HYPONATREMIA PART 1

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INTRODUCTION

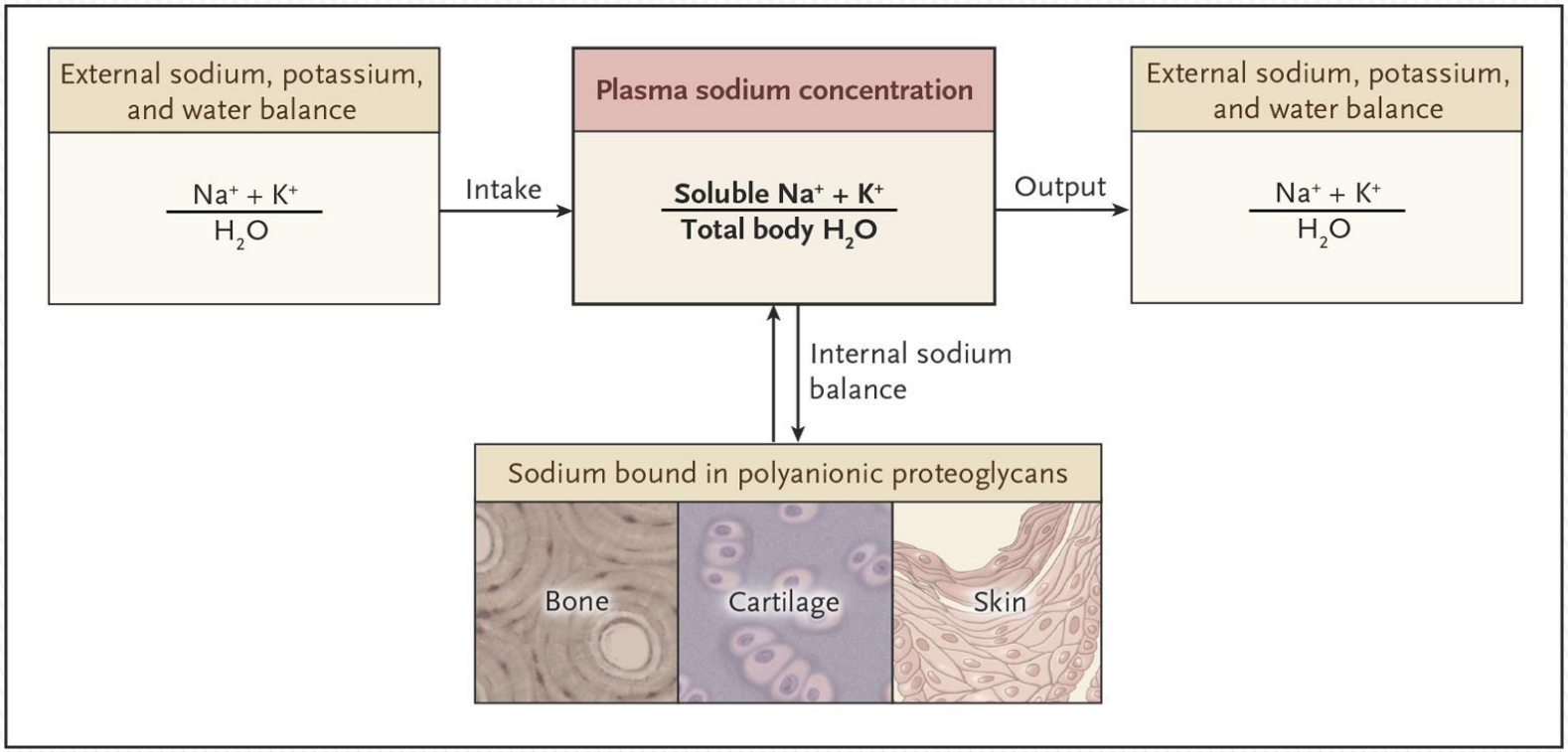
- Human cells dwell in salt water. Their well-being depends on the ability of the body to regulate the salinity of extracellular fluids.

- By controlling water intake and excretion, the osmoregulatory system normally prevents the plasma sodium concentration from straying outside its normal range (135 to 145 mmol per liter).

- Failure of the system to regulate within this range exposes cells to hypotonic or hypertonic stress.

DEFINITION

- Hyponatremia is defined as a plasma Na+ concentration <135 mmol/l.
- The absolute plasma Na+ concentration tells one nothing about the volume status of a given patient.
- Almost always the result of an ↑ in circulating AVP and/or ↑ renal sensitivity to AVP + an intake of free water;except when hyponatremia due to ↓ solute intake.



Internal and External Solute and Water Balance and the Plasma Sodium Concentration. The plasma sodium concentration is determined according to the ratio of the content of sodium and potassium in the body (the numerator of the ratio) to total body water (the denominator of the ratio). This concentration is altered by net external balances (intake minus output) of sodium, potassium, and water and by internal exchange between sodium that is free in solution and sodium that is bound to polyanionic proteoglycans in bone, cartilage, and skin.

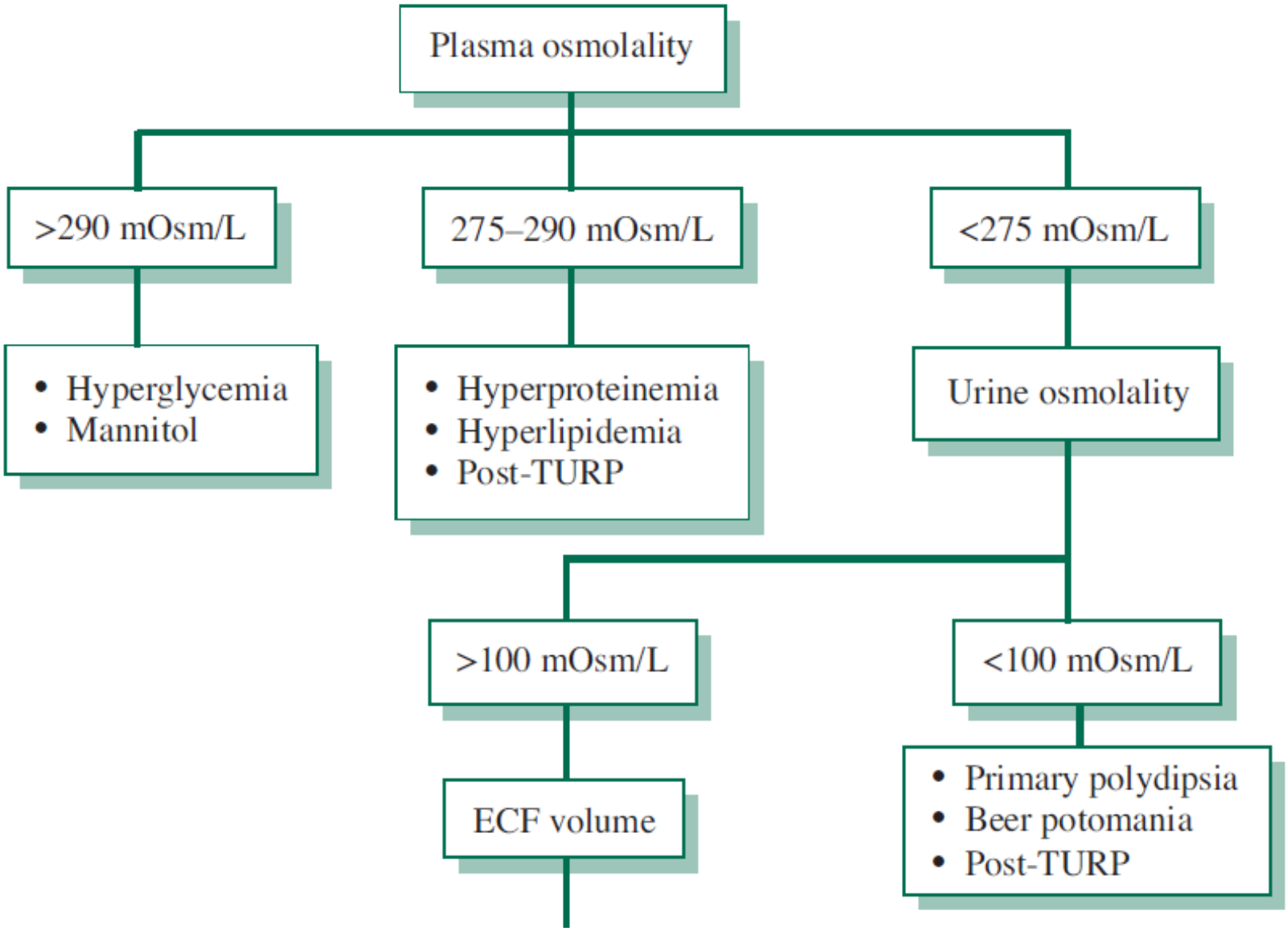
PREVALENCE

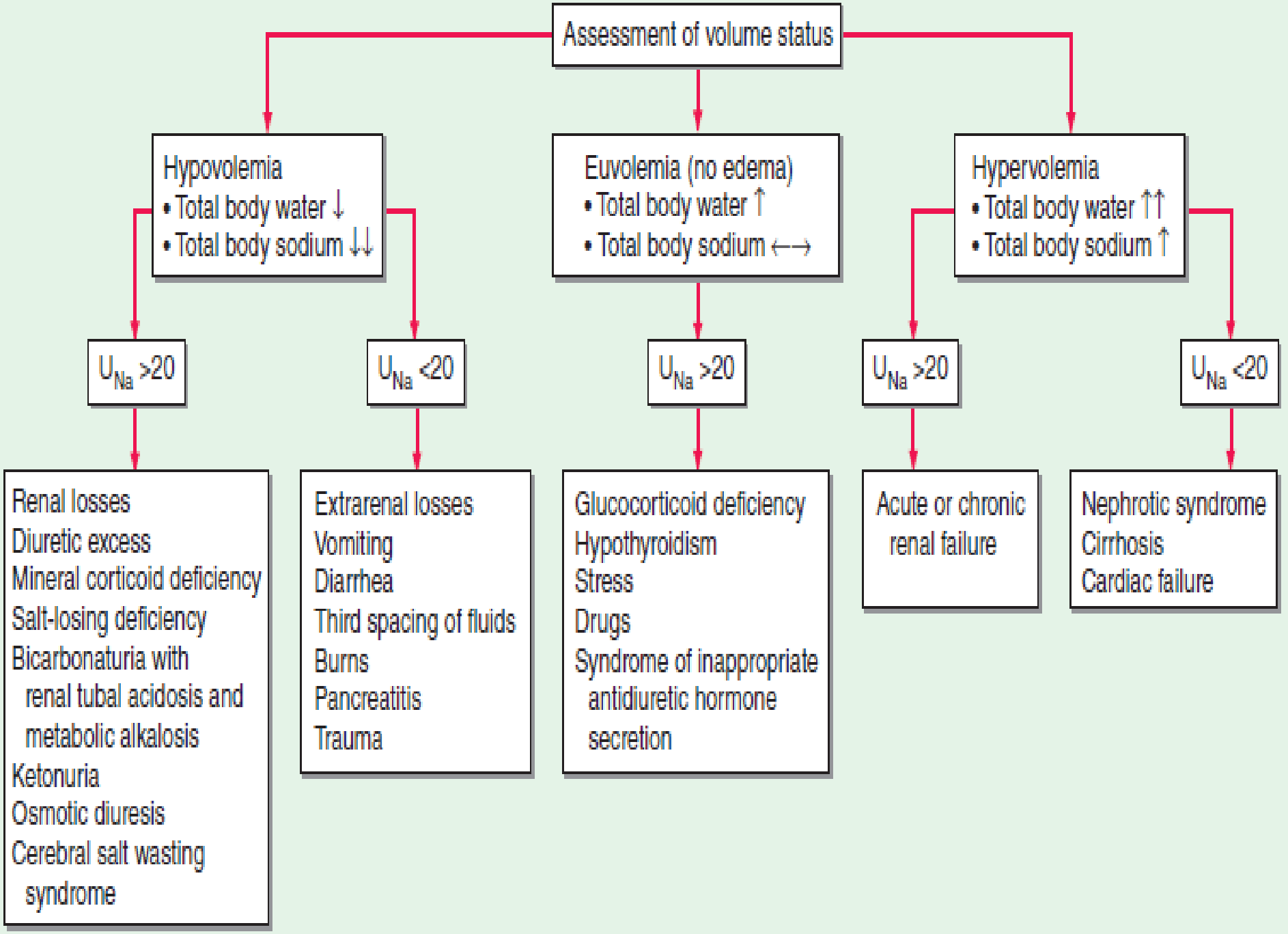
- A very common disorder, occurring in up to 22% of hospitalized patients.

TYPES & EVALUATION

- Divided into three groups depending on clinical history and volume status:

  - Hypovolumic
  - Euvolumic
  - Hypervolumic


Plasma osmolality
>290 mOsm/L
275–290 mOsm/L
<275 mOsm/L
• Hyperglycemia
• Mannitol
• Hyperproteinemia
• Hyperlipidemia
• Post-TURP
Urine osmolality
>100 mOsm/L
<100 mOsm/L
ECF volume
• Primary polydipsia
• Beer potomania
• Post-TURP


Assessment of volume status
Hypovolemia
• Total body water ↓
• Total body sodium ↓↓
Euvolemia (no edema)
• Total body water ↑
• Total body sodium ←→
Hypervolemia
• Total body water ↑↑
• Total body sodium ↑
U_{Na} >20
U_{Na} <20
U_{Na} >20
U_{Na} >20
U_{Na} <20
Renal losses
Diuretic excess
Mineral corticoid deficiency
Salt-losing deficiency
Bicarbonaturia with renal tubal acidosis and metabolic alkalosis
Ketonuria
Osmotic diuresis
Cerebral salt wasting syndrome
Extrarenal losses
Vomiting
Diarrhea
Third spacing of fluids
Burns
Pancreatitis
Trauma
Glucocorticoid deficiency
Hypothyroidism
Stress
Drugs
Syndrome of inappropriate antidiuretic hormone secretion
Acute or chronic renal failure
Nephrotic syndrome
Cirrhosis
Cardiac failure

CONSEQUENCES OF AN ABNORMAL PLASMA SODIUM CONCENTRATION

- Brain swelling from an abrupt onset of hyponatremia results in increased intracranial pressure, impairing cerebral blood flow and sometimes causing herniation.
- Extreme hypotonicity ruptures cell membranes; extreme hypertonicity damages the cytoskeleton and causes breaks in DNA, ultimately leading to apoptosis.

CONT..

- Adaptive changes in brain osmolytes permit survival, but they may also contribute to symptoms.For example, in acute hyponatremia, adaptive release of glutamate, an excitatory neurotransmitter, may increase the susceptibility to seizures.

- Organic osmolytes are small intracellular molecules (e.g., glutamate, taurine, and myo-inositol) that are found throughout nature; their concentrations can vary without perturbing cell functions.

CLINICAL FEATURES

- The symptoms of hyponatremia are primarily neurologic, reflecting the development of cerebral edema within a rigid skull.

- Early symptoms can include nausea, headache, and vomiting. However, severe complications can rapidly evolve, including seizure activity, brainstem herniation, coma, and death.

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- A key complication of acute hyponatremia is normocapneic or hypercapneic respiratory failure; the associated hypoxia may amplify the neurologic injury.
- Normocapneic respiratory failure in this setting is typically due to noncardiogenic, “neurogenic” pulmonary edema, with a normal pulmonary capillary wedge pressure.
- Acute symptomatic hyponatremia is a medical emergency, occurring in a number of specific settings.

Special Situations

- Iatrogenic Acute hyponatremia e.g., when hypotonic intravenous fluids are given to postoperative patients with an increase in circulating AVP.

- Exercise-associated hyponatremia, at marathons and other endurance events, because of “nonosmotic” increase in circulating AVP and excessive free water intake.

- The recreational drugs Molly and ecstasy (MDMA, 3,4-methylenedioxymethamphetamine), cause a rapid and potent induction of both thirst and AVP, leading to severe acute hyponatremia.

Acute Hyponatremia

- Iatrogenic
  - Postoperative: premenopausal women
  - Hypotonic fluids with cause of ↑ vasopressin
  - Glycine irrigation: TURP, uterine surgery
  - Colonoscopy preparation
- Recent institution of thiazides
- Polydipsia
- MDMA ("ecstasy," "Molly") ingestion
- Exercise induced
- Multifactorial, e.g., thiazide and polydipsia

Syndrome of Inappropriate ADH (SIADH)

- **Non-physiologic release of vasopressin** from the posterior pituitary or an ectopic source.

- Common Causes:
  - Neuropsychiatric disorders (e.g., meningitis, encephalitis, acute psychosis, cerebrovascular diseases, head trauma).
  - Pulmonary diseases (e.g., pneumonia, tuberculosis, positive-pressure ventilation, acute respiratory failure).
  - Malignant tumors (most commonly, small cell lung cancer).
  - Drugs: SSRIs, narcotics, antipsychotic agents, chlorpropamide, and NSAIDs

CONT..

- **SIADH Diagnosis**
  - Hypoosmotic hyponatremia
  - Urine osmolality >100 mOsm/L
  - Urinary Na >20
  - Euvolemia
  - The absence of conditions, which stimulate ADH secretion, including volume contraction, nausea, adrenal dysfunction, and hypothyroidism

PROTECTIVE RESPONSE IN BRAIN

- The foot processes of astrocytes, which encircle both brain capillaries and neurons, express aquaporins (such as aquaporin-4) that allow water to cross the blood–brain barrier.

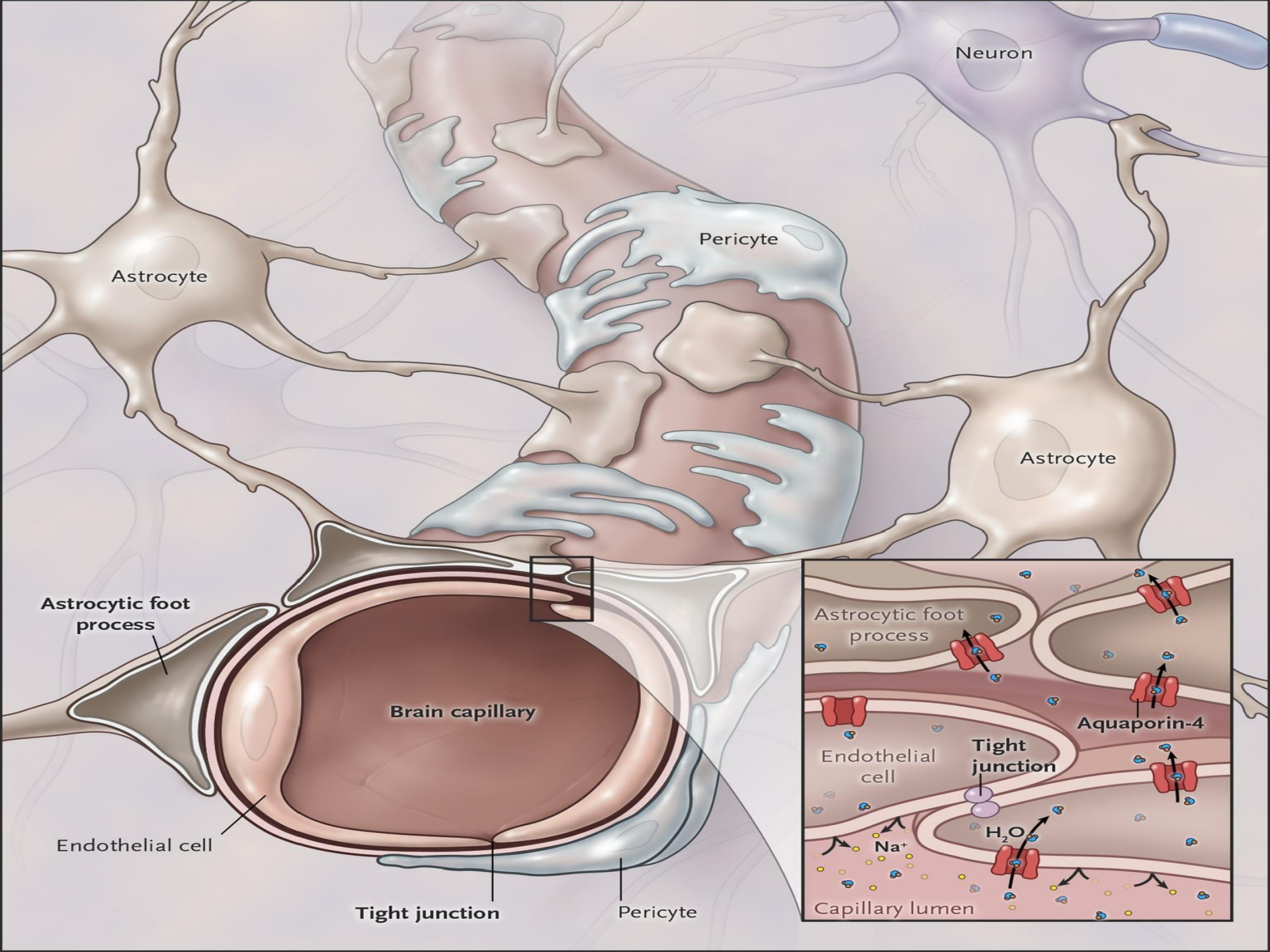
- Astrocytes protect neurons from osmotic stress; in response to hypotonicity, a cell-to-cell transfer of taurine to adjacent astrocytes allows neurons to maintain their volume while astrocytes swell.

CONT..

- Within 24 to 48 hours after this transfer, astrocytes restore their volume through loss of organic osmolytes, but this makes them vulnerable to injury from rapid normalization of the plasma sodium concentration.

- Because of the down-regulation of transporters, recovery of lost brain osmolytes may take a week or longer.

- Therefore, rapid correction of hyponatremia is a hypertonic stress to astrocytes that are depleted of osmolytes, triggering apoptosis, disruption of the blood–brain barrier, and, eventually, brain demyelination.


Neuron
Pericyte
Astrocyte
Astrocyte
Astrocytic foot process
Brain capillary
Endothelial cell
Tight junction
Pericyte
Astrocytic foot process
Aquaporin-4
Endothelial cell
Tight junction
H_2O
Na^+
Capillary lumen

OSMOTIC DEMYELINATION SYNDROME

- Rapid correction of hyponatremia is a hypertonic stress to astrocytes that are depleted of osmolytes, triggering apoptosis, disruption of the blood–brain barrier, and, eventually, brain demyelination.

- Brain injury after rapid correction of chronic hyponatremia manifests as a biphasic illness called the osmotic demyelination syndrome: an initial reduction in symptoms is followed by a gradual onset of new neurologic findings.

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- The clinical spectrum of the osmotic demyelination syndrome is broad and can include seizures, behavioral abnormalities, and movement disorders

- The lesions of ODS classically affect the pons , a structure wherein the delay in the reaccumulation of lost osmotic osmolytes is particularly pronounced.

CONT…

- Clinically, patients with central pontine myelinosis present 1 or more days after overcorrection of hyponatremia.

- The presentation can be Paraparesis, quadriparesis, dysphagia, dysarthria, diplopia, “a locked in syndrome,” and/or loss of consciousness.

CONT…

- Other regions invoved (Extra pontine myelinosis) in order of frequency:
  - Cerebellum
  - Lateral geniculate body
  - Thalamus
  - Putamen
  - Cerebral cortex or subcortex
- Clinical presentation of extrapontine myelinosis :
  - Ataxia
  - Mutism
  - Parkinsonism
  - Dystonia
  - Catatonia

THANK YOU