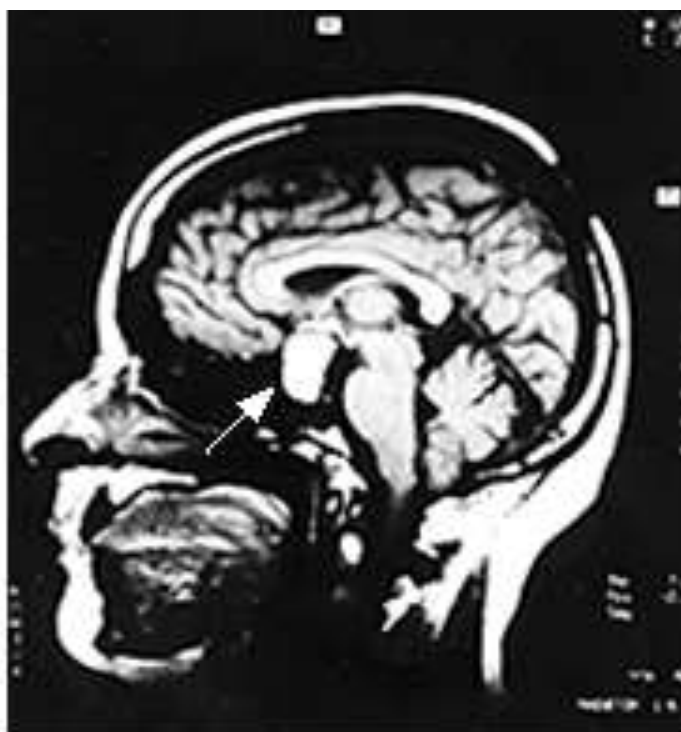
- Option if the tumor is small, does not have local mass effect, and is nonfunctional
- Not associated with clinical features that affect quality of life





Gonadotroph adenoma Magnetic resonance imaging showing, in a sagittal view of the head, a large gonadotroph adenoma extending superiorly to elevate the optic chiasm (arrow). Gonadotroph adenomas are often not recognized until they become this large. Courtesy of Peter J. Snyder, MD.





Sellar mass The MRI on the left shows in sagittal view a very large pituitary adenoma elevating the optic chiasm (arrow). The MRI on the right shows a sellar mass of similar size which has a much brighter signal than the mass on the left (arrow). The reason for the brighter signal could have been hemorrhage into a pituitary adenoma, but in this case was found surgically to be fluid in a craniopharyngioma. Courtesy of Peter J Snyder, MD.

Craniopharyngioma

Derived from Rathke's pouch.

Arise near the pituitary stalk

- extension into the suprasellar cistern common

These tumors are often large, cystic, and locally invasive

Many are partially calcified

- characteristic appearance on skull x-ray and CT images

Majority of patients present before 20yr

- usually with signs of increased intracranial pressure, including headache, vomiting, papilledema, and hydrocephalus

Craniopharyngioma

Associated symptoms include:

- visual field abnormalities, personality changes and cognitive deterioration, cranial nerve damage, sleep difficulties, and weight gain.

Children

- growth failure associated with either hypothyroidism or growth hormone deficiency is the most common presentation

Adults

- sexual dysfunction is the most common problem
- erectile dysfunction
- amenorrhea

Craniopharyngioma

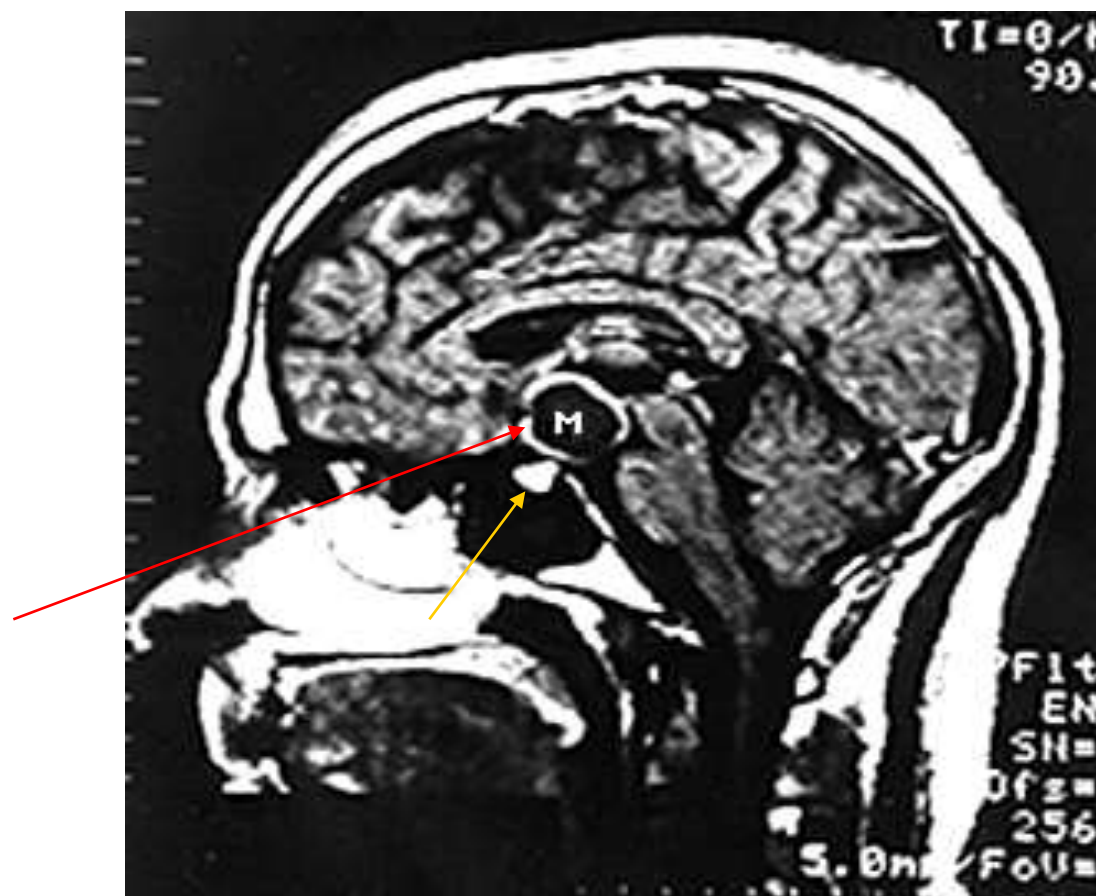
Anterior pituitary dysfunction and diabetes insipidus are common

Treatment

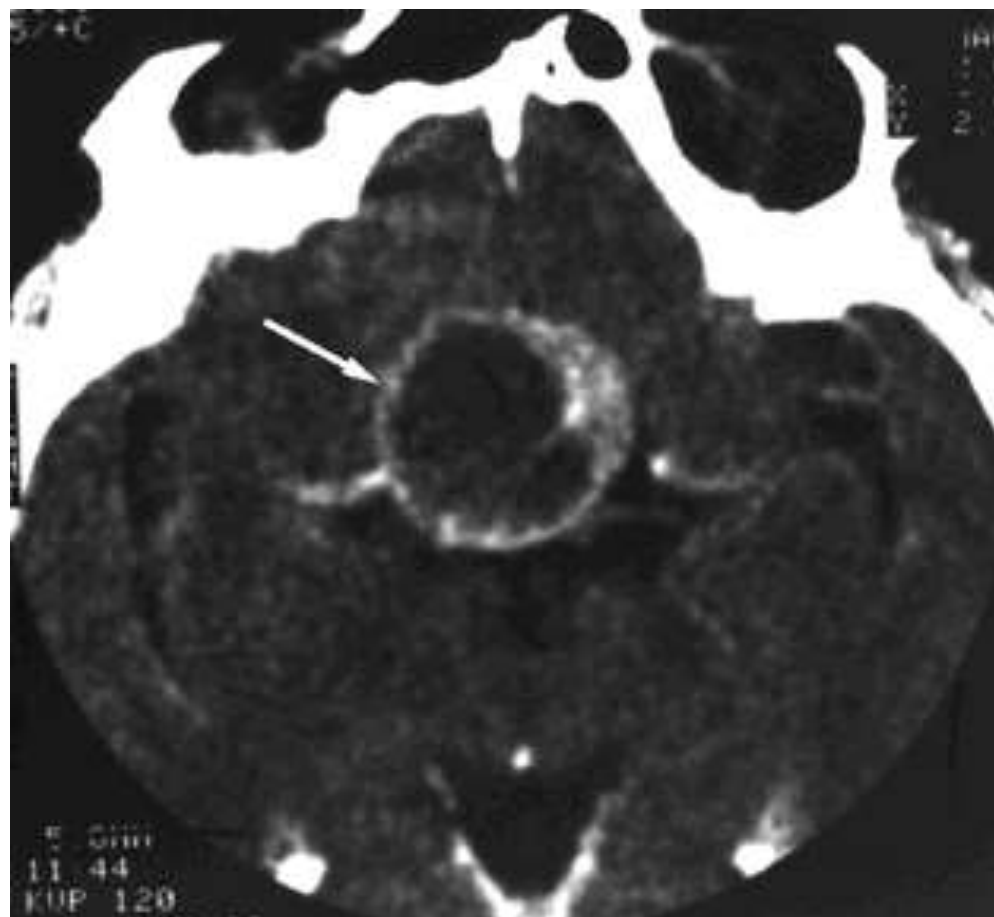
- Transcranial or transsphenoidal surgical resection
 - followed by postoperative radiation of residual tumor
 - This approach can result in long-term survival and ultimate cure
 - most patients require lifelong pituitary hormone replacement.

If the pituitary stalk is uninvolved and can be preserved at the time of surgery

- Incidence of subsequent anterior pituitary dysfunction is significantly diminished.



Sellar mass MRI shows enhancement of only the rim of a suprasellar mass (M) and of the normal pituitary inferior to it following the administration of gadolinium. The clear distinction between the mass and the normal pituitary indicates that the mass is not a pituitary adenoma. The mass was found on surgery to be a craniopharyngioma. Courtesy of Peter J Snyder, MD.



Craniopharyngioma Axial CT scan through the midbrain of a 71 year-old woman who presented with bitemporal visual field defects. There is a calcified soft tissue mass arising in the region of the sella turcica (arrows) which proved to be a craniopharyngioma. Courtesy of Jonathan Kruskal, MD.

Prolactinoma

Most common functional pituitary tumor

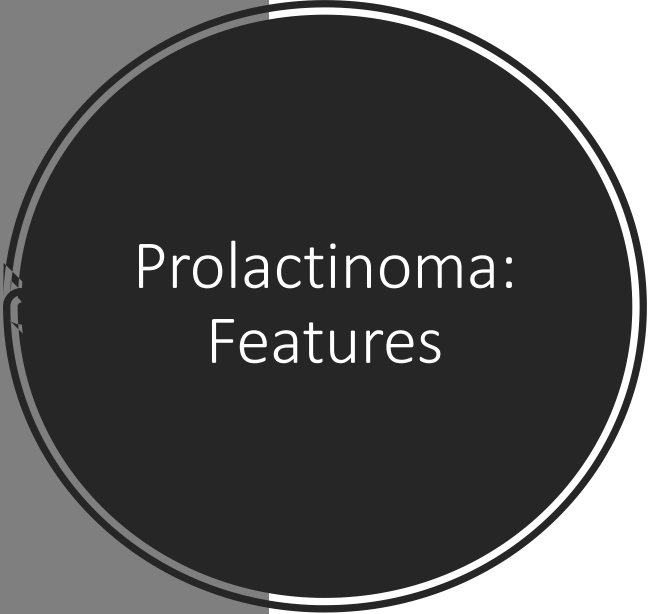
Usually a *microadenoma*

Can be a space occupying macroadenoma – often with visual field defects

Although many women with hyperprolactinemia will have galactorrhea and/ or amenorrhea

- The absence these the two signs do not excluded the diagnosis

GnRH release is decreased in direct response to elevated prolactin, leading to decreased production of LH and FSH



Prolactinoma: Features

Women

- Amenorrhea – this symptom causes women to present earlier
- Hirsutism

Men

- Impotence – often ignored
- Tend to present later
- Larger tumors
- Signs of mass effect

Prolactinoma: Diagnosis

Essential to rule out secondary causes!!

- Drugs which decrease dopamine stores
 - Phenothiazines
 - Amitriptyline
 - Metoclopramide
- Factors inhibiting dopamine outflow
 - Estrogen
 - Pregnancy
 - Exogenous sources
- Hypothyroidism

If prolactin level > 200, almost always a prolactinoma (even in a nursing mom)

Prolactin levels correlate with tumor size in the macroadenomas

- Suspect another tumor if prolactin is low with a large tumor

Prolactinoma: Diagnosis

Assess hypersecretion

- Basal, fasting morning PRL levels (normally <20 ug/L)

Multiple measurements may be necessary

- Pulsatile hormone secretion
- levels vary widely in some individuals with hyperprolactinemia

Both false-positive and false-negative results may be encountered

- May be falsely lowered with markedly elevated PRL levels (>1000 ug/L)
 - assay artifacts; sample dilution is required to measure these high values accurately
- May be falsely elevated by aggregated forms of circulating PRL, which are biologically inactive (macroprolactinemia)

Hypothyroidism should be excluded by measuring TSH and T4 levels

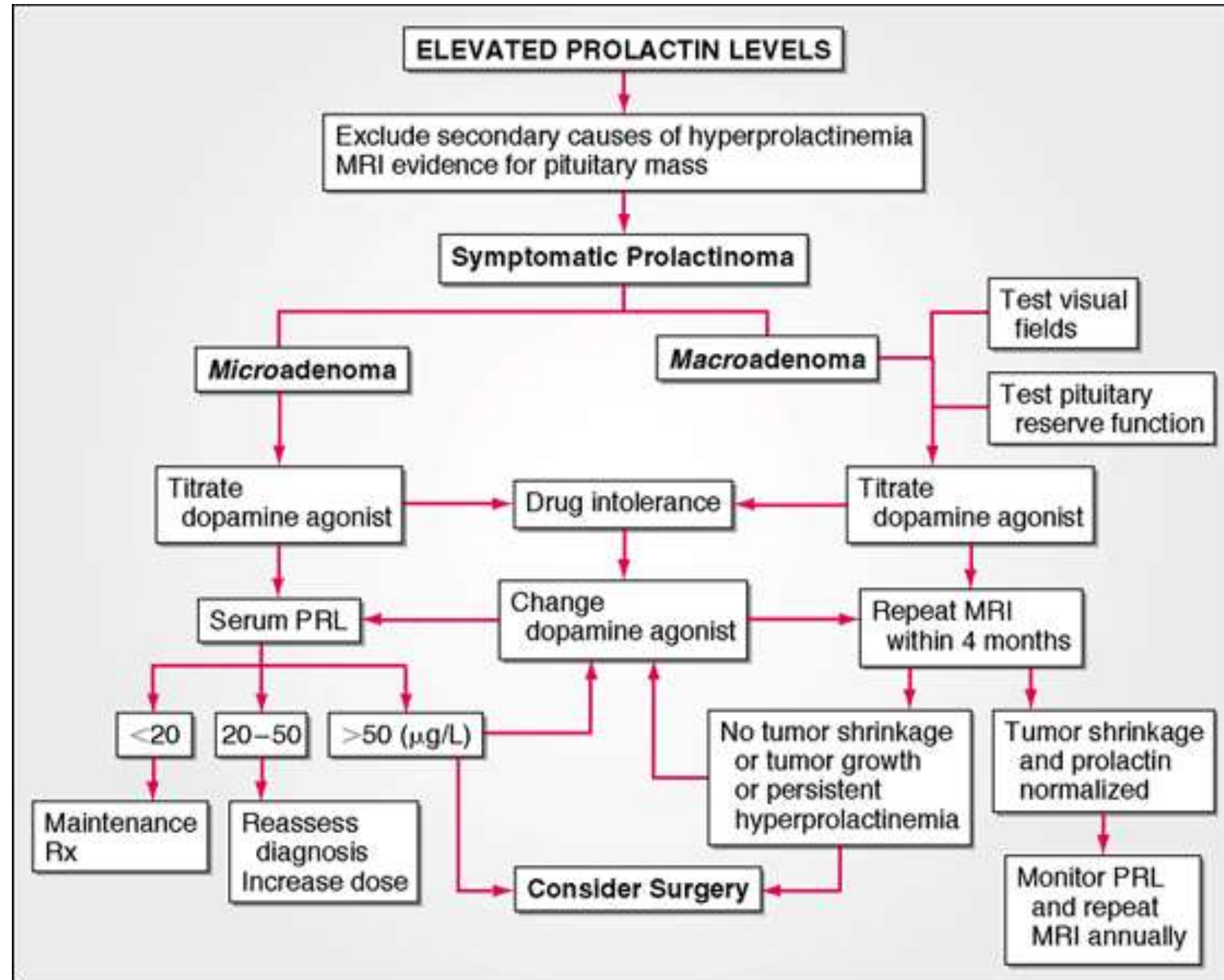
Prolactinoma: Treatment

Medical

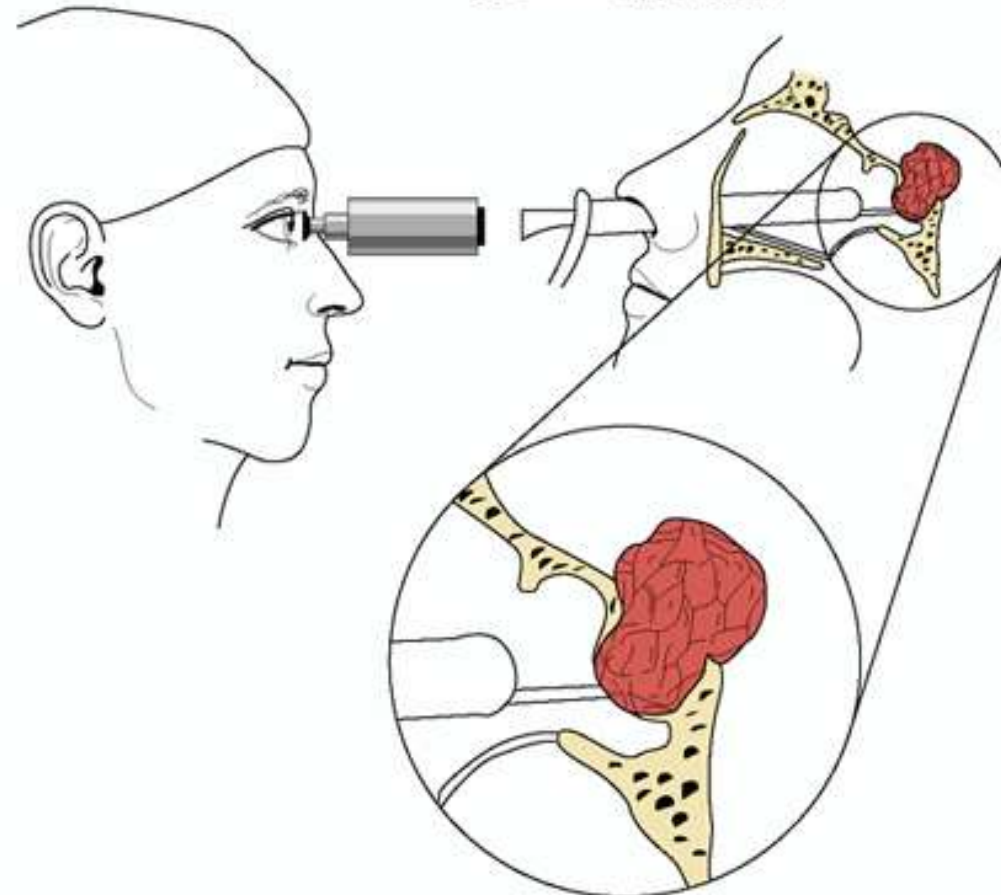
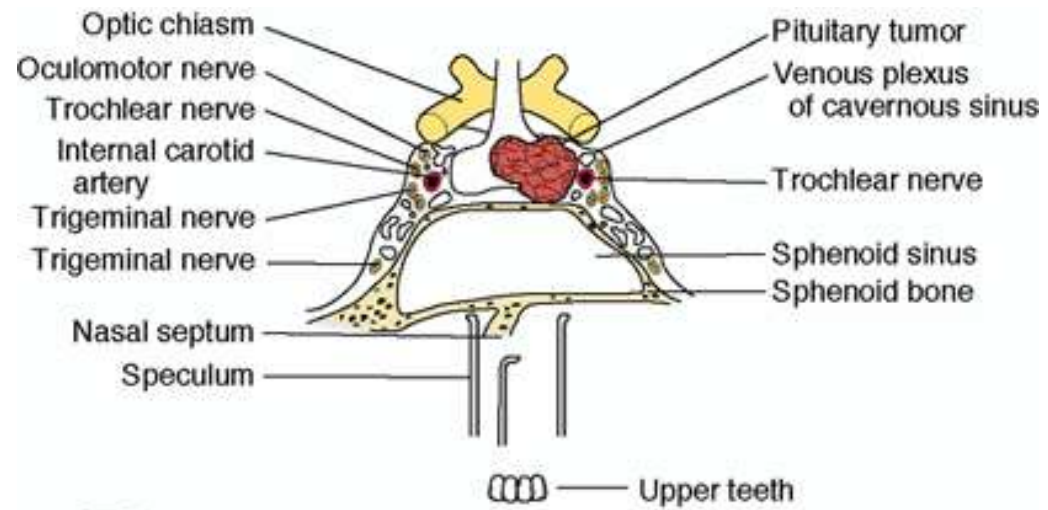
- Cabergoline – dopamine receptor agonist
- Bromocriptine - dopamine agonist
 - Safe in pregnancy
 - Will restore menses
- Decreases both prolactin and tumor size (80%)

Surgical

- Transsphenoidal surgery – irradiation (if pt cannot tolerate rx)



Transsphenoidal resection





Growth Hormone Tumors

Gigantism

- GH excess before closure of epipheseal growth plates of long bones

Acromegaly

- GH excess after closure of epipheseal growth plates of long bones
- Insidious onset
 - Usually diagnosed late

Growth Hormone Tumors

May have DM or glucose intolerance

Hypogonadism

Large hands and feet

Large head with a lowering brow and coarsening features

Hypertensive – 25%

Colon polyps

- 3-6 more likely than general population

Multiple skin tags

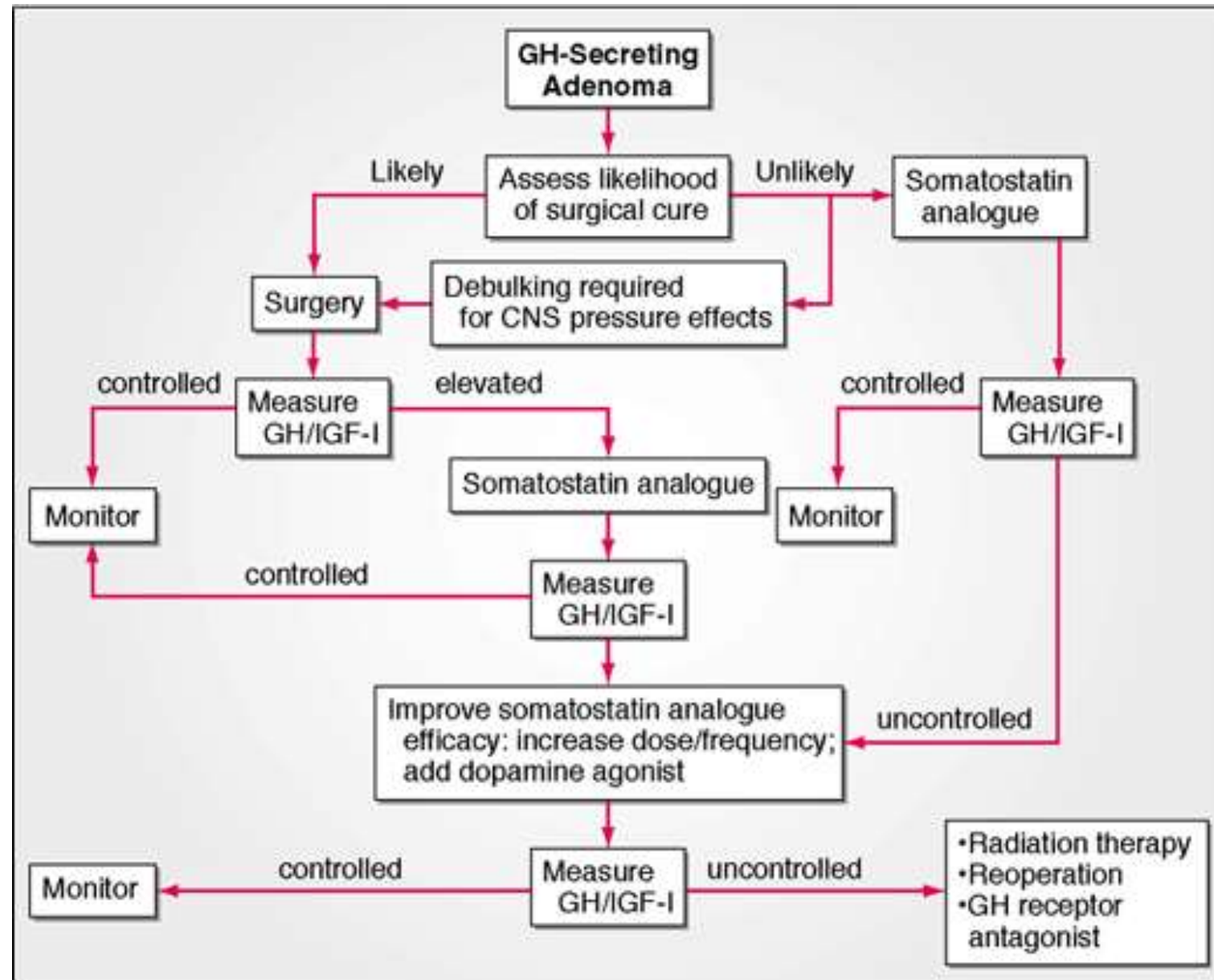
Growth Hormone Tumors: Diagnosis and treatment

Diagnosis

- Screen:
 - Check for high IGF-I levels (>3 U/ml)
 - Remember, levels very high during puberty
- Confirm:
 - 100gm glucose load
 - Positive: GH levels do not increase to <5 ng/ml

Treatment

- Surgical
- Radiation
- Bromocriptine - temporizing measure
 - May decrease GH by 50%
- Octreotide
 - For suboptimal response to other treatment





A



C



B



D



Questions?