STUDIES OF THE KIDNEY IN ACUTE INFECTION

III. Observations with the Urine Sediment Count (Addis) and the Urea Clearance Test in Lobar Pneumonia[1]

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McIntosh and Reimann (1) reviewed some previous studies on kidney function in pneumonia. They found that of six investigators, three reported impairment of renal function (2, 3, 4), two reported the absence of impairment (5, 6), and one (7) emphasized the occurrence of renal hyperfunction during the course of lobar pneumonia. It seemed to them that a further series of observations was necessary to throw some light, if possible, on the cause for such discordant results. The tests employed were the phenolsulphonphthalein test and the ure aconcentration index (8). Thirteen patients were studied. They reported renal hyperfunction, by one or the other of the tests employed, in nine patients and moderate depression of renal function in four. In no instance was there encountered serious impairment of renal function.

In a previous study (9), we showed by means of the urine sediment count, that during the course of acute rheumatic infection, there is an abnormal increase in the excretion of formed elements in the urine, persisting for some weeks after recovery, with a final return to normal. In another study (10) we showed by means of the urea clearance test, that during the acute phase of rheumatic infection there occurred a period of renal hyperfunction, followed, in the convalescent phase by a period of renal hypofunction. The latter functional state persisted for a varying number of days and in every instance where the patient was observed over a sufficient period of time, it was followed by com-

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TABLE 1

Urine sediment count in normal persons

Number	pH	Specific gravity	Urine volume per 12 hours	Protein per 12 hours*	Red cells per 12 hours	White and epithelial cells per 12 hours	Casts per 12 hours†
			cc.	*mgm.*	*millions*	*millions*	*thousands*
1	5.0	1.030	369	5.3	0	0.220	9.2
2	5.0	1.040	259	18.0	0	0.064	0
3	5.0	1.031	473	10.2	0	0.118	0
4	5.5	1.023	355	12.8	0	0.117	0
5	5.0	1.044	208	8.9	0	0.062	0
6	5.0	1.020	616	22.1	0	0.077	0
7	5.5	1.010	776	8.4	0	0.580	0
8	5.0	1.027	228	32.8	0	0.300	3.8
9	5.8	1.027	408	57.7	0	0.730	0
10	5.5	1.027	269	23.1	0	0.670	2.2
11	6.7	1.032	186	26.8	0	0.600	4.1
12	5.6	1.028	337	24.8	0	0.400	0
13	5.0	1.036	147		0.009	0.082	0
14	5.8	1.030	259	18.6	0.010	0.790	0
	5.7	1.028	234	16.8	0.260	1.100	7.8
15	5.5	1.028	285	42.0	0.010	0.810	3.2
16	5.0	1.040	158	5.6	0.013	0.115	0
17	5.5	1.018	145	10.4	0.020	0.290	2.2
18	5.0	1.035	170	18.3	0.020	0.360	0
19	5.0	1.028	80	5.8	0.022	0.520	0
20	5.5	1.032	335	21.7	0.027	1.360	
21	5.5	1.026	343	17.2	0.028	0.056	0
22	5.0	1.038	274	60.2	0.034	0.180	0
23	6.5	1.027	360	25.9	0.040	0.470	2.0
24	5.5	1.022	344	49.5	0.050	0.270	1.8
	5.0	1.027	186	26.6	0.090	0.720	1.0
25	5.5	1.036	226	26.2	0.060	0.190	0
26	5.8	1.029	239	29.3	0.070	0.370	0
27	5.7	1.020	363	52.2	0.070	0.700	2.0
28	5.0	1.032	287	15.4	0.071	0.262	0
29	6.5	1.024	387	13.9	0.072	0.097	0
30	5.0	1.034	137	2.9	0.076	0.340	0
31	5.3	1.034	220		0.088	0.638	0
32	5.0	1.034	120	7.8	0.127	3.400	0.5
33	5.5	1.037	187	26.9	0.130	0.280	2.1
34	5.5	1.030	237	34.2	0.140	0.630	2.6
35	5.0	1.036	414	17.9	0.145	0.028	0
36	5.5	1.042	210	9.0	0.157	0.131	0

* Centrifuge method (see reference 15).

† All were of the hyalin variety.

TABLE 1—*Concluded*

Number	pH	Specific gravity	Urine volume per 12 hours	Protein per 12 hours*	Red cells per 12 hours	White and epithelial cells per 12 hours	Casts per 12 hours†
			cc.	*mgm.*	*millions*	*millions*	*thousands*
37	6.5	1.026	385	22.1	0.159	0.192	0
38	5.5	1.027	205	10.2	0.205		0
39	6.0	1.031	312	33.7	0.160	0.810	0
	5.0	1.030	348	30.1	0.200	0.870	3.8
40	5.8	1.031	256	28.7	0.210	0.320	0
41	5.5	1.033	384	46.0	0.300	0.830	6.4
42	5.5	1.028	302	6.5	0.390	1.040	0
43	5.0	1.030	293	42.2	0.560	2.430	0
44	5.0	1.033	218	22.3	0.650	1.270	4 8
45	5.5	1.038	355	15.3	0.931	0.047	3.9
	5.0	1.043	280	10.0	1.530	0.024	0
Average				21.8	0.146	0.540	1.3

plete restitution of normal renal function. Since there was no reason to believe that such findings should be peculiar to acute rheumatic infection alone, we decided to repeat the same observations in a group of patients with lobar pneumonia.

Adult patients were selected from a series under investigation by the pneumonia service. No patients were selected who presented signs or gave a previous history of congestive heart failure, nephritis, or hypertension. Patients who developed reaction from pneumococcus serum were likewise excluded. The urine sediment counts were performed according to the technique described by Addis (11). The urea clearance test was performed according to the technique described by Möller, McIntosh and Van Slyke (12), and McKay (13). Blood and urine urea nitrogen determinations were made by the gasometric method of Van Slyke (14). Both urine sediment counts and blood urea clearances were made at intervals during the acute stage of the disease and during convalescence.

Table 1 indicates the results of 49 urine sediment counts performed on 45 medical students in whom there was no reason to suspect abnormality in the kidneys. The urinary protein was determined by the method described by Shevky and Stafford (15). We felt it was reasonable to accept as the upper limit of normal excretion for a

TABLE 2

Quantitative study of the 12 hour urine sediment in lobar pneumonia

Name	Number	Date	Urine volume per 12 hours	pH	Specific gravity	Protein per 12 hours	Red blood cells per 12 hours	White and epithelial cells per 12 hours	Casts per 12 hours	Temperature	Date of termination
			cc.			*mgm.*	*millions*	*millions*	*thousands*	*°F.*	
A	1	March 26, 1930	118.0	5.0	1.010	200.00	0.06	0.70	13.0	103.0	March 27, 1930
		March 29, 1930	153.0	5.0	1.016	90.00	0.20	1.48	0.0	102.6	
		April 9, 1930	143.0	5.0	1.010	2,162.00	13.50	5.24	1,120.0	99.0	Onset of diffuse glomerulonephritis April 9, 1930
		April 12, 1930	251.0	5.0	1.013	2,349.00	37.37	7.90	2,649.0	99.2	
		May 15, 1930	1,520.0	5.0	1.007	4,529.00	11,160.00	0.15	0.0	98.8	
Ba	2	January 25, 1930	636.0	5.0	1.020	230.40	46.43	2.45	44.2	101.2	January 26, 1930
		February 8, 1930	680.0	5.0	1.008	97.00	0.60	1.11	28.3	99.6	
Bb	3	October 25, 1929	510.0	5.5	1.020	826.00	0.13	1.45	7.1	103.0	Died October 26, 1929
Bc	4	March 13, 1930	400.0	5.0	1.026	2,000.00	0.05	2.45	0.0	104.8	Died March 16, 1930
Bd	5	March 25, 1930	844.0	5.5	1.013	90.00	1.27	6.00	3,446.0	103.0	Died March 26, 1930
Be	6	January 21, 1930	910.0	5.5	1.022	255.00	0.25	1.50	0.0	102.2	
		January 27, 1930	380.0	5.0	1.022	164.20	0.19	6.68	460.0	102.2	January 29, 1930
Ca	7	December 11, 1929	184.0	5.5	1.034	39.70	0.83	1.40	92.0	104.8	December 10, 1929
Cb	8	February 5, 1930	392.0	5.0	1.018	197.60	0.00	1.47	147.0	101.6	February 6, 1930
Cc	9	December 31, 1929	705.0	6.0	1.018	110.00	0.38	2.77	2,270.0	99.2	December 30, 1929
Cd	10	December 18, 1929	404.0	5.0	1.022	20.00	0.00	0.00	0.0	104.0	Died December 21, 1929
Ce	11	April 12, 1930	357.0	5.0	1.018	899.50	0.54	1.88	79.5	102.0	
		April 24, 1930	286.0	5.0	1.018	113.00	0.93	6.00	63.0	103.8	Empyema May 7, 1930
Da	12	December 20, 1929	576.0	5.0	1.018	36.00	0.59	2.66	30.0	102.6	December 21, 1929
		December 30, 1929	430.0	5.0	1.030	154.00	9.90	418.00	0.0	99.6	
		January 4, 1930	340.0	5.5	1.032	73.40	0.09	2.34	4.7	100.0	
		January 8, 1930	265.0	5.0	1.024	133.80	6.63	400.00	0.0	100.0	
Db	13	February 7, 1930	760.0	5.0	1.008	300.90	1.71	0.09	0.0	100.0	February 7, 1930

F	14	January 11, 1930	460.0	5.0	1.026	62.20	0.00	1.60	0.0	100.6	January 11, 1930
Ga	15	March 4, 1930	484.0	5.5	1.011	1,036.80	0.36	1.50	0.0	101.0	March 6, 1930
Gb	16	April 4, 1930	702.0	5.0	1.022	8,027.00	2.63	9.48	20.0	105.0	Died April 6, 1930
Gc	17	March 7, 1930	730.0	5.0	1.018	1,576.00	30.84	4.01	9,733.0	104.6	Died March 25, 1930
Gd	18	April 1, 1930	327.0	5.0	1.020	150.00	0.08	0.57	45.4	103.8	April 3, 1930
		April 15, 1930	344.0	5.0	1.021	30.00	0.09	1.41	19.0	102.0	
		April 24, 1930	367.0	5.0	1.012	53.80	0.09	0.55	50.9	99.0	
Ge	19	February 7, 1930	1,424.0	5.0	1.010	153.00	0.00	6.10	0.0	105.0	March 1, 1930
Ha	20	March 19, 1930	511.0	5.5	1.022	490.00	1.53	8.34	94.2	99.0	March 19, 1930
		March 24, 1930	710.0	5.0	1.025	50.00	0.35	2.10	9.7	99.2	
Hb	21	January 11, 1930	570.0	5.0	1.026	102.00	0.14	2.00	31.6	101.6	January 11, 1930
Ka	22	February 22, 1930	367.0	5.0	1.015	85.50	0.92	6.42	2,230.0	103.8	February 24, 1930
Kb	23	April 25, 1930	480.0	5.0	1.010	1,019.00	0.12	2.52	100.0	104.0	April 29, 1930
Kc	24	February 3, 1930	186.0	5.0	1.032	133.90	0.14	0.74	6.8	103.2	February 5, 1930
Kd	25	April 23, 1930	125.0	5.5	1.011	32.00	0.00	0.09	0.0	103.6	May 9, 1930
La	26	January 21, 1930	227.0	5.0	1.030	326.88	0.00	2.09	6.3	102.2	
Ma	27	October 24, 1929	282.0	5.5	1.017	20.30	0.07	0.70	0.0	103.6	Died November 12, 1929
Mb	28	December 31, 1929	303.0	5.5	1.020	359.90	0.37	1.89	993.2	102.8	Died January 1, 1930
Mc	29	January 25, 1930	98.0	5.0	1.020	21.20	0.01	0.09	0.0	101.0	January 28, 1930
		February 7, 1930	327.0	5.0	1.018	109.00	0.04	0.02	45.1	99.6	
Md	30	January 4, 1930	1,168.0	5.0	1.014	336.40	0.58	0.58	0.0	102.2	January 5, 1930
		January 8, 1930	780.0	5.0	1.015	168.00	0.09	1.46	0.0	100.6	
Me	31	May 9, 1930	2,592.0	5.5	1.001	170.00	0.77	28.42	0.0	99.8	April 16, 1930
		May 14, 1930	1,028.0	5.0	1.003	140.00	0.51	9.25	0.0	100.2	Onset of diffuse glomerulonephritis May 3, 1930
		May 21, 1930	941.0	5.0	1.007	135.00	0.00	1.56	0.0	99.6	
Oa	32	February 26, 1930	707.0	5.0	1.014	267.12	0.09	2.74	3,731.0	103.8	
Ob	33	January 29, 1930	250.0	5.5	1.015	1,980.00	3.70	2.77	0.0	102.0	
Pa	34	October 22, 1929	97.0	5.0	1.028	1.40	0.06	0.23	5.4	98.8	
Sa	35	March 24, 1930	463.0	5.0	1.014	572.24	1.16	0.00	0.0	105.0	Died March 24, 1930
Sb	36	April 22, 1930	289.0	5.5	1.018	1,500.00	0.96	11.16	6,036.8	104.4	Died April 23, 1930

TABLE 2—*Concluded*

Name	Number	Date	Urine volume per 12 hours	pH	Specific gravity	Protein per 12 hours	Red blood cells per 12 hours	White and epithelial cells per 12 hours	Casts per 12 hours	Temperature	Date of termination
			cc.			*mgm.*	*millions*	*millions*	*thousands*	°*F.*	
Sc	37	March 18, 1930	620.0	5.0	1.019	691.90	1.70	27.59	0.0	105.8	March 22, 1930
		March 25, 1930	1,064.0	5.5	1.010	170.00	6.38	291.54	0.0	99.8	
Sd	38	October 26, 1929	410.0	5.0	1.028	30.50	0.05	0.71	5.7	102.8	Died October 30, 1929
Ta	39	April 10, 1930	436.0	5.0	1.024	25.00	0.00	1.80	57.6	105.4	Died April 13, 1930
Ua	40	March 12, 1930	788.0	5.0	1.001	195.00	0.09	2.07	0.0	99.2	February 6, 1930
Va	41	May 20, 1930	684.0	5.0	1.018	2,462.00	0.00	0.68	38.0	104.4	
Wa	42	May 15, 1929	598.0	5.0	1.026	14.68	1.04	2.23	1,605.9	99.2	May 8, 1929
		May 20, 1929	415.0	5.0	1.026	180.00	0.78	1.38	553.0	99.0	
		May 23, 1929	590.0	5.0	1.028	53.00	0.49	0.79	190.0	98.6	
		May 31, 1929	583.0	5.0	1.023	37.80	0.17	1.92	372.0	98.6	
Wb	43	February 14, 1930	650.0	5.0	1.011	193.70	1.54	27.44	0.0	103.4	February 18, 1930
		February 22, 1930	113.0	5.5	1.018	24.40	0.56	17.80	0.0	99.0	
Za	44	February 18, 1930	388.0	5.0	1.022	83.80	0.63	1.55	882.6	104.6	
		February 24, 1930	433.0	5.5	1.020	124.70	1 95	1.41	0.0	99.6	February 24, 1930
		March 3, 1930	427.0	5.0	1.008	122.98	20.33	29.46	0.0	99.6	

period of 12 hours, 500,000 red blood cells, 1,000,000 white blood cells, and epithelial cells, 5,000 casts, and 30 mgm. of protein (16).

Table 1 in the preceeding paper, indicates the results of 34 blood urea clearance determinations in 17 patients and medical students in whom there was no past or present evidence of renal disease. The normal range varies from 75 per cent to 125 per cent of normal renal function.[2]

Table 2 shows the results of the urine sediment counts in 44 patients with lobar pneumonia. By comparison with table 1, it is evident that at some period during the precritical stage of lobar pneumonia, 38 of 44 patients showed an abnormal excretion of protein and one or more of the formed elements. There were 40 sediment counts made when the temperature was 101°F. or higher. Of these, protein was excreted in greater amount than 30 mgm. per 12 hours 34 times. Casts were excreted in greater number than 5,000 per 12 hours 26 times. White blood cells and epithelial cells were excreted in greater number than 1,000,000 per 12 hours 29 times. However red blood cells were excreted above the normal rate of 500,000 per 12 hours only 16 times. The occurrence of microscopic hematuria in the course of lobar pneumonia appears to be of greater significance than the occurrence of abnormal excretion in the urine of the other formed elements or protein (16). The extent of the microscopic hematuria appears to carry no significance as far as its interpretation goes. Of more importance is the time of occurrence of hematuria and its subsequent behavior. This fact is demonstrated by two of our patients. Patient 1 had a fairly normal urine sediment before and immediately after the crisis. However, microscopic hematuria made its first appearance 12 days after the crisis and on repeated tests this progressed to frank bloody urine. The almost concomitant occurrence of hypertension and generalized edema with progressive renal functional failure indicated the development of acute diffuse glomerulonephritis. Part of the clinical course in this patient is shown in chart 1. The same complication was observed in patient 31 with the exception that the hematuria was entirely microscopic, practically negligible in degree, and cleared up more rapidly. The clinical course in this patient is

[2] For further details of the blood urea clearance test see reference (12).

shown in chart 2. Whether the pneumococcus or a secondarily invading streptococcus was responsible for the nephritis in these two patients is not possible to say with certainty.

Of entirely different significance is the hematuria which occurred in patients 2, 20, 30, 42, and 43. In these patients microscopic hematuria occurred before or about the time of the crisis, disappearing completely, promptly after the crisis. With the onset of microscopic

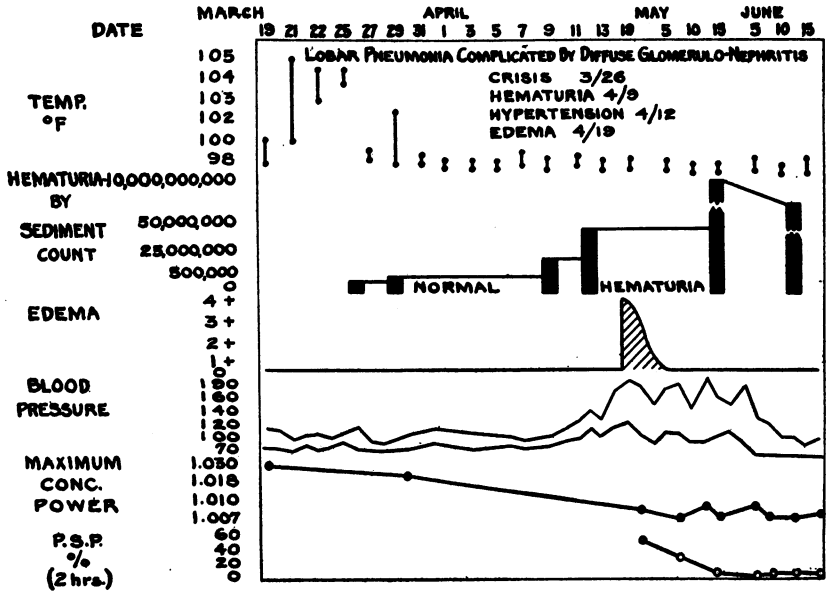

CHART 1. Patient A, Number 1. White, male, aged 39. Hematuria was first noted 14 days after the crisis. Then followed a rise in blood pressure, generalized edema including the face and impairment of renal function. Hematuria and impaired renal function were present at a subsequent examination, 2 months after discharge.

hematuria during the acute phase of the disease, its prompt disappearance and the absence of systemic manifestation, hypertension, and edema, these cases must be interpreted as instances of focal glomerulitis and are of no prognostic significance. In patient 44 the occurrence of hematuria, for the first time, in convalescence is highly suggestive of the onset of diffuse glomerulonephritis, but the absence of hypertension or edema and the lack of renal function study, makes it

impossible to be certain of any more than a focal glomerular lesion. The appearance or disappearance of microscopic hematuria apparently bears no relationship to the excretion rate of the other formed elements or protein. These appear to be of different pathogenesis as well as of different significance as far as our observations go. Apparently a more severe renal lesion is necessary to permit the excretion of red

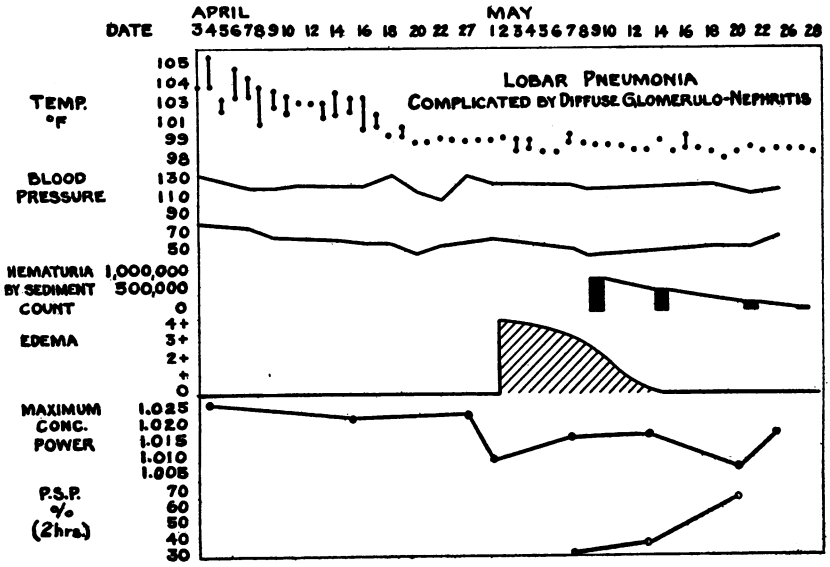

CHART 2. Patient Me, Number 31. While male, aged 31. Generalized edema involving the face was first noted 13 days after the crisis. Distinct hematuria was not present one week after the onset. The blood pressure did not rise, but renal function was temporarily impaired. Patient left the hospital apparently well.

blood cells. This fact had been previously observed in studying the urine sediment in congestive heart failure (16).

In table 3 are shown the results of the blood urea clearance test during the acute and convalescent stages of lobar pneumonia. Our results confirm the findings of McIntosh and Reimann (1). Of 13 patients studied, 9 showed a period of renal hyperfunction (increased urea excreting activity) during the acute stage, 2 showed a period of renal hypofunction (decreased urea excreting activity) during the acute stage, and 2 showed no change from normal function. Of the 9

TABLE 3

*Blood urea clearance test in lobar pneumonia**

Name	Number	Date	(B) Blood urea nitrogen	(U) Urine urea nitrogen	(V cor.) Urine volume corrected†	Kidney function per cent of average normal	Temperature	Result
			mgm. per 100 cc.	*mgm. per 100 cc.*	*cc. per minute*	*per cent*	°F.	
		March 25, 1930	24.8	1,309.0	1.310	112.0	103.0	Crisis March 27
		April 8, 1930	31.95	1,096.0	0.909	60.7	99.2	
Aa	1	April 16, 1930	31.5	591.0	1.245	39.8	99.6	
		April 17, 1930	15.5	480.0	1.425	68.4	98.4	
		May 21, 1930	12.8	474.0	1.825	9.3	99.0	
Bb	2	October 24, 1929	12.85	427.5	3.410	139.0‡	102.8	Died October 26, 1930
Bc	3	March 14, 1930	25.9	933.5	2.785	133.8‡	104.2	
		March 15, 1930	40.2	604.5	0.990	27.7	103.6	Died March 16
		April 8, 1930	19.2	1,415.0	1.770	181.0	103.8	
		April 15, 1930	5.85	1,149.0	0.675	299.0	101.8	
Ce	4	April 22, 1930	11.17	1,228.0	0.774	178.5	103.0	
		April 29, 1930	13.28	1,339.0	0.515	134.9	103.0	
		May 5, 1930	13.6	1,136.0	0.475	106.8	102.6	Empyema
D	5	April 2, 1930	14.2	1,140.0	1.175	162.0	102.0	Died April 3
		April 2, 1930	10.35	1,547.0	0.860	256.7	103.4	Crisis April 3
		April 7, 1930	7.06	630.5	1.242	186.5	99.0	
Gd	6	April 14, 1930	15.45	1,716.0	0.423	133.0	99.0	
		April 21, 1930	13.65	660.0	0.798	79.5	99.0	
		April 25, 1930	10.42	795.0	0.4975	99.6	98.6	
		May 1, 1930	15.95	521.5	1.385	71.1	98.6	
Ha	7	March 17, 1930	20.8	1,314.0	0.935	113.1	100.0	Crisis March 19
Ma	8	October 23, 1929	8.4	995.0	0.780	192.5	103.0	Died November 12

		March 19, 1930	22.85	1,627.0	0.935	128.1	105	Crisis March 22
		March 24, 1930	7.7	1,080.0	1.200	288.0	100	
Sc	9	March 27, 1930	13.4	324.0	3.695	119.0‡	99	
		April 1, 1930	12.9	93.0	6.430	61.6‡	98.8	
		April 4, 1930	12.2	90.1	7.470	73.5‡	100.0	
Ta	10	November 12, 1929	8.57	1,339.0	1.520	356.5	104.0	Crisis November 13
Ua	11	March 5, 1930	22.7	740.0	1.250	67.6	103.0	Crisis February 6
		March 18, 1930	13.55	185.2	1.088	25.4	99.6	
		May 22, 1930	8.3	129.0	7.150	147.8‡	103.2	
		May 28, 1930	7.97	595.0	0.893	136.5	98.8	May 27
Va	12	June 2, 1930	6.82	194.8	1.850	72.0	98.6	
		June 3, 1930	15.7	418.0	0.877	46.1	98.6	
		June 4, 1930	14.5	432.0	0.770	48.2	98.6	
		May 9, 1929	80.5	638.0	0.323	8.35	99.8	May 18, 1929
Wa	13	May 13, 1929	17.2	1,245.0	0.530	70.5	99.0	
		May 16, 1929	14.9	892.0	0.586	83.0	99.4	

* Each clearance value represents the average of two separate hourly determinations.

† Corrected for ideal body surface area (1.73 square meters).

‡ Maximum blood urea clearance.

patients who showed hyperfunction, 3 showed a depression of renal function following the crisis. With 4 exceptions in the entire group, all remained normal or returned to normal after a period of depressed renal function. Of these four exceptions, in only one (patient 1) did we have sufficient correlated data to establish the diagnosis of diffuse glomerulonephritis. This same likelihood is quite possible in the other three instances (patients 3, 11, 12). Return of normal function occurred in from 3 to 7 days. Patient 13 is of interest since during the acute stage of the disease he developed a blood urea clearance of 8.35 per cent of normal renal function and a blood urea nitrogen of 80.5 mgm. per 100 cc. of blood. Seven days later, the results of both tests were normal and he made an uneventful recovery.

CONCLUSIONS

1. Observations with the urine sediment count, have been made in 44 adults with lobar pneumonia. Deviations from normal sediment findings have been presented and discussed. The occurrence of microscopic hematuria appeared to be of greater prognostic significance than the appearance of the other formed elements or protein in the urine.

2. Observations with the blood urea clearance test were made in 13 patients with lobar pneumonia. Renal hyperfunction (increased urea excreting activity) was the rule during the acute stage of the disease. Slight to marked depression of renal function (decreased urea excreting activity) occurred during both the acute and convalescent stages.

3. In two patients of this series there was sufficient correlated clinical data, to be certain of a complicating acute diffuse glomerulonephritis.

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