
In the name of GOD
Fluid Therapy
N.Esfandiar,MD
Pediatric nephrologist
Mofid Children's Hospital,
Tehran,IRAN

Fluid therapy

- The goal of fluid therapy is to preserve the normal volume and electrolyte composition of body fluids. Fluid therapy is usually divided into two components:
- ●Maintenance therapy
- ●Repletion therapy

Maintenance therapy

- Maintenance therapy replaces the ongoing daily losses of water and electrolytes occurring via physiologic processes (urine, sweat, respiration, and stool), which normally preserve homeostasis
- Maintenance requirements vary depending on the patient's underlying clinical status and setting especially in postoperative or hospitalized children due to changes in their physiologic responses (eg, excess antidiuretic hormone [ADH] secretion).

Table 56-1	Goals of Maintenance Fluids
Prevent dehydration Prevent electrolyte disorders Prevent ketoacidosis Prevent protein degradation	

Water requirements

- Directly derived in relationship to caloric energy expenditures
- Daily water needs replace insensible water losses from the respiratory tract and skin, and sensible water losses in urine and stool output

Daily insensible losses

- In patients greater than 10 kg, the insensible needs are also often calculated based upon body surface area at a rate of about 300 to 400 mL/m^2/day.
  - Skin losses, due to evaporation from convection and conduction, account for two-thirds of the insensible losses (25 mL per 100 kcal). Infants and small children have a proportionally greater body surface area per unit of body weight than larger children and adults resulting in a relatively higher insensible skin loss of water.
  - Respiratory losses, due to the warming and humidification of inspired air, account for one-third of insensible losses (10 mL per 100 kcal).

Daily sensible water losses

- Account for approximately 60 mL per 100 kcal of energy expenditure. Since water loss from stool is negligible in healthy children, sensible water loss is primarily due to the daily urinary water losses required to excrete the solute load generated from typical dietary intake and cellular metabolism

Table 53-5 SOURCES OF WATER LOSS
Urine: 60%
Insensible losses: ≈35% (skin and lungs)
Stool: 5%

Methods for calculation

- **Method 1** – Maintenance fluid needed on an hourly basis:
  - •Weight less than 10 kg − 4 mL/kg per hour
  - •Weight >10 kg to 20 kg − 40 mL/hour for first 10 kg of body weight plus 2 mL/kg per hour for any increment of weight over 10 kg
  - •Weight >20 kg− 60 mL/hour for first 20 kg of body weight plus 1 mL/kg per hour for any increment of weight over 20 kg, to a maximum of 100 mL/hour (up to a maximum of 2400 mL daily)

Methods for calculation

- **Method 2** – Maintenance fluid volume for a 24-hour period :
- •Weight less than 10 kg – 100 mL/kg
- •Weight >10 kg to 20 kg – 1000 mL for first 10 kg of body weight plus 50 mL/kg for any increment of weight over 10 kg
- •Weight >20 kg- 1500 ml for first 20 kg plus 20 mL/kg for any increment of weight over 10 kg

- The total daily volume of water prescribed by the hourly format is a bit lower than the daily format, but the difference is almost always of no clinical significance

Example:

- The maintenance water needs for a 12 kg child using both methods

Example:

- Utilizing the hourly method, the maintenance needs would be 44 mL per hour or 1056 mL for 24 hours (40 mL/hour for the first 10 kg of body weight, plus 4 mL/hour for the next 2 kg [2 mL/kg per hour for each kg of body weight between 10 and 20 kg]).
- 44×24=1056

Example:

- Utilizing the 24-hour method, the maintenance needs would be slightly higher at 1100 mL for 24 hours (1000 mL for the first 10 kg, plus 100 mL for the next 2 kg [50 mL/kg per day for each kg of body weight between 10 and 20 kg]).

Maintenance electrolyte requirements

- In children, the daily sodium, chloride, and potassium requirements can be related to daily water needs as follows:
- ●Sodium and chloride − 2 to 3 mEq/100 mL of water per day
- ●Potassium − 1 to 2 mEq/100 mL of water per day
- sodium and potassium intake may need to be reduced in patients with oliguric renal failure to prevent volume expansion and hyperkalemia; conversely, their intake may need to be increased in patients with diarrhea or burns to prevent volume depletion and hypokalemia.

Dextrose

- Dextrose is added to maintenance fluids when the clinician decides to provide an additional source of glucose to the patient. Under normal circumstances, 5 to 10 percent dextrose solution administered at a maintenance rate is safe, as this amount of dextrose is taken up rapidly by cells and does not remain in the intravascular space. As a result, dextrose is not a relevant factor when considering tonicity of intravenous (IV) fluid compared to sodium
- Dextrose should not be used in patients with uncontrolled diabetes, which may increase glucose levels, or hypokalemia

Changes in maintenance needs:

- Changes in water loss : Prematurity, Burns, Fever, Mechanical ventilation , Gastrointestinal illness, Oliguria, Sweating
- Impaired ADH action

Factors affecting insensible water losses

Increased losses	% Change	Decreased losses	% Change
Prematurity	100–300	Enclosed incubator	25–50
Radiant warmer	50–100	Humidified air	15–30
Phototherapy	25–50	Sedation	5–25
Hyperventilation	20–30	Decreased activity	5–25
Increased activity	5–25	Hypothermia	5–15
Hyperthermia	12%/°C		

Table 53-6 ADJUSTMENTS IN MAINTENANCE WATER		
SOURCE	**CAUSES OF INCREASED WATER NEEDS**	**CAUSES OF DECREASED WATER NEEDS**
Skin	Radiant warmer	Incubator (premature infant)
	Phototherapy	
	Fever	
	Sweat	
	Burns	
Lungs	Tachypnea	Humidified ventilator
	Tracheostomy	
Gastrointestinal tract	Diarrhea	—
	Emesis	
	Nasogastric suction	
Renal	Polyuria	Oliguria/anuria
Miscellaneous	Surgical drain	Hypothyroidism
	Third spacing	

Action	Affect on urinary volume	Condition or disease category
Nonphysiologic or inappropriate ADH release **(SIADH)**	Decrease in urinary volume	▪ Postoperative state ▪ CNS disease – Meningitis, brain tumors, head injury ▪ Pulmonary disease – Pneumonia, bronchiolitis, asthma ▪ Immobilization ▪ Drugs • Antidepressants (eg, SSRI) • Antipsychotics (eg, haloperidol) • Seizure medications (eg, carbamazepine) • Chemotherapeutic agents (eg, vincristine, cisplatin, vinblastine) • Opiates ▪ Response to pain, stress, or anxiety
Enhanced renal ADH receptor response	Decease in urinary volume	▪ Nephrogenic SIADH – Gain of function mutations in the renal V2 receptor gene
Lack of adequate ADH release/central diabetes insipidus **(CDI)**	Increase in urinary volume	▪ CNS tumors (eg, craniopharyngioma) ▪ Congenital brain abnormalities (eg, septo-optic dysplasia) ▪ Brain trauma or injury (eg, complication of brain surgery) ▪ Genetic diseases ▪ Anorexia nervosa
Lack of renal ADH receptor response/nephrogenic diabetes insipidus **(NDI)**	Increase in urinary volume	▪ Congenital disorders (eg, loss of function mutation in renal V2 receptor gene, renal tubulopathy [Bartter syndrome]) ▪ Drugs (eg, lithium toxicity, foscarnet, ifosfamide) ▪ Renal disorders (eg, bilateral urinary tract obstruction, sickle cell nephropathy)

Isotonic versus hypotonic solution

- Systematic reviews of clinical trials showed that hospitalized children who received hypotonic fluids had an increased risk of hyponatremia compared with those who received isotonic fluids .
- This was illustrated in one meta-analysis in which of the risk of hyponatremia was greater in children who received hypotonic solutions compared to those who received isotonic solution (34 versus 17 percent, relative risk [RR] 2.08, 95% CI 1.67-2.63)

SELECTION OF MAINTENANCE FLUIDS

D5 ½NS + 20 mEq/L KCl is recommended in the child who is NPO and does not have volume depletion or risk factors for nonosmotic ADH production. Children with volume depletion, baseline hyponatremia, or at risk for nonosmotic ADH production (lung infections such as bronchiolitis or pneumonia; central nervous system infection) should receive D5 NS + 20 mEq/L KCl. Surgical patients typically receive isotonic fluids (NS, LR) during surgery and in the recovery room for 6-8 hr postoperatively; the rate is typically approximately two-thirds of the calculated maintenance rate, with dextrose added if clinically indicated. Subsequent maintenance fluids should be D5 NS or LR, with addition of 10-20 mEq/L of KCl based on the serum potassium and the clinical setting. Electrolytes should be measured at least daily in all children receiving more than 50% of maintenance fluids intravenously unless the child is receiving prolonged intravenous fluids (TPN).

These guidelines assume that there is no disease process present that would require an adjustment in either the volume or the electrolyte composition of maintenance fluids. Neonates, and especially premature infants, are outside of the scope of these guidelines given their unique physiology. Children with renal insufficiency may be hyperkalemic or unable to excrete potassium and may not tolerate 10 or 20 mEq/L of potassium. Patients with persistent ADH production because of an underlying disease process (syndrome of inappropriate ADH secretion, congestive heart failure, nephrotic syndrome, liver disease) should receive less than maintenance fluids. Children with meningitis are fluid restricted unless intravascular volume depletion is present (see Chapter 603.1). Treatment is individualized, and careful monitoring is critical.

In children with complicated pathophysiologic derangements, it may be necessary to empirically adjust the electrolyte composition and rate of maintenance fluids on the basis of electrolyte measurements and assessment of fluid balance. **In all children, it is critical to carefully monitor weight, urine output, and electrolytes to identify overhydration or underhydration, hyponatremia, and other electrolyte disturbances, and to then adjust the rate or composition of the intravenous solution accordingly.**

Example:

- The maintenance water needs for a 12 kg:
- Utilizing the hourly method, the maintenance needs would be 44 mL per hour or 1056 mL for 24 hours
- Utilizing the 24-hour method, the maintenance needs would be slightly higher at 1100 mL for 24 hours

How do you prescribe?

- Serum DW5% Half saline 1100 ml % +11 ml Kcl 15%
- Serum DW5% 1100 ml +22 ml Nacl 20% +11 ml Kcl 15%
- Serum DW5% 1100 ml +88 ml Nacl 5% +11 ml Kcl 15

- 1ml Nacl 20%=3.4mEq Na
- 1ml Nacl 5%=0.85mEq Na
- 1ml Kcl 20%=2mEq K

Calculation of water

The required water= {IWL (20-45 cc/kg/day) or 400cc/m2 or 1/3 or 25-40% of M + Uvol}+ Replacement water (ongoing loss) +Deficit (%DH×BW×10)

Table 56-7	Replacement Fluid for Diarrhea

AVERAGE COMPOSITION OF DIARRHEA
Sodium: 55 mEq/L
Potassium: 25 mEq/L
Bicarbonate: 15 mEq/L

APPROACH TO REPLACEMENT OF ONGOING LOSSES
Solution: D5 ½NS + 30 mEq/L sodium bicarbonate + 20 mEq/L KCl
Replace stool mL/mL every 1-6 hr

Table 56-8	Replacement Fluid for Emesis or Nasogastric Losses

AVERAGE COMPOSITION OF GASTRIC FLUID
Sodium: 60 mEq/L
Potassium: 10 mEq/L
Chloride: 90 mEq/L

APPROACH TO REPLACEMENT OF ONGOING LOSSES
Solution: normal saline + 10 mEq/L KCl
Replace output mL/mL every 1-6 hr

Table 56-9	Adjusting Fluid Therapy for Altered Renal Output

OLIGURIA/ANURIA

Replacement of insensible fluid losses (25-40% of maintenance) with D5 ½NS

Replace urine output mL/mL with D5 ½NS ± KCl

POLYURIA

Replacement of insensible fluid losses (25-40% of maintenance) with D5 ½NS ± KCl

Measure urine electrolytes

Replace urine output mL/mL with solution based on measured urine electrolytes

Table 57-2 | Fluid Management of Dehydration

Restore intravascular volume:
- Normal saline: 20 mL/kg over 20 min
- Repeat as needed

Calculate 24-hr fluid needs: maintenance + deficit volume

Subtract isotonic fluid already administered from 24 hr fluid needs

Administer remaining volume over 24 hr using 5% dextrose NS + 20 mEq/L KCl

Replace ongoing losses as they occur

Table 57-3	Monitoring Therapy

Vital signs:
- Pulse
- Blood pressure

Intake and output:
- Fluid balance
- Urine output

Physical examination:
- Weight
- Clinical signs of depletion or overload

Electrolytes

Assessment of Hyponatremia

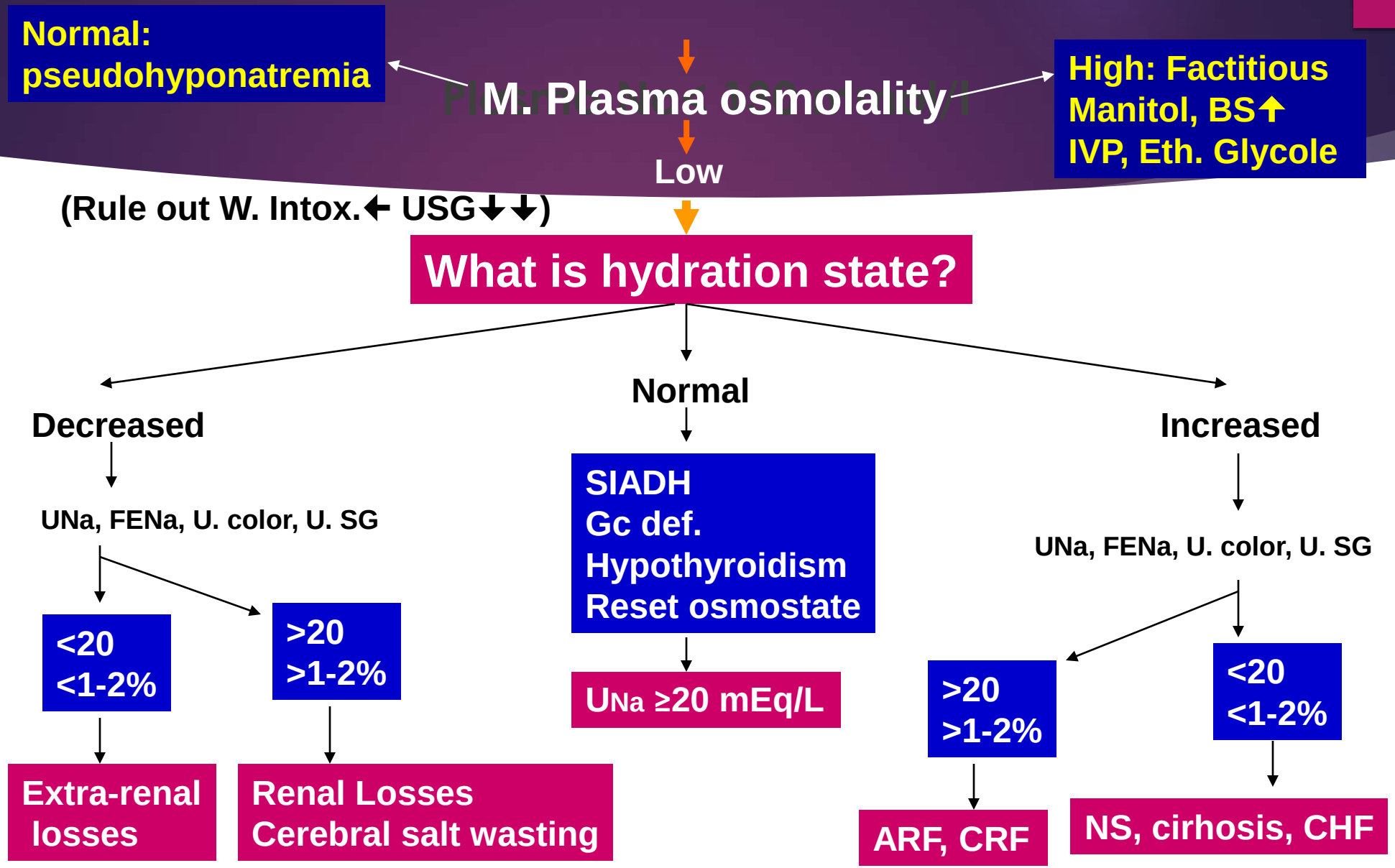


Table 55-2 Causes of Hyponatremia

PSEUDOHYPONATREMIA
Hyperlipidemia
Hyperproteinemia

HYPEROSMOLALITY
Hyperglycemia
Iatrogenic (mannitol, sucrose, glycine)

HYPOVOLEMIC HYPONATREMIA

EXTRARENAL LOSSES
Gastrointestinal (emesis, diarrhea)
Skin (sweating or burns)
Third space losses (bowel obstruction, peritonitis, sepsis)

RENAL LOSSES
Thiazide or loop diuretics
Osmotic diuresis
Postobstructive diuresis
Polyuric phase of acute tubular necrosis
Juvenile nephronophthisis (OMIM 256100/606966/602088/604387/611498)
Autosomal recessive polycystic kidney disease (OMIM 263200)
Tubulointerstitial nephritis
Obstructive uropathy
Cerebral salt wasting
Proximal (type II) renal tubular acidosis (OMIM 604278)*
Lack of aldosterone effect (high serum potassium):
- Absence of aldosterone (e.g., 21-hydroxylase deficiency [OMIM 201910])
- Pseudohypoaldosteronism type I (OMIM 264350/177735)
- Urinary tract obstruction and/or infection

EUVOLEMIC HYPONATREMIA
Syndrome of inappropriate antidiuretic hormone secretion
Nephrogenic syndrome of inappropriate antidiuresis (OMIM 304800)
Desmopressin acetate
Glucocorticoid deficiency
Hypothyroidism
Water intoxication:
- Iatrogenic (excess hypotonic intravenous fluids)
- Feeding infants excessive water products
- Swimming lessons
- Tap water enema
- Child abuse
- Psychogenic polydipsia
- Diluted formula
- Beer potomania
- Exercise-induced hyponatremia

HYPERVOLEMIC HYPONATREMIA
Heart failure
Cirrhosis
Nephrotic syndrome
Acute, chronic kidney injury
Capillary leak caused by sepsis
Hypoalbuminemia caused by gastrointestinal disease (protein-losing enteropathy)

Table 55-3	Diagnostic Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion

Absence of:

Renal, adrenal, or thyroid insufficiency

Heart failure, nephrotic syndrome, or cirrhosis

Diuretic ingestion

Dehydration

Urine osmolality >100 mOsm/kg (usually > plasma)

Serum osmolality <280 mOsm/kg and serum sodium <135 mEq/L

Urine sodium >30 mEq/L

Reversal of "sodium wasting" and correction of hyponatremia with water restriction

Hyponatremia

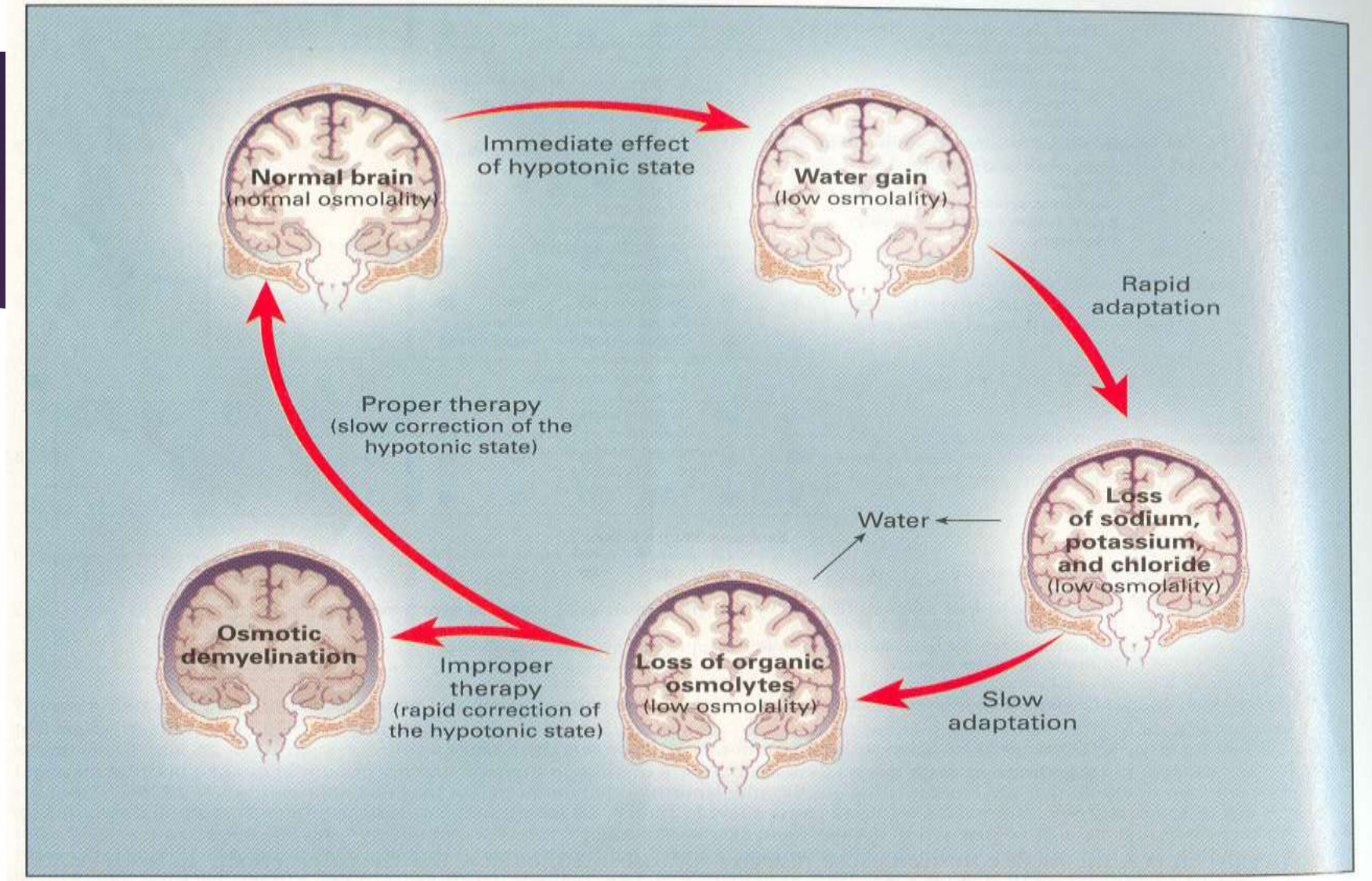
- Na < 135
- Important symptoms do not appear until < 120
- Sx result from CNS water intoxication

Types

- Dilutional
- Depletion
- Factitious

Signs and symptoms of Hyponatremia

- Increase in intracranial pressure can cause brainstem herniation and apnea
- Anorexia, nausea, emesis, malaise, lethargy, confusion, agitation, headache, seizures, coma, and decreased reflexes. Patients may have hypothermia and Cheyne-Stokes respirations. Hyponatremia can cause muscle cramps and weakness; rhabdomyolysis can occur with water intoxication.
- Brain swelling can be significantly obviated if the hyponatremia develops gradually.



Effects of Hyponatremia on the brain and Adaptive responses

Etiology of hyponatremia

Circulating volume	Urinary Na (mEq/L)	
	≤ 20	≥ 20
Decreased	Burns	Adrenal insufficiency
	Cystic fibrosis	Diuretics –early
	Diuretics – late	Salt wasting
	Gastroenteritis	
Normal or Increased	Cardiac failure	Renal failure
	Hepatic cirrhosis	SIADH
	Nephrotic syndrome	Water intoxication

Cerebral Salt Wasting Syndrome (CSWS)

- **Clinical Presentation: Acute CNS lesion specially SAH presenting with hyponatremia and high urinary sodium**
- **Key difference CSWS salt loss in face of hypovolemic**
- **Serum UA is normal in CSWS and low in SIADH**
- **Natriuretic Peptides (ANP, BNP)**

Ntriuretic peptides are the cause of persistent hyponatremia in CSW

- **Oubain like materials**

Chronic symptomatic Hyponatremia

- **Hyponatremia present for more than 48 hrs**
- **If symptoms mild correct at rate of 0.5 mEq/L/hr**
- **Correction should be slow**
- **Treat underlying disease if possible**

Osmotic Demylinating syndrome

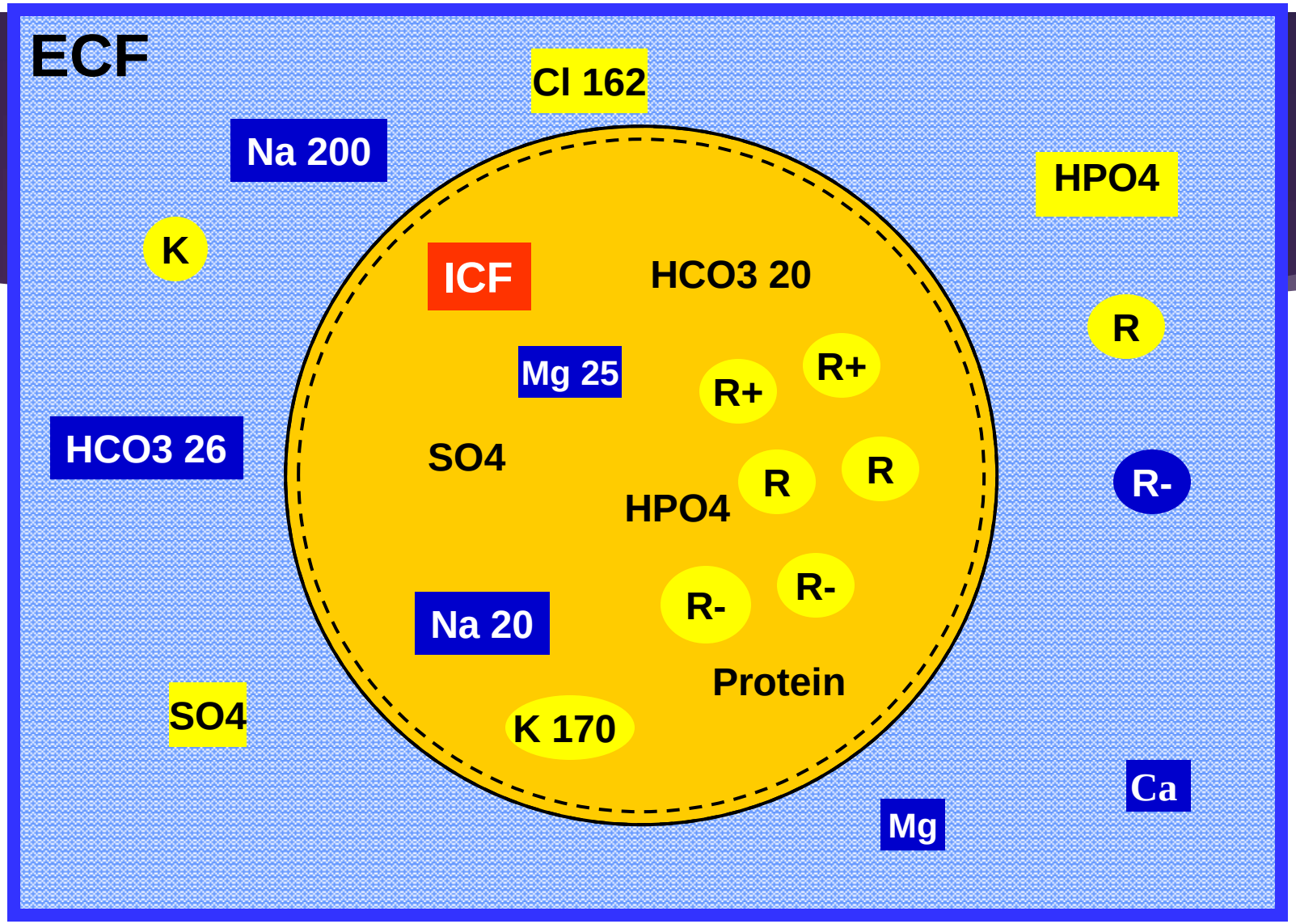
- **Often occurs 1-7 day after correction of hyponatremia**
- **Demyelination includes extrapontine area**
- **Clin.: pseudobulbar palsy, quadriparesis, movement disorders, locked in synd. Cerebellar ataxia**
- **At risk: malnutrition, alcoholism, elderly women on thiazide**
- **Mechanism: Disruption of BBB due to failure to rapidly adapt to change in osmolality**
- **Mortality: relatively low with supportive care. Majority however remain with significant morbidity**
- **Effect of reversal of osmolality?**

Hypernatremic dehydration

- ↑ sodium conc. > 150

Symptoms

- Important Sx do not appear until Na > 160
- Mainly due to CNS dehydration
- Less symptomatic initially
- Profoundly dehydrated
- Irritable, restless, weak, and lethargic
- High pitched cry and hyperpnea
- Very thirsty, fever
- Subarachnoid, subdural, and parenchymal hemorrhages
- Seizure & Coma
- CPM and extra pontine myelinolysis
- Thrombotic complications : stroke, dural sinus thrombosis, peripheral thrombosis, and renal vein thrombosis



Muscle or Brain in ECF: Hypernatremia, osmoprotective molecules

Table 57-4 | Treatment of Hypernatremic Dehydration

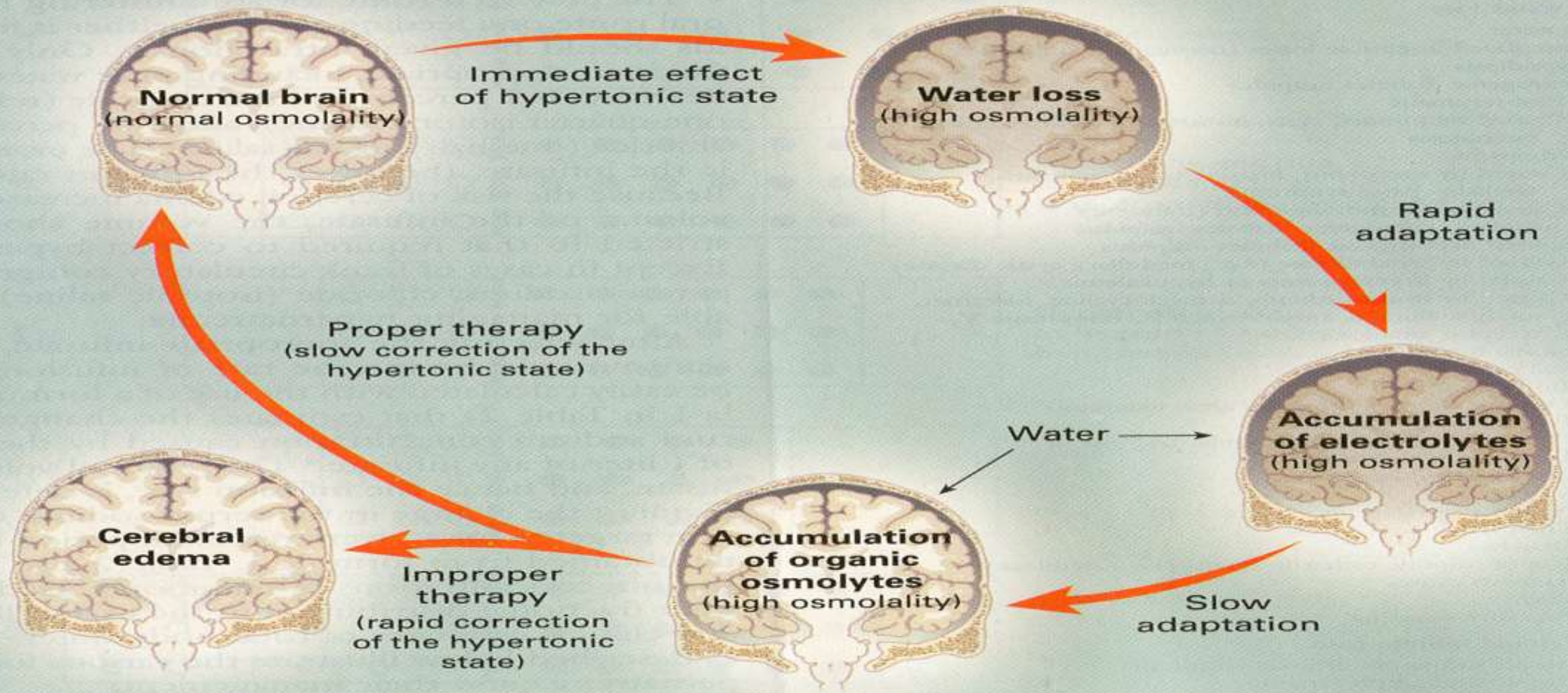
Restore intravascular volume:
- Normal saline: 20 mL/kg over 20 min (repeat until intravascular volume restored)
- Determine time for correction on basis of initial sodium concentration:
  - [Na] 145-157 mEq/L: 24 hr
  - [Na] 158-170 mEq/L: 48 hr
  - [Na] 171-183 mEq/L: 72 hr
  - [Na] 184-196 mEq/L: 84 hr

Administer fluid at constant rate over time for correction:
- Typical fluid: 5% dextrose + half-normal saline (with 20 mEq/L KCl unless contraindicated)
- Typical rate: 1.25-1.5 times maintenance

Follow serum sodium concentration

Adjust fluid on basis of clinical status and serum sodium concentration:
- Signs of volume depletion: administer normal saline (20 mL/kg)
- Sodium decreases too rapidly; either:
  - Increase sodium concentration of intravenous fluid
  - Decrease rate of intravenous fluid
- Sodium decreases too slowly; either:
  - Decrease sodium concentration of intravenous fluid
  - Increase rate of intravenous fluid

Replace ongoing losses as they occur

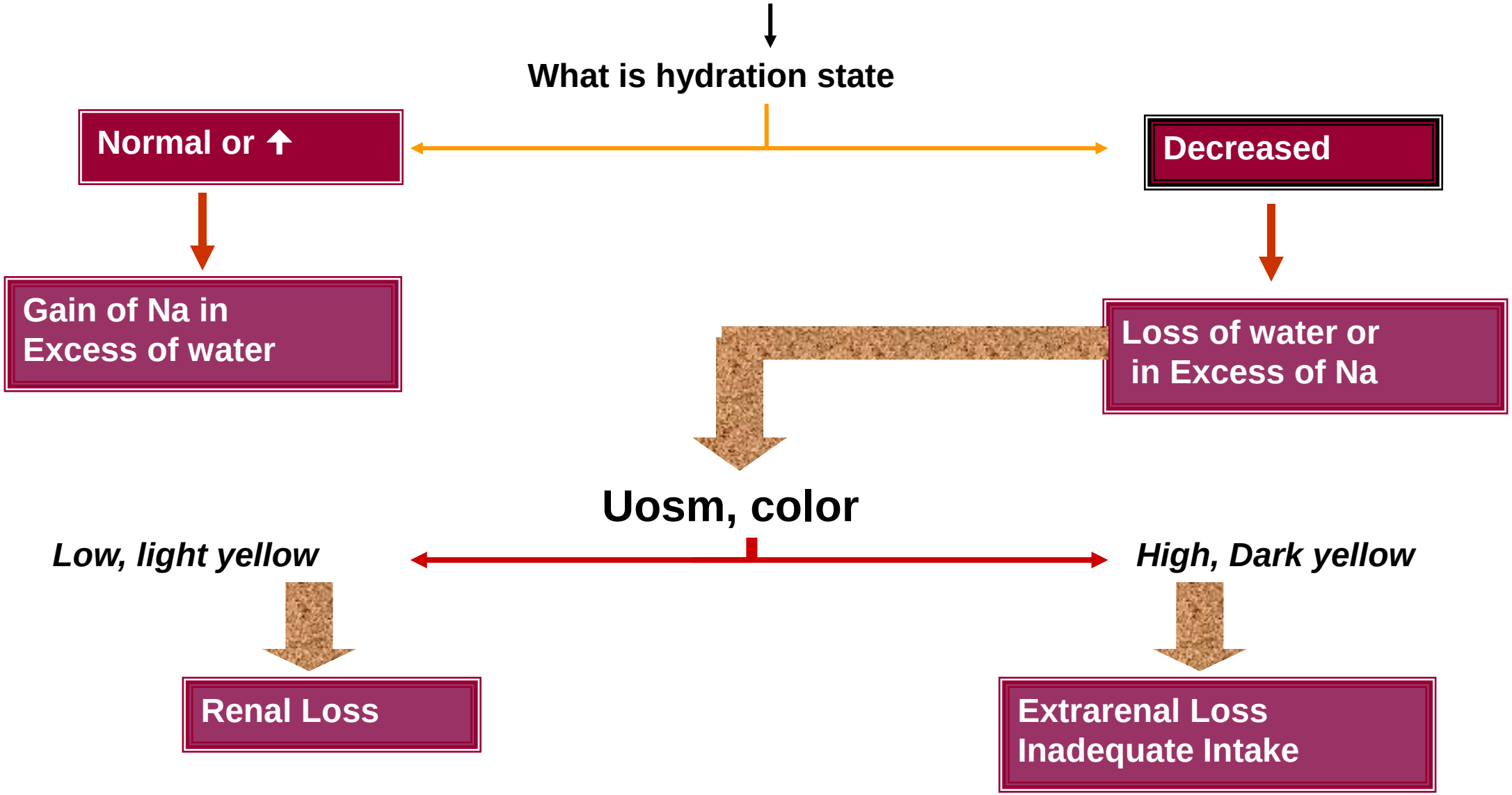


Effects of Hypernatremia on the brain and Adaptive responses

Table 52-1 CAUSES OF HYPERNATREMIA
EXCESSIVE SODIUM
Improperly mixed formula
Excess sodium bicarbonate
Ingestion of seawater or sodium chloride
Intentional salt poisoning (child abuse or Munchausen syndrome by proxy)
Intravenous hypertonic saline
Hyperaldosteronism
WATER DEFICIT
Nephrogenic diabetes insipidus:
Acquired
X-linked (MIM 304800)
Autosomal recessive (MIM 222000)
Autosomal dominant (MIM 125800)
Central diabetes insipidus:
Acquired
Autosomal recessive (MIM 125700)
Autosomal dominant (MIM 125700)
Wolfram syndrome (MIM 222300/598500
Increased insensible losses:
Premature infants
Radiant warmers
Phototherapy
Inadequate intake:
Ineffective breast-feeding
Child neglect or abuse
Adipsia (lack of thirst)
WATER AND SODIUM DEFICITS
Gastrointestinal losses:
Diarrhea
Emesis/nasogastric suction
Osmotic cathartics (lactulose)
Cutaneous losses:
Burns
Excessive sweating
Renal losses:
Osmotic diuretics (mannitol)
Diabetes mellitus
Chronic kidney disease (dysplasia and obstructive uropathy)
Polyuric phase of acute tubular necrosis
Postobstructive diuresis

$$\text{Plasma Na} \approx \frac{(\text{Nae} + \text{Ke})}{\text{TBW}}$$

Assessment Of Hypernatremia



Cause	Treatment
Na Excess	DW5% max+0.2N/s Diuretic or Dialysis
WD { NDI ↑IWL or ↓Intake	WD Approach
Central DI	Desmopressin
Water & Na Deficit	Nelson Approach

Nelson approach:

- Most patients with hypernatremic dehydration do well with a fluid sodium concentration of approximately half-normal saline, but with a fluid rate that is only 20-30% greater than maintenance fluid.
- **Patients with pure water loss may require a more hypotonic fluid (DW5% or 0.2 normal saline).**
- **Risk of hyperglycemia & hypercalcemia**

Nelson approach:

Table 57-4	Treatment of Hypernatremic Dehydration

Restore intravascular volume:
- Normal saline: 20 mL/kg over 20 min (repeat until intravascular volume restored)
- Determine time for correction on basis of initial sodium concentration:
  - [Na] 145-157 mEq/L: 24 hr
  - [Na] 158-170 mEq/L: 48 hr
  - [Na] 171-183 mEq/L: 72 hr
  - [Na] 184-196 mEq/L: 84 hr

Administer fluid at constant rate over time for correction:
- Typical fluid: 5% dextrose + half-normal saline (with 20 mEq/L KCl unless contraindicated)
- Typical rate: 1.25-1.5 times maintenance

Follow serum sodium concentration

Adjust fluid on basis of clinical status and serum sodium concentration:
- Signs of volume depletion: administer normal saline (20 mL/kg)
- Sodium decreases too rapidly; either:
  - Increase sodium concentration of intravenous fluid
  - Decrease rate of intravenous fluid
- Sodium decreases too slowly; either:
  - Decrease sodium concentration of intravenous fluid
  - Increase rate of intravenous fluid

Replace ongoing losses as they occur

WD Formula:

- Water deficit = Body weight x 0.6 (1-145/[current sodium))
- This calculation is equivalent to 3-4 mL of water per kg for each 1 mEq that the current sodium level exceeds 145 mEq.

Calculations in hypernatremia:

Water = Maintenance + Deficit +Ongoing loss

={IWL + UO} +{WD+N/S D} +Ongoing loss

Na = Maintenance Na (30meq/L)+

{0+150meq/Lit Isonatremic deficit fluid} +Ongoing loss

M: 0-10 kg 100 ml/kg

10-20 kg 50 ml/kg

>20 kg 20 ml/kg

M= IWL +UO

IWL = 400cc/m2 or 1/3 of M

Deficit =%DH×BW×10

Deficit= WD + Isonatremic deficit (150meq/L Na)

CORRECTION :

- Is hypernatremia associated with severe hypovolemia? Isotonic saline
- Does the patient have severe symptoms or is asymptomatic? patients can develop severe neurologic manifestations, including seizures, impaired mental status or coma, and death . These patients are typically treated initially with 4-6 ml/kg hypertonic saline 3%.
- Is the hypernatremia acute or chronic? hypernatremia developing over two or more days should be considered "chronic."
- What is the optimal rate of correction? Avoid overly rapid correction that can lead to a severe neurologic disorder

Urine electrolyte free water clearance

$$\text{Urine electrolyte free water clearance} = UV \times \left(1 - \frac{UNa + UK}{SNa}\right)$$

(ongoing free water loss)

As an example, the excretion of 100 mL/h of urine with a sodium plus potassium concentration one-half that of the serum sodium concentration (eg, 84 meq/L in the patient whose serum sodium is 168 meq/L) is roughly equivalent to losing 50 mL/h of electrolyte free water, regardless of the urine osmolality.

$$\text{Urine electrolyte free water clearance} = UV \times \left(1 - \frac{UNa + UK}{S\,Na}\right)$$

(ongoing free water loss)

$$\text{Urine electrolyte free water clearance} = 100 \times \left(1 - \frac{84}{168}\right)$$

$$= 50 \text{ ml/h}$$

Treatment of Hypernatremia

- **rate of correction should be maximum 0.5 meq/l/h→ correction time=2*(s Na-140)**
- **In chronic hypernatremia rate of correction should be about 10 mEq/L/day**
- **Use oral routs as much as possible**
- **IV: 0.45% saline, 0.25% saline, D5W, pure water**

Correction of hypernatremia

- **STEP ONE: ESTIMATE THE WATER DEFICIT**
- **STEP TWO: CHOOSE A RATE OF CORRECTION**
- **STEP THREE: DESIGN A FLUID REPLETION REGIMEN**
  - **WD+isosmotic fluid deficit+ ongoing water losses**
- **Concurrent electrolyte replacement**

Case study 1:

- A 10 kg child (TBW 0.6 times body weight) is estimated to have a 10 percent hypovolemic loss (about 1 liter of fluid) and a serum/plasma sodium concentration of 156 mEq/L from 24h ago due to GE.

Case study 1(Nelson Approach):

- In this case, administration of 20 ml/kg (200 ml) N/S ,then one-quarter or one-half isotonic saline at 62.5 mL/hour(1.25-1.5*1000/24 h) would provide adequate replacement of maintenance needs and remaining isotonic deficit, and would provide free water at a rate lower than the maximum threshold rate of 0.5 mEq/L per hour.

Case study 1 (WD Approach):

- The patient received a 20 mL/kg bolus of normal saline (200 mL)
- Total fluid deficit: 10 percent of 10 kg = 1000 mL
- Free water deficit: 6 L [(156/140 mEq/L) - 1] =0.686 L= 686 mL
- Isotonic loss: Total fluid deficit - water deficit = 314 mL
- 314-200=114ml (Remained isotonic loss)=17 meq Na

Case study 1:

- The water deficit should be replaced over at 32-36(156-140*2) hours so that the sodium is lowered at a rate below 0.5 mEq/L per hour.
- Over the first 24 hours, the fluid regimen, which does not include ongoing losses, would entail:
  - Free water deficit (two-thirds of total water deficit) = 686*2/3 ~460 mL
  - Remaining isotonic deficit = 114 mL of water and 17 mEq of sodium
  - Maintenance needs = 1000 mL of water and 30 mEq of sodium
  - Totally:1000+114+460 mL of water and 30+17 mEq of sodium

    =1574 mL of water and 47 mEq of sodium

Case Study 2

- A six year old (20 kg) boy has admitted due to polydipsia and polyuria following a bipolar disorder and lithium treatment since one month ago . He has about 10% DH.
- Over the last two hours, his urine output was about 130-150 ml/hour (~7ml/kg/hr).

What is your differential diagnosis?

What test would you order?

Case Study #2

Laboratory studies

Serum studies

Sodium 155 mEq/L **BUN 34 mg/dL**

Chloride 104 mEq/L **Creatinine 0.6 mg/dL**

Potassium 4.2 mEq/L **Glucose 86 mg/dL**

Bicarbonate 24 mEq/L **Serum osmolality: 320 mosmol/kg**

Other

Urine specific gravity 1.005, no glucose. **U Na= 50 mEq/L**

Urine osmolality: 175 mosmol/kg **U K = 20mEq/L**

What are the main abnormalities?

Case Study #2

Nephrogenic Diabetes Insipidus

Diagnosis

Nephrogenic Diabetes insipidus

1) Polyuria
2) Inappropriately dilute urine (urine osmolality < serum osmolality)

How do you treat this child?

Case Study 2

IV THERAPY:

- **Time of treatment=2* (155-140) =30 h**
- **Fluid=M (IWL+UO) + D (WD +Iso D)**

  = (400*0.8 *24/30 +140*30) +10*10*20

  = (320* 24/30 +4200) +2000 =6456 ml
- **WD = 0.6*BW (1- 145/155) =0.6*20*0.065=0.78 Liter =780 ml**

  or =3-4 ml/kg (155-145)=3 -4*20*10 =600 -800 ml
- **Na = M +D = M + (WD +Iso D) = (I WL+UO) +0 + Iso D**

  = 0 +50*4.2 +0 + (2000 -780) 0.15

  =210 +183 = 393 mEq Na

  ~ 215 ml/h ~60mEq Na/L

- $$\text{Urine electrolyte free water clearance} = UV \times \left(1 - \frac{UNa + UK}{S\,Na}\right)$$
  (ongoing free water loss)

- $$\text{Urine electrolyte free water clearance} = 140 \times \left(1 - \frac{50 + 20}{155}\right)$$

$$= 77 \text{ ml/h}$$

Case Study 2

IV THERAPY:

- Time of treatment=2* (155-140) =30 h
- Fluid=M + D (WD +Iso D) + ongoing water loss

  = 1500 * 24/30 +10*10*20 +77*30

  = 1200+2000+2310=5510 ml
- WD = 0.6*BW (1- 145/155) =0.6*20*0.065=0.78 Liter =780 ml

  or =3-4 ml/kg (155-145)=3 -4*20*10 =600 -800 ml
- Na = M +D = M + (WD +Iso D) = M+0 + Iso D

  = 1 2*3+0 + (2000 -780) 0.15

  =36+183 = 219 mEq Na

  ~ 184 ml/h ~40mEq Na/L

Table 553-2 CLINICAL PARAMETERS TO DISTINGUISH AMONG SIADH, CEREBRAL SALT WASTING, AND CENTRAL DIABETES INSIPIDUS

CLINICAL PARAMETER	SIADH	CEREBRAL SALT WASTING	CENTRAL DI
Serum sodium	Low	Low	High
Urine output	Normal or low	High	High
Urine sodium	High	Very high	Low
Intravascular volume status	Normal or high	Low	Low
Vasopressin level	High	Low	Low

Table 558-1	Differential Diagnosis of Polyuria and Polydipsia

Diabetes insipidus (DI)
- Central DI

Genetic (autosomal dominant)
Acquired
Trauma (surgical or accidental)
Congenital malformations (holoprosencephaly, septooptic dysplasia, encephalocele)
Neoplasms (craniopharyngioma, germinoma, metastasis)
Infiltrative (Langerhans cell histiocytosis), autoimmune (lymphocytic infundibuloneurohypophysitis), and infectious diseases
Drugs (chemotherapy)
Idiopathic
- Nephrogenic DI

Genetic (X-linked, autosomal recessive, autosomal dominant)
Acquired
Hypercalcemia, hypokalemia
Drugs (lithium, demeclocycline)
Kidney disease
Primary polydipsia
Sickle cell anemia
- Diabetes mellitus

Table 55-5 Causes of Hypokalemia

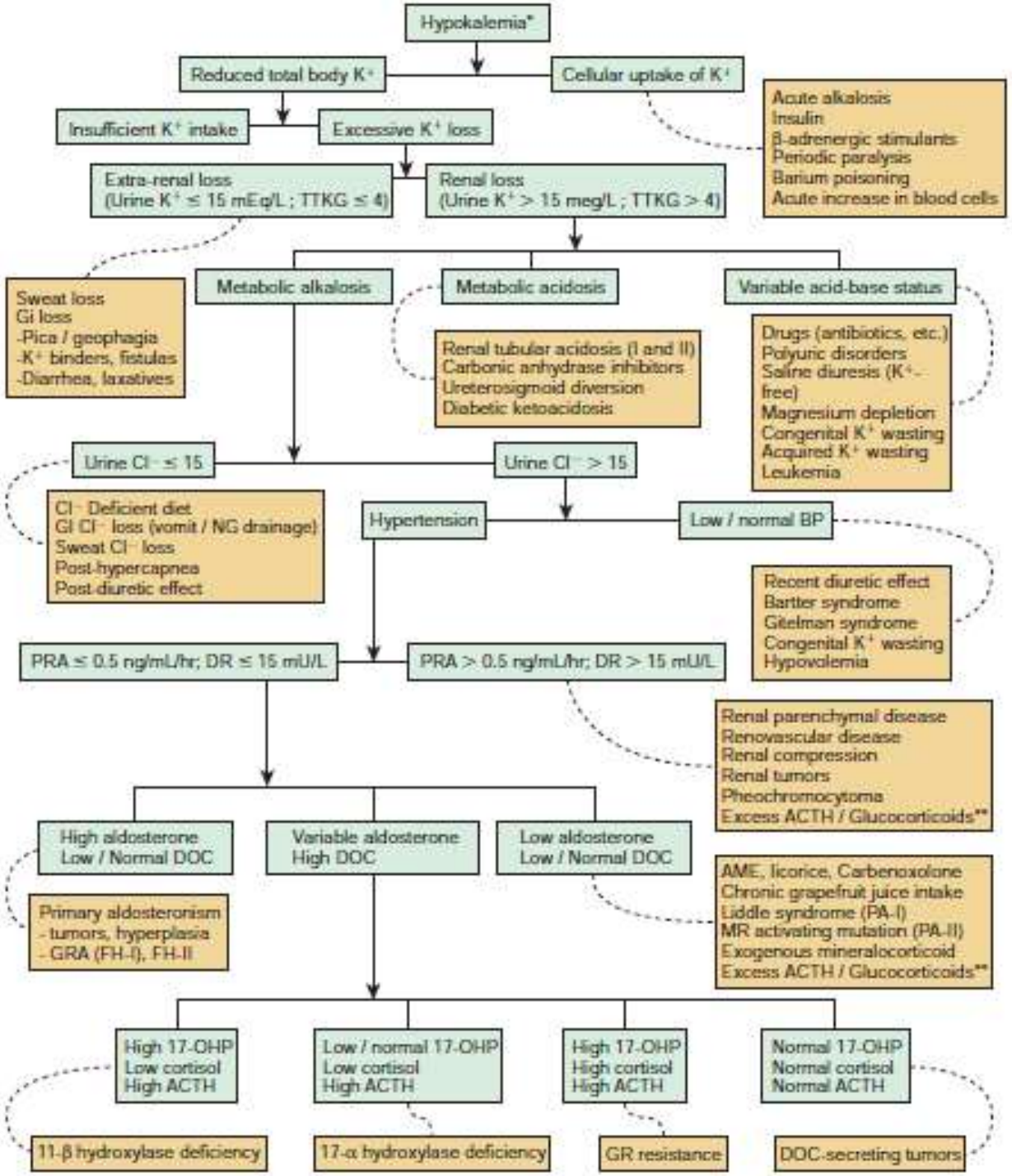
SPURIOUS
High white blood cell count

TRANSCELLULAR SHIFTS
Alkalemia
Insulin
α-Adrenergic agonists
Drugs/toxins (theophylline, barium, toluene, cesium chloride, hydroxychloroquine)
Hypokalemic periodic paralysis (OMIM 170400)
Thyrotoxic period paralysis
Refeeding syndrome

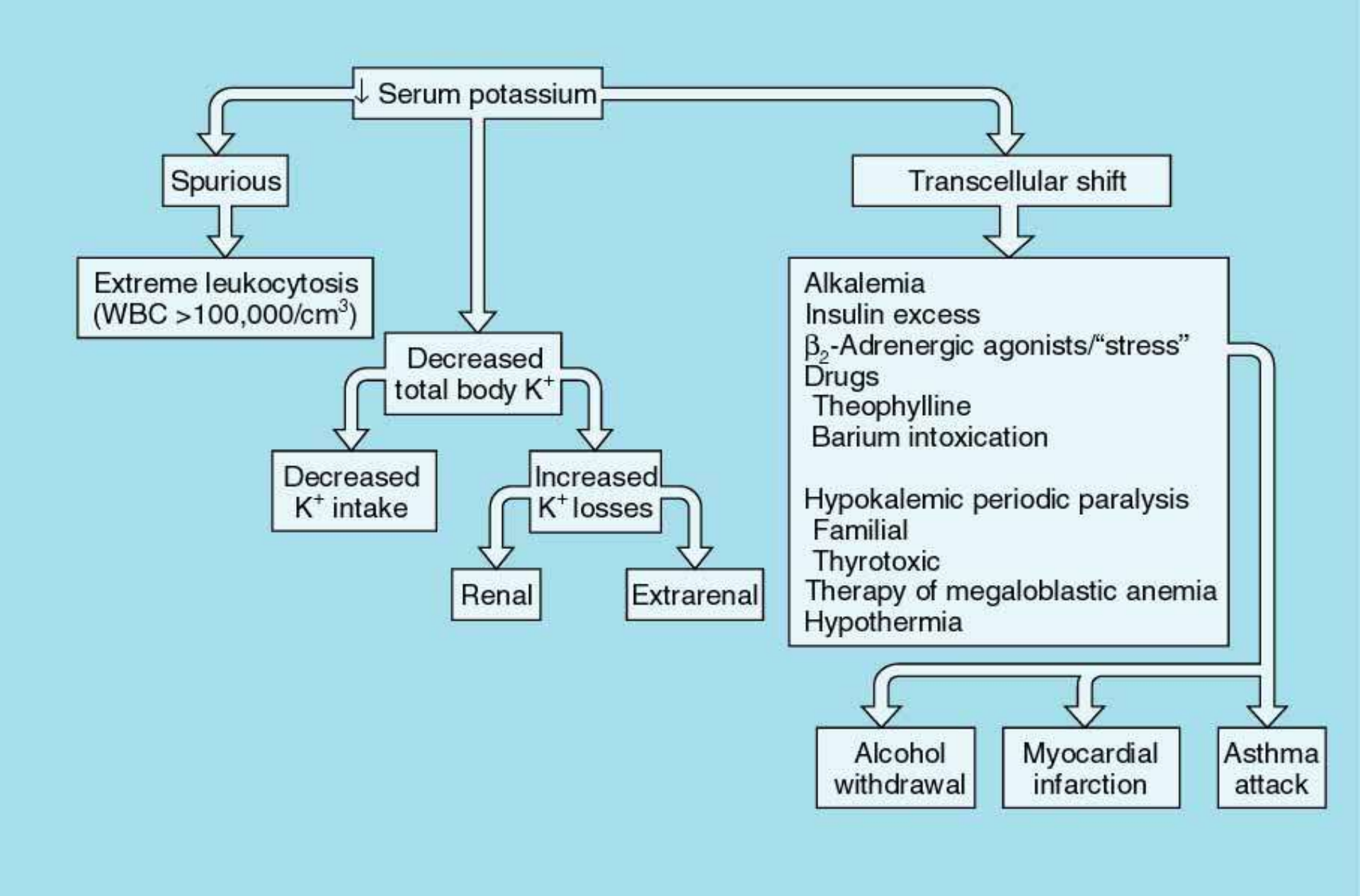
DECREASED INTAKE
Anorexia nervosa

EXTRARENAL LOSSES
Diarrhea
Laxative abuse
Sweating
Sodium polystyrene sulfonate (Kayexalate) or clay ingestion

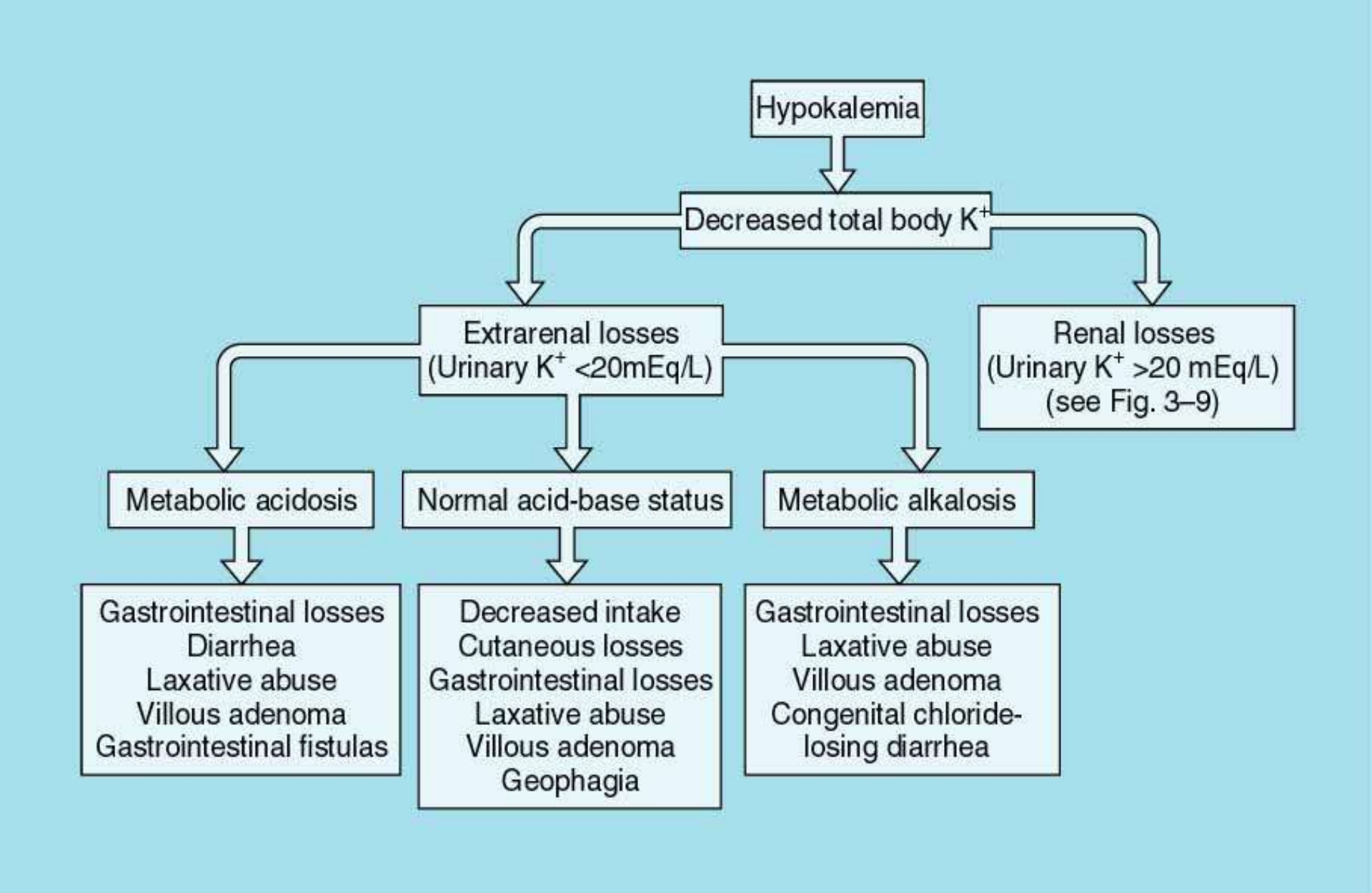
RENAL LOSSES
With metabolic acidosis
Distal renal tubular acidosis (OMIM 179800/602722/267300)
Proximal renal tubular acidosis (OMIM 604278)*
Ureterosigmoidostomy
Diabetic ketoacidosis
Without specific acid–base disturbance
Tubular toxins: amphotericin, cisplatin, aminoglycosides
Interstitial nephritis
Diuretic phase of acute tubular necrosis
Postobstructive diuresis
Hypomagnesemia
High urine anions (e.g., penicillin or penicillin derivatives)
With metabolic alkalosis
Low urine chloride
Emesis or nasogastric suction
Chloride-losing diarrhea (OMIM 214700)
Cystic fibrosis (OMIM 219700)
Low-chloride formula
Posthypercapnia
Previous loop or thiazide diuretic use
High urine chloride and normal blood pressure
Gitelman syndrome (OMIM 263800)
Bartter syndrome (OMIM 607364/602522/241200/601678)
Autosomal dominant hypoparathyroidism (OMIM 146200)
EAST syndrome (OMIM 612780)
Loop and thiazide diuretics
High urine chloride and high blood pressure
Adrenal adenoma or hyperplasia
Glucocorticoid-remediable aldosteronism (OMIM 103900)
Renovascular disease
Renin-secreting tumor
17β-Hydroxylase deficiency (OMIM 202110)
11β-Hydroxylase deficiency (OMIM 202010)
Cushing syndrome
11β-Hydroxysteroid dehydrogenase deficiency (OMIM 218030)
Licorice ingestion


Hypokalemia*
Reduced total body K+
Cellular uptake of K+
Acute alkalosis
Insulin
β-adrenergic stimulants
Periodic paralysis
Barium poisoning
Acute increase in blood cells
Insufficient K+ intake
Excessive K+ loss
Extra-renal loss
(Urine K+ ≤ 15 mEq/L ; TTKG ≤ 4)
Renal loss
(Urine K+ > 15 meq/L ; TTKG > 4)
Sweat loss
GI loss
-Pica / geophagia
-K+ binders, fistulas
-Diarrhea, laxatives
Metabolic alkalosis
Metabolic acidosis
Variable acid-base status
Renal tubular acidosis (I and II)
Carbonic anhydrase inhibitors
Ureterosigmoid diversion
Diabetic ketoacidosis
Drugs (antibiotics, etc.)
Polyuric disorders
Saline diuresis (K+-free)
Magnesium depletion
Congenital K+ wasting
Acquired K+ wasting
Leukemia
Urine Cl- ≤ 15
Urine Cl- > 15
Cl- Deficient diet
GI Cl- loss (vomit / NG drainage)
Sweat Cl- loss
Post-hypercapnea
Post-diuretic effect
Hypertension
Low / normal BP
Recent diuretic effect
Bartter syndrome
Gitelman syndrome
Congenital K+ wasting
Hypovolemia
PRA ≤ 0.5 ng/mL/hr; DR ≤ 15 mU/L
PRA > 0.5 ng/mL/hr; DR > 15 mU/L
Renal parenchymal disease
Renovascular disease
Renal compression
Renal tumors
Pheochromocytoma
Excess ACTH / Glucocorticoids**
High aldosterone
Low / Normal DOC
Variable aldosterone
High DOC
Low aldosterone
Low / Normal DOC
AME, licorice, Carbenoxolone
Chronic grapefruit juice intake
Liddle syndrome (PA-I)
MR activating mutation (PA-II)
Exogenous mineralocorticoid
Excess ACTH / Glucocorticoids**
Primary aldosteronism
- tumors, hyperplasia
- GRA (FH-I), FH-II
High 17-OHP
Low cortisol
High ACTH
Low / normal 17-OHP
Low cortisol
High ACTH
High 17-OHP
High cortisol
High ACTH
Normal 17-OHP
Normal cortisol
Normal ACTH
11-β hydroxylase deficiency
17-α hydroxylase deficiency
GR resistance
DOC-secreting tumors

Approach to Hypokalemia (1)



Approach to Hypokalemia (2)



Treatment of Hypokalemia

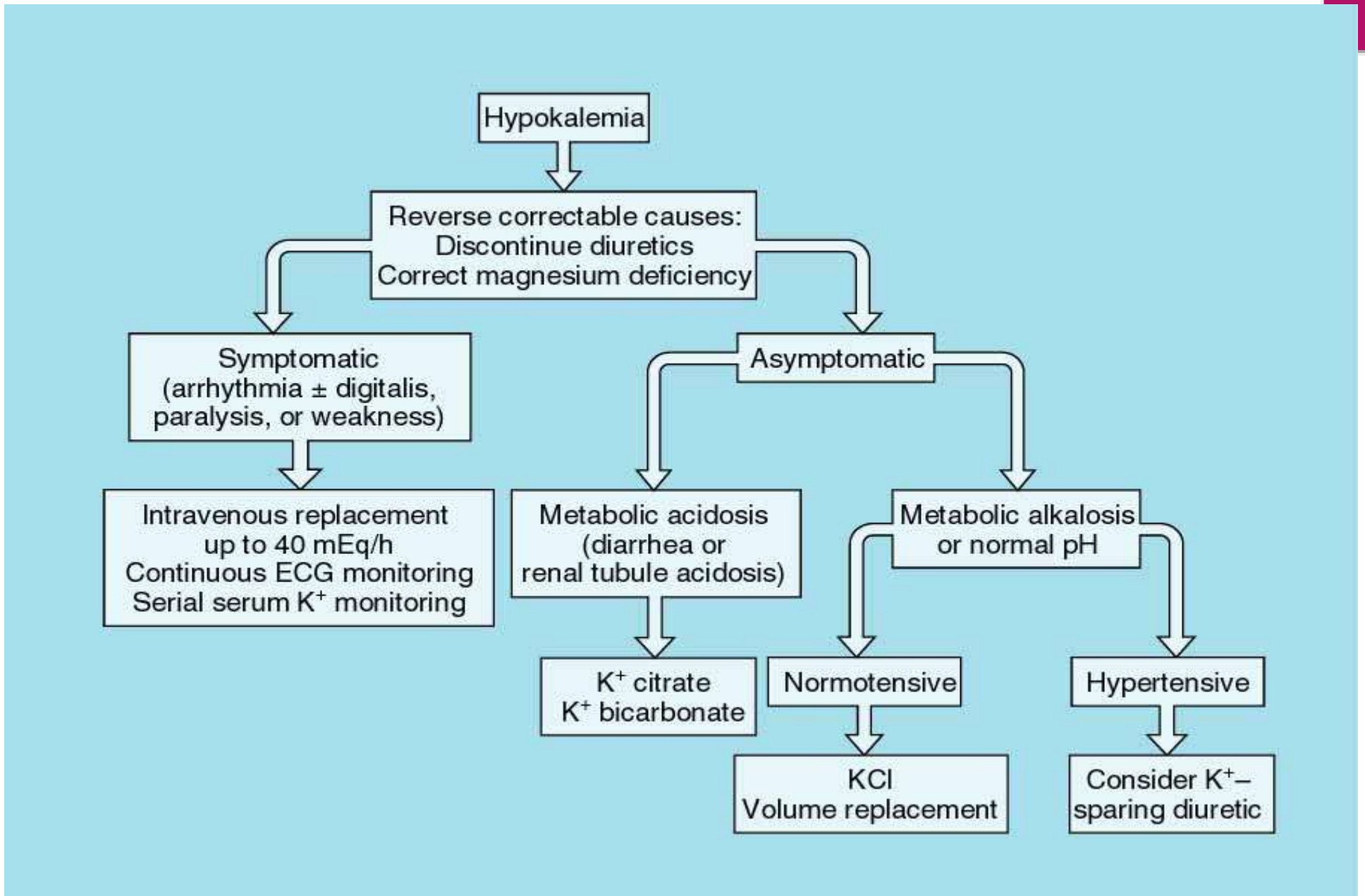


Table 55-4 Causes of Hyperkalemia

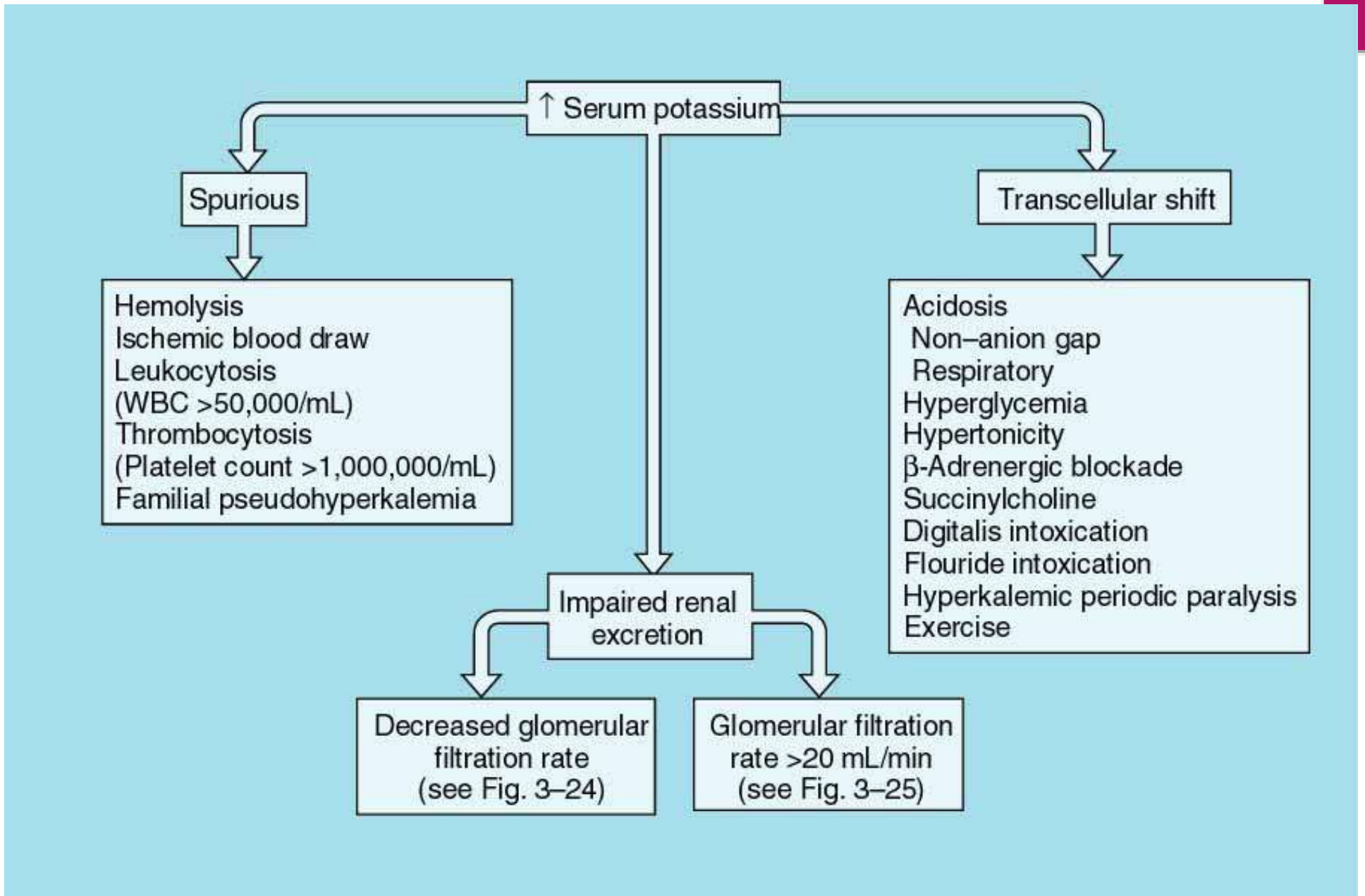
SPURIOUS LABORATORY VALUE
- Hemolysis
- Tissue ischemia during blood drawing
- Thrombocytosis
- Leukocytosis
- Familial pseudohyperkalemia (OMIM 609153/611184/612126)

INCREASED INTAKE
- Intravenous or oral
- Blood transfusions

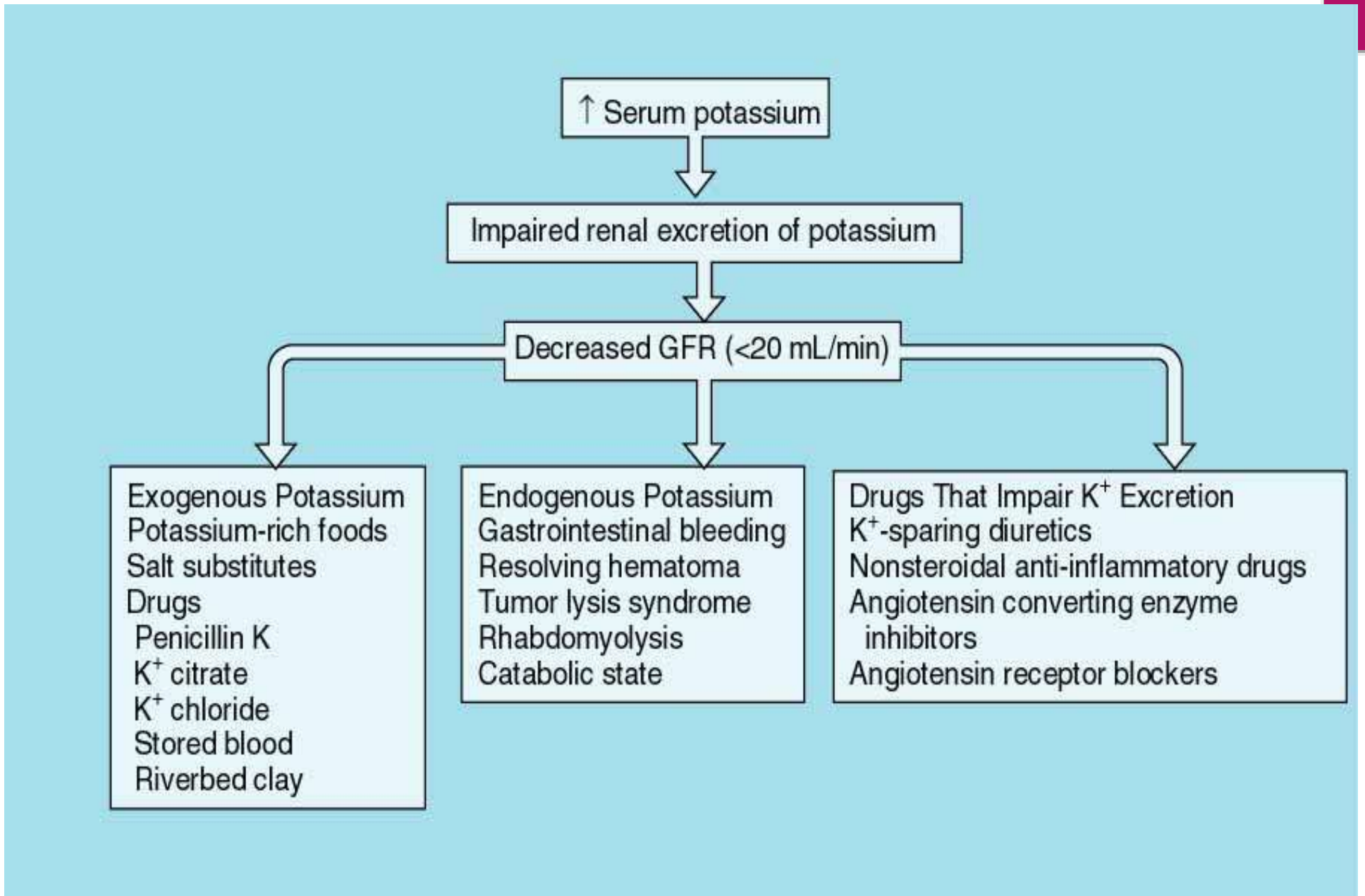
TRANSCELLULAR SHIFTS
- Acidosis
- Rhabdomyolysis
- Tumor lysis syndrome
- Tissue necrosis
- Hemolysis/hematomas/gastrointestinal bleeding
- Succinylcholine
- Digitalis intoxication
- Fluoride intoxication
- β-Adrenergic blockers
- Exercise
- Hyperosmolality
- Insulin deficiency
- Malignant hyperthermia (OMIM 145600/601887)
- Hyperkalemic periodic paralysis (OMIM 170500)

DECREASED EXCRETION
- Renal failure
- Primary adrenal disease:
  - Acquired Addison disease
  - 21-Hydroxylase deficiency (OMIM 201910)
  - 3β-Hydroxysteroid dehydrogenase deficiency (OMIM 201810)
  - Lipoid congenital adrenal hyperplasia (OMIM 201710)
  - Adrenal hypoplasia congenita (OMIM 300200)
  - Aldosterone synthase deficiency (OMIM 203400/610600)
  - Adrenoleukodystrophy (OMIM 300100)
- Hyporeninemic hypoaldosteronism:
  - Urinary tract obstruction
  - Sickle cell disease (OMIM 603903)
  - Kidney transplant
  - Lupus nephritis
- Renal tubular disease:
  - Pseudohypoaldosteronism type I (OMIM 264350/177735)
  - Pseudohypoaldosteronism type II (OMIM 145260)
  - Bartter syndrome, type 2 (OMIM 241200)
  - Urinary tract obstruction
  - Kidney transplant
- Medications:
  - Angiotensin-converting enzyme inhibitors
  - Angiotensin II blockers
  - Potassium-sparing diuretics
  - Calcineurin inhibitors
  - Nonsteroidal antiinflammatory drugs
  - Trimethoprim
  - Heparin
  - Drospirenone (in some oral contraceptives)

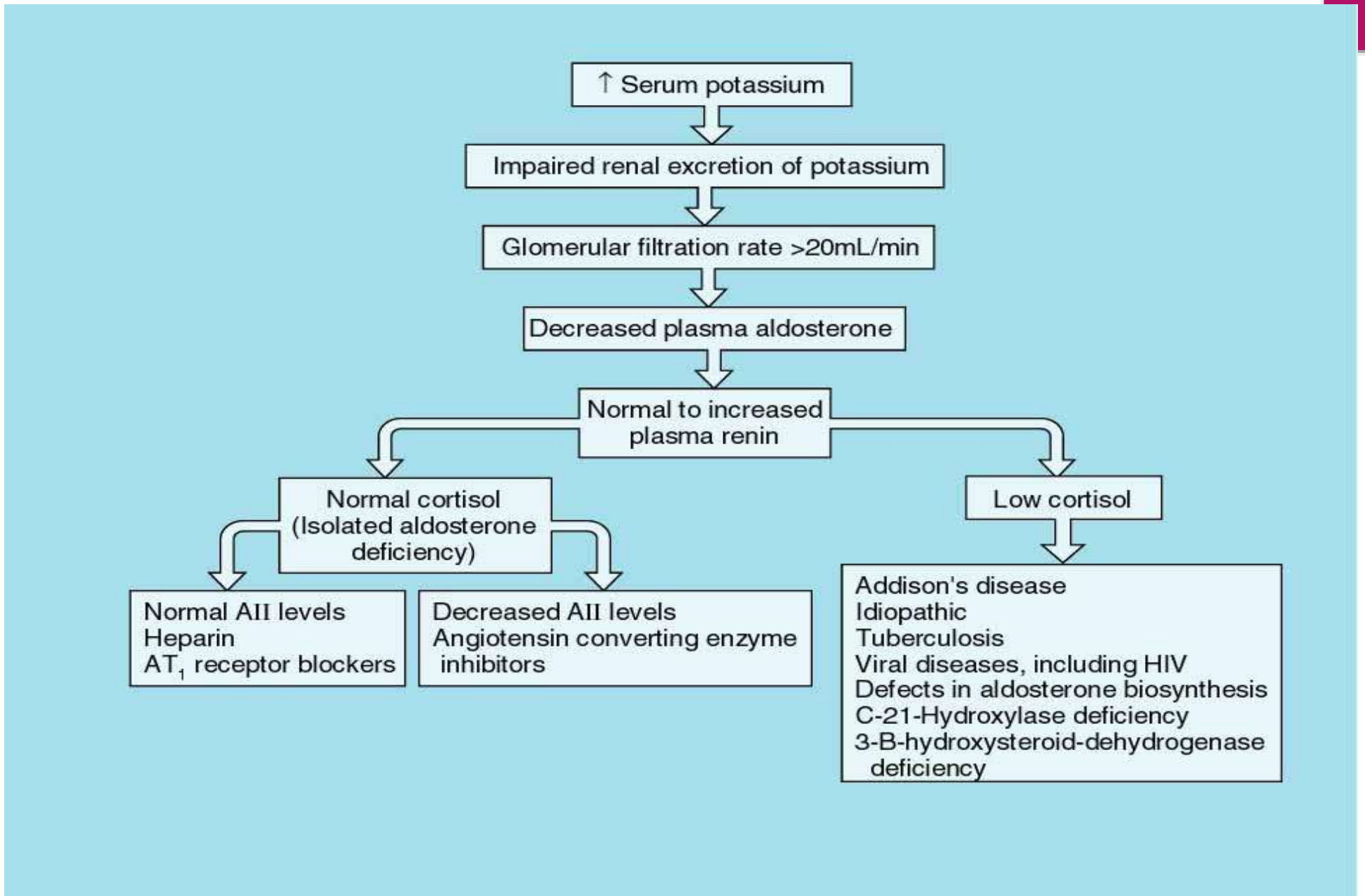
Approach To Hyperkalemia (1)



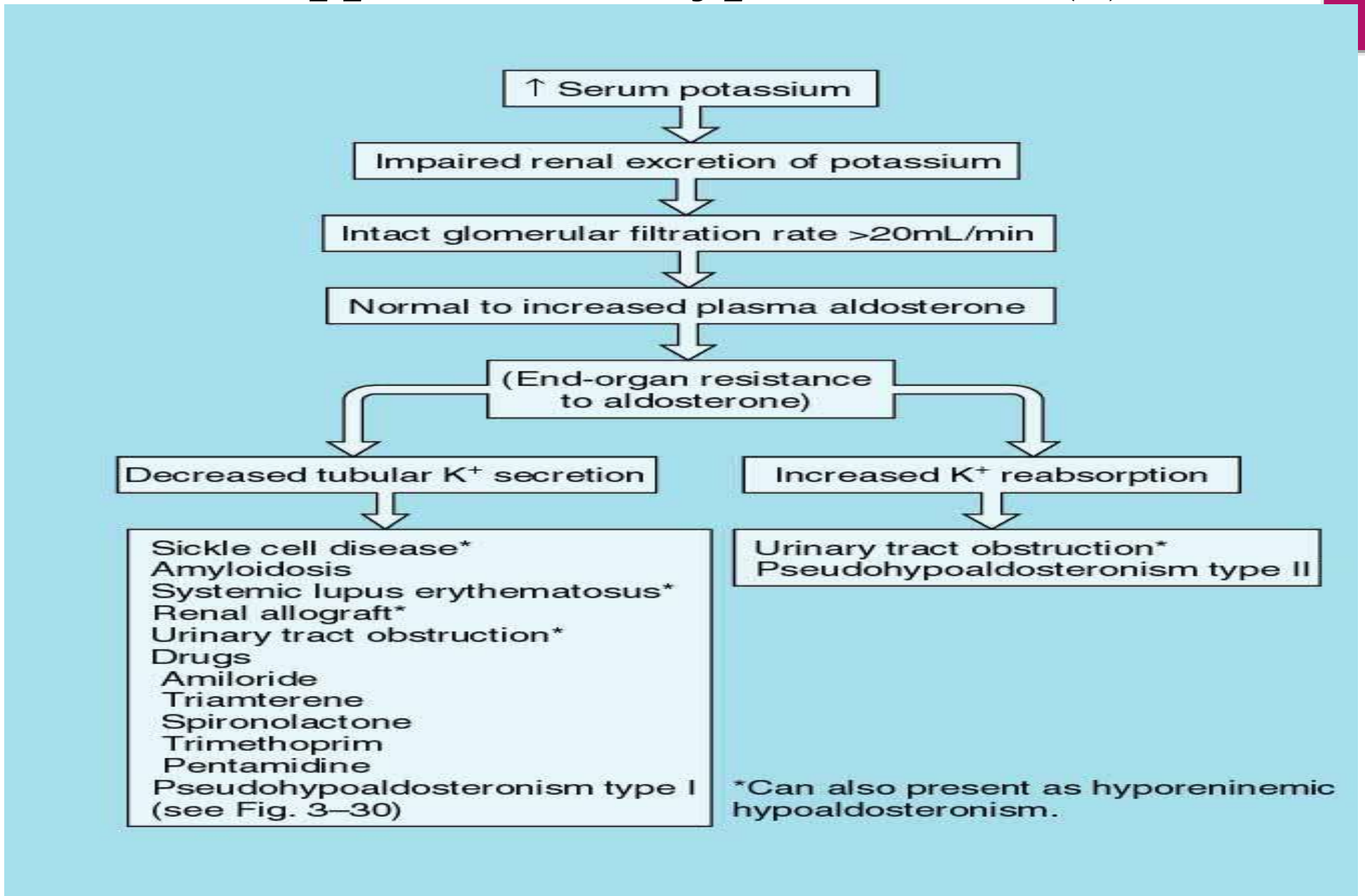
Approach To Hyperkalemia (2)



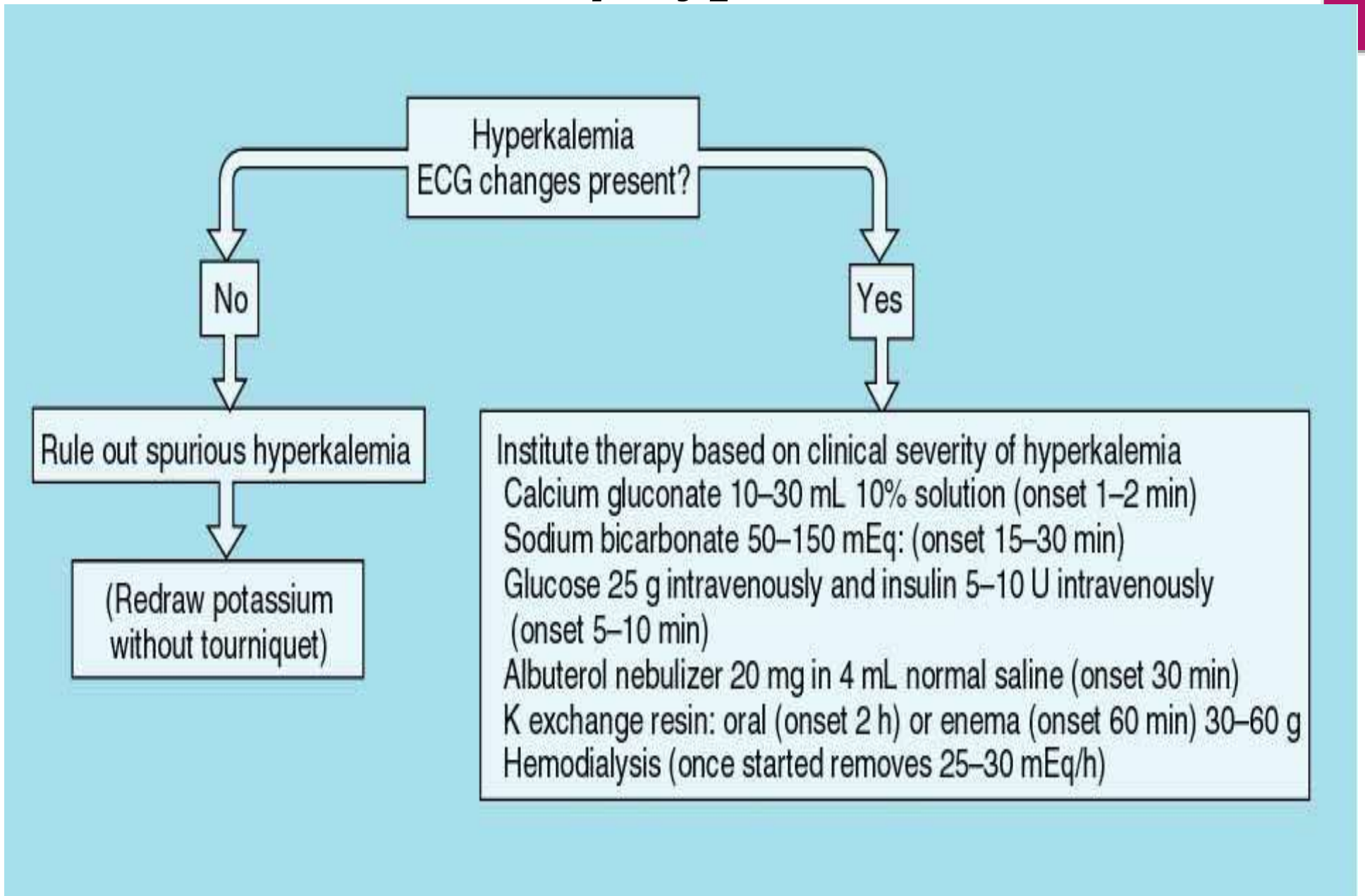
Approach To Hyperkalemia (3)

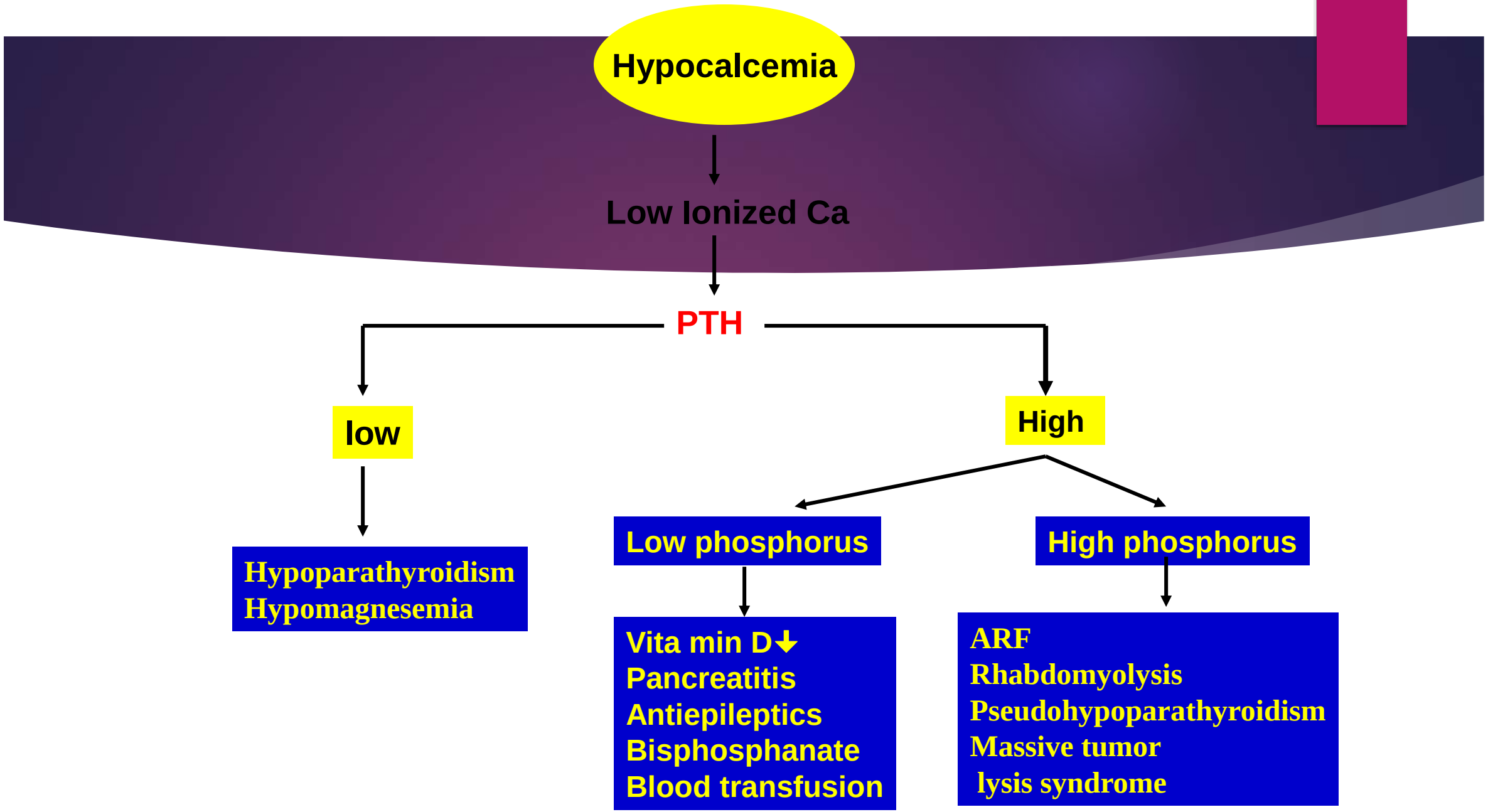


Approach To Hyperkalemia (4)



Treatment of Hyperkalemia




Hypocalcemia
Low Ionized Ca
PTH
low
Hypoparathyroidism
Hypomagnesemia
High
Low phosphorus
Vita min D↓
Pancreatitis
Antiepileptics
Bisphosphanate
Blood transfusion
High phosphorus
ARF
Rhabdomyolysis
Pseudohypoparathyroidism
Massive tumor
lysis syndrome

Flow-diagram for the work-up of patients with hypocalcemia.

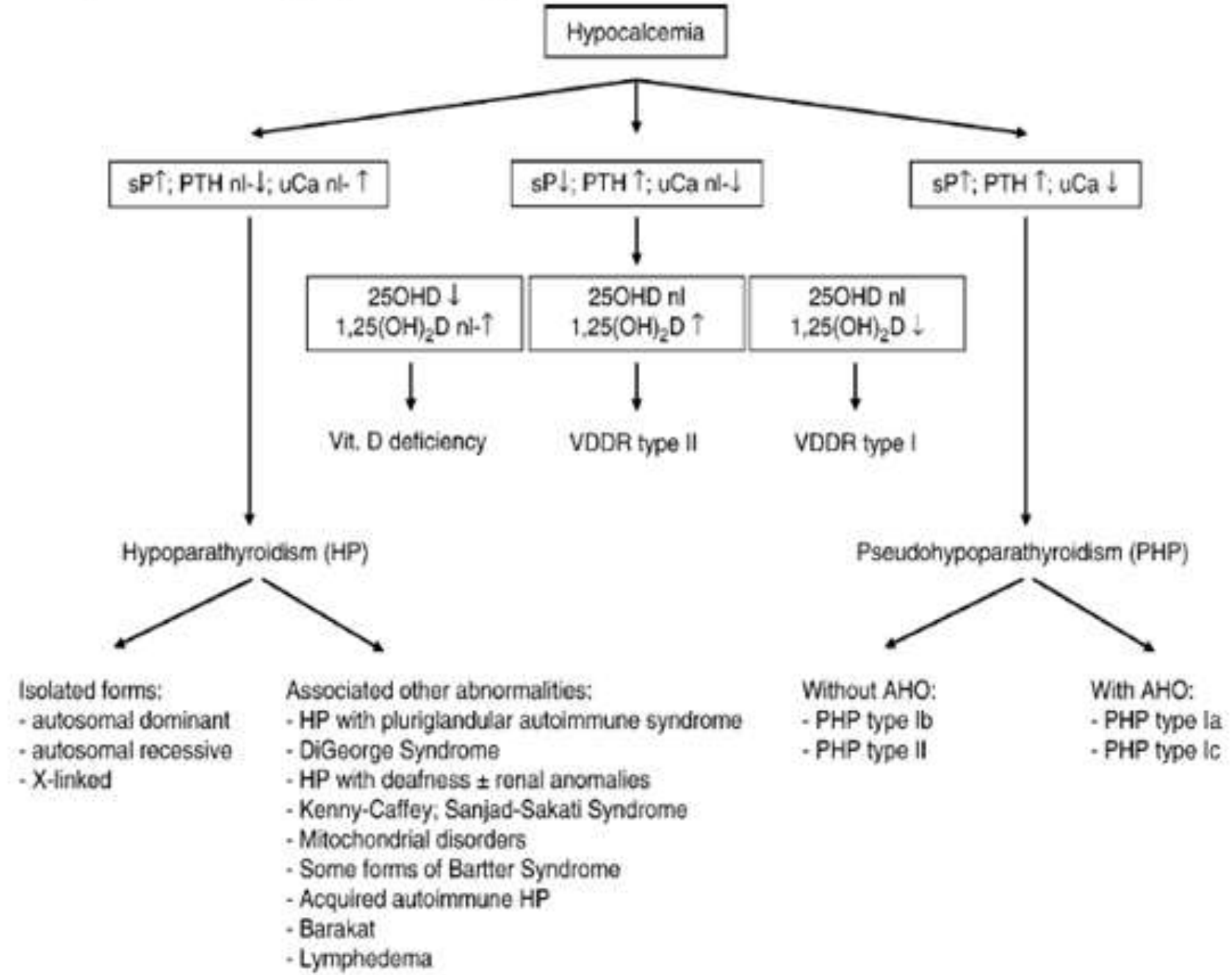


Table 571-1 Causes of Hypocalcemia

I. Neonatal
  A. Maternal Disorders
    Diabetes mellitus
    Toxemia of pregnancy
    Vitamin D deficiency
    High intake of alkali or magnesium sulfate
    Use of anticonvulsants
    Hyperparathyroidism
  B. Neonatal Disorders
    Low birthweight: prematurity, intrauterine growth restriction
    Peripartum asphyxia, sepsis, critical illness
    Hyperbilirubinemia, phototherapy, exchange transfusion
    Hypomagnesemia, hypermagnesemia
    Acute/chronic renal failure
    Nutrients/medications: high phosphate intake, fatty acids, phytates, bicarbonate infusion, citrated blood, anticonvulsants, aminoglycosides
    Hypoparathyroidism
    Vitamin D deficiency or resistance
    Osteopetrosis type II
II. Hypoparathyroidism
  A. Congenital
    1. Transient neonatal
    2. Congenital hypoparathyroidism
      a. Familial isolated hypoparathyroidism
        (1) Autosomal recessive hypoparathyroidism (GCMB, PTH)
        (2) Autosomal dominant hypoparathyroidism (CaSR)
        (3) X-linked hypoparathyroidism *(SOX3)*
      b. DiGeorge syndrome *(TBX1)*
      c. Sanjad-Sakati syndrome (short stature, retardation, dysmorphism; HRD); Kenny-Caffey syndrome 1 (short stature, medullary stenosis) *(TBCE)*
      d. Barakat syndrome (sensorineural deafness, renal dysplasia; HDR) *(GATA3)*
      e. Lymphedema-hypoparathyroidism-nephropathy, nerve deafness
      f. Mitochondrial fatty acid disorders (Kearns-Sayre, Pearson, MELAS)
    3. Insensitivity to PTH
      a. Blomstrand chondrodysplasia *(PTHR1)*
      b. Pseudohypoparathyroidism type IA *(GNAS)*
        Pseudohypoparathyroidism type IB
        Pseudohypoparathyroidism type IC
        Pseudohypoparathyroidism type II
        Pseudopseudohypoparathyroidism
      c. Acrodysostosis with hormone resistance *(PRKAR1A)*
      d. Hypomagnesemia
    4. CaSR-activating mutation
      a. Sporadic
      b. Autosomal dominant (G protein subunit α11 mutation)
  B. Acquired
    1. Autoimmune polyglandular syndrome type I *(AIRE* gene mutation)
    2. Activating antibodies to the CaSR
    3. Postsurgical, radiation destruction
    4. Infiltrative—excessive iron (hemochromatosis, thalassemia) or copper (Wilson disease) deposition; granulomatous inflammation, neoplastic invasion; amyloidosis, sarcoidosis
    5. Maternal hyperparathyroidism
    6. Hypomagnesemia/hypermagnesemia
III. Vitamin D Deficiency
IV. Other Causes of Hypocalcemia
  A. Calcium Deficiency
    1. Nutritional deprivation
    2. Hypercalciuria
  B. Disorders of Magnesium Homeostasis
    1. Congenital hypomagnesemia
    2. Acquired
      a. Acute renal failure
      b. Chronic inflammatory bowel disease, intestinal resection
      c. Diuretics
  C. Hyperphosphatemia
    1. Renal failure
    2. Phosphate administration (intravenous, oral, rectal)
    3. Tumor cell lysis
    4. Muscle injuries (crush, rhabdomyolysis)
  D. Miscellaneous
    1. Hypoproteinemia
    2. Hyperventilation
    3. Drugs: furosemide, aminoglycosides, bisphosphonates, calcitonin, anticonvulsants, ketoconazole, antineoplastic agents (plicamycin, asparaginase, cisplatinum, cytosine arabinoside, doxorubicin), citrated blood products
    4. Hungry bone syndrome
    5. Acute and critical illness: sepsis, acute pancreatitis, toxic shock
      a. Organic acidemia: propionic, methylmalonic, isovaleric

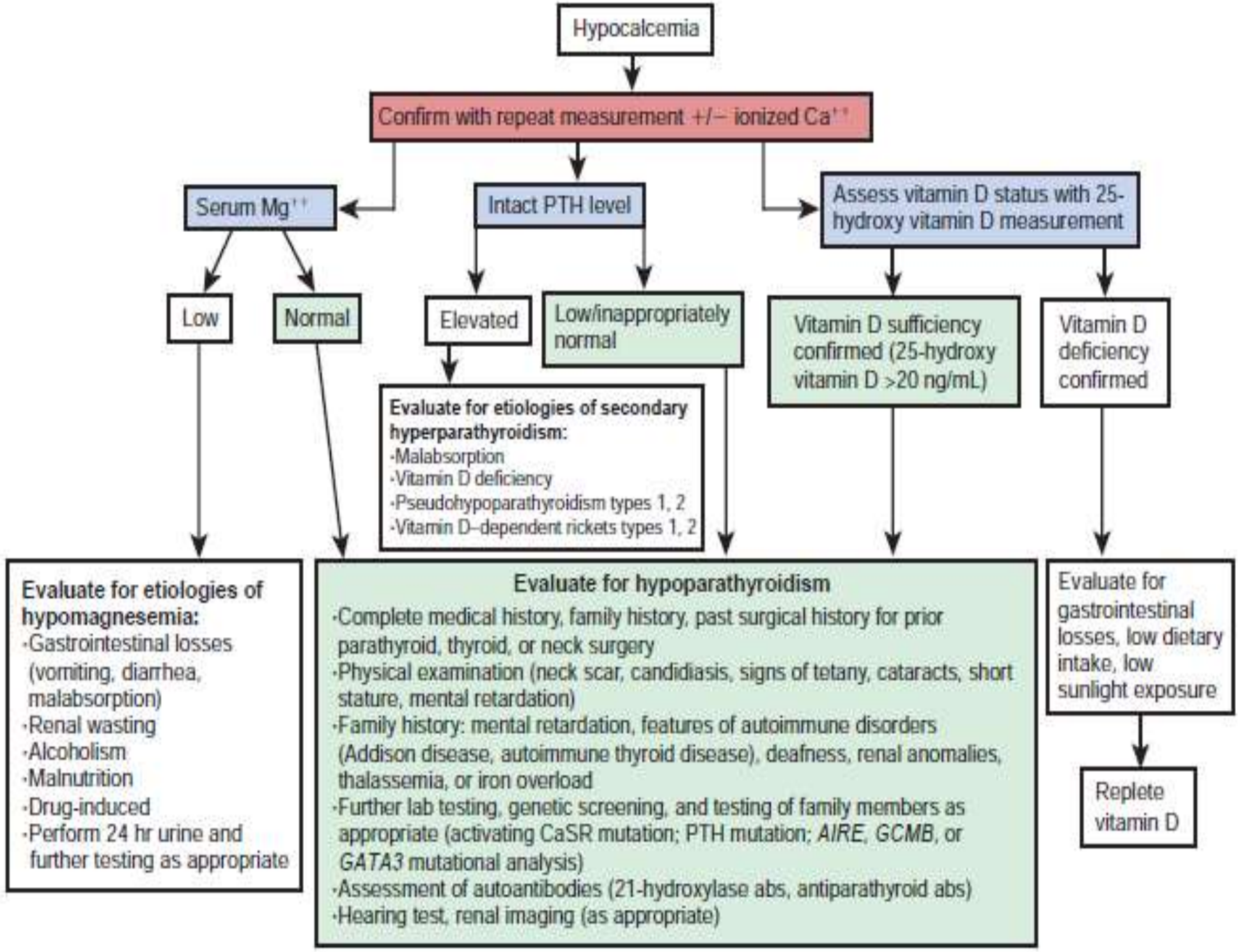

Hypocalcemia
Confirm with repeat measurement +/− ionized Ca++
Serum Mg++
Intact PTH level
Assess vitamin D status with 25-hydroxy vitamin D measurement
Low
Normal
Elevated
Low/inappropriately normal
Vitamin D sufficiency confirmed (25-hydroxy vitamin D >20 ng/mL)
Vitamin D deficiency confirmed
Evaluate for etiologies of secondary hyperparathyroidism:
·Malabsorption
·Vitamin D deficiency
·Pseudohypoparathyroidism types 1, 2
·Vitamin D–dependent rickets types 1, 2
Evaluate for etiologies of hypomagnesemia:
·Gastrointestinal losses (vomiting, diarrhea, malabsorption)
·Renal wasting
·Alcoholism
·Malnutrition
·Drug-induced
·Perform 24 hr urine and further testing as appropriate
Evaluate for hypoparathyroidism
·Complete medical history, family history, past surgical history for prior parathyroid, thyroid, or neck surgery
·Physical examination (neck scar, candidiasis, signs of tetany, cataracts, short stature, mental retardation)
·Family history: mental retardation, features of autoimmune disorders (Addison disease, autoimmune thyroid disease), deafness, renal anomalies, thalassemia, or iron overload
·Further lab testing, genetic screening, and testing of family members as appropriate (activating CaSR mutation; PTH mutation; *AIRE*, *GCMB*, or *GATA3* mutational analysis)
·Assessment of autoantibodies (21-hydroxylase abs, antiparathyroid abs)
·Hearing test, renal imaging (as appropriate)
Evaluate for gastrointestinal losses, low dietary intake, low sunlight exposure
Replete vitamin D

Table 51-2 Causes of Rickets

VITAMIN D DISORDERS
Nutritional vitamin D deficiency
Congenital vitamin D deficiency
Secondary vitamin D deficiency
Malabsorption
Increased degradation
Decreased liver 25-hydroxylase
Vitamin D–dependent rickets type 1 A and B
Vitamin D–dependent rickets type 2 A and B
Chronic kidney disease

CALCIUM DEFICIENCY
Low intake
Diet
Premature infants (rickets of prematurity)
Malabsorption
Primary disease
Dietary inhibitors of calcium absorption

PHOSPHORUS DEFICIENCY
Inadequate intake
Premature infants (rickets of prematurity)
Aluminum-containing antacids

RENAL LOSSES
X-linked hypophosphatemic rickets*
Autosomal dominant hypophosphatemic rickets*
Autosomal recessive hypophosphatemic rickets (1 and 2)*
Hereditary hypophosphatemic rickets with hypercalciuria
Overproduction of fibroblast growth factor-23
Tumor-induced rickets*
McCune-Albright syndrome*
Epidermal nevus syndrome*
Neurofibromatosis*
Fanconi syndrome
Dent disease
Distal renal tubular acidosis

Table 51-3 Clinical Features of Rickets

GENERAL
Failure to thrive
Listlessness
Protruding abdomen
Muscle weakness (especially proximal)
Fractures

HEAD
Craniotabes
Frontal bossing
Delayed fontanel closure
Delayed dentition; caries
Craniosynostosis

CHEST
Rachitic rosary
Harrison groove
Respiratory infections and atelectasis*

BACK
Scoliosis
Kyphosis
Lordosis

EXTREMITIES
Enlargement of wrists and ankles
Valgus or varus deformities
Windswept deformity (combination of valgus deformity of 1 leg with varus deformity of the other leg)
Anterior bowing of the tibia and femur
Coxa vara
Leg pain

HYPOCALCEMIC SYMPTOMS†
Tetany
Seizures
Stridor due to laryngeal spasm

*These features are most commonly associated with the vitamin D–deficiency

Table 51-4 Laboratory Findings in Various Disorders Causing Rickets

DISORDER	Ca	Pi	PTH	25-(OH)D	1,25-$(OH)_2$D	Alk Phos	URINE Ca	URINE Pi
Vitamin D deficiency	N, ↓	↓	↑	↓	↓, N, ↑	↑	↓	↑
Chronic kidney disease	N, ↓	↑	↑	N	↓	↑	N, ↓	↓
Dietary Pi deficiency	N	↓	N, ↓	N	↑	↑	↑	↓
Tumor-induced rickets	N	↓	N	N	RD	↑	↓	↑
Fanconi syndrome	N	↓	N	N	RD or ↑	↑	↓ or ↑	↑
Dietary Ca deficiency	N, ↓	↓	↑	N	↑	↑	↓	↑

Table 51-5 Biochemical Changes in Genetic Causes of Rickets

	SERUM BIOCHEMISTRY							URINE BIOCHEMISTRY		
	Phosphate	Calcium	PTH	25OHD	1,25$(OH)_2$D	FGF23	Alk Phos	Phosphate	Calcium	OTHER FEATURES
HYPOCALCEMIC VITAMIN D PATHWAY DEFECTS										
Vitamin D deficiency	Low	Variable	High	Low	Might be increased	NA	Increased	Increased	Low	Variable aminoaciduria
VDDR1B	Low	Low	High	Very low	Variable	NA	Increased	Increased	Low	25OHD does not increase after vitamin D dosing
VDDR1A	Low	Low	High	Normal or high	Very low or ND	NA	Increased	Increased	Low	25OHD does increase after vitamin D dosing
VDDR2A	Low	Low	High	Normal or high	High	NA	Increased	Increased	Low	—
VDDR2B	Low	Low	High	Normal or high	High	NA	Increased	Increased	Low	—
HYPOPHOSPHATEMIC RICKETS WITH RAISED FGF23										
XLH	Low	Normal	Normal or slightly high	Normal	Low	High	Increased	Increased	Variable	Urine calcium:creatinine used in monitoring therapy
ADHR	Low	Normal	Normal	Normal	Low	High	Increased	Increased	Variable	—
ARHR1	Low	Normal	Normal	Normal	Low	High	Increased	Increased	Variable	—
ARHR2	Low	Normal	Normal	Normal	Low	High	Increased	Increased	Variable	—
HYPOPHOSPHATEMIC RICKETS WITHOUT RAISED FGF23										
Dent's disease*	Low	Normal	Normal	Normal	Normal	Normal	Increased	Increased	High	Low molecular weight proteinuria
HHRH	Low	Normal	Normal	Normal	Normal	Normal	Increased	Increased	High	No loss of low molecular weight protein
αKlotho mutation	Low	Normal	Normal	Normal	Normal	Normal	Increased	Increased	Variable	—
OTHER INHERITED RACHITIC DISORDERS										
HPP (severe)	High	High	Low	Normal	Normal	Normal	Very low	Normal or high	High	Raised concentrations of mineralization inhibitors
HPP (mild)	Normal or high	Normal or high	Low or normal	Normal	Normal	Normal	Low	Normal	Variable	Raised concentrations of mineralization inhibitors

From Elder CJ, Bishop NJ: Rickets. Lancet 383:1665-1674, 2014.
PTH, parathyroid hormone; 25OHD, calcidiol; 1,25OH D, calcitriol; FGF23, fibroblast growth factor 23; Alk phos, alkaline phosphatase; NA, data not available; VDDR1B, vitamin D–dependent rickets due to defects in CYP27B1 encoding vitamin D 25-hydroxylase; VDDR1A, vitamin D–dependent rickets due to defects in CYP27B1 encoding 25-hydroxyvitamin D-1alpha-hydroxylase; ND, not detected; VDDR2A, vitamin D–dependent rickets due to defects in VDR encoding the vitamin D receptor; VDDR2B, vitamin D–dependent rickets due to defects in HNRNPC encoding hnRNPC1 and hnRNPC2; XLH, X-linked hypophosphatemic rickets due to mutations in PHEX; ADHR, autosomal dominant hypophosphatemic rickets due to mutations in FGF23; ARHR1, autosomal recessive hypophosphatemic rickets due to mutations in DMP1; ARHR2, autosomal recessive hypophosphatemic rickets due to mutations in ENPP1; HHRH, hereditary hypophosphatemic rickets with hypercalciuria due to mutations in SLC34A3; HPP, hypophosphatasia.
*Dent's disease is due to mutations in CLCN5.

Treatment Of Hypocalcemia

- **Asymptomatic and mild (ionized calcium concentrations above 3.2 mg/dL)**
  - ✷increasing dietary calcium intake, treat hyperphosphatemia
- **Symptomatic (ionized calcium concentration is less than 2.8 mg/dL)**
  - ✷**Intravenous calcium, Infusion**
  - ✷**Vitamin D, Calcitriol**
  - ✷**Treat hyperphosphatemia**
  - ✷**Treat Hypomagnesemia**

Calcium salt	Content of elemental Ca	comments
Calcium carbonate	10.2 (400 mg)/ 1000 mg	Preferred because least No of tablets needed
Ca lactate	1.5 mmol (60 mg) / 300mg	
Ca gluceptate	2.2 mmol (80 mg)/ 1000 mg	
Ca gluconate	2.3 mmol (90 mg)/ 1000mg	Liq form of lactate and carbonate salts are sued for pts with achlohydria or H_2anatgonist therapy because tablet dissolution will be incomplete without gastric acid

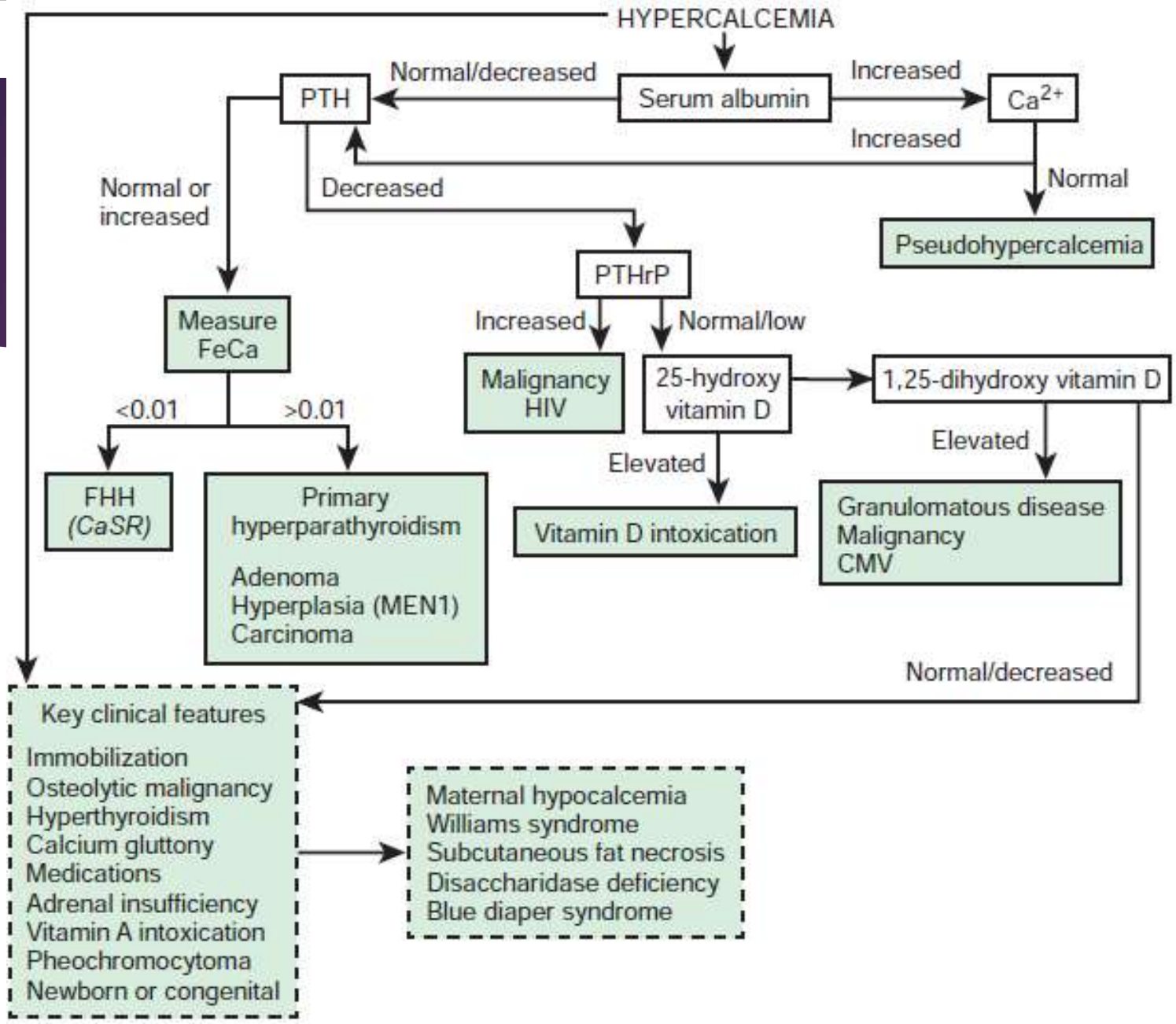
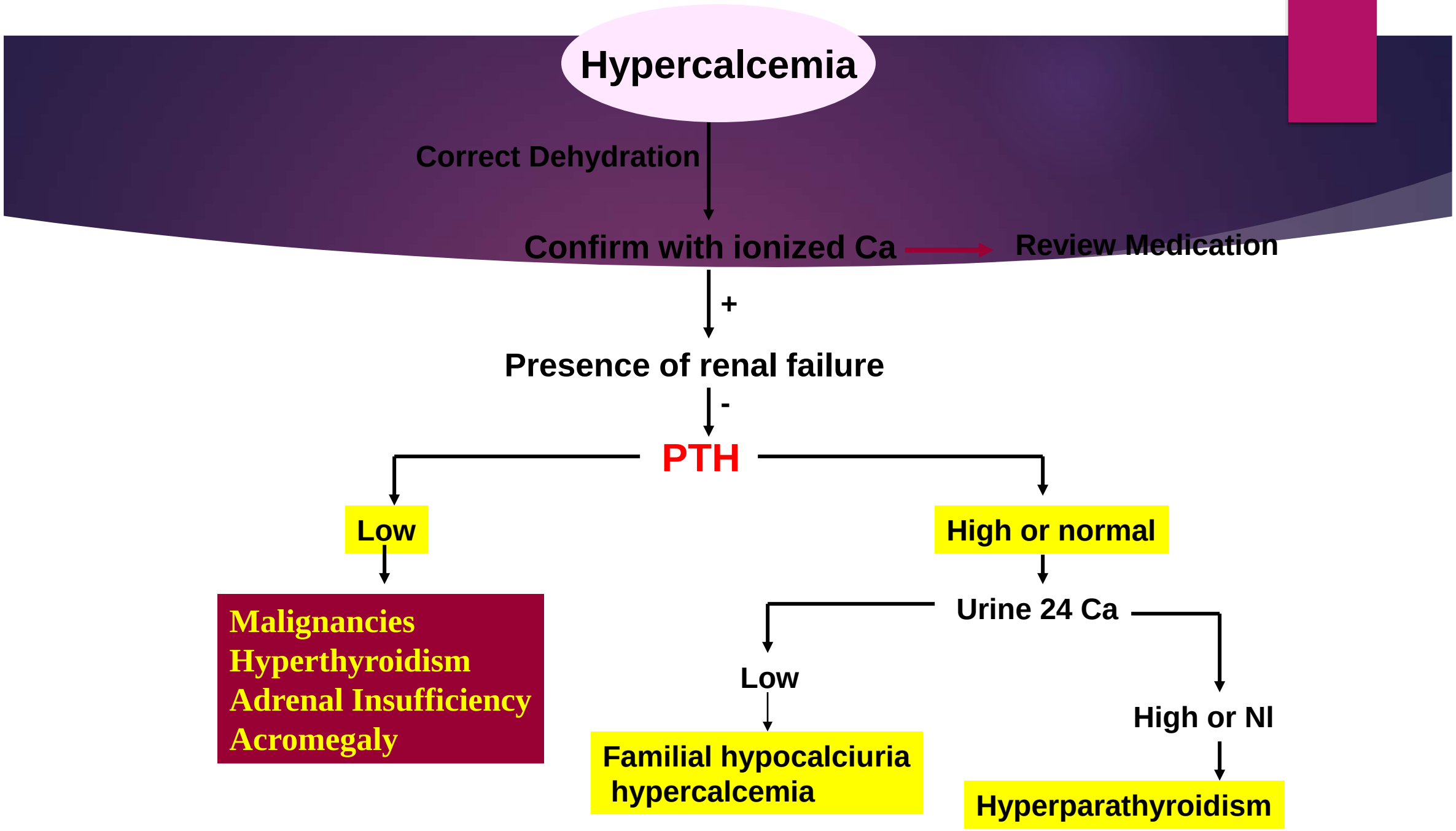
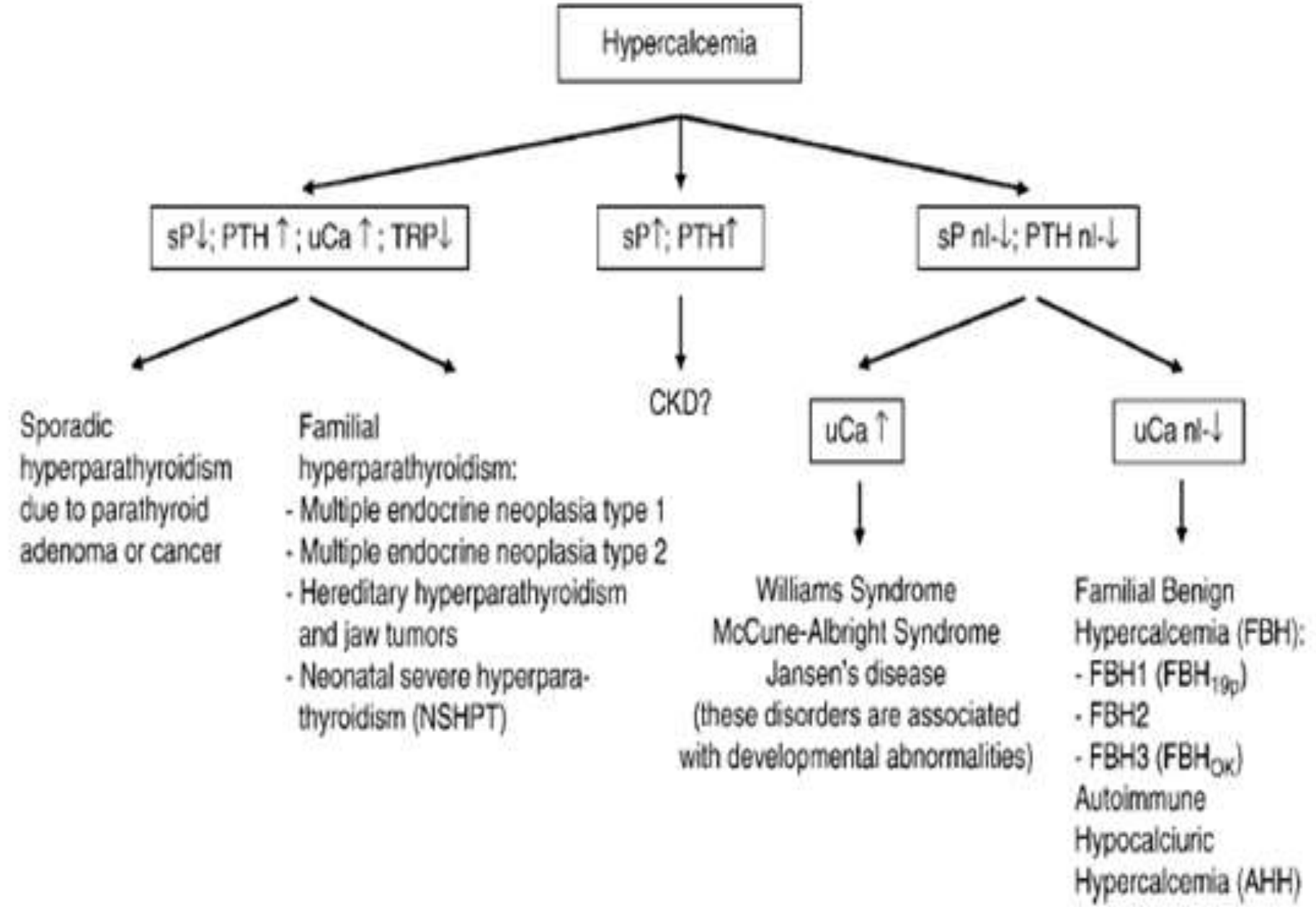

HYPERCALCEMIA
Serum albumin
Normal/decreased
Increased
PTH
Ca^{2+}
Increased
Normal
Pseudohypercalcemia
Normal or increased
Decreased
PTHrP
Measure FeCa
Increased
Normal/low
Malignancy HIV
25-hydroxy vitamin D
1,25-dihydroxy vitamin D
<0.01
>0.01
Elevated
Elevated
FHH (CaSR)
Primary hyperparathyroidism
Adenoma
Hyperplasia (MEN1)
Carcinoma
Vitamin D intoxication
Granulomatous disease
Malignancy
CMV
Normal/decreased
Key clinical features
Immobilization
Osteolytic malignancy
Hyperthyroidism
Calcium gluttony
Medications
Adrenal insufficiency
Vitamin A intoxication
Pheochromocytoma
Newborn or congenital
Maternal hypocalcemia
Williams syndrome
Subcutaneous fat necrosis
Disaccharidase deficiency
Blue diaper syndrome

Table 573-1 Causes of Hypercalcemia

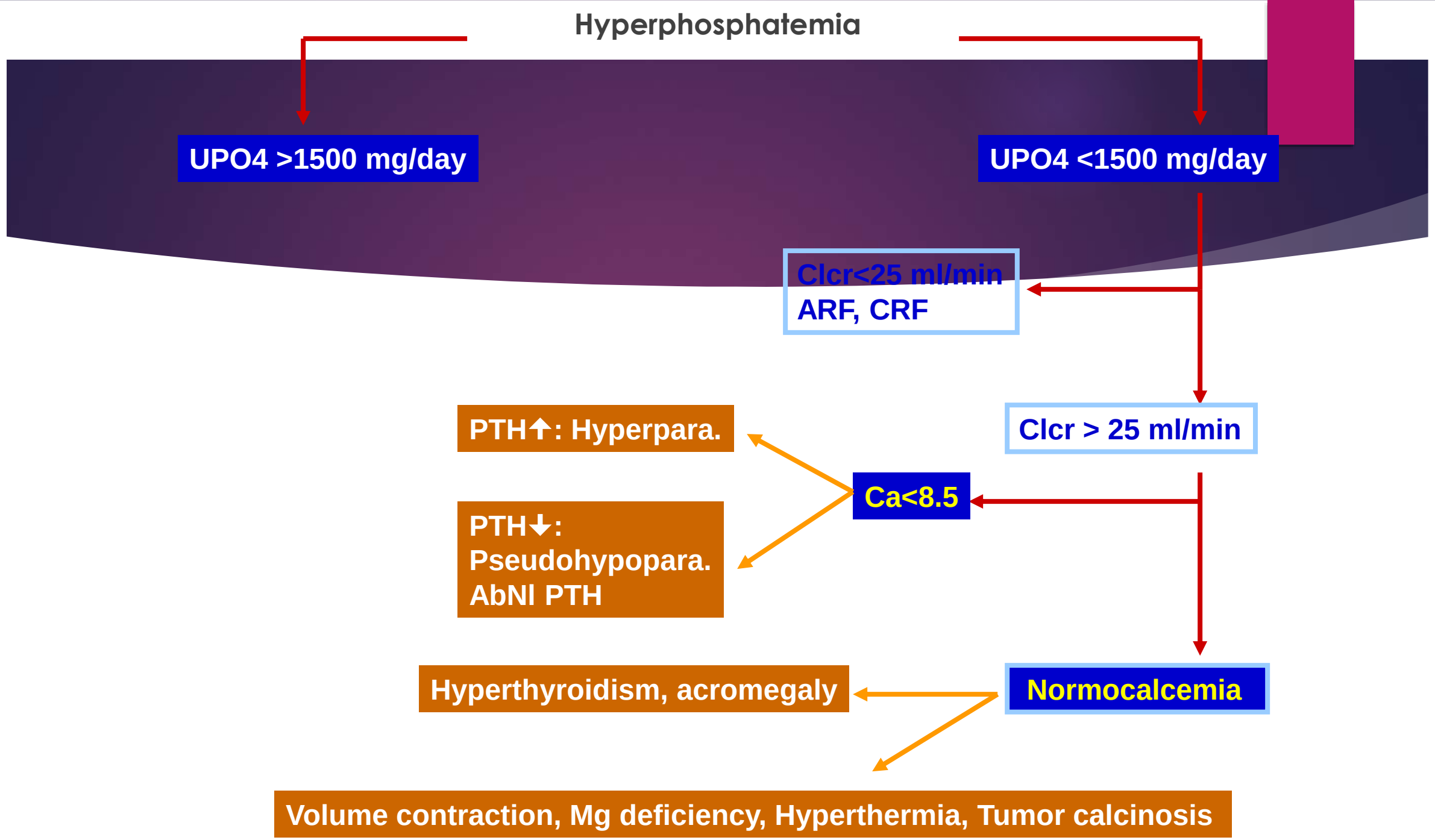
I. Neonate/Infant
  A. Maternal Disorders
    1. Excessive vitamin D ingestion, hypoparathyroidism, pseudohypoparathyroidism
  B. Neonate/Infant
    1. Iatrogenic excessive intake of calcium, vitamin D, vitamin A
    2. Phosphate depletion
    3. Subcutaneous fat necrosis
    4. Williams-Beuren syndrome (del7q11.23/*BAZ1B*) (transient receptor potential; 3-channel defect)
    5. Neonatal severe hyperparathyroidism (*CaSR*)
    6. Metaphyseal chondrodysplasia, Murk-Jansen type (*PTH1R*)
    7. Idiopathic infantile hypercalcemia (*CYP24A1*) (25-hydroxyvitamin D 24-hydroxylase)
    8. Persistent parathyroid hormone–related protein
    9. Lactase/disaccharidase deficiency (*LCT*)
    10. Infantile hypophosphatasia (*TNSALP*)
    11. Mucolipidosis type II (*GNPTAB*)
    12. Blue diaper syndrome
    13. Antenatal Bartter syndrome types 1 and 2 (*SLC12A1*, *KCNJ1*)
    14. Distal renal tubular acidosis
    15. IMAGe syndrome (*CDKN1C*)
    16. Post bone marrow transplantation for osteopetrosis
    17. Endocrinopathies: primary adrenal insufficiency, severe congenital hypothyroidism, hyperthyroidism
II. Hyperparathyroidism
  A. Sporadic
    1. Parathyroid hyperplasia, adenoma, carcinoma
  B. Familial
    1. Neonatal severe hyperparathyroidism (*CaSR*)
    2. Multiple endocrine neoplasia, type I (*MEN1*)
    3. Multiple endocrine neoplasia, type IIA (*RET*)
    4. Multiple endocrine neoplasia, type IIB (*RET*)
    5. Multiple endocrine neoplasia, type IV (*CDKN1B*)
    6. McCune-Albright syndrome (*GNAS*)
    7. Familial isolated hyperparathyroidism 1 (*CDC73*)
    8. Familial isolated hyperparathyroidism 2 (jaw tumor syndrome) (*CDC73*)
    9. Familial isolated hyperparathyroidism 3
    10. Jansen metaphyseal dysplasia (*PTH1R*)
  C. Secondary/Tertiary
    1. Postrenal transplantation
    2. Chronic hyperphosphatemia
  D. Hypercalcemia of Malignancy
    1. Ectopic production of parathyroid hormone–related peptide
    2. Metastatic dissolution of bone
III. Familial Hypocalciuric Hypercalcemia
  A. Familial Hypocalciuric Hypercalcemia I (*CaSR*)
    1. Loss-of-function mutations in CaSR
      a. Monoallelic: familial benign hypercalcemia
      b. Biallelic: neonatal severe hyperparathyroidism
  B. Familial Hypocalciuric Hypercalcemia II (*GNA11*)
  C. Familial Hypocalciuric Hypercalcemia III, Oklahoma Variant (*AP2S1*)
  D. CaSR-blocking autoantibodies
IV. Excessive Calcium or Vitamin D
  A. Milk-Alkali Syndrome
  B. Exogenous Ingestion of Calcium or Vitamin D or Topical Application of Vitamin D (calcitriol or analog)
  C. Ectopic Production of Calcitriol Associated with Granulomatous Diseases (sarcoidosis, cat-scratch fever, tuberculosis, histoplasmosis, coccidioidomycosis, leprosy; human immunodeficiency virus; cytomegalovirus; chronic inflammatory bowel disease)
  D. Neoplasia
    1. Primary bone tumors
    2. Metastatic tumors with osteolysis
    3. Lymphoma, leukemia
    4. Dysgerminoma
    5. Pheochromocytoma
    6. Tumors secreting parathyroid hormone–related peptide, growth factors, cytokines, prostaglandins, osteoclast-activating factors
  E. Williams-Beuren Syndrome (del7q11.23)
V. Immobilization
VI. Other Causes
  A. Drugs: Thiazides, Lithium, Vitamin A and Analogs, Calcium, Alkali, Antiestrogens, Aminophylline
  B. Total Parenteral Nutrition
  C. Endocrinopathies: Hyperthyroidism, Addison disease, Pheochromocytoma
  D. Vasoactive Intestinal Polypeptide–Secreting Tumor
  E. Acute or Chronic Renal Failure/Administration of Aluminum
  F. Hypophosphatasia
  G. Juvenile Rheumatoid Arthritis: Cytokine Mediated


Hypercalcemia
Correct Dehydration
Confirm with ionized Ca
Review Medication
+
Presence of renal failure
-
PTH
Low
Malignancies
Hyperthyroidism
Adrenal Insufficiency
Acromegaly
High or normal
Urine 24 Ca
Low
Familial hypocalciuria hypercalcemia
High or Nl
Hyperparathyroidism

Flow-diagram for the work-up of patients with hypercalcemia.



Hyperphosphatemia



Hyperphosphatemia

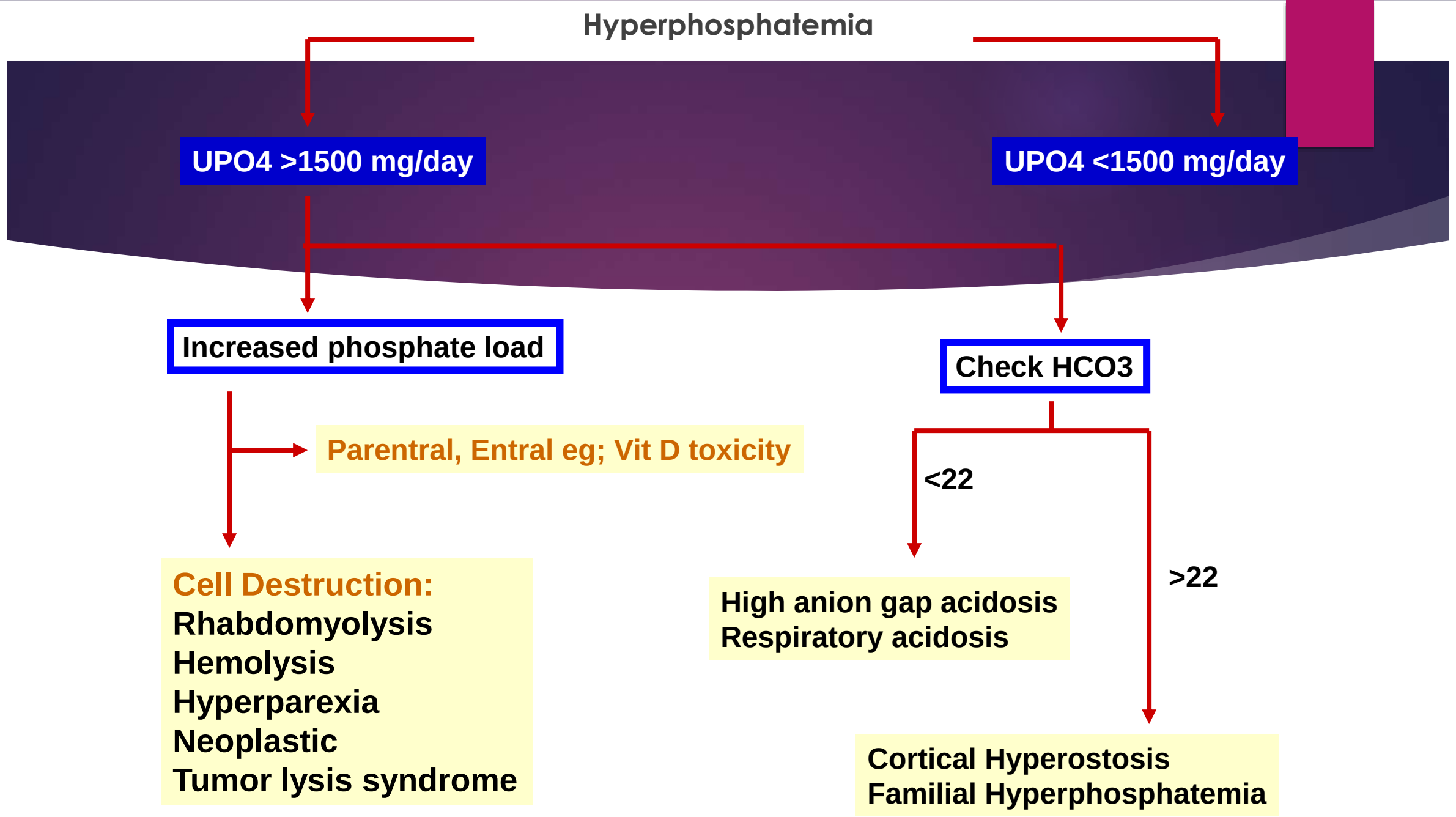


Table 55-10	Causes of Hyperphosphatemia

TRANSCELLULAR SHIFTS

Tumor lysis syndrome
Rhabdomyolysis
Acute hemolysis
Diabetic ketoacidosis and lactic acidosis

INCREASED INTAKE

Enemas and laxatives
Cow's milk in infants
Treatment of hypophosphatemia
Vitamin D intoxication

DECREASED EXCRETION

Renal failure
Hypoparathyroidism or pseudohypoparathyroidism (OMIM 146200/603233/103580/241410/203330)
Acromegaly
Hyperthyroidism
Tumoral calcinosis with hyperphosphatemia (OMIM 211900)

Table 11-1

Biochemical findings in several inherited hypo- and hyperphosphatemic disorders and underlying genetic defects

	FGF-23	TRP or TmP/GFR	1,25(OH)2D	PTH	Serum Calcium	Urinary Calcium	Mutant gene
Hypophosphatemic disorders							
XLH	Increased/ inappropriately normal	Low	Low/ inappropriately normal	Normal/ increased	Normal	Normal	PHEX
ADHR	Increased/ inappropriately normal	Low	Low/ inappropriately normal	Normal	Normal	Normal	FGF23
ARHP	Increased/ inappropriately normal	Low	Low/ inappropriately normal	normal	Normal	Normal	DMP1
HHRH	Low/normal	Low	High	Low	Normal	High	NPT2c
Hyperphosphatemic disorders							
Tumoral calcinosis	Intact: low C-terminal: very high	High	Normal-High	Low	Normal/ Increased	Increased	FGF23 or GALNT3 (glycosyltransferase)
	Extremely high (intact and C-terminal)	High	Normal-High	Elevated	Normal/ Increased	Increased	Klotho
Isolated hypoparathyroidism	Normal-increased	Elevated	Low-normal	Low-normal	Low	Increased or inappropriately normal	Calcium-sensing receptor, PTH, or GCMB, and unknown genetic defects
Pseudohypopara-thyroidism type Ia (PHP-Ia) or Ib (PHP-Ib)	Normal-increased	Elevated	Low-normal	High	Low	Low	PHP-Ia: *GNAS* exons encoding Gsα: microdeletions within or up-stream of *GNAS*

Treatment of Hyperphosphatemia

- Acute Hyperphosphatemia

  Ph restriction, phosphate binders, Dialysis,

  Intravenous fluid

- Chronic Hyperphosphatemia

  Ph restriction, phosphate binders (not aluminium), Dialysis

Hypophosphatemia

UPO4 >100 mg/day
FEPO4>10%

Hyperparathyroidism
Hypokalemia
Ketoacidosis
Tubular Defect

- **Congenital (VitDRR)**

Acquired:
fanconi, volume depletion, diuretics

UPO4 <100 mg/day
FEPO4 <10%

Ph deficiency
Ph binders
Malabsorption
Vit D deficiency

Transcellular shift

PH> 7.25
Alkalosis

Non PH related shift
Glucose, Fructose, Hyperalimentation, Hormone mediated (Insulin, androgen, glucagon)

Table 55-9	Causes of Hypophosphatemia
TRANSCELLULAR SHIFTS	
Glucose infusion	
Insulin	
Refeeding	
Total parenteral nutrition	
Respiratory alkalosis	
Tumor growth	
Bone marrow transplantation	
Hungry bone syndrome	
DECREASED INTAKE	
Nutritional	
Premature infants	
Low phosphorus formula	
Antacids and other phosphate binders	
RENAL LOSSES	
Hyperparathyroidism	
Parathyroid hormone–related peptide	
X-linked hypophosphatemic rickets (OMIM 307800)	
Overproduction of fibroblast growth factor-23	
Tumor-induced rickets	
McCune-Albright syndrome	
Epidermal nevus syndrome	
Neurofibromatosis	
Autosomal dominant hypophosphatemic rickets (OMIM 193100)	
Autosomal recessive hypophosphatemic rickets (OMIM 241520)	
Fanconi syndrome	
Dent disease (OMIM 300009/300555)	
Hypophosphatemic rickets with hypercalciuria (OMIM 241530)	
Hypophosphatemic nephrolithiasis/osteoporosis type 1 (OMIM 612286)	
Hypophosphatemic nephrolithiasis/osteoporosis type 2 (OMIM 612287)	
Volume expansion and intravenous fluids	
Metabolic acidosis	
Diuretics	
Glycosuria	
Glucocorticoids	
Kidney transplantation	
MULTIFACTORIAL	
Vitamin D deficiency	
Vitamin D–dependent rickets type 1 (OMIM 264700)	
Vitamin D–dependent rickets type 2 (OMIM 277440)	
Alcoholism	
Sepsis	
Dialysis	

Indications for different modes of therapy in ph↓

- Severe hypophosphatemia (<1.0 mg/dl [0.3 mmol/l]) in critically ill, intubated patients or those with clinical sequelae of hypophosphatemia (e.g. hemolysis) should be managed with intravenous replacement therapy (0.08–0.16 mmol/kg) over 2–6 h
- Moderate hypophosphatemia (1.0–2.5 mg/dl [0.3–0.8 mmol/l]) in patients on a ventilator should be managed with intravenous replacement therapy (0.08–0.16 mmol/kg) over 2–6 h
- Moderate hypophosphatemia (1.0–2.5 mg/dl [0.3–0.8 mmol/l]) in nonventilated patients should be managed with oral replacement therapy (1,000 mg/day)
- Mild hypophosphatemia should be managed with oral replacement therapy (1,000 mg/day)

Table 55-7 Causes of Hypomagnesemia

GASTROINTESTINAL DISORDERS
Diarrhea
Nasogastric suction or emesis
Inflammatory bowel disease
Celiac disease
Cystic fibrosis
Intestinal lymphangiectasia
Small bowel resection or bypass
Pancreatitis
Protein-calorie malnutrition
Hypomagnesemia with secondary hypocalcemia (OMIM 602014)*
RENAL DISORDERS
Medications
Amphotericin
Cisplatin
Cyclosporin
Loop diuretics
Mannitol
Pentamidine
Proton pump inhibitors
Aminoglycosides
Thiazide diuretics
Epidermal growth factor receptor inhibitors
Diabetes
Acute tubular necrosis (recovery phase)
Postobstructive nephropathy
Chronic kidney diseases
Interstitial nephritis
Glomerulonephritis
Post–renal transplantation
Hypercalcemia
Intravenous fluids
Primary aldosteronism
Genetic diseases
Gitelman syndrome (OMIM 263800)
Bartter syndrome (OMIM 607364/601678)
Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (OMIM 248250)
Familial hypomagnesemia with hypercalciuria, nephrocalcinosis, and severe ocular involvement (OMIM 248190)
Autosomal recessive renal magnesium wasting with normocalciuria (OMIM 611718)
Renal cysts and diabetes syndrome (OMIM 137920)
Autosomal dominant hypomagnesemia (OMIM 160120/613882/154020)
EAST syndrome (OMIM 612780)
Autosomal dominant hypoparathyroidism (OMIM 146200)
Mitochondrial disorders (OMIM 500005)
MISCELLANEOUS CAUSES
Poor intake
Hungry bone syndrome
Insulin administration
Pancreatitis
Intrauterine growth retardation
Infants of diabetic mothers
Exchange transfusion

Diagnostic Approach to suspected Mg Deficiency

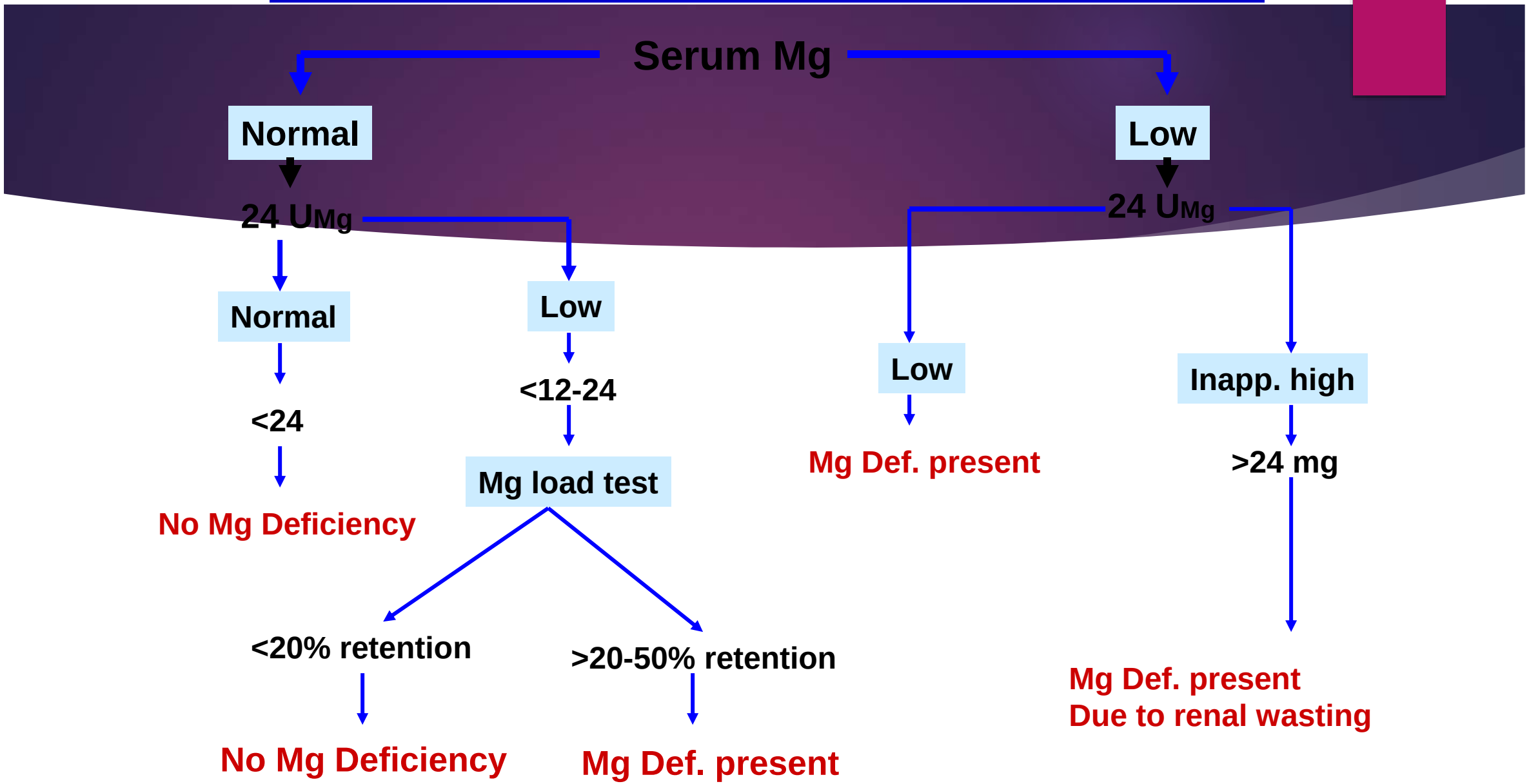


Table 38-5

Inherited disorders of renal magnesium handling

Disorder	OMIM #	Inheritance	Gene locus	Gene	Protein
Gitelman syndrome	263800	AR	16q13	*SLC12A3*	NCCT, Na^+-Cl^- cotransporter
Isolated dominant hypomagnesemia	154020	AD	11q23	*FXYD2*	γ-subunit of the Na^+-K^+-ATPase
Isolated recessive hypomagnesemia	611718	AR	4q25	*EGF*	Pro-EGF, epidermal growth factor
Autosomal dominant hypocalcemia, Autosomal dominant hypoparathyroidism	146200	AD	3q21	*CASR*	CaSR, Ca^{2+}/Mg^{2+} sensing receptor
Familial hypocalciuric hypercalcemia, Familial benign hypercalcemia	145980	AD	3q21	*CASR*	CaSR, Ca^{2+}/Mg^{2+} sensing receptor
Neonatal severe primary hyperparathyroidism	239200	AR	3q21	*CASR*	CaSR, Ca^{2+}/Mg^{2+} sensing receptor
Familial hypomagnesemia with hypercalciuria/ nephrocalcinosis	248250	AR	3q28	*CLDN16*	Claudin-16 (paracellin-1), tight junction protein
Familial hypomagnesemia with hypercalciuria/ nephrocalcinosis and severe ocular involvement	248190	AR	1p34	*CLDN19*	Claudin-19, tight junction protein
Hypomagnesemia with secondary hypocalcemia	602014	AR	9q22	*TRPM6*	TRPM6, Mg^{2+} channel
Hypomagnesemia/metabolic syndrome	500005	maternal	mtDNA	*MTTI*	Mitochondrial tRNA (Isoleucin)

Clinical and biochemical characteristics of inherited hypomagnesemia

Disorder	Age at onset	Serum Mg^{2+}	Serum Ca^{2+}	Serum K^{+}	Blood pH	Urine Mg^{2+}	Urine Ca^{2+}	Nephro-calcinosis	Renal stones
Gitelman syndrome	Adolescence	↓	N	↓	↑	↑	↓	No	no
Isolated dominant hypomagnesemia	Childhood	↓	N	N	N	↑	↓	no	no
Isolated recessive hypomagnesemia	Childhood	↓	N	N	N	↑	N	no	no
Autosomal dominant hypocalcemia, Autosomal dominant hypoparathyroidism	Infancy	↓	↓	N	N or ↓	↑	↑ – ??	yes[a]	yes[a]
Familial hypocalciuric hypercalcemia, Familial benign hypercalcemia	Often asymptomatic	N to ↑	↑	N	N	↓	↓	no	?
Neonatal severe primary hyperparathyroidism	Infancy	N to ↑	↑↑↑	N	N	↓	↓	no	?
Familial hypomagnesemia with hypercalciuria/nephrocalcinosis	Childhood	↓	N	N	N or ↓	↑↑	↑↑	yes	yes
Hypomagnesemia with secondary hypocalcemia	Infancy	↓↓↓	↓	N	N	↑	N	no	no

*frequent complication during therapy with Ca^{2+} and vitamin D

Treatment of Hypomagnesemia

- Be attentive to the ABCs
- Treat life-threatening dysrhythmias according to ACLS protocol
- Treat seizures with benzodiazepines
- Treat hypomagnesemia appropriately

✷**Symptomatic (hypocalcemic tetany, hypokalemic ventricular arrhythmias)**

Intravenous slowly over 8 to 24 hours , Mg>1 mg/dl

✷**Asymptomatic patient**

oral replacement (magnesium lactate, chloride)

✷**The underlying disease should also be corrected**

Replacement therapy

IV

- Mg sulfate 1 gm of 50% sol → 4mmol mg.
- Mg< 0.6 →0.25 mmol/kg/d
- Mg 0.7-1.2 → 0.15 mmol/kg/d
- Given over 1-4 hrs
- Levels checked in 1-2 hrs after To give time for IC shift

Oral:

- Oral replacement of large deficit is difficult
- Mg is a saline cathartic→ large doses produce diarrhea
- Up to 20 mmol/d given in divided doses
- Use Mg oxide tablets or Mg sulfate sol

Table 55-11 Appropriate Compensation During Simple Acid–Base Disorders

DISORDER	EXPECTED COMPENSATION
Metabolic acidosis	$P_{CO_2} = 1.5 \times [HCO_3^-] + 8 \pm 2$
Metabolic alkalosis	P_{CO_2} increases by 7 mm Hg for each 10 mEq/L increase in serum $[HCO_3^-]$
RESPIRATORY ACIDOSIS	
Acute	$[HCO_3^-]$ increases by 1 for each 10 mm Hg increase in P_{CO_2}
Chronic	$[HCO_3^-]$ increases by 3.5 for each 10 mm Hg increase in P_{CO_2}
RESPIRATORY ALKALOSIS	
Acute	$[HCO_3^-]$ falls by 2 for each 10 mm Hg decrease in P_{CO_2}
Chronic	$[HCO_3^-]$ falls by 4 for each 10 mm Hg decrease in P_{CO_2}

Replacement therapy

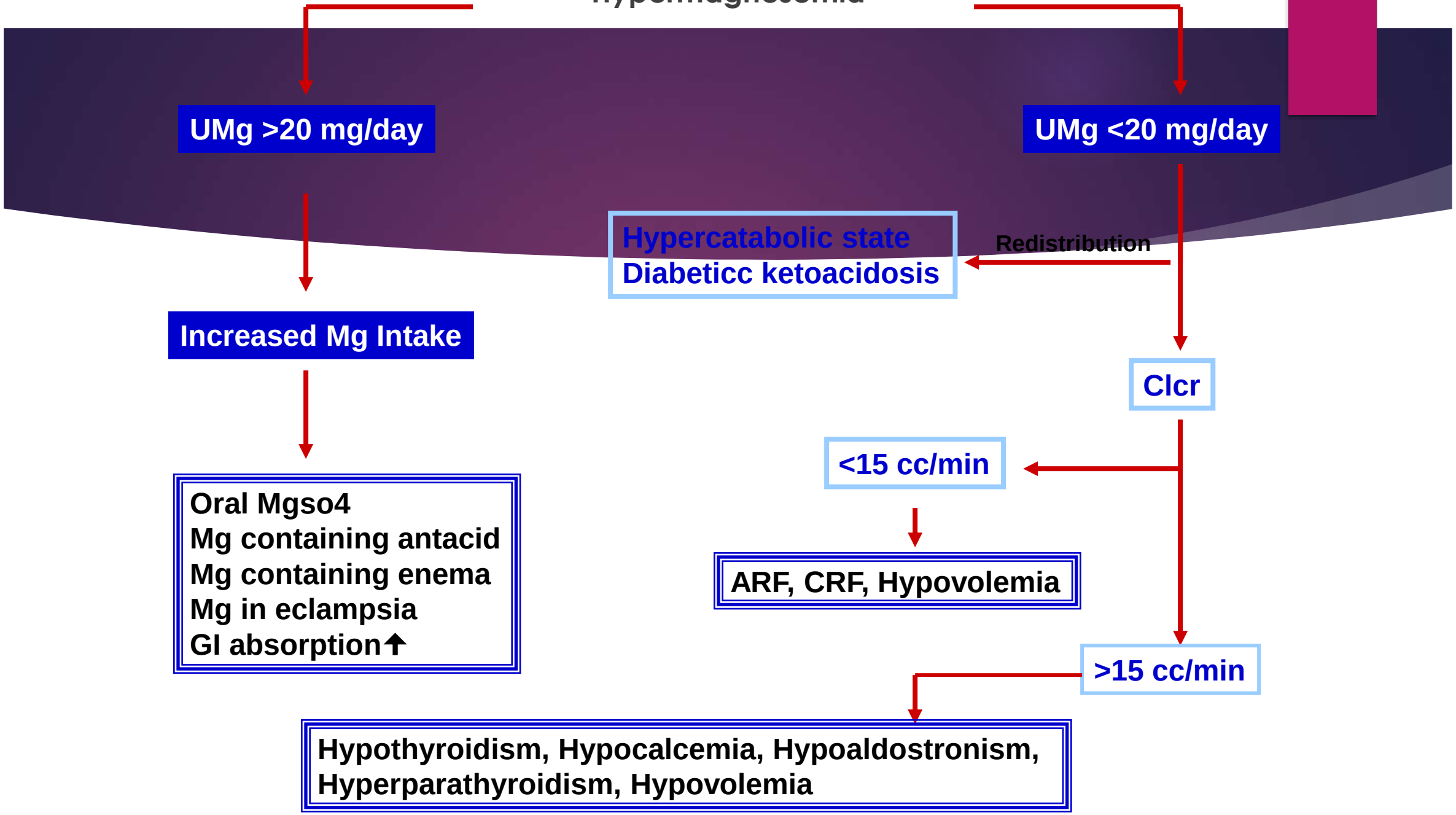
IV

- Mg sulfate 1 gm of 50% sol → 4mmol mg.
- Mg< 0.6 →0.25 mmol/kg/d
- Mg 0.7-1.2 → 0.15 mmol/kg/d
- Given over 1-4 hrs
- Levels checked in 1-2 hrs after To give time for IC shift

Oral:

- Oral replacement of large deficit is difficult
- Mg is a saline cathartic→ large doses produce diarrhea
- Up to 20 mmol/d given in divided doses
- Use Mg oxide tablets or Mg sulfate sol

Hypermagnesemia



Treatment of Hypermagnesemia

- ✓Circulatory and respiratory support with administration of 10% Ca gluconate 0.5-1 cc/kg IV.
- ✓ IV Furosmide
- ✓ Hemodialysis
- ✓ peritoneal dialysis (unstable hemodynamic)
- ✓ Exchange therapy in neonates

Table 55-11 Appropriate Compensation During Simple Acid–Base Disorders

DISORDER	EXPECTED COMPENSATION
Metabolic acidosis	$P_{CO_2} = 1.5 \times [HCO_3^-] + 8 \pm 2$
Metabolic alkalosis	P_{CO_2} increases by 7 mm Hg for each 10 mEq/L increase in serum $[HCO_3^-]$
RESPIRATORY ACIDOSIS	
Acute	$[HCO_3^-]$ increases by 1 for each 10 mm Hg increase in P_{CO_2}
Chronic	$[HCO_3^-]$ increases by 3.5 for each 10 mm Hg increase in P_{CO_2}
RESPIRATORY ALKALOSIS	
Acute	$[HCO_3^-]$ falls by 2 for each 10 mm Hg decrease in P_{CO_2}
Chronic	$[HCO_3^-]$ falls by 4 for each 10 mm Hg decrease in P_{CO_2}

Table 55-13	Causes of Metabolic Acidosis

NORMAL ANION GAP

Diarrhea
Renal tubular acidosis (RTA):
- Distal (type I) RTA (OMIM 179800/602722/267300)*
- Proximal (type II) RTA (OMIM 604278)†
- Hyperkalemic (type IV) RTA (OMIM 201910/264350/177735/145260)‡

Urinary tract diversions
Posthypocapnia
Ammonium chloride intake

INCREASED ANION GAP

Lactic acidosis
Tissue hypoxia
- Shock
- Hypoxemia
- Severe anemia

Liver failure
Malignancy
Intestinal bacterial overgrowth
Inborn errors of metabolism
Medications
- Nucleoside reverse transcriptase inhibitors
- Metformin
- Propofol

Ketoacidosis
- Diabetic ketoacidosis
- Starvation ketoacidosis
- Alcoholic ketoacidosis

Kidney failure
Poisoning
- Ethylene glycol
- Methanol
- Salicylate
- Toluene
- Paraldehyde

Table 55-14 | Causes of Metabolic Alkalosis

CHLORIDE-RESPONSIVE (URINARY CHLORIDE <15 MEQ/L)

Gastric losses
- Emesis
- Nasogastric suction

Diuretics (loop or thiazide)
Chloride-losing diarrhea (OMIM 214700)
Chloride-deficient formula
Cystic fibrosis (OMIM 219700)
Post-hypercapnia

CHLORIDE-RESISTANT (URINARY CHLORIDE >20 MEQ/L)

High blood pressure
- Adrenal adenoma or hyperplasia
- Glucocorticoid-remediable aldosteronism (OMIM 103900)
- Renovascular disease
- Renin-secreting tumor
- 17β-Hydroxylase deficiency (OMIM 202110)
- 11β-Hydroxylase deficiency (OMIM 202010)
- Cushing syndrome
- 11β-Hydroxysteroid dehydrogenase deficiency (OMIM 218030)
- Licorice ingestion
- Liddle syndrome (OMIM 177200)

Normal blood pressure
- Gitelman syndrome (OMIM 263800)
- Bartter syndrome (OMIM 607364/602522/241200/601678)
- Autosomal dominant hypoparathyroidism (OMIM 146200)
- EAST syndrome (OMIM 612780)
- Base administration

Table 55-15 Causes of Respiratory Acidosis

CENTRAL NERVOUS SYSTEM DEPRESSION

- Encephalitis
- Head trauma
- Brain tumor
- Central sleep apnea
- Primary pulmonary hypoventilation (Ondine curse)
- Stroke
- Hypoxic brain damage
- Obesity-hypoventilation (Pickwickian syndrome)
- Increased intracranial pressure
- Medications
  - Narcotics
  - Barbiturates
  - Anesthesia
  - Benzodiazepines
  - Propofol
  - Alcohols

DISORDERS OF THE SPINAL CORD, PERIPHERAL NERVES, OR NEUROMUSCULAR JUNCTION

- Diaphragmatic paralysis
- Guillain-Barré syndrome
- Poliomyelitis
- Spinal muscular atrophies
- Tick paralysis
- Botulism
- Myasthenia
- Multiple sclerosis
- Spinal cord injury
- Medications
  - Vecuronium
  - Aminoglycosides
  - Organophosphates (pesticides)

RESPIRATORY MUSCLE WEAKNESS
Muscular dystrophy
Hypothyroidism
Malnutrition
Hypokalemia
Hypophosphatemia
Medications
  Succinylcholine
  Corticosteroids

PULMONARY DISEASE
Pneumonia
Pneumothorax
Asthma
Bronchiolitis
Pulmonary edema
Pulmonary hemorrhage
Acute respiratory distress syndrome
Neonatal respiratory distress syndrome
Cystic fibrosis
Bronchopulmonary dysplasia
Hypoplastic lungs
Meconium aspiration
Pulmonary thromboembolus
Interstitial fibrosis

UPPER AIRWAY DISEASE
Aspiration
Laryngospasm
Angioedema
Obstructive sleep apnea
Tonsillar hypertrophy
Vocal cord paralysis
Extrinsic tumor
Extrinsic or intrinsic hemangioma

MISCELLANEOUS
Flail chest
Cardiac arrest
Kyphoscoliosis
Decreased diaphragmatic movement due to ascites or peritoneal dialysis

Table 55-16 | Causes of Respiratory Alkalosis

HYPOXEMIA OR TISSUE HYPOXIA

Pneumonia
Pulmonary edema
Cyanotic heart disease
Congestive heart failure
Asthma
Severe anemia
High altitude
Laryngospasm
Aspiration
Carbon monoxide poisoning
Pulmonary embolism
Interstitial lung disease
Hypotension

LUNG RECEPTOR STIMULATION

Pneumonia
Pulmonary edema
Asthma
Pulmonary embolism
Hemothorax
Pneumothorax
Respiratory distress syndrome (adult or infant)

CENTRAL STIMULATION

- Central nervous system disease
  - Subarachnoid hemorrhage
  - Encephalitis or meningitis
  - Trauma
  - Brain tumor
  - Stroke
- Fever
- Pain
- Anxiety (panic attack)
- Psychogenic hyperventilation or anxiety
- Liver failure
- Sepsis
- Pregnancy
- Mechanical ventilation
- Hyperammonemia
- Extracorporeal membrane oxygenation or hemodialysis
- Medications
  - Salicylate intoxication
  - Theophylline
  - Progesterone
  - Exogenous catecholamines
  - Caffeine


خـــدایـــا... عزیزانمان را چنان در جویبار زلال رحمتت شستشو ده که..
هر کجا تردیدی هست ایمان؛
هر کجا زخمی هست مرهم؛
هر کجا نومیدی هست امیدواری؛
و هر کجا نفرتی هست عشق جای آنرا فرا گیرد.
آمیـــن یا رب ألعالمیـــن.