Hyperprolactinemia

Diagnosis, causes, drug-induced disease, prolactinoma management, resistant/malignant disease, and pregnancy for adults with hyperprolactinemia.

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Hyperprolactinemia Clinical Practice Guideline
Melmed et al. · JCEM 2011;96:273–288

GRADE · 1 · Strong For · 2 · Suggest For · 2- · Suggest Against · 3 · Strong Against

1 Diagnosis

1	Diagnose with a **single serum prolactin** above the upper limit of normal (avoid excessive venipuncture stress). **Against** dynamic testing of prolactin secretion.
2	In **asymptomatic** hyperprolactinemia, assess for **macroprolactin**.
1	When a large tumor and only mildly elevated prolactin are discordant, obtain **serial dilution** — avoids a falsely low result from assay saturation (the "hook effect").

2 Causes

1	**Exclude** medication use, renal failure, hypothyroidism, and pituitary/parasellar tumors in patients with symptomatic, nonphysiological hyperprolactinemia.

3 Drug-Induced Hyperprolactinemia

2	If symptomatic and drug-induced is suspected, **discontinue for 3 days or substitute** then remeasure prolactin (don't stop antipsychotics without consulting the prescriber). If the drug can't be stopped and onset doesn't align with therapy start, obtain a **pituitary MRI** to exclude a mass.
2	**Do not treat** asymptomatic medication-induced hyperprolactinemia; use estrogen/testosterone for long-term hypogonadal symptoms or low bone mass if the drug can't be changed. Stepwise approach: stop drug → substitute non-causative agent → cautious dopamine agonist in consultation with prescriber.

4 Management of Prolactinoma

1	**Dopamine agonist** therapy for symptomatic microadenomas or macroadenomas — lowers prolactin, shrinks tumor, restores gonadal function. **Cabergoline preferred** over other agonists (higher efficacy, more tumor shrinkage).
2	**Do not treat** asymptomatic microprolactinomas with dopamine agonists; use a dopamine agonist or oral contraceptives if amenorrhea is present.
2	Consider **tapering/discontinuing** therapy after ≥2 years of normal prolactin with no visible tumor remnant on MRI, with careful follow-up.

5 Resistant & Malignant Prolactinoma

1	For resistant prolactinomas, **increase the dopamine agonist dose** rather than referring to surgery; switch **bromocriptine-resistant** patients to cabergoline.
2	Offer **transsphenoidal surgery** if intolerant of high-dose cabergoline or unresponsive to dopamine agonists (intravaginal bromocriptine is an option for oral intolerance); **radiation therapy** for surgical failures or aggressive/malignant tumors; **temozolomide** for malignant prolactinoma.

6 Pregnancy

1	**Discontinue dopamine agonist** as soon as pregnancy is confirmed; continuing may be prudent in select macroadenomas that are invasive or abut the optic chiasm without prior surgery/RT. **Against** routine serum prolactin measurement and routine pituitary MRI during pregnancy.
1	Obtain **formal visual field testing + MRI without gadolinium** if severe headache or visual changes develop. Counsel on **surgical resection** before conception if a macroprolactinoma shows no shrinkage or agonist intolerance.
1	**Bromocriptine** for symptomatic tumor growth during pregnancy.

Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and Treatment of Hyperprolactinemia: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2011;96(2):273–288.