RENAL PHYSIOLOGY IN LOBAR PNEUMONIA 1

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Previous studies on renal physiology during acute pneumococcus pneumonia have vielded rather discordant results. In general a hyperfunction has been reported, but this phenomenon has not always been observed. Lewis (1), Mc-Intosh and Reimann (2) and Goldring (3) found an apparent increased functional capacity of the kidney during pneumonia. Rackemann. Longcope and Peters (4) and Frothingham (5) reported that there was neither impairment of function nor hyperfunction. On the other hand, Tileston and Comfort (6) Schwartz and McGill (7) and Bookman (8) reported definite evidence of renal impairment. Interest has been stimulated in the relation of the pneumococcus to renal pathology by the work of Blackman (9) and his coworkers on the association of this organism with the nephrotic syndrome. Rake (10) and Seegal (11) have reported on the incidence of nephritis in pneumococcus infection while Winkenwerder, McLeod and Baker (12) have tabulated the incidence of pneumonia preceding nephritis. In a survey of the literature by Rake, the pneumococcus was second to the streptococcus as a bacterial incitant of Bright's' disease, while Winkenwerder, McLeod and Baker found that pneumonia was the type of infection observed at the onset of 6.5 per cent of patients in their series with Bright's disease. Seegal, however, observed but seven cases of nephritis in 1004 cases of pneu-The reasons for the variations in these monia. statistics are not clear.

The present series of observations was undertaken to determine the immediate and delayed effect of pneumococcus pneumonia on renal function and to gain some understanding of the changes in renal physiology accompanying the period of febrile illness and also convalescence.

The primary mode of approach to estimation of renal function was through the urea clearance test and estimations of protein excretion in the urine. These two procedures could be carried on without requiring too great cooperation of the patient and were independent of the treatment regime. Sediment counts were done on fresh morning specimens as an adjunct to the above tests. Other more elaborate tests were not done, as in many instances the patient was too ill to be disturbed.

METHOD OF STUDY

Twenty-eight patients admitted consecutively to the Rockefeller Institute for treatment of pneumonia were observed over varying periods of time, in some instances as long as 6 months. On admission a urea clearance test was done: the following day a sediment count was performed. Urea clearances were repeated every three days until crisis, when practicable, and were always done on the day of crisis. During the acute illness 12-hour clearances were done unless the patient was incontinent, when the periods were shortened to those over which urine collection was complete. Another urea clearance was done 5 days post-crisis and at the time of discharge. Following discharge, urea clearances were done on the patients in the Outpatient Clinic once a month until renal function had been normal for two months. Sediment counts were done on the first day after crisis and on the sixth day after crisis. Quantitative estimations of urinary protein by the method of Shevky and Stafford (13) were done daily during the febrile period and as long thereafter as protein was present. Blood pressure determinations were done daily, and retinal examinations were made on each patient during the acute illness as well as in convalescence. Urea clearances were done more frequently than noted above whenever the results were outside the usual normal range. The patients were studied without reference to the type of pneumococcus infections or method of treatment. The bacteriological findings and treatment of the disease in these patients are shown in Table I. None of the patients gave any history of preexisting renal disease. In none of the patients was any retinopathy noted nor was there any marked sclerosis

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TABLE I
Summary showing number of patients with each type of pneumococcus

Pneumococcus type	Patient	Sex	Age	Serum ther- apy	Bac- te- re- mia	Outcome
I	A. B. M. A. C. E. P. T. E. M. H. Y. R. L.	M. F. M. F. F.	years 17 18 15 17 29 40 42	+ + + + + + +	-+-+	Recovered Recovered Recovered Recovered Recovered Recovered Recovered
II	A. K. S. M.	М. М.	30 56	+++	_	Recovered Recovered
III	P. M. M. S. H. N. M. C. H. B. N. H. E. W.	M. F. M. M. F.	21 48 55 56 65 29 45	111111	111111	Recovered Recovered Recovered Recovered Recovered Recovered Died
v	E. C. O. S.	F. M.	10 39	=	=	Recovered Recovered
VII	O. K. J. T. M. B.	F. M. M.	22 28 20	- + -	<u>-</u>	Recovered Recovered Recovered
VIII	H. F. A. I.	M. M.	35 52	=	=	Recovered Recovered
IX	G. Z.	F.	49	_	_	Recovered
Unclassifiable	D. B. S. M. N. G.	F. F. M.	10 34 36	=	- -	Recovered Recovered Recovered
B. Friedländer Type C	N. G.	М.	50	_	-	Died

of peripheral vessels. Blood cultures were done routinely on admission and were negative unless otherwise noted. The number of patients with each type of pneumococcus infection is summarized in Table I. The data on the two patients who died are shown in Table II-E.

RESULTS

Urea clearance. Renal function during the febrile period before crisis as revealed by the urea clearance test varied inversely as the age of the patient. This is demonstrated in Figure 1 and Tables II-A to II-E. During the febrile period the average urea clearance for eleven patients in the age group 10 to 29 years was elevated to 147 per cent of normal. The average for four pa-

tients 30 to 39 years was 111.8 per cent of normal: of five patients 40 to 49 years, 97.7 per cent normal; and of five patients 50 to 65 years, 82.6 per cent of normal. Thus it would appear that renal function during the pre-critical period of the disease may be elevated, may be unchanged, or may be slightly impaired, and that the level is in general a function of the age of the patient. The clearances done immediately after crisis and while the patient was still in the hospital do not show a rapid return to normal. On the contrary. the clearance in the younger group remained elevated for approximately a month after the onset of the disease. At no time during the acute illness did any of these younger patients have a urea clearance below 110 per cent of normal. In fact, all of the clearance figures at this time were 130 per cent or above, except in three instances shown in Figure 1. In each of these cases the clearance was done before fluid equilibrium had been established, and it was felt that the lower values so obtained (110.5, 113 and 113 per cent respectively) could be explained in part on this basis. Furthermore, during the first 20 days of the disease a majority of the urea clearance figures were elevated to 130 per cent or above except in 3 additional instances (Cases E. M., C. E., and N. H.— 11th, 14th, and 15th days of disease). Fluid equilibrium had been established in these patients, however, and the reason for the lack of hyperfunction was not apparent.

In the age group 30 to 40 years, there was only moderate hyperfunction during the first ten days of the disease, and again in no instance was hypofunction noted. The number of patients in this group, however, is too small to warrant any conclusions.

In the age group 40 to 50 years, there was a definite absence of any increase of the urea clearance during the acute and convalescent periods of the illness. The clearance returned to an average value for this group in about three months. It is interesting to note that in this group of patients there is an apparent hyperfunction late in convalescence, occurring during the third month after onset, and that it is only after ninety days from onset that normal clearances are again observed. It was in this group that the lowest clearance was noted (first clearance 10.3 per cent on Case

H. Y.). The reason for this low value was not apparent.

In the oldest group there is no definite shift in the clearance below normal minimum, but the values during the acute illness are in general somewhat below normal average. No secondary variations in clearance values were noted in this group.

Blood urea nitrogen. The blood urea nitrogen in all of the patients at the time of admission was

that the patient was dehydrated. With restoration of fluids normal function followed, extra renal factors playing a predominant rôle.

Proteinuria. Contrary to expectation, the amount of protein lost in the urine by these patients during the febrile period was negligible. The majority of patients excreted less than 0.1 gram of protein per day throughout their entire hospital stay. In only one instance (E. C.) did

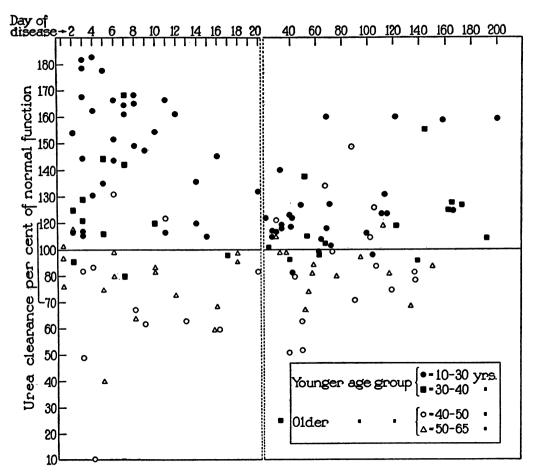


FIG. 1. SCATTER CHART SHOWING RELATION OF UREA CLEARANCE CHANGES TO DAY OF DISEASE.

within normal limits except for two patients (H. Y. and S. M.). The clearances, however, on admission, differed widely. In both exceptions noted above the blood urea nitrogen had dropped to normal five days later. In the patient H. Y. (Table II-C) there is a discrepancy between the clearance and the expected and observed blood urea nitrogen. Why this blood urea nitrogen should be lower than expected with a function of 10 per cent is not clear, unless it mirrors the fact

the protein excretion become significant, and in this patient the excretion never exceeded 3.0 grams per day and lasted for only four days. The early administration of adequate amounts of fluid to these patients seemed to depress protein excretion.

Sediment counts. In no single instance was the number of red blood cells excreted in 12 hours greater than the normal values defined by Addis. The difficulties of doing red blood cell counts on

TABLE II

Summary of laboratory examinations on patients while under observation

		Ī	Ure	a clearance	•		Sediment and protein in 12-hrs. urine (no fluid restriction)								
Patient						I					Sediment		,		······································
	Age	Day of	Defore	Blood urea	Urea clear-	Day) umc		R. B. C.	Casts					
		dis- ease	or after crisis	nitrogen	ance, average normal	dis- ease	in 12 hours	-17	Total number in 12 hours	Total number in 12 hours	Hya- line	Gran- ular	Proce	einuria	
	years			mgm. per cent	per cent		cc.				per cent	per cent	grams per liter	grams per 12 hours	
					A. PAT	IENT	S 10 TO	29 Y	EARS						
E. C. 9	10	4 8 21 34	-3 +1 +14 +27	8.17 12.72 8.59 6.54	162.1 165.0 122.7 109.5	4 5 6 7	858 305 493 514		No counts done	No counts done	+++-	+	0.7 1.58 1.8 <0.07	0.5 0.8 0.9	
D. B. 9	10	3 5 35 172	$ \begin{array}{r r} -2 \\ 0 \\ +30 \\ +167 \end{array} $	8.82 10.70 7.15 6.57	110.5 135.2 113.6 125.2	5 10	850 390	6.0 6.0	0	0			0.10 <0.07	0.08	
С. Е. ♂	15	3 7 14 27 34 91	0 +4 +11 +24 +31 +88	17.75 11.39 10.65 7.90 10.45 7.50	142.2 164.1 119.8 114.3 117.6	4 8 14	324 500 330	8.0 5.0 4+	24,000 0 0	12,000 0 0	100		<0.07 <0.07 <0.07		
A. B. ♂	17	2 20 122 159 201	0 +18 +120 +157 +199	12.26 10.80 11.29 10.20 11.65	154.5 132.0 160.9 158.5 159.3	4 21	412 575	6.0 5.0	65,000 0	20,000 18,000	100 100		1.15 <0.07	0.48	
P. T. &	17	4 9 33 65 100	-1 +4 +28 +60 +95	17.23 13.59 9.25 10.80 13.65	130.6 147.7 140.4 107.5 112.4	5 11	1,000 895	4+ 4+	0	100,000	100		<0.07		
М. А. ♀	18	3 7 41 69 113	0 +4 +38 +66 +110	7.12 7.07 7.87 8.47 11.67	167.4 160.9 117.2 116.8 131.0	3 8	540 1,090	6.0 7.0	0	16,000 0	10	90	<0.07 <0.07		
М.В. ♂	20	6 8 14 40 69 116	-1 +1 +7 +33 +62 +109	19.39 15.78 12.24 8.02 9.49 17.57	143.7 168.3 135.5 123.4 160.6 124.4	3 10 14	415 165 660	4+ 6.0 4+	120,000 0 0	12,000 0 0	100		<0.07 <0.07 <0.07		
P. M. ਨਾ	21	3 8 49 71	0 +5 +46 +68	17.76 12.22 12.34 12.95	178.5 149.0 127.3 127.2	9	740 420	7.0 7.0	8,000 40,000	0 25,000	100		0.36 <0.07	0.28	
O. K. 9	22	3 6 12 63 112	-4 -1 +5 +56 +105	5.21 5.44 7.72 5.46 5.16	181.3 166.1 161.2 98.0 123.9	13	2,550 945	6.0 6.0	0 550,000	200,000	100		<0.07 <0.07		

TABLE II-Continued

	1		Ure	a clearance	······	Sediment and protein in 12-hrs. urine (no fluid restriction)													
															Sediment				
Patient	Age	Day of	Day before or	Blood urea	Urea clear-	Day of	Volume in 12 hours		R. B. C.	B. C. Casts			Proteinuria						
		dis- ease	after crisis	nitrogen	ance, average normal	dis- ease		pН	Total number in 12 hours	Total number in 12 hours	Hya- line	Gran- ular	11000						
	years			mgm. per cent	per cent		cc.				per ceni	per ceni	grams per liter	grams per 12 hours					
A. PATIENTS 10 TO 29 YEARS—(Continued)																			
J. T. ♂	28	2 6 11 16 43 105	-6 -2 +3 +8 +35 +97	15.97 15.90 10.88 10.88 9.33 10.47	113.5 151.5 166.4 145.0 82.0 96.7	3 8 12 17	370 950 442 690	6.0 7.0 5.0	0 0 45,000 20,000	20,000 70,000 8,000 50,000	100 100 50 100	50	0.07 <0.07 <0.07 <0.07	0.02					
E. M. 9	29	3 5 11 34	-2 0 +6 +29	7.15 9.44 12.20 7.01	113.6 177.6 113.6 118.4	4 6 13	950 430 1,190	7.0 7.0 7.0	0 0 0	30,000 45,000 30,000	100 66 100	33	<0.07 <0.07 <0.07						
N. H. Q	29	4 10 15 42 72	-4 +2 +7 +34 +64	8.40 5.66 11.95 7.46 7.36	182.4 154.2 110.3 122.0 103.0	5 10 15	220 550 520	4+ 8.0 7.0	250,000 0 0	185,000 0 30,000	60 100	40	<0.07 <0.07 <0.07						
		<u> </u>			B. PAT	IENTS	30 TO	39 Y	EARS					·					
А. К. ♂	30	3 7 54	0 +4 +51	19.46 16.00 16.32	120.6 142.0 109.9	3 7	380 359	5.0 7.0	9,000	18,000 6,000	100 100		0.10 <0.07	0.04					
Н. Г. ♂	35	2 5 10 52 121 140 174	-2 +1 +6 +48 +117 +136 +170	18.96 11.82 11.24 8.12 6.66 7.06 9.21	91.2 144.1 120.0 138.1 145.0 91.9 126.9	3 7 10	540 910 920	7.0 5.0 6.0	0 0 0	20,000 55,000 60,000			0.28 <0.07 <0.07	0.14					
N. G. ♂	36	5 17 63 123	-3 +9 +54 +114	19.38 11.69 11.49 13.46	111.3 95.8 98.1 119.0	5 16	407 610	5.0 7.0	16,000 0	220,000 180,000	60 100	40	0.50 <0.07	0.20					
0. S. &	39	2 7 24 68 165	-5 0 +17 +61 +158	15.17 33.13 11.43 10.61 15.97	125.0 79.0 101.6 104.6 128.3	9 28	830 700	4+ 6.0	0	370,000 20,000	60 100	40	<0.07 <0.07						
S. M. 9	34	3 7 33 40 145 164 194	-3 +1 +27 +34 +139 +158 +188	8.71 6.24 26.43 6.60 7.59 9.50 11.36	129.5 168.0 25.1 92.8 155.3 125.0 108.9	3 8 34	215 550 360	4+ 6.0	30,000 50,000 0	22,000 85,000 0	100 100		2.6 <0.07 <0.07	0.46					

TABLE II-Continued

	1	l	Urea	clearance		Sediment and protein in 12-hrs. urine (no fluid rec							striction)		
Patient											Sediment				
	Age	Day of	Day before	Blood	Urea clear-	Day of	Vol- ume		R. B. C.	Casts		Proteinuria			
		dis- ease	or after crisis	urea nitrogen	ance, average normal	dis- ease	in 12 hours	рН	Total number in 12 hours	Total number in 12 hours	Hya- line	Gran- ular	Prote	muria	
	years			mgm. per cent	per cent		cc.				per cent	per cent	grams per liter	grams per 12 hours	
					C. PA	FIENT	s 40 TO	50 YE	ARS						
н. ү. 🌣	40	4 9 20 43 73 109 138	0 +5 +16 +39 +69 +105 +124	39.45 20.25 10.40 8.29 6.74 7.92 5.99	10.3 62.1 82.1 79.5 98.6 86.8 82.3	7	720	5.0	200,000	500,000	34	66	<0.07		
R. L. 9	42	4 8 51 105 138	0 +4 +47 +101 +134	9.02 14.63 9.65 13.30 9.58	87.0 66.7 63.0 110.0 78.6	9	312	5.0	60,000	16,000	100		<0.07		
M. S. 9	48	3 6 13 30 64 87 107	-3 0 +6 +23 +57 +80 +100	12.48 9.90 19.35 7.64 12.27 13.35 10.26	83.5 131.1 63.0 121.2 134.2 147.8 126.0	3 7 12	305 360 710	4+ 8.0 5.0	0 15,000 0	12,000 35,000 40,000	100 50 100	50	0.21 <0.07 <0.07	0.07	
G. Z. ♀	49	3 11 16 40 51 76 91 120	-6 +2 +7 +31 +42 +67 +82 +111	21.28 10.59 13.54 9.32 14.51 12.09 16.99 17.08	49.0 122.7 59.7 51.3 51.6 70.5 74.9	3 18	210 492	4+ 4+	0	350,000 0	10	90	0.43 <0.07	0.08	
		·	·		D. PATIE	NTS 5	O YEAR	RS AN	D OVER		···				
A. I. ♂	52	1 6 18 58 95	0 +5 +17 +57 +94	14.11 11.53 12.85 9.84 10.94	101.2 80.2 92.3 80.5 95.2	2 7	330 660	7.0 5.0	0	0			<0.07 <0.07		
H. N. 9	55	2 6 12 16 26 38 77	-3 +1 +7 +11 +21 +33 +72	11.40 13.15 16.29 19.90 11.93 11.04 6.82	115.6 98.3 72.7 59.9 109.9 98.6 80.0	4 12	900 500	6.0 4+	50,000 50,000	1,400,000 50,000	25 100	75	0.86 <0.07	0.78	
М. С. ♂	56	1 8 18 59 152	-6 +2 +12 +53 +146	16.89 24.48 15.31 18.47 19.54	75.9 63.5 98.2 89.3 87.5	3 19	375 650	4+ 6.0	25,000 0	45,000 18,000	75 100	25	0.14 <0.07	0.05	

TABLE II-Continued

		Urea clearance					Sediment and protein in 12-hrs. urine (no fluid restriction)								
								Sediment							
Patient	Age	Day of	Day before	Blood	Urea clear-	Day of	Vol- ume		R. B. C.	Casts		Proteinuria			
		dis- ease		urea nitrogen	ance, average normal	dis- ease	in 12 hours	рH	Total number in 12 hours	Total number in 12 hours	Hya- line	Gran- ular			
	years			mgm. per cent	per ceni		cc.				per cent	per cent	grams per liter	grams per 12 hours	
				D. PAT	IENTS 50	YEA	RS AND	OVE	R—Contin	nned					
S. M. ♂	56	5 10 16 31 55 113 135	-4 +1 +7 +22 +46 +104 +126	61.40 17.08 17.96 10.95 12.47 12.14 15.88	24.3 82.5 69.0 97.8 73.5 119.1 68.2	8 13 18	633 890 590	5.0 7.0 6.0	0 0 180,000	20,000 30,000 18,000	100 100 100		0.14 <0.07 <0.07	0.08	
Н. В. ♂	65	1 5 10 52 119	$ \begin{array}{r r} -2 \\ +3 \\ +8 \\ +50 \\ +117 \end{array} $	11.28 10.52 13.72 10.06 11.72	93.0 74.8 83.8 67.3 81.5	6 9	575 790	8.0 6.0	16,000 0	32,000 0	100		<0.07 <0.07		
					E.	PATIE	NTS WH	O DIE	D						
E. W. ♂	45	3 5		22.13 21.91	70.6 109.2	4	285	4+	120,000	3,250,000	0	100	4.82	1.37	
L. G. ♂	50	3		30.5	50.1	4	480	4+	0	2,000,000	0	100	0.72		

small samples of dilute urines must be borne in mind when interpreting these data. Casts, however, were uniformly increased in number with the hyaline type predominating. When the patients were extremely ill the proportion of granular casts increased. In the two patients who died, the differential cast count revealed 100 per cent granular casts with a large number of casts excreted in both instances.

Estimations of blood pressure. There was no significant alteration in the blood pressure accompanying the alteration in the urea clearance. In general, the blood pressure tended to be a little below normal during the febrile period of the disease, returning to the usual normal levels during convalescence.

Additional laboratory findings. Daily measurements of fluid intake and output were made on these patients and no deviations from the expected relations were noted. There was no relation between fluid intake and clearance, or be-

tween fluid intake and the number of observed formed elements in the urine. Some of the patients were given sodium chloride in therapeutic doses. This had no demonstrable effect on the urea clearance in these patients.

Relation of renal physiology to pneumococcus type and therapy

There was no demonstrable difference between the effects of different pneumococcal types on renal function. Nor did the early and effective use of therapeutic sera have any demonstrable effect on the renal function during the acute illness and also during serum disease. No effect was visible when treated and untreated patients in the same age groups were compared. It is possible that statistical analysis of a larger number of cases might show some correlation between pneumococcus type and changes in renal function. If any connection was present in our cases, however, it was quite obscured by the more marked

effects of age and increased lability of the renal function.

DISCUSSION

The outstanding revelation of these observations seems to be a decrease of renal resiliency with increasing age. The failure of older patients to develop a high urea clearance seems to be a part of their general loss of physiological elasticity. It must be emphasized here that normal children do not show urea clearances which, per square meter of body surface, exceed those of adults. It has been our experience, and also that of Cullen, Nelson and Holmes (14), that the variation in normal children from the mean, designated as "100 per cent normal," follows the same pattern as in adults. However, a marked response to alteration of some physiological factors governing the urea clearance indicating a high degree of resiliency of renal function has been observed in young children with nephrosis (Farr (15)).

The effect of age on renal behavior in pneumonia may explain, in part, the differing conclusions of previous investigators on the effect of pneumonia on renal function.

Our observations indicate no significant renal damage caused by the hyperpyrexia or the toxemia of the disease. It seems likely that the albuminuria observed in this disease is more closely allied to the benign albuminuria noted after severe exercise or cold showers than to the serious albuminuria seen in Bright's disease.

The fact that the urea clearance did not return to normal promptly with the temperature makes it seem unlikely that the clearance elevation noted is related to increase in metabolism associated with fever.

Prompt response to serum therapy did not appear to hasten the return of the inflated clearance to normal.

That hyperpyrexia of itself does not increase the urea clearance was shown by Farr and Moen (16) who observed a *decrease* in the clearance initially when artificial pyrexia was induced. Some factor other than fever must cause the increase in urea clearance in pneumonia.

These studies shed no light on the mechanism by which Bright's disease may follow pneumonia, as none occurred in this group. It seems possible that signs of renal irritation, such as red cell excretion and albuminuria, may be kept to a minimum by adequate administration of fluid.

Administration of salt to some of these patients had no appreciable effect upon the apparent renal function

CONCLUSIONS

- 1. Renal physiological studies have been made upon 28 patients with lobar pneumonia.
- 2. The urea clearance during the disease shows a sharp difference between the older and younger patients. The patients under 40 years of age show a marked elevation of the urea clearance, persisting about one month, and independent of the type of pneumonia or therapy used. The older age group show little change in the urea clearance.
- 3. Observation of the urine sediment in all groups showed a strong tendency for all abnormal elements to disappear with adequate fluid balance.
- 4. No significant changes in blood pressure were associated with the clearance changes.

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