MEDICAL GRAND ROUNDS PARKLAND MEMORIAL HOSPITAL

1 DECEMBER 1966

PATHOGENESIS OF EDEMA

Case 1.

This 19 year old [redacted] girl was brought to the hospital because of acute onset of severe breathlessness. For approximately 1 week she had noted exertional dyspnea and swelling of feet and ankles. On the night before admission she had been awakened with severe dyspnea which subsided after sitting up for 1 hour.

For 3 to 4 months she had noted increasing nervousness, sweating, heat intolerance, improved appetite and weight loss.

Physical examination revealed: regular pulse 160/min, BP 150/20, distended neck veins, enlarged thyroid with bruit, bubbling rales through both lung fields, cardiomegaly with gallop rhythm and pseudo-rub, pretibial and sacral edema, fine tremor, velvety skin, soft fine hair and onychoclysis. No eye signs of Graves disease.

Venous pressure 24 cm H_2O; circulation time 7 seconds; chest X-ray showed cardiomegaly and congested lung fields; PBI-12 μg%; RAI-54%; cardiac output was 18 liters/min.

IMPRESSION:

Thyrotoxicosis with high output venous congestive state.

Case 2.

This 56 year old [redacted] man was admitted to [redacted] for evaluation of hypertension. Aortography revealed arteriosclerotic plaques obstructing both renal arteries. Renal venous catheterization revealed pressor material coming from both kidneys. Glomerular filtration rate (creatinine clearance) was 48 ml/min. Aldosterone secretory rate was 750 μg/day. Urine sodium was 94 mEq per 24 hours. When 10 gms of salt was added to his regular diet, his weight remained stable and he did not accumulate edema.

After arterial grafting his blood pressure fell to normal and his creatine clearance rose to 95 ml/min.

CONCLUSION:

Despite bilaterally hypoperfused kidneys with reduced glomerular filtration rate and elevated aldosterone levels, the ability to regulate sodium excretion was normal.

Case 3.

This 15 year old [redacted] girl was followed in the obstetrics clinic from [redacted] to September 1966 during her first pregnancy. The expected date of delivery early in [redacted]. Her BP in the clinic was normal, but on [redacted], 1966 it had risen to 140/90. She was admitted to the hospital on [redacted] following a convulsion at home.

PHYSICAL EXAMINATION:

BP 150/120; T. 97^5; P. 100. Disoriented and confused. Pretibial, sacral and facial edema.

LABORATORY DATA:

Hematocrit 42%; BUN 18 mg%; Urinalysis - 3+ albuminuria.

COURSE IN HOSPITAL:

She was treated with $MgSO_4$ and apresoline. Labor was induced and she delivered a 5 lb. 8 oz. infant. After delivery BP fell to 130/80.

ADDITIONAL TESTS:

1. Assay of blood taken before delivery was strongly positive for the natriuretic factor.

2. Assay of blood taken 1 week after delivery was negative for natriuretic factor.

CONCLUSION:

Primagravid girl with eclampsia and edema. The high level of natriuretic factor suggests that salt retention was due to some primary intrarenal disturbance rather than to a decrease in effective arterial blood volume.

TABLE I

CAUSES OF EDEMA

I. PRIMARY REDUCTION IN PLASMA VOLUME

A. Hypoalbuminemia

Nephrosis, protein-losing enteropathy, cirrhosis, starvation.

B. Cirrhosis with ascites - increased portal pressure + decreased serum albumen.

C. Localized transudation -

Venous and lymphatic obstruction.

II. CONGESTIVE HEART FAILURE

A. Left ventricular failure

Aortic valvular disease

Mitral valvular disease

Myocardial disease

B. Right ventricular failure

Pulmonary disease with hypertension.

Constricting myocardial or pericardial disease.

III. HIGH CARDIAC OUTPUT STATES WITH DECREASED EFFECTIVE ARTERIAL BLOOD VOLUME.

A. Anemia

B. Beri-beri

C. Thyrotoxicosis

D. A - V shunts - Pagets, Cirrhosis

E. Anoxia - Cor-pulmonale

IV. HIGH OUTPUT STATES WITH INCREASED EFFECTIVE ARTERIAL BLOOD VOLUME.

A. Acute glomerulo-nephritis

B. Toxemia of pregnancy.

C. Renal shutdown with excess salt.

1. Acute tubular necrosis

2. Ureteral obstruction

3. Severe chronic renal failure

TABLE II

CRITERIA FOR CHANGES IN EFFECTIVE ARTERIAL BLOOD VOLUME

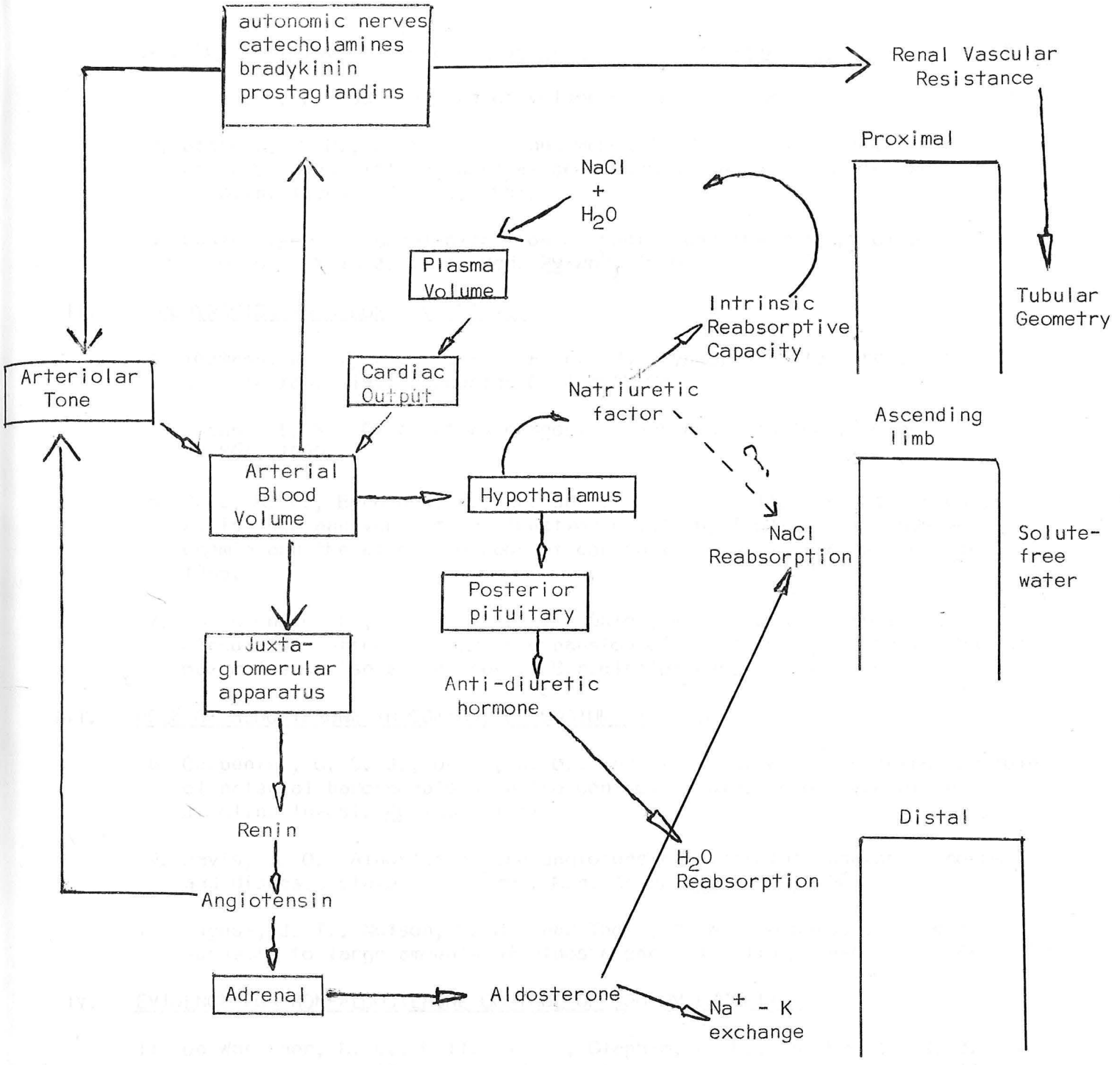
A. DECREASED EFFECTIVE ARTERIAL BLOOD VOLUME

1. Elevated antidiuretic hormone and impaired ability to excrete a water load. Tendency toward hyponatremia.
2. Increased renin and angiotensin.
3. Increased aldosterone.
4. Decreased natriuretic factor.
5. Impaired sodium excretion.

B. INCREASED EFFECTIVE ARTERIAL BLOOD VOLUME

1. Decreased antidiuretic hormone. Tendency toward hypernatremia.
2. Decreased renin and angiotensin.
3. Normal or decreased aldosterone.
4. Increased natriuretic factor.
5. Enhanced ability to excrete salt loads.

Figure 2. FACTORS INVOLVED IN HOMOSTATIC CONTROL OF ARTERIAL BLOOD VOLUME



BIBLIOGRAPHY

I. EVIDENCE THAT VOLUME RECEPTORS ARE LOCATED IN ARTERIAL SIDE OF CIRCULATION.

1. Smith, H. W. Salt and water volume receptors. Am. J. Med. 23:623, 1957.

2. Epstein, F. H., Post, R. S., and McDowell, M. The effect of an arteriovenous fistula on renal hemodynamics and electrolyte excretion. J. clin. Invest. 32:233, 1953.

3. Epstein, F. H. Renal excretion of sodium and the concept of a volume receptor. Yale J. Biol. Med. 29:282, 1956.

II. HEMODYNAMICS IN CONGESTIVE STATES.

4. Youmans, W. B., and Huckins, A. R. Hemodynamics in failure of the circulation. 1951. Charles C. Thomas Co.

5. Eichna, L. W. Circulatory congestion and heart failure. Circulation 22:864, 1960.

6. Case, R. B., Berglund, E., and Sarnoff, S. J. VII. Changes in coronary resistance and ventricular function resulting from acutely induced anemia and the effect thereon of coronary stenosis. Am. J. Med. 18:397, 1955.

7. Robinson, B. F., Epstein, S. E., Kahler, R. L., and Braunwald, E. Circulatory effects of acute expansion of blood volume: Studies during maximal exercise and at rest. Circulation Res. 19:26, 1966.

III. ROLE OF ALDOSTERONE IN CONTROL OF SODIUM EXCRETION.

8. Carpenter, C. C. J., Davis, J. O., and Ayers, C. R. Concerning the role of arterial baroreceptors in the control of aldosterone secretion. J. clin. Invest. 40:1160, 1961.

9. Davis, J. O. Aldosterone and angiotensin interrelationships in normal and diseased states. J. Amer. Med. Assoc. 188:1062, 1964.

10. August, J. T., Nelson, D. H., and Thorn, G. W. Response of normal subjects to large amounts of aldosterone. J. clin. Invest. 37:1549, 1958.

IV. EVIDENCE FOR NON-ALDOSTERONE CONTROL OF SODIUM EXCRETION.

11. De Wardener, H. E., Mills, I. H., Clapham, W. F., and Hayter, C. J. Studies on the efferent mechanism of the sodium diuresis which follows the administration of intravenous saline in the dog. Clin. Sci. 21:249, 1961.

12. Rector, F. C., Jr., Van Giesen, G., Kiil, F., and Seldin, D. W. Influence of expansion of extracellular fluid volume on tubular reabsorption of sodium independent of changes in glomerular filtration rate and aldosterone activity. J. clin. Invest. 43:341, 1964.

13. Levinsky, N. G., and Lalone, R. C. The mechanism of sodium diuresis after saline infusion in the dog. J. clin. Invest. 42:1261, 1963.

14. Davis, J. O., Holman, J. E., Carpenter, C. J., Urquhart, J., and Higgins, J. T. An extra-adrenal factor essential for chronic renal sodium retention in presence of increased sodium-retaining hormone. Circulation Res. 14:17, January 1964.

V. EVIDENCE THAT THE NON-ADRENAL FACTOR IS HORMONAL.

15. Lichardus, B., and Pearce, J. W. Evidence for a humoral natriuretic factor released by blood volume expansion. Nature 209:407, 1966.

16. Johnston, C. I., and Davis, J. O. Evidence from cross circulation studies for a humoral mechanism in the natriuresis of saline loading. Proc. Soc. Expt. Biol. 121:1058, 1966.

17. Cort, J. H. Electrolytes, Fluid Dynamics and the Nervous System. 1965. Academic Press.

VI. EVIDENCE THAT SODIUM EXCRETION IS CONTROLLED BY INTRARENAL HEMODYNAMICS.

18. Barger, A. C., Muldowney, F. P., and Liebowitz, M. R. Role of the kidney in the pathogenesis of congestive heart failure. Circulation 20:273, 1959.

19. Friedler, R. M., Belleau, L., and Earley, L. E. Hemodynamically induced reversal of the sodium retention resulting from acute suprahepatic inferior vena caval constriction. J. clin. Invest. 45:1009, 1966.

20. Earley, L. E., and Friedler, R. M. Changes in renal blood flow and possibly the intrarenal distribution of blood during the natriuresis accompanying saline loading in the dog. J. clin. Invest. 44:929, 1965.

21. Earley, L. E., and Friedler, R. M. The effects of combined renal vasodilation and pressor agents on renal hemodynamics and the tubular reabsorption of sodium. J. clin. Invest. 45:542, 1966.

22. Gill, J. R., Jr., Mason, D. T., and Bartter, F. C. Adrenergic nervous system in sodium metabolism: Effects of guanethidine and sodium-retaining steroids in normal man. J. clin. Invest. 43:177, 1964.

23. Earley, L. E., Martino, J. A., and Friedler, R. M. Factors affecting sodium reabsorption by the proximal tubule as determined during blockade of distal sodium reabsorption. J. clin. Invest. 45:1668, 1966.

VII. THE ROLE OF PROXIMAL TUBULE IN SODIUM EXCRETION.

24. Dirks, J. H., Cirksena, W. J., and Berliner, R. W. The effect of saline infusion on sodium reabsorption by the proximal tubule of the dog. J. clin. Invest. 44:1160, 1965.

25. Cortney, M. A., Mylle, M., Lassiter, W. E., and Gottschalk, C. W. Renal tubular transport of water, solute, and PAH in rats loaded with isotonic saline. Amer. J. Physiol. 209:1199, 1965.

26. Rector, F. C., Jr., Brunner, F. P., and Seldin, D. W. Mechanism of glomerulotubular balance. I. Effect of aortic constriction and elevated ureteropelvic pressure on glomerular filtration rate, fractional reabsorption, transit time, and tubular size in the rat. J. clin. Invest. 45:590, 1966.

27. Brunner, F. P., Rector, F. C., Jr., and Seldin, D. W. Mechanism of glomerulotubular balance. II. Regulation of proximal tubular reabsorption by tubular volume, as studied by stopped-flow microperfusion. J. clin. Invest. 45:603, 1966.

VIII. ROLE OF ANTIDIURETIC HORMONE IN VOLUME CONTROL.

28. Gauer, O. H. Regulation of fluid volume. Proc. Internat. Union Physiol. Sci. 4:222, 1965.

IX. EVIDENCE FOR INCREASED EFFECTIVE ARTERIAL BLOOD VOLUME IN TOXEMIA OF PREGNANCY.

29. Brown, J. J., Davies, D. L., Doak, P. B., Lever, A. F., Robertson, J. I. S., and Trust, P. Plasma renin concentration in hypertensive disease of pregnancy. Lancet, December 11, 1965, p 1219.

30. Watanabe, M., Meeker, C. I., Gray, M. J., Sims, E. A. H., and Solomon, S. Aldosterone secretion rates in abnormal pregnancy. J. clin. Endo. and Metab. 25:1665, 1965.

Addendum. Davis, J. O., Urquhart, John, Higgins, James T., Rubin, Ellis C., and Hartroft, Phyllis M. Hypersecretion of Aldosterone in Dogs with a Chronic Aortic-caval Fistula and High Output Heart Failure. Circulation 14:471, 1964.