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Further Studies of Renal Function in Renal, Cardiorenal and Cardiac Diseases

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FURTHER STUDIES OF RENAL FUNCTION IN RENAL,
CARDIORENAL AND CARDIAC DISEASES*

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The objects of this investigation are (1) to ascertain the value of quantitative determinations of the diastatic activity¹ of urine in revealing renal functional capacity in cardiac, cardiorenal and renal cases; (2) to compare in the same group of cases the findings of diastase, urea and phthalein in the urine with those of urea, total incoagulable nitrogen and cryoscopy in the blood, and (3) to compare the relative value and limitations of the tests of retention with those of excretion.

Renal functional capacity is usually ascertained in one of two ways: (1) *Tests of excretory capacity* through the quantitative determination of the secretion of various substances in the urine—dyes, methylene blue, indigocarmin, rosanilin and phthalein; other chemicals, potassium iodid, lactose, salicylates, sodium chlorid, urea, sugar following phloridzin and the enzyme, diastase. (2) *Tests of retention* through the determination of the concentration of certain substances in the blood, ions—through electrical conductivity, molecules and ions—through cryoscopy, and urea, total incoagulable nitrogen and cholesterolin.

The number of functional tests has increased to such an extent that it is essential to determine which can be discarded without loss. Only through familiarity with the reliability, value, limitations, peculiarities, and the significance of the findings of each test in the various types of disease is the most profitable selection of tests made possible.

THE TESTS EMPLOYED AND THEIR TECHNIC

1. The *phthalein* test² was used according to the usual technic.
2. *Diastase*.³ Diastase has recently been introduced into functional renal work by Wohlgemuth⁴ for determining the relative functional

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1. The expression "diastatic activity of the urine" is used in place of "diastase content" or "quantitative urinary diastase," because at present we have no method for the quantitative estimation of an enzyme, but only methods for the quantitative expression of relative enzymatic activity.

2. Rowntree and Geraghty: *THE ARCHIVES INT. MED.*, 1912, ix, 284.

3. For the results of our diastase studies in unilateral and bilateral surgical diseases of the kidneys, see *Ann. Surg.*, 1913, xxxvii, 801; *Surg., Gynec. and Obst.*, 1914, xviii, 196.

4. Wohlgemuth: *Biol. Ztschr.*, 1909, xxi, 432.

capacity of the two kidneys. A modification of this method was devised by us to make the test adaptable for determining total renal functional capacity. The technic employed was elaborated in conjunction with Dr. Thomas R. Brown, who has demonstrated with it that the total daily output in urine is fairly constant.⁵ The technic was as follows:

One-fifth of the twenty-four-hour urine collected under toluol was neutralized and diluted to 1 L. By means of a graduated 2 c.c. pipet, decreasing amounts of urine were placed in a series of twelve tubes (arranged in a rack) as follows: 1.8, 1.6, 1.4, 1.2, 1, 0.8, 0.6, 0.4 c.c. Ten c.c. of the diluted urine was further diluted to 20 c.c. and of this decreasing amounts placed in the remaining tubes of the series as follows: 0.4, 0.2, 0.1, 0.05 c.c. To each tube was added sufficient 1 per cent. NaCl solution to bring the total volume in each tube to 2 c.c. Two c.c. of a 0.1 per cent. freshly prepared soluble starch solution was added to each tube. The rack with the tubes was placed in a water-bath at 38 C. for a half-hour, then transferred to cold water for three minutes.

^N₅₀ — iodine solution was added drop by drop in amounts sufficient to elicit a permanent color. The occurrence of blue or violet shows incomplete digestion, while the last tube without the violet color indicates the diastatic activity of the urine and from it "d" is calculated. The diastatic activity is expressed by $d \frac{38^\circ}{30'}$, which represents the number of c.c. of 0.1 per cent. starch solution which 1 c.c. of the diluted urine can digest at 38 C. in thirty minutes to products not yielding a blue color with iodine.

The urea content of the twenty-four-hour specimens of urine was determined by the Marshall method.⁶

The principle of Marshall's method consists in the conversion of the urea into ammonium carbonate by means of an enzyme, urease, present in an extract of the soy bean, and the titration of the ammonia with standard hydrochloric acid and methyl orange, directly or after its removal with an air current.

The freezing point of serum was made in the ordinary way, utilizing the Beckman apparatus, 25 to 50 c.c. of blood usually being taken.

The blood urea was determined according to Marshall's⁷ method.

The total non-protein nitrogen of the serum was determined as follows: Ten c.c. of serum was added to 115 c.c. of 95 per cent. alcohol, 100 c.c. of the filtrate being evaporated to dryness. The residue was subjected to Kjeldahl nitrogen determination. The result represents the nitrogen in 8 c.c. of blood.

The values which we accept as normal are as follows: Phthalein, 50 to 60 per cent. for one hour, 60 to 80 per cent. for two hours, $d \frac{38^\circ}{30'}$ = 5 or more, freezing point of serum -56° , total non-protein N of blood .22 — .26 gm. per L. as determined by Folin, and blood urea .20 — .30 gm. per L. Retention of a mild grade occurs in many conditions without apparently serious renal involvement. Only when the retention is considerable do we consider the findings of importance. Such retention we refer to as cumulative phenomena, which means that the freezing-point of blood is at least -0.60 C., the total non-protein nitrogen 0.500 gm. and the urea of blood 0.550 gm. per L.

5. Brown and Smith: Bull. Johns Hopkins Hosp., July, 1914.

6. Marshall: Jour. Biol. Chem., 1913, xiv, 283; xv, 495.

7. Marshall: Jour. Biol. Chem., 1913, xv, 487.

TABLE I.—GROUP A, MILD NEPHRITIS

No.	Name	Date	Clinical Diagnosis	Phthalein Per Cent.		Dias- tase 38° d— 30°	Albu- min	Urea in 24-hr. Urine Gm.	Cryo- copy —()*	Urea per L. Blood Gm.	Total Non- protein N.per L. Blood Gm.	Remarks
				1 hr.	2 hr.							
1	B. 31744	3/26/13	Chronic nephritis; psychasthenia	37	21	0	+	13.5	0.56	0.380	Slight elevation of blood-pressure. Trace albumin and few casts in urine. Lactose excreted in 6 hours, 64 per cent.
2	P. Har- riet Lane	2/12/13	Orthostatic albumin- uria	5	55	2.5	—	8.3	Patient child of 12 years. Albumin dis- appeared in recumbent posture.
3	T. 30165	1/18/13	Febrile albuminuria; mild typhoid fever	42	20	1.7	+	0.530	Trace of albumin present after recovery.
4	S. 30162	1/ 3/13	Acute nephritis.....	20	23	5	+	..	0.58	0.160	Nephritis following turpentine ingestion. Recovery without albuminuria. Guaiae positive.
5	P. 30492	3/12/13	Chronic nephritis; arteriosclerosis	25	15	1.4	++	0.420	Lactose, 6 hours. Discharged, improved, March 14, 1913.
6	P. 30520	3/18/13	Chronic nephritis; neurasthenia	26	18	5	+	Discharged March 12, 1913.
7	H. 30506	3/ 7/13	Chronic nephritis; acute exacerbation	20	21	?	++	15.4	0.64	March 7, 1913, guaiae positive.
		3/31/13	0	±	March 31, 1913, guaiae positive. Dis- charged April 19, 1913, improved.
8	C. 31673	11/ 8/13	Chronic nephritis; albuminuria	60	15	10	±	0.584	Discharged Nov. 14, 1913, unimproved.
9	C.	12/20/13	Chronic nephritis....	49	16	20	±	0.185	
10	L.	2/ 9/14	Albuminuria; mild nephritis	51	9	3.3	0.120	0.294	Lactose normal.
11	S. 32071	2/ 3/14	Acute nephritis.....	23	31	5	+	0.290	0.472	Lactose 12 hours. Guaiae positive. Dis- charged Feb. 18 1914.
12	C. 32178	3/ 8/14	Mild nephritis.....	47	15	6.6	+	0.210	0.455	Lactose 6 hours. Guaiae positive. Dis- charged March 14, 1914, improved.

RESULTS

In a series of 56 cases of medical nephropathies, 60 diastase, 41 phthalein, 30 urea determinations in the urine, together with 27 freezing points, 44 urea or total incoagulable nitrogen estimations in the blood-serum have been made. Opportunity to compare the functional findings with the anatomical changes present in the kidney at autopsy has been afforded in fifteen instances. For ease of presentation and discussion of the results, the cases presented in the accompanying table have been grouped as previously⁸ into Section A, mild nephritis; B, severe nephritis; C, myocardial insufficiency; D, cardiorenal disease.

Group A—Mild Nephritis.—Twelve cases fall into this group. The lowest phthalein encountered was 40 per cent. for two hours, yet no diastatic activity could be detected in two cases, while $d \frac{38^\circ}{30'}$ was less than 2 in two other instances. Details concerning two of these cases can be seen from the following case reports:

CASE 1.—W. B., 31,744. The patient, a physician, aged 45, consulted Dr Barker concerning his shortness of breath. His family history was not of particular interest, nor was his past history, except for two attacks of gout and occipital headache persisting for years. Under strain the patient became weak, nervous and irritable.

For some years he had been aware of the fact that he had a slight albuminuria, a few casts and a slightly increased B. P. The blood picture was practically normal. The eye grounds normal except for slight blurring of upper and nasal margin. Except a B. P. varying from 130 to 160 the physical examination revealed nothing of importance. The Wassermann was negative.

CASE 5.—J. B. P., 30,492.—This patient, 64 years of age, had had the ordinary diseases of childhood, pneumonia as a young man, one attack of gonorrhea followed by stricture, pyorrhea alveolaris for twenty years and an attack of rheumatism fourteen years ago. For four years he has had to urinate once during the night.

Present illness dated back six weeks, starting with slight pain in region of left kidney. Urinalysis showed albumin and casts whereupon his family sent him in for study.

Physical examination revealed slightly palpable radials, B. P. 135, an occasional extrasystole which later disappeared, and a faint aortic systolic murmur which frequently disappeared in erect posture. The Roentgen-ray showed slight dilatation of the arch. The blood picture was normal and the eye grounds showed slight blurring of part of margin of disc. The vessels were slightly tortuous, two small patches suggesting exudate in the left eye. There were no scars or hemorrhages in either eye.

In the remaining eight cases the diastatic findings were in harmony with those of the other tests, two cases showing but a slight reduction in diastatic activity, the others appearing normal.

The findings in Case 7 are interesting. This was considered an acute exacerbation, mild in type, in the course of a chronic nephritis. However, the phthalein was considerably reduced, 41 per cent. for

8. Rowntree and Fitz: THE ARCHIVES INT. MED., 1913, xi, 258.

TABLE 2.—GROUP B, SEVERE NEPHRITIS

No.	Name	Date	Clinical Diagnosis	Phthalein Per Cent.		Diastase 38° d— 30°	Albu- min	Urea in 24-hr. Urine Gm.	Cryos- copy —()*	Urea per L. Blood Gm.	Total Non- protein N.per L. Blood Gm.	Remarks
				1 hr.	2 hr.							
13	M. 30537	4/10/13	Chronic diffuse nephritis	±	±	7.4	+	0.58	Discharged April 29, 1913, improved.
14	K. M. ...	3/ 1/13	Chronic diffuse nephritis; arteriosclerosis	2.5	20.3	0.59	0.846	Diastase at March 12, 1913, 0. Patient better; discharged March 18, 1913.
		3/12/13	0						
15	R. 30228	1/18/13	Chronic diffuse nephritis	±	±	1.7	+++	1.000	Discharged Feb. 20, 1913, improved.
16	R. 30696	3/25/13	Chronic diffuse nephritis; arteriosclerosis	10	14	1.3	±	10.0	0.53	0.460	Discharged March 31, 1914, improved.
17	H. 30585	3/25/13	Parenchymatous nephritis	9	++	10.5	Guaic ++. Discharged March 24, 1913, unimproved.
18	N.	12/ 9/12	Chronic nephritis; hemiplegia	1.3	0	0.61	Died one month later.
19	T. 30253	3/18/13	Parenchymatous nephritis	58	12	5	++	11.5	0.50	0.160	Persistent edema over six months, heavy albuminuria; retention of NaCl.
20	T. 30073	12/12/12	Chronic diffuse nephritis; uremia	±	±	1.7	++	0.880	Died. Incoag. N 2.00 just before death.
21	S. 29680	12/ 8/12	Chronic diffuse nephritis; gout	±	±	1.7	+	0.590	Necropsy 2847. Discharged Dec. 14, 1912, improved.
22	McC.30286	1/21/13	Chronic diffuse nephritis; arteriosclerosis	30	14	1.7	±	0.080	Discharged Jan. 22, 1913.
23	W. 31769	10/ 8/13	Chronic nephritis....	10	7	5	1.030	Discharged Dec. 12, 1913, improved.
24	R. 31674	11/20/13	Chronic nephritis....	8	10	10	++	0.414	0.588	
25	F. 31862	12/19/13	Chronic nephritis....	22	18	2	+	0.222	Discharged Jan. 7, 1914, improved.
26	W.	1/28/14	Chronic nephritis....	20	6	0	+	0.360	0.420	Lactose 12 hours.

two hours (20 per cent. for first hour), which is the lowest phthalein in this group. $D \frac{38^{\circ}}{30'}$ was only 2, while the freezing point was reduced to $-.64$. All the findings are in harmony and point to a more serious involvement than clinically was thought to exist. The drop in $d \frac{38^{\circ}}{30'}$ to 0 three weeks later, at which time the albumin had practically disappeared, is inexplicable as the patient seemed much improved in every way and was discharged in good condition.

No evidence of cumulative phenomena has been encountered in this group except in the instance just referred to, in which the finding was in keeping with the phthalein and diastase findings.

It appears, therefore, that findings of all the tests are in harmony in nine of the twelve cases and that the findings of all the tests, with the exception of diastase, are in accord throughout. The diastatic activity has indicated severe functional involvement in three cases of nephritis in which the clinical picture, history, phthalein test, tests of retention and the subsequent course of events, all showed that the involvement was but slight.

Group B—Severe Nephritis.—Fourteen cases of severe nephritis were studied. The diastatic activity was decreased in all but three instances — $d \frac{38^{\circ}}{30'}$ being 1.7 or lower in ten cases. Two of these patients died, but only one came to necropsy. Zero value for diastase was encountered three times. K. M., No. 14, showed a zero value shortly before leaving the hospital, at which time clinically he seemed much improved. Normal diastatic values were found in Nos. 19, 23 and 24.

In No. 19 the finding is in harmony with all other tests with the exception of salt, toward which a retention existed. The case is of great interest as an instance of hyperpermeability in nephritis and has been reported in detail. Normal diastase findings in Nos. 23 and 24 are irreconcilable with other findings, since the phthalein was markedly decreased and cumulative phenomena were present in both cases.

Depression of the freezing point to $-.61$ was only once encountered (No. 18), the patient dying one month later. In the presence of very severe nephritis, the freezing point was not markedly decreased in three instances (Nos. 13, 14 and 16). Cumulative phenomena as evidenced by urea and total non-protein N of the blood were present in six cases. The low N content in Case 19⁹ (referred to above) is of interest in connection with the high freezing point and normal phthalein

9. This case has been classed as severe nephritis because of clinical findings—marked albuminuria and considerable edema. The findings of the functional studies are prognostically correct, since the patient's condition is now no worse than it was when she was observed two years ago.

TABLE 3.—GROUP C, CARDIAC CASES

No.	Name	Date	Clinical Diagnosis	Phthalein Per Cent.		Dias- tase — d— 30'	Albu- min	Urea in 24 hr. Urine Gm.	Cryos- copy —()°	Urea per L. Blood Gm.	Total Non- protein N.per L. Blood Gm.	Remarks
				1 hr.	2 hr.							
27	S. 30622	4/ 9/13	Myocardial insufficiency; aortic and mitral insuffi- ciency; mitral stenosis	10	+	5.1	Died three days after tests.
28	B. 30875	5/29/13	Myocarditis; miliary TB; pericarditis; chronic pas- sive congestion	18	10	0	0	Extreme chronic passive conges- tion at autopsy. Kidneys other- wise normal.
29	K. 30655	6/ 5/13	Arteriosclerosis; myocarditis	40	2.5	+	Broken compensation present at time of test. Lactose 9 hours. Discharged Aug. 8, 1913. Improved.
30	J. 30704	5/29/13	Myocardial insufficiency; aortic insufficiency; myo- carditis	23	18	0	+++	Died in broken compensation, which was severe at time of all tests. Kidneys showed only chronic passive congestion.
		6/ 5/13	5	+++
31	B. 30625	4/ 9/13	Myocardial insufficiency; aortic insufficiency; arterio- sclerosis	10	0	Convalescing at time of test. Dis- charged April 13, 1913; condition improved.
32	L. 30618	3/31/13	Myocardial insufficiency...	1.4	+	3.7	0.54	Moderate broken compensation at time of test. Discharged June 24, 1913, unimproved.
33	H. 30380	3/ 7/13	2.3	+	8.1	Patient died without recovering compensation. Autopsy 3915.
		3/26/13	Acute endocarditis; acute lobar pneumonia; poly- serositis	10	+	19.2	0.56	0.355
34	J. 30461	3/ 7/13	Myocardial insufficiency; aortic and mitral insuffi- ciency	10	0	17.6	Broken compensation at time of test. Discharged April 3, 1913, improved.
35	E. 30398	2/25/13	Myocardial insufficiency; aortic and mitral insuffi- ciency	99	25	2.3	++	10.2	0.48	0.168	Severe broken compensation; death without recovery. Kidneys nor- mal at autopsy except chronic passive congestion.
36	C. 30178	1/18/13	Myocardial insufficiency; pericarditis; myocarditis	2.5	+	0.56	Died. Kidneys normal at autopsy, 3870.
37	A. 30291	1/17/13	Myocarditis	36	19	1.7	+	...	0.67	0.470	Autopsy: Chronic passive conges- tion, myocarditis. Kidneys other- wise normal. 3858.
			0	+	13.4	Died May 3, 1913.
38	K. 30802	5/ 2/13	Myocardial insufficiency; mitral insufficiency; arterio- sclerosis	16	17	0	+	13.4
39	M. 30503	3/ 7/13	Myocardial insufficiency; aortic insufficiency; arterio- sclerosis	0	±	8.6	0.58	0.422	Guaiac +. Discharged March 28, 1913, improved.
40	H. 30666	3/10/13	Myocardial insufficiency; arteriosclerosis	2.5	—	13.4	In broken compensation at time of test. Discharged May 13, 1913, improved.
			Mitral stenosis; mitral in- sufficiency; hemiplegia	2.3	±	39.7	Severe broken compensation at time of test. Died. Kidneys nor- mal except for chronic passive congestion.
41	G. 30499	3/ 7/13	2.3	±	39.7

and normal diastatic activity. The rapid increase in the total non-protein N in Case 20, reaching 2 gm. per L. just prior to death, is also worthy of note.

No serious disagreement in the findings of the various tests in this group is encountered, except that diastatic activity is normal in two cases of severe nephritis which show cumulative phenomena.

In considering diastase as an index of the functional capacity of the kidney in uncomplicated nephritis, it is evident that in the majority of instances it is of some value. In three cases of mild nephritis, however, severe involvement of function has been indicated where the other tests and the clinical history fail to substantiate this, while in two cases of severe nephritis with very low phthalein output and with cumulative phenomena, no decrease at all in functional capacity is indicated. Since its findings are entirely out of harmony in five cases in a series of twenty-six, obviously no absolute reliance can be placed in it. The test must be considered of only corroborative¹⁰ value.

Group C—Cardiac Cases.—Fifteen cardiac cases, myocardial insufficiency, endocarditis, etc., unassociated with nephritis were studied, eight of them coming to necropsy. As previously pointed out, these cases rarely have the markedly decreased phthalein output which is seen in severe grades of nephritis, although they may present a similar clinical picture. Only when the passive congestion is of an extreme grade is the phthalein output much reduced. With restoration of compensation, the phthalein rapidly becomes normal again. Of the six cases in which the phthalein output was studied, five patients died. Two had more than a 50 per cent. output, two 40 per cent., one 33 and one 28 per cent. In severe myocardial breaks there is some tendency to a reduction of the output for the first hour (the highest output for the first hour was 36 per cent.), with a fair output the second hour. In many instances the outputs for the first and second hours are nearly equal. In this condition the first hour excretion is often a truer index to function than that for two hours.

Diastase determinations were made in all these cases. Three patients died with a perfectly normal diastatic activity, although two of these had earlier showed a decreased content. Four others died with a fair activity, two with a zero output, while two did not die, although the diastase was very low—zero in one instance. Therefore, little dependence, prognostically or diagnostically, can be placed on the diastase findings.

As has been previously pointed out by Strauss and Hohlweg, marked increase in blood urea and total non-protein N is not fre-

10. Where the findings of the diastase test conflict with those of the phthalein, blood urea or blood nitrogen, we would discard the former.

TABLE 4.—GROUP D, CARDIO-RENAL CASES

No.	Name	Date	Clinical Diagnosis	Phthalein Per Cent.		Dias- tase 38° d— 39°	Albu- min	Urea in 24-hr. Urine Gm.	Cryo- copy —()	Urea per L. Blood Gm.	Total Non- protein N. per L. Blood Gm.	Remarks
				1 hr.	2 hr.							
42	Z. 31821	12/12/13	Chronic nephritis; myocar- dial insufficiency	60	13	2.5	++	0.320	Discharged Dec. 13, 1913, improved.
43	J. 30469	2/25/13	3.3	+	15.9	0.57	0.480	Mild broken compensation at time of test. Discharged March 14, 1913, improved.
		3/ 7/13	Myocardial insufficiency; aortic and mitral insuffi- ciency; chronic nephritis	21	5	5	+	
44	B. 30117	12/21/12	Myocardial insufficiency; chronic nephritis	14	21	++	0.58	0.320	In broken compensation at time of test. Discharged Feb. 19, 1913, improved.
45	G. 31757	1/ 3/13	Myocardial insufficiency; chronic nephritis	51	15	20	+	0.56	0.340	Convalescent at time of test.
46	B. 30599	2/25/13	Myocardial insufficiency; chronic nephritis	50	13	2.5	++	20.1	0.050	In broken compensation at time of test. Discharged April 9, 1913, improved.
47	J. 30482	3/12/13	Myocardial insufficiency; hemiplegia; chronic neph- ritis	40	18	5	+	30.2	0.390	In broken compensation at time of test. Died.
48	S.	5/29/13	Myocardial insufficiency; mitral insufficiency; arterio- sclerosis; chronic nephritis	12	45	0	Fair compensation at time of test.
49	B. 30486	3/ 7/13	Myocardial insufficiency; chronic nephritis	44	11	5	+	19.8	0.59	0.280	0.280	Discharged Mar. 21, 1913, improved.
50	S. 30632	4/ 9/13	Myocardial insufficiency; aortic insufficiency; arterio- sclerosis; chronic nephritis	40	17	1.3	--	19.8	0.00	0.460	In moderate broken compensation at time of test. Discharged May 3, 1913, improved.
51	C. 30679	4/ 9/13	Myocardial insufficiency; aortic insufficiency; chronic nephritis	2	+	6.2	In moderate broken compensation at time of test. Discharged April 11, 1913, improved.
52	G. 30554	4/ 2/13	Myocardial insufficiency; myocarditis; acute endo- carditis; chronic diffuse nephritis	0	+	19.4	0.50	1.100	Chronic passive congestion of kid- neys; otherwise normal at au- topsy, 3069.
53	G. 30658	4/ 2/13	Myocardial insufficiency; arteriosclerosis; chronic nephritis	0	+	19.1	0.55	0.650	In broken compensation at time of test. Discharged May 28, 1913, improved.
54	J. 30680	3/26/13	Myocardial insufficiency.....	5	++	Discharged Mar. 30, 1913, improved.
55	J. 31796	12/18/13	Myocardial insufficiency; chronic nephritis	90	10	±	0.300	0.322	Discharged Dec. 30, 1913, improved.
56	R. 31752	11/27/13	Myocardial insufficiency; chronic nephritis	48	20	2.5	+	0.518	Discharged Dec. 10, 1913, improved.

quently seen¹¹ in pure passive congestion. A cumulative phenomenon is only seen once in six cases in which such studies were made, e. g., Case 37 in which the freezing point was $-.67$ and total incoagulable nitrogen on the upper limit of normal, $.47$ gm. per L.

Group D—Cardiorenal Cases.—Fifteen cases fell into this group, three of which ended fatally. The relative and absolute degree of cardiac and renal involvement varied much in the different cases, so that practically all types of cardiorenal cases are included.

One patient (No. 47) died showing a normal diastase during a cardiac break in nephritis. The phthalein here was 40 per cent. first hour and 18 per cent. second hour. Two patients (Nos. 52 and 53) died with a zero output and one of these showed only a chronic passive congestion at necropsy. Two (Nos. 48 and 51) left the hospital improved after exhibiting a zero output. In six cases a normal diastase was encountered, but in three of these the renal function was good as indicated by the other tests.

It has been previously pointed out that diseases of the kidney may be clinically identical, but functionally and pathologically different, and that by the aid of the phthalein test it is possible to determine in any given cardiorenal case whether the heart or the kidney is relatively more responsible for the clinical picture presented. This is not possible by the diastase test, since the diastatic activity seems to be markedly but inconstantly depressed in both cardiac and renal disease.

Cumulative phenomena were encountered in only three cases, all of which died. Case 52 is of special interest as the necropsy showed no changes other than passive congestion, although the blood urea was 1.1 gm. per L. The freezing point was at the same time not at all depressed.

*Influence of Blood and of Albumin on Diastatic Activity.*¹²—In the foregoing table blood is recorded in the urine in seven instances. In the other cases microscopical examination or the guaiac test failed to show its presence. Three cases of mild nephritis showed blood and a normal or high "d." A mild nephritic on two occasions showed a low "d," one severe nephritic and one cardiac case a zero "d" value in the

11. We have now seen three cases in which cumulative phenomena have been encountered in pure chronic congestion, e. g., Cases 37 and 52 and a third case which has been reported by Marshall and Davis.

12. As stated above, this test deals only with "diastatic activity" and not with "diastase content." The activity is dependent on environment and not on actual amount of diastase. Only the influence of albumin and blood have been considered here, since they have entered into the interpretation of the findings of the test in the hands of certain authors.

presence of blood. According to Wohlgemuth¹³ and to Corbett,¹⁴ blood accelerates diastatic activity.

Wohlgemuth¹⁵ and Neumann¹⁶ do not consider that the presence of albumin affects the diastatic activity of the urine, while Corbett and Geyelin¹⁷ think that it may, claiming that higher findings are encountered in cases with marked albuminuria.

In the sixty diastase determinations made, the presence or absence of albumin was noted in fifty-six instances, with forty-eight positive findings. Exact quantitative studies of the albumin content were not made, the amount present being indicated as a trace, +, + +, etc.

In the twelve cases of mild nephritis six cases showed a normal or high "d" value. In none of these was there much albumin in the urine, but in three the guaiac test was positive. Only once (Case 7) was much albumin present, the "d" value was low, but later with less albumin the "d" sank to 0—blood still persisting in the urine.

In fourteen cases of more severe nephritis much albumin was present in five instances and in two of these a normal "d" was encountered. One of these cases (No. 19) had normal function indicated by all other tests except the salt test, so that it is not necessary to assume that the albumin was responsible for the high "d" value in this instance. In Case 17, despite the presence of large amounts of albumin and the presence of blood, a zero "d" value was present.

In fifteen cardiac cases much albumin was present in three instances and a normal diastase value only once. Case 29 with about the same amounts on each occasion gave a 0 value at first and a normal one later. The patient died. The phthalein here showed definite functional impairment, 23 and 18 per cent. for the first and second hours, respectively—the first hour reading being probably the truer index to the function.

In fifteen cardiorenal cases much albumin was present in four cases and normal diastase once in three of the four cases in which it was determined. In the series of severe renal and cardiorenal cases, twelve instances of marked albuminuria were found and in only four cases was "d" normal or higher, while in four it was 1.7 or 0.

Analysis of our data does not indicate that albumin plays a great rôle in activating diastase. Are we justified, then, in ascribing high or normal values in the presence of marked albuminuria to activation of diastase by the albumin? In Case 19 we have an instance of hyper-

13. Wohlgemuth: *Ztschr. f. Urol.*, 1911, v, 801.

14. Corbett: *Quart. Jour. Med.*, 1913, vi, 365.

15. Wohlgemuth states that with the technic here employed no activation occurs unless the albumin is present in large amount.

16. Neumann: *Deutsch. Arch. f. klin. Med.*, 1913, cxi, 164.

17. Geyelin: *THE ARCHIVES INT. MED.*, 1914, xiii, 96.

permeability of the kidney—high phthalein, 70 per cent. for two hours, normal diastase, normal urea output, no cumulative phenomena but retention of salt. It is not necessary to assume that the diastatic activity has been accelerated by the albumin.

First it seems advisable to determine whether or not albumin does activate diastase, and if it does, to what extent. In case it does, then it must be determined whether the character of the albumin or the quantity plays a rôle and to what extent. Since albuminuria is almost constant in conditions in which the diastatic activity is determined, and since marked albuminuria may be associated with zero and low "d" values, it constitutes a serious defect in the test to attempt to ascribe normal or high findings in certain instances to the presence of albumin. Uncertainty as to the interpretation of the findings of a test must of necessity decrease the practical value of that test.

CONCLUSIONS

1. The quantitative estimation of the diastatic activity of the urine as it is employed at present shows low values in the majority of cases of mild and severe nephritis, while in cardiac and cardiorenal cases the diastase findings are bizarre. Owing to the frequent occurrence of normal diastatic values in cases in which considerable or grave renal functional involvement is unquestionably present, and of low diastatic values which are not in accord with the clinical course of the case or with findings of other functional tests, no diagnostic or prognostic significance attaches to this test, other than that which is corroborative in character. As a single test it is unreliable. Further data as to the influence of albumin on the "d" value are desirable.

2. The phthalein test is the one of choice and unquestionably the most valuable single test in this group of cases.

The total non-protein N and urea content of the blood are of about equal value in severe cases, while the freezing point of the serum is probably of somewhat less value since depression in the freezing point is lacking in several instances in which one or both of the other tests indicate that retention is present.

3. Both tests of excretion and of retention are valuable. In all cases a phthalein test is advisable. *Whenever the phthalein output is decreased even but slightly the total non-protein nitrogen or the blood urea or both should be determined.*

