[Hyponatremia]

MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

March 19, 1959

Case I. [redacted] Pathological Water Drinker

A 65 year old white woman was admitted to the hospital in coma following a convulsion. There was history of extreme polydipsia (1 glass water every 5 minutes) and equally great polyuria dating back to a "stroke" one year previously. Examination disclosed: BP 140/90, T 102°, P 100, semicoma, cyanosis, slight papilledema, tissue wastage and diminished skin turgor. Incontinence with passage of large volume of dilute urine (sp. gr. 1.005).

A diagnosis of diabetes insipidus was made. The patient was treated with rapid intravenous infusions of 5% dextrose in distilled water and the injection of 10 units pitressin tannate in oil. Urine volume decreased and the specific gravity rose to 1.025.

Shortly thereafter blood chemistries, drawn before treatment, were reported as: Na - 117 mEq/L, K - 4.3 mEq/L, Cl - 82 mEq/L, CO_2 - 21 mEq/L and BUN - 12 mg.%. It was apparent that the patient had physiological diabetes insipidus secondary to pathologically excessive water intake. Following the administration of 400 cc of 5% NaCl the serum Na^+ to 142 mEq/L and Cl to 103 mEq/L. The patient's mental status improved markedly. Thereafter, fluid intake was restricted to 2000 cc daily.

Case II. [redacted] Acute Renal Failure with Hyponatremia

This 51 year old negro woman was admitted to the hospital for gastrointestinal bleeding. In preparation for surgery 2 pints of whole blood were transfused and sulfasuxidine was given for bowel sterilization. Three days later her temperature was 103° C and she became oliguric. Seven days later she was transferred to the medicine service.

Past history revealed that the patient had been treated for myxedema for 4 years. She also had HCVD with congestive heart failure, treated with digitalis for 8 months.

Examination revealed: BP 160/60-0, P-60, R-26, T 97°. Acutely ill; stuporous and moderately dyspneic. Moist basilar rales, cardiomegaly, hepatomegaly and 1+ pitting sacral and pretibial edema. Venous pressure was 23 cm.

Laboratory data: Na - 113 mEq/L, K - 6.3 mEq/L, Cl - 72.8 mEq/L, CO_2 - 8.6 mEq/L, BUN - 136 mg.%.

Course in hospital: Urine output on the day of transfer was approximately 500 cc. The patient was given 350 cc 1 M sodium lactate slowly over a 24 hour period, despite evidence of incipient pulmonary edema. The patient's mental status improved dramatically. The following day blood chemistries were Na - 127 mEq/L, K - 4.4 mEq/L, Cl - 94.8 mEq/L, CO_2 - 26 mEq/L, BUN - 122 mg.%. Urine output increased to 1500 cc and the next day it rose to 3700 cc. The patient improved rapidly and was discharged 3 weeks later with normal blood chemistries.

Physical examination: BP 104/70, P 100, R-A, lethargy, moderate bilateral pleural effusions, cardiomegaly, hepatomegaly, and massive anasarca.

Laboratory data: Venous pressure 25 cm H_2O, circulation time 15 sec. Blood chemistries: Na - 127 mEq/L, K - 3.5 mEq/L, Cl - 84.3 mEq/L, CO_2 - 30.7 mEq/L, BUN 17 mg.%, and serum albumen 3.0 gm.%.

Course: Restriction of fluid intake to 700 cc daily resulted in prompt correction of the hyponatremia (to 140 mEq/L). Treatment with digitoxin failed to effect diuresis. The patient was then given 100 mg. chlorothiazide daily. BP rose from 110/70 to 160/100 within 12 hours and there was a 35 lb. weight loss in the following 10 days.

Case IV. [redacted] Water Retention in Cerebral Disease

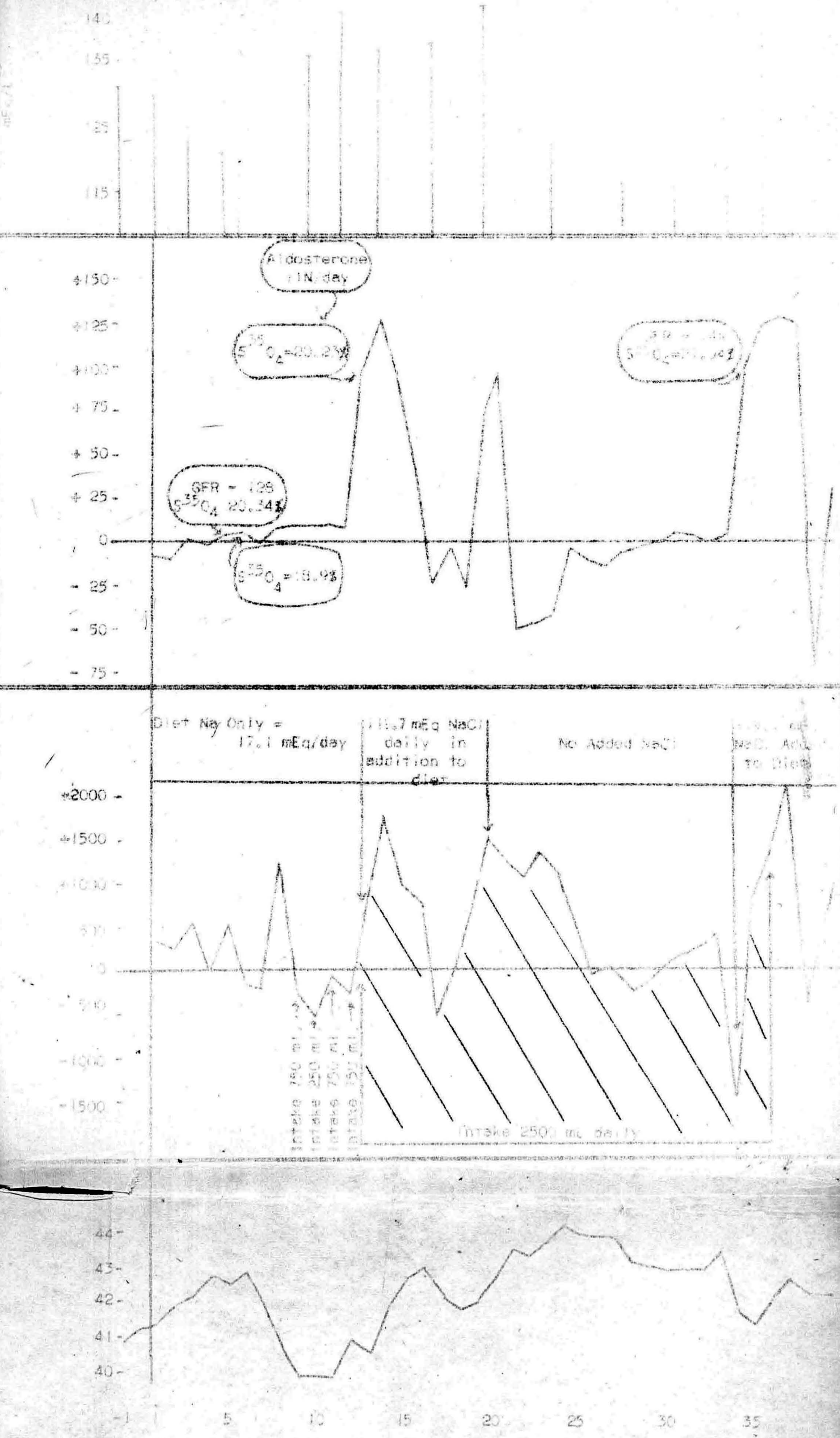
This 40 year old woman sustained a basilar skull fracture in an automobile accident and was unconscious for an indeterminate period of time.

Physical examination revealed an intoxicated, lethargic woman with bleeding from the right ear.

Course in hospital: Patient's sensorium cleared transiently, but she then became more lethargic and began to hallucinate. At that time examination showed BP 110/70 and P 92. There was no evidence of ECF volume deficit and no localizing neurological signs. Serum Na+ was 117 mEq/L and Cl - 83.7 mEq/L. Mental symptoms cleared spontaneously, but the patient remained hyponatremic. Administration of 3000-4000 cc of isotonic saline failed to elevate serum Na. Large amounts of sodium were excreted into the urine each day. 200-300 cc of 5% NaCl produced only slight transient elevations in serum Na, with the administered sodium being rapidly excreted into the urine.

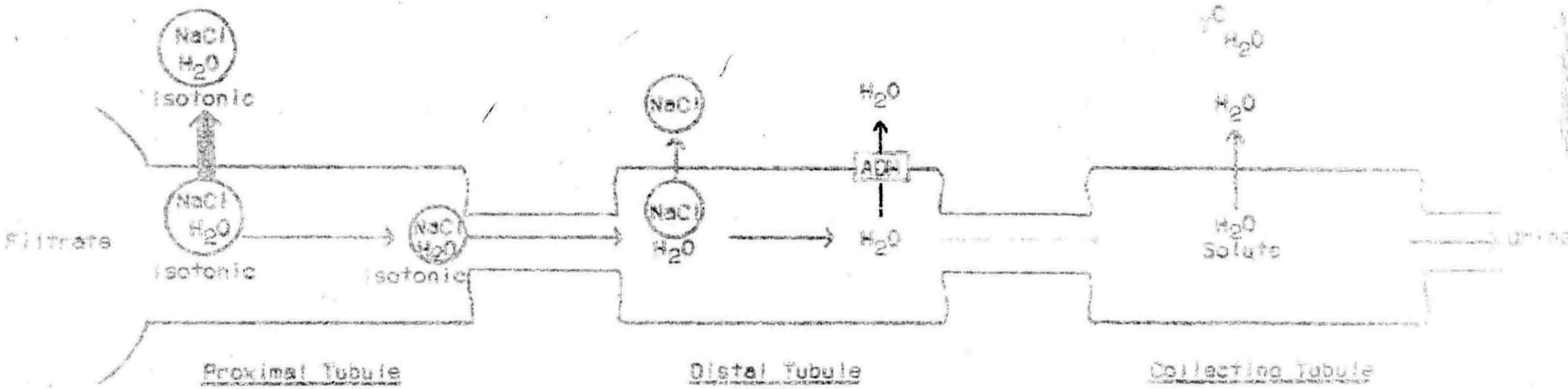
The patient was considered to have a cerebral salt-wasting syndrome and was transferred to the metabolic ward for further studies.

The results of these studies are charted on the next page.



Aldosterone
IN/day
GFR = 128
Diet Na Only = 17.1 mEq/day
daily in addition to diet
No Added NaCl
Intake 750 ml
Intake 250 ml
Intake 750 ml
Intake 2500 ml daily

REABSORPTION AND EXCRETION OF WATER BY THE KIDNEY



Proximal Tubule

1. Complete H_2O permeability.
2. Sodium and H_2O reabsorbed isotonically.
3. Obligatory reabsorption of 85% of glomerular filtrate.

Distal Tubule

1. Sodium reabsorbed independently of H_2O.

3. **Completely permeable to H_2O in presence of ADH -- small volume of isotonic fluid leaves distal tubule.**

Collecting Tubule

1. H_2O removed in excess of solute.
2. Independent of ADH.
3. Concentration of final urine is dependent on the volume and concentration of fluid entering the collecting duct.

b. ADH -- small volume of isotonic fluid - final urine is hypertonic.

Terms used to describe renal metabolism of H_2O:

1. Osmolar clearance = volume of H_2O required to excrete all urinary solutes as solution isotonic to plasma. $Cosm = \frac{Uosm\ V}{Posm}$

   When urine is isotonic, Uosm = Posm and Cosm = V. Therefore, water is neither conserved nor dissipated.

2. Free-water clearance = the amount of solute-free water in urine in excess of that osmotically obligated by excreted solute. $C_{H_2O} = V - Cosm$

   C_{H_2O}, which is liberated by the active reabsorption of solute (sodium salts) in the ascending loop of Henle and the distal tubule, represents the rate of water dissipation by the kidney.

3. $T^{C}_{H_2O}$ = the volume of solute-free water abstracted from the isotonic fluid traversing the collecting tubule in forming hypertonic urine.

   $T^{C}_{H_2O} = Cosm - V$

   $T^{C}_{H_2O}$ represents the renal conservation of water.

Factors necessary for rapid excretion of water in excess of solute (C_{H_2O}).

1. Delivery of sufficient quantities of sodium-containing fluid to the distal tubule.
2. Adequate capacity of the distal tubule to actively reabsorb sodium.
   a. Intact distal tubule.
   b. Adrenal steroids - aldosterone, DOC.
3. Low permeability of distal tubule to water.
   a. Absence of antidiuretic hormone.
   b. ? Presence of cortisone or hydrocortisone.
   c. ? Presence of thyroid hormone.

Pathogenesis of hyponatremia (hypo-osmolarity):

Hyponatremia always results from an imbalance between the rate of water intake and the rate of water loss from the body.

A. Abnormal water intake:

1. Iatrogenic water loads

2. Excessive thirst
   a. anxiety - pathological water drinkers
   b. hypothalamic polydipsia
   c. salt depletion - vomiting, diarrhea, post-diuresis, post-paracentesis, adrenal-insufficiency, diabetic acidosis.
   d. shock - trauma, blood loss

3. Normal thirst in present of hypo-osmolarity of plasma. Humans drink more from habit rather than need.

B. Impaired renal excretion of water.

1. Decreased delivery of salt-containing fluid to distal tubule:
   a. decreased glomerular filtration rate - heart failure, renal vascular disease, salt depletion.
   b. increased reabsorption of sodium in proximal tubule - heart failure, cirrhosis, nephrosis.

2. Diminished capacity of distal tubule to reabsorb sodium.
   a. damaged distal tubule - salt-losing nephritis, acute tubular necrosis.
   b. absence of aldosterone - Addison's disease, primary hypoaldosteronism.

3. Increased permeability of distal tubule.
   a. Inappropriate secretion of antidiuretic hormone:
      1) decreased blood volume (?arterial) - salt depletion, heart failure, cirrhosis, adrenal-insufficiency, hypoalbuminuria, blood loss.
      2) pain - post-operative, carcinoma
      3) loss or inactivation of cellular cations - "pulmonary salt-wasters", "cerebral salt-wasters," chronic debilitating diseases
      4) altered sensitivity of posterior pituitary to osmotic or volume stimuli
   b. absence of cortisone - Addison s disease, panhypopituitarism, primary myxedema.
   c. absence of thyroid hormone - primary myxedema, panhypopituitarism.
   d. damaged distal tubule - renal poisons, acute tubular necrosis.

TYPES AND TREATMENT OF HYPONATREMIA

Condition	Pathogenetic Factors: Water Intake	Distal tubules: Na^+ Load	Distal tubules: Reab. Capacity	Distal tubules: Permeability: ADH	Distal tubules: Permeability: Other	Symptoms: H_2O Intox.	Symptoms: ↓ ECF	Response to Hypertonic saline: Clinical	Response to Hypertonic saline: Serum $[Na^+]$	Treatment of choice: H_2O Restriction	Treatment of choice: NaCl: Isotonic	Treatment of choice: NaCl: Hypertonic	Treatment of choice: Diuretics
I. Diminished body sodium													
A. Salt wasting states													
1. Pulmonary	N, ↑	N, ↑	N, ↓	↑		-	±	Thirst	Trans. ↑	+		±	
2. Cerebral	N, ↑	N, ↑	N, ↓	↑		-	±	Thirst	Trans. ↑	+		±	
3. Renal	N, ↑	N, ↑	↓	↑		-	±	Partial	Correct.		+	±	
4. Post-obstructive	↑	↑, ↓	↓, N, ↑	↑		±	+	"	"		+		
5. Addison's	↑	↑, ↓	↓	↑	↓ steroid	±	+	"	"		+	±	
6. Primary hypo-aldosteronism	N	↑	↓	?		±	+	"	"		+	±	
B. Salt depletion													
1. Vomiting, diarrhea	↑	↓	↑	↑		+	+	"	"		+		
2. G. I. drainage	↑	↓	↑	↑		+	+	"	"		+		
3. Sweating	↑	↓	↑	↑		+	+	"	"		+		
4. Post-paracentesis	↑	↓	↑	↑		+	+	Mixed	"	+		±	
5. Post-diuresis	↑	↓	↑	↑		+	+	"	"	+		±	
6. Ion-exchange resins	↑	↓	↑	↑		+	+	"	"	+		±	
7. Exudates & Transudates	↑	↓	↑	↑		+	+	Good	"		+		
II. Normal body sodium													
A. Renal failure													
1. Chronic	N, ↑	N, ↓	↓	?		±	-	Good	Correct.	+		±	
2. Acute	N, ↑	↑, ↓	↓	?	damaged	+	-	"	"	±		±	
B. Post-operative	↑	N	N	↑		+	-	"	"	+		±	
C. Myxedema	N	N, ↓	N	N, ↑	↓ thyroid	-	-	Thirst	Trans. ↑	+			
D. Panhypopituitarism	N	N	N ?	N, ↑	↓ steroid	-	-	"	"	+			
E. Pathological water drinker	↑	↑	↓	↓		+	-	Good	Correct.	+		±	
III. Increased body sodium													
A. Heart failure	N	↓	↑	↑		±	-	↑ Edema	Trans. ↑	+		? ±	+
B. Cirrhosis	N	↓	↑	↑		±	-	"	"	+		? ±	+
C. Hypoalbuminemia													
1. Nephrosis	N	↓	N, ↑	N, ↑		-	±	"	"	+			+
2. Nutritional	N	↓	N, ↑	N, ↑		-	±	"	"	+			+

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