MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

November 17, 1966

HYPOKALEMIA

I. The Physiology of Body Potassium

A. Normal values

1. Total body potassium

a. Adult male = 36 - 56 mEq/Kg body weight
b. Adult female = 32 - 43 mEq/Kg body weight

2. Distribution

a. Extracellular - 3.5 to 5.3 mEq per L or about 60 mEq
b. Intracellular - 120 mEq per L or between 3,000 and 4,000 mEq

3. Content in intestinal fluids

a. Gastric: 5 to 25 mEq/L, but may be up to 40 mEq/L
b. Intestinal: 2 to 10 mEq/L of small intestinal fluid but may be as high as 80 mEq per liter of diarrheal stool

B. Renal mechanisms: average excretion = 50 - 100 mEq/day

1. Glomerular filtration - about 700 mEq/day
2. Tubular reabsorption - probably complete in proximal tubule
3. Tubular secretion - active process in distal tubule in exchange for sodium

1. Pitts, R. F. Physiology of the Kidney and Body Fluids. Year Book Publishers, 1963.

2. Leaf, A. and R. F. Santos. Physiologic mechanisms in potassium deficiency. New Eng. J. Med. 264:335, Feb. 16, 1961.

3. Berliner, R. W., T. J. Kennedy, Jr. and J. Orloff. Relationship between acidification of the urine and potassium metabolism. Am. J. Med. 11:274, 1951.

4. Davidson, D. G., N. G. Levinsky and R. W. Berliner. Maintenance of potassium excretion despite reduction of glomerular filtration during sodium diuresis. J. Clin. Invest. 37:548, 1958.

C. Response to potassium restriction

1. Hypokalemia may result from decreased intake

a. Renal conservation not complete so that 5 to 25 mEq/day may be lost

b. Losses in stool may also be considerable

c. Renal losses dependent upon presence of sodium in diet and will not occur in absence of sodium

2. Metabolic alkalosis

a. Mechanisms

1) As extracellular K+ is lost, K+ leaves cells and H+ (and Na+) enters cells, leaving the extracellular fluid alkaline.

2) As renal tubular intracellular K+ decreases, there is a reciprocal increase in H+ secretion, resulting in elevation of HCO_3-reabsorptive capacity and increased net excretion of acid, primarily as NH^4.

b. Correction of alkalosis

1) NaCl will usually correct the alkalosis unless excessive adrenal salt-retaining hormone is present or the potassium depletion is severe.

2) K+, when administered with a non-reabsorptive anion such as gluconate, may worsen the alkalosis by requiring addition H+ secretion (and HCO_3 formation) to buffer the non-reabsorbable anion.

5. Tarail, R. and J. R. Elkinton. Potassium deficiency and the role of the kidney in its production. J. Clin. Invest. 28:99, 1949.

6. Fourman, P. The ability of the normal kidney to conserve potassium. Lancet 1:1042, 1952.

7. Squires, R. D. and E. J. Huth. Experimental potassium depletion in normal human subjects. J. Clin. Invest. 38:1134 and 1149, 1959.

8. Seldin, D. W., L. G. Welt and J. H. Cort. The role of sodium salts and adrenal steroids in the production of hypokalemic alkalosis. Yale J. Biol. & Med. 29: 229, 1956.

9. Kassirer, J. P. and W. B. Schwartz. Correction of metabolic alkalosis in man without repair of potassium deficiency. Am. J. Med. 40:19, 1966.

10. Grollman, A. P. and J. L. Gamble, Jr. Metabolic alkalosis, a specific effect of adrenocortical hormones. Am. J. Physiol. 196:135, 1959.

D. Interpretation of the Serum Potassium Concentration

1. Relationship to intracellular stores

   a. Serum K+ usually falls about 1 mEq/L with loss of 200 mEq

   b. In general, good correlation between serum level and cellular stores.

2. Factors affecting serum K+

   a. pH: reciprocal change with inverse change of 0.6 mEq/L in serum K+ for each 0.1 unit change in extracellular pH.

   b. ECF volume changes have little if any effect per se.

   c. Rapid tissue breakdown may induce hyperkalemia, particularly if renal function is impaired.

   d. Glucose and insulin will lower serum K+

   e. Muscular exercise will release K+

   f. Hemolysis, prolonged standing or clotting of blood will release K+ from RBC's

* Therefore, for proper interpretation of a serum K+, the blood should be obtained without excessive pumping or other exercise, analyzed rapidly without allowing hemolysis to occur and the level considered in relation to the pH of the extracellular fluid. For many situations, the serum bicarbonate concentration will indicate the direction of pH change.

11. Scribner, B. H. and J. M. Burnell. Interpretation of the serum potassium concentration. Metabolism 5:468, 1956.

12. Burnell, J. M. et al. The effect in humans of extracellular pH change on the relationships between serum potassium concentration and intracellular potassium. J. Clin. Invest. 35:935, 1956.

13. Skinner, S. C. A cause of erroneous potassium levels. Lancet 1:478, 1961.

II. The Effects of Hypokalemia

A. Renal

1. Structural changes.

a. Swelling and degeneration of tubular epithelial cells with vacuolar or hydropic lesion

b. Secondary changes may be irreversible and predispose to pyelonephritis

2. Functional changes

a. Impaired concentrating mechanism with polyuria

1) Maximum urinary specific gravity below 1.015

2) Vasopressin resistant

b. Impaired bicarbonate excretion with inappropriately acid urine in presence of extracellular alkalosis

c. Sodium retention with slight expansion of ECF volume; sodium conservation on a low salt diet may be impaired

B. Polydipsia

1. Probably more than just secondary to polyuria related to impaired concentrating ability

2. Circumstantial evidence for a primary effect of K+ depletion; mineralocorticoid excess may also be a factor

14. Surawicz, B. et al. Clinical manifestations of hypopotassemia. Am. J. Med. Sci. 233:603, 1957.

15. Hollander, W., Jr. Nephropathy of potassium depletion in Diseases of the Kidney, ed by M. B. Strauss and L. G. Welt, Little, Brown & Co., 1963.

16. Relman, A. S. and W. B. Schwartz. The nephropathy of potassium depletion: a clinical and pathological entity. New England J. Med. 255:195, 1956.

17. Muehrcke, R. C. Prolonged potassium deficiency and chronic pyelonephritis in man and animals, in Biology of Pyelonephritis, ed. by E. L. Quinn and E. H. Kass, Little, Brown & Co., 1960.

18. Fourman, P., R. A. McCance and R. A. Parker. Chronic renal disease in rats following a temporary deficiency of potassium. Brit. J. Exper. Path. 37:40, 1956.

19. Welt, L. G., W. Hollander, Jr. and W. B. Blythe. The consequences of potassium depletion. J. Chronic Dis. 11:213, 1960.

C. Cardiac

1. Structural
   a. Muscle necrosis, mainly subendocardial
   b. Lesions similar to focal lesions of coronary artery disease

2. Functional
   a. ECG abnormalities: no consistent pattern, and may be found in only about 1/2 of patients with potassium depletion
      1) depression of S-T segment
      2) decrease in amplitude and inversion of T wave
      3) exaggeration of U wave

   b. Arrhythmias
      1) auricular and ventricular extrasystoles
      2) A-V conduction disturbances
      3) Increased incidence and severity when patients are on digitalis

D. Gastro-intestinal

1. Decrease motility and propulsive ability

2. Paralytic ileus may occur

E. Metabolic

1. Carbohydrate metabolism

   a. in vitro decrease in hepatic glucose uptake, increase in glucose output, decrease in glycogen formation
   b. decreased glucose tolerance
   c. interference with insulin secretion

2. Protein metabolism - questionable in man

F. Neuromuscular

1. Structural: waxy degeneration and necrosis of muscle
2. Functional
   a. weakness and paralysis (quadriplegia)
   b. tetany (probably related to alkalosis)

20. Bellet, S., et al. Electrocardiographic patterns in hypopotassemia. Am.J. Med. Sci. 219:542, 1950.
21. Davidson, S. and B. Surawicz. Incidence of supraventricular and ventricular ectopic beats and rhythms and of atrioventricular conduction disturbances in patients with hypopotassemia. Circulation, Supplement III, Oct. 1966 (abstract)
22. Webster, D. C. et al. Effect of potassium deficiency on intestinal motility and gastric secretion. Ann. Surg. 132:779, 1950.
23. Eliel, L. P. et al. Postoperative potassium deficit and metabolic alkalosis. J. Clin. Invest. 31:419, 1952.
24. Conn, J. W. Hypertension, the potassium ion and impaired carbohydrate tolerance. New England J. Med. 273:1135, 1965.

The Causes of Hypokalemia

A. Cellular Shifts

1. Acute alkalosis

2. Periodic paralysis

3. Cortisol in large doses
4. Rapid glycogen formation

B. Decreased intake

1. Starvation probably not a cause of hypokalemia
   a. Renal losses minimal without dietary salt
   b. Decreased total tissue "potassium capacity" but in keeping with loss of tissue

2. Propensity toward hypokalemia increased with any cause of increased loss

C. Increased loss

1. Gastro-intestinal

   a. vomiting and G-I drainage
      1) decreased intake
      2) loss of K+ in vomitus or drainage
      3) increased renal loss via metabolic alkalosis

   b. diarrhea

   c. enemas and laxatives

   d. fistulas

   e. ureterosigmoidostomy

2. Extracorporeal circulation (may be mainly cellular shifts from respiratory alkalosis)
3. Renal

   a. Primary renal disease
      1) Renal tubular acidosis
      2) Fanconi syndrome
      3) Potassium-wasting renal disease: metabolic hyperchloremic acidosis, hyponatremia, hypovolemia, salt-wastage, evidence of pyelonephritis

         a) with hypomagnesemia (Welt) - familial, chronic dermatitis, normotensive
         b) with sodium conservation (Liddle) - familial, hypertensive, increased renal reabsorption of sodium, decreased aldosterone

25. Bagshawe, K. D., J. R. Curtis and E. S. Garnett. Effect of prolonged hydrocortisone administration on potassium metabolism. Lancet 1:18, 1965.

26. Elkinton, J. R. and E. J. Huth. Body fluid abnormalities in anorexia nervosa and undernutrition. Metabolism 8:376, 1959.

27. Schwartz, W. B. and A. S. Relman. Metabolic and renal studies in chronic potassium depletion resulting from overuse of laxatives. J. Clin. Invest. 32:258, 1953.

28. Seldin, D. W. and J. D. Wilson. Renal tubular acidosis in The Metabolic Basis of Inherited Disease, ed. by Stanbury et al., 2nd edition, 1965.

29. Stanbury, S. W. Some aspects of disordered renal tubular function in Advances in Internal Medicine, Vol. 9, ed by W. Dock and I. Snapper. Year Book Publishers, 1958.

30. Stanbury, S. W., A. H. Gowenlock and R. F. Mahler. Interrelationships of potassium deficiency and renal disease in Aldosterone, ed by A. F. Muller and C. M. O'Connor, Little, Brown & Co., 1958.

31. Earle, D. P., et al. Low potassium syndrome due to defective renal tubular mechanisms for handling potassium. Am. J. Med. 11:283, 1951.

32. Brooks, R. V., et al. Potassium deficiency of renal and adrenal origin. Am. J. Med. 23:391, 1957.

33. France, R. et al. Further studies in a case of potassium depletion of undetermined cause. Trans. Am. Clin. & Climat. Assoc. 71:45, 1959.

34. Gitelman, H. J., J. B. Graham and L. G. Welt. A new familial disorder characterized by hypokalemia and hypomagnesemia. Clin. Res. 14:108, 1966. (Trans. Ass. Am. Phys., in press)

35. Liddle, G. W., T. Bledsoe and W. S. Coppage, Jr. A familial renal disorder simulating primary aldosteronism but with negligible aldosterone secretion. Trans. Ass. Am. Phys. 76:199, 1963.

b. Adrenocortical hormone excess

1) Exogenous steroids - usually only with large doses of cortisone or cortisol

2) Cushing's syndrome with high levels of cortisol production

a) More common with adrenal tumor

b) Often the first evidence of non-pituitary "ACTH"-producing tumors

3) Primary aldosteronism: metabolic alkalosis, hypernatremia, hypervolemia, normal sodium retention, suppressed plasma renin activity

4) Secondary aldosteronism (non-edematous)

a) Accelerated or malignant hypertension (50%)

b) Renovascular hypertension (variable)

c) Juxta-glomerular hyperplasia (Bartter's syndrome)

5) Hyperdesoxycorticosteronism (Biglieri) - normotensive, normal aldosterone.

36. Bartter, F. C. and P. Fourman. The different effects of aldosterone-like steroids and hydrocortisone-like steroids on urinary excretion of potassium and acid. Metabolism 11:6, 1962.

37. Christy, N. P. and J. H. Laragh. Pathogenesis of hypokalemic alkalosis in Cushing's syndrome. New England J. Med. 265:1083, 1961.

38. Allott, E. N. and M. O. Skelton. Increased adrenocortical activity associated with malignant disease. Lancet 2:278, 1960.

39. Conn, J. W., R. F. Knopf and R. M. Nesbit. Clinical characteristics of primary aldosteronism from an analysis of 145 cases. Am. J. Surgery 107:159, 1964.

40. Relman, A. S. and W. B. Schwartz. The effect of DOCA on electrolyte balance in normal man and its relation to sodium chloride intake. Yale J. Biol. & Med. 24:540, 1952.

41. Hilden, R. and A. R. Krogsgaard. Low serum potassium level in severe hypertension. Am. J. Med. Sci. 236:487, 1958.

42. Laragh, J. H. et al. Electrolyte metabolism and aldosterone secretion in benign and malignant hypertension. Ann. Int. Med. 53:259, 1960.

43. Goldberg, J. and D. K. McCurdy. Hyperaldosteronism and hypergranularity of the juxtaglomerular cells in renal hypertension. Ann. Int. Med. 59:24, 1963.

44. Bartter, F. C. et al. Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. Am. J. Med. 33:811, 1962.

45. Biglieri, E. G. Hyperdesoxycorticosteronism with hypokalemic alkalosis with edema. J. Clin. Invest. 42:917, 1963 (abstract).

Differential diagnosis of hypokalemia with renal potassium loss

Clinical State	Aldosterone	Plasma Renin	Hypertension	Hypokalemia
Renal potassium-wasting	Variable	-	Benign when present	Present
With hypomagnesemia	Variable	Increased	Absent	Present
With sodium conservation	Decreased	Decreased	Present	Present
Adrenocortical hormone excess				
Cushing's syndrome	Normal	Suppressed or normal	Usually benign	Occasional
Primary aldosteronism	Increased	Suppressed	Usually benign	Usual
Secondary aldosteronism				
Malignant hypertension	Usually increased	Increased	Accelerating or malignant	Frequent
Renovascular hypertension	Normal or increased	Increased	Benign or malignant	Frequent
Juxtaglomerular hyperplasia	Increased	Increased	Absent	Present
Excessive DOC Production	Normal	?	Absent	Present
Diuretic-induced	Elevated initially	Elevated initially	Usual	Frequent

3. Renal potassium loss (continued)

c. Diuretic-induced

1) More common with thiazides

a) chronic use
b) patients usually given access to salt
c) some carbonic anhydrase inhibition, thereby decreasing H+ secretion.
d) probably blocks proximal tubular reabsorption of Na+, thereby delivering more Na+ to distal site where exchange for K+ occurs.
e) with diuresis and shrunken plasma volume, secondary aldosteronism may increase Na+ absorption and K+ wastage.

2) Incidence: varies from 0 to 50% of hypertensives.

3) Patients with edema (secondary aldosteronism) have increased susceptibility: often start with depleted total K+ and have marked renal loss when large amounts of Na+ are delivered into distal tubule.

4) Mercurials will also produce hypokalemia but lose effectiveness and potassium depletion is self-limited.

46. Remenchik, A. P., et al. Depletion of body potassium by diuretics. Circulation 33:796, 1966.

47. Cranston, W. I. Effects of oral diuretics on raised arterial pressure. Lancet 2:966, 1963.

IV. Therapy of hypokalemia

A. Oral

1. "Natural" - mEq per 100 gm

a. Orange (fresh or juice) - 3
b. Banana - 6
c. Apricot, dried - 22
d. Broccoli - 6
e. Celery - 4
f. Carrott - 6
g. All-bran celery - 16
h. Ry-Krisp crackers - 8
i. Litchi nuts - 14
j. Peanuts - 9
k. Herring - 7

2. Supplemental

a. KCl-liquid, as 20% solution, diluted in tomato juice
b. Need for chloride to correct alkalosis
c. Danger of tablets

B. Parenteral

1. Insure adequate renal function
2. Concentrations greater than 40 mEq/L and amounts of greater than 20 mEq per hour may be locally irritating and cardiotoxic

48. Darrow, D. C. Physiological basis of potassium therapy. J.A.M.A. 162:1310, 1956.

Suggested Protocol for Evaluation of Patients with Hypokalemia

When patients are found to have serum potassiums below 3.5 mEq/L, the following evaluation will be useful in determining the etiology:

A. Collect a 24 hour urine for total Na and K before any replacement therapy. If immediate supplemental K+ is indicated, at least obtain a single specimen for Na and K concentration.

1. If the total urine K+ is below 30 mEq/day (while the urine Na is above 100 mEq/day), hypokalemia has probably been caused by extra-renal losses (vomiting, diarrhea, chronic laxative use) or prior diuretic therapy.

2. If the total urine K+ is above 30 mEq/day, the possibility of hyperaldosteronism (primary or secondary) or some form of potassium-wasting renal disease is suggested. If it is above 50 mEq/day, primary aldosteronism is strongly suggested.

B. An attempt to replenish potassium should then be made: This may take weeks.

1. Stop diuretic therapy, laxatives, etc.

2. Give KCl - 40 to 120 mEq/day. Simultaneous sodium deprivation will hasten K+ repletion but may lead to sudden hyperkalemia.

3. Both serum and urine K+ measurements may be misleading during supplemental K+ therapy. The serum K+ may become normal but, if total body stores are not repleted, it may rapidly fall again when the K+ is stopped. The urine may contain large amounts of K+ while K+ is being given, even though the serum K+ is still low.

C. If urinary K+ was high when the patient was hypokalemic, a work-up for primary aldosteronism should be done.

1. When the serum K+ is normal, the supplemental K+ should be stopped and the patient given access to sodium. (A low salt intake will stimulate aldosterone production in a normal subject and decrease potassium excretion even in a patient with aldosteronism, since Na will not be available in the distal tubule for exchange with K+.)

2. A 24 hour urine should be obtained for total Na, K and aldosterone, five to seven days after discontinuing the supplemental K+.

   a. Obtain a serum K+ on the same day the urine is brought in.

   b. Aldosterone production, even from a tumor, may be suppressed by hypokalemia and stimulated by potassium loading.

   c. If the urine aldosterone is high (normal range = 5 to 20µg/day) under these conditions, hyperaldosteronism exists.

3. Accelerated or malignant hypertension will frequently produce significant secondary hyperaldosteronism (presumably by renal ischemia inducing increased renin-angiotensin production with direct stimulation of aldosterone synthesis).

4. Primary aldosteronism is usually associated with a benign form of hypertension, hypernatremia, and an expanded plasma volume.

5. As emphasized by Dr. Conn, endogenous renin production is suppressed in primary aldosteronism presumably by the expanded plasma volume and cannot be stimulated by the usual physiologic stimuli (sodium depletion and upright posture).

   a. Blood for renin assay should be obtained first in the "control" state, i.e. with the patient on a normal salt intake and in bed overnight, and then after 3 days on a 500 mg low salt diet + 4 hours upright.

      1) 25 ml. peripheral venous blood should be collected in heparinized tubes and cooled immediately in an ice-water bath.

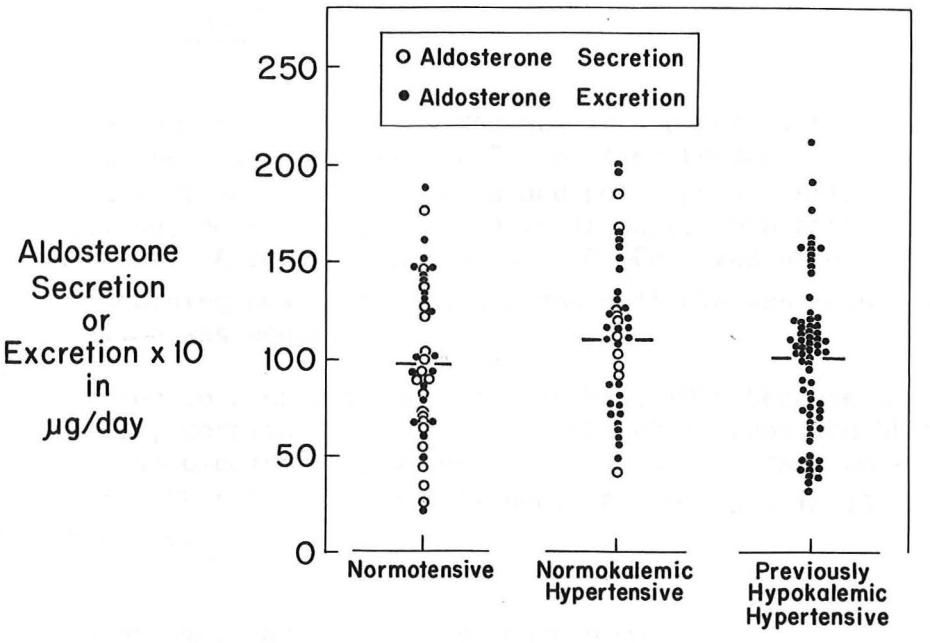
      2) The plasma should be separated immediately after centrifugation, placed into a clean test tube and frozen.

   b. Even after salt deprivation and standing for 4 hours, renin activity should remain suppressed in patients with primary aldosteronism (presumably because the initial expanded plasma volume has not been shrunken enough to stimulate renin release). In patients with essential hypertension, the renin activity should be markedly elevated (3 to 10 fold) after these stimuli.

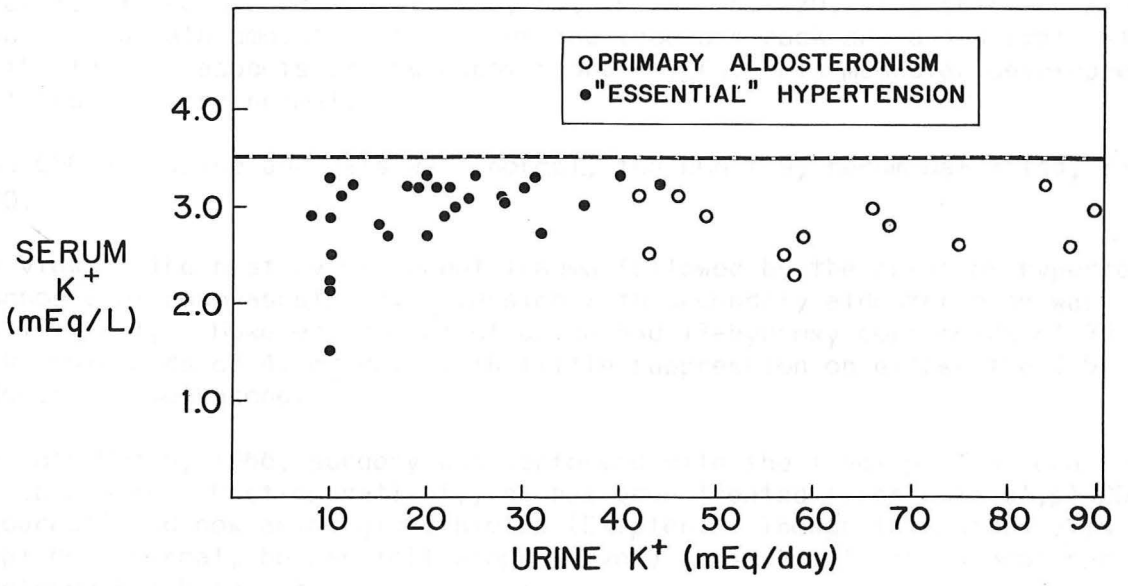
Reference 49. Cannon, P. J., R. P. Ames and J. H. Laragh. Relation between potassium balance and aldosterone secretion in normal subjects and in patients with hypertensive or renal tubular disease. J. Clin. Invest. 45:865, 1966.

"Southwestern" Series - Primary Aldosteronism

Patient	While hypokalemic			While normokalemic		
	Serum K+ (mEq/L)	Urine K+ (mEq/day)	Urine Aldosterone (µg/day)	Serum K+ (mEq/L)	Urine K+ (mEq/day)	Urine Aldosterone (µg/day)
1. [redacted]*	2.8	68	14.9	3.5	43	23.2
2. [redacted]	3.1	42	12.8	3.7	64	25.1
3. [redacted]*	2.9	49	18.7	3.6	43	30.8
4. [redacted]	2.3	58	26.2			
5. [redacted]*	2.5	43	31.8			
6. [redacted]	3.1	46	19.4	3.5	49	26.1
7. [redacted]	2.5	57	23.1	3.5	86	34.0
8. [redacted]	2.7	59	53.3			
9. [redacted]	3.0	90	38.8	3.5		31.6
10. [redacted]	3.0	66		3.5	118	43.0
11. [redacted]	2.6	88	52.0			
12. [redacted]	2.6	76	23.8			
13. [redacted]	3.2	85	37.3			



#12218



#12218
Dr. Kaplan

CASE REPORTS

I. Renal tubular acidosis

[redacted] is a 42 year-old [redacted] man who was in apparently normal health until [redacted], 1965 when he developed the "flu". He soon became very weak, started to lose weight rapidly and noted polyuria and polydipsia. After the onset of severe nausea with vomiting, he was hospitalized in January, 1966 because of profound generalized weakness. A serum potassium of 1.0 mEq/L was noted in association with a low CO_2 combining power and the diagnosis of RTA was made. Therapy with KCl and Shohl's solution was begun.

He was admitted to [redacted] in [redacted], 1966 because of left flank pain. On admission, despite continuation of KCl-45 mEq/day and Shohl's solution, 15 ml tid, his serum electrolytes were: sodium = 147, potassium = 2.6, CO_2 = 22, Cl = 111. When the Shohl's was discontinued, the CO_2 fell to 13.5, but the urinary pH remained above 6.0.

II. Cushing's syndrome: adrenocortical carcinoma

[redacted] is an 18 year-old man who was in apparently normal health until being severely traumatized in a cave-in in [redacted], 1965. After recovery from the acute trauma, he experienced the onset of early morning headaches, plethora, acne and peripheral edema in [redacted], 1965.

When first seen in [redacted], 1966, his BP was 160/120. The skin was flushed, there was a moderate amount of acne over the face and back and a few small striae across the lateral aspects of the abdomen and thighs. His muscular development and fat distribution were normal.

The CBC and urine analysis were normal, the BUN = 9, serum Na+ = 145, K+ = 2.6, CO_2 = 30.

In view of the history of recent trauma followed by the onset of hypertension, the diagnosis of renovascular hypertension with secondary aldosteronism was considered initially. However, a control urine had 17-hydroxy corticoids of 70 mg/day and 17-ketosteroids of 41 mg/day, with little suppression on either the 0.5 or 2.0 mg q 6 h doses dexamethasone.

In late [redacted], 1966, surgery was performed with the finding of a local metastasized adrenal carcinoma. Post-operatively, he has been treated first with o',p'-DDD, then 5-fluorouracil and now amino-glutethimide (Elipten). Though this steroid levels have been kept near normal, he has felt progressively worse and further local spread of the carcinoma has been noted.

11.

Primary hyperplasia of the juxtaglomerular complex with hyperaldosteronism (Bartter's syndrome)

[redacted] a 39 year-old [redacted] woman, has been bothered for about 3 years with easy fatigue, increasing weight gain with edema of the feet, hands and peri-orbital tissue, arthralgias and muscle cramps. In [redacted], 1965, bronchoscopy was performed for evaluation of a slowly resolving and recurrent pneumonia. Pentothal and a "muscle relaxant" were given and she remained unable to move for a prolonged period post-anesthesia. The serum potassium was measured and found to be 1.5 mEq/L. Since then, she has been kept almost continually on large amounts of supplemental potassium but her serum concentration was never brought up to the normal range.

She had been given mercurial injections and thiazide tablets since [redacted], 1966 for relief of edema. Her stools have become more frequent and softer while taking potassium supplements.

The patient had a normal childhood and adolescence with a pattern of growth and development in keeping with her two younger sisters. Menses have been normal and she had 3 uneventful pregnancies. She smokes heavily and drinks as many as 20 cups of coffee each day. Other than for recurrent pneumonias since 1960, her past medical history and review of systems are essentially negative.

On physical examination, the blood pressure was initially 140/90 but after the first day was never above 120/80. Height was 61 1/4 inches, weight 173 lbs. She was moderately and symmetrically obese with no gross abnormalities of physical or mental development. The retinal vessels were normal. The heart, lungs, abdomen and genitalia were normal. Moderate pitting pre-tibial edema was present. Muscle strength was slightly decreased, particularly in the more central groups and all muscles were tender to pressure. The neurological examination was normal.

The laboratory evaluation included: hemoglobin = 15.6, urine negative, BUN = 12, FBS - 101, CO_2 from 29 to 38, chloride from 87 to 99, sodium = 135 to 141, serum albumin = 4.4, globulin = 3.3, calcium = 9.2, phosphorus = 3.9, arterial blood pH = 7.54 and PCO_2 = 37, liver function tests normal. Plasma 17-hydroxycorticoids (8 a.m.) were 13 µg%. Urinary 17-hydroxycorticoids were normal as was an I.V.P.

	[redacted]/65	[redacted]/65	[redacted]/65	[redacted]/66
Diet	Regular No KCl	Day 4-500 mg Na No KCl	Regular Off KCl 3 days	Day 5-500 mg Na + 80 mEq KCl
Serum K+ (mEq/L)	2.2	2.5	2.6	4.2
Urine Na+ (mEq/L)	198	57	171	74
Urine K+ (mEq/L)	42	35	42	110
Urine aldosterone (µg/day)	18.6	58.1		31.6
Plasma renin (ng/100 ml*)	1,085	1,293	603	

* Performed by Dr. J. Caulie Gunnells, Jr. using the Helmer technique for preparation of the plasma with a 1 hour incubation and bio-assay by measuring the pressor response of the specially prepared rat.

Her pressor response to intravenous angiotensin and l-norepinephrine were measured before and immediately after rapid infusion of 500 and 1,000 ml of normal saline.

		Angiotensin mμg/Kg/Min			Norepinephrine mμg/Kg/Min		
	Blood Pressure	4.0	8.0	12.0	40	60	80
Control	110/70	10	15	18	-	-	-
After 500 ml N.S.	105/70	-	15	20	16	20	24
After 1,000 ml N.S.	118/78	-	16	-	-	-	-

A renal biopsy has been interpreted to show increased granularity and number of juxtaglomerular cells.