Hypothalamic and pituitary drugs

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Introduction

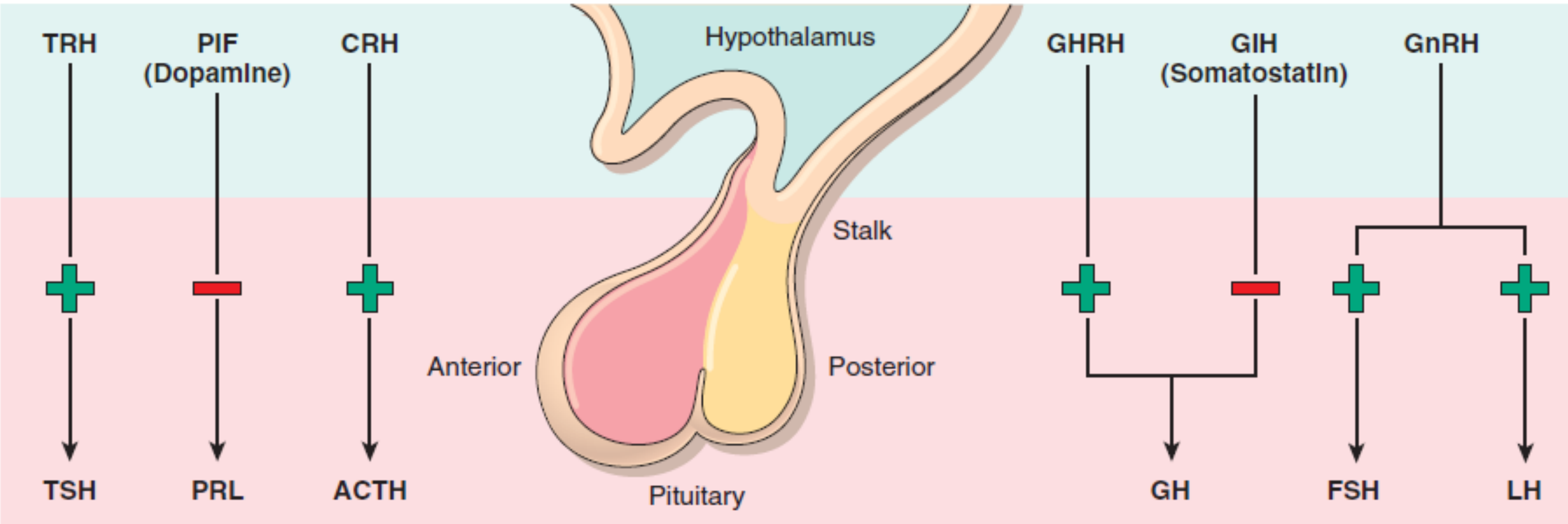

Fig. 20.2 The hypothalamic/pituitary axis. The hypothalamus regulates the secretion of hormones from the adenohypophysis (anterior pituitary gland) by releasing stimulatory (corticotropin-releasing hormone, CRH; growth hormone–releasing hormone, GHRH; gonadotropin-releasing hormone, GnRH; thyrotropin-releasing 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
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Hypothalamic & pituitary drugs

- **Recombinant form of human GH**

  * somatropin (S.C.)

  * acts through GH receptor ---> increase production of IGF-1 ที่ตับ ออกฤทธิ์ที่ bone, muscle

  * 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

(idiopathic intracranial hypertension)

* ADRs: pseudotumor cerebri, edema,

effect GH อยู่แล้ว

hyperglycemia, slipped capital femoral epiphysis

Hypothalamic & pituitary drugs

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Hypothalamic & pituitary drugs

จาก hypothalamus ลง inhibit GH

- Somatostatin analogues

= GHIH

long-acting

แท่ไหนไม่รู้

* octreotide, lanreotide (I.M., S.C., I.V.)

* agonists at somatostatin receptor

main

* inhibit production of GH, and to a lesser extent, of TSH, glucagon, insulin and gastrin

Hypothalamic & pituitary drugs

- Somatostatin analogues

  รักษา GH excess

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

  ลด splanchnic blood flow, ลด portal hypertension

  * also use in acute control of bleeding from esophageal varices

  if ใช้นาน > 6 เดือน

  * ADRs: gallstone, bradycardia

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Hypothalamic & pituitary drugs

- GH receptor antagonists ไทยไม่มีเลย

  * 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 = octreotide analogues)

  * ADR: increased liver enzymes

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Hypothalamic & pituitary drugs

- Dopamine agonists

long-acting

ใช้บ่อย ∴ ถูกกว่า

แพง

* bromocriptine, cabergoline (P.O.)

* ergot derivatives โครงสร้าง ergot nucleus

* activate dopamine (D_2) receptor

* suppress pituitary secretion of

prolactin (tuberoinfundibular pathway)

hypothalamus → ant. pituitary gland

Dopamine ในสมองมี 4 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

nausea, vomiting ~: center ในสมองโดน DA กระตุ้น

* ADRs: N/V, orthostatic hypotension, psychiatric problems, pulmonary

มีน้ำเกิดในปอด

infiltration (high dose)

Hypothalamic & pituitary drugs

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- **Vasopressin receptor agonists**
- Vasopressin receptor antagonists

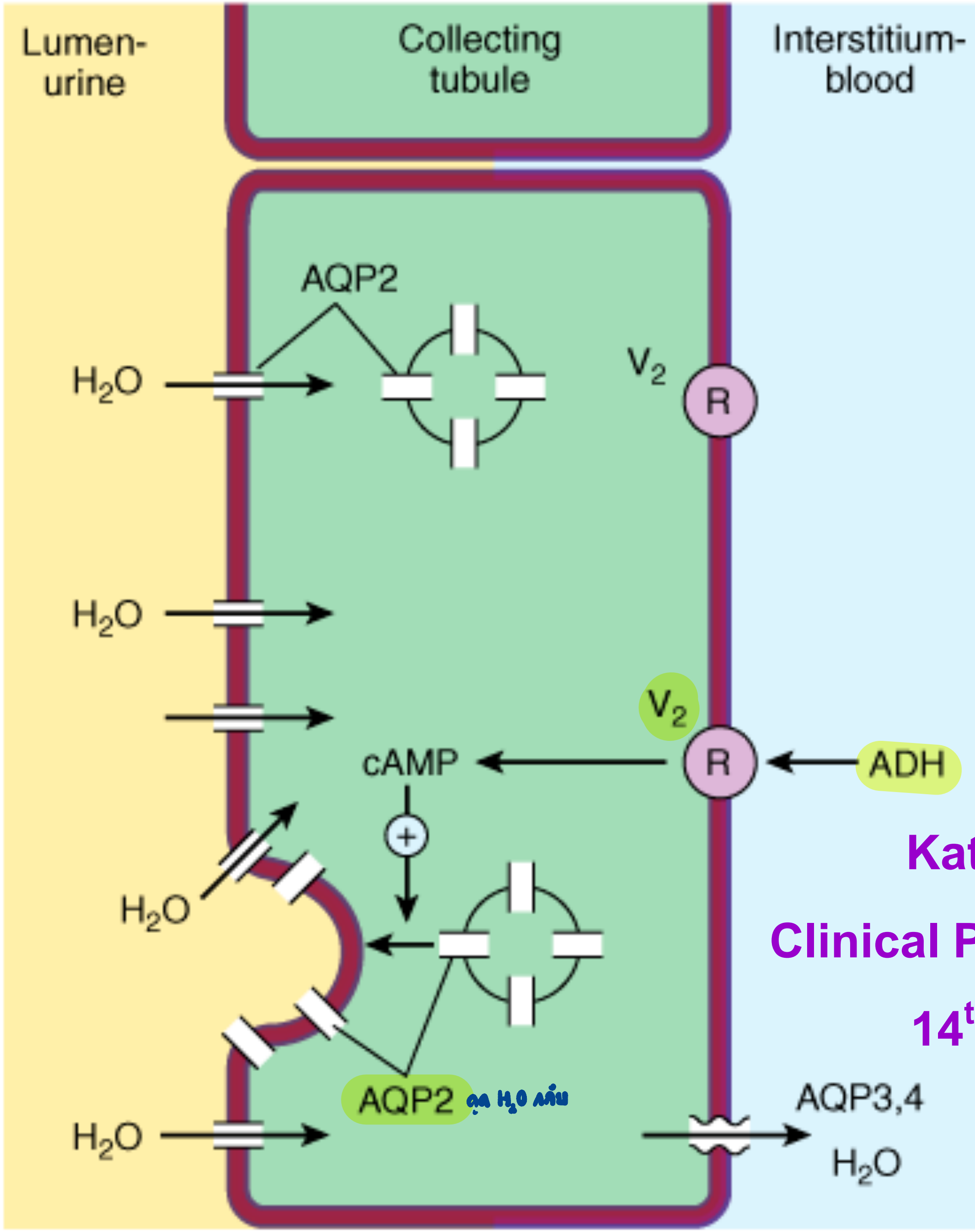
Hypothalamic & pituitary drugs

- Vasopressin receptor agonists

  * desmopressin (dDAVP)

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

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



Katzung Basic & Clinical Pharmacology 14th edition 2018

Hypothalamic & pituitary drugs

- **Vasopressin receptor agonists**

  ∵ AVP deficiency

  * use in R_x of central DI & pediatric

  ฉี่รดที่นอนตอนกลางคืน

  primary nocturnal enuresis

  * also stimulate the release of vWF

  von Willebrand disease

  from endothelial cells (vWD, uremic bleeding)

  ∵ H_2O ↑ → dilute เลือด

  * ADRs: hyponatremia, allergic reactions

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- **Vasopressin receptor antagonists**

Hypothalamic & pituitary drugs

- **Vasopressin receptor antagonists**

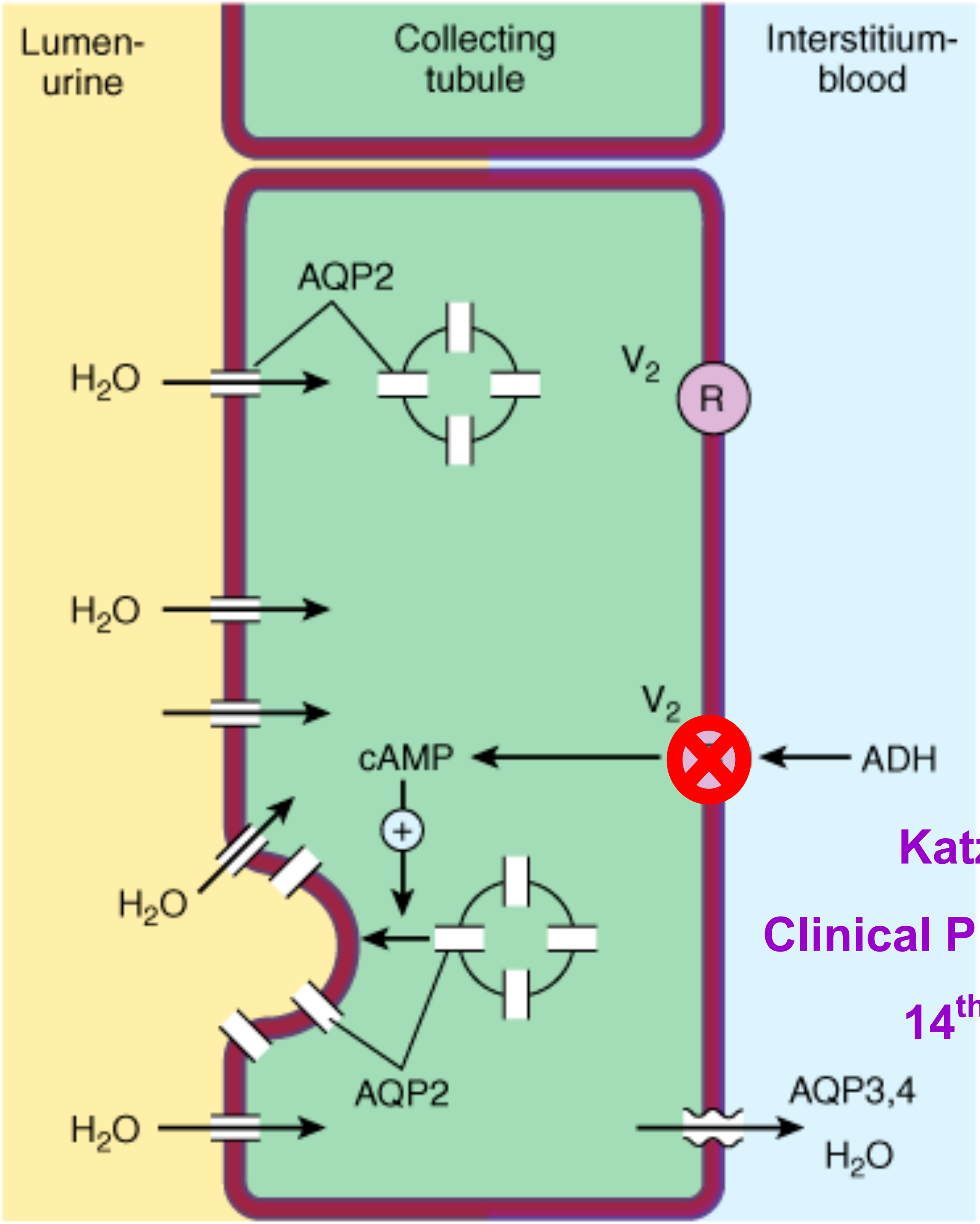
$\boxed{\text{-vaptan}}$ = vasopressin antagonist

ปจบ.ใช้อันนี้มากกว่า

* 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

  ใช้ร่วมกับ diuretic

  adjunct to standard diuretic therapy in patients with CHF

  -: ขับ H_2O ออก ↑

  * ADRs: hypernatremia, dehydration

Additional reading