Fluid and electrolyte therapy in newborns

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INTRODUCTION — Water and electrolyte homeostasis in newborn infants is influenced by numerous factors, including gestational age, postnatal physiological changes in renal function, altered response to hormones, redistribution of total body water, and water loss secondary to environmental factors. As a result, management of neonatal fluid and electrolyte therapy is challenging as these factors and the clinical setting need to be accounted for while caring for neonates, especially preterm infants.

Fluid and electrolyte therapy in newborns, including the underlying principles of fluid and electrolyte homeostasis, determination of fluid and electrolyte requirements, influence of the care environment (eg, radiant warmers, humidity), and management of electrolyte and water abnormalities is discussed here.

WATER AND ELECTROLYTE HOMEOSTASIS — Water and electrolyte balance is primarily dependent on renal function and fluid intake versus losses. However, a newborn is more susceptible to derangements in water and electrolyte homeostasis because of the normal postnatal changes in body water components, functional immaturity of the neonatal kidney, increased insensible water losses compared with older individuals, and an inability to independently access water. In particular, the magnitude of postnatal diuresis, immaturity of renal function, and insensible fluid loss is higher at lower gestational age (GA). Thus, it is important for the clinician caring for the neonate, especially very preterm (VPT) infants, to have an understanding of the basic physiologic mechanisms that regulate and maintain water and electrolyte balance.

Changes in total body water — Total body water (TBW) is composed of extracellular fluid (ECF), which includes intravascular and interstitial fluid, and intracellular fluid. The amount of TBW as a percentage of body weight and its distribution in various fluid compartments vary with GA [1]. As an example, in a newborn term infant, the TBW is 75 percent of the body weight as compared with 80 percent in an infant born at 27 weeks gestation; the ECF volumes are 45 and 70 percent, respectively.

After birth, there is a physiologic diuresis of ECF resulting in a weight loss during the first week of life. The magnitude of diuresis and relative weight loss decreases with increasing GA. Normal weight loss is approximately 10 to 15 percent in preterm and 5 percent for term breastfed infants in the first day of life [2]. Fluid loss results primarily from an isotonic reduction in extracellular water, although the mechanism for this process is uncertain. The postnatal diuresis is approximately 1 to 3 mL/kg per hour in term infants and is greater in preterm infants. Since fluid administration in these infants is entirely regulated by caregivers, recognition of normal physiologic fluid loss is a major determinant for fluid management. In addition, other
concomitant fluid losses vary depending on the clinical setting. (See 'Sources of water loss' below.)

**Fluid and electrolytes homeostasis in preterm infants** — Prospective studies involving very low birth weight (VLBW) infants (BW ≤1500 g) and extremely low birth weight (ELBW) infants (BW ≤1000 g) demonstrated a consistent pattern of fluid and sodium homeostasis despite varying intakes of sodium and water over the first five to seven days of life [3,4]. Results demonstrated that in these preterm neonates there were three consistent phases of water and sodium changes:

- **Pre-diuretic phase** – Day 1 of life is characterized by oliguria with low glomerular filtration rate (GFR) and low fractional excretion of sodium (FENa). It is speculated that birth-associated renal nerve stimulation increases renal vascular resistance, thus GFR and renal flow are suppressed.

- **Diuretic and natriuretic phase** – Days 2 to 3 of life are characterized by both increased urine output and sodium losses caused by increased GFR and high FENa. In this second phase, lung fluid is thought to be absorbed, resulting in increased extracellular volume. This leads to inhibition of sympathetic activity with subsequent reduced renal vascular resistance causing an increase in GFR, FENa, and urine output.

- **Post-diuretic phase** – Days 4 to 5 are characterized by varied urine output dependent upon changes in fluid intake, with a reduction of GFR and FENa compared with days 2 to 3.

**Renal function** — Neonatal renal function is varied due to:

- Developmental immaturity – Renal function improves with increasing GA.

- Postnatal hemodynamic changes at birth that affect renal function. The magnitude and rate of changes vary with GA

Developmental immaturity, especially in the preterm infant, affects the following renal functions, which can result in water and electrolyte imbalance:

- Glomerular filtration

- Ability to concentrate urine

- Tubular reabsorption of sodium and bicarbonate and secretion of potassium and hydrogen

**Glomerular filtration** — Embryogenesis is complete by approximately 35 weeks gestation, at which time there are between 0.6 and 1.2 million nephrons in each kidney. As a result, GFR in preterm infants with GAs below 35 weeks is lower. So, for example, a full term infant has a GFR of approximately 26 mL/min per 1.73 m², whereas a preterm infant at 27 weeks gestation will have a GFR of 13.4 mL/min per 1.73 m².

GFR increases at birth in all infants due to recruitment of superficial nephrons and a substantial increase in renal blood flow (RBF) due to a decrease in renal vascular resistance and increases in systemic blood pressure. However, the velocity of change is greater in term infants compared with preterm infants, especially VPT infants. So for term infants, GFR doubles by two weeks of age to 54 mL/min per 1.73 m² compared with a GFR of 16.2 mL/min per 1.73 m² for a neonate born at 27 weeks gestation.

**Serum creatinine** — Clinically, serum creatinine (SCr) values are the most convenient method to estimate GFR. Similar to GFR, SCr normally varies with GA and postnatal age. At birth, SCr concentration is the same as the concentration in the mother (usually less than 1 mg/dL [88 micromol/L]), and normally falls
over time. For term infants, the decline is rapid to nadir values (SCr 0.2 to 0.4 mg/dL [18 to 35 micromol/L]) by the first or second week of life. For preterm newborns, the decline is slower, and may take up to two months to reach normal baseline (table 1). (See "Neonatal acute kidney injury: Pathogenesis, etiology, clinical presentation, and diagnosis", section on 'Serum creatinine'.)

The diagnosis of either acute kidney injury or chronic kidney disease (CKD) is suspected with an abnormally elevated serum creatinine (SCr) for GA and postnatal age or increasing SCr from a previous baseline. (See "Neonatal acute kidney injury: Pathogenesis, etiology, clinical presentation, and diagnosis", section on 'Diagnosis' and "Chronic kidney disease in children: Definition, epidemiology, etiology, and course", section on 'Children less than two years of age'.)

**Blood urea nitrogen** — In preterm infants, blood urea nitrogen (BUN) is not a reliable marker for renal function or protein intolerance, especially for infants who receive parenteral amino acid [5-7].

**Urinary concentration** — Urine concentrating ability is limited in the newborn compared with older infants and children. The maximum urine concentration that can be achieved increases from 400 mosmol/kg in the first few days after birth to 1200 mosmol/kg at one year of age. As a result, the risk of volume depletion is increased in the newborn because of the inability to maximally concentrate urine and due to increased insensible fluid loss compared with older individuals. If fluid repletion is inadequate, this results in hypovolemia and hypernatremia. (See 'Sources of water loss' below.)

Limited concentrating ability in newborn infants is due to the following [8-10]:

- **Limited toxicity of the medullary osmotic gradient** — This is due in part to the short loop of Henle in newborns that restricts the countercurrent multiplication that forms the osmotic gradient from the corticomedullary junction to the inner medulla. In addition, toxicity within the medullary interstitium is limited by reduced availability of osmolar molecules (eg, urea) due to a low dietary intake of sodium and protein from human milk and formula and reduced urea synthesis due to the typical anabolic state of the newborn.

- **Diminished response to antidiuretic hormone (ADH, also referred to as arginine vasopressin)** — ADH increases the water permeability of the collecting tubule by activation of its receptors. In the newborn, the collecting tubule is relatively unresponsive to changes in ADH, and the response diminishes with decreasing GA [11].

Concentrating ability matures after birth, but the pace of this maturation is lower in infants of lower GA.

**Other tubular function**

- **Sodium** — In the neonate, maximum reabsorption of sodium is limited due to tubular immaturity and tubuloglomerular imbalance, which improves with increasing GA. Limited sodium reabsorption is in part due to reduced responsiveness to aldosterone [12-14]. Sodium transport throughout the kidney also depends on the Na-K-ATPase pump located on the basolateral membrane of various sections of the tubule and membrane transporters. In the neonate, especially VPT infants (GA <32 weeks), the immature developmental expression and function of the Na-K-ATPase pump and membrane transporters result in decreased sodium reabsorption [15]. As a result, the fraction of the filtered sodium that is excreted (FENa) is as high as 5 percent in preterm infants less than 30 weeks gestation compared with less than 2 percent in older infants and children.
- **Bicarbonate** – Bicarbonate resorption in the proximal tubule is reduced due to decreased expression and activity of the NA-K-ATPase pump and carbonic anhydrase and sodium-hydrogen antiporter. This leads to a lower resorptive threshold for bicarbonate of 19 to 21 mmol/L in term infants, and 16 to 20 mmol/L in preterm infants [16,17].

- **Potassium** – Potassium excretion primarily occurs in the gastrointestinal tract, with only approximately 10 to 15 percent excreted in the urine. In the neonate, this excretion is dependent largely on the NA-K-ATPase pump. Low renal excretion is due to the decreased expression and activity of this pump, decreased responsiveness of the neonatal kidney to aldosterone, and lower GFR. This leads to higher normal values of potassium (table 2) and an increased risk of hyperkalemia, especially in ill preterm infants. (See "Causes, clinical manifestations, diagnosis, and evaluation of hyperkalemia in children".)

**Sources of water loss** — Water loss is divided into insensible losses through the skin and lungs, and sensible losses through the kidney (urine output). The absolute and relative amounts of water loss through these routes change with GA. Other fluid losses may include stool, gastric drainage, ileostomy drainage, or thoracostomy output.

**Renal** — After birth, most neonates demonstrate low urinary volume <1 mL/kg per hour) in the first day of life [3,4]. After 24 hours of life, urine output (sensible losses) increases and is approximately 45 mL/kg per day, or 2 mL/kg per hour. As noted above, neonates have a limited ability to concentrate their urine. (See 'Urinary concentration' above.)

**Skin** — Evaporation through the skin can result in large insensible water losses in newborns. These may be excessive in extremely low birth weight (ELBW; BW <1000 g) infants with very thin skin (increased skin permeability). In addition, the surface area-to-volume (related to body weight) ratio increases with deceasing GA, which also increases fluid loss.

As the skin matures with increasing GA and postnatal age, the surface area-to-volume ratio decreases and evaporative loss is reduced. These factors are less significant for infants born after 28 weeks GA. For more immature infants, these losses become less important one week after birth. As an example, insensible water loss in an infant born at 24 weeks gestation may be as high as 200 mL/kg per day compared with a loss of 20 mL/kg per day for a term infant. Water loss also may be excessive in conditions in which skin integrity is compromised (eg, epidermolysis bullosa, abdominal wall defect) [18-20].

Other factors that may increase skin losses include:

- **Radiant warmers**, which increase evaporative water loss by approximately 50 percent [21]. Use of humidification and plastic wrap may minimize this loss [22]. Newer incubators that provide humidification and easier access to infants have been developed, resulting in a decreased use of radiant warmers [23].

- **Heat-emitting phototherapy devices**, which increase transepidermal water loss [24,25]. However, these devices are rapidly being replaced by newer ones using high-intensity gallium nitride light-emitting diode (LED) phototherapy, which have no effect on transepidermal water loss [26].

**Respiratory** — With the typical ambient humidity in the nursery, approximately one-half of insensible losses in term infants are caused by water loss through the respiratory system [27,28]. Respiratory loss increases with increasing respiratory rate and decreases for infants who receive humidified air, including those who are intubated and mechanically ventilated. Although respiratory water loss increases with decreasing GA, transepidermal loss increases even more [28]. Thus, in preterm infants, skin water loss is
greater than respiratory loss.

**Effect of antenatal glucocorticoids** — Antenatal administration of glucocorticoids to promote lung maturation in preterm infants also results in maturation of the skin and kidneys (see "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery").

In one report, water and sodium homeostasis during the first week after birth were compared in ELBW infants exposed and not exposed to antenatal glucocorticoids [29]. Exposed infants had lower insensible water loss, less hypernatremia, and an earlier diuresis and natriuresis than unexposed infants. These changes were thought to result from enhanced epithelial cell maturation that improved the barrier function of the skin. In experimental studies, glucocorticoid exposure resulted in maturation of ion channels in the proximal renal tubular epithelium [30,31].

In another report, exposure to antenatal glucocorticoids prevented nonoliguric hyperkalemia that frequently occurs in ELBW infants [32]. The mechanism is uncertain, but may be related to enhanced stabilization of cell membranes and upregulation of Na-K-ATPase activity, leading to a decrease in the movement of potassium from intracellular to extracellular compartments.

**MONITORING**

**Overview** — Fluid and electrolyte management in the newborn is made more difficult by several factors that include gestational age (GA), postnatal age, and the clinical setting (environmental factors, severity of illness, and therapeutic intervention). It is important to be aware of variations in lab values at different GAs for appropriate neonatal fluid and electrolyte management. Monitoring and consideration of the various concomitant and changing factors are essential to correcting and maintaining optimal balance of fluid and electrolytes in newborns. Management requires performing serial physical examinations, including measuring (and interpreting) body weight, monitoring intake and output, and frequent serial measurements of serum sodium.

**Physical examination** — Physical examination begins with a general assessment of the patient, including determining GA and postnatal age. These factors affect the degree of water loss (especially skin loss). Other factors that will influence fluid losses and need to be considered include loss of skin integrity and the use of humidified air or radiant heater. As care proceeds, serial examination should include daily weights, signs of cardiovascular stability (heart rate, blood pressure, capillary refill), state of hydration (skin turgor, mucus membrane status, fullness of the anterior fontanelle), and the presence or absence of edema.

**Body weight** — Body weight should be measured at least daily and in some cases more frequently. There is an expected physiologic weight loss in the first several days of life of 5 to 10 percent in term infants [2], and as high as 15 percent in preterm infants [33].

With appropriate nutrition and fluid intake, weight typically reaches a nadir at approximately three to four days and rebounds to near birth weight (BW) by seven days, although a significant percentage of otherwise normal infants may not regain BW for 14 days or longer. The absence of this normal weight loss or weight gain over the first few days suggests excess fluid intake or abnormally low losses.

However, it is important to note that body weight measurements in extremely low birth weight (ELBW) infants (BW <1000 g) may be unreliable or subject to technical errors. In some neonatal units, routine weights to minimize handing of these extremely preterm (EPT) infants are not obtained until several days after birth. In other units, weights are measured but considered in the context of all clinical information. The addition of
built-in scales as part of the radiant warmer/incubator has made obtaining daily weights easier to achieve.

When weight measurements are available, changes are obviously dependent on adequate nutrition as well as hydration status. Body weight changes in conjunction with serum sodium concentration are the best measure of fluid status. The frequency of serial electrolyte measurements is increased when there is fluid and electrolyte imbalance. (See 'Serum sodium' below.)

- Excess body water is suggested by weight gain often in conjunction with a low serum sodium concentration. In infants with diminished renal function, volume overload may be identified by an increase in blood pressure and physical findings of generalized edema.

- Inadequate fluid intake (hypovolemia) is manifested by excessive weight loss, a high sodium concentration, tachycardia, and poor capillary refill. In the most severe cases, hypotension may be observed as a prelude to neonatal shock. (See "Etiology, clinical manifestations, evaluation, and management of neonatal shock", section on 'Physical findings' and "Etiology, clinical manifestations, evaluation, and management of low blood pressure in extremely preterm infants".)

- Decrease in effective circulation can occur when third spacing takes place, such as with sepsis or ileus. In this case, body weight may be increased with evidence of edema or ascites and a diminished sodium concentration.

**Intake and output** — For the first few days after birth, fluid intake and output of urine and stool should be measured and the net difference recorded for preterm or term infants with acute illness.

The input should exceed the output by the estimated insensible fluid needs of the infant based on the GA, which varies due to skin permeability and surface area-to-volume ratio (see 'Skin' above) and clinical setting minus the estimated normal fluid loss due to diuresis following delivery. The estimated insensible fluid loss is adjusted based on body weight changes outside of the normal range and abnormal sodium levels. For example, in an EPT infant, an estimation of insensible loss of 100 mL/kg is inadequate if there is an excess weight loss and a concomitant increase in serum sodium. In this case, the estimated insensible fluid loss should be increased, resulting in an increase in intake, which is reflected by a corresponding increase in the net difference between intake and output. (See 'Changes in total body water' above and 'Sources of water loss' above.)

**Serum sodium** — Serial serum or plasma sodium determinations are essential for monitoring the fluid and electrolyte balance of ill neonates, including EPT infants (GA <28 weeks). When body weights are used in conjunction with serum sodium determinations, the etiology of any sodium derangement and plan for treatment can more readily be established. During the first days of life, changes in sodium concentration primarily reflect changes in water intake and loss, and not changes in sodium balance. (See "General principles of disorders of water balance (hyponatremia and hypernatremia) and sodium balance (hypovolemia and edema)", section on 'Disorders of sodium balance'.)

- Hyponatremia suggests excess of free water (hypervolemia) (see "Hyponatremia in children", section on 'Hypervolemia')

- Hypernatremia suggests depletion of free water or dehydration (hypovolemia) (see "Hypernatremia in children", section on 'Excess water losses')

The frequency of monitoring serum sodium is increased when the risk of abnormalities in increased. The
specific monitoring schedule depends upon GA and postnatal age, as well as the infant's clinical condition. In general, EPT infants who have very high insensible water losses will require monitoring as frequently as every six to eight hours over the first two to three days after birth, while older preterm and term infants may be adequately monitored with daily determinations [34]. Once a normal serum sodium is established with stable body weights and the rate or type of fluid administration is not changing significantly, monitoring frequency can be reduced.

**FLUID REQUIREMENTS** — Calculation of fluid and electrolyte requirements must account for correction of fluid abnormalities (deficit or excess water) and ongoing maintenance requirements. Maintenance fluid requirements are those needed for neutral water balance after accounting for obligatory losses (eg, urine and stool) and insensible losses (eg, skin and lungs) (table 3).

Requirements will be influenced by factors that include the gestational age (GA) and postnatal age, environmental temperature and humidity, renal function, and ventilator dependence (which affects respiratory losses). Excessive loss of other fluids, such as ileostomy or gastric drainage, thoracostomy output, polyuria caused by osmotic diuresis, diuretic use, or repeated removal of cerebrospinal fluid, must also be measured and replaced.

During the first few days, physiologic fluid loss should be anticipated, approximating 2 to 3 percent of body weight per day in term infants and 3 to 5 percent in preterm infants:

- Larger than normal losses should prompt an assessment for excess losses and/or inadequate intake, taking into consideration urine output and insensible fluid losses. Normal urine output is approximately 1 to 3 mL/kg/hr. Fluid intake is increased until water balance is achieved as determined by body weight and sodium concentration.

- Deficits associated with cardiovascular changes (tachycardia and poor capillary refill) require prompt correction with a bolus infusion of normal saline (10 to 20 mL/kg); in severe cases, this may need to be repeated. Once hemodynamic stability has been restored, the remaining deficit may be more slowly corrected over one to two days.

- Abnormal weight gain coupled with:
  - Decreased urine output should prompt evaluation for renal dysfunction as well as inappropriate secretion of ADH or a significant inflammatory response, such as severe inflammatory response syndrome (SIRS). (See "Neonatal acute kidney injury: Pathogenesis, etiology, clinical presentation, and diagnosis", section on 'Diagnosis'.)
  - Markedly increased urine output suggests excess intake, impaired renal concentrating ability due to an underlying congenital tubular defect, or diabetes insipidus. In this setting, fluid intake is adjusted until water balance is achieved as determined by monitoring the intake and output, body weight, and sodium concentration.

**ELECTROLYTE REQUIREMENTS** — Maintenance requirements for sodium, potassium, and chloride are approximately 2 to 3 mEq/kg per day. For infants receiving intravenous (IV) fluids, these electrolytes generally are not given during the first 48 hours after birth because of the relatively volume-expanded state, and normal isotonic losses during the first days of life. Urine flow should be adequate before potassium is added.

In addition to maintenance requirements, electrolyte deficits should be replaced. Usually replacement with
dextrose solutions containing half-normal or normal saline will be adequate. Depending upon the volume of fluid output, electrolyte losses from gastric or ileostomy drainage can be large, with the following electrolyte composition [35]:

- Gastric output is composed of 20 to 80 mEq/L sodium, 5 to 20 mEq/L potassium, and 100 to 150 mEq/L chloride.
- Small bowel output is composed of 100 to 140 mEq/L sodium, 5 to 15 mEq/L potassium, 90 to 130 mEq/L chloride, and 40 to 75 mEq/L bicarbonate.

DISORDERS OF SODIUM BALANCE — In the first week of life, disorders of sodium balance are primarily due to abnormalities of water balance.

Hyponatremia

**Early newborn period** — During the early newborn period (first four to five days of life), hyponatremia, defined as a serum sodium concentration of 128 mEq/L or less, most often reflects excess total body water (TBW) with normal total body sodium. This likely results from excessive fluid intake or, infrequently, water retention due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH). SIADH may accompany pneumonia or meningitis, pneumothorax, or severe intraventricular hemorrhage [36]. (See "Pathophysiology and etiology of the syndrome of inappropriate antidiuretic hormone secretion (SIADH)" and "Hyponatremia in children", section on 'Syndrome of inappropriate ADH secretion'.) Hyponatremia due to these causes is treated by fluid restriction, which usually results in a slow return to normal levels. Adjustment of fluid intake is based on changes of body weight, sodium concentration, and net fluid intake.

**Later newborn period** — After the first 4 to 5 days of life, hyponatremia is usually caused by negative sodium balance [37]. It is most commonly seen as a result of inadequate replacement of large renal sodium losses in extremely preterm (EPT) infant (gestational age [GA] ≤28 weeks) due to immature tubular function or infants who receive diuretic therapy [37]. In these patients, correction of hyponatremia is based on the repletion of the sodium deficit. This is calculated as the product of the total body volume times the sodium deficit per liter (ie, 140 minus the serum sodium concentration). The volume of distribution of sodium is the total body water because of the rapid osmotic equilibration between the extracellular and intracellular fluid. Although the total body water is 75 percent in normal term infants and increases with immaturity, most clinicians use a volume of distribution of 60 percent to minimize the likelihood of overly rapid correction. Sodium intake also needs to provide maintenance sodium based on the patient's ongoing needs.

Rarely, hyponatremia is caused by congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency, which may present as hyponatremia, hyperkalemia, metabolic acidosis, and shock in the newborn. This disorder most commonly is diagnosed as part of the standard newborn screening. For these patients, management includes correction of hypovolemia with normal saline followed by repletion of the sodium deficit along with appropriate replacement steroids. (See "Genetics and clinical presentation of classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency" and "Treatment of classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency in infants and children", section on 'Management in neonates'.)

**Factitious hyponatremia** — Hyponatremia occasionally is factitious due to increased serum glucose
level. Hyperglycemia causes an osmotic shift of fluid into the intravascular space, diluting the true sodium concentration. The measured level decreases by 1.6 mEq/L for every 100 mg/dL increase in glucose level. Erroneously low sodium level may also be caused by sample collection error (eg, drawing blood out of a central line that was not adequately cleared or upstream from an intravenous infusion).

**Hypernatremia** — Neonatal hypernatremia is serum sodium concentration ≥150 mEq/L due to either excessive fluid loss or excessive sodium intake.

**Excessive fluid loss** — Neonatal hypernatremia is most commonly due to excessive fluid loss and presents as abnormally high weight loss in the first few days after delivery. Hypovolemia and hypernatremia result from inadequate fluid replacement of fluid loss due to insensible water loss (skin and respiratory loss) and urine (inability for maximal urinary concentration). In full term infants, this is most frequently caused by inadequate breastfeeding resulting in insufficient water replacement [38]. Affected infants often have >10 percent weight loss, which exceeds the weight loss normally observed due to diuresis after delivery. (See "Initiation of breastfeeding", section on 'Excessive weight loss' and 'Changes in total body water' above.)

An unusual cause of hypernatremia in newborns is diabetes insipidus, which is sometimes associated with hypoxic-ischemic encephalopathy or central nervous system malformations. Affected patients typically manifest polyuria and hypernatremia results due to inadequate fluid replacement.

For patients with hypernatremia due to excessive fluid loss, treatment consists of increasing free water administration. Rapid correction of the hypernatremia (generally defined as more than 0.5 mEq/L per hour) should be avoided since this may result in cerebral edema and seizures [39]. Adequacy of therapy is based on serial sodium measurements.

**Excess sodium intake** — Hypernatremia without significant weight loss should prompt a search for inadvertent high sodium administration. Neonatal hypernatremia can be caused by excessive sodium delivered through parenteral fluids, medication, or blood products, even in preterm infants despite their normally high urinary loss [37]. If hypernatremia is caused by excessive sodium intake, sodium administration should be reduced and, if necessary, water intake increased.

**DISORDERS OF POTASSIUM BALANCE**

**Hypokalemia** — Hypokalemia, defined as a serum potassium concentration <3 mEq/L, usually results from excessive losses of potassium. Contributing factors include chronic diuretic use, renal tubular defects, or significant loss due to output from a nasogastric tube or ileostomy.

Hypokalemia usually is asymptomatic. However, it can cause weakness and paralysis, ileus, urinary retention, and conduction defects detected on the electrocardiogram (ECG) (eg, ST segment depression, low voltage T waves, and U waves).

In most cases, treatment consists of increasing the daily potassium intake by 1 to 2 mEq/kg. In severe or symptomatic hypokalemia, potassium chloride (KCl) (0.5 to 1 mEq/kg) is infused intravenously (IV) over one hour with continuous ECG monitoring to detect arrhythmias. (See "Hypokalemia in children".)

**Hyperkalemia** — Hyperkalemia is defined as a serum potassium concentration >6 mEq/L. However, neonates have a higher normal range of potassium because of their reduced urinary potassium excretion.
caused by their relatively increased aldosterone insensitivity, perhaps due to low expression of mineralocorticoid receptors [40] and decreased glomerular filtration rate (GFR) (table 2). Both of these factors are accentuated in preterm infants, resulting in normally higher serum potassium levels than their term counterparts. Pathologic hyperkalemia may result from multiple causes, including decreased potassium clearance (eg, renal failure, certain forms of congenital adrenal hyperplasia), increased potassium release caused by bleeding or tissue destruction (eg, intraventricular hemorrhage, cephalohematoma, hemolysis, bowel infarction), and inadvertent excessive administration of potassium (eg, supplementation for hypokalemia associated with diuretic therapy).

Hyperkalemia occurs frequently in extremely low birth weight (ELBW) infants [41-43]. The mechanism may be an exaggerated shift from intracellular to extracellular potassium after birth [41]. As noted above, antenatal glucocorticoids may be protective [32].

Depending upon severity and the rate of onset, hyperkalemia can be asymptomatic or so severe as to constitute a medical emergency. Signs include arrhythmias and cardiovascular instability. ECG findings associated with hyperkalemia consist of peaked T waves, flattened P waves, increased PR interval, and widening of the QRS complex. Bradycardia, supraventricular or ventricular tachycardia, and ventricular fibrillation may occur. (See "Causes, clinical manifestations, diagnosis, and evaluation of hyperkalemia in children", section on 'Clinical manifestations'.)

When the diagnosis is made, administration of any fluid that contains potassium should be discontinued immediately. Treatment is aimed at three factors (algorithm 1) (see "Management of hyperkalemia in children"):

- Reversal of the effect of hyperkalemia on the cell membrane by infusion of 10 percent calcium gluconate (0.5 mL/kg) or calcium chloride (dose of 20 mg/kg or 0.2 mL/kg) over five minutes.

- Promotion of potassium movement from the extracellular fluid compartment into the cells by administering intravenous (IV) glucose and insulin (0.05 units/kg human regular insulin with 2 mL/kg 10 percent dextrose in water), followed by a continuous infusion of insulin (0.1 units/kg per hour with 4 mL/kg per hour of 10 percent dextrose in water [100 mL/kg per day]). Glucose levels must be monitored and infusion rate of glucose adjusted as necessary.

Other treatment methods that promote intracellular movement of potassium that may also be used after administration of glucose and insulin include:

- Administration of IV sodium bicarbonate (in a dose of 1 to 2 mEq/kg over 30 to 60 minutes).

- Administration of beta agonists, such as albuterol, via nebulization.

- Increasing urinary excretion with IV administration of furosemide (1 mg/kg per dose) in infants with adequate renal function.

Dialysis can be considered in infants with oliguria or anuria.

**SUMMARY AND RECOMMENDATIONS** — Water and electrolyte homeostasis in newborn infants is shaped by gestational and postnatal effects on the distribution of total body water (TBW), renal function, and water loss. Fluid and electrolyte therapy must account for these factors when determining maintenance requirements and correction of any abnormalities:
• After birth, there is a physiologic diuresis of extracellular fluid (ECF) resulting in a weight loss during the first week of life. The magnitude of diuresis and relative weight loss increases with decreasing gestational age (GA). Normal weight loss is approximately 5 percent for term infants and is approximately 10 to 15 percent in preterm infants. (See 'Changes in total body water' above and 'Body weight' above.)

• Renal function is affected by both GA and postnatal age.
  - Glomerular filtration rate (GFR) is low in neonates and decreases with GA. Although GFR increases in all infants after delivery, the rate of rise decreases with GA. (See 'Glomerular filtration' above.)
  - Tubular function is immature in the neonate, resulting in limited ability to concentrate urine, reduced sodium and bicarbonate reabsorption (leading to increased renal losses), and low renal potassium excretion. (See 'Urinary concentration' above and 'Other tubular function' above.)

• The neonate has a proportionally greater fluid loss compared with older individuals. This is primarily due to increased evaporative losses through the skin, which increase with decreasing GA and with the use of radiant heaters. (See 'Sources of water loss' above.)

• Monitoring to maintain the correct balance of fluid and electrolytes in the neonate consists of the following:
  - Physical examination to assess the infant's GA and other factors that contribute to fluid loss (eg, loss of skin integrity). Sequential physical examinations to assess fluid status that include evaluation of cardiovascular stability, daily weights, and the presence of edema. Normal weight loss over the first three to five days should be expected. Volume overload is suggested by inadequate weight loss in this time period or excessive weight gain, edema, and increased blood pressure. Inadequate fluid administration may be accompanied by excessive weight loss, tachycardia, poor capillary refill, and, in severe cases, hypotension. (See 'Physical examination' above.)
  - Monitoring fluid intake and output of urine and stool. (See 'Intake and output' above.)
  - For infants receiving parenteral fluids, serial measurement of serum sodium. During the first days of life, changes in sodium concentration primarily reflect changes in water intake with hyponatremia associated with excess water (hypervolemia) and hypernatremia with excessive water loss (hypovolemia). The frequency of monitoring is dependent on the infant's clinical condition and GA. (See 'Serum sodium' above.)
  - Calculation of fluid and electrolyte requirements must account for correction of fluid abnormalities (deficit or excess water) and ongoing maintenance requirements. Maintenance fluid requirements are those needed for neutral water balance after accounting for obligatory losses (eg, urine and stool) and insensible losses (eg, skin and lungs) (table 3), and are influenced by postnatal age and birth weight (BW), environmental factors, renal function, and ventilator dependence. (See 'Fluid requirements' above.)
  - Maintenance requirements for sodium, potassium, and chloride are approximately 2 to 3 mEq/kg per day. For infants receiving intravenous fluids, these electrolytes are not given during the first 48 hours after birth. Additional electrolyte losses beyond maintenance requirements should be replaced. (See 'Electrolyte requirements' above.)
In the newborn, particularly preterm infants, electrolyte disorders are common and include:

- Hyponatremia (see 'Hyponatremia' above)
- Hypernatremia (see 'Hypernatremia' above)
- Hypokalemia (see 'Hypokalemia' above)
- Hyperkalemia (see 'Hyperkalemia' above)

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REFERENCES


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## Serum creatinine values for very preterm infants (gestational age less than 33 weeks)

<table>
<thead>
<tr>
<th>Age</th>
<th>50&lt;sup&gt;th&lt;/sup&gt; percentile value mg/dL (micromol/L)</th>
<th>95&lt;sup&gt;th&lt;/sup&gt; percentile value mg/dL (micromol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7 days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 to 27 weeks gestation</td>
<td>0.87 (76.9)</td>
<td>1.23 (108.7)</td>
</tr>
<tr>
<td>28 to 29 weeks gestation</td>
<td>0.84 (74.3)</td>
<td>1.18 (103.9)</td>
</tr>
<tr>
<td>30 to 33 weeks gestation</td>
<td>0.66 (58.3)</td>
<td>0.95 (83.9)</td>
</tr>
<tr>
<td><strong>10 to 14 days</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 to 27 weeks gestation</td>
<td>0.75 (66.3)</td>
<td>1.10 (97.3)</td>
</tr>
<tr>
<td>28 to 29 weeks gestation</td>
<td>0.69 (61)</td>
<td>1.02 (90.3)</td>
</tr>
<tr>
<td>30 to 33 weeks gestation</td>
<td>0.57 (50.4)</td>
<td>0.84 (74.1)</td>
</tr>
<tr>
<td><strong>One month</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 to 27 weeks gestation</td>
<td>0.48 (42.4)</td>
<td>0.72 (63.6)</td>
</tr>
<tr>
<td>28 to 29 weeks gestation</td>
<td>0.41 (36.2)</td>
<td>0.64 (57)</td>
</tr>
<tr>
<td>30 to 33 weeks gestation</td>
<td>0.35 (30.9)</td>
<td>0.57 (50.2)</td>
</tr>
<tr>
<td><strong>Two months</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 to 27 weeks gestation</td>
<td>0.31 (27.4)</td>
<td>0.51 (44.9)</td>
</tr>
<tr>
<td>28 to 29 weeks gestation</td>
<td>0.33 (28.8)</td>
<td>0.58 (51.6)</td>
</tr>
<tr>
<td>30 to 33 weeks gestation</td>
<td>0.25 (22.2)</td>
<td>Data not available</td>
</tr>
</tbody>
</table>


Graphic 111831 Version 2.0
### Normal serum potassium levels in children*

<table>
<thead>
<tr>
<th>Age</th>
<th>Range (mEq/L or mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature infant</td>
<td>4 to 6.5</td>
</tr>
<tr>
<td>Newborn</td>
<td>3.7 to 5.9</td>
</tr>
<tr>
<td>Infant</td>
<td>4.1 to 5.3</td>
</tr>
<tr>
<td>Child &gt;1 year old</td>
<td>3.5 to 5</td>
</tr>
</tbody>
</table>

* Local laboratory reference ranges for normal may vary depending on laboratory and assay technique. Clinical implications of variation from normal or reference range levels must be considered individually.
Fluid requirements (mL/kg per day) in newborns

<table>
<thead>
<tr>
<th>Birth weight (g)</th>
<th>Days 1 to 2</th>
<th>Day 3</th>
<th>&gt; Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1000</td>
<td>90 to 120</td>
<td>140</td>
<td>150</td>
</tr>
<tr>
<td>1001 to 1250</td>
<td>80 to 100</td>
<td>120</td>
<td>150</td>
</tr>
<tr>
<td>1251 to 1500</td>
<td>80</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>1501 to 2000</td>
<td>60 to 80</td>
<td>100</td>
<td>140 to 160</td>
</tr>
<tr>
<td>&gt;2000</td>
<td>60 to 80</td>
<td>100</td>
<td>140 to 160</td>
</tr>
</tbody>
</table>

These values are intended as guidelines and should be adjusted according to the infant’s clinical status. Adjustments should be made based on monitoring the infant's hydration status, including serial measurements of the infant's weight and serum or plasma sodium levels.

Other adjustments include the following:

- For very low birth weight (VLBW) infants (BW <1500 g), the above values assume that the infant is being cared for in a humidified incubator with appropriate thermal control, and if respiratory support is provided, humidified gas is used.
- For VLBW infants cared for in an open warmer or receiving respiratory support with non-humidified gases, the required amount of daily fluid is higher. In this clinical setting, fluid administration is started at the upper end of the normal range and increased in increments of 20 mL/kg per day based on frequent monitoring of hydration status performed at least every eight hours until a stable regimen is established.
- For term infants, fluid adjustments are not needed for those cared for in an open warmer or bassinette if they are adequately wrapped, as they have less fluid skin loss than preterm infants due to more mature, thicker skin.
- For term infants receiving therapeutic hypothermia, many practitioners will restrict fluids to 40 to 60 mL/kg/d if there is evidence of acute kidney injury.
- For infants receiving conventional phototherapy using fluorescent blue lights, requirements are approximately 10 percent higher (10 to 15 mL/kg per day).
- For infants that receive therapy using LED lights that use high-intensity blue gallium nitride, there is no need for additional adjustment because there is no increased insensible skin losses.
**Management of acute pediatric hyperkalemia**

- Does the patient have one or more of the following:
  - ECG changes*
  - Muscular weakness or paralysis
  - Serum or plasma potassium > 7 mEq/L (mmol/L)
  - Serum or plasma potassium between 6 and 7 mEq/L (mmol/L) with an ongoing risk of a continued rise due to tissue breakdown (e.g., tumor lysis or major crush injury)

- Emergent therapy
  - Does the patient have IV access?
    - Yes
      - IV calcium infusion
      - IV insulin and glucose infusion
    - No
      - Inhaled beta-adrenergic agent
      - Continue to obtain IV access
  - Monitor response:
    - Serial lab testing of potassium
    - Continuous or serial ECG monitoring

- Patient responds to initial emergent therapy by meeting all of the following criteria:
  - Serum or plasma potassium decreases < 7 mEq/L (mmol/L)
  - Clinical findings (e.g., ECG change or muscular symptoms) resolve
  - No ongoing increase in potassium for at-risk patients

- Nonemergent therapy:
  - Correction of reversible causes of hyperkalemia
  - Removal of excess potassium from the body. One or more of the following measures are performed:
    - Diuretics
    - Gastrointestinal cation exchanger
    - Dialysis in patients with renal insufficiency or who do not respond to medical management

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ECG: electrocardiogram; IV: intravenous.

* Electrocardiographic changes suggestive of hyperkalemia include widening of the QRS complex, loss of P waves, or arrhythmias, but not isolated peaked T waves.

¶ For details of therapy, please refer to UpToDate topics on the management of hyperkalemia in children.

Δ Nonemergent therapy given as adjunctive therapy to patients who receive emergent therapy and for patients with acute asymptomatic hyperkalemia with potassium levels <7 mEq/L not at risk for continued rise in potassium.
Contributor Disclosures

Steven Ringer, MD, PhD  Nothing to disclose  Steven A Abrams, MD  Consultant/Advisory Boards: MilkPep [Childhood nutrition (Diary)].  Tej K Mattoo, MD, DCH, FRCP  Nothing to disclose  Melanie S Kim, MD  Nothing to disclose

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