

The role of the kidney in electrolyte imbalance

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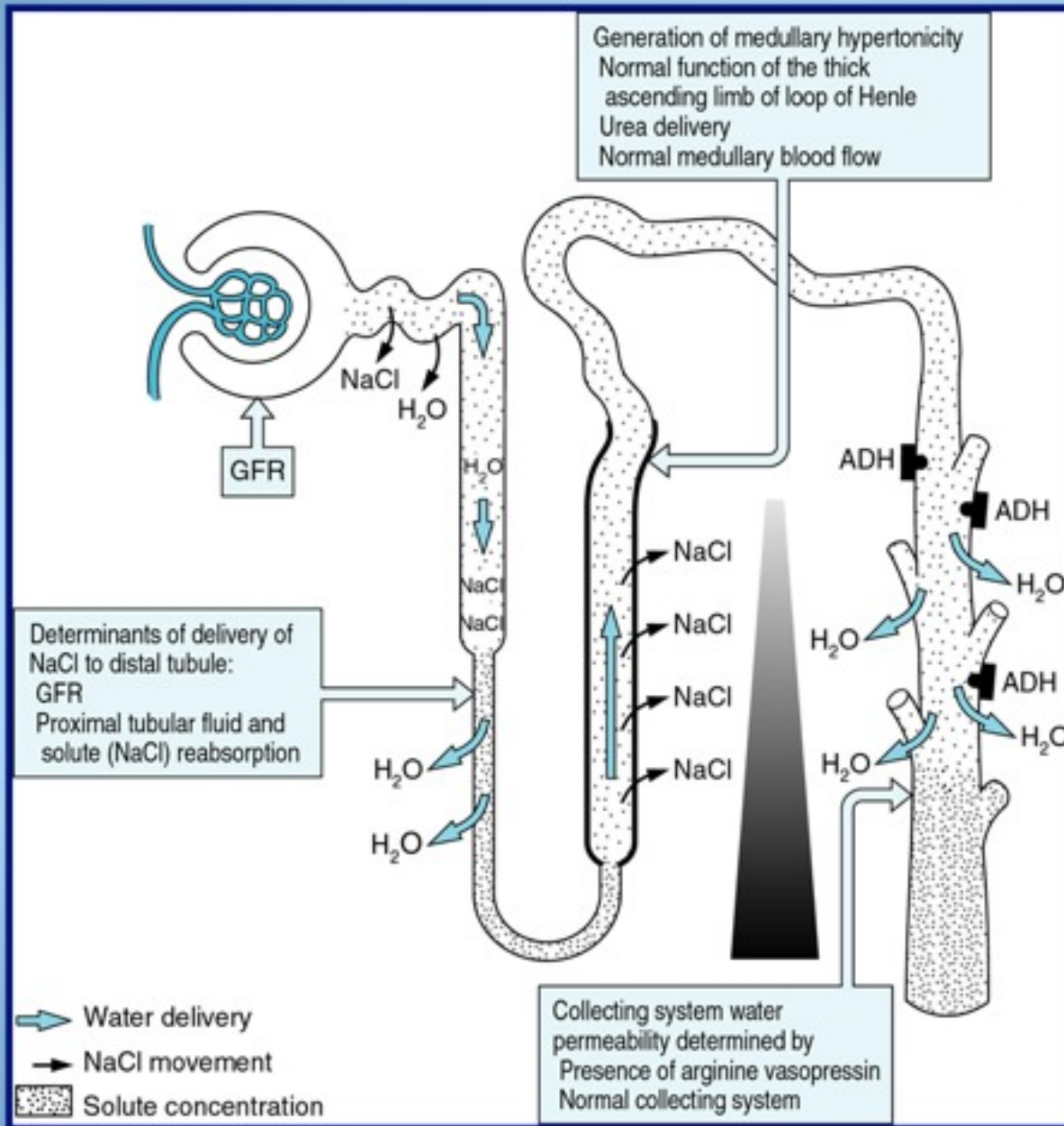
Hyponatraemia: Definition

- Low serum $[\text{Na}^+] \leq 135 \text{ mEq/L (mmol/L)}^1$
 - May have low, normal or high total body sodium¹
 - Not due to lab artifact¹
 - High glucose (and hypo-insulinaemic)
 - High lipids/proteins (if using flame photometry)
 - Mannitol, maltose, glycine
 - Permeable osmolites do not cause hyponatraemia¹
 - Ethanol, mannitol, ethylene glycol
 - BUN
 - Two primary factors to evaluate: Na^+ deficit and water surplus²
 - Na^+ deficit: With non-renal causes, the urine $[\text{Na}^+]$ is usually $< 15 \text{ mmol/L}$
 - Water surplus: No longer excrete the maximum volume (0.5-1 L/hr) of the most dilute urine (around 60 mOsm/kg H_2O)

1. Berl T, Robertson GL. In: *The Kidney*. W.B. Saunders, 2000.

2. Halperin ML. In: *The ACID truth and BASIC facts with a Sweet Touch, an enLYTEment (5th ed)*. Toronto, RossMark Medical Publishers, 2004.

Urine concentration

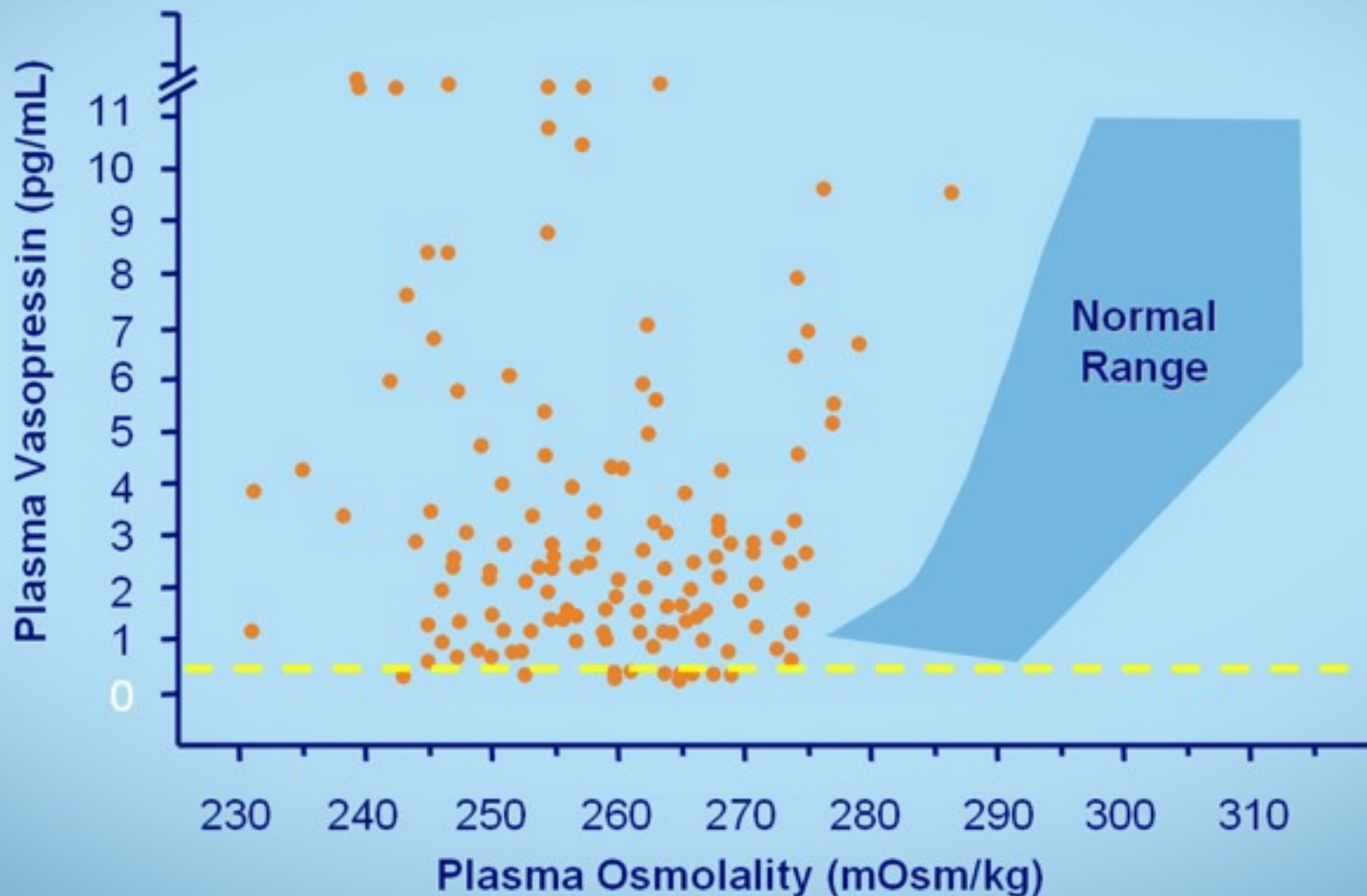


- Glomerular filtration rate
- Sodium reabsorption
- Urea delivery
- Water reabsorption
 - Vasopressin
 - Aquaporin

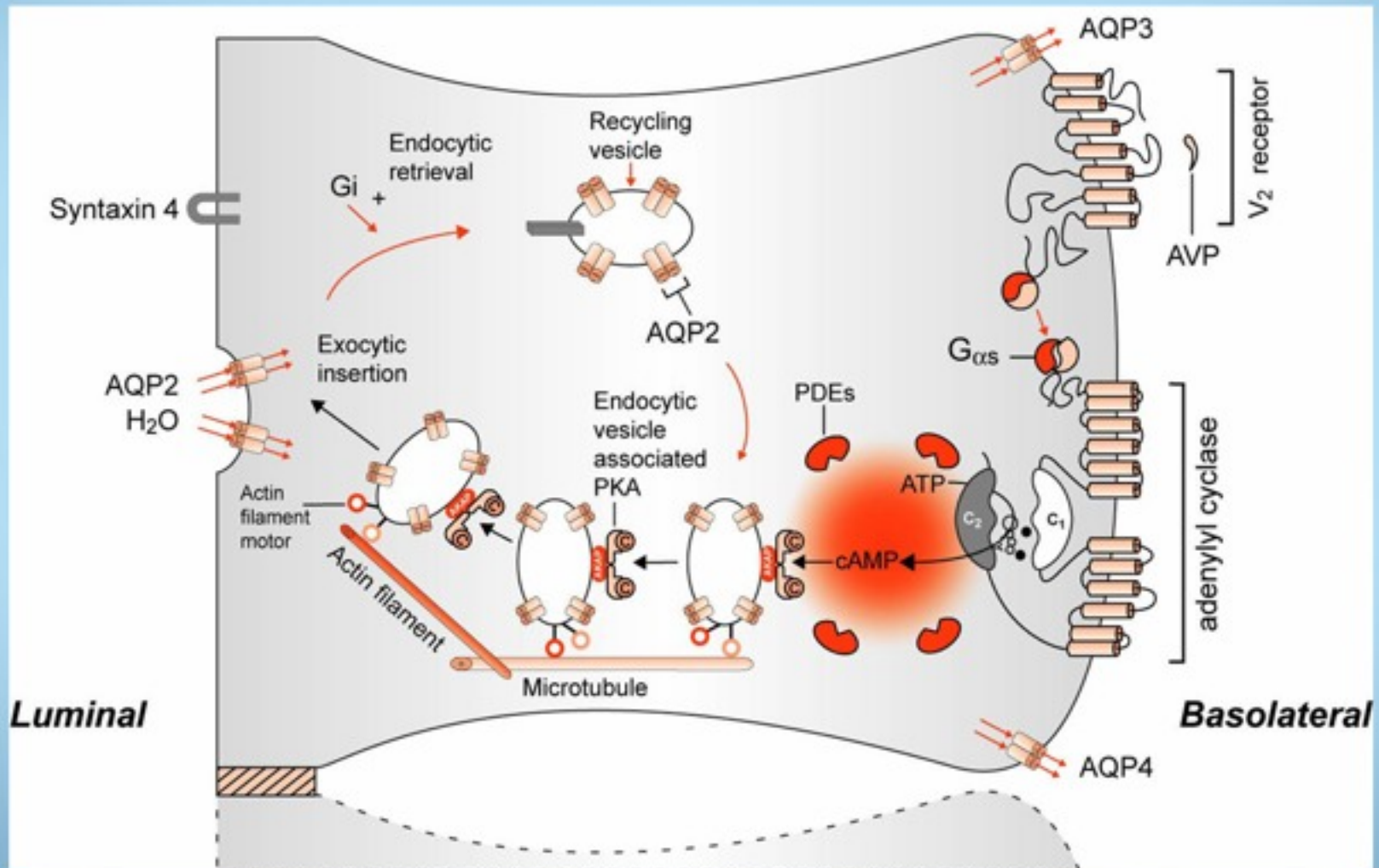
Vasopressin (AVP, ADH)

- Nonapeptide hormone synthesised in the hypothalamus
- Released into the circulation by the posterior pituitary
- V_{1a} vascular receptor:
 - Vasoconstriction
 - Increased peripheral vascular resistance, afterload
- V_2 renal tubular receptor:
 - Water retention
 - Increased intra- and extra-cellular volume overload
 - Hyponatraemia

Plasma vasopressin levels are inappropriately elevated in most patients with SIADH



Vasopressin makes the cortical and medullary collecting ducts permeable to water



Mechanism of action of V₂ antagonists

- Replacing/overlapping with vasopressin in the binding pocket of the vasopressin V₂ receptor
- Inducing a loss-of-function of the V₂ receptor: analogy with Nephrogenic Diabetes Insipidus due to mutations in the vasopressin V₂ receptor gene
- No stimulation of intracellular cAMP in response to vasopressin, no insertion of aquaporin 2 water channels in the luminal membrane in response to vasopressin
- Therefore an aquaretic state is induced with excretion of electrolyte-free water and correction of hyponatraemia¹⁻³

1. Verbalis JG, et al. *Am J Med.* 2007;120(11A):S1–S21.

2. Schrier RW, et al. *N Engl J Med.* 2006;355:2099–2112.

3. Berl T, et al. *J Am Soc Nephrol.* 2010;21:705–712.