BODY FLUID COMPARTMENTS

* TOTAL BODY WATER = 60 % OF TOTAL BODY WEIGHT

  SOLIDS = 40 %

* HIGH ADIPOSE TISSUE - % WATER IS (FAT HAS LOWEST H2O CONTENT) LOWER.
  60 % TOTAL BODY WATER = 42 L

70 kg MAN

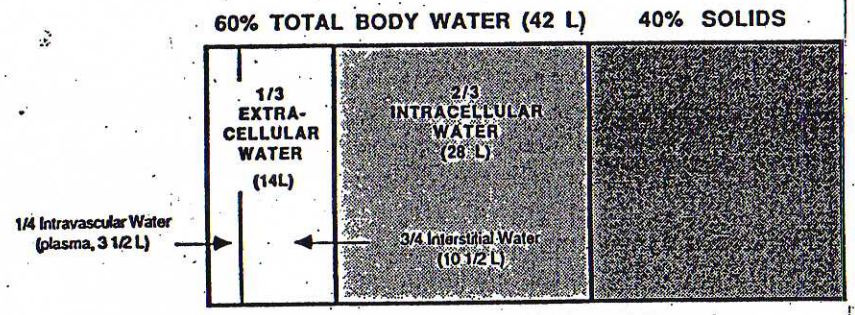
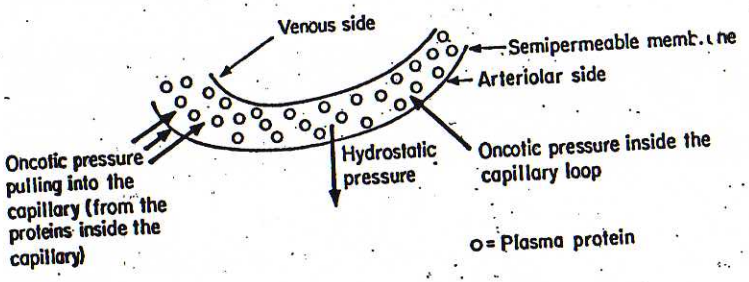


Figure 1.5. Body fluid compartments in an average 70-kg man.



* 2 % BODY WATER = TRANSCELLULAR WATER
  * CSF
  * INTRO-OCULAR FLUID
  * GIT

* WATER + SOLUTES IN CONTINUOUS DYNAMIC EQUILIBRIUM
  FACTORS : - STARLING FORCES

  ON AVERAGE

  * NET ONCOTIC PRESSURE - (PLASMA PROTEINS) DIRECTED INWARDS OF : 20,7 mmHg

  * NET HYDROSTATIC PRESSURE - (BLOOD PRESSURE) DIRECTED OUTWARDS OF : 21 mmHg

OUTWARD FORCE = 0,3 mmHG - MOVES FLUID (H2O) FROM PLASMA TO INTERSTITITIAL SPACE

SIZE OF INTERSTITIAL SPACE IS RELATIVELY CONSTANT

REASON :

FLUID DRAINED BACK BY
* VENOUS SIDE OF CAPILLARIES
* LYMPHATICS

FLUID BALANCE BETWEEN INTRA VASCULAR SPACE AND INTERSTITIUM

↓

DEPENDS : FLUID FILTRATION FROM CAPILLARIES AND LYMPHATIC RETURN

Tissue	Water content as %
Brain	82
Skeletal muscle	76
Liver	68
Kidney	83
Blood	83
Skin	72
Bone	22
Adipose tissue	10

TONICITY AND SOLUTE CONTENT OF BODY COMPARTMENTS

* MOST CELLULAR MEMBRANES ARE FREELY PERMEABLE TO WATER

* OSMOLARITY OF ONE COMPARTMENT CHANGES -----> WATER SHIFTS
  RAPIDLY TO EQUALIZE OSMOLARITY DIFFERENCES

* ALL BODY FLUID COMPARTMENTS HAVE THE SAME OSMOLARITY

* FLUID VOLUME OF A COMPARTMENT = REFLECTION OF THE AMOUNT OF OSMOTIC PARTICLES IN THAT COMPARTMENT
  (EXCEPTION - NEPHRON CERTAIN PARTS IMPERMEABLE TO WATER)

* TONICITY

  TONICITY / EFFECTIVE OSMOTIC PRESSURE IS OFTEN INTERCHANGED WITH OSMOLARITY. OSMOLARITY IS USUALLY ABOUT THE SOME AS TONICITY.

  REASON :

MOST SOLUTED IN BODY :

GLUCOSE
SODIUM
POTASSIUM
CHLORIDE

→ PRODUCE OSMOTIC PRESSURE DIFFERENCES

DUE TO THEIR INABILITY TO FREELY MOVE ACROSS MEMBRANES

EXCEPT UREA : - MOVES FREELY

* UREA - NO EFFECT ON OSMOTIC PRESSURE. TONICITY OF UREA IS ZERO

* NET OSMOTIC EFFECT OF INTRA AND EXTRACELLULAR SOLUTES IS OSMOLARITY OF 285 MOSM/L

* OSMOTIC PRESSURE MEASURED BY DEPRESSION OF FREEZING POINT
  BY SOLUTES : - SOLUTION
  = MOSML/KG. A 180 KNOWN AS OSMOLALITY

* LOW SOLUTE CONCENTRACTIONS IN BODY FLUIDS ----- DIFFERENCE BETWEEN OSMOLARITY AND OSMOLALITY IS NEGLIGIBLE. TERMS USED INTERCHANGEABLY

* MOST IMPORTANT EXTRACELLULAR OSMOTIC PARTICLES ARE THE ELECTROLYTES, NA+ , ET AND BICARBONATE (HCO3)

* MOST IMPORTANT INTRACELLULAR OSMOTIC PARTICLES ARE : K+ AND PHOSPHATE

* PARTITION OF IONS BETWEEN CELLS AND THE EXTRACELLULAR SPACE DEPENDS ON THEIR CONTINUOUS ACTIVE AND PASSIVE TRANSPORT ACROSS CELL MEMBRANES EG.

NA+ - K+ - ATP ASE PUMP

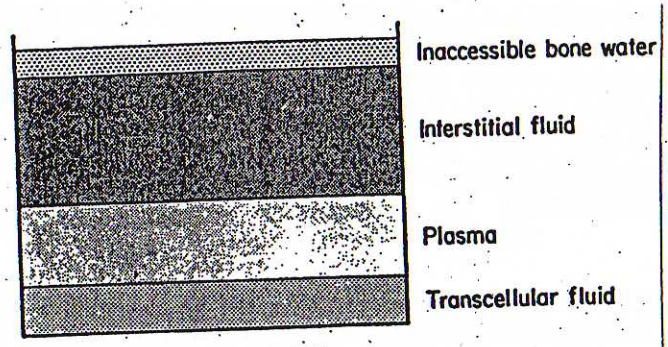
* DISTRIBUTION OF NONIONIC OSMOTIC PARTICLES EG. GLUCOSE AND AMINO ACIDS DEPENDS ON

BOTH : MEMBRANE TRANSPORT

METABOLISM

* VOLUME OF CELLS - THE WHOLE INTRACELLULAR SPACE REFLECTS THE NUMBER OF OSMOTIC PARTICLES MAINTAINED WHITIN THE CELLS BY MULTIPLE METABOLIC AND TRANSPORT PROCESSES

* BRAIN : REGULATE VOLUME BY ALTERATION OF INTRACELLULAR OSMOTIC PARTICLES



Subdivisions of ECF

RENAL REGULATION OF BODY FLUID COMPARTMENTS

EXTRACELLULAR VOLUME (SODIUM) REGULATION.

* KIDNEY REGULATES ECV THROUGH HANDLING OF NA+ (MAJOR CATION OF EC -SPACE) EG:

(A)

NA+ ADDED → EXTRA CELLULAR VOLUME

↑TONICITY (TRANSIENTLY)

BODY MAINTAINS CONSTANT TONICITY BY REGULATING WATER CONTENT

WATER ACCUMULATED BY : (1) THIRST MECHANISM
(2) RENAL CONSERVATION (ADH)

TONICITY RETURNS TO NORMAL !

(B)

NA+ LOST FROM THE BODY :

INCREASED WATER EXCRETION BY KIDNEY TO NORMALIZE TONICITY AND EXTRA CELLULAR VOLUME WILL FALL.

* CHANGES IN EXTRA CELLULAR VOLUME ARE REFLECTED IN PARALLEL CHANGES IN INTRAVASCULAR VOLUME AND EVENTUALLY IN CARDIAC OUTPUT AND TISSUE PERFUSSION OF ORGANS.

* SEVERE FALL IN EXTRACELLULAR VOLUME ----> DECREASE IN BLOOD PRESSURE AND ORGAN PERFUSSION ----> SHOCK.

* SEVERE RISE IN EXTRA CELLULAR VOLUME ----> HYPERTENSION AND CIRCULATORY CONGESTION OCCURS.

VOLUME RECEPTORS

* RECEPTORS CARDIO PULMONARY CIRCULATION AND CAROTID SINUS

SENSED LOSS OF INTRAVASCULAR VOLUME

RESULT : SYMPATHETIC NEURAL SIGNALS OF THE KIDNEY

* BARO RECEPTORS IN AFFERENT GLOMERULAR ARTERIOLE ALSO SENSE REDUCTION IN PERFUSSION PRESSURE ---- RELEASE RENIN FROM JGA. INCREASED SYMPATHETIC NEURAL TONE TO THE KIDNEY AND DECREASED DELIVERY OF NACL TO THE MACULA DENSA OF THE DISTAL CONVOLUTED TUBULE AS A RESULT OF A REDUCED GFR ALSO STIMULATE RENIN RELEASE. (AI - AII - STIMULATE RELEASE OF ADRENAL CORTEX - ALDOSTERONE)

* ATRIAL NATRIURETIC FACTOR (ANF) - RELEASED FROM CARDIAC ATRIA IN RESPONSE TO VOLUME EXPANSION. ANF INCREASES NA+ EXCRETION BY RAISING GFR AND DECREASING TUBULAR REABSORPTION OF NA+ . ALSO OPPOSES RENIN AND ALDOSTERONE

NORMAL SODIUM BALANCE

* NORMAL DIETARY NAT = 150 MMOL/24H IS EXCRETED IN URINE

* CHANGES SODIUM INTAKE ---> MINIMUM ALTERATIONS IN CIRCULATING VOLUME ARE SENSED - URINE NA+ RISES OR FALLS TO MAINTAIN EXTRA CELLULAR VOLUME. HOMEOSTATIC RANGE - CAN MANAGE DIETARY NA+ FROM < 1 TO OVER 1000 MMOL/24H BY APPROPRIATE CHANGES IN URINE NA+ OUTPUT

RENAL NA+ HANDLING

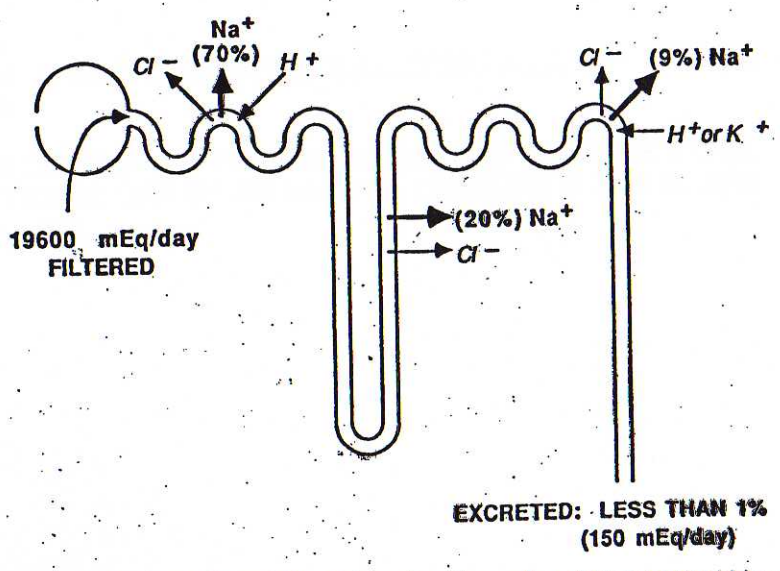


Figure 1.8. Overview of filtration and reabsorption of Na^+ by the kidney.

MACHANISMS CONTROLLING URINE NA+ EXCRETION :

NA+ EXCRETION :

* FILTRATION OF 140 L / 24H
* CONTAINS 25,500 MMOL NA+
* 99 % REABSORBED
* ± 150 MMOL/24H EXCRETED

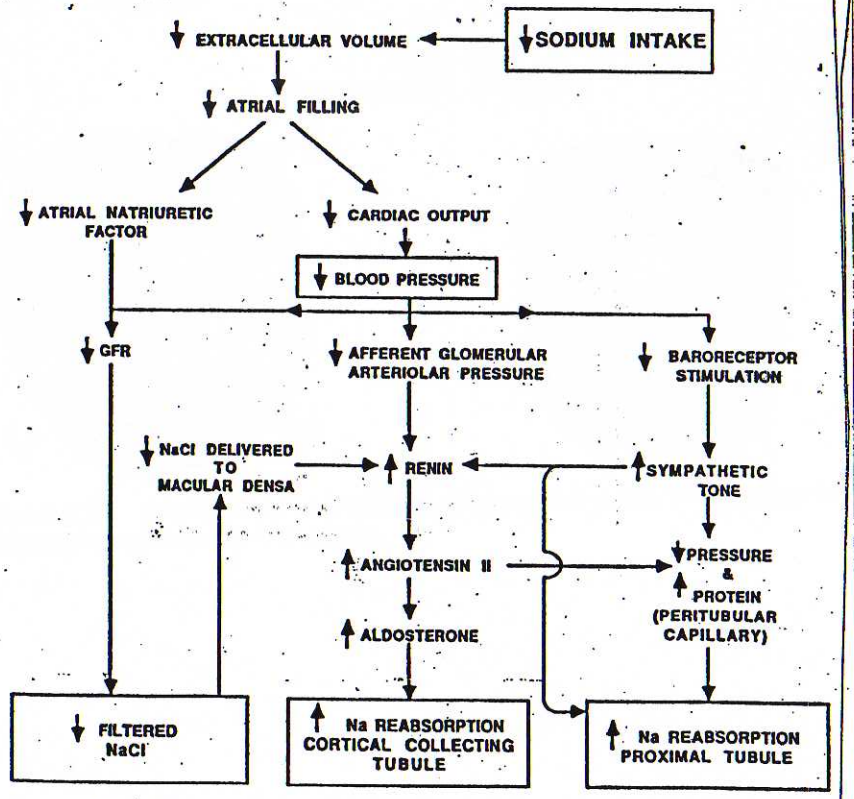


Figure 1.9. The mechanisms involved in the reduction of urine Na^+ excretion in response to reduced Na^+ intake.

BODY TONICITY (WATER) REGULATION.

WATER ADDED :

OSMOLARITY FALLS IN EXTRA CELLULAR SPACE AND AS CELLS TAKE UP WATER, IN THE INTRA CELLULAR SPACE

WATER LOST

OSMOLARITY INCREASES IN EXTRACELLULAR SPACE AND AS CELLS GIVE UP WATER IN THE INTRACELLULAR SPACE

KIDNEY

COUNTERACTS THESE CHANGES THROUGH GREATER OR LESSER EXCRETION OF INGESTED WATER, AND THE BODY OSMOLARITY NORMALLY VARIES LITTLE DESPITE WIDE RANGES OF WATER INTAKE.

SEVERE FALL OF EXTRACELLULAR OSMOLARITY : BELOW 280 - 290 MOSM/L
---- SIGNIFICANT SWELLING OF BODY CELLS

SEVERE RISE IN EXTRACELLULAR OSMOLARITY --- CELLS SHRINK

* IN CENTRAL NERVOUS SYSTEM MARKED CHANGES IN CELL VOLUME CAN CAUSE MENTAL CHANGES, SEIZURES AND DEATH.

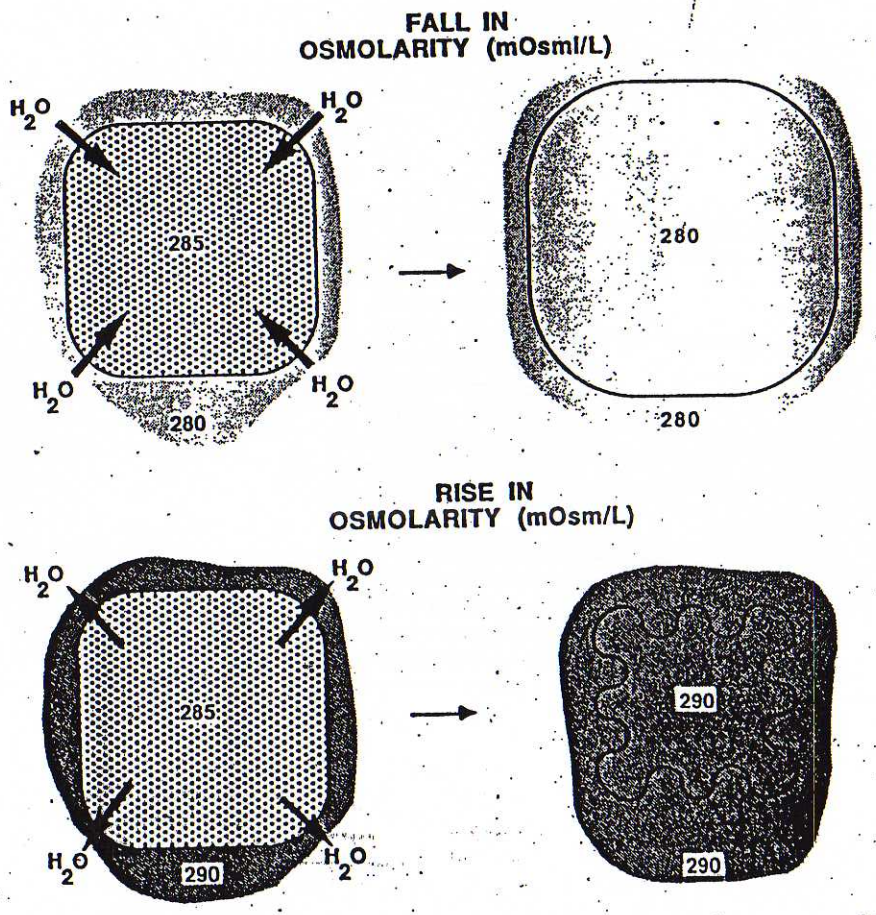


Figure 1.10. Depiction of cell volume changes that occur in response to changes in extracellular osmolarity.

Principal Causes of Respiratory Alkalosis

I. Hypoxemia
   A. Congestive heart failure
   B. Pneumonia
   C. Pulmonary emboli
   D. High altitude
II. Pulmonary disease
III. Stimulation of respiratory center
   A. Salicylate intoxication
   B. Sepsis
   C. Psychogenic hyperventilation
   D. Brain lesions
IV. "Excessive" mechanical ventilation

Principle Causes of Respiratory Acidosis

I. Inhibition of respiratory center
   A. Drug overdose: opiates, etc.
   B. Oxygen therapy in chronic hypercapnia
II. Musculoskeletal disorders
   A. Muscle weakness, e.g., myasthenia gravis
   B. Extreme obesity
   C. Chest cage abnormalities, e.g., kyphoscoliosis
III. Airway obstruction
   A. Aspiration of foreign body
   B. Asthma
   C. Chronic obstructive lung disease
IV. Abnormal pulmonary capillary gas exchange
   A. Pulmonary edema
   B. Severe lung disease
V. Inadequate mechanical ventilation

Principal Causes of Metabolic Alkalosis

I. Loss of acid (urine Cl^- <15 mEq/L)
   A. Extrarenal
      1. Vomiting
      2. Gastric drainage
   B. Renal
      1. Diuretics[a]
         a. Thiazides
         b. Furosemide
         c. Ethacrynic acid
      2. Posthypercapneic alkalosis
II. Gain of Alkali (urine Cl^- >20mEq/L)
   A. Rapid administration of $NaHCO_3$
   B. Primary mineralocorticoid excess
      1. Endogenous
         a. Primary aldosteronism
         b. Cushing's disease
      2. Exogenous
         a. High dose corticosteroid administration
         b. Disorders simulating mineralocorticoid excess[b]
            i. Licorice
            ii. Chewing tobacco
      3. Primary aldosteronism

[a]If the diuretic agent has been given recently, urine Cl^- may be > 15 mEq/L, as a result of the direct chloriuretic action.
[b]Licorice acts with a mechanism similar to that of corticosteroids because of the properties of its basic constituent, glycyrrhizic acid. Chewing tobacco also contains glycyrrhizic acid.

Principal Causes of Metabolic Acidosis

I. Increased Anion Gap
   A. Ketoacidosis
      1. Diabetes mellitus
      2. Starvation
   B. Lactic acidosis
   C. Ingestions
      1. Salicylates
      2. Methyl alcohol
      3. Ethylene glycol
   D. Renal failure
II. Normal Anion Gap
   A. Loss of alkaline intestinal secretions (hypokalemic)
      1. Diarrhea
      2. Fistulae
      3. Biliary or pancreatic drainage tubes
   B. Acetazolamide (hypokalemic)
   C. Renal tubular acidosis (hypokalemic)
      1. Proximal
      2. Distal
   D. Aldosterone deficiency (hyperkalemic)
      1. Primary adrenal insufficiency
      2. Hyporeninemic hypoaldosteronism
      3. Inhibitors of aldosterone effect (K^+ sparing diuretics)
         a. Spironolactone
         b. Triamterene
         c. Amiloride

Table 3.1.
Principal Causes of Hypertonic States

I. Decreased water intake (increased serum Na^+ concentration)
   A. Inability to respond to thirst
      1. Inability to communicate
         a. Infants
         b. Altered sensorium
      2. Inability to swallow
      3. Lack of water source
   B. Defective thirst center
II. Water loss (increased serum Na^+ concentration)
   A. Extrarenal
      1. Diarrhea
      2. Vomiting
      3. Insensible loss
   B. Renal
      1. Central diabetes insipidus
         a. Hereditary
         b. Trauma
         c. Neoplasms
      2. Nephrogenic diabetes insipidus
         a. Hereditary
         b. Hypokalemia, hypercalcemia
         c. Pathological processes in the medulla
III. Solute gain
   A. Hyperglycemia (diabetes mellitus; reduced serum Na^+ concentration)
   B. Mannitol (reduced serum Na^+ concentration)
   C. Excessive intake of Na^+ (increased serum Na^+ concentration)
IV. Pseudohypertonicity: Increase in osmolality without change in tonicity
   A. Ingested substances
      1. Ethanol
      2. Methanol
      3. Ethylene glycol (antifreeze)
   B. High BUN

Table 3.2.
Principal Causes of Hypotonic States

I. Impaired water excretion (true hyponatremia)
   A. Volume depletion
      1. Whole blood loss-hemorrhage
      2. Plasma loss
         a. Renal (diuretics, aldosterone deficiency)
         b. Extrarenal (gastrointestinal loss, skin loss and third spacing)
   B. Euvolemic or slightly volume expanded states
      1. Tumors[a]
      2. Intracranial lesions[a]
      3. Lung diseases[a]
      4. Drugs[a]
      5. Thyroid and glucocorticoid deficiency
   C. Edematous states
      1. Renal failure
      2. Congestive heart failure
      3. Nephrotic syndrome
      4. Cirrhosis
II. Excess water intake, e.g. psychogenic polydipsia (true hyponatremia)
III. Pseudohypotonicity (pseudohyponatremia)
   A. Accumulation of non-Na^+ solutes (hypertonic hyponatremia)
      1. Glucose
      2. Mannitol
   B. Increased nonaqueous phase of plasma (isotonic hyponatremia)
      1. Hyperlipidemia
      2. Hyperproteinemia

[a]Syndrome of inappropriate ADH secretion.

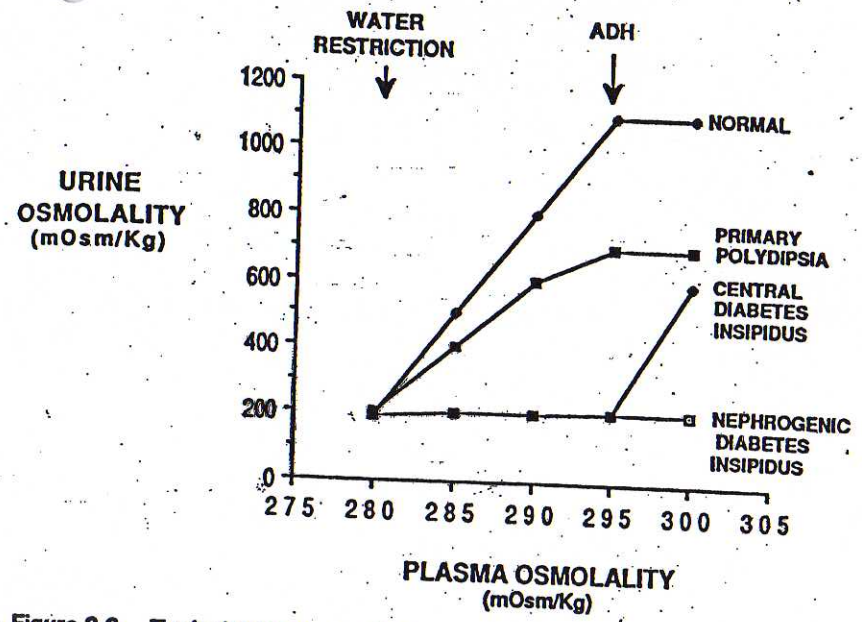


Figure 3.3. Typical responses of urine concentration during the water deprivation test. (Modified from Rose BD. Clinical physiology of acid-base and electrolyte disorders. 2nd ed. New York: McGraw-Hill Book Company, 1984:532.)

Major Causes of Edema According to Primary Mechanism

Increased capillary hydraulic pressure

A. Increased plasma volume due to renal Na+ retention
  1. Heart failure, including congestive
  2. Primary renal sodium retention
    a. Renal disease, including the nephrotic syndrome
    b. Drugs: minoxidil, diazoxide, hydralazine
      anti-inflammatory drugs, glucocorticosteroids, estrogens
    c. Refeeding edema
  3. Early cirrhosis
  4. Pregnancy and premenstrual edema
  5. Idiopathic edema (when diuretics induced)
B. Venous obstruction
  1. Cirrhosis or hepatic venous obstruction
  2. Acute pulmonary edema
  3. Local venous obstruction
C. Decreased arteriolar resistance
  1. Calcium channel blockers
  2. Idiopathic edema (?)

Hypoalbuminemia

A. Proteinuria
  1. Nephrotic syndrome
  2. Protein-losing enteropathy
B. Reduced albumin synthesis
  1. Liver disease
  2. Malnutrition

Increased capillary permeability

A. Idiopathic edema (?)
B. Burns
C. Trauma
D. Inflammation or sepsis
E. Allergic reactions, including certain forms of angioedema
F. Adult respiratory distress syndrome
G. Diabetes mellitus
H. Interleukin-2 therapy
I. Malignant ascites

Lymphatic obstruction or increased interstitial oncotic pressure

A. Postmastectomy
B. Nodal enlargement due to malignancy
C. Hypothyroidism
D. Malignant ascites

Uncertain mechanism

A. Docetaxel
B. Pramipexole