The role of the kidney in electrolyte imbalance

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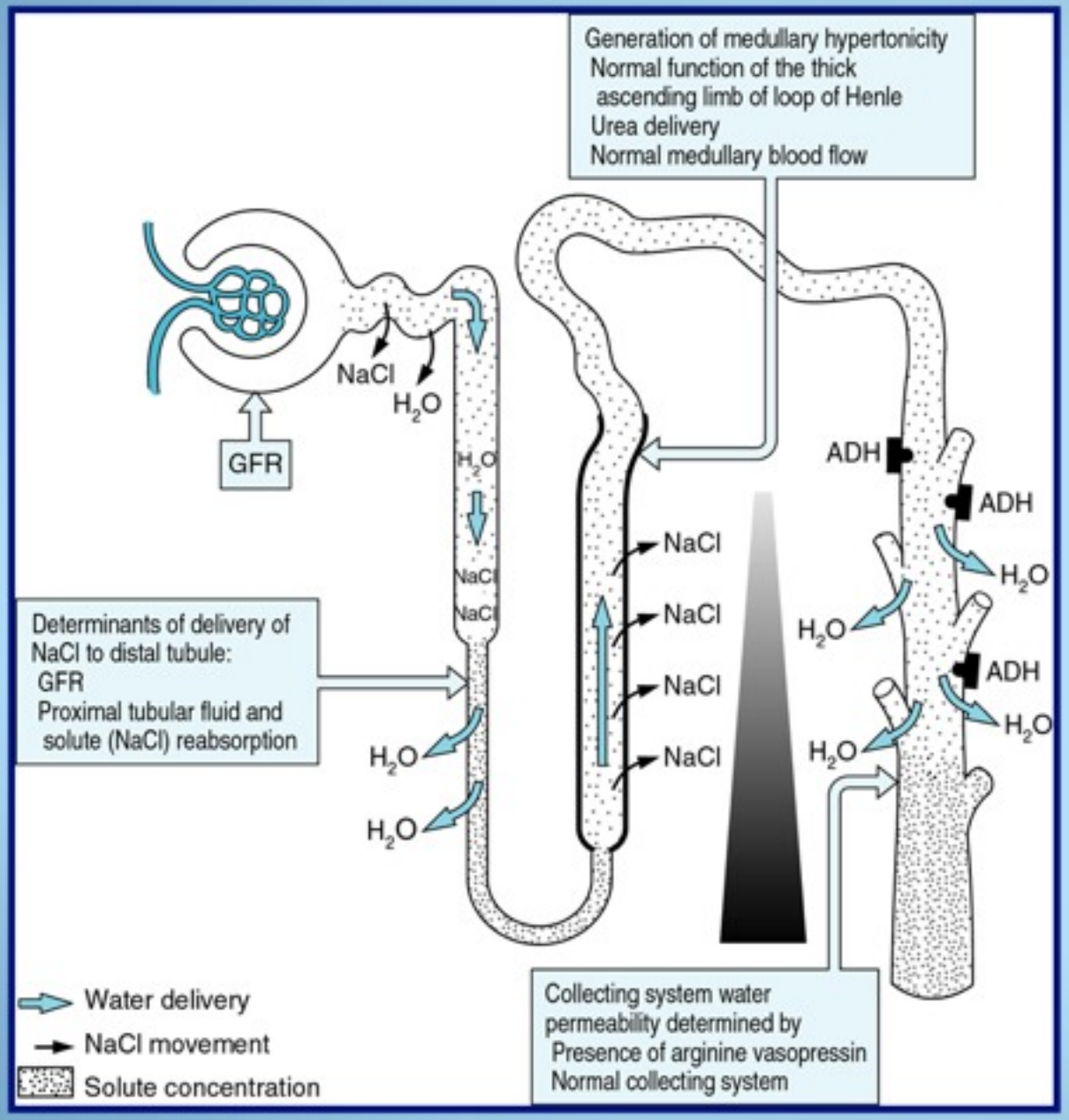
Hyponatraemia: Definition

- Low serum [Na^+] ≤ 135 mEq/L (mmol/L)[1]
  - May have low, normal or high total body sodium[1]
  - Not due to lab artifact[1]
    - High glucose (and hypo-insulinaemic)
    - High lipids/proteins (if using flame photometry)
    - Mannitol, maltose, glycine
  - Permeable osmolites do not cause hyponatraemia[1]
    - Ethanol, mannitol, ethylene glycol
    - BUN
  - Two primary factors to evaluate: Na^+ deficit and water surplus[2]
    - Na^+ deficit: With non-renal causes, the urine [Na^+] is usually < 15 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 enLYTEnment (5th ed)*. Toronto, RossMark Medical Publishers, 2004.

Urine concentration



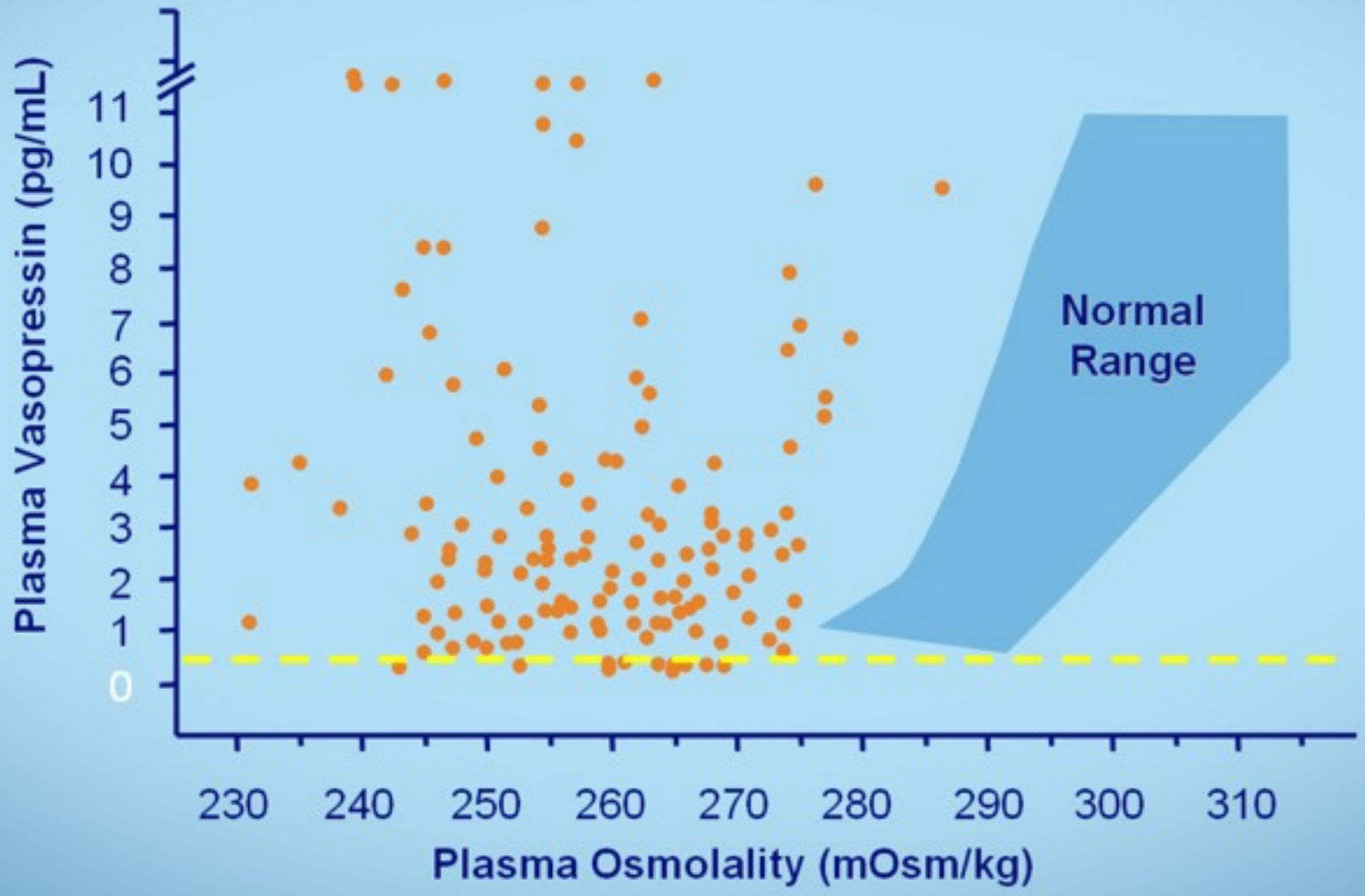
- Glomerular filtration rate
- Sodium reabsorption
- Urea delivery
- Water reabsorption
  - Vasopressin
  - Aquaporin

Kumar S, Berl T. In: Disorders of Water Metabolism, *Comprehensive Clinical Nephrology*. Mosby. 2007.

Vasopressin (AVP, ADH)

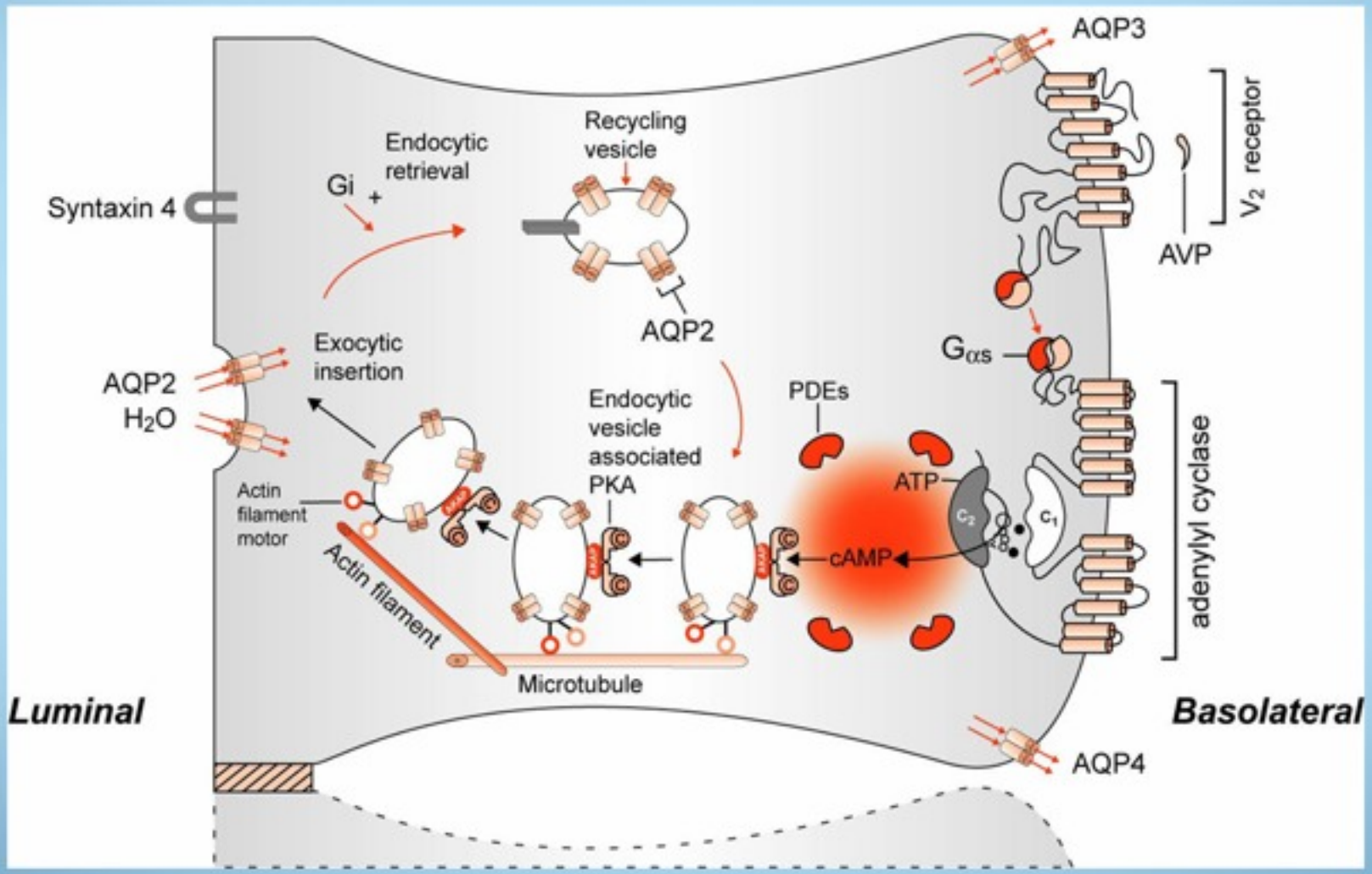
- Nonapeptide hormone synthesised in the hypothalamus
- Released into the circulation by the posterior pituitary
- V_{1a} vascular receptor:
  - Vasoconstriction
  - Increased peripheral vascular resistance, afterload
- V_2 renal tubular receptor:
  - Water retention
    - Increased intra- and extra-cellular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

Plasma vasopressin levels are inappropriately elevated in most patients with SIADH



Robertson GL, et al. *Am J Med.* 1982;72:339–353.

Vasopressin makes the cortical and medullary collecting ducts permeable to water



Bichet DG. *Semin Nephrol.* 2008;28(3):245–251.

Mechanism of action of V_2 antagonists

- Replacing/overlapping with vasopressin in the binding pocket of the vasopressin V_2 receptor
- Inducing a loss-of-function of the V_2 receptor: analogy with Nephrogenic Diabetes Insipidus due to mutations in the vasopressin V_2 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 hyponatraemia[1-3]

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.