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Comprehensive Overview of Hypernatremia: Pathophysiology, Diagnosis, and Management

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Abstract

Hypernatremia, defined as an elevated serum sodium concentration, is a critical electrolyte imbalance with significant neurological and systemic effects. Effective management hinges on understanding the condition's underlying aetiology, such as dehydration, excessive sodium intake, or impaired renal water handling. The approach to treatment varies by onset and severity: acute hypernatremia (<48 hours) necessitates rapid but controlled correction to prevent complications like vascular rupture or cerebral bleeding, while chronic hypernatremia (≥48 hours) requires gradual intervention to mitigate the risk of cerebral edema. Treatment focuses on restoring water balance through intravenous fluids (typically hypotonic solutions) while monitoring serum sodium levels to prevent overcorrection. Identifying and addressing associated conditions, such as diabetes insipidus (DI) or volume depletion, is crucial. Advances in the understanding of pathophysiology have informed clinical guidelines, emphasizing personalized care based on patient-specific factors, such as age, comorbidities, and the underlying cause of hypernatremia. Despite improvements in treatment protocols, challenges remain in managing hypernatremia in critically ill patients, where both rapid and excessively slow corrections are associated with increased mortality. Further research is needed to refine management strategies, develop predictive biomarkers for better risk assessment, and optimize outcomes in diverse patient populations. This review highlights the importance of a multidisciplinary approach in diagnosing, treating, and preventing complications of hypernatremia, ensuring safer and more effective care delivery.

Key words: hypernatremia; water-electrolyte balance; fluid balance; diabetes insipidus

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Introduction

Hypernatremia, defined as a serum sodium level greater than 145 mmol/L, is commonly encountered both in the community and in-patient settings (Al-Absi et al, 2012; Liu et al, 2024; Nasser et al, 2024; Yun et al, 2023). The global prevalence of hypernatremia has been reported as being anywhere between 1–5% and varies across clinical settings, with reports of 0–5% in hospitalized patients and 0.2–1% in the emergency department (Arzhan et al, 2022; Nasser et al, 2024; Yun et al, 2023). However, this figure can be as high as 6–47% in the intensive care setting (Brennan et al, 2021; Kitisin et al, 2025; Nasser et al, 2024; Oude Lansink-Hartgring et al, 2016; Yun et al, 2023). According to a Dutch cohort study, the incidence of hypernatremia has increased significantly, rising from 13% to 24% over

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the past two decades which reflects a broader trend observed where the prevalence of dysnatremia (hyponatremia and hypernatremia) has shifted from predominantly hyponatremia to hypernatremia (Oude Lansink-Hartgring et al, 2016).

Acute hypernatremia, often overlooked, significantly increases morbidity and mortality rates due to severe complications such as neurological damage and dehydration (Feigin et al, 2023; Jansch et al, 2023; Kamatam et al, 2023; Mc Causland et al, 2014). Such severe symptoms are likely to manifest following an acute elevation in serum sodium levels above 160 mmol/L, while increased mortality risks occur with levels above 180 mmol/L (Kamatam et al, 2023). The rapid onset of hypernatremia can result in brain cells being impacted by the differences between the intracellular and extracellular compartments (Kamatam et al, 2023). This osmotic imbalance is particularly hazardous for the elderly as age-related physiological changes and impaired thirst perception hinder their ability to compensate for these shifts effectively (Kamatam et al, 2023; Sam and Ing, 2023; Yun et al, 2023). While published studies have demonstrated hypernatremia to be associated with higher rates of mortality among older, hospitalised patients than any other electrolyte abnormality, other studies have attributed this to underlying comorbidities (Arzhan et al, 2022; Feigin et al, 2023; Pokhriyal et al, 2024; Wu et al, 2023; Yun et al, 2023).

Effective management of hypernatremia requires a multidisciplinary approach that includes accurate diagnosis, identification of underlying causes, and tailored treatment strategies. The optimal treatment of hypernatremia should consider its severity, duration and mode of clinical presentation to avoid neuronal cell shrinkage and resultant brain injury (Jansch et al, 2023; Wang et al, 2024; Wu et al, 2023; Yun et al, 2023). The importance of integrating evidence-based clinical guidelines, emerging technologies, and patient-centred care help to improve outcomes for hypernatremia.

As the global burden of electrolyte imbalances continues to grow due to aging populations and rising prevalence of chronic illnesses, addressing hypernatremia with precision medicine and interdisciplinary care is becoming increasingly critical (Issa et al, 2025). Wootton et al (2024) stated in their recent comprehensive review that there exists a complex interplay between anthropogenic climate change and dysnatremia, which is postulated to be linked to significant morbidity and mortality. While recent literature provides robust evidence supporting a correlation between higher environmental temperatures and increased rates of hyponatremia, the relationship between elevated temperatures and hypernatremia remains less well-established and requires further investigation (Kutz et al, 2020; Mannheimer et al, 2022; Meade et al, 2020; Wootton et al, 2024).

Epidemiology

Hypernatremia is a serious electrolyte imbalance that disproportionately affects vulnerable populations, including neonates, infants, children, the elderly, and nursing home residents, particularly those with restricted mobility or cognitive impairments such as dementia (Brennan et al, 2021; Hu et al, 2022; Imai et al, 2019;

Sam and Ing, 2023). In hospitalized patients, its prevalence ranges from 1.9% to 30.8% and is strongly associated with both in-hospital and long-term mortality and increased healthcare costs (Brennan et al, 2021; Gautam et al, 2024; Jansch et al, 2023; Otterness et al, 2023; Wootton et al, 2024).

Critically ill individuals, who are particularly prone to osmotic imbalances due to altered fluid and electrolyte management, are at an even higher risk, with prevalence reaching up to 10% in this population (Yun et al, 2023). Hypernatremia in the hospital setting often results from inadequate water intake due to impaired self-hydration and insufficient clinical monitoring, compounded by inappropriate fluid prescriptions, such as hypertonic saline administration (Braun et al, 2015; Kamatam et al, 2023; Yun et al, 2023). These issues are further exacerbated in intensive care units (ICUs), where a considerable number of studies have focused on hypernatremia prevalence and outcomes, highlighting its association with fluid management challenges and renal dysfunction (Feigin et al, 2023; Fried and Palevsky, 1997; Jansch et al, 2023; Molin et al, 2025; Moradi et al, 2020).

As the global burden of electrolyte imbalances continues to grow due to aging populations and rising prevalence of chronic illnesses, addressing hypernatremia with precision medicine and interdisciplinary care is becoming increasingly critical (Issa et al, 2025; Meade et al, 2020; Regati and Vijayakumar, 2020; Sasai et al, 2023).

Classification and Aetiology

Hypernatremia is a clinical finding characterized by serum sodium concentrations exceeding 145 mmol/L, reflecting a water deficit relative to sodium levels in the body. Normal sodium levels in adults range between 135–145 mmol/L (normonatremia), with hypernatremia further classified into

- mild (146–149 mmol/L),
- moderate (150–169 mmol/L), and
- severe ($\geq$170 mmol/L) (Cabassi and Tedeschi, 2017; Nur et al, 2014; Sam and Ing, 2009).

Severe hypernatremia has been variably defined in the literature as serum sodium levels exceeding >152 mmol/L, >155 mmol/L, or >160 mmol/L (Sam and Ing, 2023). However, there is no universally accepted consensus on the exact threshold, reflecting variability in clinical practice and study methodologies (Sam and Ing, 2023). Recent literature suggests adding "extreme hypernatremia" (>190 mmol/L) as a rare category seen infrequently in clinical practice (Arambewela et al, 2016; Kamatam et al, 2023). This inconsistency highlights the need for standardized definitions to help guide diagnosis and treatment.

Hypernatremia is a disruption in homeostasis, characterized by a laboratory finding indicative of a water imbalance in the body, resulting from either water loss or excessive sodium intake (Yun et al, 2023). It reflects a disruption in homeostasis that requires careful clinical evaluation to determine its underlying cause and appropriate management. This highlights the importance of viewing hypernatremia as a symptom of a broader systemic issue rather than an isolated condition.

Table 1. Causes of hypernatremia.

Condition	Common causes	Less common causes
Water deficit	Renal losses: osmotic diuretics, hyperglycaemia, polyuria of acute tubular necrosis	Diabetes insipidus: central, nephrogenic, systemic disease, drugs
	Non-renal losses: gastrointestinal loss (diarrhoea, vomiting, stomal losses) & Skin loss: excess sweating/burns	Increased insensible losses: pyrexia, hyperventilation
	Inability to obtain water: lack of access to free water or inadequate water intake (dehydration)	Impaired thirst mechanism: secondary to underlying neurological abnormalities or hypothalamic dysfunction
Sodium excess	Ingestion of high sodium: inappropriate formula concentration, high osmolality rehydration solutions, salt poisoning	Hyperaldosteronism: primary hyperaldosteronism: Conn's syndrome
	Iatrogenic causes: hypertonic saline or sodium bicarbonate infusions	Secondary hyperaldosteronism: congestive cardiac failure (CCF), nephrotic syndrome, steroids

Hypernatremia can be acute, i.e., developing within 48 hours, or chronic, persisting beyond this period with distinct implications for management and outcomes (Muhsin and Mount, 2016; Pokhriyal et al, 2024; Sterns, 2015; Yun et al, 2023). Acute hypernatremia often requires rapid yet controlled correction to prevent complications like vascular rupture or cerebral bleeding. Chronic hypernatremia elicits adaptive intracellular osmolyte production, reducing immediate risks but making the brain susceptible to cerebral edema if corrected too quickly (Muhsin and Mount, 2016; Sterns, 2015). Understanding these temporal and severity classifications is essential for tailoring therapeutic interventions and improving patient outcomes.

Causes of Hypernatremia

Hypernatremia typically arises from a combination of water and electrolyte deficits, with free water loss exceeding sodium loss. This leads to concentrating the sodium in extracellular fluid (ECF) (Moradi et al, 2020). Although less common, hypernatremia can also result from an increase in sodium intake or retention.

Several conditions can lead to a state of water deficit (Table 1). This condition is primarily caused by a net loss of water, usually through renal routes. For example, in osmotic diuresis or diabetes insipidus, the kidneys lose excessive amounts of water due to either a deficiency of antidiuretic hormone (ADH) or resistance to its effects, resulting in a water depletion state. On the other hand, non-renal losses (e.g., insensible losses or gastrointestinal (GI) losses) can occur when more water than sodium is lost, resulting in a net concentration of sodium in the blood (Lewis, 2023; Sonani et al, 2024).

The inability to obtain water is especially common in elderly individuals, infants or babies that are breastfed (due to inadequate milk supply) and critically ill patients (Moradi et al, 2020). Less commonly, hypernatremia results from hypertonic sodium gain, often due to medical interventions or accidental sodium loading.

Renal causes include conditions like hyperglycaemia and mannitol administration, which increase urinary solute excretion and osmolality. These aetiologies underscore the complexity of diagnosing and managing hypernatremia effectively.

Pathophysiology

Understanding the normal physiological mechanisms for maintaining eunatremia (serum sodium 135–145 mmol/L) is crucial for correctly identifying the cause of hypernatremia (Muhsin and Mount, 2016; Sonani et al, 2024; Yun et al, 2023). Serum sodium level and osmolality are both normally tightly regulated by three major mechanisms, namely thirst, ADH and the renin-angiotensin system (RAS) (Sonani et al, 2024; White et al, 2025; Yun et al, 2023) (Fig. 1).

Normal serum osmolality, maintained within the range of 280–295 mOsm/kg, relies on the coordinated actions of vasopressin, thirst mechanisms, and renal responses to vasopressin. Hypernatremia arises when these regulatory mechanisms fail, leading to imbalances in water and sodium homeostasis.

Hypernatremia occurs due to an excess of sodium relative to water in the body, resulting in plasma hyperosmolality (Agrawal et al, 2008; Muhsin and Mount, 2016; Sonani et al, 2024; White et al, 2025; Yun et al, 2023). The increase in osmolality drives water out of cells, causing cellular dehydration, particularly in the brain. Increased plasma osmolality, generally due to elevated sodium levels, activates the body's thirst mechanism via osmosensors primarily located in the anterior hypothalamus, with arginine vasopressin (AVP) (antidiuretic hormone, ADH) serving as the primary regulator. This hormone triggers thirst and works to conserve water in the kidneys by concentrating urine to restore balance (Agrawal et al, 2008; Muhsin and Mount, 2016; Robertson, 2016; Sonani et al, 2024; White et al, 2025).

Top Tips

1. Thirst mechanism: When sodium levels rise, the osmoreceptors situated in the hypothalamus detect an increase in osmolality. This firstly initiates the neural mechanisms of thirst and prompts drinking, and secondly triggers the posterior pituitary gland to release ADH (McKinley and Johnson, 2004; Augustine et al, 2020).
2. ADH secretion: From stimulation of the hypothalamus, the posterior pituitary gland releases ADH which increases water reabsorption in the kidneys, helping to dilute the excess sodium in the blood (Cecil et al, 2012).

Signs and Symptoms of Hypernatremia

Neurological Symptoms

Hypernatremia predominantly affects the central nervous system due to brain cell shrinkage caused by osmotic imbalances. The severity of symptoms depends on the rate and magnitude of sodium concentration increases, becoming critical when levels exceed 160 mEq/L (Braun et al, 2015; Sonani et al, 2024). Early symptoms include thirst, weakness, neuromuscular excitability, and hyperreflexia, which

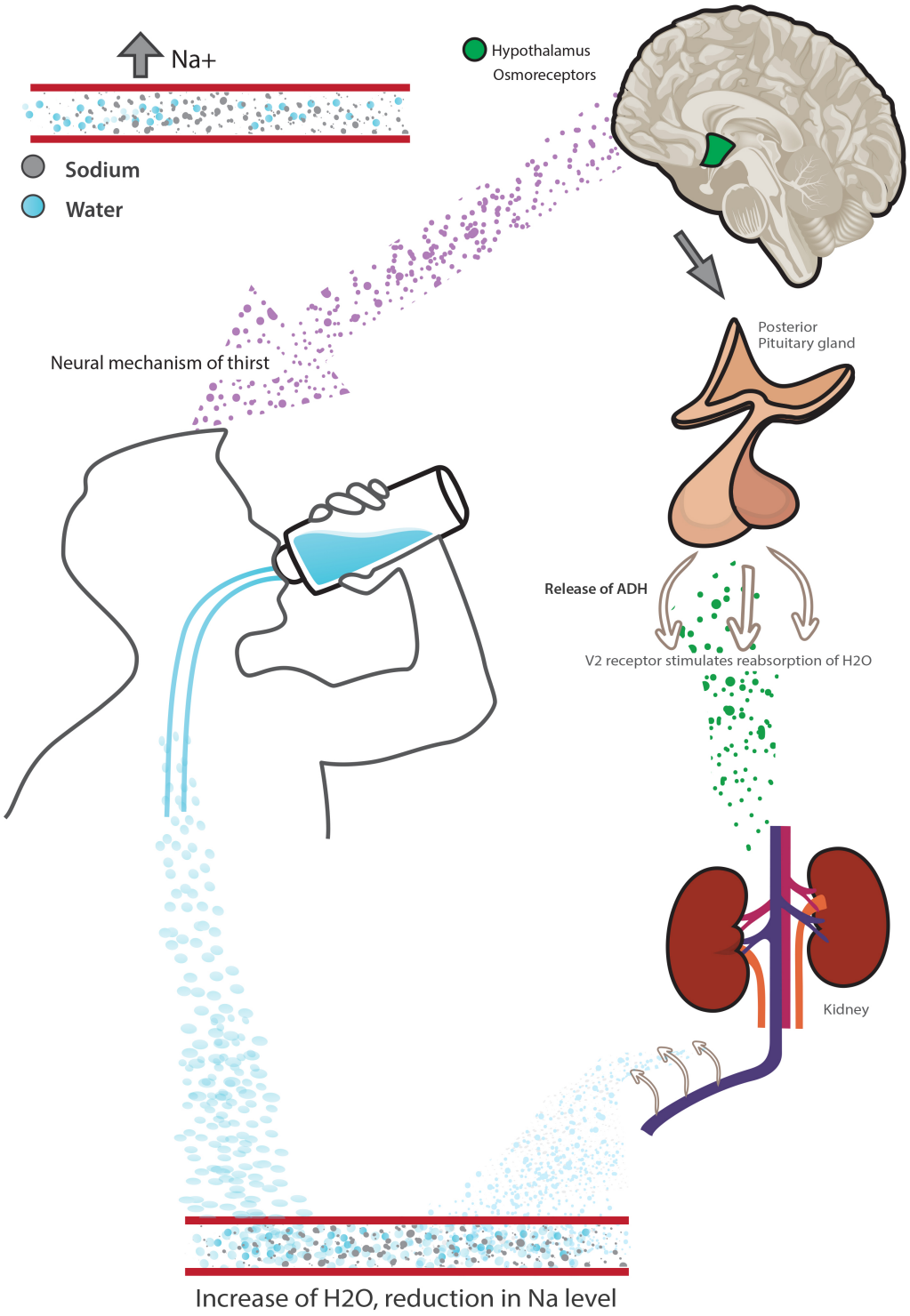

Fig. 1. Diagram showing normal physiological response to hypernatremia. The figure was created using Adobe Illustrator, version 29.5.1 (Adobe Inc., San Jose, CA, USA). Artwork for brain section contains imagery from: Adobe stock: ref AdobeStock_762647807. ADH, antidiuretic hormone.

can progress to confusion, seizures, and coma in severe cases. In later stages, symptoms such as muscle cramps and coma are more pronounced, especially when serum sodium exceeds 160 mmol/L (Table 2 lists other common symptoms).

Table 2. Signs and symptoms of hypernatremia.

Clinical manifestation	Common symptoms	Less common symptoms
Cognitive dysfunction and neurologic symptoms	Lethargy, confusion, irritability, obtundation, abnormal speech	Seizures, nystagmus, myoclonic jerks, and focal neurologic deficits (less common in adults)
Dehydration and volume depletion	Orthostatic hypotension, tachycardia, oliguria, dry oral mucosa, abnormal skin turgor, intense thirst	
Other clinical findings to suggest the cause of hypernatremia	Weight loss, generalized weakness, fever, and laboured respiration	

Mortality of Hypernatremia Across Settings

Hypernatremia is associated with significant mortality, varying by severity and clinical setting. Mortality rates range from 40% to 55%, though this is often attributed to the underlying condition rather than hypernatremia itself (Ates et al, 2016; Bataille et al, 2014; Kamatam et al, 2023). Without treatment, mortality rates may range from 20% to 60% (Ates et al, 2016; Bataille et al, 2014). Severe complications include subarachnoid or subdural haemorrhage caused by ruptured bridging veins and dural sinus thrombosis, particularly in acute hypernatremia cases where osmotic imbalances are pronounced (Sonani et al, 2024). These complications can lead to permanent brain damage or death.

In emergency departments, hypernatremia occurs in approximately 1% of patients and is linked to mortality rates between 20% and 60% (Bataille et al, 2014). Among hospitalized patients, about 3% present with serum sodium levels >145 mEq/L, with an in-hospital mortality rate of 12% compared to 2% in normonatremic patients (Arzhan et al, 2022).

In intensive care units (ICUs), approximately 9% of patients develop hypernatremia, with mortality rates reaching 43% for those admitted with hypernatremia and 39% for ICU-acquired cases, compared to 24% in normonatremic patients (Lindner et al, 2007). In neuro-ICUs, particularly among traumatic brain injury (TBI) patients, hypernatremia presents an even greater risk. Severe hypernatremia is an independent risk factor for mortality in these patients, with higher mortality rates observed in cases of mild, moderate, and severe hypernatremia (Li et al, 2013).

Furthermore, rapid correction of chronic hypernatremia increases the risk of cerebral edema, seizures, and additional brain damage (Kim, 2006). These findings highlight the need for careful management and monitoring of hypernatremia to minimize its impact on patient outcomes.

Systemic Effects

Hypernatremia and the accompanying hyperosmolar state can impair various physiological functions and organ systems (Sonani et al, 2024). This includes neuropsychiatric impairments, reduced cardiac contractility, and metabolic disturbances such as increased peripheral insulin resistance and impaired hepatic gluco-

neogenesis (Zhi et al, 2019). These complications can lead to prolonged ICU stays, additional complications, and increased mortality (Lindner et al, 2007).

Acute vs. Chronic Hypernatremia

Acute Hypernatremia

Acute hypernatremia, developing within 48 hours, poses serious risks, including vascular rupture, cerebral bleeding, and death. Neonates and children are particularly vulnerable (Durrani et al, 2022). Adults may also experience severe symptoms such as seizures, particularly during rapid rehydration or sodium loading (Braun et al, 2015; Sonani et al, 2024).

Chronic Hypernatremia

Chronic hypernatremia elicits brain adaptations, such as the production of osmolytes, which reduce the immediate risks of brain cell shrinkage but increase susceptibility to cerebral edema during rapid correction. Adults with chronic hypernatremia may present with milder symptoms, such as anorexia, nausea, and restlessness, but severe cases can involve life-threatening complications during inappropriate treatment (Braun et al, 2015; Sonani et al, 2024).

Diagnostic Challenges

Chassagne et al (2006) conducted a multicentre study involving 150 geriatric patients with hypernatremia, revealing significant associations with symptoms like low blood pressure, tachycardia, dry oral mucosa, and altered consciousness. Physical signs such as orthostatic hypotension and abnormal skin turgor were observed in over 60% of cases. However, these findings lacked diagnostic specificity and sensitivity, highlighting the limitations of physical examination alone in detecting hypernatremia.

Clinical Assessment

A thorough clinical evaluation is crucial to determine the severity, duration, and cause of hypernatremia. Patient history should focus on symptom onset, duration, signs of fluid loss (e.g., vomiting, diarrhea), dehydration, and underlying conditions (Brennan et al, 2021). Hypernatremia symptoms primarily manifest as central nervous system dysfunction, particularly with rapid sodium increases over hours (Braun et al, 2015; Kim, 2006; Sonani et al, 2024). Physical examination, including assessments of skin turgor, tachycardia, and orthostatic hypotension, helps evaluate volume status and guide management (Brennan et al, 2021; Yun et al, 2023). Edema, often resulting from salt and water retention, signifies a hypervolemic state and is indicative of sodium excess (Table 3).

In chronic or severe hypernatremia, clinical signs may underestimate hypovolemia. Patients who have diabetes insipidus and hypernatremia often present with physical signs of volume depletion (Robertson, 2016; Yun et al, 2023). Hydration assessment can be unreliable in cases of chronic hypernatremia, where clinical

Table 3. Clinical assessment of fluid status.

Fluid status	Clinical findings	Causes
Hypovolemic Total body water deficit/less degree of total body sodium deficit	Orthostatic hypotension Oliguric Dry mucosal membranes Skin turgor Increased thirst Delayed capillary refill	Body fluid loss (burns, sweat) Diuretic use GI loss Osmotic diuresis Post-renal obstruction
Euvolemic Decreased total body water/normal total body sodium	Edema is absent	Central DI/nephrogenic DI Fever Hyperventilation Medications Hypodipsia
Hypervolemic Increased total body water/greater degree of increase in total body sodium	Edema may be present Raised JVP Peripheral edema Shortness of breath Hypertension	Iatrogenic Cushing's syndrome Hyperaldosteronism

GI, gastrointestinal; DI, diabetes insipidus; JVP, jugular venous pressure.

signs may underestimate degree of hypovolemia (The Royal Children's Hospital Melbourne, 2012).

Investigations

Investigating hypernatremia begins with requesting a comprehensive biochemical profile including urea, electrolytes, creatine, calcium, magnesium, phosphate and glucose to assess the patient's metabolic and renal status (Lee et al, 2022). These tests provide critical insights into the underlying cause of hypernatremia and help identify concurrent abnormalities, such as renal dysfunction, electrolyte imbalances, or hyperglycaemia, which may require immediate attention. To help differentiate between renal and extrarenal causes, assessing plasma volume, plasma osmolality, urine volume, concentrating ability and osmolality can further help. If results are delayed, a urine dipstick for specific gravity will also give an indication of urinary concentration.

When nephrogenic or central diabetes insipidus (DI) is suspected, a water deprivation test followed by desmopressin administration may be performed. In central DI, desmopressin increases urine osmolality, whereas nephrogenic DI shows no response (Flynn et al, 2025). Imaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI) scans, are indicated to identify the underlying cause of DI, particularly in cases of suspected central DI due to hypothalamic or pituitary damage. Conditions like brain surgery, head trauma, or tumours may impair antidiuretic hormone (ADH) production, leading to central DI (Farrell et al, 2021; Gubbi et al, 2000).

In extrarenal causes, the body attempts to conserve water, resulting in appropriately low urine volume, high urine specific gravity, and urine osmolality significantly exceeding serum osmolality (Fig. 2). These tests should ideally be performed before initiating treatment to accurately identify the underlying cause and guide further management.

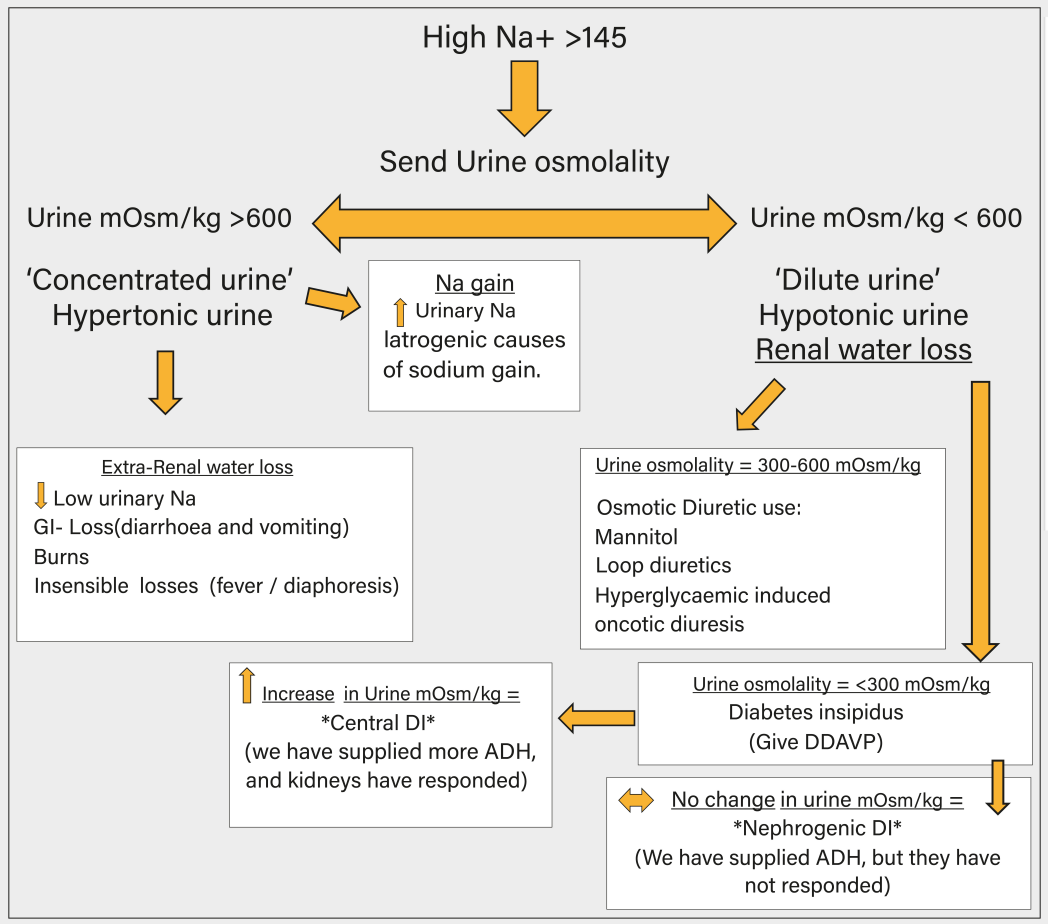

Fig. 2. Identifying the underlying aetiology. The figure was created using Adobe Illustrator, version 29.5.1 (Adobe Inc., San Jose, CA, USA). Na^+, sodium ion; DDAVP, 1-deamino-8-D-arginine vasopressin; Osm, osmoles.

Treatment of Hypernatremia

The treatment of hypernatremia should take into account its cause, severity, and duration (Sonani et al, 2024; Yun et al, 2023). Rapid correction must be avoided to prevent the potentially devastating and often irreversible complication of cerebral edema. The primary objectives of treatment are to normalize serum sodium levels while simultaneously addressing intravascular volume depletion and free water deficit (Sonani et al, 2024; Yun et al, 2023).

Oral hydration is effective for conscious patients, but in cases of severe hypernatremia where patients cannot drink due to persistent vomiting or altered mental status, intravenous (IV) hydration is preferred (Lewis, 2023; Yun et al, 2023). Co-

Table 4. Treatment strategies for varying volume statuses seen in hypernatremia.

Volume status	Treatment approach	Considerations
1. ECF volume overload	Replace free water with IV 5% dextrose in water or enteral water. Administer a loop diuretic to manage excess volume.	Monitor serum potassium and replace if necessary.
2. Euvolemia (normal volume status)	Replace free water with 5% dextrose in water or twice the volume of 0.45% saline.	Tailor fluid type based on clinical scenario (e.g., severity of hypernatremia).
3. Hypovolemia	Use 0.45% saline to restore both volume and free water. Alternatively, use a combination of 0.9% normal saline and 5% dextrose in water.	Special consideration for diabetes or nonketotic hyperglycemic coma patients.
4. Severe acidosis (pH <7.10)	Add sodium bicarbonate to 5% dextrose in water or 0.45% saline, ensuring the final solution remains hypotonic (e.g., 50–75 mEq/L of sodium bicarbonate).	Use cautiously to avoid overcorrection of acidosis and worsening hypernatremia.
Alternative approach	Separate replacement for ECF volume and free water using the estimated free water deficit formula.	This approach allows precise fluid and sodium management.

ECF, extracellular fluid; IV, intravenous.

matose patients may require enteral access via a nasogastric (NG) tube or percutaneous endoscopic gastrostomy (PEG) tube, enabling the administration of water and liquid nutrition directly into the stomach (Sonani et al, 2024). The choice of IV fluid depends on the type of hypernatremia being treated. For patients experiencing severe dehydration or shock, initial fluid resuscitation with isotonic fluids is recommended as the first step (Lewis, 2023; Sonani et al, 2024; Yun et al, 2023).

Hypernatremia is primarily a water management issue, where water loss exceeds sodium loss, while volume resuscitation focuses on restoring extracellular fluid. Treatment involves correcting the water deficit gradually, using hypotonic fluids, while isotonic fluids address volume depletion. Table 4 outlines treatment approaches based on different volume statuses and corresponding strategies that one can encounter in hospital settings.

Serum sodium should be monitored every 2–4 hours during the acute phase (Seay and Greenberg, 2019; Sonani et al, 2024). Neurological symptoms may indicate cerebral edema from rapid osmolality shifts, and hypotonic fluids should be stopped immediately. The rate of correction, urine output, and ongoing losses must be carefully always documented (Brennan et al, 2021; Yun et al, 2023).

Overcorrection of Hypernatremia

Overcorrection of hypernatremia, or reducing serum sodium levels too quickly, poses significant risks, primarily due to the rapid osmotic shifts that can lead to

severe complications, including cerebral edema and neurological damage (Feigin et al, 2023; Sterns, 2015). A rapid reduction in serum sodium levels can cause water to enter brain cells, resulting in swelling and increased intracranial pressure, manifesting as headaches, nausea, vomiting, altered mental status, seizures, or, in extreme cases, brain herniation (Feigin et al, 2023; Sonani et al, 2024; Sterns, 2015).

The risk of cerebral edema is particularly pronounced in chronic hypernatremia, where the brain has adapted to a hyperosmolar state over time, making rapid correction more likely to cause irreversible neurological deficits (Feigin et al, 2023). For instance, neonatal cases of hypernatremia dehydration have documented seizures and permanent cognitive impairments associated with aggressive correction strategies (Del Castillo-Hegyi et al, 2022). Conventional guidelines advocate for gradual correction at a rate not exceeding 8–10 mmol/L per day (Chauhan et al, 2019; Gilbert, 2025; Nur et al, 2014). However, emerging evidence suggests that carefully monitored faster correction may be safe and effective in acute hypernatremia, without associated neurological complications (Kitisin et al, 2025; Sonani et al, 2024).

In contrast to chronic hypernatremia, acute hypernatremia can be treated more rapidly since the brain has not had time to synthesize new osmoles (Osm) to counter the increased sodium concentration. These findings highlight the need to tailor management strategies based on the underlying aetiology, chronicity of hypernatremia, and individual patient factors to optimize outcomes while minimizing risks (Al-Absi et al, 2012; Sonani et al, 2024; Yun et al, 2023).

Undercorrection of Hypernatremia

Conversely, undercorrection of hypernatremia, where serum sodium levels are insufficiently lowered, is a common occurrence and is associated with increased mortality (Bataille et al, 2014; Kamatam et al, 2023). Prolonged elevation of serum sodium levels can exacerbate the detrimental effects of dehydration, resulting in persistent hyperosmolarity. This, in turn, may perpetuate symptoms such as lethargy, confusion, and, in severe cases, seizures or coma (Bataille et al, 2014; Kamatam et al, 2023; Sonani et al, 2024).

Table 5. TBW fraction across age/sex.

Age/Sex	Fraction
Male	0.6
Female	0.5
Elderly male	0.5
Elderly female	0.45

TBW, total body water.

If hypernatremia is not corrected at an appropriate rate, particularly in patients with underlying comorbidities such as diabetes insipidus or chronic dehydration, it can worsen both neurological and renal complications (Arzhan et al, 2022; Feigin et al, 2023; Pokhriyal et al, 2024; Wu et al, 2023; Yun et al, 2023). Gradual correction is critical to avoid complications like cerebral edema from overcorrection, but

undercorrection should also be avoided to ensure proper fluid balance and recovery (Bataille et al, 2014; Chacon-Palma et al, 2025; Sonani et al, 2024). Current guidelines recommend a cautious reduction in serum sodium levels, to minimize risks. However, the authors of recent studies emphasize the need for further research to better understand the impact of correction rates on mortality and neurological outcomes (Chauhan et al, 2019; Pokhriyal et al, 2024).

Key Take Home Point

Both overcorrection and undercorrection of hypernatremia can lead to serious complications, emphasizing the need for careful monitoring and gradual correction of sodium levels.

Total Body Water

Total body water (TBW) is a critical parameter in assessing a person's hydration status, body composition, and overall health. It plays a vital role in maintaining sodium balance (Sonani et al, 2024). Common formulas, such as the Watson formula—which considers factors like age, sex, and weight—and others based on regression models, provide estimates of TBW (Churchill and Patri, 2021; Kim et al, 2005; Noori et al, 2018). However, these formulas are inherently limited by their reliance on population-based averages, leading to variability in accuracy (Johansson et al, 2001; Roumelioti et al, 2018). Generally, TBW constitutes approximately 60% of body weight in men and 50% in women, with variations influenced by factors such as age and body composition (Table 5) (Muhsin and Mount, 2016).

Despite inherent limitations, TBW calculations remain essential for estimating clinical parameters such as free water deficit (FWD), which assumes a stable total body sodium level (Table 6). In practice, however, the actual FWD in patients with hypernatremia often exceeds predictions from standard formulas (Lewis, 2023). Estimating TBW and serum sodium concentration (expressed in mmol/L or mEq/L) is critical for assessing fluid depletion and guiding appropriate therapy. Clinicians must proceed with caution, as rapid correction of significant deficits—for example, 7 litres—can lead to serious complications and is generally avoided within a 24-hour period. In contrast, smaller deficits (e.g., 5 litres) may be corrected safely over shorter durations. TBW-based formulas, derived from anthropometric models originally developed by Watson and colleagues (Watson et al, 1980), offer a foundational approach to calculating fluid requirements in these scenarios.

Digital Tools and Advanced Techniques for Estimating Fluid Management

Tools like MDCalc, a widely used online calculator, assist healthcare professionals in estimating water deficits and guiding fluid replacement therapy in acute or hospital settings (Elovic and Pourmand, 2019). While online calculators based on TBW estimation formulas offer convenience and reasonable accuracy for general populations, they may be less reliable for individuals with atypical body composi-

Table 6. Formulas used to calculate free water deficit.

Formula	Description	Considerations
Formula 1: Total body water (TBW) × [0.6 in men or 0.5 in women × body weight (kg)] × [(plasma sodium/140) – 1]	Calculates free water deficit based on body weight and plasma sodium levels	Helps guide hydration therapy for hypernatremia correction
Formula 2: 4 mL × body weight (kg) × (desired change in serum sodium mEq/L)	An alternative formula to estimate free water deficit using body weight and desired change in serum sodium	Offers a practical approach for gradual correction while avoiding complications like cerebral edema
Considerations	Gradual correction of hypernatremia is essential to avoid complications like cerebral edema	Both formulas aim to guide safe and effective hydration therapy

tions, such as athletes or those with significant muscle or fat variations (Johansson et al, 2001; Roumelioti et al, 2018).

Advanced techniques like bioelectrical impedance analysis (BIA) or dilution methods provide greater precision but are less practical for routine use (Martinoli et al, 2003; Matias et al, 2016; Tahar et al, 2024). Despite these challenges, the rise of digital health tools has improved accessibility to TBW and hydration level estimations, providing clinicians and patients with valuable, non-invasive resources for monitoring hydration and fluid management (Liaqat et al, 2022; Mehra et al, 2025; Sandys et al, 2022).

Regional Variations in Hypernatremia Management

The management of hypernatremia varies significantly across regions, shaped by healthcare infrastructure, prevalent underlying causes, and resource availability. In developed countries, access to advanced diagnostic tools and timely interventions enables precise and gradual correction. Conversely, low- and middle-income countries often face challenges such as limited access to diagnostic tests, IV fluids, and healthcare facilities, resulting in treatment delays (Bello et al, 2024; Ulasi et al, 2022). In regions with high infectious disease burdens, such as Sub-Saharan Africa, or chronic conditions like diabetes prevalent in the Middle East, hypernatremia frequently arises from dehydration or comorbidities. Cultural and socioeconomic factors, including dietary habits and access to clean water, also play a crucial role in influencing the prevalence and management of hypernatremia in various populations (Abohajir et al, 2019; Bello et al, 2024).

Pseudohypernatremia

As highlighted in numerous published studies, measuring serum sodium concentration is critical for the correct diagnosis and safe management of dysnatremia,

emphasizing the need for reliable laboratory techniques to guide appropriate clinical interventions (Goldwasser et al, 2015; Kelly, 2019; Sterns and Hix, 2009). Pseudohypernatremia, or spurious hypernatremia, refers to a falsely elevated serum sodium concentration caused by laboratory methods affected by abnormal plasma composition rather than an actual increase in sodium levels (Callewaert et al, 2013; Goldwasser et al, 2015; Kelly, 2019). This artifact typically arises in the context of conditions such as hypolipidaemia or severe hypoproteinaemia, which alter the plasma's water phase proportion, leading to measurement errors in certain laboratory techniques (Callewaert et al, 2013; Goldwasser et al, 2015; Kelly, 2019).

Modern laboratory techniques, such as direct ion-selective electrode (ISE) methods, have largely mitigated the impact of pseudohypernatremia. However, indirect ISE methods, which rely on plasma dilution, are still susceptible to this artifact. Recognizing pseudohypernatremia is crucial to avoid unnecessary treatment, as the true sodium levels in the plasma water phase are typically normal in these cases. Diagnosis relies on correlating laboratory findings with clinical presentation and assessing for conditions such as dyslipidaemia or monoclonal gammopathies.

Clinical Vignette 1

A 74-year-old female weighing 65 kg has presented to the emergency department with a week's history of feeling generally unwell, accompanied by her husband who reports some subtle confusion and increased lethargy—all acute findings.
On further collateral history taken from the husband, specifically related to fluid status, he explained that his wife has had loose stools for the past three days and has been unable to keep fluids down for the past 72 hours.
A focused physical examination showed dry mucosal membranes, decreased skin turgor and delayed capillary refill. Abbreviated mental test score (AMTS) is 7, implying cognitive impairment.
Serum sodium ion (Na^+) was found to be 165 mEq/L.
Q1: What is the likely cause of hypernatremia?
Q2: What further testing should be done?
Q3: What is an appropriate treatment?

Answer

A1: The above presentation is in keeping with fluid loss hypernatremia, commonly seen in the elderly population, secondary to loose stool and inability to take in free water.

Investigations

A2: Send urine osmolality to confirm diagnosis before starting therapies. Urine osmolality should be high (more than 500), as ADH function should be intact.

Calculate total body water deficit-

$$0.45 \times 65 \times \frac{(165 - 145)}{145} = 4.034\ L\ deficit$$

Considerations

It is difficult to calculate the duration of hypernatremia in the clinical setting; one is often presented with a set of bloods on a patient who has not had bloods in the past 48 hours to differentiate between acute or chronic hypernatremia. Unless acute onset of hypernatremia can be proven, we must assume chronic hypernatremia and treat more cautiously.

Treatment

A3:

Admission to hospital

Aim for reduction in serum sodium of no more than 10 mEq/L in the first 24 hours.

Intravenous access

$$0.45 \times 65 \times \frac{(165 - 155)}{155} = 1.887\ L\ deficit\ in\ 24\ hours$$

To replete this water deficit, we can commence 5% dextrose at a rate of 85 mL/hour, to administer a bit more than the deficit of 2.017 L, given the need to account for ongoing water losses. However, given patient's volume depletion, administration of 1/2 normal saline (NS) at 170 mL/hour would be preferable. This can be changed to 5% dextrose at 85 mL/hour once the patient is euvolemic.

This patient does not require admission to ICU for serial blood sampling, however, will require twice daily bloods until the sodium is within range. The rate of free water administration can be changed to ensure that patient corrects at an appropriate rate, without over- or under correction.

This clinical vignette represents a virtual case, designed for educational purposes. The case is hypothetical, and the patient details are not based on any real individual. The aim is to illustrate important clinical concepts, diagnostic strategies, and treatment approaches. The case encourages critical thinking and provides a safe, simulated environment for learning without real-world consequences.

Osmotic Demyelination Syndrome

Osmotic demyelination syndrome (ODS), encompassing central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM), results from extreme shifts in serum sodium concentration and plasma osmolality (Han et al, 2015; Lambeck et al, 2019; Suppadungsuk et al, 2025; Treves et al, 2024). Current knowledge suggests that rapid increases in osmolality disrupt cellular homeostasis, leading to myelin sheath damage, particularly in the central pons (Suppadungsuk et al, 2025). While most documented cases of ODS occur during rapid correction of hyponatremia, hypernatremia-related ODS due to diverse causes has been reported in the literature but remains poorly understood (An et al, 2010; Han et al, 2015; Ismail et al, 2013). Further research is needed to elucidate the precise pathophysiological processes, risk factors, and preventative strategies specific to hypernatremia-induced ODS (Hegazi and Nawara, 2016).

Endocrine Causes of Hypernatremia

Hypernatremia can result from a variety of underlying conditions that disrupt the body's water and sodium balance. Among these, Cushing syndrome, diabetes insipidus (DI), and hyperaldosteronism are significant contributors due to their distinct pathophysiological mechanisms and pathophysiological mechanisms.

Cushing Syndrome

Cushing syndrome, characterized by excessive cortisol production, can cause hypernatremia due to cortisol's mineralocorticoid-like effects, which increase sodium retention and promote water loss. This hormonal imbalance contributes to hypervolemic hypernatremia, a rare but severe condition linked to elevated morbidity and mortality (Schernthaner-Reiter et al, 2021). Cortisol stimulates mineralocorticoid receptors, promoting increased sodium reabsorption and fluid retention (Nieman et al, 2025; Schernthaner-Reiter et al, 2021). The syndrome may arise from pituitary adenomas, chronic corticosteroid use, tumours, cancer, or inherited endocrine disorders (Gadelha et al, 2023; Simon and Theodoropoulou, 2022).

In Adrenocorticotropic hormone (ACTH)-dependent Cushing syndrome, excessive pituitary secretion of ACTH or ectopic production from paraneoplastic tumours further exacerbates the condition (Simon and Theodoropoulou, 2022). Complications such as cardiovascular disease, thrombotic events, and infections are common (Gadelha et al, 2023; Schernthaner-Reiter et al, 2021). Treatment focuses on addressing cortisol excess through medical or surgical interventions, or a combination of both, to mitigate these systemic effects.

Hyperaldosteronism

Hyperaldosteronism is characterized by excessive aldosterone secretion, which increases sodium reabsorption and promotes the loss of potassium and hydrogen ions (Vedere and Khalifa, 2025). It can be classified as primary (autonomous) or secondary, with differentiation based on laboratory and diagnostic evaluations (Funes Hernandez and Bhalla, 2023; Lattanzio and Weir, 2020; Vaidya et al, 2022; Vedere and Khalifa, 2025).

In primary hyperaldosteronism, mild hypernatremia (146–149 mmol/L) results from renal salt retention, although the "aldosterone escape" mechanism typically prevents significant fluid overload or edema (Wang et al, 2023). Secondary hyperaldosteronism, associated with elevated renin levels, often requires addressing the underlying cause to mitigate the condition.

Hyperaldosteronism is linked to various complications, including an elevated risk of cardiovascular diseases (e.g., atrial fibrillation, left ventricular hypertrophy, myocardial infarction), kidney diseases (e.g., glomerular hyperfiltration, proteinuria, end-stage kidney disease), and metabolic disorders (e.g., Type II diabetes mellitus, metabolic syndrome, obesity) (Funes Hernandez and Bhalla, 2023; Vaidya et al, 2022; Vedere and Khalifa, 2025). Treatment strategies are tailored to the underlying aetiology and may include surgical intervention, pharmacological therapy, and lifestyle modifications to manage associated risks effectively.

Hypernatremia and Diabetes Insipidus

Hypernatremia and DI are closely interrelated, as DI causes excessive urination (polyuria) and thirst (polydipsia), leading to significant water loss. Without adequate fluid replacement, this water loss results in dehydration, concentrating sodium levels in the blood and causing hypernatremia. In DI, this fluid imbalance arises from the kidneys' inability to conserve water, which may be due to either a deficiency in antidiuretic hormone or resistance to its action (Fig. 3).

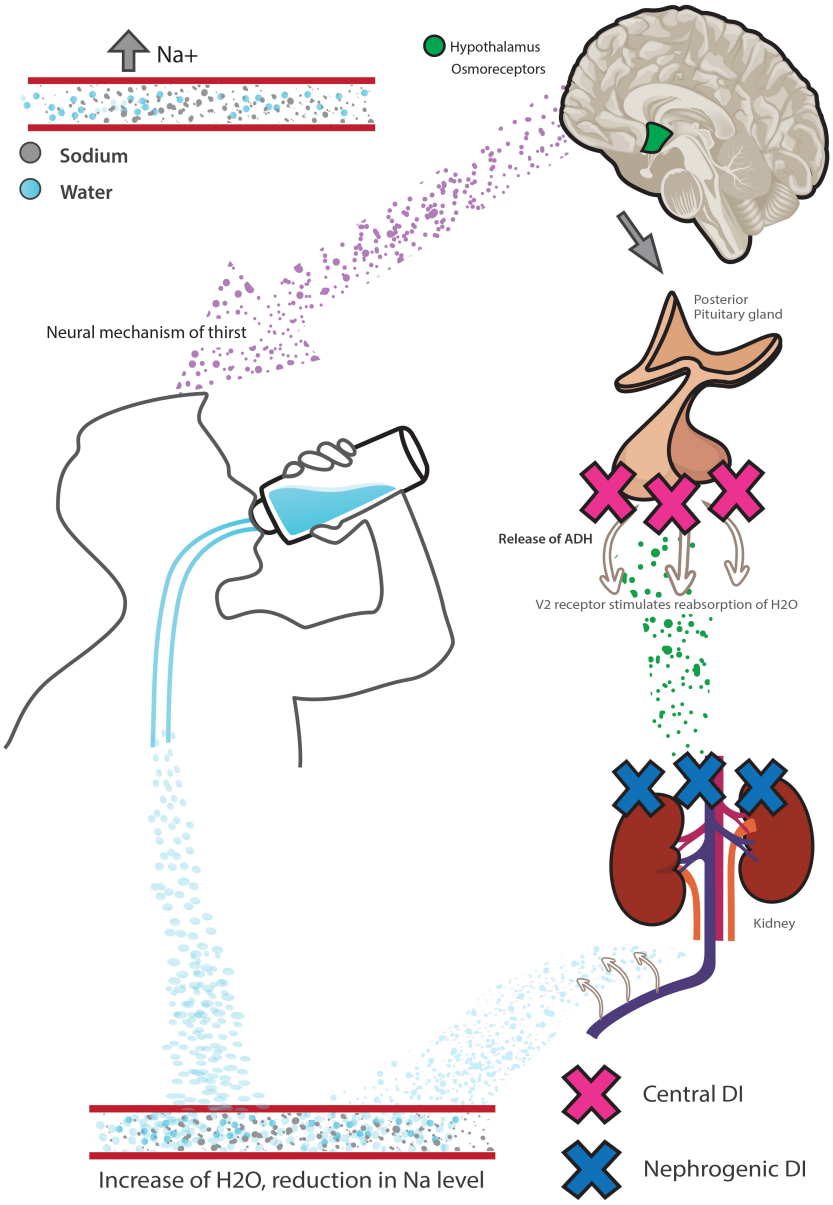

Fig. 3. Hypernatremia in C-DI and N-DI. The figure was created using Adobe Illustrator, version 29.5.1 (Adobe Inc., San Jose, CA, USA). Artwork for brain section contains imagery from: Adobe stock: ref AdobeStock_762647807. C-DI, central diabetes insipidus; N-DI, nephrogenic diabetes insipidus.

There are three possible types of DI, each with distinct mechanisms.

Central Diabetes Insipidus

This type occurs when the hypothalamus or posterior pituitary gland is impaired, resulting in reduced production or secretion of ADH. Causes of impairment include trauma, tumours, infections, or genetic conditions (Farrell et al, 2021; Flynn et al, 2025; Gubbi et al, 2000). Without sufficient ADH, the kidneys lose their ability to conserve water, leading to excessive urination and thirst. If fluid intake is inadequate to replace losses, dehydration ensues, and hypernatremia can develop.

Key Take Home Point

The analogy of the "water faucet" with no one to turn it off aptly illustrates how the kidneys continue to excrete large amounts of dilute urine without the necessary hormonal control.

Nephrogenic Diabetes Insipidus

In nephrogenic diabetes insipidus (N-DI), the kidneys are resistant to the effects of ADH, despite normal or elevated ADH production. This resistance prevents the kidneys from reabsorbing water effectively, leading to excessive urination (polyuria) and thirst (polydipsia). Common causes include genetic mutations affecting water reabsorption pathways, certain medications (e.g., lithium), or chronic kidney disease (Farrell et al, 2021; Flynn et al, 2025; Gubbi et al, 2000). Without appropriate water retention, patients are at risk of dehydration, and hypernatremia may develop if fluid losses are not adequately replaced.

Key Take Home Point

The analogy here—"the tap has broken off"—captures the concept that while ADH is available, the kidneys cannot act on it, preventing water reabsorption.

Mixed Diabetes Insipidus (Mixed-DI)

Mixed-DI involves a combination of central and nephrogenic mechanisms, where both reduced ADH production and kidney resistance to ADH contribute to the condition. This dual pathology results in excessive urination (polyuria) and thirst (polydipsia), complicating both diagnosis and treatment. The overlapping symptoms of central diabetes insipidus (C-DI) and N-DI require careful evaluation to identify the extent of hypothalamic or pituitary dysfunction and kidney resistance. This type of DI is often associated with complex clinical scenarios, such as severe trauma, extensive brain injuries, or prolonged use of nephrotoxic medications, necessitating a multifaceted approach to management (Robertson, 2016; Wu et al, 2016).

Key Take Home Point

In all forms of DI, the body's inability to concentrate urine leads to a persistent state of water diuresis, which is effectively captured in the analogy that in both cases, the "tap" can't be turned off, leading to excessive fluid loss.

It's critical to differentiate between these types, as they have distinct causes and treatment strategies, with C-DI often treated with synthetic ADH (desmopressin), while N-DI may require measures like a low-salt diet, adequate fluid intake, and in some cases, medications to improve kidney response to ADH (Farrell et al, 2021; Flynn et al, 2025; Gubbi et al, 2000).

Clinical Vignette 2

A 35-year-old male was admitted to ICU with an out-of-hospital cardiac arrest (OOHCA), with a suspected down-time of 45 minutes.
He was admitted to ICU for post return of spontaneous circulation (post-ROSC) management which included neuroprotection and targeted temperature control.
On admission, his serum sodium level was 137 mEq/L (normal range).
His CT brain on admission showed evidence of hypoxic ischemic encephalopathy.
12 hours into his admission, he became significantly hypertensive, with a widened pulse pressure, altered respirations, and bradycardia. Serum sodium increased to 154 mEq/L within 12 hours.
Q1: What is the most likely pathophysiologic cause of this man's sudden increase in serum sodium?
Q2: What testing should be done to confirm this diagnosis, and what is the best treatment?

Answer

A1: This patient has developed central diabetes insipidus (C-DI): The presence of widened pulse pressure, bradycardia, and irregular respirations (Cheyne-Stokes breathing) constitutes Cushing's triad, which occurs with a sudden increase in intracranial pressure. Due to the rise in intracranial pressure (ICP), ADH is not being released from the pituitary gland (unable to switch the tap off- lack of supply), resulting in large urinary loss of free water, manifesting as high urine output.
A2: The patient's urine osmolality should be measured before and after administration of 1-deamino-8-D-arginine vasopressin (DDAVP), which would demonstrate inappropriately low urine osmolality corrected after administration of DDAVP.
Desmopressin is a synthetic, longer lasting form of ADH, and using this will remedy the loss of ADH production and reduce free water loss and significant increase in sodium.

This clinical vignette is a virtual case created for educational purposes to simulate a real-life scenario. The patient and details are fictional, designed to highlight key clinical concepts, diagnostic approaches, and treatment strategies. The case encourages critical thinking and allows learners to practice decision-making in a safe, simulated environment.

Hypernatremia and Coronavirus Disease 2019

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) , is often associated with dysnatremias, including hypernatremia, which is linked to adverse outcomes such as increased mortality,

ICU admissions, prolonged hospital stays and heightened healthcare utilisation (Ma et al, 2023; Shrestha et al, 2022; So et al, 2023). Shrestha et al (2022) conducted a systematic review and meta-analysis that emphasized these associations, highlighting the significant clinical impact of hypernatremia in COVID-19 patients (Hirsch et al, 2021; Shrestha et al, 2022; So et al, 2023; Zimmer et al, 2020).

Hypernatremia in COVID-19 patients often develops secondary to fever, diarrhoea, anorexia, and inadequate fluid intake, and it tends to persist despite targeted therapy (Zimmer et al, 2020). A territory-wide retrospective cohort study by So et al (2023) reported a high prevalence of hypernatremia in hospitalized COVID-19 patients, correlating it with worse clinical outcomes and increased mortality rates (Ma et al, 2023; Shrestha et al, 2022; So et al, 2023). These findings underscore the critical importance of diligent monitoring and aggressive management of hypernatremia in COVID-19 patients, especially in high-risk groups, to improve survival and reduce complications (Hirsch et al, 2021; Ma et al, 2023; Shrestha et al, 2022; So et al, 2023; Zimmer et al, 2020).

Hypernatremia and Biomarkers in Acute Kidney Injury

Emerging biomarkers show promise in identifying the onset, risk, severity, and mortality associated with acute kidney injury (AKI). Jansch et al (2023) classified these biomarkers into three categories: markers of impaired kidney function, structural damage, and stress markers, as also noted by Ostermann et al (2020). Among these, serum sodium, particularly hypernatremia, has demonstrated its utility in providing critical prognostic information regarding AKI risk, mortality, and kidney recovery (Jansch et al, 2023; Marahrens et al, 2023; Zhi et al, 2021).

Despite advancements, no current biomarker or combination of biomarkers has been shown to reliably replace serum creatinine for AKI diagnosis (Jansch et al, 2023). This limitation highlights the importance of integrating hypernatremia assessment into routine patient monitoring to identify individuals at elevated risk for AKI. By recognizing hypernatremia early, healthcare providers can implement targeted preventative strategies, including precise fluid management and robust clinical monitoring, to mitigate risks and improve outcomes for patients, particularly in critical care settings.

Climate and Dysnatremia

Wootton et al (2024) investigated the influence of meteorological and patient-related factors on dysnatremia, highlighting the critical role of climate change—particularly rising temperatures—in serum sodium imbalances. The study emphasizes the need for further research into the relationship between climate metrics, such as temperature and humidity, and the incidence of dysnatremia, as well as the physiological adaptations to heat exposure.

Key recommendations include striking a balance in hydration messaging during extreme heat events to prevent both dehydration and overhydration. Tailored interventions are particularly important for vulnerable populations, including the el-

derly, individuals with unstable housing, those with chronic illnesses, and patients on medications that affect sodium balance. These strategies aim to reduce the risk of dysnatremia and its associated complications, especially as climate change continues to pose growing challenges to public health (Kutz et al, 2020; Mannheimer et al, 2022; Meade et al, 2020; Wootton et al, 2024).

Future Research

Recent studies underscore the need for continued research into hypernatremia, its underlying mechanisms, and innovative management strategies. Hu et al (2022) conducted a prospective cohort study implementing exome or targeted panel genetic sequencing in neonates with recurrent hypernatremia. They identified single-gene disorders, with over 50% of cases linked to an arginine vasopressin receptor-2 (*AVPR2*) deficiency associated with congenital nephrogenic diabetes insipidus, a rare X-linked recessive mutation responsible for approximately 90% of these cases (Yang et al, 2022). The findings emphasize the potential of early genetic testing to identify genetic aetiologies, optimize treatments, and improve therapeutic outcomes.

In another study, Fuse et al (2024) highlighted the detrimental impact of hypernatremia on microglia, the central nervous system's immune cells. Elevated sodium levels activate microglia, triggering the release of pro-inflammatory cytokines, which contribute to neuroinflammation and neuronal damage. Morphological changes in microglia, such as a transition to an amoeboid shape, further indicate stress and inflammation. Additionally, studies have shown that admission hypernatremia not only increases hospital mortality but also impairs immune response in sepsis, leading to reduced Granulocyte Colony-Stimulating Factor (G-CSF) and Tumor Necrosis Factor alpha (TNF-α) levels (Lin et al, 2022). These findings suggest hypernatremia may exacerbate brain injuries, such as those resulting from stroke or trauma, making it a critical focus for research into neuroinflammation and brain health.

Despite these advancements, progress in hypernatremia management has been limited (Arzhan et al, 2022; Yun et al, 2023). The integration of artificial intelligence (AI) into clinical care presents an exciting avenue for innovation (Kwon et al, 2021; Thongprayoon et al, 2022). AI's predictive analytics capabilities could enable earlier identification of at-risk patients, particularly in vulnerable populations such as the elderly or critically ill (Kwon et al, 2021; Thongprayoon et al, 2022). Future studies should explore whether AI-driven tools can improve morbidity and mortality outcomes in these groups. Such research has the potential to revolutionize hypernatremia management, fostering data-driven, proactive healthcare solutions that prioritize early detection and timely intervention.

Clinical Trials

Current clinical trials focus on optimizing fluid management strategies to improve electrolyte correction and patient outcomes (Tahar et al, 2024). Research em-

phasizes individualized treatment protocols to minimize complications like cerebral edema and seizures (Sonani et al, 2024; Yun et al, 2023).

Advances in hypernatremia pathophysiology reveal complex osmoregulatory mechanisms, highlighting the need for sensitive diagnostic tools for earlier detection (Nasser et al, 2024; Sonani et al, 2024). Prevention strategies target better hydration practices and reduced hospital-acquired cases. Future research aims to identify novel therapeutic targets and design precision medicine trials, enhancing the prevention, diagnosis, and management of hypernatremia.

Education and Training of Medical Personnel

Effective hypernatremia management requires healthcare professionals to understand its pathophysiology, diagnosis, and treatment. Training programs should emphasize core competencies, including identifying risk factors, interpreting laboratory results, and implementing safe correction strategies. Simulation-based learning and case discussions enhance decision-making in complex scenarios, while continuing medical education (CME) ensures professionals stay updated on evolving guidelines and digital tools like MDCalc (Berg, 2023; Elovic and Pourmand, 2019). Interdisciplinary collaboration among physicians, nurses, dietitians, and pharmacists is essential for optimal care (Bendowska and Baum, 2023; World Health Organization, 2010). Regional challenges, particularly in resource-limited settings, must be addressed with practical approaches, such as oral rehydration solutions (Ezezika et al, 2021). If unsure, doctors should refer to local hospital guidelines to ensure appropriate and context-specific management (Appendix Table 7). Investing in medical education equips healthcare providers to recognize and manage hypernatremia effectively, improving patient outcomes and minimizing complications (Majumder et al, 2023).

Conclusion

Hypernatremia is a common electrolyte imbalance in hospitalized patients, and it is linked to notably higher rates of morbidity and mortality. A systematic and individualized approach is essential for its diagnosis, evaluation, and management. Key considerations include the severity, duration, and underlying cause of hypernatremia, as these factors guide effective treatment strategies.

Timely intervention is critical to prevent complications such as neuronal cell shrinkage, brain injury, and the risks of overcorrection, which can result in brain oedema. Although mild cases may not need immediate intervention, it's essential to quickly assess and begin the right treatment to reduce the risk of worsening and potential complications.

These findings emphasize the importance of controlled sodium management in preventing severe neurological sequelae, underscoring the need for vigilance and precision in managing this electrolyte disorder.

Key Points

- Hypernatremia is primarily associated with a free water deficit due to inadequate water intake and/or excessive water loss.
- Patients with diabetes insipidus are unable to concentrate their urine due to a lack of ADH effect; central DI patients respond to DDA.
- Most outpatients with DI present with polyuria/polydipsia rather than hypernatremia, since thirst causes them to maintain eunatremia (until access to free water is lost).
- Manifestations include thirst with intact sensorium, decreased mental status, confusion, abnormal neuromuscular signs, hyperreflexia, seizures, convulsions and coma.
- The optimal treatment of hypernatremia should consider its severity, duration and mode of clinical presentation to avoid neuronal cell shrinkage and consequent brain injury.

Curriculum Checklist: Hypernatremia

This article addresses the following requirements of the internal medicine and critical care curriculum:

- Physiology and pathophysiology of sodium balance and water homeostasis.
- Causes and classification of hypernatremia (e.g., dehydration, diabetes insipidus, iatrogenic causes).
- Clinical presentation and symptoms of hypernatremia.
- History-taking and examination in patients with suspected hypernatremia.
- Indications for and interpretation of serum sodium, urine osmolality, and other relevant laboratory tests.
- Complications of hypernatremia, including neurological effects and osmotic demyelination syndrome.
- Principles of fluid resuscitation and correction of sodium imbalance.
- Monitoring and prevention strategies for hypernatremia in hospitalized patients.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

RM was responsible for conceptualizing the study, drafting the original manuscript, critically reviewing and editing the content, overseeing project administration, and supervising the overall work. AMWL contributed substantially to drafting the

original manuscript, critically reviewing and editing the manuscript. RC was involved in drafting and revising the manuscript critically and contributed to the preparation and development of visual elements. JMK participated in the critical review and editing of the manuscript and provided supervision throughout the project. JD was engaged in critically reviewing and editing the manuscript and also contributed to supervisory responsibilities, fulfilling important intellectual and leadership functions within the project. All authors made substantial contributions to conception. All authors gave final approval of the version to be published. All authors have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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Appendix

See Table 7.

Table 7. Electrolyte Disturbances (all).

Derangement	Action to be taken
Severe Hypernatraemia (above 150 mmol/L)	For patients whose serum sodium is >150 mmol/L who are receiving CRRT, this guidance must be carefully followed to avoid over-rapid correction of serum sodium, which can cause neurological injury. When possible, free water hydration must be the first line treatment for hypernatraemia. Serum sodium levels should not be lowered by more than 8–10 mmol/L over 24 hours. In those cases of hypernatraemia where CRRT is necessary, the sodium concentration of the replacement fluids ($[Na]_{replacement}$) should be increased by adding concentrated Sodium Chloride (NaCl) 30% solution in order to avoid a quick overcorrection of the hypernatraemia. An aseptic technique must be used to infuse the 30% NaCl into the replacement bags. The targeted $[Na]_{replacement}$ should be 10 mmol/L below the patient's $[Na]_{serum}$. As these volumes are small, they will not significantly affect the concentration of other electrolytes in the bag. The following should be reserved for severe hypernatraemia patients with serum NA >150 mmol/L who require CRRT. Remember to only use CRRT with heparin/no anticoagulation and maintain an effluent dose of 30 mL/kg/h.
Hyponatraemia (below 130 mmol/L)	For patients whose serum sodium is <130 mmol/L who are receiving CRRT, this guidance must be carefully followed to avoid over-rapid correction of serum sodium, which can cause neurological damage. An overly rapid correction of hyponatraemia can lead to osmotic demyelination syndrome, which can potentially result in permanent neurological injury. The cornerstone of managing severe hyponatraemia in the critically ill patient is to ensure a gradual rise in serum sodium concentrations by not >8–10 mmol/L over 24 hours. Adjust the sodium concentration in the dialysate and replacement fluids by adding sterile water. Sodium serum concentration will not rise above that of the dialysate/replacement fluid. A stepwise switch every 24 hours to fluid bags with 8–10 mmol/L higher serum concentration than the patient's current serum sodium can be considered. These modifications can be performed in all modalities of CRRT except when using regional anticoagulation with citrate. Bicarbonate and potassium may need to be replaced during the use of these modified CRRT as their concentration will be lower than normal in the modified fluid bags.

CRRT, continuous renal replacement therapy.