Electrolyte Abnormalities in Neonates

Jon Palmer, VMD, DACVIM
Director of Neonatal/Perinatal Programs
Graham French Neonatal Section, Connelly Intensive Care Unit
New Bolton Center, University of Pennsylvania

Electrolyte Abnormalities

- Sodium/Water Balance
- Hyponatremia/Hypernatremia
- Hypokalemia/Hyperkalemia

Sodium/Water Balance

- Transition from fetal physiology
  - Late term fetus
  - High F_{xNa}
  - Transition – to low F_{xNa}
    - Most species during 1st day
    - Fetal foal - before birth
- Sodium conserving mode
  - Na requirement for growth
    - Bone growth
    - ↑ body mass
      - Increase in interstitial space
  - Milk diet
    - Fresh milk is sodium poor
      - 9-15 mEq/l

Sodium/Water Balance
Sodium Overload

- Sodium containing intravenous fluids
  - 6-7 mEq Na/kg/day
  - Mare's milk – 1.8 mEq Na/kg/day
  - 3-4 X normal Na
- Sodium overloading
  - Expansion of the extracellular fluid space
  - Sodium fractional excretion will remain low
- Difficulty dealing with volume loading

Hyponatremia

Hyponatremia

Spurious hyponatremia

Dilutional hyponatremia

Depletional hyponatremia

Redistribution hyponatremia

Spurious Hyponatremia

- Normal plasma sodium concentration
- Laboratory reports a low concentration
  - Presence of interfering substances
    - Lipids or large proteins
    - Artificially dilutes sample
    - Not with modern assay techniques
  - Mistakes in sampling
    - Venipuncture site distal to a low Na drip
    - Sample is taken from a catheter
      - Infusion of a low Na solution
      - Insufficient dead space clearing

Dilutional Hyponatremia

- Lack of balance
  - Fluid intake/urine output
- Loss of integrity of the urinary system
  - Ruptured bladder
  - Ruptured/necrotic urachus
  - Fenestrated ureters
- Renal failure
  - Low GFR
  - Na wasting

Dilutional Hyponatremia

- Failed/delayed renal transition fetal to neonatal physiology
  - Low GFR
- Water overload
  - Management mistakes
    - Dilute milk replacer
    - Excessive water enemas (retained)
    - Fluid therapy errors (Na wasting renal syndromes)
  - Syndrome of inappropriate antidiuresis (SIA)
  - Appropriate antidiuresis
    - Decreased arterial volume

Dilutional Hyponatremia

- Most common form hyponatremia in neonates
- Only occurs with intake of hyponatremic fluid
  - Fresh milk
  - Hyponatremic rehydration formulas
    - Dextrose in water or half strength saline
- Not with isotonic Na containing fluids
  - Normisol-R, Lactated Ringers, Plasmalyte
  - Less marked on milk replacer than fresh milk

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- Synonym: SIADH
  - Syndrome of Inappropriate Antidiuretic Hormone Secretion
- Hyponatremia secondary to
  - Inappropriate reabsorption of water from urine
- Diagnosis
  - High urine osmolarity
  - Hyposmolar hyponatremia - plasma
  - Normal renal function
  - Normal adrenal function
  - Euvolemia
- Can have excessive renal sodium excretion
  - Often absent in the neonate
  - Low sodium intake

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- Clinical syndrome
  - Sudden decrease in urine output
  - High urine specific gravity
  - Weight gain
    - 10-15% of body weight overnight
  - No edema
  - Decreasing plasma sodium concentration
- ADH increased
  - No osmotic stimulus
  - No hypovolemic stimulus

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- SIADH
  - Inappropriate vasopressin release
    - Erratic and unpredictable release vasopressin
    - Reset of the osmostat
      - Threshold for release is lowered
    - Vasopressin release not fully suppressed at low osmolarity
      - But normal at higher osmolarity
  - Receptor abnormality (vasopressin release normal)
    - Hypersensitive receptors
    - Receptors continue to respond
      - After vasopressin levels decrease
      - Hypovasopressinemic antidiuresis

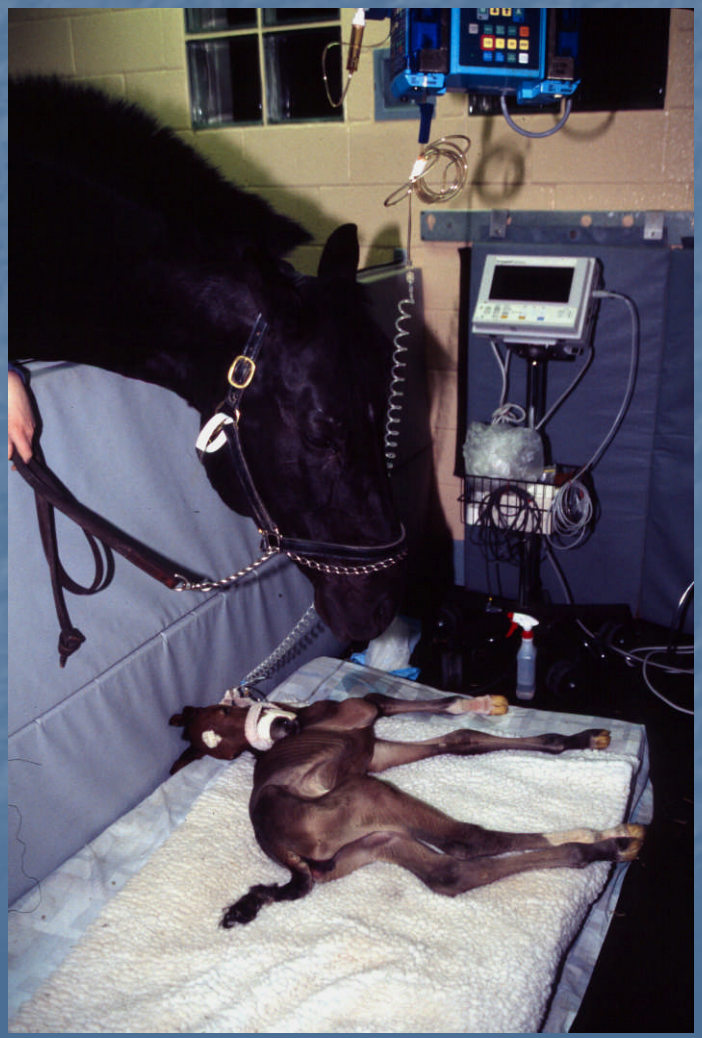
Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- SIAD not SIADH
  - High urine osmolarity
  - Hyposmolar hyponatremia
  - Hypovolemia
    - Appropriate vasopressin release
    - Defense of volemia

Hyponatremia
Syndrome of Inappropriate Antidiuresis (SIAD)

- Nonosmotic ADH release
  - Subclinical volume depletion
  - Pain
  - Stress
  - Administration of hypotonic fluids
- Abnormal adrenal function
- Abnormal renal function

Depletional Hyponatremia



- Na loss > water
- Diarrhea
  - Excessive sodium loss in feces
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water
- Renal sodium wasting
  - Tubular disease
  - Use of diuretics
  - Endocrine disturbances
  - Rehydration with Na poor fluids
    - Fresh/frozen milk
    - Fresh water

Redistribution Hyponatremia

- Low sodium concentration
  - Osmolarity normal
  - Isosmotic hyponatremia
    - Hyperosmotic hyponatremia
- Other osmotically active particles present
  - Redistribute fluid from intracellular space
    - Appropriate decrease Na concentration
    - Hyperglycemia (Na, Glu in mmol/L)
      - $Na_{corrected} = Na_{measured} + [(Glu - 5)/3.5]$
      - 1.6 mEq/l Na decrease for 5.55 mmol/L glu increase
    - Iatrogenic addition of osmoles
      - Mannitol
    - Extreme hyperproteinemia
    - Secondary to sick cell syndrome

Hyponatremia
Sick Cell Syndrome

- Critically ill patients
  - Cellular insult
  - Loss of cell wall integrity
  - Solutes leak
    - Fluid follows
    - Dilution of extracellular sodium

Hyponatremia
Clinical Assessment

- Classify hyponatremia
  - Hypervolemic
  - Euvolemic
  - Hypovolemic

Hyponatremia
Clinical Assessment

- Hypervolemic hyponatremia
  - Impaired water excretion
    - Renal failure
    - Ruptured bladder
    - Decreased GFR
    - Na retention
    - ADH excess
  - Increased total body water + Na
    - Water > Na
  - Edema, ascites
  - Decreased arterial volume/BP
    - Stimulate ADH secretion

Hyponatremia
Clinical Assessment

- Euvolemic hyponatremia
  - Most common in hospitalized patients
  - ADH mediated water retention
    - Increased ECF
  - Iatrogenic
    - Rx hypotonic fluids in patients
    - When stimulus for increased ADH secretion
  - Total body Na normal
  - No edema
    - Defines euvolemic

Hyponatremia
Clinical Assessment

- Hypovolemic hyponatremia
  - Deficit water & Na
    - Na deficit > water deficit
  - Etiology
    - Diarrhea
    - Na wasting nephropathy
    - Diuretics

Hypotonic Hyponatremia Clinical Findings

- Asymptomatic or symptomatic
- Severe
  - < 115 mEq/l – arbitrary definition
- Acute
  - < 36-48 hr
- Progressive brain edema
  - Weakness, depressed reflexes
  - Obtunded, abnormal sensorium
  - Hypothermia
  - Cheyne-Stokes respiration
  - Seizures, Coma
  - Brainstem herniation
  - Respiratory arrest

Hypotonic Hyponatremia Brain Edema

- Abrupt hypo-osmolarity
  - Aquaporin-4 mediated
  - Water moves into brain cells
- Compensation
  - Decreased cerebral venous pooling
  - Decreased CSF volume
    - Pediatric – less relative CSF volume
- Cell volume regulatory ions
  - Na, K, Cl
  - Released within 5 min from cells
  - Can continue for 4 hours
  - Stretched cell membranes open ion channels
  - Hormone regulated cellular ion differences
    - Predisposes females to more damage

Hypotonic Hyponatremia Brain Edema

- Reduction of cellular osmolytes
  - Polyalcohols
    - Sorbitol
    - Inositol
  - Amino acids
  - Methylamines
  - Within 2-4 days
    - Up to 50% reduction osmolytes

Hypotonic Hyponatremia Brain Edema

- Early and late phase changes
  - Limit cellular edema
  - Limit damage
- Hypoxic ischemic encephalopathy
  - Compounds hyponatremia damage
    - Interferes with compensation
  - Cerebral edema
    - Interferes with cerebral perfusion
    - Impairs central respiratory centers

Hypotonic Hyponatremia Chronic, severe

- Asymptomatic
  - Oligosymptomatic
  - Not treat?
- Only for days
  - Somnolent
  - Disoriented
  - Often Rx
- Causes
  - Diuretics
  - SIADH
  - Malnourishment/liver disease
  - Diarrhea

Hypotonic Hyponatremia Chronic, severe - treated

- Risk of cerebral myelinolysis
  - Central pontine myelinulysis
  - Initial report 12 patients – weak evidence
  - Other reports extrapontine
  - May occur in 25% cases
    - Over rapid correction
    - Other risk factors
      - Hypokalemia
      - Alcoholism
  - Experimental studies – Na 118 to 140 mEq/l
    - 48 hrs – OK
    - 8 hr – 90% myelinolysis
      - Rx hypertonic saline
      - Rx ADH antagonist

Hypotonic Hyponatremia Myelinolysis - Pathogenesis

- Osmotic reloading fails
  - Rapid correction
  - Brain cell Na, K
    - Normal
    - High because of overshoot
  - Amino acid content low
- Osmotic reloading
  - Organic osmolytes take up to 5 days
    - Normal metabolic molecules
    - Parts of cellular proteins/lipids
  - External addition not speed
  - Transport depends on new gene expression
    - RNA transcription – protein production
  - Slowest where lesions occur
  - Blood brain barrier has role

Hypotonic Hyponatremia Myelinolysis - Pathogensis

- Blood brain barrier
  - Major target of cellular edema
  - Vascular endothelial cell
  - Astrocyte foot processes
  - Cell shrink opens cell junctions
- BBB disrupted
  - Not protect
  - Plasma constituents have access

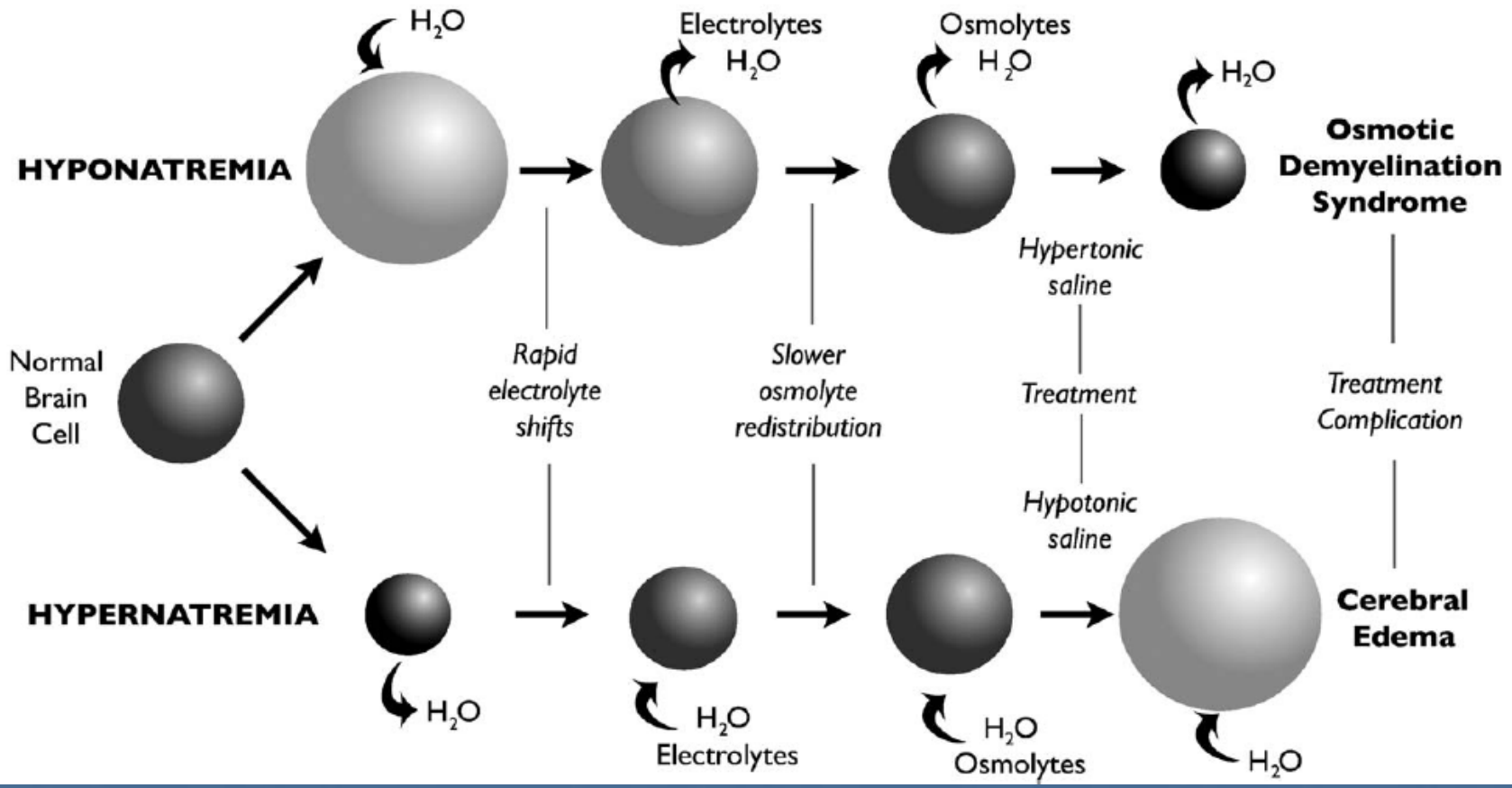
Hypotonic Hyponatremia Myelinolysis - Pathogenesis

- Factors associated
  - Overshoot hypernatremia
  - Increasing Na > 25 mEq/L 24-48 hr
  - Concurrent hypoxic event
  - Liver disease
- Rate of Na rise
  - Less important than magnitude
- Symptomatic hyponatremia
  - More important to treat
  - Than threat of myelinolysis
- Signs days after Na correction
- MRI lesions best seen 2 weeks after

Hypotonic Hyponatremia Treatment

- Recognize cause
  - Don’t treat spurious, redistribution hyponatremia
- Symptomatic – euvolemia/hypervolemia, with concentrated urine
  - Hypertonic saline
  - Furosemide – limit volume expansion
  - Stop water intake
- Symptomatic – hypovolemia
  - Isotonic fluids
- Mild symptomatic – dilute urine
  - Evaporative losses only

Hyponatremia/Hypernatremia Osmotic Shifts



Hypotonic Hyponatremia Treatment - Correction rate

- Acute – rapid
- Chronic
  - Increase Na < 0.5 mmol/L/hr
  - Stop once serum Na = 120-126
- If seizures
  - Increase Na 1 – 1.5 mmol/L/hr for 1st 3 hr
  - Or until seizures stop
  - Give 1-2 ml/kg/hr 3% saline
    - If seizures severe up to 4-6 ml/kg/hr
  - Add furosemide
  - Stop when Na = 118 mEq/l
    - Goal 125 mEq/l

Hypotonic Hyponatremia
Estimate Effect of Infusate

$$\text{For each liter given Change in serum [Na]} = \frac{(\text{Infusate Na} + \text{Infusate K}) - \text{serum Na}}{\text{Total body water} + 1}$$

Total body water

- early neonate = 0.75 X body wt
- pediatric = 0.6 X body wt
- adult = 0.5-0.6 X body wt
- geriatric = 0.45-0.5 X body wt

Hypotonic Hyponatremia Treatment

- Vasopressin Antagonists
  - Better predictability
  - Better fine tuning
- Hyponatremia and ADH
  - Primarily disease of excess ADH
  - In face of continued hypotonic fluid intake
- Not use with hyponatremia because of
  - Renal disease
  - Volume contraction
- Oral products being tested

Hypotonic Hyponatremia Vasopressin Antagonists

- Demeclocycline
  - Blocks at tubules
- Aquaretics
  - V_{1a} & V_2
    - Conivaptan
  - V_2
    - Lixivaptan
    - Satavaptan
    - Tolvaptan

Hypernatremia

Hypernatremia

- Uncommon
- Deficit of water relative to Na stores
- Hypertonic hyperosmolality
- Causes of hypernatremia
  - Spurious
  - Excessive free water loss
    - Pure water loss
    - Hypotonic fluid loss
  - Hyperosmotic intake
  - Iatrogenic

Spurious hypernatremia

- Sampling errors
  - Blood samples from the intravenous catheter
    - Not large enough presample
    - Sample contamination
      - with saline

Hypernatremia
Increased free water loss

- Increased insensible loss
  - Increased respiratory rate
  - Low humidity
  - High body temperature
  - External warming
    - Radiant heat
    - Hot air heat
- Increased insensible loss with limited intake
  - Hot weather
  - Neonate unable to nurse
    - Lack opportunity
    - NE

Hypernatremia
Increased free water loss

- Water loss
  - Diabetes insipidus
    - Unusual because of neonate's diet
- Hypotonic fluid loss
  - Furosemide
  - Osmotic diuresis
    - Glucosuria
    - Mannitol
  - Renal disease
  - Diarrhea
  - Excessive sweating

Hypernatremia Hyperosmotic Intake

- High sodium maternal milk
  - Excessive sodium intake relative to free water
- Iatrogenic mishaps
  - Improperly mixed electrolyte solutions
    - Without the opportunity/ability to drink fresh water
  - Improperly mixed milk replacer
    - All powdered milk replacers are sodium rich
  - Use of hypernatremic intravenous fluids solutions
    - 5% sodium bicarbonate
    - Hypertonic saline
  - Use of saline in oxygen humidifiers
  - Hypertonic enemas (retained)

Hypernatremia
Normal defense against

- Concentrate urine
  - Osmolar release ADH
- Thirst
  - Only develops if can't get to water

Hypernatremia Treatment

- Recognize cause
  - Eliminate/manage underlying problem
- If developed acutely (hours)
  - Can be corrected over hours (↓Na 1 mmol/hr)
  - Usually acute sodium loading
- If developed slowly (over days)
  - Intracellular accumulation organic osmolytes
  - Correct slowly to avoid cerebral cellular edema
  - ↓Na < 0.5 mmol/hr (target ↓Na 10 mmol/day)

Hypernatremia Treatment

- If Na > 170
  - Don’t decrease < 150 for 48-72 hr
- Oral fluid therapy
  - As soon as possible
  - Na and K in milk
- Seizures during treatment
  - Common
  - From cerebral edema
  - Slow correction

Hypernatremia
Estimate Effect of Infusate

$$\text{For each liter given Change in serum [Na]} = \frac{(\text{Infusate Na} + \text{Infusate K}) - \text{serum Na}}{\text{Total body water} + 1}$$

Total body water

- early neonate = 0.75 X body wt
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Hypokalemia

Hypokalemia

- Hypokalemia common in neonates
- Anabolic increase in cell mass (growth)
  - Potassium major intracellular ion
- Renal K wasting
  - Diuresis
  - Renal pathology

Hypokalemia
Stress/sepsis

- Resting muscle
  - Uses 10% of available Na^+:K^+ ATPase activity
- Stimulated acutely by
  - Insulin
  - Epinephrine
  - Contractile activity

Hypokalemia
Stress/sepsis

- Stress/Sepsis →↑ epinephrine
  - ↑ Na^+:K^+ ATPase activity
  - Significant intracellular shifts of K → hypokalemia
  - ↑ ATPase demand
    - ↑ glucose utilization/requirement
    - ↑ glucose transport into the cell resulting
    - → further shift K intracellular??

Hypokalemia Pathogensis

- Loss of 1% total body potassium
  - Disturbs transcellular distribution
  - Results in physiological changes
- Blood levels
  - Not correlate total body stores
  - Rapid drop more likely clinical signs
- Loss 100 mEq K
  - Blood level decreases by 0.3 mEq/l
  - If there are no confounders

Hypokalemia
Signs - man

- Muscle weakness
- Paralytic ileus
- Cardiac arrhythmias
  - Atrial tachycardia
  - Atrioventricular dissociation
  - Ventricular tachycardia/fibrillation
  - Flat or inverted T-waves
  - ST-segment depression
  - U-waves

Hypokalemia
Signs - man

- K < 2.5
  - Rhabdomyolysis with myoglobinuria
  - Acute renal failure
- K < 2.0
  - Ascending paralysis
  - Impairment of respiratory function
- Not recognize in neonatal foals

Hypokalemia

- High levels of potassium in milk
  - Will support growth requirements
- Stressed/Septic neonates
  - Not tolerate oral feeding
- Neonates require significant K supplementation
  - Prolonged intravenous glucose
  - Parenteral nutrition
  - Limited or no milk feeding
- Glucocorticoid administration
  - Mineralocoritcoid receptor stimulation
  - $\rightarrow$ urine loss of potassium

Hypokalemia Treatment

- Neonates
  - Milk diet – not need supplement
  - Fluids only
    - If normal plasma levels – 3 mEq/kg/d
    - If hypokalemic – 6-12 mEq/kg/d or more

Hyperkalemia

- Differential diagnosis
  - Ruptured bladder
  - Urinary tract defect
  - Sick cell syndrome
  - Iatrogenic

Hyperkalemia

- Loss of integrity lower urinary tract
  - ↑K only when on a milk diet
    - Also true for ↓Na, ↓Cl
  - Receiving parenteral nutrition
    - ↑K only occur with overzealous K administration
- Sick cell syndrome
  - Suffer global cell insult
    - Perinatal hypoxic ischemic asphyxial insults
  - ↑K = 6-8 mEq/l
- Hyperglycemia – no insulin response
- Iatrogenic in the face of renal insufficiency

Hyperkalemia
Signs

- Impaired neuromuscular transmission
  - Cardiac
  - Neuromuscular paresis/paralysis
- General fatigue
- Weakness
- Paresthesia

Management of Hyperkalemia

Questions to be asked:

Is there an emergency related to hyperkalemia?

- If so, what is the plan for therapy?

Is pseudohyperkalemia present?

Did this hyperkalemia develop acutely?

- Toxicity more related to rate of increase than level
- Toxicity associated with acid-base status

What role of

- High K intake
- Decreased renal K excretion
- Transcellular K shift

Management of Hyperkalemia

- ECG changes
  - Peaked T wave
    - False + depending on lead placement
  - Decrease/absence P waves
    - False + depending on lead placement
  - Prolonged PR interval
  - Widened QRS
  - Sine wave QRS
  - Asystole
- ECG not sensitive indicator of hyperkalemia
  - K > 6.0 – 46% abnormal ECG (in man)
  - K > 6.8 – 55% abnormal ECG (in man)
- Not predicable progression

Management of Hyperkalemia

- Pseudohyperkalemia
  - Sample hemolysis
  - Long, tight tourniquet (man)
  - Leukocytosis (>70,000; serum)
  - Thrombocytosis (>1,000,000; serum)
    - Measure plasma vs serum
    - If serum > 0.3 higher - pseudohyperkalemia

Management of Hyperkalemia Urgent Therapy

- Oppose direct toxic effects
  - Ca therapy
- Promote cellular uptake K
  - Insulin (glucose)
  - β_2-agonists (albuterol)
  - $NaHCO_3$ - not
- Remove from body
  - Drain uroabdomen
  - Diuretics
  - Cation exchange resins

Management of Hyperkalemia Urgent Therapy

- Calcium
  - Ca gluconate – less irritating
  - CaCl – Ca more biologically available
  - Slow IV push
    - ECG changes within 1-3 minutes
    - Lasts 30-60 minutes

Management of Hyperkalemia Urgent Therapy

- Insulin
  - Increase Na/K pump – primarily muscle/liver
    - Increase Na/H exchanger as well – may be important
  - Onset 20 min with peak 30-60 min
  - Dose related
  - Use glucose only to prevent hypoglycemia
  - Dose – 10 units as a bolus
    - Lasts 4-6 hr
  - CRI use in neonates
  - Hypoglycemia risk – monitor

Management of Hyperkalemia Urgent Therapy

- Adrenergic Agents
  - $ß_2$-receptor in the muscle and liver
  - Directly activate Na/K-ATPase
    - Increase cAMP
  - Albuterol
    - By insufflation or IV
    - K drop within 30 min, peak 90-120 min
    - Drop 0.6-1 mEq/l
  - Has no effect 40% dialysis patients (man)
  - Effect additive to insulin

Management of Hyperkalemia Urgent Therapy

- $NaHCO_3$
  - Poor response
  - Requires 4 hrs for effect
  - K decreased < 0.35 mEq/l at 6 hr
- Combined therapy
  - Insulin + β_2
    - Different mechanisms
    - In theory additive 60-100%
    - But not all respond to β_2
    - Combination – less frequent hypoglycemia
  - Insulin + $NaHCO_3$
    - Potentiate effect?

Management of Hyperkalemia Direct Elimination from Body

- Gastrointestinal Route
  - Sodium polystyrene sulfonate
    - Cation exchange resin
    - 1 gm removes 0.5-1 mEq/l K
    - 4-6 hr required for full effect
  - Oral, enema
    - Constipates – give with laxative
  - Minimal short term effect
  - Depends on gut perfusion

Management of Hyperkalemia Direct Elimination from Body

- Renal
  - Na diuresis
  - Deliver Na to distal K secreting sites
  - Renal disease often attenuates effect
- Abdomen
  - Draining uroabdomen
  - Peritoneal dialysis