

# Prolactin Antagonist

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## SOURCE :

Bertram G. Katzung Basic & Clinical  
Pharmacology 15th Edition  
Google for images & research article

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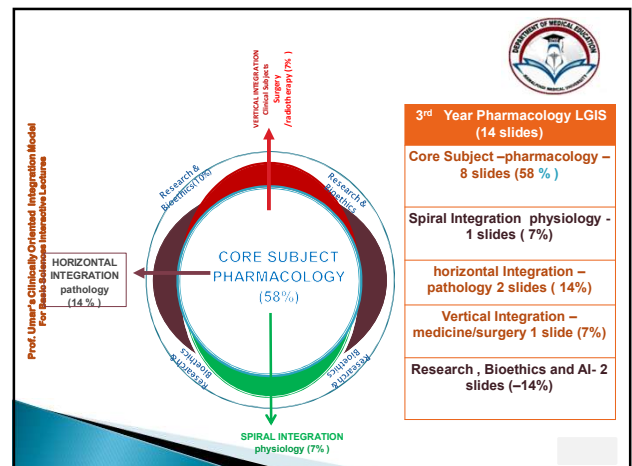
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## MOTTO AND VISION

- ▶ To impart evidence based research oriented medical education
- ▶ To provide best possible patient care
- ▶ To inculcate the values of mutual respect and ethical practice of medicine

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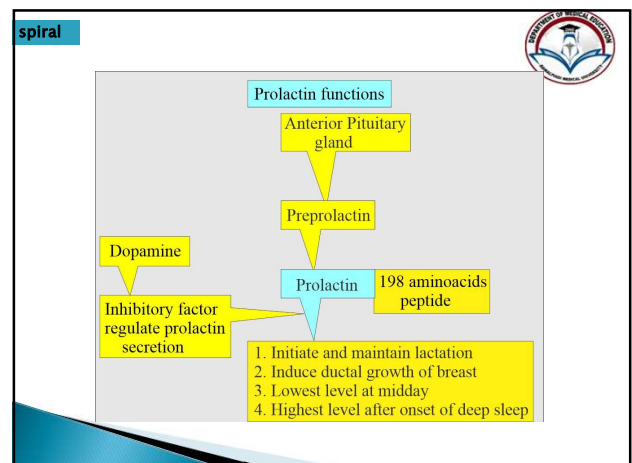
## Learning Objectives



**By the end of lecture students should be able to :**

- ▶ Enumerate prolactin antagonists
- ▶ Describe mechanism of action , uses as well as adverse effects of prolactin antagonist

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TABLE  
Causes of Hyperprolactinemia

| Physiologic   | Pharmacologic   | Pathologic  |
|---|---|---|
| Pregnancy<br>Nursing<br>Nipple stimulation<br>Exercise<br>Stress<br>Sleep<br>Seizures | Dopamine antagonist (phenothiazines, haloperidol, risperidone, metoclopramide, reserpine, methyldopa, opioids)<br>Monoamine oxidase inhibitors<br>Cimetidine (intravenous)<br>Verapamil<br>Thyrotropin-releasing hormone stimulation test | Pituitary tumors (prolactinoma, acromegaly that co-secretes growth hormone and prolactin, nonsecretory adenoma)<br>Hypothyroidism<br>Chronic renal insufficiency<br>Severe liver failure<br>Hypophyseal stalk lesion ("stalk effect")<br>Neuraxis irradiation<br>Spinal cord lesions<br>Hypophysitis (inflammation of hypophyseal stalk)<br>Polycystic ovarian syndrome |

\* Hyperprolactinemia secondary to medications is usually mild (25 to 100 ng/mL), except for the highlighted agents, in which cases levels can exceed 200 ng/mL.

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**Drugs used in hyperprolactinemia (dopamine agonists)**

- ▶ **Ergot derivatives**
  - Bromocriptine
  - Cabergoline
- ▶ **Nonergot derivatives**
  - Quinagolide

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**Mechanism of action:**

- ▶ D2 agonist
- ▶ Inhibit prolactin secretion
- ▶ Inhibit growth hormone release

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**Pharmacokinetics:**

- ▶ Oral preparations
- ▶ Elimination-----metabolism
- ▶ T<sub>1/2</sub> :
  - Cabergoline 65 hrs
  - Quinagolide 20 hrs
  - bromocriptine 7 hrs.
- ▶ After vaginal administration, serum levels peak more slowly

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**Clinical uses**

**1) Hyperprolactinemia**

- ▶ shrink prolactin-secreting tumors, ↓ prolactin levels, and restore ovulation in 70% of women with microadenomas and 30% of women with macroadenomas
- ▶ **Cabergoline :**
  - 0.25 mg twice weekly orally or vaginally
  - increased gradually, according to serum prolactin determinations, up to a maximum of 1 mg twice weekly.
- ▶ **Bromocriptine**
  - initial dose of 1.25 mg; increased as tolerated.
  - Long-acting oral bromocriptine formulations (Parlodel SRO) and intramuscular formulations (Parlodel LAR).

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## II) Inhibit Physiological lactation:

- prevent breast engorgement when breast-feeding not desired.
- Use for this purpose-----discouraged because of toxicity.

## III) Acromegaly:

- Alone or in combination with pituitary surgery, radiation therapy, or octreotide administration
- Doses required are higher than those used to treat hyperprolactinemia.

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## IV) Parkinson's disease

Cabergoline and bromocriptine

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## Toxicity



1. Nausea, headache, light-headedness, orthostatic hypotension, and fatigue.
2. Psychiatric manifestations
3. Erythromelalgia ---- rarely.
4. Cold induced peripheral digital vasospasm----- High dosages of ergot-derived
5. Pulmonary infiltrates -----chronic high-dosage therapy.
6. higher risk of valvular heart disease -----Cabergoline at high dose bt not with low dose
7. Cabergoline appears to cause nausea less often than bromocriptine.
8. Vaginal administration can reduce nausea, but may cause local irritation.

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## Cautions and Contraindications



### ► Pregnancy

- In small pituitary adenomas, dopamine agonist therapy is discontinued upon conception because the risk of growth of microadenomas during pregnancy is low (2.7%).
- Patients with macroadenomas require vigilance, as the risk for tumor progression is high (22.9%) and such patients often require a dopamine agonist throughout pregnancy.

### ► stroke or coronary thrombosis

- postpartum women taking bromocriptine to suppress postpartum lactation....rare reports

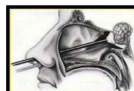
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## Surgery



1. Patient drug intolerance,
  2. Tumors resistant to medical therapy,
  3. Persistent visual-field defects in spite of medical treatment, and
  4. Patients with large cystic or hemorrhagic tumors.
- **Trans-sphenoidal surgery** is the conventional procedure.



## Radiotherapy

1. Macroadnoma
2. Resistant to medical therapy or when surgery is failed

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Further reading

## Research and bioethics

- *Dehelean L, Romosan AM, Papava I, Bredicean CA, Dumitrascu V, Ursoniu S, Romosan RS. Prolactin response to antipsychotics: An inpatient study. PLoS One. 2020 Feb 4;15(2):e0228648.*
- We must be cautious when prescribing and monitoring dopamine agonist therapy to avoid social harm to patients and balance this with depriving patients of effective non-invasive treatments.

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## Further reading

## Artificial intelligence

- ▶ Artificial intelligence programs are widely used by both healthcare professionals and patients.
- ▶ patients benefit from effectively managing their treatment through features like drug reminders, self-monitoring, dosage guidance, and accessing information on the potential side effects of therapy
- ▶ healthcare professionals benefit from utilizing artificial intelligence in the process of diagnostic radiology and medical education, as well as in the planning, execution, and composition of medical research within the field

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