AN APPRAISAL OF THE WATER TEST OF ADRENAL FUNCTION

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The water excretion test of adrenal function as described by Robinson, Power and Kepler[1] has been used in the diagnosis and exclusion of adrenal insufficiency. The test is made in two parts*. Part 1 consists of a comparison between the volume of urine excreted during the night and the largest volume of a single hourly specimen supplied in the forenoon. In the original description of the test it was stated that "if the volume of any single hourly specimen provided during the morning is greater than the volume of urine provided during the night, the response to the test is negative, that is, such a response indicates the absence of Addison's disease." It was further stated that if part 1 was negative, part 2 need not be carried out. However, in our study both parts of the test were completed in all instances regardless of the results obtained in part 1, principally because we wished to verify the findings advanced by Robinson, Power and Kepler.

In the 194 consecutive tests comprising this study the results obtained were divided into four groups. Group 1 included tests in which both parts gave negative results. Group 2 included tests in which part 1 was negative and part 2 positive. Group 3 included tests in which part 1

* Procedure 1: On the day before the test, the patient is instructed that the usual salt intake is neither to be restricted nor to be supplemented by additional salt tablets. He is to eat or drink nothing after 6 o'clock in the evening. Until this hour he may eat and drink as desired. At 10:30 p. m. he is required to empty his bladder and discard the urine. All urine voided from 10:30 p. m. until and including 7:30 a. m. is collected as the night specimen. The volume of the night specimen is determined and the urine saved for chemical analysis. Breakfast is omitted and fasting blood drawn for urea and chloride determination. At 8:30 a. m. the patient voids again, and the urine is discarded. Between 8:30 a. m. and 9:15 a. m. he is asked to drink a volume of water equal to 9 cc. per pound of body weight. At 9:30 a. m., 10:30 a. m., 11:30 a. m., and 12:30 p. m. he is requested to empty his bladder, each time in a separate container. The volume of the largest morning specimen is then measured. He is kept at rest during the morning period.

Procedure 2: The fasting plasma urea and chloride are determined in mg. per cent. The night volume of urine and the largest morning specimen of urine are measured in cc. The night urine specimen is analyzed for urea and chloride in mg. per cent. From these data the following equation is then solved.

$$X = \frac{\text{urea in urine (mg. per cent)}}{\text{urea in plasma (mg. per cent)}} \times \frac{\text{chloride in plasma (mg. per cent)}}{\text{chloride in urine (mg. per cent)}} \times \frac{\text{largest volume of day urine in cc.}}{\text{total volume of night urine in cc.}}$$

If X is greater than 30, the test is negative; if less than 25, the test is considered positive.

was positive and part 2 negative. Group 4 included tests in which both parts gave positive results.

Group 1 — Part 1 and part 2 negative, 113 tests in 112 cases. In 111 of 112 patients the test gave negative results and assisted in the exclusion of adrenal insufficiency. In the remaining patient the results of the test were negative on two occasions. However, because the patient presented characteristic pigmentation and other clinical features of Addison's disease, the results of the water test were considered inadequate to exclude Addison's disease completely. All other tests of adrenal insufficiency including the Cutler-Power-Wilder salt deprivation test were also negative. Excretion of 17-ketosteroids in the urine was 7.8 mg. in the 24 hour period. The diagnosis of adrenal insufficiency therefore could not be substantiated except for the pigmentation and response to adrenal therapy. This case indicated that the water test was no less reliable than any other test of adrenal function.

Group 2—Part 1 negative and part 2 positive, 2 cases. In both cases the result in part 2 was incorrectly positive. One of these patients had a duodenal ulcer, pyloric obstruction, and loss of chlorides. The other had an elevated blood urea. In both instances these changes were sufficient to render the test positive. In no other instance in the series was evidence of adrenal insufficiency found by completing part 2 when the result of part 1 was negative.

Group 3—Part 1 positive and part 2 negative, 20 cases. The presence of adrenal insufficiency was excluded only after part 2 had been completed. The only feature common to these patients was fatigue or exhaustion of varying degree. Final diagnoses included anorexia nervosa, carcinoma of the stomach, chronic nervous exhaustion, hyperventilation tetany, and undulant fever. The test had value in excluding adrenal insufficiency as a cause of symptoms.

Group 4—Part 1 and part 2 positive, 59 tests in 39 cases. From the results of the test alone, all patients in this group were considered as having adrenal insufficiency.

Sixteen patients had proven Addison's disease. The diagnosis in all was substantiated by other tests of adrenal function and by the patient's response to replacement therapy.

In 12 patients the test gave presumptive evidence of adrenal failure of pituitary origin. Frank pituitary disease was present in each case. Two patients had acromegaly associated with enlargement of the sella turcica. In 8 cases neoplasm of the pituitary without acromegaly was associated with varying degrees of hypogonadism. One patient had a

Rathke pouch cyst. Another patient had pituitary cachexia as a result of surgical trauma to the anterior lobe of the pituitary.

Three cases were classified as miscellaneous adrenal disease. One patient had carcinoma of the adrenal cortex with a high titer of urinary 17-ketosteroids and hirsutism. One patient had the characteristic features of Cushing's syndrome. In the third case positive proof of an adrenal defect was lacking. This patient had generalized anasarca without measurable renal, cardiac, or nutritional factors. Chronic constrictive pericarditis, hypoproteinemia, chronic nephritis, and other conditions which might have been causing anasarca were excluded insofar as possible. After dehydration with a low-sodium high-potassium intake and mercupurin, the water excretion test became negative. We wondered if this excessive water retention was associated with an adrenal abnormality.

The 8 remaining patients giving positive results to the test were not considered to have adrenal insufficiency. Five had diseases not usually accepted as embodying adrenal failure. One of these had disseminated lupus erythematosus and marked cachexia. Two had generalized carcinomatosis and malnutrition. One had grade III rheumatoid arthritis and inanition. In a woman with renal tuberculosis the test was positive twice and negative once. Assays for 17-ketosteroid excretion were normal.

Two patients had duodenal ulcer with partial pyloric obstruction and vomiting, which apparently disturbed the water and chloride balance.

One positive test was the result of an error in technic, and upon repetition the test was negative.

COMMENT

In my experience the water excretion test of adrenal function is satisfactory and of definite value in the diagnosis and exclusion of adrenal insufficiency. The chief advantages are that it is safe, that a special diet is not a prerequisite, and that it does not require hospitalization. In these respects it offers an advantage over the Cutler-Power-Wilder test. The chief disadvantage is that in the absence of adrenal insufficiency other conditions such as renal disease, duodenal ulcer, and chronic cachexia may give a positive result. In such instances adrenal insufficiency must be excluded by the salt deprivation test, assays for 17-ketosteroids, and so forth.

In our experience the test is of little value in determining response to the treatment of adrenal insufficiency. In some instances the test has become negative following treatment, but in other instances with more intensive treatment, it has remained positive.

SUMMARY OF PATIENTS WITH POSITIVE RESULTS IN PART 1 AND PART 2

1.	Addison's disease		16
2.	Pituitary disease		
	a. Acromegaly	2	
	b. Basophilic adenoma	8	
	c. Rathke pouch cyst	1	
	d. Pituitary cachexia	1	
	Total		12
3.	Miscellaneous adrenal disease		
	a. Carcinoma of adrenal	1	
	b. Cushing's syndrome	1	
	c. Water retention (?)	1	
	Total		3
4.	Other conditions giving positive results		
	a. Disseminated lupus erythematosus	1	
	b. Diffuse carcinomatosis	2	
	c. Rheumatoid arthritis	1	
	d. Renal tuberculosis	1	
	e. Duodenal ulcer	2	
	f. Incorrect technic	1	
	Total		8
	Grand total		39

CONCLUSIONS

The results of 194 consecutive water excretion tests for adrenal function in 173 patients indicate its value in the diagnosis and exclusion of adrenal insufficiency.

Only one of the 112 patients giving negative results in both parts of the test was considered to have Addison's disease. All other tests for adrenal insufficiency gave comparable results in this instance.

Adrenal insufficiency was not proved to exist in any patient by completing part 2 of the test after part 1 was negative.

False positive results were obtained in 8 patients. Chronic cachexia, duodenal ulcer, or renal disease appeared to be the explanations for the incorrect results.

REFERENCE

1. Robinson, F. V., Power, M. H., and Kepler, E. J.: Two new procedures to assist in the recognition and exclusion of Addison's disease: A preliminary report. Proc. Staff Meet., Mayo Clinic 16:577 (Sept. 10) 1941.

ERRATUM

In the article "Exstrophy of the Bladder in Twins" in the October, 1943 issue of the CLEVELAND CLINIC QUARTERLY the following error appeared on page 140, "M.T. had complete exstrophy of the bladder with an associated hypospadias," which should read, "M.T. had complete exstrophy of the bladder with an associated epispadias."