MEASURES OF RENAL TUBULAR FUNCTION

Comparison of the Addis and Pituitrin Concentration Tests

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ESTIMATION of the ability of renal tubules to concentrate urine is of as great value as any single test in establishing diagnosis and prognosis of renal disease. Further, it can be performed accurately and simply, at no cost to the patient and with minimal effort to the examiner. With this to recommend it, the principle should be widely applied.

In the measurement of concentrating ability the aim should be to determine maximal or "ceiling" specific gravity. Possibly because many of the methods suggested do not furnish such values they are infrequently used. General acceptance and usage of a single, practical method of testing for maximal specific gravity might contribute toward more uniformity in the understanding of the various types of renal disease.

The method described by Lashmet and Newburgh[1] probably most nearly measures maximal concentrating ability. They proposed that the oral intake of solids be controlled for seven days before and three days during water deprivation. However, the duration and rigorous restrictions of the test make routine application unlikely.

Brunn, 1921;[2] Sodeman and Engelhardt, 1941-1943;[3,4] and more recently Horne and Morris, 1947,[5] have utilized the antidiuretic principle of posterior pituitary extract as a means of estimating the ability of the kidneys to concentrate urine. After subcutaneous injection of 10 units of surgical pituitrin, they observed a sharp decrease of urinary output and an increase of specific gravity which attained its maximum degree at two hours and persisted for three to four hours. The specific gravities of the specimens collected from normal persons ranged from 1.022 to 1.036 (Sodeman and Engelhardt)[4] and 1.020 to 1.029 (Horne and Morris).[5] These authors have suggested that the convenience of the test and the results obtained might justify substituting it for tests that depend upon fluid deprivation.

Taylor, Peirce and Page[6] compared the results obtained by the method described by Sodeman and Engelhardt to those recorded following a period of 24 hours fluid deprivation (Addis).[7]

They found that injection of pituitary extract into normal subjects yielded urinary specific gravities of 1.015 to 1.033, a spread only slightly greater than that reported by proponents of the test. On the other hand, the Addis test, as has been previously shown by its author and by Alving and Van Slyke[8] produced specimens whose specific gravities among normal persons always exceeded 1.026.

Comment

Since the antidiuretic action of posterior pituitary extract is maximal two hours after injection, the pituitary tests can be performed in a short period without preparation. However, this apparent advantage may be offset by the inconveniences imposed by volumes of urine formed during the two hour period of oliguria induced by pituitrin. Many patients will form but 5 to 15 cc. of urine under such conditions, a volume which prevents measurement of gravity by an urinometer. In such instances a pyknometer and analytical balance must be used. Further, scanty amounts of urine may make quantitative estimation of proteinuria difficult. Without this information an accurate specific gravity determination is impossible, for 1 per cent proteinuria can elevate the specific gravity 0.003.

In addition to these mechanical disadvantages of the pituitary test, patients must spend at least two hours waiting in a laboratory or office, while the Addis test may be performed by almost anyone during normal activity. Simple instructions are rarely misinterpreted. The test requires only fluid deprivation for twenty-four hours and collection of the urine formed during the second twelve hours of this period. Normal subjects produce specimens with specific gravities which range from 1.026 to 1.032. Further, the specimen is always large enough so that its gravity can be measured quickly with a urinometer and its protein content determined. If indicated, an Addis count[7] of the sediment can be made.

Instructions for Addis Test

1. No fluid or frozen foods of any kind from 8 a.m. until 8:00 a.m. of following day.
2. Dry diet is permissible.
3. At 8:00 p.m. empty bladder and discard urine.
4. Save all urine passed from 8:00 p.m. until 8:00 a.m.
   Keep in jar in icebox or cool place.
5. Bring specimen to desk from which list of instructions was received.

Although this test of concentrating ability seems to be the most satisfactory for routine use, there are cases in which it has limitations. Patients with diabetes insipidus or edema, regardless of origin, may produce dilute urine regardless of the degree of dehydration and thus vitiate the Addis test as a measure of renal efficiency. If a test of renal function is desired among such patients, the urea clearance serves admirably.

Interpretation of Urinary Specific Gravity Measurements

Values of urinary specific gravity which do not approximate the "ceiling" or maximal value for the individual patient can have little meaning save in a

very broad sense. In the early or moderately advanced stages of most renal disease and especially in chronic glomerulonephritis, pyelonephritis, and essential or malignant hypertensive vascular disease, it is commonplace to have isolated urine specimens with specific gravities of 1.020 or above. This is possibly the result of relative dehydration occurring by chance. In those tests which depend upon the effects of pituitary extract on the kidneys or brief periods of fluid restriction there is no way of separating this type of patient from the normal as far as tubular function is concerned. Patients to whom this might occur are those in whom accurate estimation of urinary concentrating ability is of most value. If the disease is far enough advanced to permit formation of urine with specific gravity constantly below 1.020, even the crudest tests or the history of frequency and nocturia are adequate evidences of extensive tubular deterioration.

The interpretation of tests of concentrating ability must naturally be made in relation to other observations in the patient. For instance, retinal arteriolar sclerosis, arterial hypertension and cardiac hypertrophy may be present in similar degrees in a patient with chronic glomerulonephritis and one with essential hypertension both of whom concentrate urine to 1.021. The former, however, will have proteinuria usually in excess of 3-4 Gm. per twenty-four hours and the urea clearance will be depressed to a considerable degree, while these two findings may be within normal limits in the patient with essential hypertension. In those patients with pyelonephritis, acute glomerulonephritis and the malignant phase of hypertension, the degree of pyuria, hematuria or cylindruria may be the determining factor in establishing differential diagnosis.

Since renal and vascular diseases vary in their rate of progression from patient to patient, an isolated test of concentrating power is of limited value for purposes of prognostication. The rate of deterioration can be known only by serial observations made at intervals spaced according to the nature of the disease involved. In the cases of patients with early essential hypertension this information is of more than academic interest. At present, probably the best indication for lumbodorsal sympathectomy as treatment for these patients is evidence of advancing arteriolar disease (Page, Corcoran, and Taylor).[9] Corcoran and Page[10] have indicated that one of the earliest signs of such change is diminishing tubular function which can well be demonstrated by measuring the ability of kidneys to concentrate urine.

Summary

1. Estimation of "ceiling" or maximal ability of kidneys to concentrate urine is a reliable test for renal functions.

2. The Addis test is inexpensive and convenient. It approximates "ceiling" specific gravity and sharply segregates abnormal and normal values.

3. Single measurements of maximal concentrating ability are of diagnostic value but for prognosis in chronic progressive disease of the kidneys serial estimates at six to twelve month intervals are necessary.

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