Hypothalamic and pituitary drugs

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Introduction

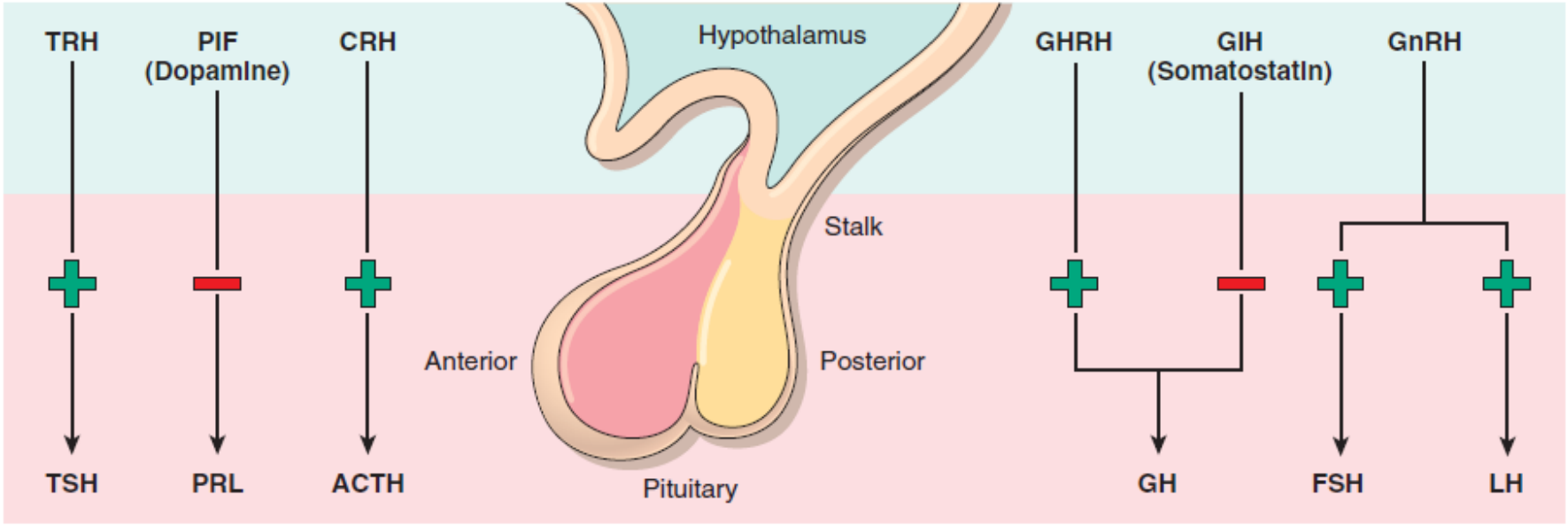

Fig. 20.2 The hypothalamic/pituitary axis. The hypothalamus regulates the secretion of hormones from the adenohypophysis (anterior pituitary gland) by releasing stimulatory (corticotropin-releasing hormone, CRH; growth hormone–releasing hormone, GHRH; gonadotropin-releasing hormone, GnRH; thyrotropin-releasing hormone (TRH) and inhibitory factors (growth hormone inhibitory hormone, GIH or somatostatin; prolactin inhibitory factor, PIF or dopamine). These in turn modulate the release of six hormones from the anterior pituitary: adrenocorticotropic hormone (ACTH or corticotropin); follicle-stimulating hormone (FSH); growth hormone (GH, or somatotropin); luteinizing hormone (LH); prolactin (PRL); and thyroid-stimulating hormone (TSH, or thyrotropin).

Robbins Basic Pathology 10th edition 2018

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- Somatostatin analogues
- GH receptor antagonists
- Dopamine agonists
- Vasopressin receptor agonists
- Vasopressin receptor antagonists

Hypothalamic & pituitary drugs

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Hypothalamic & pituitary drugs

- **Recombinant form of human GH**

  * somatropin (S.C.)

  * acts through GH receptor ---> increase production of IGF-1

  * restores normal growth and metabolic GH effects in GH-deficient individuals

Hypothalamic & pituitary drugs

- Recombinant form of human GH

  * replacement in GH deficiency

  * increased final adult height in children with certain conditions associated with short stature

Hypothalamic & pituitary drugs

- Recombinant form of human GH

  * ADRs: pseudotumor cerebri, edema, hyperglycemia, slipped capital femoral epiphysis

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- **Somatostatin analogues**
- GH receptor antagonists
- Dopamine agonists
- Vasopressin receptor agonists
- Vasopressin receptor antagonists

Hypothalamic & pituitary drugs

- **Somatostatin analogues**

  long-acting

  * octreotide, lanreotide (I.M., S.C., I.V.)
  * agonists at somatostatin receptor
  * inhibit production of GH, and to a lesser extent, of TSH, glucagon, insulin and gastrin

Hypothalamic & pituitary drugs

- **Somatostatin analogues**

  * use in R_x of acromegaly and several other hormone-secreting tumors

  * also use in acute control of bleeding from esophageal varices

  * ADRs: gallstone, bradycardia

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- Somatostatin analogues
- **GH receptor antagonists**
- Dopamine agonists
- Vasopressin receptor agonists
- Vasopressin receptor antagonists

Hypothalamic & pituitary drugs

- GH receptor antagonists
  - * pegvisomant (S.C.)
  - * block GH receptor
  - * ameliorate effects of excess GH production

Hypothalamic & pituitary drugs

- **GH receptor antagonists**

  * use in R_x of acromegaly (given alone or in combination with somatostatin analogues)

  * ADR: increased liver enzymes

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- Somatostatin analogues
- GH receptor antagonists
- **Dopamine agonists**
- Vasopressin receptor agonists
- Vasopressin receptor antagonists

Hypothalamic & pituitary drugs

- **Dopamine agonists**

  long-acting

  * bromocriptine, cabergoline (P.O.)
  * ergot derivatives
  * activate dopamine (D_2) receptor
  * suppress pituitary secretion of prolactin (tuberoinfundibular pathway)

Hypothalamic & pituitary drugs

- **Dopamine agonists**

  * dopaminergic effects on CNS motor control and behavior

  * use in R_x of hyperprolactinemia from prolactinoma and Parkinson's disease

Hypothalamic & pituitary drugs

- **Dopamine agonists**

  * **ADRs: N/V, orthostatic hypotension, psychiatric problems, pulmonary infiltration (high dose)**

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- Somatostatin analogues
- GH receptor antagonists
- Dopamine agonists
- **Vasopressin receptor agonists**
- Vasopressin receptor antagonists

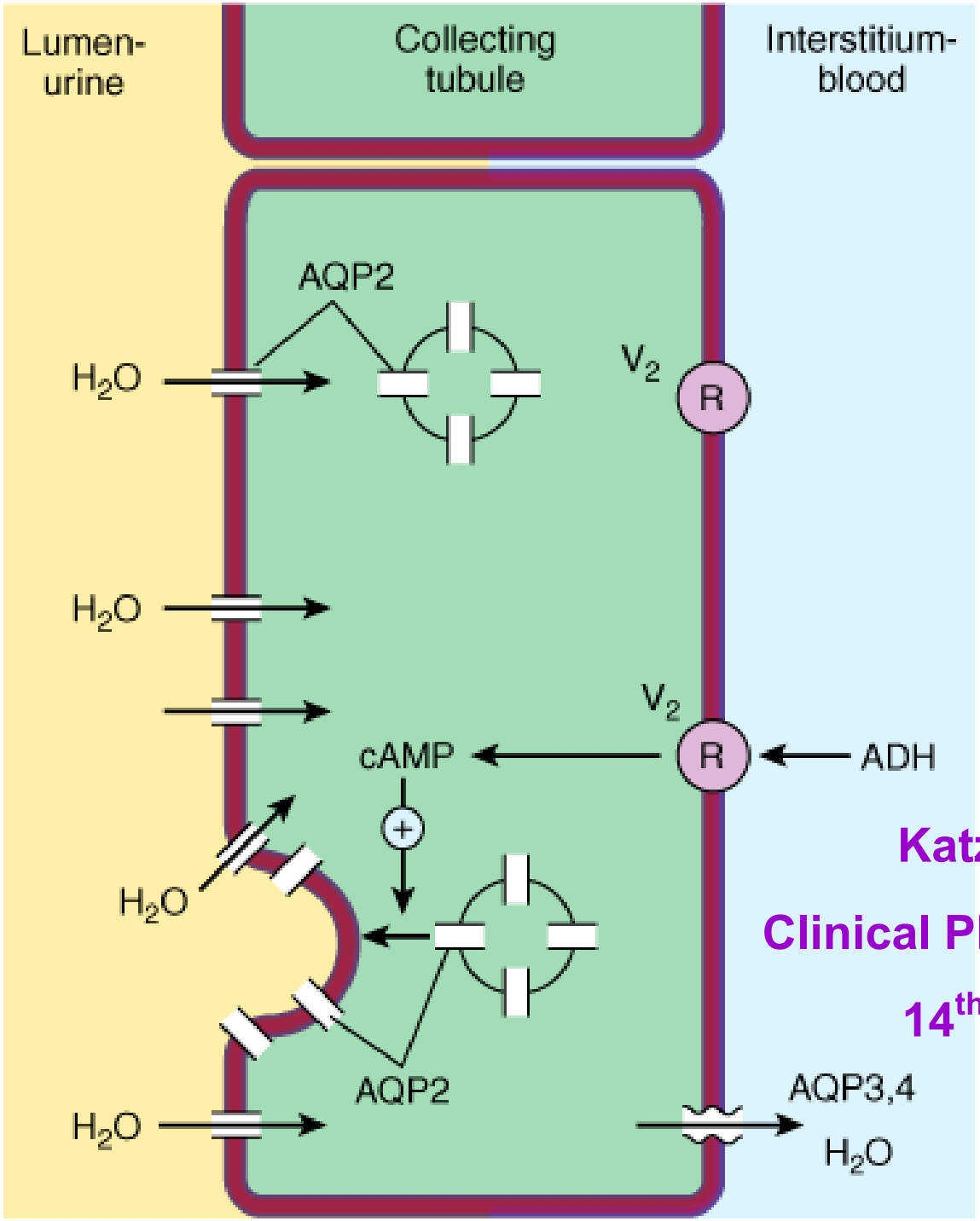
Hypothalamic & pituitary drugs

- **Vasopressin receptor agonists**

  * desmopressin (dDAVP)

  * nasal spray, intranasal sol., P.O., I.V.

  * activate V_2 receptor at cortical collecting duct ---> decreased water excretion



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Hypothalamic & pituitary drugs

- **Vasopressin receptor agonists**

  * use in R_x of central DI & pediatric primary nocturnal enuresis

  * also stimulate the release of vWF from endothelial cells (vWD, uremic bleeding)

  * ADRs: hyponatremia, allergic reactions

Hypothalamic & pituitary drugs

- Recombinant form of human GH
- Somatostatin analogues
- GH receptor antagonists
- Dopamine agonists
- Vasopressin receptor agonists
- **Vasopressin receptor antagonists**

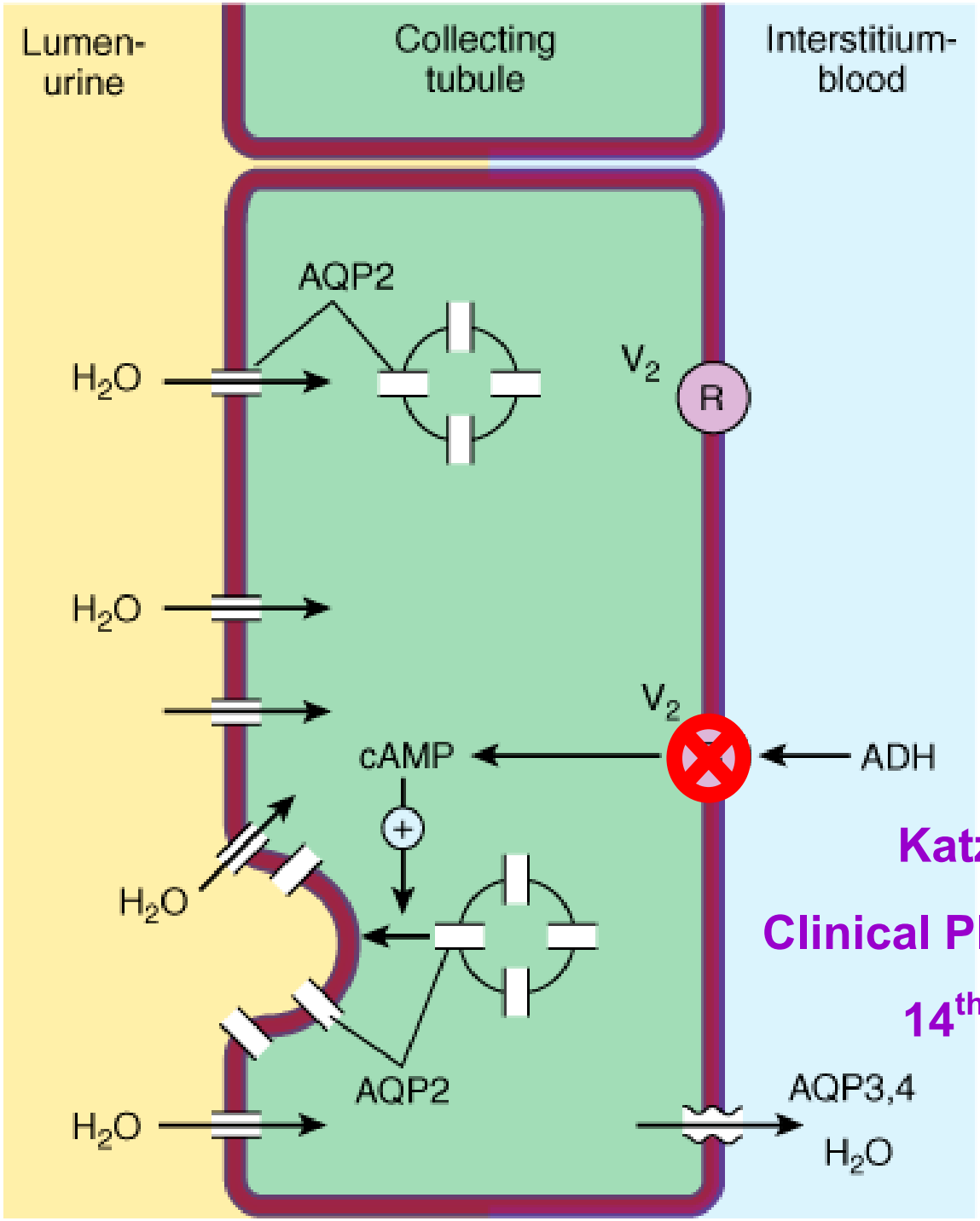
Hypothalamic & pituitary drugs

- **Vasopressin receptor antagonists**

  * conivaptan (I.V.), tolvaptan (P.O.)

  * conivaptan: nonselective V_{1a} and V_2 antagonist

  * tolvaptan: selective V_2 antagonist



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Hypothalamic & pituitary drugs

- **Vasopressin receptor antagonists**

  * very effective in treatment of hyponatremia (esp. SIADH) and as an adjunct to standard diuretic therapy in patients with CHF

  * ADRs: hypernatremia, dehydration

Additional reading