**Pathophysiology**

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- Course website: rci.rutgers.edu/~advis  

- Lectures, tests, grades, office hours, textbook,  

- Material to be covered:  
  - Lectures 1-2: Introduction to Pathophysiology (2)  
  - Lectures 3-4: Mechanisms of Self-Defense and Stress (2)  
  - Lectures 5-8: Endocrine and Nervous System Dysfunctions (4)  
  - Lecture 9: Alterations of Skeletal Muscle Function (1)  
  - Lecture 10: Cardiovascular, Respiratory and Renal Dysfunctions (7)  
  - Lecture 11: Alterations of the Reproductive System (2)  
  - REVIEW AND TEST #1  
  - REVIEW AND TEST #2  
  - REVIEW AND TEST #3  

- About lecture slides:  
  - There are not intended to be the sole source for studying the course material !!!!!!!!!!!!!!!!  
  - Slides are good to review the course material after you have study your course textbook  
  - Slides are a good indicator of the relative importance of lecture topics (see slide # per topic  
  - Group slides by titles when using them to review course material. Match lectures and text.  

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**Symptoms of Tissue Disease**

**Water movement**  
- water from plasma to ICF  
- water from ICF to ECF  
- alteration: edema  

**Na, Cl, H2O balance**  
- water balance  
- Na and Cl balance  

**Na, Cl, H2O alterations**  
- isotonic alterations  
- hypertonic alterations  
- hypotonic alterations  

**K & others alterations**  
- K alterations  
- hyperkalemia  
- other electrolytes  

**Acid – base balance**  
- H ion and pH  
- buffer systems  
- acid – base imbalances  

The cells in the body live in a fluid environment with an electrolyte and acid – base concentration maintained within a narrow range.  

Changes in electrolyte concentration affect the electrical activity of nerve and muscle cells and cause shifts of fluid from one compartment to another. Alterations in acid-base balance disrupts cellular functions. Fluid concentrations also affect blood volume and cellular function. Disturbances in these functions are common and can be life threatening.  

Understanding how alterations occur and how the body compensates or correct the disturbance is important to understand many pathophysiological conditions.  

Your course textbook, chapter 4, introduction.
Water Movement

Water movement
water from plasma to ICF
water from ICF to ECF
alteration: edema

Na, Cl, H2O balance
water balance
Na and Cl balance

Na, Cl, H2O alterations
isotonic alterations
hypertonic alterations
hypotonic alterations

K & others alterations
K alterations
hyperkalemia
other electrolytes

Acid – base balance
H ion and pH
buffer systems
acid – base imbalances

Water movement across capillary walls depend on the Starling forces: hydrostatic and oncotic pressures.
Water Movement

DISTRIBUTION OF BODY FLUIDS:
Body fluids are distributed among functional compartments and are classified as ICF and ECF; TBW=ICF+ECF and varies with age and the amount of body fat.

Water moves between ICF and ECF by osmosis and it moves between plasma and ICF compartments, across capillary membranes by osmosis and hydrostatic pressure.

Movement across the capillary wall is called net filtration and is described according to Starling law (the balance between hydrostatic and osmotic forces).

Edema or water accumulation in interstitial spaces results from increase filtration to tissue from capillaries or lymphatic channels due to arterial dilation, venous or lymphatic obstruction, raised vascular volume, or increased capillary permeability. It may be localized or generalized and is associated with weight gain, swelling and puffiness, tighter-fitting clothes and shoes, and limited movement of the affected areas.

Water movement across capillary walls depend on the Starling forces: hydrostatic and oncotic pressures.

DISTRIBUTION OF BODY FLUIDS:
Body fluids are distributed among functional compartments and are classified as ICF and ECF; TBW=ICF+ECF and varies with age and the amount of body fat.

Water movement from plasma to ICF

Water movement from ICF to ECF

Alteration: edema

Na, Cl, H2O balance

Na and CI balance

Na, Cl, H2O alterations

Isotonic alterations

Hypertonic alterations

Hypotonic alterations

K & Others alterations

K alterations

Hyperkalemia

Other electrolytes

Acid – base balance

H ion and pH

Buffer systems

Acid – base imbalances

Water movement across capillary walls depend on the Starling forces: hydrostatic and oncotic pressures.
Water Movement

Water movement across capillary walls depend on the Starling forces: hydrostatic and oncotic pressures.

INCREASED CAPILLARY PERMEABILITY (burns, allergic inflammation reaction)
- Decreased production of plasma proteins (cirrhosis, malnutrition)
- Loss of plasma proteins
- Increased tissue oncotic pressure
- EDEMA
- Na, H2O renal retention
- Increased absorption of interstitial fluid

DECREASED CAPILLARY ONCOTIC PRESSURE
- Decreased transport of capillary filtered protein
- LYMPH OBSTRUCTION
- Decreased absorption of interstitial fluid

INCREASED CAPILLARY HYDROSTATIC PRESSURE (venous obstruction, salt & water retention, heart failure)
- Fluid movement into tissue
- Decreased transport of capillary filtered protein
- Decreased absorption of interstitial fluid

Na, Cl, H2O balance
- water balance
- Na and Cl balance

Na, Cl, H2O alterations
- isotonic alterations
- hypertonic alterations
- hypotonic alterations

K & others alterations
- K alterations
- hyperkalemia
- other electrolytes

Acid – base balance
- H ion and pH
- buffer systems
- acid – base imbalances

Water movement from plasma to ICF
- alteration: edema

Na, Cl, H2O balance
- alteration: edema

Water movement from ICF to ECF
- alteration: edema

Na, Cl balance
- alteration: edema

INCREASED CAPILLARY PERMEABILITY
- Burns, allergic inflammation reaction
Fluids and Electrolytes Balance

Water movement
- Water from plasma to ICF
- Water from ICF to ECF
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K & others alterations
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- Other electrolytes

Acid – base balance
- H ion and pH
- Buffer systems
- Acid – base imbalances

Na and H2O balance are intimately related. Cl is pp to Na levels. Water balance is regulated by ADH. Na balance is regulated by ALDO through RAS and by ANH.

Changes in electrolytes affect electrical activity of nerve / muscle cells and cause shifts of fluid from one compartment to another.
Fluids and Electrolytes Balance

**Water movement**
- Water from plasma to ICF
- Water from ICF to ECF

**Alteration: edema**

**Na, Cl, H2O balance**
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**Fluids and Electrolytes Alteration**

**Water movement**
- Water from plasma to ICF
- Water from ICF to ECF
- Edema

**Na, Cl, H2O balance**
- Na and H2O balance
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**ALTERATIONS IN SODIUM, CHLORIDE & WATER BALANCE:**
Alterations in H2O balance might be isotonic, hypertonic, or hypotonic. In isotonic alterations changes in TBW are pp to changes in electrolytes. Hypertonic alteration develop when ECF osmolality is above normal, mostly due to Na increase or H2O decrease. In hypotonic alterations ECF osmolality is below normal.

Hypernatremia may be caused by acute increase in Na or H2O loss. Water deficit or hypertonic dehydration is rare, but can be caused by no H2O, pure H2O loss, hyperventilation, arid climate, and high renal loss of H2O. Hyperchloremia is caused by an excess of Na or a deficit of bicarbonates.

Hyponatremia usually causes movement of H2O into cells. It may be caused by Na loss, inadequate Na intake, or dilution of body’s Na by excess water (rare but can be caused by compulsive H2O drinking, low urine formation, and SIADH.

Hypochloremia usually result of hyponatremia or high HCO3 conc. 

Changes in electrolytes affect electrical activity of nerve / muscle cells and cause shifts of fluid from one compartment to another.
CAUSES AND CONSEQUENCES OF HYPERTONIC IMBALANCES

<table>
<thead>
<tr>
<th>Cause</th>
<th>Mechanism</th>
<th>ECF effect</th>
<th>ICF effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased Sodium</td>
<td>Excessive intake IV hypertonic solution</td>
<td>Hyperhydration</td>
<td>Dehydration in ICF</td>
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<tr>
<td></td>
<td>Saline induced abortion</td>
<td>Weight gain</td>
<td>Thirst</td>
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<tr>
<td></td>
<td>Decreased Na loss</td>
<td>Bounding pulse</td>
<td>Fever</td>
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<td></td>
<td>Hyperaldosteronism</td>
<td>Increased BP</td>
<td>Low urine output</td>
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<td></td>
<td>Cushing syndrome</td>
<td>Edema</td>
<td>Brain cell shrinkage</td>
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<tr>
<td></td>
<td>Renal failure</td>
<td>Venous distention</td>
<td>Confusion</td>
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<td></td>
<td>Congestive heart failure</td>
<td>Neuromuscular symptoms</td>
<td>Coma</td>
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<td>Muscle weakness</td>
<td>Cerebral hemorrhage</td>
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<td></td>
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<td>Seizures</td>
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<td>Water Deficit</td>
<td>Water deprivation</td>
<td>Hypovolemia</td>
<td>Dehydration in ICF</td>
</tr>
<tr>
<td></td>
<td>Confusion or coma</td>
<td>Weight loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unable to communicate</td>
<td>Weak pulse</td>
<td></td>
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<td></td>
<td>Loss of thirst</td>
<td>Postural hypotension</td>
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<td></td>
<td>Unable to swallow</td>
<td>Taquicardia</td>
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<td>Water loss</td>
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<td>Watery diarrhea</td>
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<td>Diabetes Insipid</td>
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<td></td>
<td>Excessive diuresis</td>
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<td></td>
<td>Excessive diaphoresis</td>
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<tr>
<td>Other Factors</td>
<td>Hyperglycemia</td>
<td>Dilutional hyponatremia</td>
<td>Dehydration in ICF</td>
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<tr>
<td></td>
<td></td>
<td>Polyuria</td>
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<tr>
<td></td>
<td></td>
<td>Weight loss</td>
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<tr>
<td></td>
<td></td>
<td>Hypovolemia</td>
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<tr>
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<td></td>
<td>Late hyponatremia</td>
<td></td>
</tr>
</tbody>
</table>
## Fluids and Electrolytes Alteration

### Water movement
- Water from plasma to ICF
- Water from ICF to ECF

### Sodium, Chloride, and Water Balance
- **Na, Cl, H2O balance**
  - Water balance
  - Na and Cl balance
- **Na, Cl, H2O alterations**
- **Hypotonic alterations**
- **Hypertonic alterations**
- **Isotonic alterations**

### Potassium and Other Electrolytes
- **K & other alterations**
  - **K alterations**
  - **Hyperkalemia**
  - **Other electrolytes**

### Acid-Base Balance
- **Acid – base balance**
  - H ion and pH
  - Buffer systems
  - Acid-base imbalances

### Causes and Consequences of Hypotonic Imbalances

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</thead>
<tbody>
<tr>
<td>Decreased Sodium</td>
<td>Inadequate Na intake Hypoaldosteronism Increased Na loss Diuresis Profuse sweating Gastrointestinal losses</td>
<td>ECF contraction and hypovolemia (but may not occur if there is water excess)</td>
<td>Increased ICF water; edema Brain cell swelling, irritability, depression, confusion Systemic cellular edema, including weakness, anorexia, nausea, and diarrhea Edema</td>
</tr>
<tr>
<td>Water Excess</td>
<td>Na dilution IV hypotonic solution H2O for isotonic loss Tap H2O enemas Psychogenic polydipsia Renal H2O retention Increased ADH</td>
<td>ECF volume expands with hypervolemia (but may not occur if fluid is trapped in ICF)</td>
<td>Dehydration in ICF</td>
</tr>
<tr>
<td>Other Factors</td>
<td>Nephrotic syndrome Cirrhosis Cardiac failure</td>
<td>Hypervolemia or hypovolemia</td>
<td>Dehydration in ICF</td>
</tr>
</tbody>
</table>

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Page 8
### Fluids and Electrolytes Alteration

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#### ALTERATIONS IN POTASSIUM & OTHER ELECTROLYTES:

- K is the main ICF ion; it regulates ICF osmolality, maintains resting membrane potential, and is required for glycogen deposition in liver & skeletal muscle. Its balance is regulated by kidney, by ALDO & insulin secretion, & by changes in pH. The mechanism of K tolerance allows the body to adapt slowly to increase levels of K intake.

- Hypokalemia indicates loss of total body (TB) K, although ECF hypokalemia can develop without losses of TB-K, and plasma K may be normal or elevated when TB-K is depleted. Hypokalemia may be caused by low K intake, a K shift from ECF to ICF, increased ALDO, and increased renal excretion.

- Hyperkalemia may be caused by increased K intake, a shift of K from ICF to ECF, or decreased renal excretion.

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**Changes in electrolytes affect electrical activity of nerve / muscle cells and cause shifts of fluid from one compartment to another.**
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**Fluids and Electrolytes Alteration**

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### CLINICAL MANIFESTATIONS OF POTASSIUM ALTERATIONS

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<tr>
<th>Organ system</th>
<th>Hypokalemia</th>
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<tr>
<td>Cardiovascular</td>
<td>Dyssrhythmias</td>
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<td></td>
<td>EKG changes</td>
<td>Bradycardia</td>
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<tr>
<td></td>
<td>Cardiac arrest</td>
<td>Heart block</td>
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<tr>
<td></td>
<td>Weak irregular pulse</td>
<td>Cardiac arrest</td>
</tr>
</tbody>
</table>

| Nervous | Lethargy | Anxiety |
| Fatigue | Confusion | Tinnitus |
| Paresthesia | | |

| Gastrointestinal | Nausea and vomiting | Nausea and vomiting |
| | Diarrhea | Colicky pain |

| Kidney | Water loss | Oliguria |
| Thirst | Kidney damage |
| Inability to concentrate urine | |

| Skeletal and smooth muscle | Weakness | Early: hyperactive muscles |
| Flaccid paralysis | Late: weakness and flaccid paralysis |
| Respiratory arrest | |
| Constipation | |
| Bladder dysfunction | |
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<td>Numbness</td>
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<td>Decreased motility</td>
<td>Diarrhea</td>
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<td>Distension</td>
<td>Colicky pain</td>
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<td>Decreased bowel sounds</td>
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<td>ileus</td>
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<td>Kidney</td>
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</table>

### Fluids and Electrolytes Alteration

**ALTERATIONS IN POTASSIUM & OTHER ELECTROLYTES:**

Ca is a necessary ion in the structure of bones and teeth, in blood clotting, in hormone secretion and the function of cell receptors, and in membrane stability. PO4 acts as buffer in acid–base regulation and provides energy for contraction of muscles. Ca and PO4 are controlled by PTH, VitD and CT.

Hypocalcemia is related to inadequate intestinal absorption, deposition of Ca into bones or soft tissue, blood infusion, or decreased PTH and VitD levels. Hypercalcemia is caused by a number of diseases, including hyperparathyroidism, bone metastases, sarcoidosis, and excess VitD.

Hyperphosphatemia develops with renal failure w/low GFR.

Mg functions in enzymatic reactions and often interacts with Ca at the cell level. Hypomagnesemia may be caused by malabsorption syndromes. Hypermagnesemia is rare and is usually cause by renal failure.

Changes in electrolytes affect electrical activity of nerve / muscle cells and cause shifts of fluid from one compartment to another.
# Fluids and Electrolytes Alteration

## Water movement
- Water from plasma to ICF
- Water from ICF to ECF

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## Na, Cl, H2O alterations
- Isotonic alterations
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## K & others alterations
- K alterations
- Hyperkalemia
- Other electrolytes

## Acid – base balance
- pH ion and pH buffer systems
- Acid – base imbalances

### CALCIUM

<table>
<thead>
<tr>
<th>Excess causes</th>
<th>Excess effects</th>
<th>Deficit causes</th>
<th>Deficit effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>HyperPTH; bone metastases w/Ca resorption from breast, prostate, renal, and</td>
<td>Fatigue, weakness, lethargy, anorexia, nausea, impaired renal function, kidney</td>
<td>Low G1 absorption, deposits of ionized Ca in bones / soft tissue, blood administration, low</td>
<td>Neuromuscular excitability, tingling, muscle spasm, gut cramps, hyperactive bowel</td>
</tr>
<tr>
<td>cervical cancer; sarcoidosis; high vitD; PTH- tumors</td>
<td>stone, dysrhythmias, bradycardia, cardiac arrest, bone pain, osteoporosis,</td>
<td>PTH or VitD, nutritional deficiencies occur with sources of dairy products or green</td>
<td>sounds, severe cases show convulsions, tetany, long QT interval, cardiac arrest</td>
</tr>
<tr>
<td></td>
<td>constipation</td>
<td>leafy vegetables</td>
<td></td>
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<tr>
<td>Renal failure w/ low GFR, PO4 releasing anticancer drugs, long-term use of</td>
<td>Symptoms linked to low calcium from high PO4 in prolonged soft tissue calcification</td>
<td>Most common by gut malabsorption related to VitD deficiency, use of MgAI and Al-containing</td>
<td>Low O2 transport and disturbed energy metab; WBC, platlet dysfunction; deranged</td>
</tr>
<tr>
<td>laxative / enema w/ PO4, hypoparathyroidism</td>
<td>of lungs, kidneys and joints</td>
<td>antacids, long-term EIOH abuse, respiratory alkalosis, phosphaturia due to hyperPTH</td>
<td>nerve / muscle function; irritability, confusion, numbness, coma, convulsions, resp. failure</td>
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<tr>
<td>Renal failure w/ low GFR, PO4 releasing anticancer drugs, long-term use of</td>
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<tr>
<td>Usually renal failure; also high intake of Mg-containing antacids, adrenal</td>
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<td>insufficiency</td>
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### POSPHATE

<table>
<thead>
<tr>
<th>Excess causes</th>
<th>Excess effects</th>
<th>Deficit causes</th>
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### MAGNESIUM

| Excess causes                                                                 | Excess effects                                                                 | Deficit causes                                                                 | Deficit effects                                                                 |
|                                                                              |                                                                                  |                                                                                |                                                                                 |
|                                                                              |                                                                                  |                                                                                |                                                                                 |
ACID–BASE BALANCE:

H ions, which maintain membrane integrity and the speed of enzymatic reactions, must be concentrated within a narrow range if the body is to function normally.

The renal and respiratory systems, together with the body’s buffer systems are the main regulators of acid-base balance. Lungs & kidneys compensate for pH changes by increasing or decreasing ventilation, and by producing more acidic or more alkaline urine.

Acid-base imbalances, caused by changes in blood H conc., are acidosis and alkalosis. Abnormal increase or decrease in bicarbonate concentration causes metabolic alkalosis or acidosis; changes in alveolar ventilation and removal of CO2 produce respiratory acidosis or respiratory alkalosis.

Alterations in acid-base balance disrupts cellular functions.
ACID – BASE BALANCE:

Metabolic acidosis is caused by an increase in non-carbonic acids or loss of bicarbonate from the ECF.

Metabolic alkalosis occurs with an increase in bicarbonate, usually caused by loss of metabolic acid from conditions such as vomiting, or gastrointestinal suctioning, or from excessive bicarbonate intake, from hyperaldosteronism, and diuretic therapy, which increase plasma bicarbonate.

Respiratory acidosis occurs with a decrease in alveolar ventilation, which in turn causes hypercapnia (increase in CO2) and increases in carbonic acid concentration.

Respiratory alkalosis occurs with alveolar hyperventilation and excessive reduction of CO2, or hypercapnia with decreases in carbonic acid.

Alterations in acid-base balance disrupts cellular functions.

### Water movement
- water from plasma to ICF
- water from ICF to ECF alteration: edema

### Na, Cl, H2O balance
- water balance
- Na and Cl balance

### Na, Cl, H2O alterations
- isotonic alterations
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### K & others alterations
- K alterations
- hyperkalemia
- other electrolytes

### Acid – base balance
- H ion and pH
- buffer systems
- acid – base imbalances

 Alterations in acid-base balance disrupts cellular functions.
Acid – Base Balance Alteration

Water movement
- water from plasma to ICF
- water from ICF to ECF

alteration: edema

Na, Cl, H2O balance
water balance
Na and Cl balance

Na, Cl, H2O alterations
isotonic alterations
hypertonic alterations
hypotonic alterations

K & others alterations
K alterations
hyperkalemia
other electrolytes

Acid – base balance
H ion and pH
buffer systems
acid – base imbalances

Alterations in acid-base balance disrupts cellular functions.
Your first Case Study

SUMMARY:
You examine a 2-year-old cow that has been grazing on a poor quality pasture. The owner states that the cow seems to have a poor appetite, walks slowly, and stands apart from the rest of the herd. The cow has developed swelling beneath the skin of her brisket and ventral thorax. On examination, you find a listless cow standing on a pasture littered with various metal objects. Examination of her cardiovascular system reveals distended jugular veins and abnormal heart sounds characterized by irregular sloshing sounds throughout the cardiac cycle that drastically muffle the first and second heart sounds. Subcutaneous edema can be seen throughout the chest and abdomen, but most prominent in the dependent ventral areas of the thorax. Pushing on these swollen areas leaves a dent (pitting edema).

TENTATIVE DIAGNOSIS:

LAB TESTS:

FINAL DIAGNOSIS:

TREATMENT:

A 2-year-old cow with subcutaneous edema throughout the chest and abdomen.