

Anterior Pituitary Gland

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學習目標

- Anatomy
- Anterior pituitary hormones
 - Prolactin(PRL)
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 - Adrenocorticotrophic Hormone(ACTH)
 - Gonadotropins: FSH, LH
 - Thyroid-Stimulating Hormone (TSH)
- Hypopituitarism
- Pituitary Tumor
 - Prolactinoma
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Introduction

- 腦下垂體前葉常被稱為「主導腺體」，因為它與下視丘共同協調許多其他內分泌腺體的複雜調節功能。
- 主要荷爾蒙：：泌乳素 (PRL)、生長激素 (GH)、促腎上腺皮質素 (ACTH)、黃體素 (LH)、濾泡刺激素 (FSH) 和促甲狀腺素 (TSH)。
- 分泌模式與調控：這些荷爾蒙以脈衝方式分泌，反映了下視丘釋放因子的調控。
- 回饋機制：周邊腺體產生的荷爾蒙反過來在下視丘和腦下垂體層面進行回饋控制，調節腦下垂體功能。

Anatomy

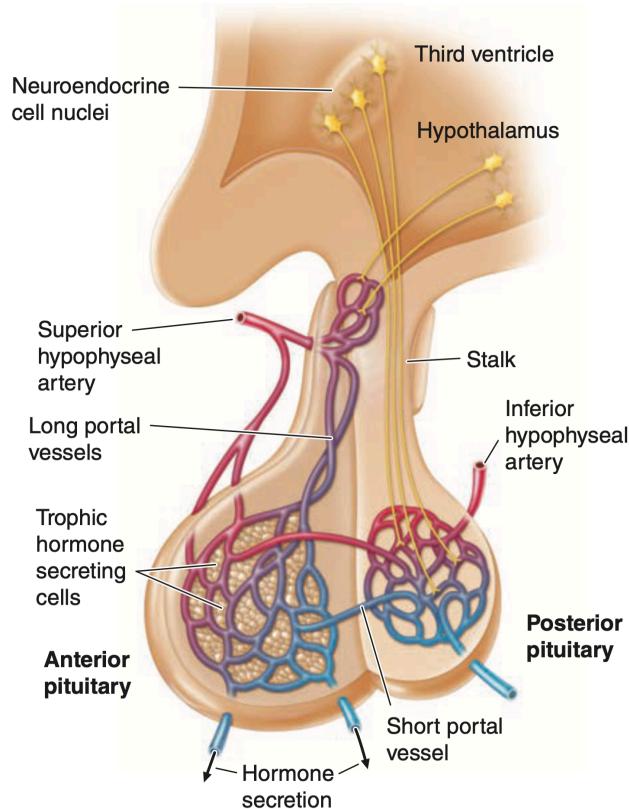


FIGURE 378-2 Diagram of hypothalamic-pituitary vasculature. The hypothalamic nuclei produce hormones that traverse the portal system and impinge on anterior pituitary cells to regulate pituitary hormone secretion. Posterior pituitary hormones are derived from direct neural extensions.

- **位置與大小：**腦下垂體重量約 600 毫克，位於蝶鞍 (sella turcica) 內，在鞍膈 (diaphragma sella) 的腹側。它由解剖和功能上不同的前葉和後葉組成。
- **周圍結構：**蝶鞍骨質結構毗鄰重要的血管和神經結構，包括海綿竇 (cavernous sinuses)、顱神經和視交叉 (optic chiasm)
- 腦下垂體前葉的主要血液供應來自上、下腦下垂體動脈 (superior and inferior hypophyseal arteries) 形成的**下視丘-腦下垂體門脈叢 (hypothalamic-pituitary portal plexus)**
- 後葉由下腦下垂體動脈(inf. hypophyseal artery)供應

Anterior Pituitary Hormone Expression and Regulation

TABLE 378-1 Anterior Pituitary Hormone Expression and Regulation

CELL	CORTICOTROPE	SOMATOTROPE	LACTOTROPE	THYROTROPE	GONADOTROPE
Tissue-specific transcription factor	T-Pit	Prop-1, Pit-1	Prop-1, Pit-1	Prop-1, Pit-1, TEF	SF-1, DAX-1
Fetal appearance	6 weeks	8 weeks	12 weeks	12 weeks	12 weeks
Hormone	POMC	GH	PRL	TSH	FSH, LH
Protein	Polypeptide	Polypeptide	Polypeptide	Glycoprotein α , β subunits	Glycoprotein α , β subunits
Amino acids	266 (ACTH 1–39)	191	198	211	210, 204
Stimulators	CRH, AVP, gp-130 cytokines	GHRH, ghrelin	Estrogen, TRH, VIP	TRH	GnRH, activins, estrogen
Inhibitors	Glucocorticoids	Somatostatin, IGF-1	Dopamine	T_3 , T_4 , dopamine, somatostatin, glucocorticoids	Sex steroids, inhibin
Target gland	Adrenal	Liver, bone, other tissues	Breast, other tissues	Thyroid	Ovary, testis
Trophic effect	Steroid production	IGF-1 production, growth induction, insulin antagonism	Milk production	T_4 synthesis and secretion	Sex steroid production, follicle growth, germ cell maturation
Normal range	ACTH, 4–22 pg/L	<0.5 μ g/L ^a	M <15 μ g/L; F <20 μ g/L	0.1–5 mU/L	M, 5–20 IU/L; F (basal), 5–20 IU/L

^aHormone secretion integrated over 24 h.

Abbreviations: F, female; M, male. For other abbreviations, see text.

Source: Adapted with permission from Melmed S: Hypothalamic-pituitary regulation, in P Conn (ed): *Conn's Translational Neuroscience*. San Diego, CA: Elsevier; 2017.

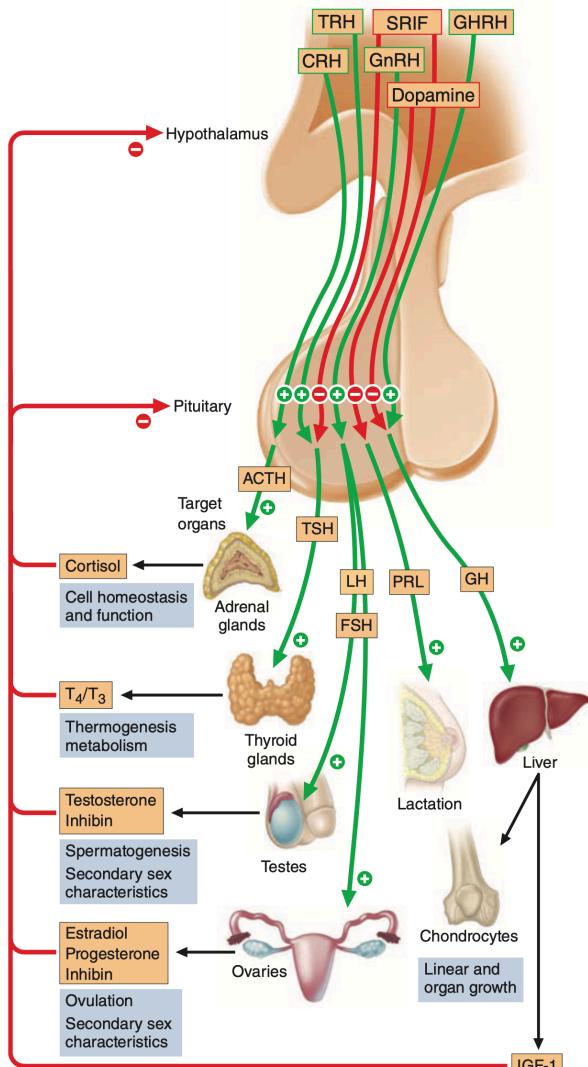
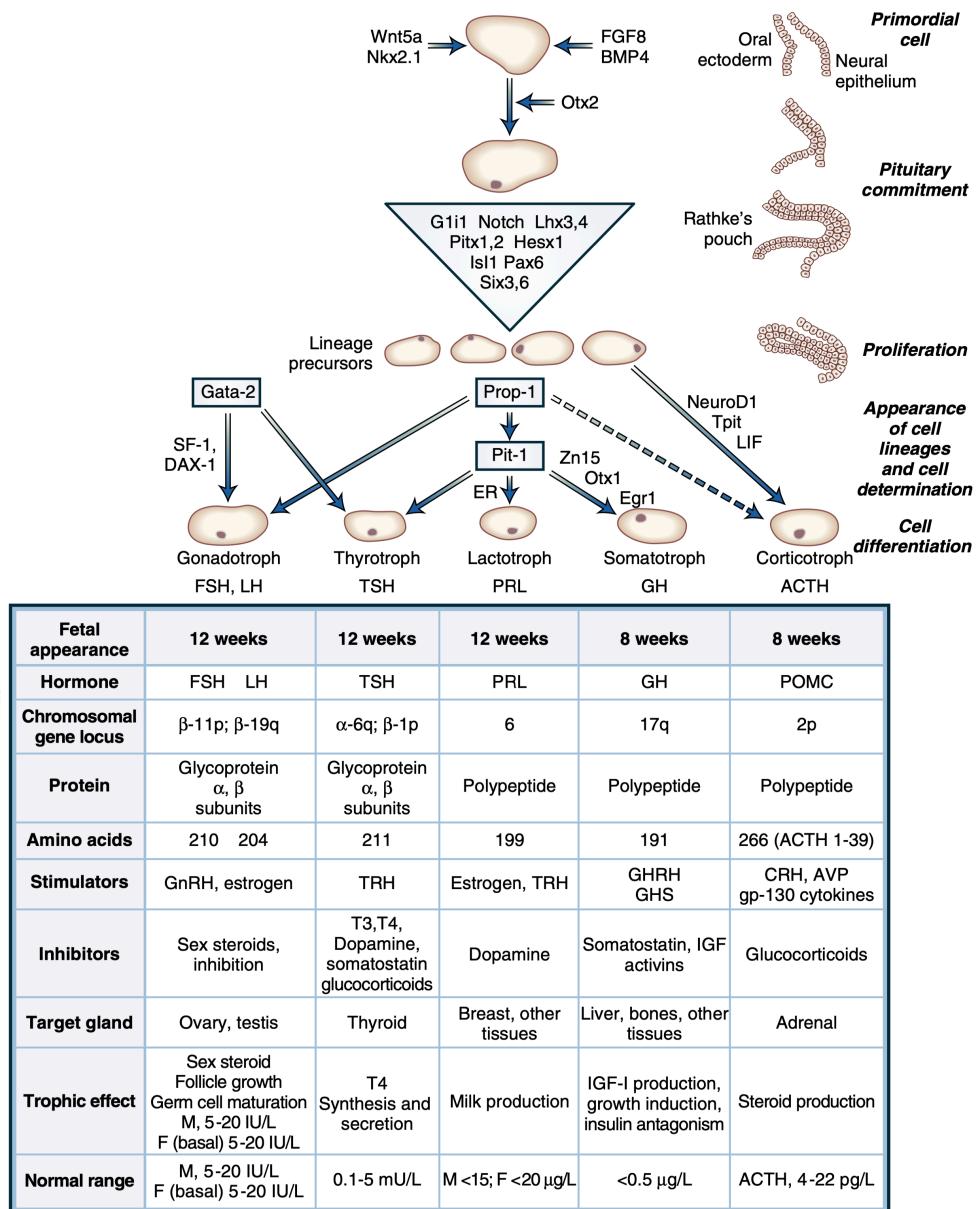
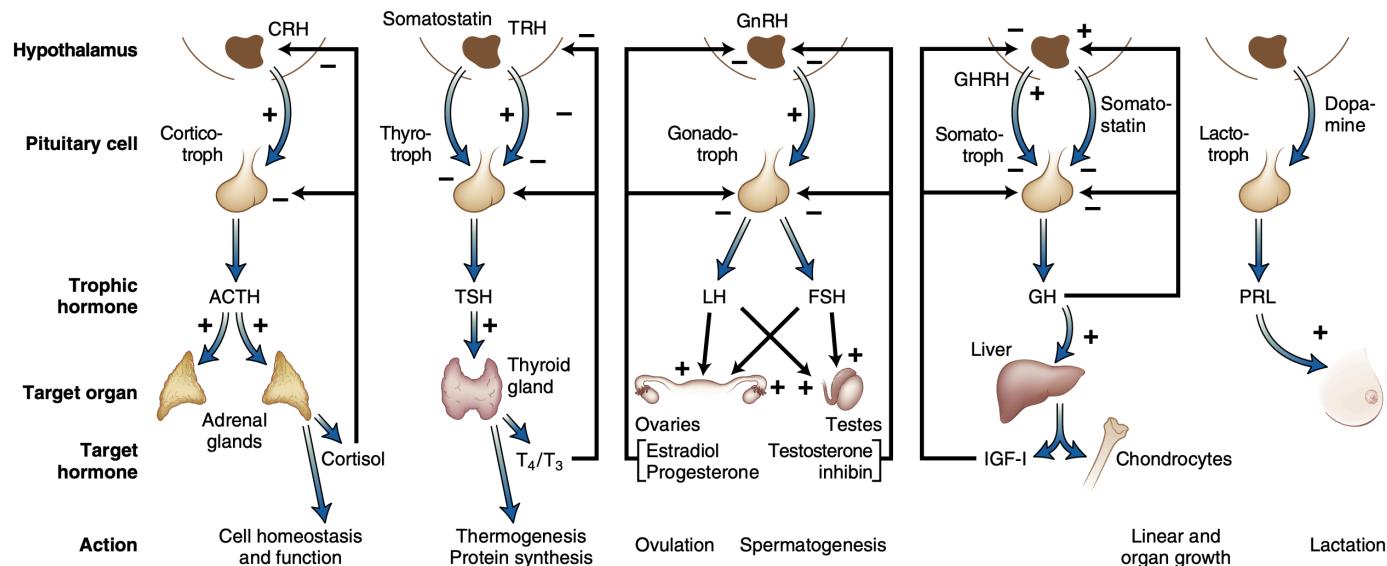
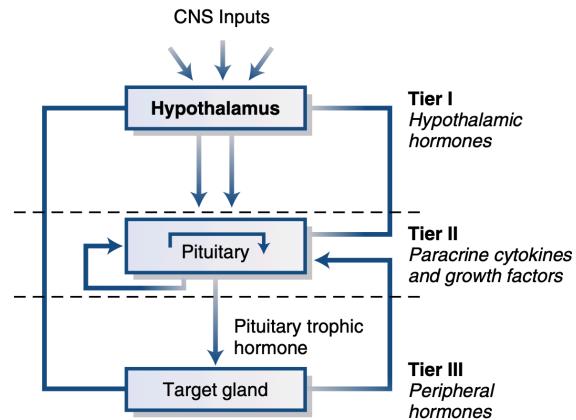


FIGURE 378-1 Diagram of pituitary axes. Hypothalamic hormones regulate anterior pituitary trophic hormones that in turn determine target gland secretion. Peripheral hormones feed back to regulate hypothalamic and pituitary hormones. For abbreviations, see text.



Pituitary Hormone Axes



• **Fig. 8.4** Control of hypothalamic-pituitary target organ axes. ACTH, adrenocorticotrophic hormone; CRH, corticotropin-releasing hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone-releasing hormone; GnRH, gonadotropin-releasing hormone; IGF, insulin-like growth factor; LH, luteinizing hormone; PRL, prolactin; T_3 , triiodothyronine; T_4 , thyroxine; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone. (Adapted from Melmed S. Mechanisms for pituitary tumorigenesis: the plastic pituitary. *J Clin Invest*. 2003;112:1603–1618.)

泌乳素 (Prolactin, PRL)

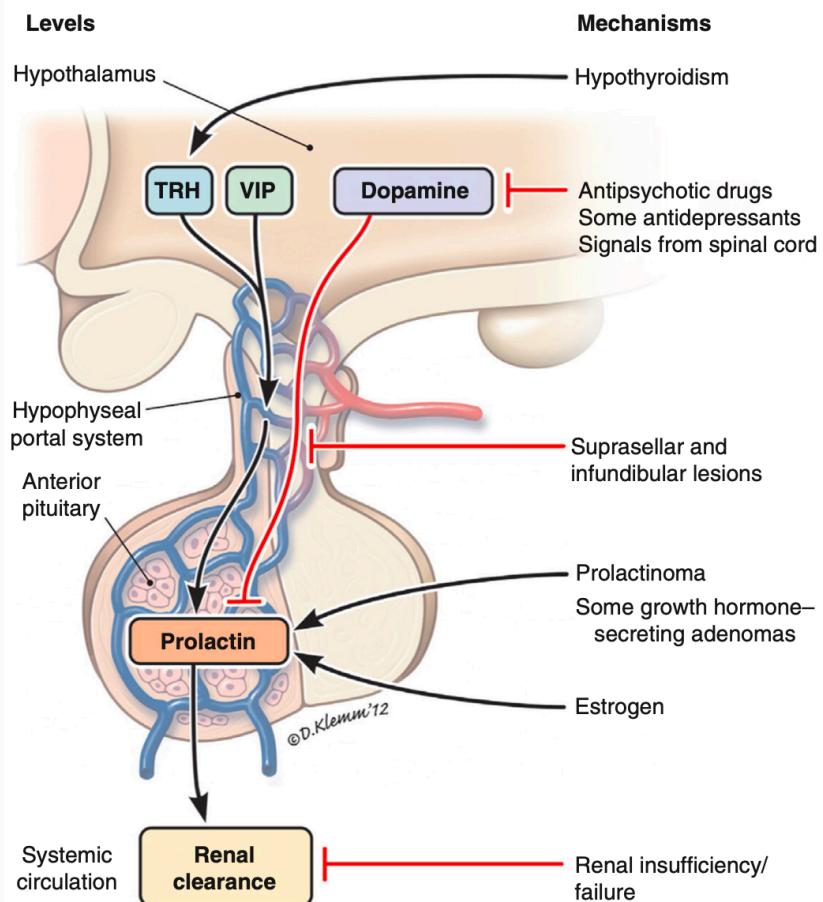
- 泌乳素 (PRL) 主要由腦下垂體前葉的泌乳促素細胞 (Lactotrophs) 產生。
- 其分泌受到下視丘多巴胺 (Dopamine) 的持續性抑制 (tonic inhibition)，這是其最顯著的調控特徵。
- 泌乳促素細胞 (Lactotroph Cells)：
 - 佔前葉功能細胞數量的 15% 至 25%。
 - 多數研究認為泌乳促素細胞主要起源於生長促素細胞 (Somatotrophs) 或共同的乳腺生長促素祖細胞 (Mammosomatotroph progenitor)。
- 分泌：
 - 正常濃度：女性約 10-25 µg/L，男性約 10-20 µg/L。
 - 分泌模式：脈衝式分泌，最高峰在非快速動眼睡眠期(凌晨4-6 點可達 30 µg/L)半衰期約 50 分鐘。

泌乳素的調控 (Regulation)

- 主要為抑制性調控：PRL 是唯一主要受下視丘抑制性控制的腦下垂體前葉荷爾蒙。
 - 下視丘的多巴胺結合泌乳素細胞 (Lactotropes) 膜上的多巴胺第 2 型受體 (Dopamine D2 receptor, D2R)，提供持續性的抑制控制。
 - PRL 本身可以通過短環負回饋 (short-loop negative feedback) 調節自身分泌
- 刺激性調控，刺激因子 (PRL-Releasing Factors, PRFs)：
 - 雌激素 (Estrogen)：顯著刺激 PRL 基因轉錄和分泌。是造成女性 PRL 濃度高於男性、排卵期和孕期 PRL 升高的主要原因。
 - 促甲狀腺素釋放激素 (TRH)：可刺激 PRL 分泌。
 - 吸吮刺激 (Suckling)：哺乳期間，吸吮動作通過神經反射強烈刺激 PRL 釋放。
 - 壓力 (Stress)：生理或心理壓力可導致 PRL 短暫升高。

泌乳素的作用 (Actions)

- 主要生理功能：
 - 泌乳：PRL 是產後啟動和維持乳汁製造所必需的激素。
 - 吸吮刺激不僅促進 PRL 釋放，也刺激垂體後葉釋放催產素 (Oxytocin)。Oxytocin 引起乳腺肌上皮細胞收縮，導致乳汁噴射 (milk ejection)。乳汁在乳腺內積聚會抑制進一步合成。
- 生殖功能調節 (Reproductive Function)：高濃度的 PRL 會抑制下視丘 GnRH 的脈衝式分泌，進而抑制 LH 和 FSH 的分泌，導致性腺功能低下，引起月經失調 (無月經/月經稀少) 和不孕。
 - 在產後哺乳期，生理性的高 PRL 是造成泌乳性閉經 (Lactational Amenorrhea) 和暫時性不孕的主要原因。



• **Fig. 6.6** Neuroendocrine regulation of PRL secretion. Regulation of prolactin under physiologic and pathologic conditions. Black arrows indicate stimulation, whereas red bars depict inhibition. The regulation of serum prolactin occurs at different levels, as illustrated on the left. Common causes of hyperprolactinemia and relevant mechanisms are shown on the right. TRH, thyrotrophin-releasing hormone; VIP, vasoactive intestinal peptide. (From Huang W, Molitch ME. Evaluation and management of galactorrhea. *Am Fam Physician*. 2012;85:1073–1080.)

生長激素 (Growth Hormone, GH)

- 生長促素細胞 (Somatotroph Cells)：
 - GH 主要由腦下垂體前葉的生長促素細胞合成、儲存和分泌。
 - 這些細胞是前葉中數量最多的細胞類型，約佔 35% 至 45%。
 - 主要分佈在前葉的兩側翼 (lateral wings)。

生長激素的調控 (Regulation)

- GH 的分泌受到下視丘、周邊信號和回饋機制的複雜調控，呈現明顯的脈衝式和晝夜節律性。
- 下視丘調控：
 - 生長激素釋放素 (GHRH)：由下視丘弓狀核分泌，是主要刺激因子。
 - 體抑素 (Somatostatin, SST/SRIF)：由下視丘腹周核分泌，是主要抑制因子。SST 結合到體促素細胞的 SST 受體 (SSTRs，主要是 SSTR2 和 SSTR5)，抑制 GH 釋放。
- 飢餓素 (Ghrelin)：主要由胃部分泌的肽類荷爾蒙，是一種強效的 GH 促分泌劑 (secretagogue)

生長激素的調控 (Regulation)

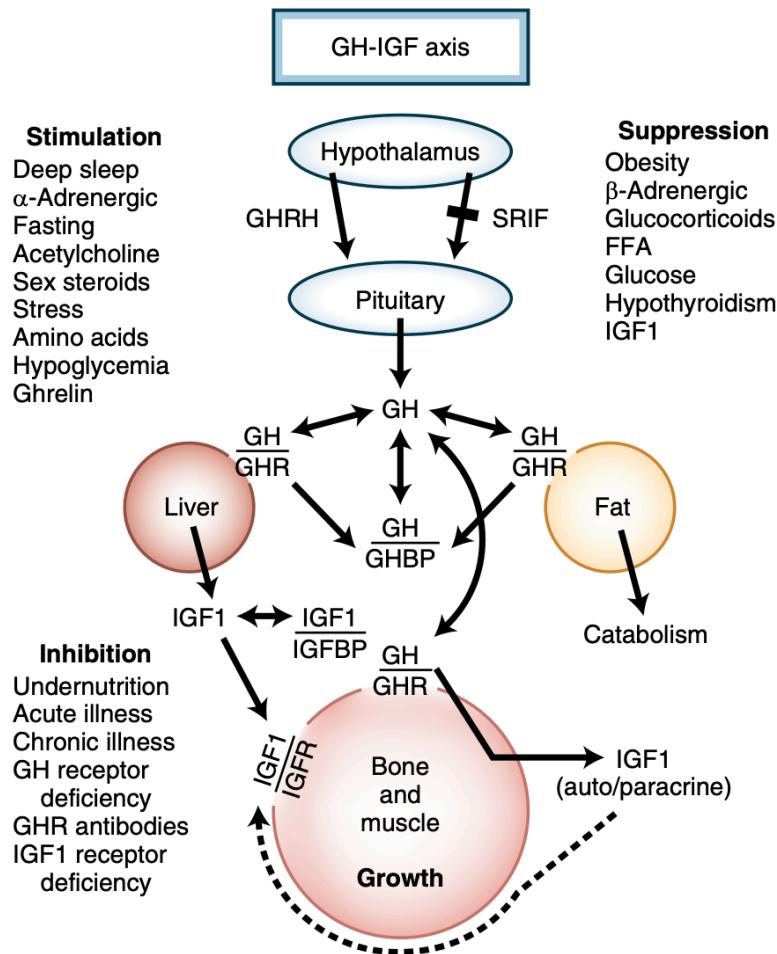
- 負回饋調控：
 - 類胰島素生長因子-1 (IGF-1)：是 GH 的主要周邊介質，主要由肝臟在 GH 刺激下產生。IGF-1 發揮主要的負回饋作用：刺激下視丘釋放體抑素 (SST)。抑制下視丘釋放 GHRH (作用較弱)。直接抑制腦下垂體體促素細胞分泌 GH。
 - 生長激素 (GH)：GH 自身也透過短迴路負回饋抑制其分泌，可能是透過刺激下視丘釋放體抑素。
- 其他激素的交互影響：
 - 糖皮質素 (Glucocorticoids)：急性給予可刺激 GH 釋放，但慢性過量則會抑制 GH 分泌和作用，導致生長遲緩。
 - 甲狀腺素 (Thyroid Hormones)：甲狀腺功能低下會導致 GH 分泌減少和反應性降低。

類胰島素生長因子 (Insulin-Like Growth Factors, IGFs)

- IGF-1：主要由肝臟產生（受 GH 調控），也在周邊組織局部產生，介導 GH 的許多促生長和分化作用。
- IGFBPs：IGF-1 和 IGF-2 與高親和力的 IGF 結合蛋白 (IGFBPs) 結合。IGFBP3 是主要的循環載體蛋白，其濃度受 GH 調控 (GH 缺乏和營養不良時降低) 。
IGFBP1/2 主要調節局部組織 IGF 作用。
- IGF-1 濃度影響因素：青春期升高，16 歲達高峰，隨年齡下降 (>80%)；女性高於男性；GH 異常 (缺乏或過多如肢端肥大症) 影響顯著；分解代謝狀態 (惡病質、營養不良、敗血症) 導致 GH 阻抗，IGF-1 降低。
- IGF-1 生理與治療：注射 IGF-1 可引起低血糖；低劑量可改善胰島素敏感性；具有合成代謝作用 (促進蛋白質合成)。已批准用於 GH 抵抗症候群。副作用與劑量相關 (低血糖、水腫、下頷痛等)。

GH 的代謝作用 (Metabolic Action)

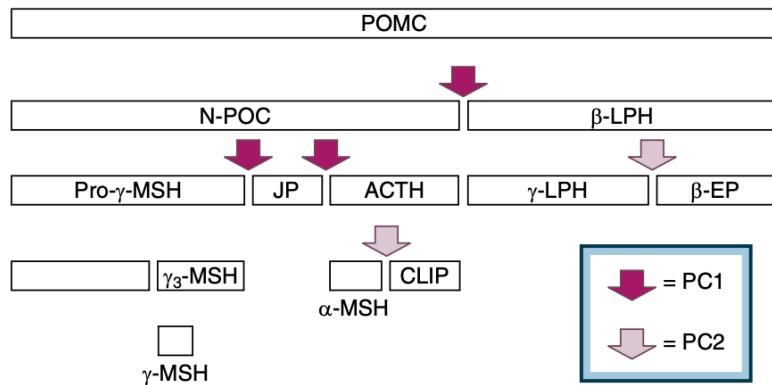
- 直接作用：主要影響代謝，常被描述為具有抗胰島素或致糖尿病 (diabetogenic) 的效應。
 - 抑制周邊組織（肌肉、脂肪）對葡萄糖的攝取和利用。
 - 增加肝臟的糖質新生作用 (gluconeogenesis)。
 - 促進脂肪組織分解 (lipolysis)，釋放游離脂肪酸。
 - 刺激多種組織（尤其是肝臟）產生 IGF-1。
- 間接作用 (透過 IGF-1)：主要介導 GH 的促生長效應。
 - 線性生長：刺激骨骼生長板的軟骨細胞增生和分化，促進骨骼的線性生長（長高）。這是 GH 在兒童和青少年期最重要的作用。
 - 合成代謝 (Anabolic Effect)：促進胺基酸攝取和蛋白質合成，抑制蛋白質分解，增加肌肉量和器官大小。



• **Fig. 6.10** The growth hormone/insulin-like growth factor (GH-IGF) axis. Simplified diagram of GH axis involving hypophysiotropic hormones controlling pituitary GH release, circulating GH-binding protein (GHBP) and its GH receptor (GHR) source, insulin-like growth factor 1 (IGF-1) and its largely GH-dependent binding proteins (IGFBP), and cellular responsiveness to GH and IGF-1 interacting with their specific receptors. FFA, free fatty acids; GHRH, growth hormone-releasing hormone; IGFR, IGF-1 receptor; SRIIF, somatotropin release-inhibiting factor (somatostatin). (From Rosenblom A. Growth hormone insensitivity: physiologic and genetic basis, phenotype and treatment. *J Pediatr*. 1999;135:280–289.)

促腎上腺皮質素 (Adrenocorticotrophic Hormone, ACTH)

- 合成：由促皮質素細胞 (corticotropes, 約佔 20%) 合成。源自前腦啡黑細胞促素皮質素 (Proopiomelanocortin, POMC) 前驅蛋白，POMC 也產生 β -lipotropin, β -endorphin, met-enkephalin, α -MSH 等。POMC 基因受糖皮質素 (cortisol) 強力抑制，受 CRH、AVP、促炎細胞激素 (如 IL-6) 誘導。



• Fig. 6.26 Processing and cleavage of pro-opiomelanocortin (POMC). The mature POMC precursor peptide is sequentially cleaved by prohormone convertase 1 (PC1) in the anterior pituitary corticotroph. In the neuro-intermediate lobe and other cell types, cleavage by PC2 allows release of β -MSH or β -endorphin or both. Carboxypeptidase H (not shown) removes residual basic amino acids at cleavage sites. ACTH, adrenocorticotrophic hormone; CLIP, corticotropin-like intermediate lobe peptide; EP, endorphin; JP, joining peptide; LPH, lipotropin; MSH, melanocyte-stimulating hormone; N-POC, N-terminal pro-POMC fragment. (From Clark AJL, Swords FM. Molecular pathology of corticotroph function. In: Rappaport R, Amselem S, eds. *Hypothalamic-Pituitary Development*. Basel, Switzerland: Karger; 2001.)

ACTH的調控 (Regulation)

- 主要刺激因子：
 - 促腎上腺皮質素釋放素 (CRH)：下視丘旁室核分泌，是最強的 ACTH 促分泌因子。
 - 血管加壓素 (Arginine Vasopressin, AVP)：在壓力狀態下常與 CRH 協同釋放，增強 CRH 對 ACTH 釋放的刺激作用。
- 主要抑制因子 - 負回饋：
 - 皮質醇 (Cortisol)：由腎上腺皮質在 ACTH 刺激下分泌。皮質醇是 HPA 軸最主要的負回饋抑制物。作用於腦下垂體：抑制 ACTH 的釋放和 POMC 基因的轉錄。作用於下視丘：抑制 CRH 和 AVP 的合成與釋放。
- 壓力 (Stress)
 - 生理（如低血糖、手術、感染）和心理壓力是 HPA 軸的強烈刺激因子。壓力信號可以超越皮質醇的負回饋抑制，導致 CRH、AVP、ACTH 和皮質醇的顯著升高。
- 畫夜節律 (Circadian Rhythm)
 - ACTH 和皮質醇的分泌具有非常明顯的畫夜節律，其濃度在清晨（約醒來時）最高，而在傍晚和入睡初期最低。

ACTH的作用 (Actions)

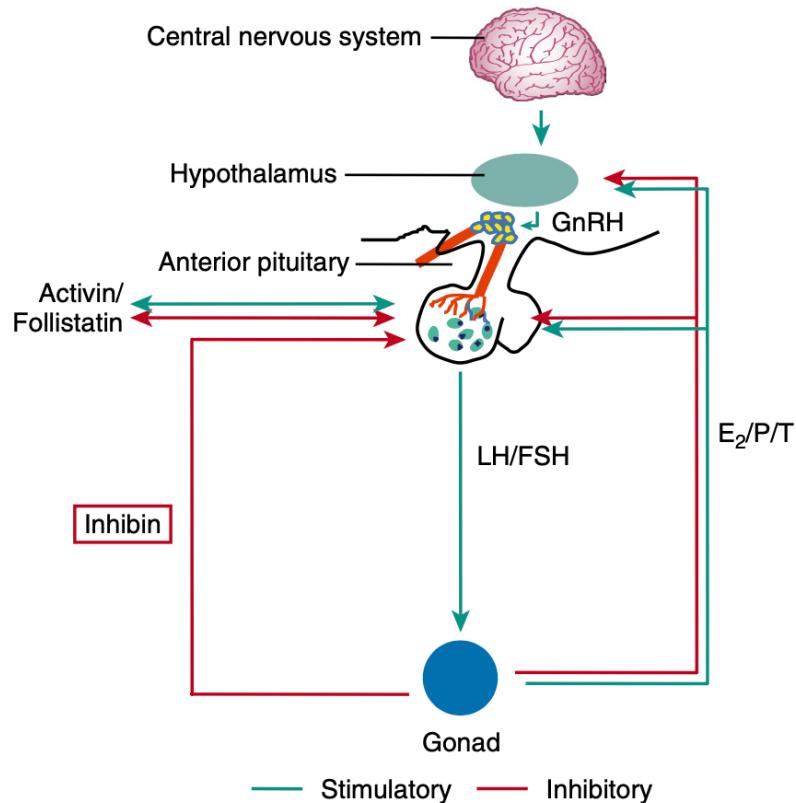
- **主要作用 - 刺激腎上腺皮質**：ACTH 的主要目標器官是腎上腺皮質。
 - 結合到腎上腺皮質細胞（主要是束狀帶 Zona Fasciculata 和網狀帶 Zona Reticularis）表面的 MC2R (Melanocortin-2 Receptor)。
 - 刺激類固醇生成 (Steroidogenesis)：增加類固醇（主要是糖皮質素/皮質醇，以及腎上腺雄激素）的合成與分泌。
 - 維持腎上腺皮質結構：長期的 ACTH 刺激對維持腎上腺束狀帶和網狀帶的大小和功能至關重要。缺乏 ACTH 會導致這些區域萎縮；過量 ACTH 則導致增生 (hyperplasia)。

ACTH的作用 (Actions)

- 黑素細胞刺激作用 (Melanocyte Stimulation)：
 - ACTH 分子本身以及其前體 POMC 的其他衍生物（如 α -MSH, γ -MSH, β -LPH）都含有可以結合到皮膚黑素細胞表面 MC1R (Melanocortin-1 Receptor) 的序列。
 - 在生理濃度下，ACTH 對膚色的影響很小。但在 ACTH 病理性極度升高的情況下（例如，原發性腎上腺功能不全/愛迪生氏病，或切除腎上腺後的庫欣氏病/尼爾森氏症候群），過量的 ACTH 及相關 POMC 肽段會刺激黑素細胞產生黑色素，導致皮膚和黏膜（如口腔、牙齦、疤痕處）出現色素沉著過度 (Hyperpigmentation)。
- 續發性腎上腺功能低下(Secondary adrenal insufficiency)不會有色素沉著(ACTH低)

促性腺激素 (Gonadotropins: FSH and LH)

- 合成與分泌：由促性腺細胞 (gonadotropes, 約佔 10%) 產生 LH 和 FSH
- 調控 (Regulation)
 - LH 和 FSH 的分泌受到下視丘-腦下垂體-性腺軸 (HPG Axis) 的精確調控，涉及下視丘的刺激、性腺的複雜回饋以及旁分泌/自分泌因素。



• **Fig. 6.32** The hypothalamic-pituitary-gonadal axis. See text for discussion. $E_2/P/T$, estrogen/progesterone/testosterone; FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone. (Adapted from Kaiser UB. Gonadotrophin hormones. In: Melmed S, ed. *The Pituitary*, 3rd ed. San Diego, CA: Elsevier; 2011:205–260.)

Gonadotropin(FSH/LH) 的調控

- 下視丘刺激：
 - 促性腺素釋放素 (GnRH)：是 HPG 軸的關鍵啟動者。由下視丘神經元以脈衝形式 (pulsatile manner) 分泌至腦下垂體門脈系統。
 - 脈衝式釋放 (Pulsatile release)：GnRH 必須以脈衝形式釋放進入垂體門脈系統才能有效刺激 LH 和 FSH 的分泌。持續、非脈衝性的 GnRH 暴露反而會導致 GnRH 受體脫敏和促性腺激素分泌的抑制
 - 差異性調控：GnRH 脈衝的頻率 (frequency) 和幅度 (amplitude) 可以差異性地調控 LH 和 FSH 的分泌。較高頻率的 GnRH 脈衝有利於 LH 的分泌，而較低頻率的脈衝則有利於 FSH 的分泌。這種差異性調控在女性月經週期中尤為重要。

Gonadotropin(FSH/LH) 的調控

- 雌激素(Estrogens)：在下視丘和腦下垂體調控 gonadotropin的分泌。慢性雌激素的曝露為抑制；排卵前升高的雌激素則產生正回饋，增加 GnRH 脈衝頻率和幅度，形成LH Surge，觸發排卵。
- 黃體素(Progesterone)：減緩 GnRH 脈衝頻率，但增強對 GnRH 的反應。
- 罂固酮 (Testosterone)：也作用於下視丘和腦下垂體（部分透過轉化為雌激素）。
- 性腺勝肽：抑制素 (Inhibin) 選擇性抑制 FSH 合成；活化素 (Activin) 刺激 FSH 合成。

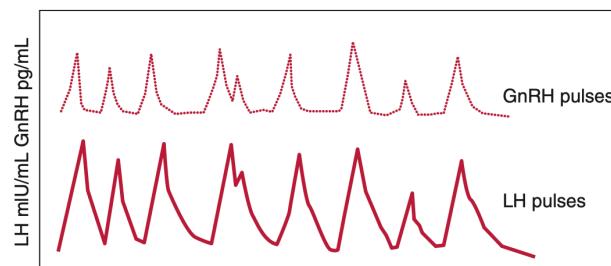


FIGURE 378-3 Hypothalamic gonadotropin-releasing hormone (GnRH) pulses induce secretory pulses of luteinizing hormone (LH).

LH 的作用 (Actions)

- 女性：

- 刺激卵巢的莢膜細胞 (Theca Cells) 合成雄激素（主要是雄烯二酮 androstenedione），這些雄激素隨後被顆粒細胞利用來合成雌激素。
- 觸發排卵 (Ovulation) (LH 峰)。
- 維持排卵後形成的黃體 (Corpus Luteum) 功能，刺激黃體分泌黃體素和雌激素。

- 男性：

- 刺激睪丸的萊氏細胞 (Leydig Cells) 合成和分泌睪固酮 (Testosterone)。

FSH 的作用

- 女性：

- 刺激卵巢濾泡 (Ovarian Follicles) 的生長和發育成熟。
- 刺激濾泡的顆粒細胞 (Granulosa Cells) 增生。
- 誘導顆粒細胞上的芳香化酶 (Aromatase) 活性，將來自莢膜細胞的雄激素轉化為雌激素 (Estradiol)。
- 增加顆粒細胞上的 LH 受體表現，為 LH surge的作用做準備。

- 男性：

- 作用於睪丸曲細精管中的 Sertoli Cells。
- 精子生成 (Spermatogenesis) 的啟動和維持。
- 刺激 Sertoli 細胞產生雄激素結合蛋白 (Androgen-Binding Protein, ABP) (維持曲細精管內高濃度的睪固酮) 、抑制素 B (Inhibin B) (回饋抑制 FSH)

甲狀腺刺激素 (Thyroid-Stimulating Hormone, TSH)

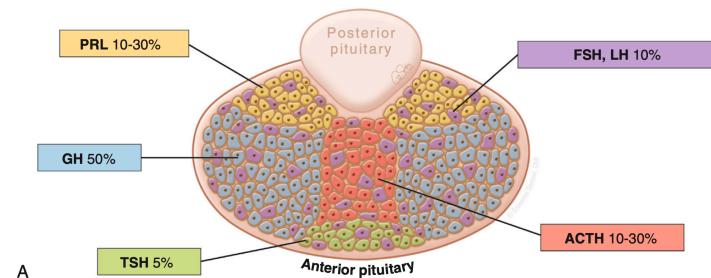
- 合成與分泌：由促甲狀腺激素細胞 (thyrotropes, 約佔 5%) 分泌。糖蛋白，共用 α 次單元，具特異的 TSH β 次單元。
- 主要調控：
 - 刺激：下視丘 TRH (三勝肽) 是主要刺激因子。TRH 也刺激 PRL 分泌。
 - 抑制：甲狀腺荷爾蒙 (T4,T3) 是主要抑制因子，透過負回饋作用於腦下垂體（主要是 TR β 2 受體）和下視丘，抑制 TSH 和 TRH。多巴胺、體抑素、糖皮質素也抑制 TSH (藥理劑量下較明顯)。
 - 回饋反應：甲狀腺功能低下時 TSH 升高；甲狀腺功能亢進時 TSH 受抑制。長期未治療的甲狀腺功能低下可導致 TSH 升高及促甲狀腺激素細胞增生、腦下垂體增大。

TSH的作用 (Actions)

- **主要目標器官**：甲狀腺濾泡細胞 (Thyroid Follicular Cells)。
- **作用機制**：TSH 結合到甲狀腺濾泡細胞表面的 TSH 受體 (TSHR)。
- **主要效應**：TSH 刺激甲狀腺素合成與分泌的所有步驟：
 - 增加碘離子的攝取（活化 NIS）。
 - 刺激甲狀腺球蛋白 (Tg) 的合成與碘化。
 - 促進碘化酪胺酸的耦合反應（生成 T₃/T₄）。
 - 促進溶酶體水解 Tg，釋放 T₃ 和 T₄ 進入血液。
- **滋養效應 (Trophic Effect)**：TSH 對甲狀腺具有促生長作用，刺激甲狀腺細胞增生和甲狀腺血流增加。長期或過度的 TSH 刺激會導致**甲狀腺腫 (Goiter)**。
- **分泌模式**：呈脈衝式分泌，但因半衰期較長（約 50 分鐘），血清濃度相對穩定，單次測量即可評估。

Anterior pituitary hormones

- Growth Hormone(GH)
- Adrenocorticotropic Hormone(ACTH)
- Prolactin(PRL)
- Gonadotropins: FSH, LH
- Thyroid-Stimulating Hormone (TSH)



Hormone	Stimulators	Inhibitors	Target
GH	GHRH, ghrelin	Somatostatin, IGF-1	Liver, bone, other tissues
ACTH	CRH, AVP, gp-130 cytokines	Glucocorticoids	Adrenal
PRL	Estrogen, TRH, VIP	Dopamine	Breast, other tissues
FSH, LH	GnRH, activins, estrogen	Sex steroids, inhibin	Ovary, testis
TSH	TRH	T3, T4, dopamine, somatostatin, glucocorticoids	Thyroid

腦下垂體功能低下 Hypopituitarism

- 腦下垂體功能低下 (Hypopituitarism) 是指前葉腦下垂體荷爾蒙產生不足 。
- 病因可分為遺傳性疾病，或更常見的後天性因素，包括：
 - 腫瘤壓迫效應 。
 - 局部腦下垂體或下視丘的創傷、自體免疫、發炎或血管損傷 。
 - 下視丘荷爾蒙合成或分泌受損，導致續發性腦下垂體衰竭 。
- 腦下垂體功能低下常遵循一定的荷爾蒙喪失順序：通常是生長激素 (GH) 最先受影響 → 其次是促性腺激素 (FSH → LH) → 接著是促甲狀腺激素 (TSH) → 最後是促腎上腺皮質素 (ACTH) 。
- 兒童期常以生長遲緩為表現；成人則以性腺功能低下為最早症狀 。

發育性病因 (Developmental Causes)

- 腦下垂體發育不良 (Dysplasia)：可導致腦下垂體無發育 (aplasia)、發育不全 (hypoplasia) 或異位 (ectopic)
- 基因突變：多種轉錄因子和生長因子對下視丘和腦下垂體發育至關重要，從單一荷爾蒙缺乏到合併性腦下垂體荷爾蒙缺乏 (CPHD) 或尿崩症。
 - 已知相關基因：HESX1, SOX2, SOX3, LHX3, LHX4, OTX, GLI2, PAX6, BMP4, ARNT2, FGF8, FGFR1, SHH, PROKR2, GPR161, IGSF1, PITX2, CHD7 等
- 特定譜系缺陷的基因突變：
 - Pit-1 (POU1F1)：突變導致 GH、PRL、TSH 合併缺乏。患者通常表現為生長失敗和不同程度的甲狀腺功能低下
 - Prop-1 (PROP1)：突變導致 GH、PRL、TSH 及促性腺激素缺乏，少數成年後可能出現 ACTH 缺乏。患者生長遲緩，無法自發進入青春期
 - T-Pit (TBX19)：突變導致 ACTH 缺乏，引起低皮質醇血症
 - SF-1 (NR5A1)：突變損害促性腺細胞發育，以及腎上腺/性腺發育

下視丘內分泌功能障礙 (Hypothalamic Endocrine Dysfunction)

- 當下視丘本身受損，導致腦下垂體分泌的荷爾蒙減少，稱為次發性 (Secondary)或下視丘性(Hypothalamic) 腦下垂體功能低下症。
- **Kallmann Syndrome**
 - 痘因：下視丘 GnRH 合成缺陷，常伴有嗅覺喪失或減退（因嗅球發育不全）。由多種基因突變引起，包括影響 GnRH 神經元遷移的 KAL 基因 (X-link)，以及 GPR54 (體染色體隱性)、FGFR1 (體染色體顯性) 等十多種基因。
 - 臨床表現：青春期延遲，男性有小陰莖等顯著性腺功能低下特徵；女性為原發性閉經和第二性徵發育失敗。可能伴有色盲、視神經萎縮、耳聾、腭裂、腎異常、隱睾、鏡像運動等。
 - 診斷：低 LH、FSH 及低性類固醇（睪固酮或雌二醇）。重複給予 GnRH 可恢復腦下垂體反應，提示為下視丘缺陷。
 - 治療：男性用 hCG 或睪固酮；女性用週期性雌激素和黃體素恢復第二性徵。欲恢復生育能力可用促性腺激素或脈衝式 GnRH 輸注。

下視丘內分泌功能障礙 (Hypothalamic Endocrine Dysfunction)

- Bardet-Biedl Syndrome：
 - 病因：罕見的遺傳異質性疾病，與至少九個基因座相關，部分涉及基底纖毛功能。
 - 臨床表現：智力障礙、腎異常、肥胖、多指/短指/併指。常有 GnRH 缺乏（男性 75%，女性 50%）。視網膜變性，多在 30 歲前失明。
- 瘦素 (Leptin) 及瘦素受體突變：導致廣泛的下視丘異常，包括食慾過盛、肥胖和中樞性性腺功能低下（因 GnRH 產生減少）。
- Prader-Willi Syndrome(小胖威利)：
 - 病因：父系染色體 15q 上 SNRPN、NECDIN 等印記基因缺失。
 - 臨床表現：促性腺激素功能低下性性腺功能低下、食慾過盛-肥胖、慢性肌張力低下、智力遲緩、成人型糖尿病。多種軀體缺陷。可能與下視丘催產素/血管加壓素核減少有關。GnRH 合成缺陷。

後天性腦下垂體功能低下 (Acquired hypopituitarism)

- 常見原因：意外或神經外科創傷、血管事件（如中風、Sheehan syndrome）、腫瘤（腦下垂體/下視丘、顱咽管瘤、淋巴瘤、轉移癌）、發炎性疾病（淋巴球性/自體免疫性腦下垂體炎，包括檢查點抑制劑引起）、浸潤性疾病（類肉瘤病、血鐵沉積症、結核病）、放射治療。
- 腦損傷/放射治療後遺症：頭部創傷（包括運動傷害、車禍、爆炸傷）、蜘蛛膜下腔出血和放射治療後，有 25-40% 患者會發生暫時性或永久性腦下垂體功能低下，需長期追蹤。放射治療後，功能低下通常在 5-15 年內發生，多因下視丘損傷，GH 缺乏最常見，其次依序是促性腺激素、TSH、ACTH。

後天性腦下垂體功能低下 (Acquired hypopituitarism)

- 淋巴球性/自體免疫性腦下垂體炎：
 - 最常見於產後女性，常表現為高泌乳素血症和類似腺瘤的腦下垂體腫塊。
 - 可由檢查點抑制劑 (CTLA-4 或 PD-1/PD-L1 抑制劑) 誘發。
 - 引起的腦下垂體衰竭可能是暫時性或永久性的。糖皮質素治療可能使發炎過程緩解。
- 空蝶鞍症 (Empty Sella)：
 - 常為 MRI 偶然發現，可能是部分或看似完全的空蝶鞍。
 - 患者通常腦下垂體功能正常，提示周圍殘餘組織功能完好。但功能低下也可能潛隱發生。可由腦下垂體腺瘤的無症狀性梗塞和退化，隨後被腦脊液填充硬腦膜疝所致。偶爾，小的功能性腺瘤可發生在正常腦下垂體組織邊緣內，影像學不易發現。
- 下視丘浸潤性疾病：類肉瘤病、組織細胞增生症 X、澱粉樣變性、血鐵沉積症常同時累及下視丘和腦下垂體，尿崩症 (DI) 是常見表現（半數患者）。

後天性腦下垂體功能低下 (Acquired hypopituitarism)

- 腦下垂體中風 (Pituitary Apoplexy)：
 - 指腦下垂體急性出血或梗塞，常發生於已存在的腦下垂體腺瘤中，或產後 (Sheehan's syndrome)、糖尿病、高血壓、鐮狀細胞貧血、休克等情況下。懷孕期腦下垂體生理性增大增加風險。
 - 臨床表現：內分泌急症，可導致嚴重低血糖、低血壓/休克、中樞神經出血甚至死亡。急性症狀包括劇烈頭痛伴腦膜刺激徵、雙側視力改變、眼肌麻痺，嚴重時心血管衰竭、意識喪失。
 - 診斷：CT 或 MRI 可見腫瘤內或蝶鞍出血、腦下垂體柄偏移、組織受壓。
 - 治療：無明顯視力喪失或意識障礙者可保守治療（高劑量糖皮質素）；有顯著或進行性視力喪失、顱神經麻痺或意識喪失者需緊急手術減壓。術後視力恢復與事件發生時間相關，嚴重眼肌麻痺或視力缺損是早期手術的指徵。中風後常發生腦下垂體功能低下。

Hypopituitarism

TABLE 379-1 Etiology of Hypopituitarism^a

Development/structural	
Midline cerebral defect syndromes	
Pituitary dysplasia/aplasia	
Primary empty sella	
Congenital hypothalamic disorders (septo-optic dysplasia, Prader-Willi syndrome, Bardet-Biedl syndrome, Kallmann syndrome)	
Congenital central nervous system mass, encephalocele	
Genetic	
Combined pituitary hormone deficiencies	
Isolated primary hormone deficiencies	
Traumatic	
Surgical resection	
Radiotherapy damage	
Head injuries	
Neoplastic	
Pituitary adenoma	
Parasellar mass (germinoma, ependymoma, glioma)	
Rathke's cyst	
Craniopharyngioma	
Hypothalamic hamartoma, gangliocytoma	
Pituitary metastases (breast, lung, colon carcinoma)	
Lymphoma and leukemia	
Meningioma	
Infiltrative/inflammatory	
Lymphocytic hypophysitis	
Hemochromatosis	
Sarcoidosis	
Histiocytosis X	
Granulomatous hypophysitis	
Transcription factor antibodies	
Immunotherapy	
Vascular	
Pituitary apoplexy	
Pregnancy-related (infarction with diabetes; postpartum necrosis)	
Subarachnoid hemorrhage	
Sickle cell disease	
Arteritis	
Infections	
Fungal (histoplasmosis)	
Parasitic (toxoplasmosis)	
Tuberculosis	
<i>Pneumocystis jirovecii</i>	

腦下垂體功能低下症的臨床表現 (Clinical Features of Hypopituitarism)

- 臨床表現：取決於缺乏哪種荷爾蒙及缺乏程度。
 - GH 缺乏：兒童期生長障礙；成人期異常身體組成。
 - 促性腺激素缺乏：女性月經失調、不孕；男性性功能下降、不孕、第二性徵喪失。
 - TSH 缺乏：兒童期生長遲緩；兒童和成人甲狀腺功能低下。
 - ACTH 缺乏：引起繼發性腎上腺功能不全，導致低皮質醇血症，但鹽皮質激素產生相對保留。
 - PRL 缺乏：導致泌乳失敗。血管加壓素缺乏（若後葉被影響）：引起尿崩症 (DI)，表現為多尿、煩渴。
- 預後：長期腦下垂體損傷患者死亡率增加，主要死於心血管和腦血管疾病。既往頭頸部放療也是決定因素。

診斷 (Diagnosis)

- 一般原則 (General Approach)
 - 臨床懷疑：基於病史（如頭部創傷、放療史、產後大出血史等）和臨床表現（如生長遲緩、性腺功能低下症狀、不明原因疲勞等）產生懷疑。
 - 生化學評估：測定基礎荷爾蒙濃度，必要時進行動態功能測試。
 - 影像學檢查：主要是腦部 MRI，以尋找腦下垂體或下視丘的結構性病變。
 - 視野檢查：若懷疑有腫塊壓迫視交叉，需進行視野檢查。
- 基礎荷爾蒙評估 (Basal Hormone Evaluation)
- 動態功能測試 (Dynamic Function Testing / Provocative Tests)

TABLE 379-2 Tests of Pituitary Sufficiency

HORMONE	TEST	BLOOD SAMPLES	INTERPRETATION
Growth hormone (GH)	Insulin tolerance test: Regular insulin (0.05–0.15 U/kg IV)	–30, 0, 30, 60, 120 min for glucose and GH	Glucose <40 mg/dL; GH should be >3 µg/L
	GHRH test: 1 µg/kg IV	0, 15, 30, 45, 60, 120 min for GH	Normal response is GH >3 µg/L
	L-Arginine test: 30 g IV over 30 min	0, 30, 60, 120 min for GH	Normal response is GH >3 µg/L
	L-Dopa test: 500 mg PO	0, 30, 60, 120 min for GH	Normal response is GH >3 µg/L
Prolactin	TRH test: 200–500 µg IV	0, 20, and 60 min for TSH and PRL	Normal prolactin is >2 µg/L and increase >200% of baseline
ACTH	Insulin tolerance test: regular insulin (0.05–0.15 U/kg IV)	–30, 0, 30, 60, 90 min for glucose and cortisol	Glucose <40 mg/dL Cortisol should increase by >7 µg/dL or to >20 µg/dL
	CRH test: 1 µg/kg ovine CRH IV at 8 A.M.	0, 15, 30, 60, 90, 120 min for ACTH and cortisol	Basal ACTH increases 2- to 4-fold and peaks at 20–100 pg/mL Cortisol levels >20–25 µg/dL
	Metyrapone test: Metyrapone (30 mg/kg) at midnight	Plasma 11-deoxycortisol and cortisol at 8 A.M.; ACTH can also be measured	Plasma cortisol should be <4 g/dL to assure an adequate response Normal response is 11-deoxycortisol >7.5 µg/dL or ACTH >75 pg/mL
	Standard ACTH stimulation test: ACTH 1-24 (cosyntropin), 0.25 mg IM or IV	0, 30, 60 min for cortisol and aldosterone	Normal response is cortisol >21 g/dL and aldosterone response >4 ng/dL above baseline
	Low-dose ACTH test: ACTH 1-24 (cosyntropin), 1 µg IV	0, 30, 60 min for cortisol	Cortisol should be >21 µg/dL
	3-day ACTH stimulation test consists of 0.25 mg ACTH 1-24 given IV over 8 h each day		Cortisol >21 µg/dL
TSH	Basal thyroid function tests: T_4 , T_3 , TSH	Basal measurements	Low free thyroid hormone levels in the setting of TSH levels that are not appropriately increased indicate pituitary insufficiency
	TRH test: 200–500 µg IV	0, 20, 60 min for TSH and PRL ^a	TSH should increase by >5 mU/L unless thyroid hormone levels are increased
LH, FSH	LH, FSH, testosterone, estrogen	Basal measurements	Basal LH and FSH should be increased in postmenopausal women Low testosterone levels in the setting of low LH and FSH indicate pituitary insufficiency
	GnRH test: GnRH (100 µg) IV	0, 30, 60 min for LH and FSH	In most adults, LH should increase by 10 IU/L and FSH by 2 IU/L Normal responses are variable
Multiple hormones	Combined anterior pituitary test: GHRH (1 µg/kg), CRH (1 µg/kg), GnRH (100 µg), TRH (200 µg) are given IV	–30, 0, 15, 30, 60, 90, 120 min for GH, ACTH, cortisol, LH, FSH, and TSH	Combined or individual releasing hormone responses must be elevated in the context of basal target gland hormone values and may not be uniformly diagnostic (see text)

^aEvoked PRL response indicates lactotrope integrity.Abbreviations: T_3 , triiodothyronine; T_4 , thyroxine; TRH, thyrotropin-releasing hormone. For other abbreviations, see text.

TABLE 8.15 Assessment of Anterior Pituitary Function

Test	Dose	Normal Response	Side Effects
ACTH			
Insulin tolerance	0.1–0.15 U/kg IV	Peak cortisol response $>18 \mu\text{g}/\text{dL}$, or increase by $7 \mu\text{g}/\text{dL}$	Sweating, palpitation, tremor
Metyrapone	Oral administration of 30 mg/kg at 11 PM	Peak 11-DOC $\geq 7 \mu\text{g}/\text{dL}$ Peak cortisol $\leq 7 \mu\text{g}/\text{dL}$ Peak ACTH $>75 \text{ pg/mL}$	Nausea, insomnia, adrenal crisis
CRH stimulation	100 μg IV	Peak ACTH \geq twofold to fourfold Peak cortisol $\geq 20 \mu\text{g}/\text{dL}$ or $\uparrow \geq 7 \mu\text{g}/\text{dL}$	Flushing
ACTH stimulation	250 μg IV or IM or 1 μg IV	Peak cortisol $\geq 20 \mu\text{g}/\text{dL}$	Rare
TSH			
Serum T ₄ (free T ₄)			
Total T ₃			
TSI—third generation			
TRH stimulation	200–500 μg IV	Peak TSH \geq 2.5-fold or $\uparrow \geq 5$ –6 mU/L (females), $\uparrow \geq 2$ –3 mU/L (males)	Flushing, nausea, urge to micturate
PRL			
Serum PRL			
TRH stimulation	200–500 μg IV	PRL \geq 2.5-fold	Flushing, nausea, urge to micturate
LH/FSH			
Serum LH and FSH		Elevated in menopause and in men with primary testicular failure	
Serum testosterone		300–900 ng/mL (age-adjusted normal ranges)	
GnRH stimulation	100 μg IV	LH \geq twofold to threefold, or by 10 IU/L FSH 1.5–2-fold, or by 2 IU/L	Rare
GH			
Insulin tolerance	0.1–0.15 U/kg	GH peak $>5 \mu\text{g}/\text{L}$	Sweating, palpitation, tremor
Glucagon	1–1.5 mg IM	GH peak $>3 \mu\text{g}/\text{L}$	Nausea, headaches
L-Arginine plus GHRH		Peak GH $>9 \mu\text{g}/\text{L}$	
L-Arginine	0.5 g/kg (max 30 g) IV over 30 min		Nausea
GHRH	1 $\mu\text{g}/\text{kg}$		Flushing

ACTH, Adrenocorticotrophic hormone; CRH, corticotropin-releasing hormone; 11-DOC, 11-deoxycorticosterone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone-releasing hormone; GnRH, gonadotropin-releasing hormone; IM, intramuscular; IV, intravenous; LH, luteinizing hormone; PRL, prolactin; T₃, triiodothyronine; T₄, thyroxine; TSH, thyroid-stimulating hormone; TRH, thyrotropin-releasing hormone.

Treatment of hypopituitarism

- 治療根本病因：如果可能，治療導致腦下垂體功能低下的潛在疾病（如切除腫瘤、治療感染或發炎）。
- 荷爾蒙補充治療：以生理劑量補充缺乏的荷爾蒙，以恢復正常的生理功能、改善症狀、提高生活品質並預防長期併發症。這通常需要終身治療。
 - ACTH : Hydrocortisone 10-20 mg/d ; 或 Cortisone acetate 15-25 mg/d ; 或 Prednisone 5 mg QD
 - TSH : L-Thyroxine 0.075-0.15 mg/d 。
 - FSH/LH : 男性 : 罂粟固酮凝膠 (5-10 g/d) 、皮膚貼片 (5 mg/d) 或 Testosterone enanthate 200 mg 每 2 週肌注 。女性 : 週期性雌孕激素 (如結合型雌激素 0.625-1.25 mg/d + 黃體酮 5-10 mg/d 第 16-25 天) ；或雌二醇貼片加黃體酮 。
 - FSH/LH 缺乏 (生育需求) : hMG, hCG 或脈衝式 GnRH
 - GH 缺乏 (成人) : Somatotropin 0.1-1.25 mg/d 皮下注射
 - GH 缺乏 (兒童) : Somatotropin 0.02-0.05 mg/kg/d
 - 血管加壓素缺乏 : Desmopressin 300-600 µg qd

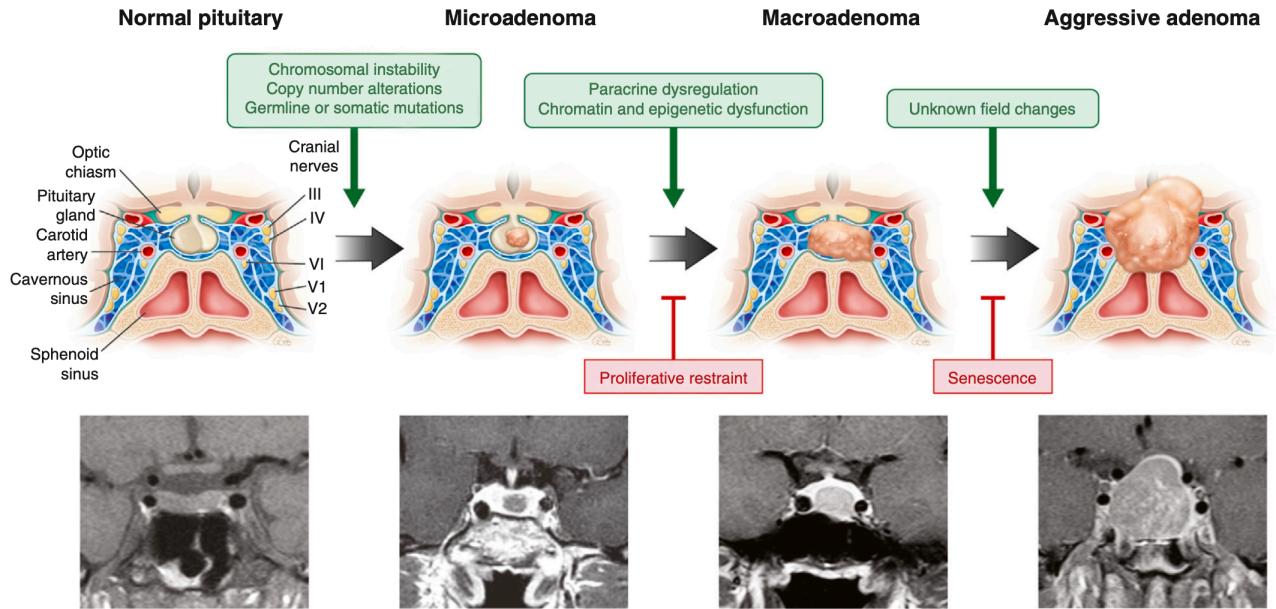
Treatment of hypopituitarism

TABLE 379-3 Hormone Replacement Therapy for Adult Hypopituitarism^a

HORMONE DEFICIT	HORMONE REPLACEMENT
ACTH	Hydrocortisone (10–20 mg/d in divided doses)
	Cortisone acetate (15–25 mg/d in divided doses)
	Prednisone (5 mg A.M.)
TSH	L-Thyroxine (0.075–0.15 mg daily)
FSH/LH	Males
	Testosterone gel (5–10 g/d)
	Testosterone skin patch (5 mg/d)
	Testosterone enanthate (200 mg IM every 2 weeks)
	Females
	Conjugated estrogen (0.65–1.25 mg qd for 25 days)
	Progesterone (5–10 mg qd) on days 16–25
	Estradiol skin patch (0.025–0.1 mg every week), adding progesterone on days 16–25 if uterus intact
GH	For fertility: menopausal gonadotropins, human chorionic gonadotropins
	Adults: Somatotropin (0.1–1.25 mg SC qd)
Vasopressin	Children: Somatotropin (0.02–0.05 mg/kg per day)
	Intranasal desmopressin (5–20 g twice daily) Oral 300–600 µg qd

腦下垂體腫瘤 (Pituitary Tumor)

- The most frequent cause of pituitary disorders is pituitary gland tumors.
- Two types of tumors exist (secretory and non-secretory).
- The problems fall into three categories:
 - Hypersecretion
 - It is usually caused by a secretory pituitary gland tumor.
 - Hyposecretion
 - It is usually caused by a non-secretory tumor, interfering the ability of the normal pituitary gland to create hormones.
 - It can also be caused by a large secretory tumor. It can also happen after surgery or the radiation therapy.



Cell type	PROP1						TPIT	Null
	PIT1				Gonadotroph	Corticotroph		
Hormone secreted	Lactotroph	Mammosomatotroph	Somatotroph	Thyrotroph	FSH/LH	ACTH	None	
Clinical phenotype	High PRL Pituitary failure	High PRL, high GH, and/or high IGF1 Pituitary failure	High GH, high IGF1 Pituitary failure	High/low TSH, high/low T4 Pituitary failure	High/low FSH, high/low LH Pituitary failure	High ACTH, high cortisol Pituitary failure	Pituitary failure	

• **Fig. 7.19** Pathogenesis of pituitary adenomas. Specific transcription factors determine development and differentiation of hormone-expressing cell lineages. Pituitary adenomas arise from a differentiated hormone-expressing cell, or from a null cell devoid of hormone products. Clinical phenotype is determined by the cell of origin and the presence or absence of autonomous, specific hormone hypersecretion. (From Melmed S, Kaiser UB, Lopes MB, et al. Clinical biology of the pituitary adenoma. *Endocr Rev*. 2022;43:1003–1037. Copyright Giovanna Santoni, CMI. Used by permission.)

局部壓迫效應 (Local Mass Effects)

- 蝶鞍腫塊（最常見為腦下垂體腺瘤）常向上方（阻力最小的鞍膈方向）擴展，也可侵犯蝶鞍底部進入蝶竇（圖 380-1）。
- 頭痛：常見，即使腫瘤很小且未向上擴展，可能因鞍內壓力改變牽拉硬腦膜引起，嚴重程度與腺瘤大小或擴展程度關聯不大。
- 視力喪失：最常見原因是向上壓迫視交叉，導致典型的雙顳側偏盲（上方更明顯）。少數情況下，直接侵犯視神經或阻塞腦脊液流動也可致視力障礙。
- 腦下垂體柄壓迫：可中斷下視丘荷爾蒙和多巴胺到達腦下垂體，導致高泌乳素血症（早期）及後續其他腦下垂體荷爾蒙缺乏（"柄切斷"現象）。
- 海綿竇侵犯：向兩側擴展可壓迫海綿竇及其中的第 III、IV、VI 對顱神經和三叉神經的眼支、上頷支，導致複視、眼瞼下垂、眼肌麻痹、面部感覺減退。
- 其他侵犯：向下侵入蝶竇；罕見侵犯鼻咽頂、顳葉或額葉（可致癲癇、人格改變、嗅覺喪失）；侵犯下視丘可致性早熟/性腺功能低下、尿崩症、睡眠障礙、體溫調節異常、食慾紊亂。

Mass effect

TABLE 9.1 Local Effects of an Expanding Pituitary, Parasellar, or Hypothalamic Mass

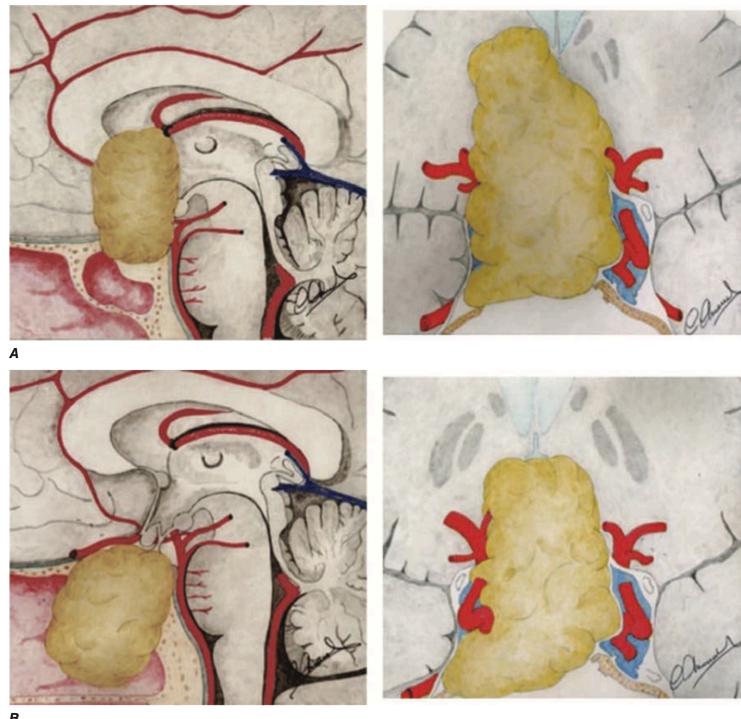
Impacted Structure	Clinical Effect
Pituitary	Growth failure, adult hyposomatotropism, hypogonadism, hypothyroidism, hypoadrenalinism
Optic tract	Loss of red perception, bitemporal hemianopia, superior or bitemporal field defect, scotoma, blindness
Hypothalamus	Temperature dysregulation, obesity, diabetes insipidus; thirst, sleep; appetite, behavioral, and autonomic nervous system dysfunctions
Cavernous sinus	Ptosis, diplopia, ophthalmoplegia, facial numbness
Temporal lobe	Uncinate seizures
Frontal lobe	Personality disorder, anosmia
Central	Headache, hydrocephalus, psychosis, dementia, laughing seizures

Neuro-ophthalmologic tract	<i>Field defects:</i> Bitemporal hemianopia (50%), amaurosis with hemianopia (12%), contralateral or monocular hemianopia (7%)
	Scotomas—junctional; monocular central, arcuate, altitudinal; hemianopic
	<i>Homonymous hemianopia</i>
	<i>Acuity loss:</i>
	Snellen
	Contrast sensitivity
	Color vision
	Visual evoked potential
	<i>Pupillary abnormality:</i>
	Impaired light reactivity
	Afferent defect
	<i>Optic atrophy:</i>
	Papilledema
	Cranial nerve palsy—oculomotor, trochlear, abducens, sensory trigeminal
	Nystagmus
	Visual hallucinations
	Postfixation blindness

TABLE 380-1 Features of Sellar Mass Lesions^a

IMPACTED STRUCTURE	CLINICAL IMPACT
Pituitary	Hypogonadism Hypothyroidism Growth failure, adult growth hormone deficiency Hypoadrenalinism Hyperprolactinemia (stalk compression)
Optic chiasm	Loss of red perception Bitemporal hemianopia Superior or bitemporal field defect Scotoma Blindness
Hypothalamus	Temperature dysregulation Appetite and thirst disorders Obesity Diabetes insipidus Sleep disorders Behavioral dysfunction Autonomic dysfunction
Cavernous sinus	Ophthalmoplegia with or without ptosis or diplopia Facial numbness
Frontal lobe	Personality disorder Anosmia
Brain	Headache Hydrocephalus Psychosis Dementia Laughing seizures

^aAs the intrasellar mass expands, it first compresses intrasellar pituitary tissue, then usually invades dorsally through the dura to lift the optic chiasm or laterally to the cavernous sinuses. Bony erosion is rare, as is direct brain compression. Microadenomas may present with headache.



380-1 Expanding pituitary mass. Pituitary mass expansion may (A) impinge vital soft tissue structures and (B) invade the sphenoid sinus. (Reproduced with permission from P Cappabianca et al: Size does not matter. The intrigue of giant adenomas: a true surgical challenge. *Acta Neurochir (Wien)* 156:2217, 2014.)

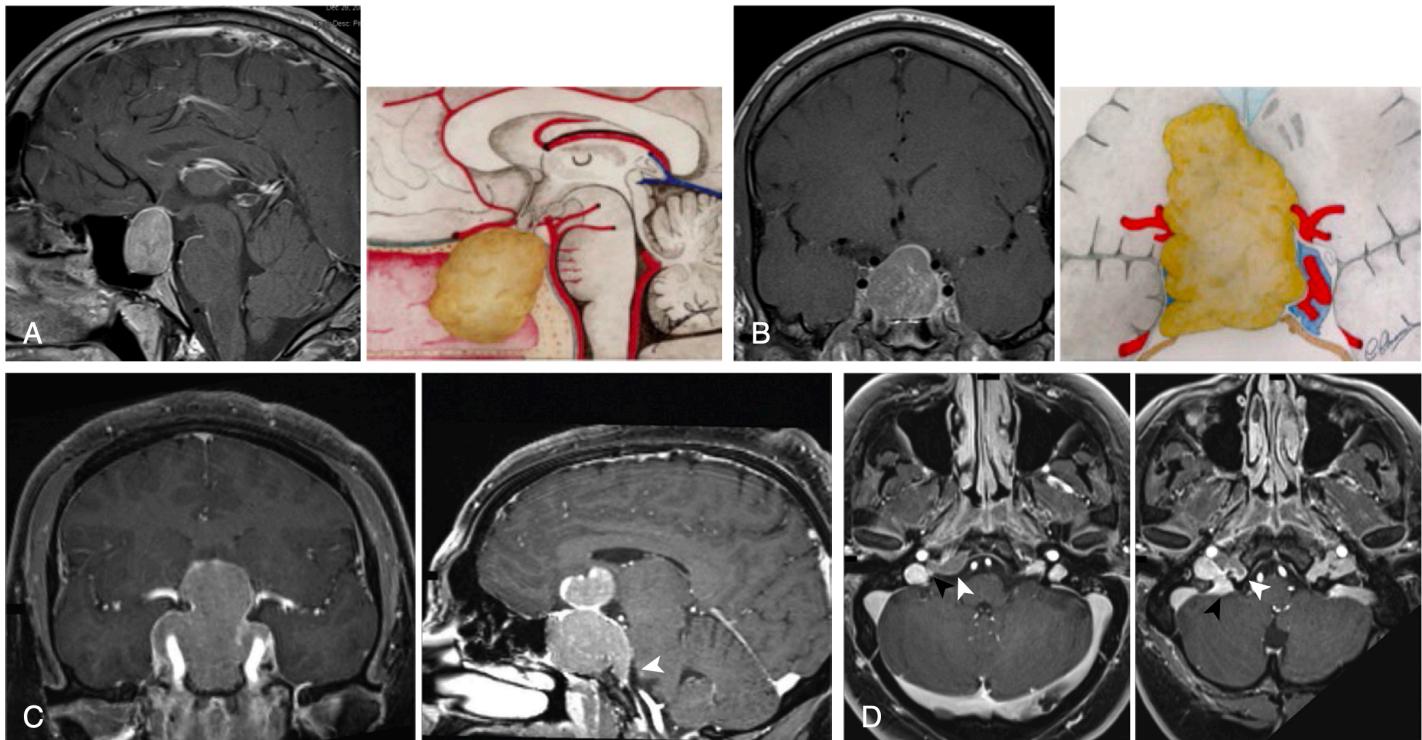
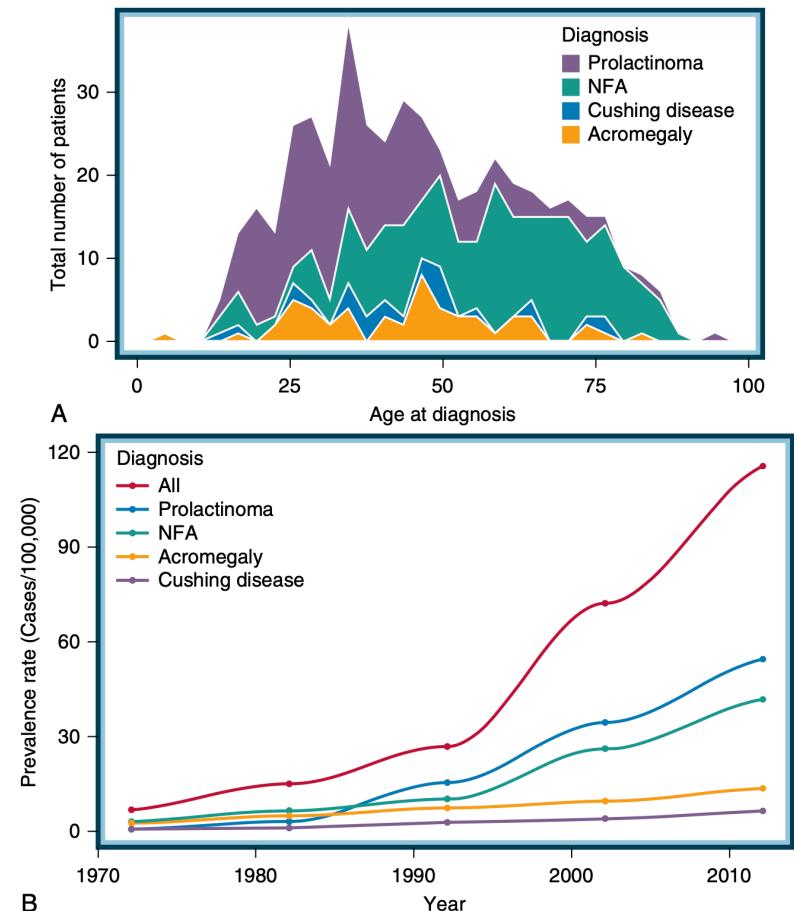


Fig. 7.2 Invasive pituitary adenomas. (A) Sagittal view of a large pituitary adenoma (left) and schematic illustration (right) of a lesion extending into the sphenoid sinus cavity down to the floor of nasal cavities. (B) Coronal view (left) and schematic illustration (right) of a lesion extending upward with eccentric sprout into the paraventricular space, encroaching the internal and middle carotid arteries, and their branches, and compressing perforating vessels of basal ganglia and internal capsule. (C) Coronal view (left) of bilobed homogeneous hypoenhancing adenoma with invasion of the cavernous sinus and suprasellar cistern; on sagittal view (right), inferior extension into the sphenoid sinus anteriorly and retroclival region via the petrosal/basilar plexus posteriorly (arrowhead) is seen. (D) Left, T1-weighted axial image at the level of the inferior pons demonstrates extension of the mass to the right inferior petrosal sinus (white arrowhead). Further extension on the right to the pars nervosa of the jugular foramen is seen (black arrowhead). Right, more inferiorly at the level of the upper medulla, mass extension to the right hypoglossal canal is seen (white arrowhead), within the hypoglossal plexus. The pars vascularis of the jugular foramen, seen more posteriorly, is patent (black arrowhead). (A–B, schematic illustrations from Cappabianca P, et al. Size does not matter. The intrigue of giant adenomas: a true surgical challenge. *Acta Neurochir [Wien]*. 2014;156:2217–2220. C–D, from Kuo AH, et al. Giant pituitary adenoma with inferior petrosal sinus, jugular foramen, and hypoglossal canal extension. *JAMA Otolaryngol Head Neck Surg*. 2020;146:82–84.)

盛行率

- Prolactinoma 最多
→ non-functional
→ Acromegaly
→ Cushing disease



• **Fig. 7.22** Epidemiology of pituitary adenomas. (A) Number of patients with a prolactinoma, acromegaly, Cushing disease, or a nonfunctional pituitary adenoma (NFA) by age at diagnosis. (B) Increasing prevalence of clinically significant pituitary adenomas between 1972 and 2012 showing a clear rise since around 1990, mainly explained by the increased prevalence of prolactinomas and nonfunctional adenomas. (Redrawn from Melmed S, Kaiser UB, Lopes MB, et al. Clinical biology of the pituitary adenoma. *Endocr Rev*. 2022;43:1003–1037. Copyright Giovanna Santoni, CMI. Used by permission.)

Imaging studies

- 磁振造影 (MRI)：是評估腦下垂體及周圍結構的首選
 - 注射顯影劑 (Gadolinium) 前後的矢狀面和冠狀面 T1 加權影像。
 - 正常影像：腦下垂體高度兒童約 6mm，成人約 8mm；懷孕期和青春期可達 10-12mm。
 - 腺瘤影像：T1 加權像上通常呈低信號，T2 加權像上呈高信號。顯影劑注射後強化程度通常低於周圍正常組織。

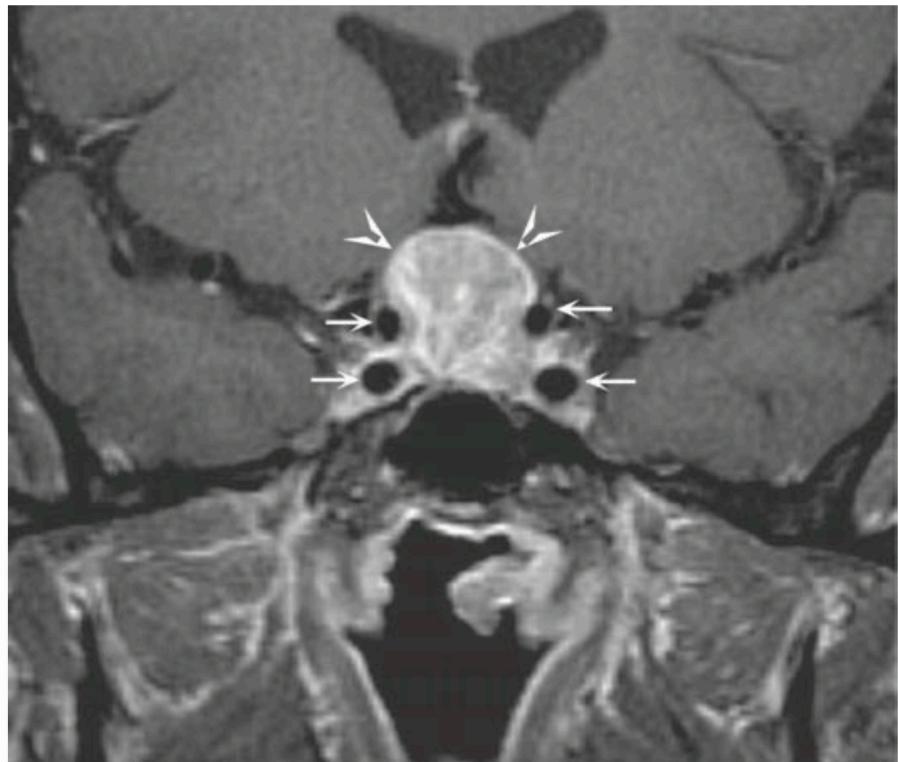


FIGURE 380-2 Pituitary adenoma. Coronal T1-weighted postcontrast magnetic resonance image shows a homogeneously enhancing mass (arrowheads) in the sella turcica and suprasellar region compatible with a pituitary adenoma; the small arrows outline the carotid arteries.

Laboratory Investigation

- 目的：確定腫瘤性質（功能性 vs. 無功能性）、評估是否存在荷爾蒙過量或缺乏。
- 依臨床表現選擇：若有典型荷爾蒙過量症候群（如肢端肥大症、庫欣氏病、泌乳素瘤），應針對性檢查。
- 若 MRI 懷疑腺瘤但無明顯症狀，建議初步篩檢包括：
 - 泌乳素 (PRL)
 - 類胰島素生長因子-1 (IGF-1)
 - 24小時尿游離皮質醇 (UFC) 及/或 Overnight 1mg Dexamethasone 抑制試驗
 - FSH、LH
 - 甲狀腺功能 (TSH, Free T4)
- 評估腦下垂體功能低下：在進一步檢查或手術前，通常需評估是否存在需要補充的荷爾蒙缺乏

TABLE 380-2 Screening Tests for Functional Pituitary Adenomas

	TEST	COMMENTS
Acromegaly	Serum IGF-1 Oral glucose tolerance test with GH obtained at 0, 30, and 60 min	Interpret IGF-1 relative to age- and sex-matched controls Normal subjects should suppress growth hormone to <1 µg/L
Prolactinoma	Serum PRL	Exclude medications MRI of the sella should be ordered if PRL is elevated
Cushing's disease	24-h urinary free cortisol Dexamethasone (1 mg) at 11 P.M. and fasting plasma cortisol measured at 8 A.M. Late night salivary cortisol ACTH assay	Ensure urine collection is total and accurate Normal subjects suppress to <5 µg/dL Distinguishes adrenal adenoma (ACTH suppressed) from ectopic ACTH or Cushing's disease (ACTH normal or elevated)
Gonadotropinoma	Baseline FSH, LH, free α subunit, ovarian hyperstimulation, estrogen (females), testosterone (males) TRH stimulation test with assays for LH, FSH, free α subunit, free LHβ, free FSHβ subunits	Rare; more commonly nonfunctioning adenomas Consider screening for hypopituitarism Some gonadotropinomas exhibit an inappropriate gonadotropin response to TRH
TSH-producing adenoma	Free T ₄ , free T ₃ , TSH, free α subunit	Key feature is an inappropriately normal or high TSH in the setting of elevated free T ₄ and T ₃

Abbreviations: ACTH, adrenocorticotropin hormone; FSH, follicle-stimulating hormone; GH, growth hormone; IGF-I, insulin-like growth factor I; LH, luteinizing hormone; MRI, magnetic resonance imaging; PRL, prolactin; TSH, thyroid-stimulating hormone.

TABLE 380-3 Classification of Pituitary Adenomas^a

ADENOMA CELL ORIGIN	HORMONE PRODUCT	CLINICAL SYNDROME
Lactotrope	PRL	Hypogonadism, galactorrhea
Gonadotrope	FSH, LH, subunits	Silent, ovarian hyperstimulation, hypogonadism
Somatotrope	GH	Acromegaly/gigantism
Corticotrope	ACTH/none	Cushing's disease or silent
Mixed growth hormone and prolactin cell	GH, PRL	Acromegaly, hypogonadism, galactorrhea
Other plurihormonal cell	Any	Mixed
Acidophil stem cell	PRL, GH	Hypogonadism, galactorrhea, acromegaly
Mammosomatotrope	PRL, GH	Hypogonadism, galactorrhea, acromegaly
Thyrotrope	TSH	Thyrotoxicosis
Null cell	None	Hypopituitarism/none
Oncocytoma	None	Hypopituitarism/none

^aHormone-secreting tumors are listed in decreasing order of frequency. All tumors may cause local pressure effects, including visual disturbances, cranial nerve palsy, and headache.

Note: For abbreviations, see text.

Source: Adapted with permission from S Melmed: Pathogenesis of pituitary tumors. Nat Rev Endocrinol 7:257, 2011.

TABLE 7.2**Laboratory Testing for Diagnosis of Hormone-Secreting Pituitary Adenomas**

	Test	Results Requiring Further Evaluation
Prolactinoma	Serum PRL measurement	PRL level elevated
Acromegaly	Serum IGF1 level OGTT (75 g glucose) with GH measured at 0, 30, and 60 min	Age-adjusted IGF1 level elevated GH >0.4 µg/L with use of an ultrasensitive assay
Cushing disease	24-h UFC measurement Midnight salivary cortisol measurement Plasma cortisol measurement at 08:00 after dexamethasone (1 mg) at 21:00 Serum ACTH measurement	Elevated UFC on at least two tests Elevated free salivary cortisol level Failure to suppress cortisol level to <1.8 µg/dL Low ACTH level suggests adrenal adenoma; very high level may indicate ectopic ACTH source
Thyrotrophin-secreting tumor	Serum TSH measurement Free T ₄ measurement	Normal or increased T ₄ level with measurable TSH may suggest TSH-secreting tumor

ACTH, adrenocorticotrophic hormone; GH, growth hormone; IGF1, insulin-like growth factor type 1; OGTT, oral glucose tolerance test; PRL, prolactin; T₄, thyroxine; TSH, thyroid-stimulating hormone; UFC, urinary free cortisol.

From Melmed S. Pituitary-tumor endocrinopathies. *N Engl J Med*. 2020;382:937–950.

治療 (Treatment) 原則

- 目標：使過多的荷爾蒙分泌正常化、改善荷爾蒙過多導致的症狀、縮小或切除腫塊以緩解壓迫症狀、保留剩餘垂體功能、預防復發。
- 方法：經蝶竇手術、放射治療、藥物治療。需根據腫瘤性質、大小、位置、患者年齡、專家經驗等選擇最佳方案。
- 藥物治療 (Medical Therapy)：
 - 泌乳素瘤：多巴胺激動劑，**藥物治療是首選**
 - 肢端肥大症：生長抑素受體配體 (SRLs)、GH 受體拮抗劑
 - TSH 分泌性腫瘤：SRLs，偶用多巴胺激動劑
 - 庫欣氏病：SRLs (Pasireotide)、腎上腺皮質類固醇生成抑制劑
 - 非功能性腫瘤：通常對藥物無反應，需手術和/或放療

經蝶竇手術 (Transsphenoidal Surgery)

- 多數垂體腫瘤的首選手術方式
- 適應症：具壓迫效應的腫塊、荷爾蒙過度分泌
- 目標：盡可能選擇性切除腫瘤，保護正常垂體組織
- 效果：可逆轉術前的壓迫效應（如視野缺損）和部分垂體功能低下
- 併發症：取決於腫瘤大小、侵襲性及外科醫生經驗。死亡率約 1%。
 - 常見併發症（發生率可達 10-20%）：暫時性尿崩症、垂體功能低下。
 - 較少見 (<10%)：永久性尿崩症、顱神經損傷、鼻中隔穿孔、視力障礙、腦脊液漏 (4%)。
 - 罕見：頸動脈損傷、失明、下視丘損傷、腦膜炎。微腺瘤手術併發症罕見。

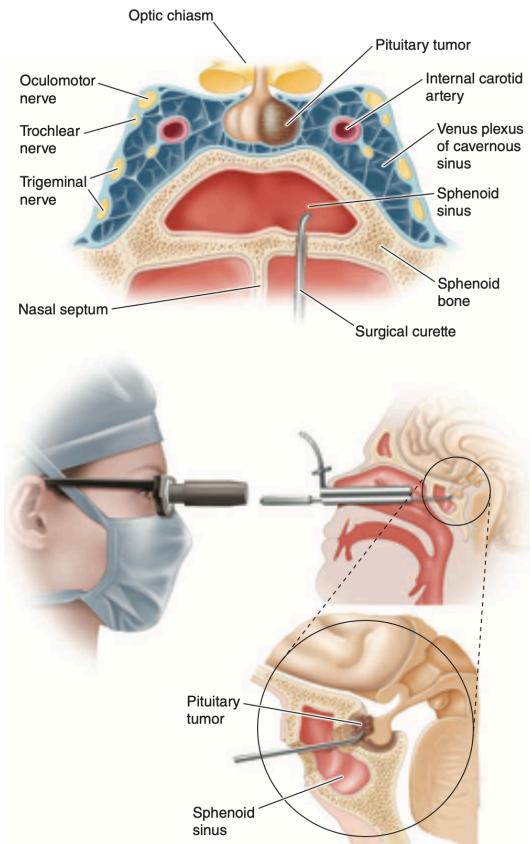


FIGURE 380-3 Transsphenoidal resection of pituitary mass via the endonasal approach.

放射治療 (Radiation)

- 用途：原發治療或更常見的術後輔助治療（治療殘留腫瘤、預防復發/再生長）。對無法手術切除的非功能性腫瘤殘留是主要治療手段之一。
- 技術：聚焦式高能量直線加速器（需精確固定頭部）、立體定向放射手術（伽瑪刀、直線加速器、迴旋加速器，單次大劑量）、質子刀。
- 缺點：起效慢 (5-15 年達最大效果)，常需輔助藥物治療；高發生率的遲發性垂體功能低下 (10 年內 >50%，多因下視丘損傷)。
- 副作用：短期（噁心、無力、脫髮、味覺/嗅覺喪失）；遲發性（垂體功能低下、視神經損傷 [約 2%]、顱神經損傷 [罕見]、繼發性腫瘤風險增加 [傳統放療 10 年 1.3%，20 年 1.9%]、腦血管疾病風險增加）。立體定向放療風險較低

Other Sellar masses

- Craniopharyngiomas
- Rathke's cysts
- Sella chordomas
- Meningiomas
- Histiocytosis
- Pituitary metastases
- Hypothalamic hamartomas and gangliocytomas
- Hypothalamic gliomas and optic gliomas
- Brain germ cell tumor

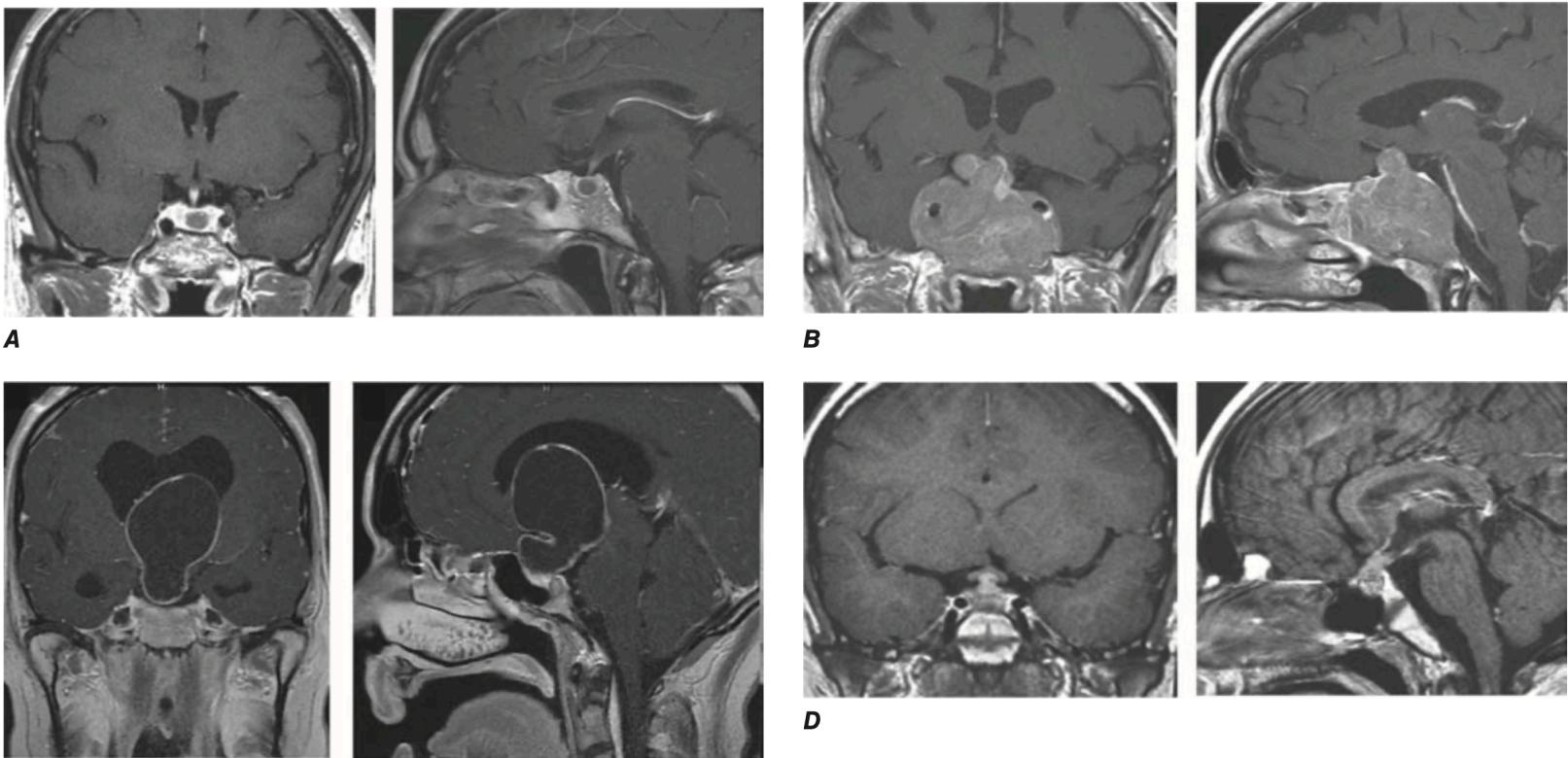
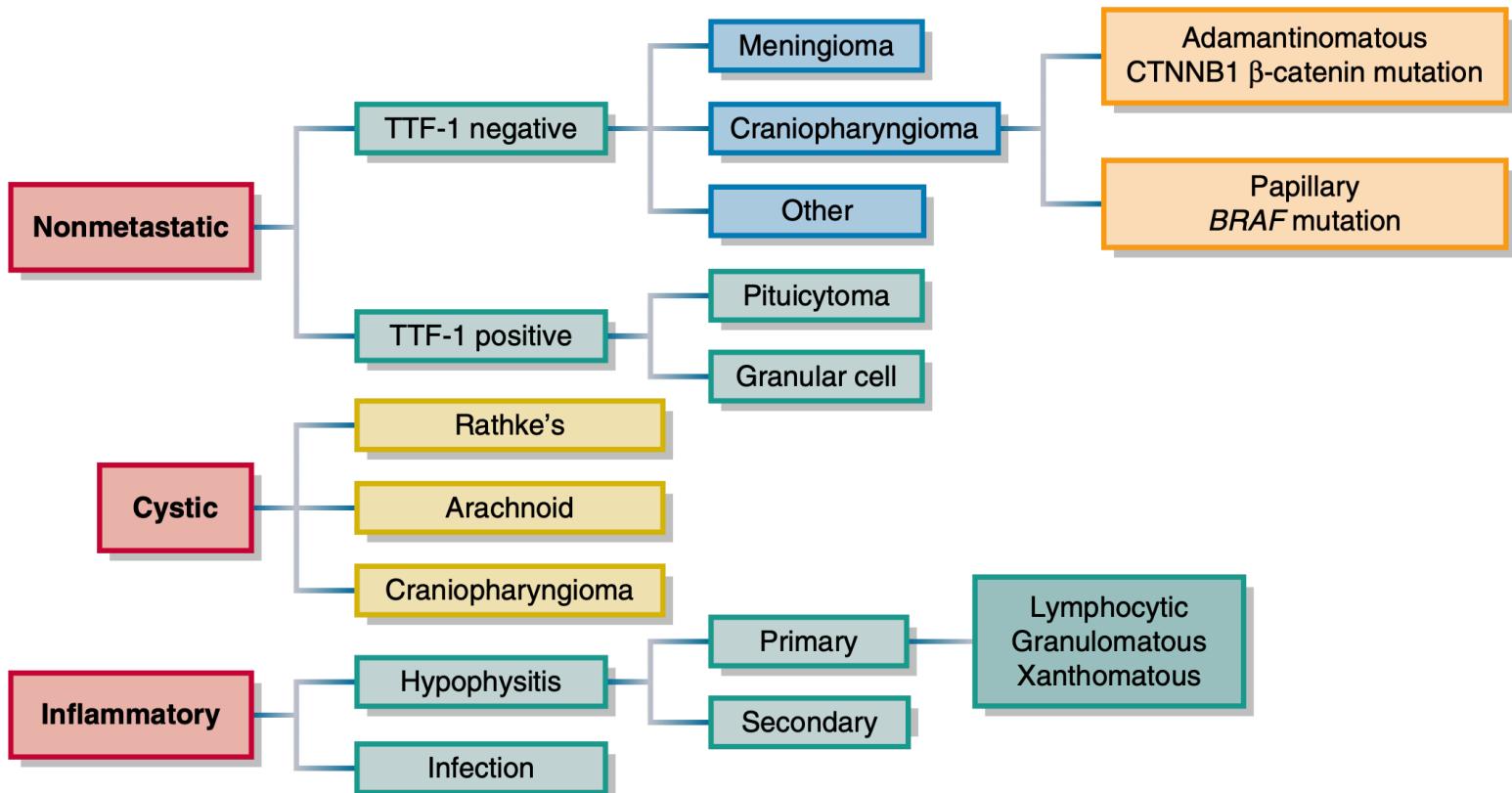
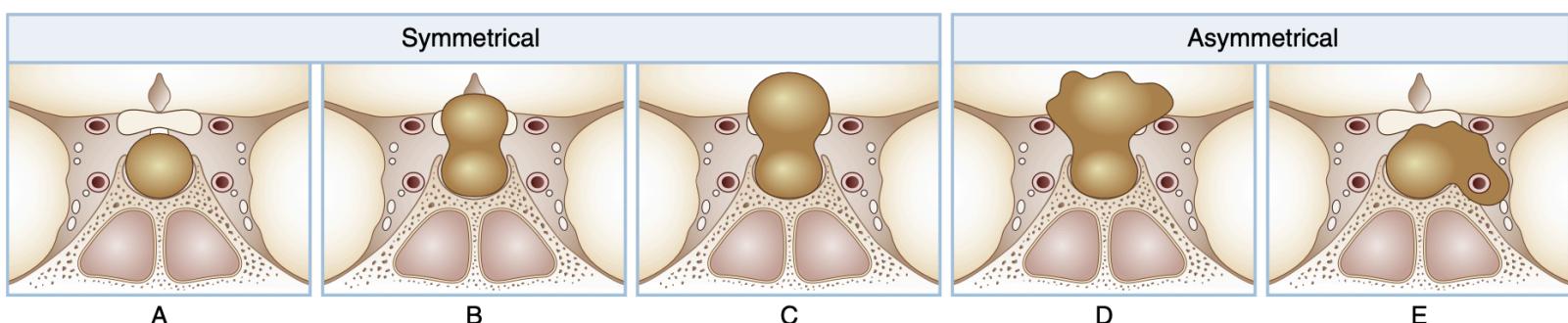
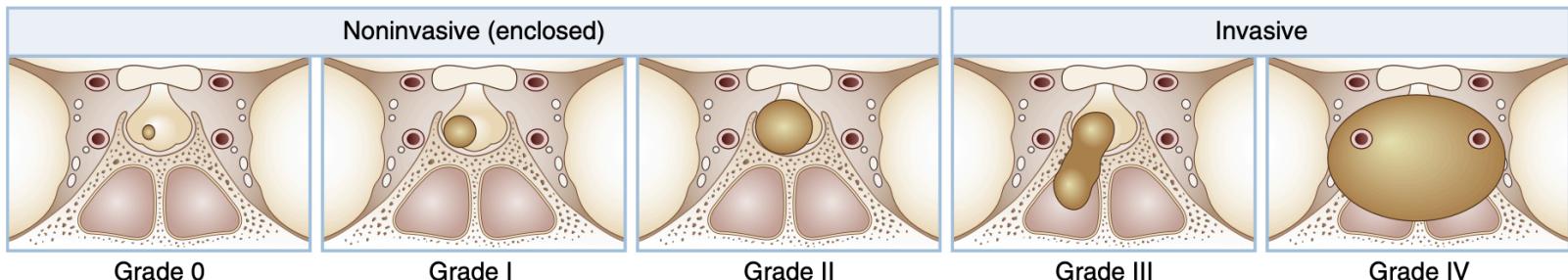


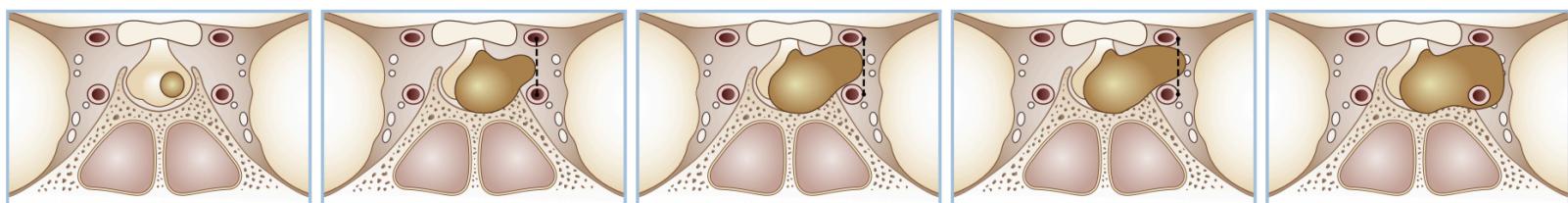
FIGURE 380-4 Imaging differential diagnosis of sellar masses. **A.** Microadenoma. **B.** Macroadenoma. **C.** Craniopharyngioma. **D.** Hypophysitis with stalk thickening. (C: Reproduced with permission from Muller HL: Childhood craniopharyngioma. Recent advances in diagnosis, treatment and follow-up. *Horm Res* 69:193, 2008. A, B, D: Used with permission from Vivien Bonert, MD.)



• **Fig. 7.12** Differential diagnosis of nonadenomatous sellar masses. (Adapted from Syro LV, Rotondo F, Moshkin O, Kovacs K. Nonpituitary sellar masses. In: Melmed S, ed. *The Pituitary*. 5th ed. Elsevier; 2022.)



HARDY CLASSIFICATION SYSTEM



B

KNOSP CLASSIFICATION SYSTEM

Prolactinoma

Etiology and Prevalence

- Prolactin: Normal range: M<15, F<20 µg/L
- Prolactinomas are the most frequently encountered secretory pituitary tumors
- incidence of approximately 30 per 100,000 population
- The female:male ratio for microprolactinomas is 20:1; macroprolactinomas is 1:1
- Macroprolactinomas have a greater propensity to grow and tumor size correlates with serum PRL levels
- PRL level higher than 200 ng/mL is strongly indicative of a PRL- secreting pituitary tumor
 - < 100 µg/L → microadenomas
 - > 200 µg/L → macroadenomas
- MRI should be performed in all patients with hyperprolactinemia

TABLE 380-5 Etiology of Hyperprolactinemia**I. Physiologic hypersecretion**

- Pregnancy
- Lactation
- Chest wall stimulation
- Sleep
- Stress

II. Hypothalamic-pituitary stalk damage

- Tumors
 - Craniopharyngioma
 - Suprasellar pituitary mass
 - Meningioma
 - Dysgerminoma
 - Metastases
- Empty sella
- Lymphocytic hypophysitis
- Adenoma with stalk compression
- Granulomas
- Rathke's cyst
- Irradiation
- Trauma
 - Pituitary stalk section
 - Suprasellar surgery

III. Pituitary hypersecretion

- Prolactinoma
- Acromegaly

IV. Systemic disorders

- Chronic renal failure
- Hypothyroidism
- Cirrhosis
- Pseudocyesis
- Epileptic seizures

V. Drug-induced hypersecretion

- Dopamine receptor blockers
 - Atypical antipsychotics: risperidone
 - Phenothiazines: chlorpromazine, perphenazine
 - Butyrophenones: haloperidol
 - Thioxanthenes
 - Metoclopramide
- Dopamine synthesis inhibitors
 - α -Methyldopa
- Catecholamine depletors
 - Reserpine
- Opiates
- H_2 antagonists
 - Cimetidine, ranitidine
- Imipramines
 - Amitriptyline, amoxapine
- Serotonin reuptake inhibitors
 - Fluoxetine
- Calcium channel blockers
 - Verapamil
- Estrogens
- Thyrotropin-releasing hormone

臨床表現 Clinical Presentation

- 女性：
 - 月經失調amenorrhea(無月經/稀少)、乳漏galactorrhea、不孕infertility 是典型的traid。
 - 約80% 高泌乳血症的女性會有乳漏的症狀
 - 長期低雌激素可致骨密度下降。
 - 其他症狀：性慾減退、體重增加、輕度多毛。
- 男性：
 - 性慾減退、不孕、陽痿是常見主訴，常伴有因腫瘤壓迫引起的視力喪失或頭痛。
 - 乳漏罕見。
 - 長期低睽固酮可導致骨質疏鬆、肌肉減少、鬍鬚生長減少。
 - 男性腫瘤常常較大才被發現。

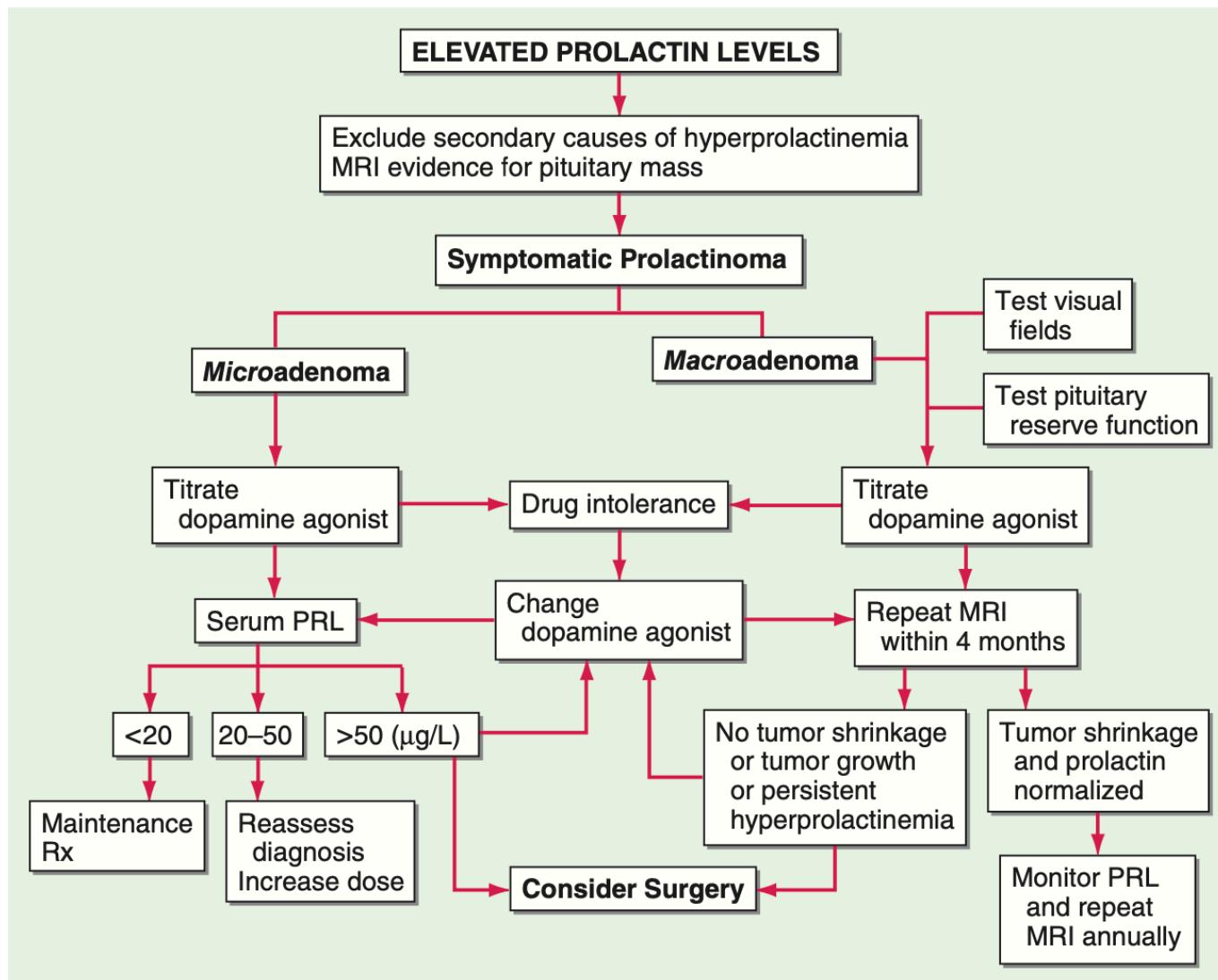
TABLE 9.16 Signs and Symptoms of Prolactinomas

Associated With Tumor Mass	Associated With Hyperprolactinemia
Visual field abnormalities	Amenorrhea, oligomenorrhea, infertility
Blurred vision or decreased visual acuity	Decreased libido, impotence, pre-mature ejaculation, oligospermia
Symptoms of hypopituitarism	Galactorrhea
Headaches	Osteoporosis
Cranial nerve palsies	
Pituitary apoplexy	
Seizures (temporal lobe)	
Hydrocephalus (rare)	
Unilateral exophthalmos (rare)	

診斷 Diagnosis

- 血清 Prolactin 測定：基礎、空腹、早晨檢測。
- 排除其他原因：詳細用藥史(例如精神科用藥)、評估腎功能、甲狀腺功能 (TSH, FT4)。
- MRI：所有高泌乳素血症患者均應進行腦下垂體 MRI，以確定是否存在腫瘤或其他蝶鞍病變。
- 鑑別診斷：
 - PRL > 200-250 µg/L 強暗示示泌乳素瘤。
 - PRL < 100 µg/L 可能是微腺瘤、柄壓迫或其他原因。
 - PRL < 50 µg/L 可能是生理因素或藥物引起。

Management of prolactinoma



Medical treatment

- 治療目標：使Prolactin正常化，恢復性腺功能，改善乳漏，保護骨密度，縮小腫瘤（若是泌乳素瘤）。
- Oral dopamine agonists：對幾乎所有原因引起的高泌乳素血症均有效。是泌乳素瘤(不論Macro or micro)的首選和主要治療方法
 - 藥物：Cabergoline (長效，D2 親和力高，耐受性好，每週1-2 次) 是首選；Bromocriptine (短效，需每日多次，適用於備孕期)。
- 療效：抑制 PRL 分泌和合成，抑制細胞增生。多數 microadenoma和約 70% macroadenoma可使 PRL 正常化並縮小腫瘤。壓迫症狀常在用藥數日內改善。部分患者長期治療後可嘗試停藥 (約 20% 微腺瘤可緩解)。約20%患者可能耐藥
- Side Effects of dopamine agonists:
 - 常見：便秘、鼻塞、口乾、失眠、眩暈、噁心、嘔吐、姿勢性低血壓。
 - 罕見：精神症狀、胸膜纖維化等。

Cabergoline

1. A long-acting dopamine agonist (0.5 to 1.0 mg twice weekly).
2. Normalizes PRL and resumption of normal gonadal function in 80% of microadenomas; normalizes PRL and shrinks 70% of macroadenomas.
3. Mass effect symptoms usually improve within days after cabergoline initiation; improvement of sexual function requires several weeks of treatment .

Bromocriptine mesylate

1. A short-acting dopamine agonist, preferred when pregnancy is desired.
2. Initiated by administering a low bromocriptine dose (0.625–1.25 mg) at bedtime with a snack, followed by gradually increasing the dose. Most patients are controlled with a daily dose of 7.5 mg (2.5 mg tid)

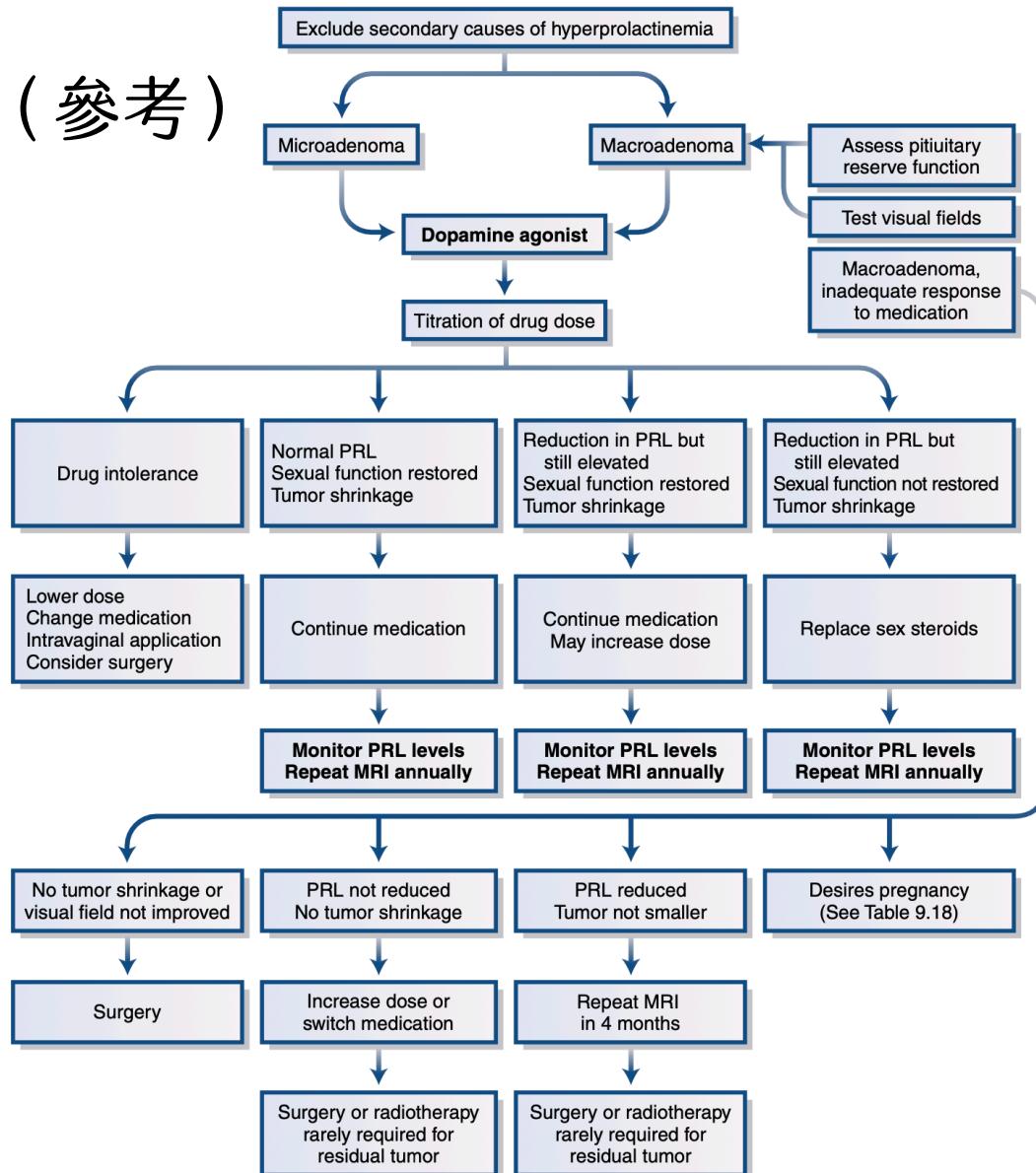
手術 Surgery

- 僅用於對dopamine resistance or intolerance，或出現急性視力障礙且藥物無效的侵襲性Macroadenoma
- Microadenoma 術後初期緩解率約 70%，
Macroadenoma約 30%。
- 術後復發率高：Microadenoma 1 年 20%，
Macroadenoma 長期復發率 >50%

放療 Radiation Therapy

- 保留給對藥物和手術均無效的侵襲性腫瘤。
- Linear accelerator radiotherapy 可以用來降低或控制腫瘤的大小。
- 高劑量可能會引起其他併發症

另一個流程圖（參考）



• Fig. 9.26 Prolactinoma management. After secondary causes of hyperprolactinemia have been excluded, subsequent management decisions are based on clinical imaging and biochemical criteria. *MRI*, magnetic resonance imaging; *PRL*, prolactin.

特殊情況 - 妊娠

- 計劃懷孕前應盡量使 PRL 正常化。
 - 若需藥物促孕，優先選 Bromocriptine (超過30年的使用經驗，短效)，確認懷孕後停藥，降低嬰兒曝露。
 - 不推薦 Cabergoline (長效) 用於備孕。
- 懷孕期間通常建議停用多巴胺促效劑（尤其在 microadenoma患者）。
- 懷孕期腦下垂體增大，腺瘤有生長風險
 - Microadenoma 5%，Macroadenoma 15-30%
 - 需密切監測視野。若出現顯著增大伴壓迫症狀，可考慮恢復使用 Bromocriptine (懷孕安全性資料較多) 或手術。

Management of patients planning pregnancies

Microadenoma	Macroadenoma
Discontinue dopamine agonist when pregnancy test is positive	Consider surgery before pregnancy Ensure bromocriptine sensitivity before pregnancy
Periodic visual field examinations during pregnancy	Monitor visual fields expectantly and frequently
Postpartum magnetic resonance imaging (MRI) after 6 weeks ^a	Administer bromocriptine if vision becomes compromised Or continue bromocriptine throughout pregnancy if tumor previously affected vision Consider high-dose steroids or surgery during pregnancy if vision is threatened or adenoma hemorrhage occurs Postpartum MRI after 6 weeks

^aPituitary MRI may be performed during pregnancy if deemed necessary.

Acromegaly

Acromegaly and Gigantism

- 肢端肥大症 (Acromegaly)：是一種慢性進行性疾病，主要由於成人期（骨骼生長板閉合後）腦下垂體 生長激素 (Growth Hormone, GH) 分泌過多，導致骨骼（尤其是肢體末端和面部）、軟組織及內臟器官異常增生和代謝紊亂。
- 巨人症 (Gigantism)：若 GH 過度分泌發生在兒童或青少年期（骨骼生長板閉合前），則會導致線性生長過度，身材異常高大，稱為巨人症。

Etiology

- 純多數 (98%) 由分泌 GH 的腦下垂體腺瘤引起（生長激素細胞瘤；或混合分泌 GH/PRL 的腫瘤）。
- 罕見原因 (<1%)：異位垂體組織 GH 瘤；異位 GH 分泌（胰臟、卵巢、肺腫瘤）；過量 GHRH 分泌（下視丘腫瘤如錯構瘤；或周邊腫瘤如支氣管/胰臟類癌瘤），後者引起垂體增生。

Etiology

TABLE 380-6 Causes of Acromegaly

	PREVALENCE, %
Excess Growth Hormone Secretion	
Pituitary	98
Densely or sparsely granulated GH cell adenoma	60
Mixed GH cell and PRL cell adenoma	25
Mammosomatotrope cell adenoma	10
Plurihormonal adenoma	
GH cell carcinoma or metastases	
Multiple endocrine neoplasia 1 (GH cell adenoma)	
McCune-Albright syndrome	
Ectopic sphenoid or parapharyngeal sinus pituitary adenoma	
Extrapituitary tumor	<1
Pancreatic islet cell tumor	
Lymphoma	
Excess Growth Hormone-Releasing Hormone Secretion	
Central	<1
Hypothalamic hamartoma, choristoma, ganglioneuroma	
Peripheral	<1
Bronchial carcinoid, pancreatic islet cell tumor, small-cell lung cancer, adrenal adenoma, medullary thyroid carcinoma, pheochromocytoma	

Abbreviations: GH, growth hormone; PRL, prolactin.

Source: Data from S Melmed: Medical progress: Acromegaly. N Engl J Med 355:2558, 2006.

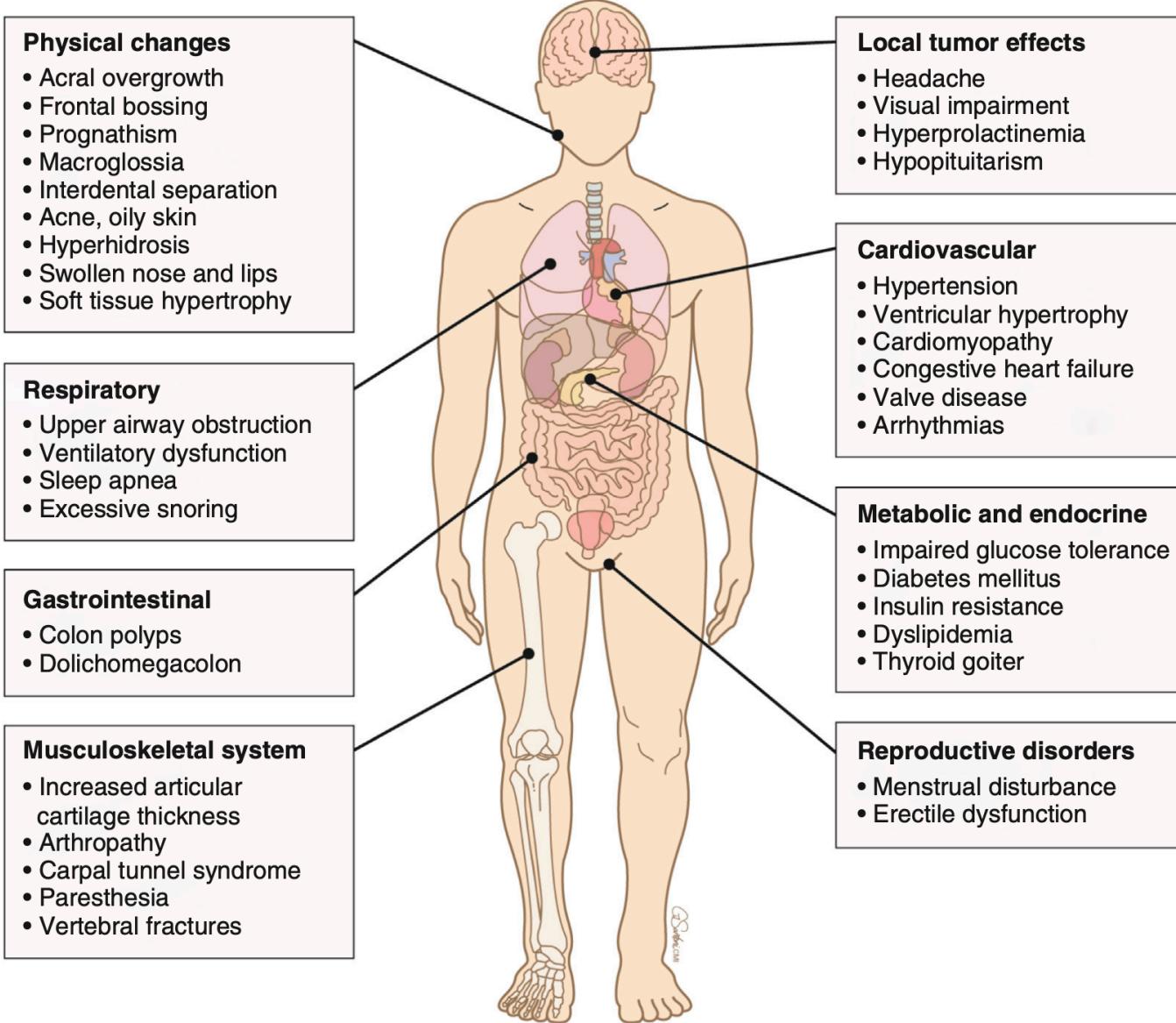
盛行率 (Prevalence)

- 不同地區和研究的報導有所差異，估計範圍約為每百萬人口 28 至 137 例。
- 年發生率 (Annual Incidence)：近年來的調查數據顯示，年發生率有所上升，估計約為每百萬人口 3 至 11 例。發生率的增加可能部分歸因於診斷意識的提高和檢測技術的進步。
- 美國數據：估計美國每年約有超過 3000 例新診斷的肢端肥大症病例，總患病人數約 25,000 人。

Cause	Prevalence (%)	Hormonal Products	Clinical Features	Pathologic Characteristics
Excess GH Secretion				
Pituitary	98			
Densely granulated GH cell adenoma	30	GH	Slow growing, clinically insidious	Resemble normal somatotrophs, numerous large secretory granules
Sparingly granulated adenoma	30	GH	Rapidly growing, often invasive	Cellular pleomorphism, characteristic ultrastructure
Mixed GH cell and PRL cell adenoma	25	GH and PRL	Variable	Densely granulated somatotrophs, sparsely granulated lactotrophs
Mammosomatotroph cell adenoma	10	GH and PRL	Common in children; gigantism, mild hyperprolactinemia	Both GH and PRL in same cell, often same secretory granule
Acidophil stem cell adenoma		PRL and GH	Rapidly growing, invasive, hyperprolactinemia dominant	Distinctive ultrastructure, giant mitochondria
Plurihormonal adenoma		GH (PRL with α GSU, FSH/LH, TSH, or ACTH)	Often secondary hormonal products are clinically silent	Variable; either monomorphic or plurimorphous
GH cell carcinoma or metastases		GH	Usually aggressive	Documented metastasis
MEN1 (adenoma)		GH or PRL	Pancreatic, parathyroid, or pituitary tumors	Adenoma
McCune-Albright syndrome		GH, PRL	Classic triad	Hyperplasia
Ectopic sphenoid or parapharyngeal sinus pituitary adenoma		GH	Ectopic mass	Adenoma
Familial acromegaly		GH	Young patients	Large adenomas
Carney syndrome		GH	Classic syndrome	Adenoma
Extrapatuitary Tumor				
Pancreatic islet cell tumor	<1			Small pituitary
Excess GHRH Secretion				
Central—hypothalamic hamartoma, choristoma, ganglion-neuroma	<1		Hypothalamic mass	Somatotroph hyperplasia
Peripheral—bronchial carcinoid, pancreatic islet cell tumor, small cell lung cancer, adrenal adenoma, medullary thyroid carcinoma, pheochromocytoma	1	GH, PRL	Systemic features	Somatotroph hyperplasia, rarely adenoma
ACTH, Adrenocorticotrophic hormone; FSH, follicle-stimulating hormone; GH, growth hormone; GHRH, growth hormone-releasing hormone; α GSU, glycoprotein α -subunit; LH, luteinizing hormone; MEN1, multiple endocrine neoplasia type 1; PRL, prolactin; TSH, thyroid-stimulating hormone.				
Adapted from Melmed S. Medical progress: Acromegaly. <i>N Engl J Med</i> . 2006;355:2558–2573; Melmed S, Braunstein GD, Horvath E, et al. Pathophysiology of acromegaly. <i>Endocr Rev</i> . 1983;4:271–290.				

臨床表現

- 起病隱匿，診斷常延遲 10 年以上 。
- 骨骼改變：肢端（手、足）增大、顱骨（額骨隆起、下頷前突、牙縫增寬）、脊柱後凸。兒童期發病導致巨人症 。
- 軟組織改變：面容粗糙、鼻大唇厚、舌體增大、皮膚增厚（油膩、多汗、皮贅）、聲音低沉、腕隧道症候群 。
- 系統性影響：
 - 心血管：最重要！心肌病、心律不整、左室肥厚、舒張功能下降、高血壓 。
 - 呼吸：睡眠呼吸中止症 ($>60\%$)，因軟組織阻塞和中樞因素 。
 - 代謝：糖尿病 (25%) 或糖耐量異常 (GH 拮抗胰島素) 。
 - 腫瘤：結腸息肉風險增加 (1/3)，**結腸癌**死亡率增加 。
 - 其他：關節病、近端肌無力、疲勞、內臟腫大 。
- 預後：未控制者死亡率增高約三倍，平均壽命縮短 10 年，主因心腦血管及呼吸系統疾病 。



• **Fig. 7.38** Clinical features of acromegaly. (From Melmed S, Kaiser UB, Lopes MB, et al. Clinical biology of the pituitary adenoma. *Endocr Rev*. 2022;43:1003–1037. Copyright Giovanna Santoni, CMI. Used by permission.)

• **BOX 7.4**

Clinical Features of Acromegaly^a

Local Tumor Effects

Pituitary enlargement
Visual field defects
Cranial nerve palsy
Headache

Somatic Effects

Acral Enlargement

Thickening of soft tissues in hands and feet

Musculoskeletal

Gigantism
Prognathism
Jaw malocclusion
Arthralgias and arthritis
Carpal tunnel syndrome
Acroparesthesia
Proximal myopathy
Hypertrophy of frontal bones

Skin

Hyperhidrosis
Oily
Skin tags

Colon

Polyps

Cardiovascular

Left ventricular hypertrophy
Asymmetric septal hypertrophy
Cardiomyopathy
Hypertension
Congestive heart failure

Pulmonary

Sleep disturbances
Sleep apnea—central and obstructive
Narcolepsy

Visceromegaly

Tongue
Thyroid
Salivary gland
Liver
Spleen
Kidney
Prostate

Endocrine-Metabolic Effects

Reproductive

Menstrual abnormalities
Galactorrhea
Decreased libido, impotence, low sex hormone–binding globulin

Multiple Endocrine Neoplasia Type 1 (MEN1)

Hyperparathyroidism
Pancreatic islet cell tumors

Carbohydrates

Impaired glucose tolerance
Insulin resistance and hyperinsulinemia
Diabetes mellitus

Lipids

Hypertriglyceridemia

Minerals

Hypercalciuria, increased 1,25-hydroxyvitamin D3
Urinary hydroxyproline

Electrolytes

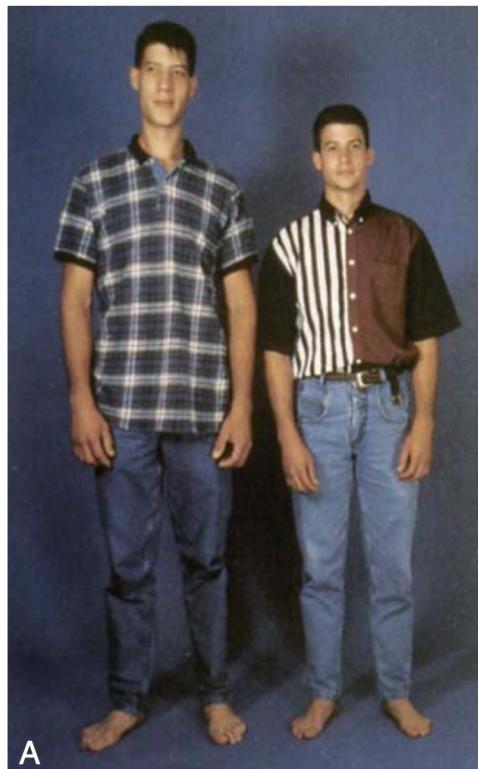
Low renin
Increased aldosterone

Thyroid

Low thyroxine-binding globulin
Goiter

^aMost soft tissue and metabolic changes are reversible by tight hormonal control. Bony changes, hypertension, and central sleep apnea are generally not reversible.

Modified from Bonert V, Melmed S. Acromegaly. In: Bar S, ed. Contemporary Endocrinology. Humana Press; 2002:201–228.



Acromegaly

- More than 95% acromegaly harbor a GH-secreting pituitary adenoma
- Mixed GH-cell and PRL-cell adenomas are composed of distinct somatotrophs expressing GH and lactotrophs expressing PRL.
- Screening colonoscopy for colon cancer should be performed at diagnosis
- The most significant mortality determinants are GH levels and the presence of coexisting cardiac disease.
- Control of GH levels to less than 2.5 µg/L significantly reduces morbidity and mortality

診斷 (Diagnosis)

- 篩檢：血清 IGF-1 濃度（需根據年齡和性別判讀）。IGF-1 升高提示 GH 過量，是最佳篩檢指標。
- 確診：口服葡萄糖耐量試驗 (Oral Glucose Tolerance Test, OGTT)。口服 75g 葡萄糖後，在 2 小時內多次檢測 GH 的濃度。
 - 正常人 GH 的濃度 會被高血糖抑制到很低；肢端肥大症患者 GH 無法被充分抑制（通常以 GH 最低值 $< 1 \text{ ng/mL}$ 或更低 $< 0.4 \text{ ng/mL}$ 作為抑制標準）。
- 隨機 GH 無用：因其脈衝式分泌。
- 影像學：腦下垂體 MRI，尋找腺瘤。若 MRI 陰性但生化證據確鑿，需考慮異位 GHRH 或 GH 分泌，可測量血漿 GHRH 濃度。
- 併發症評估：血糖/糖化血色素、血壓、心臟評估（心電圖、心臟超音波）、睡眠呼吸監測、大腸鏡檢查

Oral Glucose Tolerance Test (OGTT)

For the diagnosis of acromegaly

Blood sampling: GH at 0 min, 30 min, 60 min, 90 min, 120min

- Normal response: GH nadir < 1 ng/mL, usually at 60 min
- Acromegaly:
 - GH nadir > 1 ng/mL (lower cut-off in newer more sensitive assays); 1/3 increase, 1/3 remain unchanged, 1/3 fall modestly (but not < 1 ng/mL)
- False positive: starvation, protein-caloric malnutrition, anorexia nervosa

治療 Management

- 治療目標：生化學緩解（GH $\backslash < 1 \text{ ng/mL}$ 且 IGF-1 正常化）、控制腫瘤體積、緩解症狀和壓迫效應、治療合併症、降低死亡率、保留正常垂體功能。
- 手術治療 - 經蝶竇手術 (TSS)：對於大多數可切除的腺瘤（尤其微腺瘤和非侵襲性大腺瘤）是首選的一線治療。目標是完全切除腫瘤達到生化學治癒。
 - 微腺瘤緩解率約 70%，大腺瘤 $< 50\%$ 。
 - 術後 GH 快速下降，IGF-1 需 3-4 天恢復正常 。
 - 術後可能復發 (10%) 或出現垂體功能低下 (15%)
- 放射治療：作為輔助治療，起效慢 (5-15 年)，常需藥物過渡，遲發性垂體功能低下常見。IGF-1 正常化效果相對差 。

藥物治療 (Medical Management)

- Somatostatin Receptor Ligands, SRLs:
 - 機制：GH 分泌腺瘤細胞表面主要表達 SST2 和 SST5 受體亞型。SRLs 模擬內源性體抑素作用，優先結合這些受體，從而抑制 GH 分泌。
 - Octreotide (長效微球 LAR)、Lanreotide (長效緩釋 depot) 是主要藥物，透過結合 SST2/SST5 抑制 GH 分泌。可作為術前輔助（縮瘤、緩解症狀）或術後/原發治療。約 50% 患者 GH/IGF-1 可正常化，約 50% 腫瘤縮小。口服 Octreotide 可用於已穩定的患者。Pasireotide LAR(二線) 對其他 SRLs 耐藥者有效，但高血糖副作用更常見。
 - SRLs 副作用多為短期胃腸道反應、膽泥/膽石 (30%)、輕度糖耐量異常、心動過緩。
- GH 受體拮抗劑 (Pegvisomant)：阻斷外周 GH 作用，使 IGF-1 正常化 (約 70%)，但 GH 濃度仍高，需監測肝酶和腫瘤體積。可與 SRLs 併用
- 多巴胺激動劑 (Cabergoline)：高劑量可能有效，尤其對混合分泌 PRL 者，常與 SRLs 併用

診斷&治療

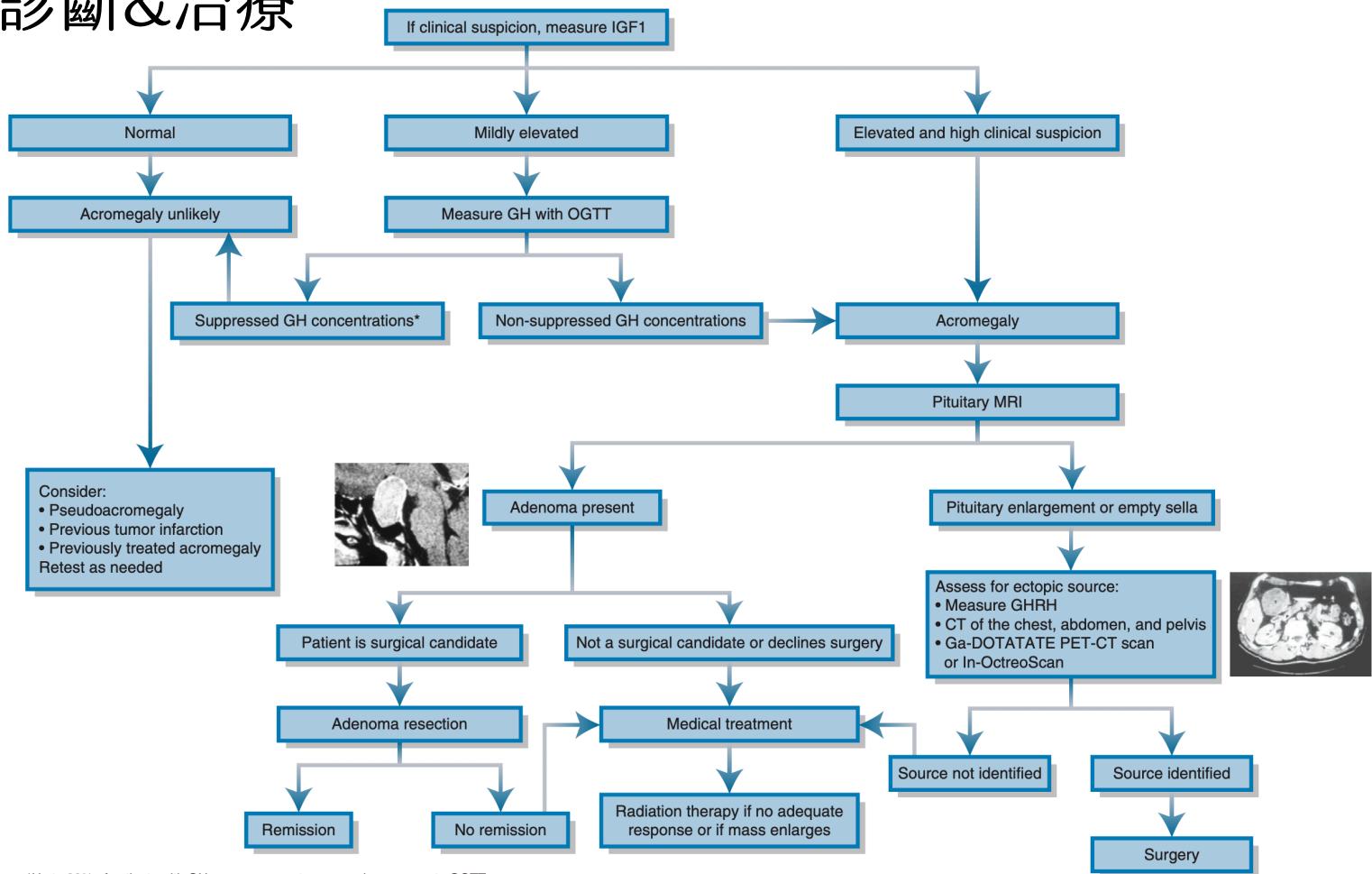
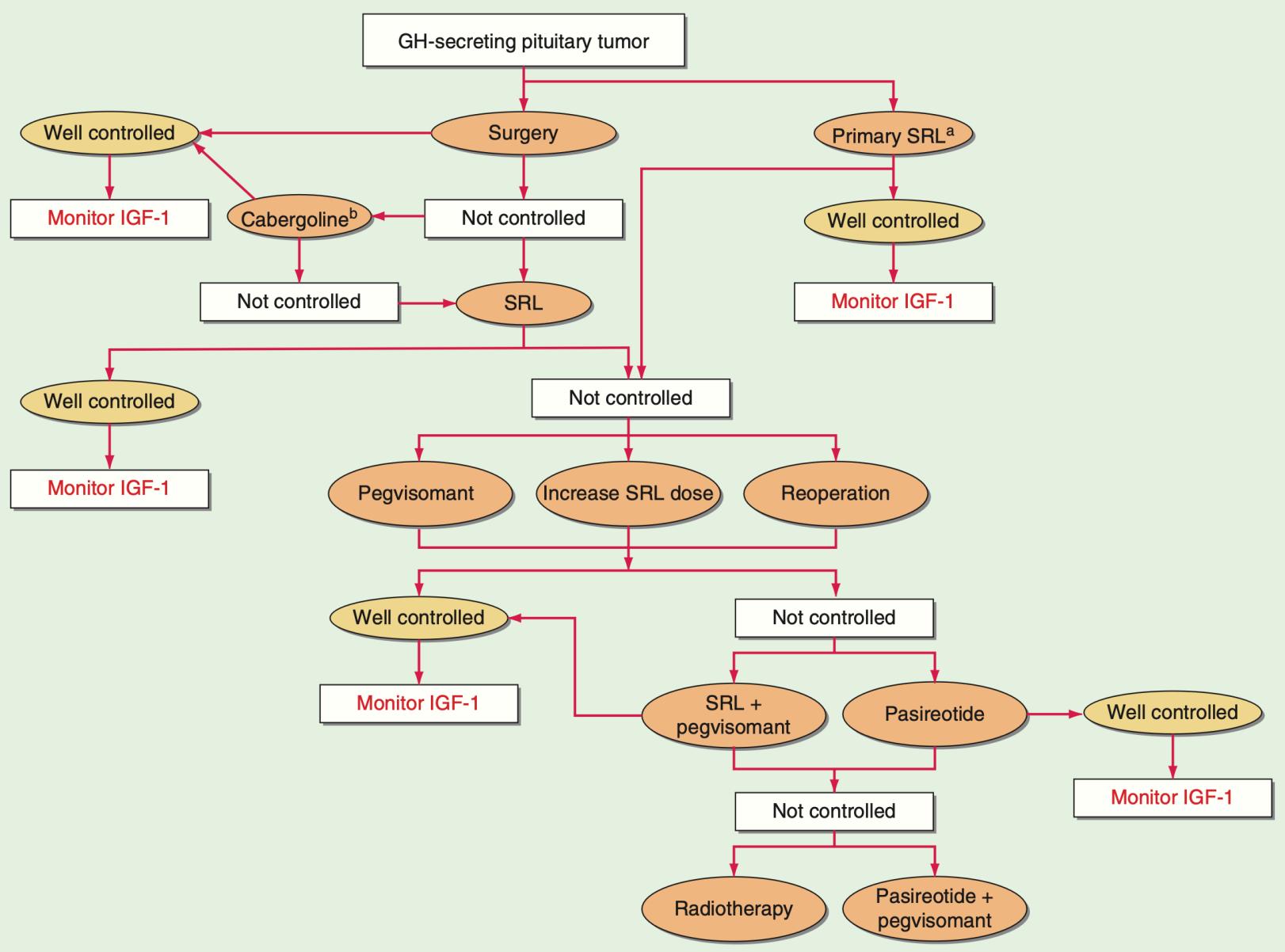


Fig. 7.43 Acromegaly diagnosis and management. (Modified from Fleseriu M, Langlois F, Lim DST, Varlamov EV, Melmed S. Acromegaly: pathogenesis, diagnosis, and management. *Lancet Diabetes Endocrinol.* 2022;10:804–826.)



治療目標、治療方式

TABLE 7.24 Management of Acromegaly

Goals

- Control GH and IGF1 secretion
- Control tumor growth
- Relieve central compressive effects, if present
- Preserve or restore pituitary trophic hormone function
- Treat comorbidities (hypertension, cardiac failure, hyperglycemia, sleep apnea, arthritis)
- Normalize mortality rates
- Prevent biochemical recurrence

TREATMENTS					
Characteristic	Surgery	Radiotherapy	SRL	GHR Antagonist	Dopamine Agonist
Advantages					
Mode	Transsphenoidal resection	Noninvasive	Monthly injection	Daily injection	Oral
Biochemical control					
GH <2.5 µg/L	Macroadenomas, <50% Microadenomas, >80%	~35% in 10 years	~55%–65%	Increases	<15%
IGF1 normalized					
Onset	Rapid	Slow (years)	Rapid	Rapid	Slow (weeks)
Patient compliance	One-time consent	Good	Must be sustained	Must be sustained	Good
Tumor mass	Debulked or resected	Ablated	Growth constrained or shrinks ~50%	Unknown	Unchanged
Disadvantages					
Cost	One-time	One-time	Ongoing	Ongoing	Ongoing
Hypopituitarism	~10%	>50%	None	Very low IGF1 if overtreated	None
Other	Tumor persistence or recurrence, 6% AVP deficiency, 3% Local complications, 5%	Local nerve damage Second brain tumor Visual and CNS disorders, ~2% Cerebrovascular risk	Gallstones, 20% Nausea, diarrhea	Elevated liver enzymes (rare)	Nausea, ~30% Sinusitis High dose required

OUTCOMES		
Feature	Evaluation	Treatment
Safe Biochemical Activity		
Nadir GH < 0.4 µg/L	Assess GH/IGF1 axis Evaluate adrenal, thyroid, and gonadal axes Periodic but less frequent MRI	None or no change in current treatment
Age-matched normal IGF1		
Asymptomatic		
No comorbidities		
Unsafe Biochemical Activity		
Nadir GH > 0.4 µg/L	Assess GH/IGF1 axis Evaluate pituitary function Periodic MRI	Weigh treatment benefit vs. risks Consider new treatment if being treated
Elevated IGF1		
Discordant GH and IGF1		
Asymptomatic		
No comorbidities		
Unsafe Biochemical and Clinical Activity		
Nadir GH >1 µg/L	Assess GH/IGF1 axis Evaluate pituitary function Assess cardiovascular, metabolic, and tumoral comorbidity Periodic MRI	Actively treat or change treatment
Elevated IGF1		
Clinically active tumor growing		
AVP, arginine vasopressin; CNS, central nervous system; GH, growth hormone; GHR, growth hormone receptor; IGF1, insulin-like growth factor type 1; MRI, magnetic resonance imaging; SRL, somatostatin receptor ligand.		
Modified from Melmed S. Acromegaly. <i>N Engl J Med</i> . 2006;355:2558–2573.		

藥物

TABLE 7.25 Medical Therapy of Acromegaly

Therapy	Receptor Target	Route of Administration	Dose	Frequency	Side Effects	Efficacy (GH/IGF1 Normalization)
Cabergoline	D2 receptor	Oral	1–4 mg	Biweekly up to daily	Nausea, dizziness, orthostatic hypotension	30%–40%
Octreotide	SST2, SST5	SC	50–400 µg/d	1–3 times daily	Nausea, vomiting, diarrhea, constipation, abdominal pain, cholelithiasis/biliary sludge, bloating, bradycardia, fatigue, headache, alopecia, dysglycemia	50%–60%
Octreotide LAR Lanreotide	SST2, SST5 SST2, SST5	IM Deep SC	20–40 mg 60–120 mg	Monthly Every 4–6 weeks		
Pasireotide LAR	SST1, SST2, SST3, SST5	IM	40–60 mg	Monthly	Same as above, with more hyperglycemia	Up to 80%
Oral octreotide	SST2, SST5	Oral	40–80 mg	Twice daily	Nausea, vomiting, diarrhea, dyspepsia, cholelithiasis, headache, dizziness, dysglycemia	65%
Pegvisomant	GH receptor	SC	10–40 mg	Daily to once weekly (less frequent when used in combination)	Transaminase elevation, lipodystrophy, arthralgias	60%–90%

D2, dopamine type 2; GH, growth hormone; IGF1, insulin-like growth factor type 1; IM, intramuscular; SC, subcutaneous; SST, somatostatin receptor.

Modified from Langlois F, McCartney S, Fleseriu M. Recent progress in the medical therapy of pituitary tumors. *Endocrinol Metab*. 2017;32:162–170.

Summary

- Surgery is the preferred primary treatment for GH-secreting microadenomas.
- The high frequency of residual GH hypersecretion after macroadenoma resection usually necessitates adjuvant or primary medical therapy for these larger tumors.
- Patients unable to receive or respond to unimodal medical treatment may benefit from combined treatments, or they can be offered radiation.
- Very rarely, repeat surgery may be required.

ACTH-Secreting Tumors (Cushing Disease)

Etiologies of hypercortisolism

- Most commonly iatrogenic caused by exogenous glucocorticoids (though underreported)
- Cushing's disease (60–70% of non-iatrogenic CS): ACTH- secreting pituitary adenoma (usually microadenoma) or hyperplasia
- Adrenal tumor (10–15%): adenoma or (rarely) carcinoma
- Ectopic ACTH (10–15%): small cell lung carcinoma, carcinoid, islet cell tumors, medullary thyroid cancer, pheochromocytoma
- Cushing's disease is 5–10 times more common in women than in men.

Cushing's disease

- 定義：庫欣氏病特指由於**腦下垂體促腎上腺皮質素細胞腺瘤 (Corticotrope Adenoma)** 分泌過量 ACTH，導致雙側腎上腺皮質增生並產生過量皮質醇 (Cortisol) 所引起的**庫欣氏症候群 (Cushing's Syndrome)**。必須與其他導致庫欣氏症候群的原因（如腎上腺腫瘤、異位 ACTH 分泌）相區分。
- 盛行率：庫欣氏病是**內源性庫欣氏症候群中最常見的病因**（約佔 70%，不包括外源性類固醇使用者）。
- 好發族群：女性較男性多見（約 3:1）。發病年齡通常在 20-50 歲之間。
- 腫瘤特徵：絕大多數（約 80-90%）為**微腺瘤 (< 10 mm)**，位於**腦下垂體前葉內**。大腺瘤較少見。

Clinical presentation

- **代謝與外觀**：中心性肥胖（軀幹肥胖、四肢相對細）、**月亮臉** (Moon Facies)、**水牛肩** (Buffalo Hump)（頸後脂肪墊）、鎖骨上窩脂肪墊飽滿、皮膚變薄、容易瘀青、**紫色皮紋** (Purple Striae)（寬 >1cm，位於腹部、脅腹、大腿、乳房）、痤瘡、多毛症（女性）。
- **肌肉骨骼**：**近端肌肉無力**（從椅子上站起困難、爬樓梯困難）、骨質疏鬆（導致骨折、身高變矮、背痛）。
- **心血管**：高血壓、低血鉀（較少見，皮質醇過量時可作用於鹽皮質素受體）。
- **內分泌/代謝**：糖耐量異常或糖尿病、血脂異常。
- **神經精神**：情緒不穩（易怒、焦慮、憂鬱）、失眠、記憶力下降，嚴重者可出現精神病。
- **免疫**：免疫功能受抑制，易發生感染（尤其是伺機性感染）。
- **生殖**：女性月經失調（稀少或無月經）、男性性慾減退。
- **色素沉著**：通常不明顯，因為 ACTH 濃度雖升高但未達極高濃度（與原發性腎上腺功能不全或 Nelson 症候群不同）。

Clinical presentation

TABLE 380-7 Clinical Features of Cushing's Syndrome (All Ages)

SYMPTOMS/SIGNS	FREQUENCY, %
Obesity or weight gain (>115% ideal body weight)	80
Thin skin	80
Moon facies	75
Hypertension	75
Purple skin striae	65
Hirsutism	65
Menstrual disorders (usually amenorrhea)	60
Plethora	60
Abnormal glucose tolerance	55
Impotence	55
Proximal muscle weakness	50
Truncal obesity	50
Acne	45
Bruising	45
Mental changes	45
Osteoporosis	40
Edema of lower extremities	30
Hyperpigmentation	20
Hypokalemic alkalosis	15
Diabetes mellitus	15

Source: Adapted with permission from MA Magiokou et al, in Wierman ME: Diseases of the Pituitary. Totowa, NJ: Humana; 1997.

TABLE 15.9 Symptoms and Signs for the Diagnosis of Cushing Syndrome

Discriminatory	Less Discriminatory
<p>Signs</p> <ul style="list-style-type: none"> • Facial plethora • Proximal myopathy • Cutaneous striae (red-purple, >1 cm wide) • Bruising • In children—weight gain with reduced height percentile 	<p>Signs</p> <ul style="list-style-type: none"> • Central obesity • Buffalo hump, supraclavicular fullness • Facial fullness • Acne and hirsutism • Skin thinning • Poor wound healing • Peripheral edema
<p>Symptoms and complications (especially at a young age)</p> <ul style="list-style-type: none"> • Hypertension • Diabetes mellitus • Osteoporosis and vertebral fractures 	<p>Symptoms and complications</p> <ul style="list-style-type: none"> • Fatigue • Weight gain • Depression, mood and appetite change, impairment of concentration and memory • Back pain • Oligomenorrhea, polycystic ovary syndrome • Recurrent infections • Kidney stones

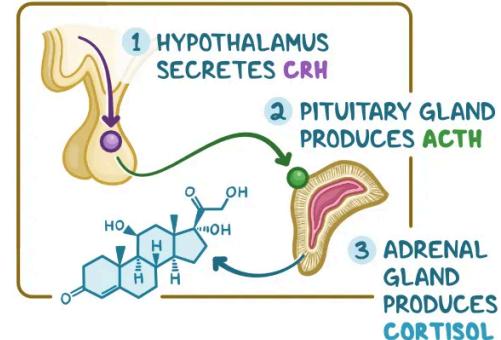
Data from Nieman LK, Biller BM, Findling JW, et al. Diagnosis of Cushing's syndrome, an Endocrine Society Clinical Guideline. *J Clin Endocrinol Metab.* 2008;93:1526–1540.

SYMPTOMS of CUSHING SYNDROME



BACKGROUND

- * SET of SYMPTOMS RESULTING from EXPOSURE to ↑↑ LEVELS of CORTISOL
~ aka HYPERCORTISOLISM
- * ENDOGENOUS or EXOGENOUS SOURCES of EXCESS CORTISOL



CAUSES

- * LONG-TERM USE of GLUCOCORTICOID MEDICATIONS
- * PITUITARY TUMOR
~ CUSHING DISEASE
- * ECTOPIC ACTH-PRODUCING TUMOR
- * ADRENAL TUMOR



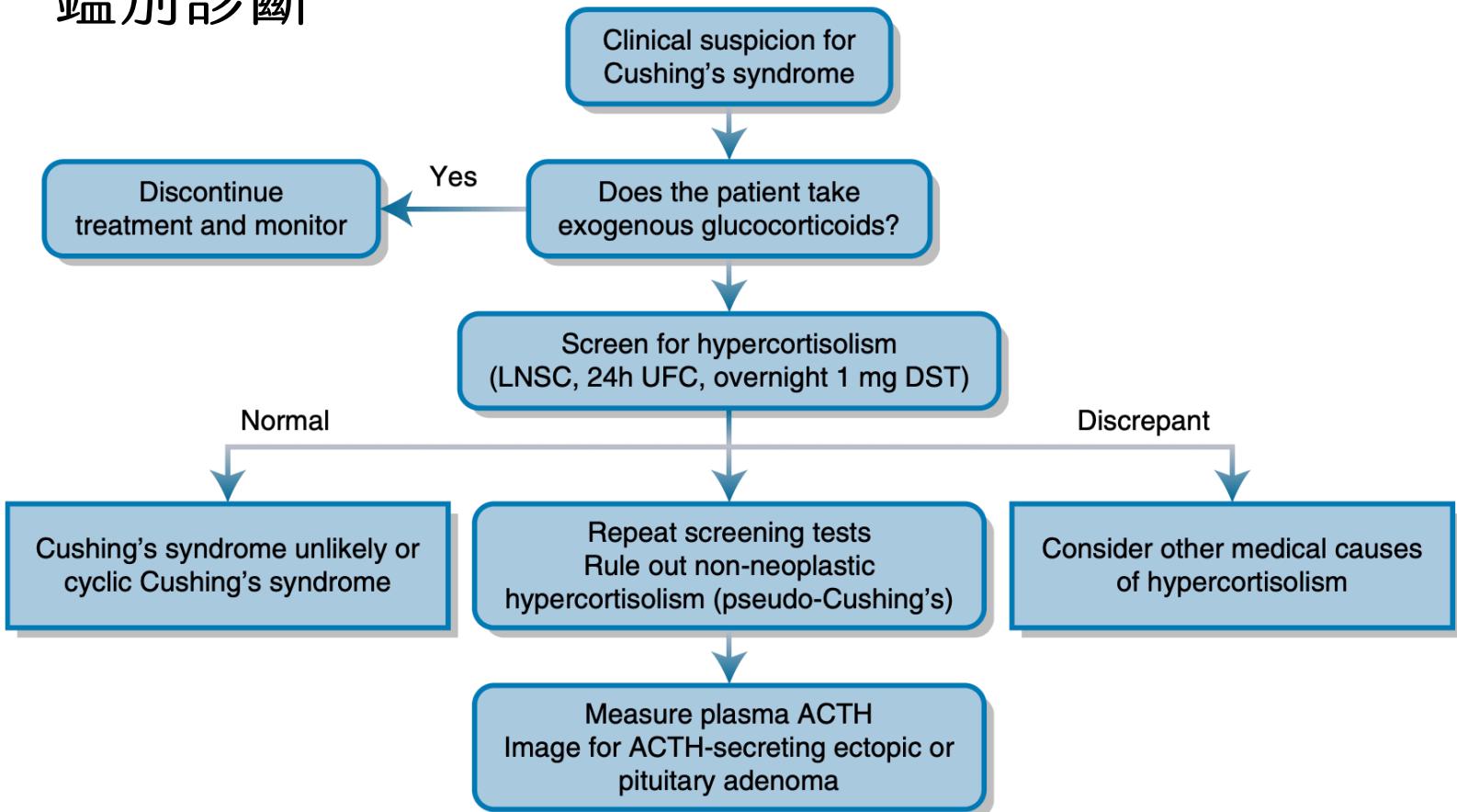
DIAGNOSIS

- * MEDICAL HISTORY
- * PHYSICAL EXAM
- * LAB TESTS
 - ~ 24-HOUR URINARY FREE CORTISOL TEST
 - ~ LATE-NIGHT SALIVARY CORTISOL
 - ~ LOW- or HIGH-DOSE DEXAMETHASONE TEST
- * IMAGING





鑑別診斷



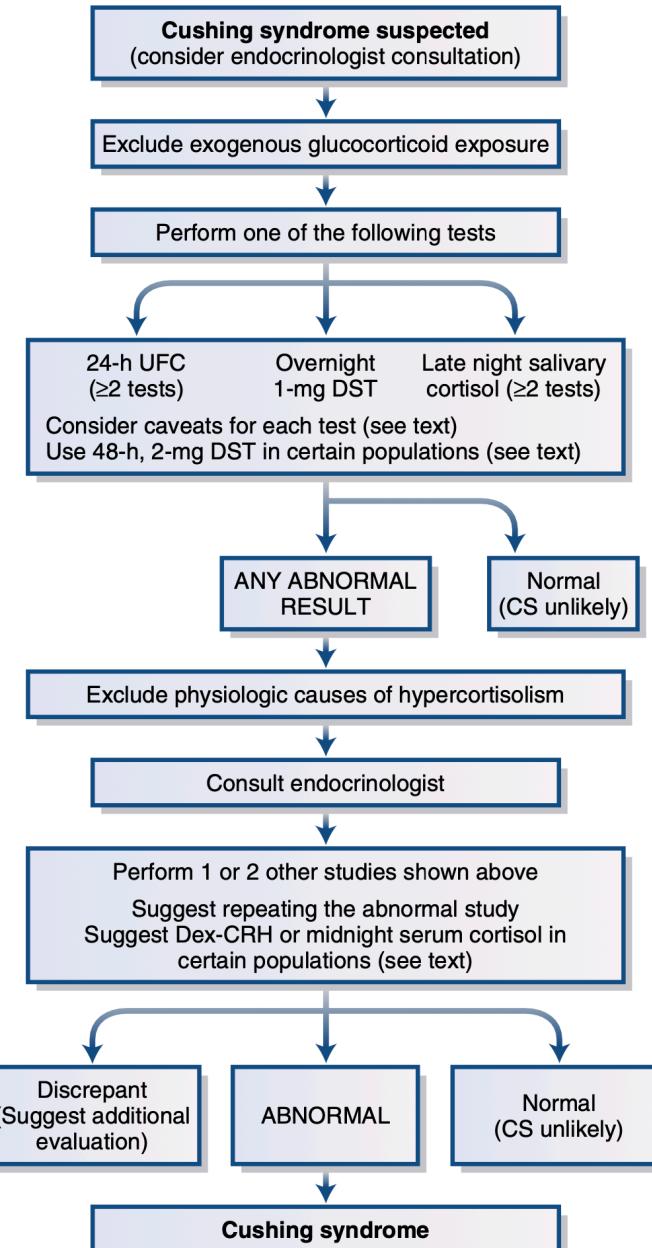
• **Fig. 7.52** Differential diagnosis of Cushing syndrome. *ACTH*, adrenocorticotrophic hormone; *DST*, dexamethasone suppression test; *LNSC*, late-night salivary cortisol; *UFC*, urinary free cortisol. (Modified from Fleseriu M, Auchus R, Bancos I, et al. Consensus on diagnosis and management of Cushing disease: a guideline update. *Lancet Diabetes Endocrinol*. 2021;9:847–875.)

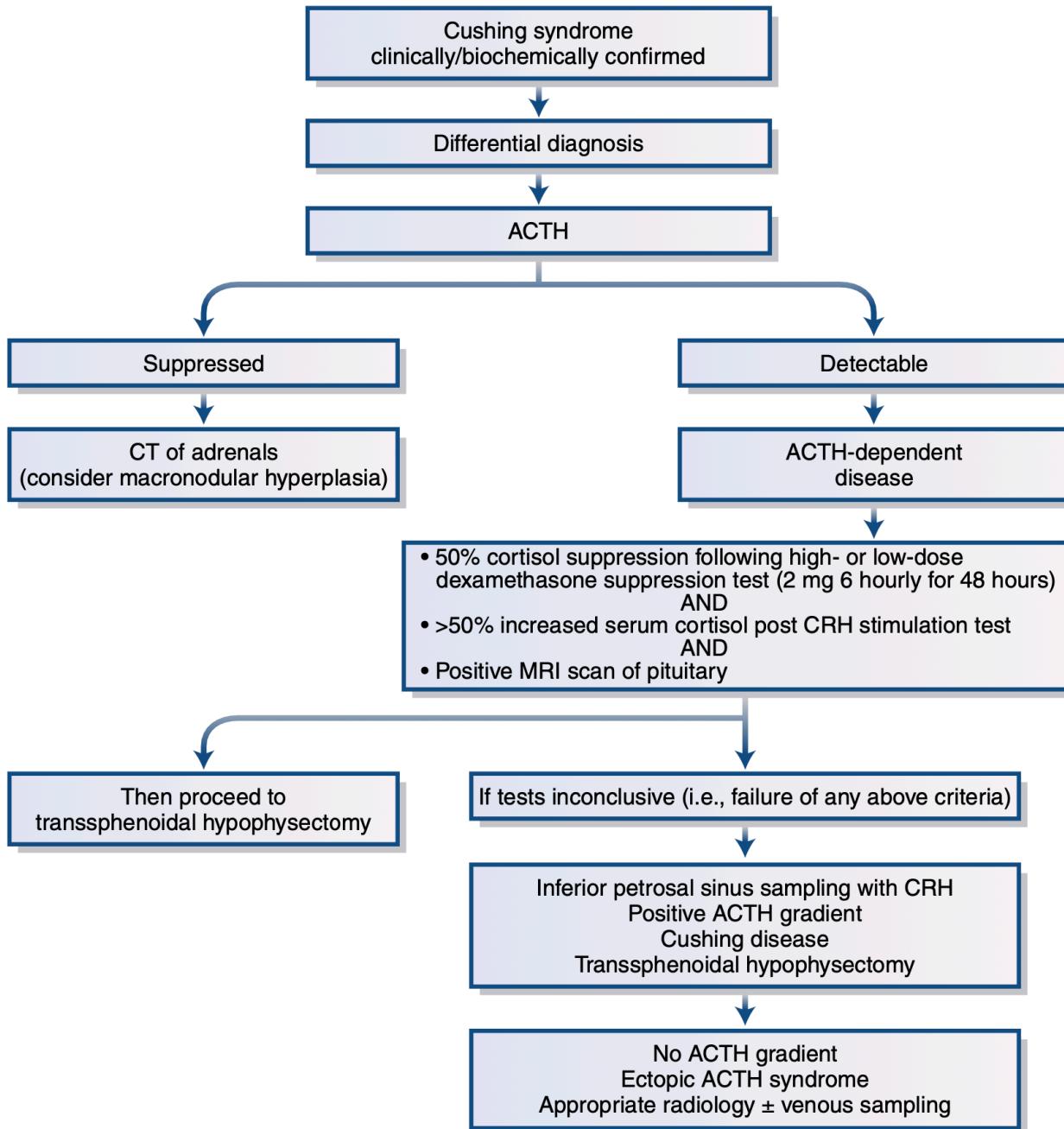
診斷流程

- 第一步：篩檢→確認皮質醇過多
 - 篩檢：(1) 24 小時尿液游離皮質醇 (UFC) 多次升高；(2) 過夜 1mg 地塞米松抑制試驗失敗（晨間皮質醇 $> 1.8 \mu\text{g/dL}$ 或 50 nmol/L ）；(3) 晚夜唾液皮質醇升高。
 - 確認：Low dose dexamethathone test($0.5\text{mg Q6H} \times 2\text{days}$)
- 第二步：區分 ACTH 依賴性與非依賴性
 - 測定血漿 ACTH。ACTH 顯著抑制 ($< 5 \text{ pg/mL}$) 提示 ACTH 非依賴性（腎上腺來源）；ACTH 正常或升高提示 ACTH 依賴性（垂體或異位來源）。

診斷流程

- 第三步：區分垂體性（庫欣氏病）與異位性 ACTH
 - High dose dexamethathone test: 庫欣氏病通常可被抑制（cortisol下降 >50%），異位 ACTH 通常不被抑制
 - CRH 刺激試驗：庫欣氏病通常對 CRH 有反應（ACTH 和皮質醇升高），異位 ACTH 通常無反應
 - 腦下垂體 MRI：首選影像學檢查，但約 40% 庫欣氏病微腺瘤 MRI 無法檢出
 - 雙側海綿竇旁靜脈竇取樣 (Bilateral Inferior Petrosal Sinus Sampling, BIPSS)：當 MRI 未能發現確切腺瘤，或影像學結果模棱兩可時，BIPSS 是鑑別 ACTH 來源是腦下垂體還是異位分泌的黃金標準。海綿竇旁靜脈竇 ACTH 濃度與周邊靜脈 ACTH 濃度的比值 > 2.0 ，或CRH 刺激後比值 ≥ 3 可確診庫欣氏病。





Diagnostic Tests (參考)

- 24 hour Urine Free Cortisol
 - A. Purpose: Screening for Cushing's syndrome
 - B. Procedure: 24 hour urine free cortisol level.
(Normal range: 4.3~176.0 µg/24hr)

- Overnight Dexamethasone Suppression Test
 - A. Purpose: Screening for Cushing's syndrome
 - B. Procedure
 - Give 1 mg dexamethasone orally at 11 pm
 - Check cortisol at 8 am of the following day prior to food intake
 - C. Interpretation
 - Normally serum cortisol are suppressed to < 1.8 (2.0) $\mu\text{g/dL}$
 - Depression, restless sleep, emotional or physical stress, recent heavy alcohol consumption, obesity, thyrotoxicosis, acromegaly, pregnancy, oral contraceptives, phenytoin, rifampin and barbiturates → false positive

- Low Dose Dexamethasone Suppression Test (LDDST)
 - A. Purpose: Confirmation of Cushing's syndrome
 - B. Procedure
 - Day 1: Obtain baseline serum cortisol, ACTH at 8 am
 - Day 1-2: Give dexamethasone 0.5 mg q6h po x 2 days
 - Day 3: Check serum cortisol level at 8 am
 - C. Interpretation: normal response → serum cortisol < 2 µg/dL at 8 am on D3

- High Dose Dexamethasone Suppression Test (HDDST)
 - A. Purpose: D/D of Cushing's disease or ectopic ACTH secretion
 - B. Procedure
 - Day 1: Obtain baseline serum cortisol, ACTH at 8 am
 - Day 1-2: Give dexamethasone 2 mg q6h po x 2 days
 - Day 3: Check serum cortisol level at 8 am
 - C. Interpretation
 - Cushing's disease: D3 cortisol level is < 50% of D1 baseline cortisol level;
 - Ectopic ACTH: non-suppressible

Management of Cushing's Disease

- 首選：經蝶竇選擇性切除垂體腺瘤，經驗豐富者初期緩解率 70-80% (microadenoma); <50% (macroadenoma)
- 術後：出現暫時性腎上腺皮質功能低下（需要補充皮質醇數月至一兩年）
- 復發：長期復發率約 10-20%。

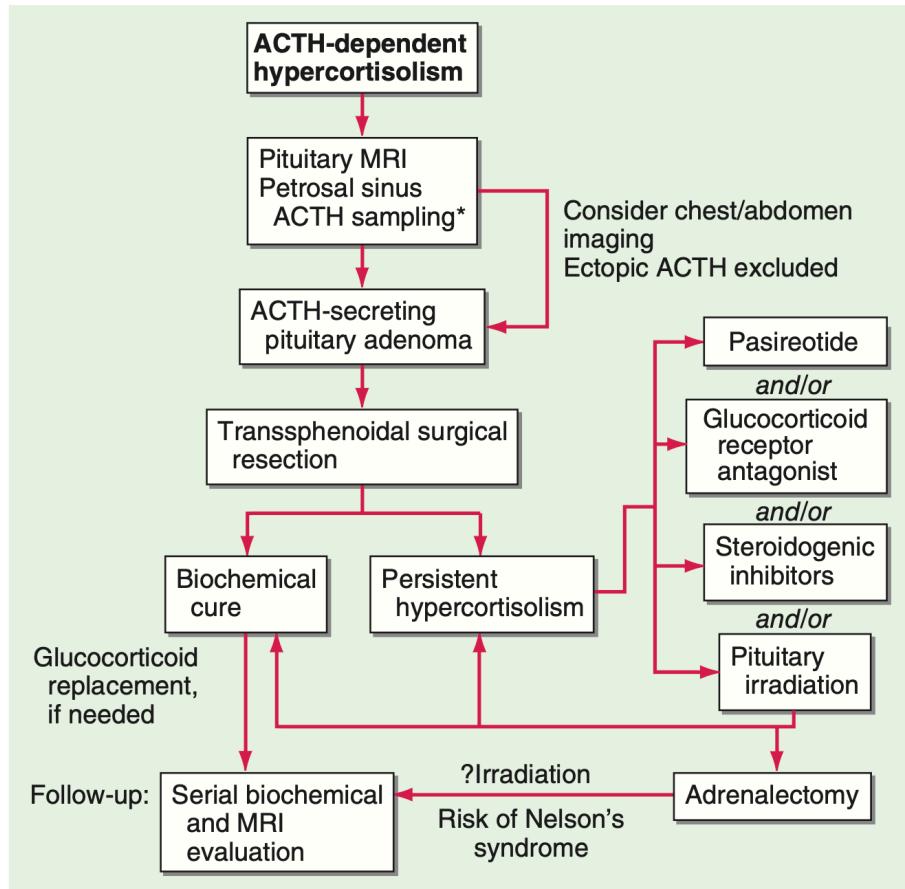
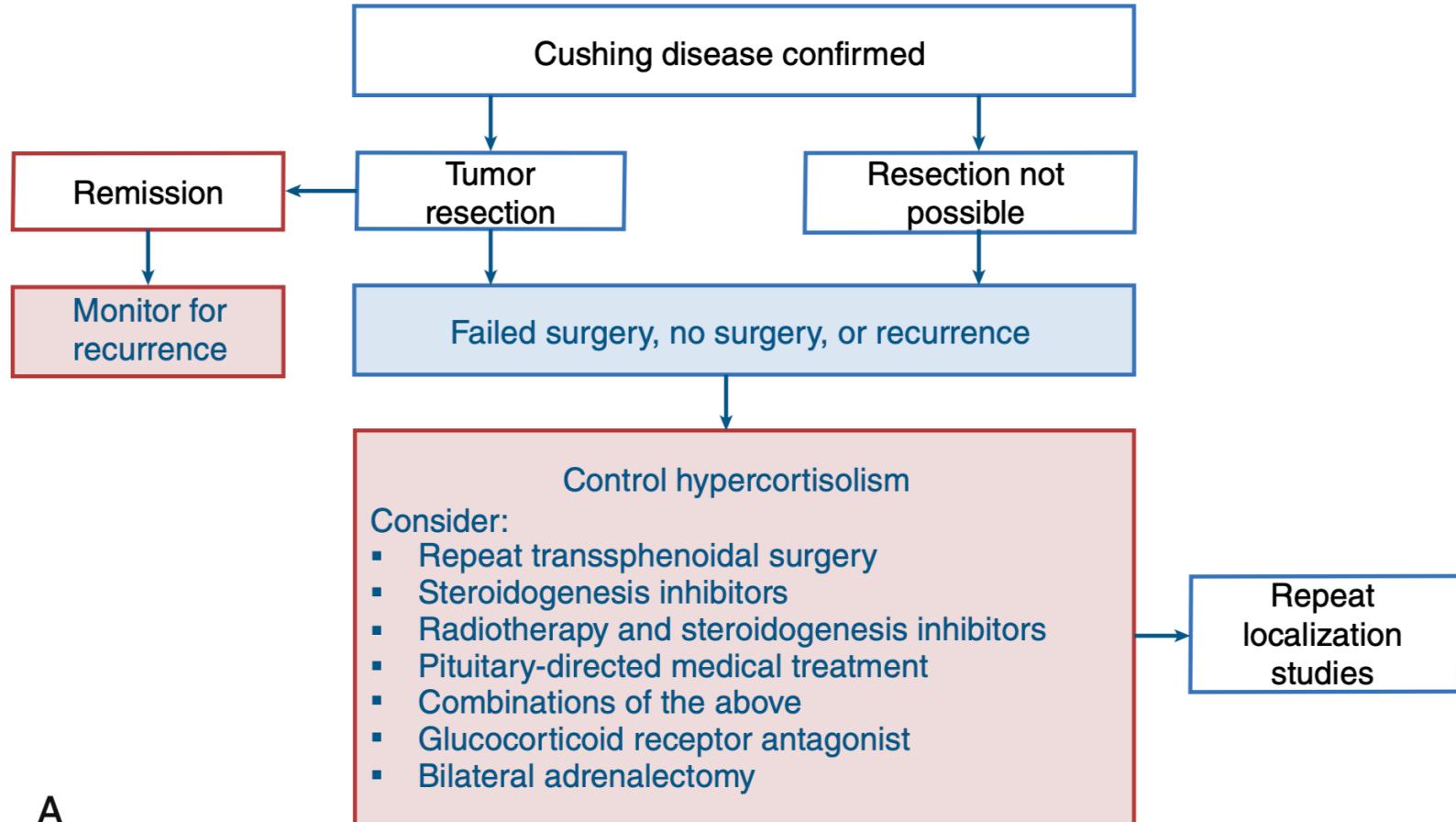


FIGURE 380-9 Management of Cushing's disease. ACTH, adrenocorticotropin hormone; MRI, magnetic resonance imaging; *, Not usually required.



Medical treatment for Cushing's disease

- 垂體導向：
 - Pasireotide (SRL，對 SST5 親和力高，可降 ACTH、UFC，但易致高血糖)。
- 腎上腺導向 (抑制類固醇合成)：
 - Osilodrostat (11 β -羥化酶抑制劑，效果好)、Ketoconazole (抑制早期步驟)、Metyrapone (11 β -羥化酶抑制劑)、Etomidate (IV，抑制 11 β -羥化酶/醛固酮合成酶)、Mitotane (腎上腺皮質溶解劑，主要用於 ACC)。
 - 使用這些藥物需監測皮質醇濃度防腎上腺危象。
 - 糖皮質素受體拮抗劑：Mifepristone (阻斷外周皮質醇作用，用於改善高血糖，不影響 ACTH/皮質醇濃度)。

Take Home Message

- Hormone
 - TSH/ACTH/GH/PRL/FSH,LH
- Pituitary tumors
 - Prolactinoma
 - Acromegaly (IGF1, GH, OGTT tests)
 - Cushing's disease (overnight/low dose/high dose Dexamethasone Suppression Test)

References

- Harrison's Principles of Internal Medicine, 21e
- William's Endocrinology, 15e
- Pocket Medicine, 8e
- 臺大醫院代謝內分泌檢查工作手冊

Thanks for your attention!

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