The value of tests for renal function in early and advanced Bright's disease / by R. Fitz, M.D., Boston, Massachusetts.

The Value of Tests for Renal Function in Early and Advanced Bright's Disease

BY

R. FITZ, M.D.

BOSTON, MASSACHUSETTS

FROM THE

AMERICAN JOURNAL OF THE MEDICAL SCIENCES

September, 1914, No. 3. vol. cxlviii, p. 330

Extracted from the American Journal of the Medical Sciences,
September, 1914, No. 3, vol. cxlviii, p. 330.

THE VALUE OF TESTS FOR RENAL FUNCTION IN EARLY AND ADVANCED BRIGHT'S DISEASE.[1]

By R. Fitz, M.D.,
BOSTON, MASSACHUSETTS.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.)

Since Richard Bright[2] described characteristic anatomical changes in various forms of kidney disease the problem of nephritis has occupied the attention of many observers. It is admitted that there are several types of nephritis, each one showing a different clinical course and different pathological lesions. It has been generally recognized that in the course of a nephritis, symptoms referable to toxemia have developed which have been given the inclusive name of "uremia," and that nephritic patients have died of uremia, of cardiac failure, or of some intercurrent cause. But it has been found impossible to predict in an individual case by clinical study alone what course the disease will take in its development or what anatomical changes will be found at autopsy. Therefore, during recent years, methods have been devised for estimating renal function in order to make possible an early diagnosis of existent kidney disease and to offer information in regard to its prognosis and treatment.

In 1881 Fleischer[3] followed the excretion of nitrogen, sodium chloride, and phosphoric acid in a series of nephritic cases. His patients were given a known diet, and were controlled by normal individuals with similar food. Fleischer found that the excretion of nitrogen in ratio to its intake in the pathological cases showed considerable variation, that phosphoric acid was poorly excreted, while the chloride balance was nearly perfect. These observations justify the assumption that in a diseased kidney, different parts show selective excretory functions tending to retain certain substances from the diet and to excrete others normally.

In 1910 Schlayer[4] and his co-workers began a series of experimental and clinical studies which have been of great value in the

[1] Read before the Section in Medicine of the New York Academy of Medicine, March 5, 1914.

[2] Guy's Hosp. Rep., 1836, i, 358.

[3] Deutsch. Arch. f. klin. Med., 1881, xxiv, 129.

[4] Schlayer and Takayasu, Deutsch. Arch. f. klin. Med., 1910, xcviii, 17; Ibid., 1911, ci, 333; Ibid., 1911, cii, 311; Verh. des. Cong. f. innere Med., 1912, xxix, 501; Beihefte zur med. Klin., 1912, ix, 211; Münch. med. Woch., 1913, lx, 800.

early diagnosis of abnormal renal function. Schlayer's original observations were based on acute experimental nephritis in rabbits. He injected potassium bichromate, cantharidin, or uranium nitrate into animals and produced a tubular, vascular, or mixed type of nephritis in which he studied renal function. He recognized the close relation which exists between renal blood-supply and the amount of urine excreted, and accordingly he studied general blood-pressure in his animals, changes in renal volume as recorded in an oncometer, and the diuretic response to various forms of stimuli, controlling the experiments by autopsy and histological examination. The various toxic substances produced different effects. In tubular nephritis Schlayer found that the renal vascular system reacted to vasodilators and constrictors normally. The urine, however, was dilute and the kidney was unable to concentrate and excrete sodium chloride when it was injected intravenously. In vascular nephritis, on the other hand, the kidney's concentrative powers were unaffected while the vascular response to vasomotor stimuli was lost or exaggerated. This led him to determine whether the excretion of other substances in addition to that of chloride might be used as a measure of the efficiency of the vascular or tubular apparatus of the kidney to replace observations with the oncometer. One of the prominent features of his experiments was the amount of fluid excreted. In tubular nephritis it was not remarkable; but in vascular nephritis it varied directly with the vascular functional condition. In cases where the renal vessels were hypersensitive to vasodilators there resulted a diuresis; when the vessels were insensitive there was oliguria. Thus the amount of urine obtained was one index to glomerular function. Voit[5] discovered that if lactose was injected into an animal intravenously or subcutaneously the entire amount could be recovered in the urine. Schlayer, however, found in experimental nephritis that intravenous injections of this sugar were only well excreted when the renal vascular system was normal, and were held back when the glomeruli were damaged. Therefore he assumed that lactose in addition to water might be used as a test for the vascular condition of the kidney. Schlayer recognized the complexity of chloride metabolism. Duckworth[6] had already introduced potassium iodide as a test for renal function, and Schlayer, comparing its excretion with that of sodium chloride, found that both were distinctly interfered with in tubular lesions. So Schlayer adopted the excretion of water and lactose as indicators of renal vascular activity, and that of sodium chloride and potassium iodide as measures of tubular activity. Experimentally there was a close agreement between the excretion of these substances and the respective types of nephritis, which confirmed Schlayer's views as to their place of excretion.

[5] Deutsch. Arch. f. klin. Med., 1897, lviii, 545.
[6] Saint Bartholomew's Hosp. Rep., 1867, iii, 216.

He turned these methods to the study of patients. His technique for the various tests was simple. While under observation the patient was ordered a constant diet containing known amounts of fluid and salt. The total amount of fluid and sodium chloride excreted was followed from day to day. To make the lactose test 2 gm. of the sugar dissolved in 20 c.c. of distilled water were injected intravenously. After the injection the urine was collected at the end of four hours and every hour or two thereafter to twelve hours. Each specimen was tested for the presence of sugar with Nylander's reagent, and the total amount of sugar excreted was determined polarimetrically. Normally 60 per cent. or more of the amount injected was regained in from four to six hours.

On a certain day the patient was given 10 gm. of salt by mouth. Normally this should be excreted in from twenty-four to forty-eight hours, either by an increase of salt concentration in the urine or by diuresis. Schlayer found, however, that there were two types of abnormal salt excretion. In experimental tubular nephritis, with intact glomeruli, the kidney could not concentrate chloride and the salt was retained in the body. The specific gravity of the urine was low, and to this type of dilute urine Schlayer gave the name "tubular" hyposthenuria. The other type of abnormal chloride excretion occurred in experimental nephritis, where the tubules were normal but where the vessels were hypersensitive to stimulation. As a result the diuretic action of the salt was marked, and the added salt was excreted in an excess of fluid, its concentration remaining low and the specific gravity of the urine remaining unchanged. Schlayer called such a dilute urine "vascular" hyposthenuria. Both types of chloride excretion were found to occur clinically.

The length of time required by the kidney to excrete 500 mg. of potassium iodide given by mouth served as a criterion for the iodide test. Janeway[7] has pointed out that this depends upon the qualitative reaction which is used to determine the presence of iodine in the urine. Schlayer selected Sandow's test and considered sixty hours normal, while von Monakow,[8] taking starch paste and nitric acid, made forty-four hours the upper limit.

By using these various tests, Schlayer claims to be able to distinguish certain types of acute and chronic nephritis and to find their distinguishing characteristics to be sharply demarcated. Vascular nephritis, whether acute or chronic, is characterized by a delayed lactose excretion, by oliguria or polyuria, depending on the sensitiveness of the renal vessels, and by a normal chloride and iodide excretion. Tubular nephritis is shown by a normal water and lactose excretion, but with delayed chloride and iodide outputs. All grades of mixed functional disturbances are found between these two extremes. In a general way the tests point out

[7] Trans. Cong. Amer. Phys. and Surg., 1913, ix, 14.
[8] Deutsch. Arch. f. klin. Med., 1911, cii, 248.

the severity of the disease, and since they are all delicate, often show functional changes before clinical signs of nephritis develop. Schlayer has shown this prettily by observing cases over a long interval of time. He has been able to see cases with abnormal function by the tests later develop albuminuria, cylindruria, and hypertension. Repetition of the tests in such cases has demonstrated a progressively worse renal function with the increasing clinical severity of the disease. The work of Conzen,[9] Eppinger and Barrenscheen,[10] Rowntree and Fitz,[11] Herringham and Trevan,[12] Eisner,[13] Michaud and Schlecht,[14] and Frank and Benrenroth[15] confirms the value of Schlayer's methods in the diagnosis of nephritis.

In regard to the anatomical changes producing the functional disturbances, however, there is a difference of opinion. Von Monakow found a delayed potassium iodide excretion when the salt excretion was undisturbed, and believed that disturbance of water excretion depended on tubular degeneration. Rowntree and Fitz considered lactose an index of the vascular condition of the kidney, but showed in the frog at least that the tubules in the absence of a glomerular system were capable of excreting the sugar. In summing up the relation of functional tests to pathological diagnosis in nephritis, Christian[16] states that "so far too few cases are recorded with these functional tests and subsequent histological examination of the kidneys to justify final conclusions, but such as are recorded do not seem to indicate that any very close correlation between function and anatomical lesion can be made on the basis of the rate of excretion of such substances as lactose, potassium iodide, salt, and water."

Von Monakow, repeating Schlayer's work, added a nitrogen test to the others. This consisted in following the nitrogen balance during the period of observation, and on one day giving 20 gm. of urea, containing 9.3 gm. of nitrogen. According to his observations it was normally excreted within forty-eight hours, but was retained in nephritides with glomerular lesions. Although subsequent work has not proved the place of its excretion, there seems little doubt at present that the kidney has selective excretory capacities. The excretion of lactose, water, and nitrogen differs from that of sodium chloride and potassium iodide. By following the excretion of these substances and by adding test amounts it is possible to discover an abnormal renal function before marked clinical signs of kidney disease are manifest. The different types

[9] Deutsch. Arch. f. klin. Med., 1912, cviii, 353.
[10] Wien. med. Woch., 1912, lxii, 1408, 1497.
[11] Arch. Int. Med., 1913, xi, 121; ibid., 258.
[12] Quart. Jour. Med., 1913, vi, 505.
[13] Deutsch. Arch. f. klin. Med., 1913, cxii, 442.
[14] Jahreskurse, f. ärtzl. Fortbildung, 1913, iv, 3.
[15] Verh. des Cong. f. innere Med., 1913, xxx, 217.
[16] Trans. Cong. Amer. Phys. and Surg., 1913, ix, 1.

of functional disturbance are well illustrated by the following cases:

CASE I.—Tubular nephritis. Peter Bent Brigham Hospital. Medical No. 782.

A man, aged forty years, came to the hospital with acute articular rheumatism. His history was unimportant except for a previous attack of rheumatic fever. Three months ago he became unconscious while at work, remaining in this condition for four days. No paralysis was noted at the time. He made a normal recovery.

At entry, physical examination showed an enlarged heart. There was a faint systolic murmur at the apex. The aortic second sound was accentuated. The systolic blood-pressure was 185. There was moderate thickening of the peripheral vessels, and the urine showed a trace of albumin with occasional casts. The fundi oculorum were normal. There was no edema.

At the time the tests for renal function were made the acute stage of rheumatic fever had passed. The results of the functional tests are charted below.[17]

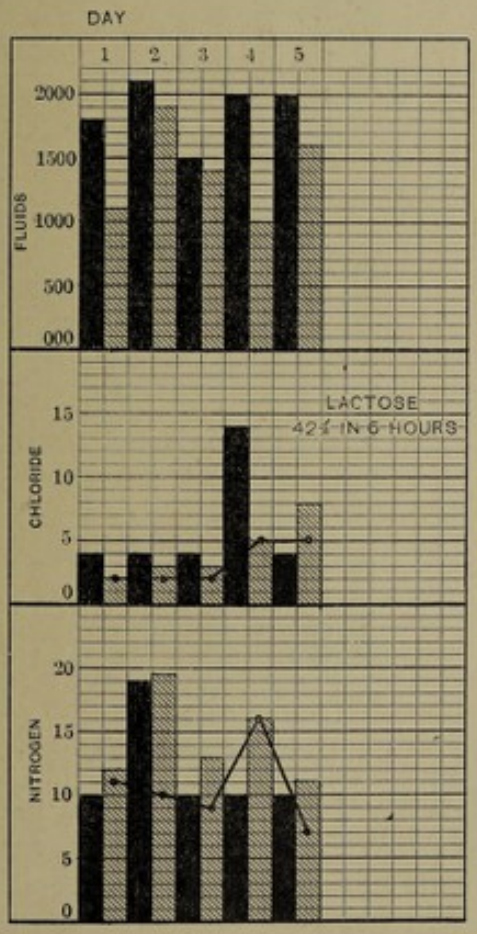

CHART I.—"Tubular" nephritis.

[17] The black column in the accompanying charts represents intake, the cross-column output, the dotted lines the concentration of chloride or nitrogen per 100 c.c. of urine.

While the functional findings are not absolutely typical the striking feature is retention of chloride and water when added salt was given, while added nitrogen is excreted normally. This suggests tubular involvement. On the other hand the lactose excretion is somewhat delayed, and therefore vascular function must be interfered with to a certain extent. The case is called "tubular" because it illustrates with more than usual distinctness the type of excretion which characterizes abnormal tubular function.

Case II.—Vascular nephritis. Peter Bent Brigham Hospital. Medical No. 131.

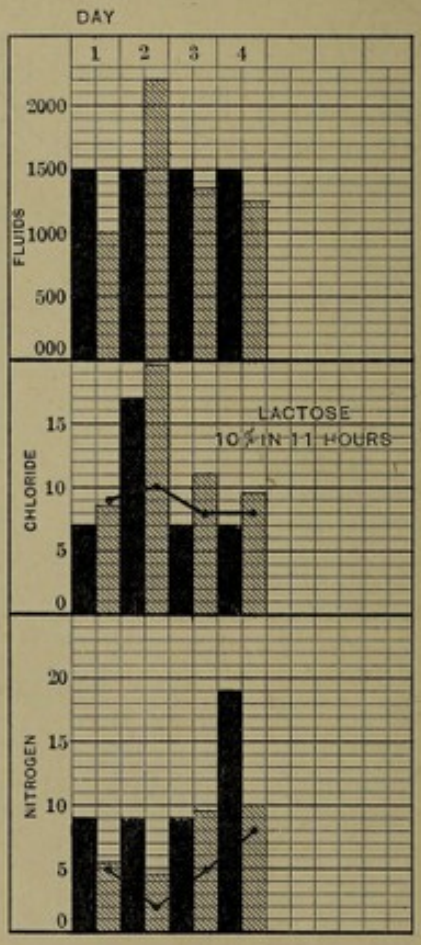

Chart II.—"Vascular" nephritis.

A woman, aged thirty years, entered the hospital complaining of "shortness of breath." As a girl she had scarlet fever and "convulsions." Ten years ago she noted shortness of breath on exertion. Two years ago her face and eyes were swollen at times. During the past year her physician had observed a high blood-pressure. On two or three occasions during this time she had mild convulsions, from which she recovered quickly. There was more or less headache.

Physical examination showed marked cardiac hypertrophy. There was a systolic murmur at the apex, and another of different pitch and intensity at the base. The aortic second sound was accentuated. The systolic blood-pressure was 200. The urine showed albumin and casts. The specific gravity was between 1010 to 1015. Fundus examination showed edema and hemorrhage of the disks without exudate.

In this case the vascular system was especially at fault. The lactose and nitrogen were poorly excreted. The tubules were able to increase the concentration of chloride, but the salt acted mainly as a diuretic, increasing the urinary output markedly. Thus the vessels were hypersensitive and as the specific gravity showed a relative fixation during the period of observation, the functional findings are those of "vascular hyposthenuria."

CASE III.—Mixed nephritis. Peter Bent Brigham Hospital. Medical No. 75.

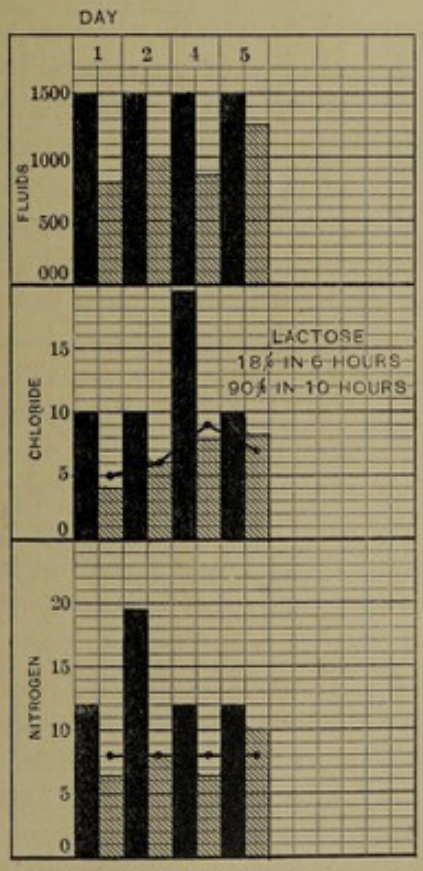

CHART III.—"Mixed" nephritis.

A painter, aged forty-five years, came to the hospital complaining of weakness of the arms and legs. His previous and family histories were negative. Physical examination gave signs of a peripheral neuritis, probably due to lead poisoning. In addition his heart was slightly enlarged, the aortic second sound was ringing, the

blood-pressure was 160, and the urine was of a fixed gravity, between 1014 to 1015, and contained albumin and casts. His renal functions were studied with the results shown above.

Here the function of both the tubules and vascular system was involved. There was a delayed lactose and nitrogen excretion; the vessels were insensitive to chloride stimulation. Salt concentration increased slightly, following the added amount, but not enough to increase the total output. Thus a mixed type of functional derangement was found, without a typical "vascular" or "tubular" hyposthenuria.

On the whole, Schlayer's tests are significant, chiefly because they show early functional disturbances in the kidney, and by repetition illustrate the rapidity of development of an early disease. But whether vascular and tubular function on an anatomical basis can be differentiated in Bright's disease with the same definition as in experimental toxic nephritis, remains to be determined by a careful study of more clinical and pathological material.

In advanced nephritis these tests are less useful. In the first place it is difficult to conceive of such a kidney in which pathological and functional lesions are not found in both tubules and vascular system to so great a degree as to make differentiation of function impossible. In the second place, whatever disturbances are found may be identical with those occurring in an early disease, and so give little prognostic information. The latter point is well demonstrated by the cases quoted. The most advanced case to all clinical appearances was the one recorded as "vascular" nephritis. Yet by the tests the worst case functionally was the one which showed the "mixed" type of excretion, and occurred in a man who had no symptoms of kidney disease whatever. Therefore in advanced Bright's disease, tests which estimate the total renal function and which are directed to determining the cause of symptoms encountered are of more value than finer ones which attempt to study individual functions of different anatomical units of the organ.

It is generally agreed that the kidney is the main excretory channel of the body, and that retention of substances through faulty elimination may lead to toxic manifestations. Prevost and Dumas,[18] in 1821, found an increase in the urea content of the blood after extirpation of the kidneys. From that time various observers have isolated specific substances from the blood of uremic patients which they have considered the cause of symptoms. But each body successively incriminated has been successively rejected. At present renal insufficiency or uremia is regarded as a complex intoxication arising from unknown causes. But the degree of renal insufficiency can be estimated in a variety of ways.

[18] Quoted by Schöndorff, Pflüger's Arch. f. d. ges. Phys., 1899, lxxiv, 307.

In phenolsulphonephthalein, Rowntree and Geraghty[19] have given the most valuable single aid to the estimation of total renal function, which is known at present. Phenolsulphonephthalein is a dye devoid of toxicity, and is eliminated from the body almost entirely through the kidney. Rowntree and Geraghty have shown from careful studies in nephritis that the amount of phthalein excreted varies in direct proportion to the severity of the disease. In fatal uremia only traces of the dye are found in the urine, while in mild nephritis the amount recovered is nearly normal. In cardio-renal disease where the heart is chiefly at fault and the kidneys are congested without a marked nephritis a low phthalein output may be observed at first, rapidly rising as the circulation is restored, while if a severe nephritis is present no change in the phthalein excretion accompanies the improved circulation.

In addition to its accuracy the test has the added advantages of being rapid and so simple that it may be used by the general practitioner. A solution of phenolsulphonephthalein is made containing 6 mg. of the dye to 1 c.c. of salt solution. This is injected either intravenously or intramuscularly under aseptic conditions. Following the injection all the urine excreted is collected at the end of one hour and two hours, is diluted to a suitable amount with alkaline water, and its phthalein content is estimated by colorimetry. The Du Boscq colorimeter may be used or the simpler Autenrieth-Königsberger machine or even a series of test-tubes containing varying amounts of the dye in varying dilutions. If the colorimeter is used a standard solution for comparison is made which contains 6 mg. of phthalein in a liter of alkaline water. Normally from 40 to 60 per cent. of the amount injected is recovered in one hour, and from 60 to 80 per cent. in two hours following intramuscular injection. The test has been used successfully by so many observers that its value must be accepted as a fact.

In a few cases, however, the excretion of the dye gives unreliable information. This appears to be because a diseased kidney may be hyperpermeable to one substance, while it is impermeable to another. Thus it may be permeable to a dye and impermeable, possibly, to an unknown poison causing certain symptoms of the disease. Bard and Bonnet,[20] in studies on renal function in which potassium iodide and methylene blue were used as tests, found that in interstitial nephritis the excretion of both substances was faulty, in "epithelial" nephritis the kidney was hyperpermeable for both, and in secondary interstitial nephritis the methylene-blue excretion was normal or increased, while that of potassium iodide was diminished. Pepper and Austin[21] have lately called attention to a case of nephritis with marked albuminuria, cylindruria, and

[19] Jour. Pharm. and Exp. Ther., 1909, i, 579; Arch. Int. Med., 1912, ix, 284.
[20] Arch. Gén. de Méd., 1898, 3d ser., ix, 129, 283, 464.
[21] Amer. Jour. Med. Sci., 1913, cxlv, 254.

edema in which the phthalein output was normal, and Baetjer[22] reports nearly similar cases. Foster[23] illustrates the difficulty of prognosis by the use of any one kind of functional test giving as examples cases which died of uremia with a practically normal phthalein output shortly before death. In this regard the following case is of interest.

CASE IV.—Peter Bent Brigham Hospital. Medical No. 4.

A woman, aged sixty-three years, was admitted to the hospital with a history of dyspnea of one year's duration. Her family and previous histories were negative. Her habits were good. Two months before entry her eyesight had failed, and she began to have mild occipital headaches. Physical examination was unimportant except for marked cardiac hypertrophy, an apical systolic murmur, an increased blood-pressure (232 mm. systolic), and a urine which contained albumin and casts. She appeared to be a case of advanced interstitial nephritis, confirmed by a phthalein excretion of 12 per cent. for two hours. Rest in bed produced no benefit. In two weeks she became drowsy and was bled. On the following day the phthalein excretion was 30 per cent. for one hour and twenty minutes. Her general condition did not improve. A week later she became comatose and put out only traces of phthalein in two hours. She was bled again. She became brighter temporarily, and her phthalein excretion on the next day was 54 per cent. for two hours. She lapsed into coma soon and died shortly. On the day of her death she put out 8 per cent. of phthalein in two hours. Autopsy showed typical contracted kidneys. It is difficult to explain this rapid premortal rise in the excretion of phthalein on any other ground than that bleeding had in some way rendered the kidney hyperpermeable to the dye without having any definite influence on the disease.

But, on the whole, the phthalein test is of great value. These latter observations merely emphasize that to judge the degree of renal insufficiency with accuracy more than one test must be used.

Of substances studied in the blood of nephritics the concentration of the incoagulable nitrogen and urea has been found to be of most importance. Folin and Denis[24] and Marshall[25] have recently devised relatively simple methods for performing these analyses, making possible such estimations as a matter of routine in hospitals with well-equipped laboratories. In regard to the technique employed, readers are referred to the original articles. The older methods required large amounts of blood, and were time-consuming. Nevertheless, Ascoli,[26] Strauss,[27] and others found in severe grades

[22] Arch. Int. Med., 1913, xi, 593.
[23] Arch. Int. Med., 1913, xii, 452.
[24] Jour. Biol. Chem., 1912, xi, 527.
[25] Ibid., 1913, xv, 487.
[26] Pflüger's Arch. f. d. ges. Phys., 1901, lxxxvii, 103.
[27] Die Chronische Nierentzündungen in ihrer Einwirkung auf die Blutflüssigkeit und deren Behandlung, Berlin, 1902, A. Hirschwald.

of nephritis the nitrogen usually though not invariably increased, the increase being much more marked toward death. Obermayer and Popper[28] showed that cases of uremia have a higher incoagulable nitrogen content in the blood than do normal individuals or cases of nephritis without uremia, and that of this nitrogen the urea fraction increases with the development of intoxication. Widal[29] has gone so far as to believe that it is possible to base an approximate prognosis as to length of life on the degree of urea retention.

Opposed to this, Strauss,[30] in a recent paper, describes different clinical types of uremia, and says that high values for blood-nitrogen are usually accompanied by uremic manifestations, but that a low concentration for nitrogen does not mean a favorable outcome for the disease, because fatal uremia may develop when low figures are present as well as when high figures are found. Foster's results bear out this statement. Thus this test is not infallible, and proves again that to judge accurately the degree of renal insufficiency more than one test for renal function must be made.

The relation of faulty sodium chloride excretion to edema in nephritis and its independence of nitrogen retention has been proved by Widal,[31] although Bickel[32] in a series of analyses was unable to find any relationship between the development of uremia and the amount of chloride accumulation in the blood as estimated by electrical conductivity. The apparent contradiction of faulty chloride elimination without an increase of its blood-concentration has been explained by two hypotheses. Bohne,[33] by determining the chloride content of nephritic organs at autopsy in a limited number of cases, believed that the salt was stored in the tissues rather than in the blood, while Marie[34] has assumed that in nephritis, chlorides are retained in a "free" state where they increase the concentration of the blood and tissues, and in this way produce accumulation of fluid or circulate as a "fixed" compound when they are inactive. Whatever the relation of salt retention to edema may be, there is no doubt that certain cases of advanced nephritis with normal function in other regards are unable to excrete sodium chloride and develop edema. The cases reported by Austin and Pepper and by Baetjer show this strikingly. In Baetjer's cases, which were of well-marked nephritis, the phthalein and lactose outputs were normal or increased; yet the patients were unable to excrete chloride, and after its administration retained water. Apparently Austin and Pepper's case is of the same type. This

[28] Ztsch. f. klin. Med., 1909. lxvii, 332.
[29] Bull. et mém. d. hôp. de Paris, 1911, series 3, xxxii, 627.
[30] Deutsch. Arch. f. klin. Med., 1912, cvi, 219.
[31] Verh. des. Cong. f. innere Med., 1909, xxvi, 43.
[32] Deutsch. med. Woch., 1902, xxviii, 501.
[33] Fortschr. der Med., 1897, xv, 121.
[34] Sem. Méd., 1903, xxiii, 385.

shows from another point of view that more than one kind of test must be made to estimate the total renal function.

Finally, there is considerable evidence at hand that certain manifestations of renal insufficiency are produced by the retention of acids in the body, with a consequent acidosis. This can be measured by direct determination of blood-alkalinity, by following the carbon dioxide tension of expired air, since it has been shown to be diminished in various acidoses, or by determining the urinary acidity. Older methods for determining blood-reaction based upon its direct titration against normal acids are inaccurate. Nevertheless, von Jaksch,[35] in 1888, found the reaction of the blood abnormally acid in uremia, and this was confirmed by Peiper[36] and Orlowski.[37] Brandenburg[38] compared the nitrogen of the blood with its reaction in a variety of cases, and made the interesting observation that in uremia there was often an acidosis which bore no relation to the degree of nitrogen retention. While these observations are not beyond criticism, the recent work of Straub and Schlayer,[39] and of Porges and Leimdörfer[40] proves that the results obtained are important. Working with Haldane's instrument, these observers have noted independently a lowering of the carbon dioxide tension in uremic cases, concluding that the condition has to do with acidosis. Sellards,[41] Palmer,[42] and Palmer and Henderson[43] have considered an increased urinary acidity as another sign of acidosis, and have found it a frequent occurrence in nephritis.

All these observations show that the study of renal function in advanced nephritis is extremely complex. A diseased kidney affords as varied a picture in regard to its functional diagnosis as it does in regard to its clinical manifestations. None of the tests, alone, which have been considered, justify a definite estimate of the renal function in every case, nor has their relationship to each other and to the clinical and pathological condition associated with them been controlled in a sufficient number of cases to establish their real meanings. There is no doubt, however, that a variety of tests for renal function helps to make a diagnosis of kidney disease before definite signs of nephritis manifest themselves, and affords accurate information in regard to prognosis by estimating the degree and type of renal insufficiency. Moreover, a series of such tests is of help in treatment.

Widal[44] believes that three distinct symptom complexes occur

[35] Ztschr. f. klin. Med., 1888, xiii, 350.
[36] Virchows Arch., 1889, cxvi, 337.
[37] Cent. f. Stoffw. v. verd. Krankh., 1902, iii, 123.
[38] Ztschr. f. klin. Med., 1899, xxxvi, 267.
[39] Münch. med. Woch., 1912, lix, 568.
[40] Ztsch. f. klin. Med., 1913, lxxvii, 464.
[41] Johns Hopkins Hosp. Bull., 1912, xxiii, 289.
[42] Boston Med. and Surg. Jour., 1913, clxix, 464.
[43] Jour. Biol. Chem., 1913, xiii, 393; Arch. Int. Med., 1913, xii, 146.
[44] Le Mouvement Médical, 1913, i, 1.

in cardiorenal disease. Patients with high blood-pressure suffer from one train of symptoms which include circulatory disturbances, like tinnitus, vertigo, headache, cerebral hemorrhage, or cardiac decompensation. Patients with chloride retention suffer from equally characteristic symptoms. Here edema is the underlying factor. The digestive, nervous, or respiratory organs may be affected, depending on the situation of the edema, with diarrhea, delirium and convulsions, or dyspnea. Patients with nitrogen retention do not develop edema, but show albuminuric retinitis, a progressive loss of appetite, anemia, and coma. Such individuals are subject to ulcerative gastro-enteritis, pleuritis, or pericarditis. Naturally the symptoms become intermixed in advanced cases, so that a sharp division is impossible. But Widal considers that in the "hypertensive" cases the heart must be watched, in the chloride retention cases with edema, a salt-poor diet is indicated, and that the nitrogen retention cases are the most severe and hopeless.

Such a dogmatic division of symptoms in cardiorenal disease needs confirmation. But a rational diet based upon the kidney's selective excretory capacity can be instituted by following the excretion and blood-concentration of nitrogen, salt and water. Von Noorden[45] has formulated general rules for the protective treatment of nephritis. A case can be treated on a less empirical basis, and more as an individual by making these simple tests. It is fair to assume that cases unable to excrete chloride should be given a salt-poor diet; cases unable to excrete nitrogen and with nitrogen accumulation in the blood should be given low protein diets, and cases of acidosis with normal functions in other respects should receive alkalies.

For these reasons, tests for renal function in Bright's disease are important for diagnosis, prognosis, and treatment. The lactose, salt, water, potassium iodide, and nitrogen tests are of special value in the early diagnosis of nephritis. In advanced nephritis the functional condition is so complex that tests to estimate total function are more useful than those designed to study the function of different parts of the kidney. The phthalein excretion is the most satisfactory single test. The non-protein nitrogen of the blood offers additional information in regard to faulty eliminative powers on the part of the kidney. Yet cases occur in which both blood-nitrogen and phthalein are normal, and chloride retention is an important factor in the disease. Finally, acidosis has been shown to exist in uremia. Since no one test is perfect in determining total renal function, cases must be studied from several points of view. A rational dietetic treatment can be given in individual cases based on the conditions disclosed by the study of the kidney's selective excretory capacity.

[45] Metabolism and Practical Medicine, Chicago, 1907, ii, 433.

THE AMERICAN JOURNAL
OF THE MEDICAL SCIENCES

Edited by GEORGE MORRIS PIERSOL, M.D. Monthly. Illustrated. 1920 pa
yearly. Price, $5.00 per annum.

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, founded in 1820, l
long been recognized as the leading medical journal of the English-speaking race. Fr
the first it sought the epoch-making papers, and becoming recognized as their medi
it has, in turn, been sought by those who have had discoveries or real advances in
art and science of medicine to announce in its Department of Original Articles. Dur
1914 *The American Journal* will still further develop a feature that has proved m
useful and popular, namely, a series of Special Articles, written by prearrangement w
men of the highest authority, and covering present-day topics of the greatest imp
tance and interest. These articles are designed to be clinical and practical, and to pres
important advances and the latest knowledge clearly and concisely, with particular refere
to application in daily work. The Department of Book Reviews will continue to comp
critical and discriminating estimates of important new books, as well as briefer notices of bo
of less importance and of new editions. The Department of Progress of Medical Scien
under the charge of recognized specialists, will continue to summarize the actual advances
the art and science of medicine appearing in the leading medical periodicals of the world.

PROGRESSIVE MEDICIN

**A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMEN
IN THE MEDICAL AND SURGICAL SCIENCES, COVERING THE ENTIRE DOMA
OF MEDICINE.** Edited by HOBART AMORY HARE, M.D., Professor of Therapeut
in Jefferson Medical College, Philadelphia; Physician to the Jefferson Medical Colle
Hospital, etc. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeut
Jefferson Medical College, Philadelphia. In four octavo volumes, containing 1200 pag
amply illustrated. Annual subscription price, in heavy paper covers, $6.00, *net;* in clo
binding, $9.00, *net.* Carriage paid to any address.

PROGRESSIVE MEDICINE is the story of the progress, discoveries and improvemen
in the various branches of the medical and surgical sciences, and is published four tim
a year, in March, June, September and December. The matter presented is the digest
essence of the entire medical literature of the world published during the previous twel
months, modified, explained and criticised in the light of the personal experience of the co
tributor. By this method useless information is discarded and only that which is valuable a
really helpful to the practitioner is retained. Practicality and thoroughness are the control
features. The contributors are authorities in their respective lines, and their experience
private and hospital practice enables them to choose unerringly that which their broth
workers require. Every article is original, the veritable product of the author whose na
it bears. The style is narrative in form, hence easy to read. The interpretation of the fa
stated is given and their bearing upon the whole subject under consideration is clearly s
simply indicated.

COMBINATION RATES

THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES	per annum,	$5 00
PROGRESSIVE MEDICINE (heavy paper covers)	"	6 00
PROGRESSIVE MEDICINE (cloth binding)	"	9 00
PROGRESSIVE MEDICINE (paper covers) and the AMERICAN JOURNAL	"	10 00

PHILADELPHIA
706-8-10 SANSOM ST.

LEA & FEBIGER

NEW YORK
2 WEST 45TH ST