with γ_G-globulin. The present report demonstrates that an allergic individual, containing γ_M-, γ_G- and γ_A-globulins in his serum, has reaginic antibody activity entirely in a γ_G-globulin fraction. These observations would suggest that a certain degree of caution should be used in concluding that all reaginic antibodies are of a distinct molecular species. The methods for detection of reagin take advantage of the skin-fixing properties of this antibody. Although it has been demonstrated that γ_A-globulin will fix to the skin of human and various non-human primates, this report suggests that the property of skin fixation is not limited to γ_A-globulin. The presence of reaginic antibody actively associated with a γ_G-globulin fraction may be analogous to the skin fixing properties of guinea pig $7S\gamma_1$-globulin described by Ovary, Benacerraf and co-workers(16-18). Sera of several additional timothy sensitive patients are being investigated to determine the nature of the reaginic antibody activity.

Summary. 1. Serum from untreated timothy sensitive patient (E.F.) was fractionated by Sephadex G-200 gel-filtration and DEAE-cellulose ion-exchange chromatography, and resulted in the isolation of a single fraction with reagin activity. 2. The isolated reagin possesses chromatographic and immunochemical characteristics of γ_G-globulin.

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Production of Urea Nitrogen and Creatinine in Chronic Azotemia And Effect of Hemodialysis.* (31079)

N. J. BLONDEEL,† S. GOODMAN, N. M. SIMON AND F. DEL GRECO

Department of Medicine and Clinical Research Center, Northwestern University Medical School, Chicago, Ill.

The rate of urea nitrogen production in patients with chronic azotemia has not been adequately investigated. Since unlimited pro-

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tein intake may lead to the development of uremia, low protein diets of various composition have been proposed(1,2,3,4). From the available evidence it is not clear whether the rate of urea nitrogen production during limited protein intake differs from normal, and whether it is affected by dialysis. The present study was undertaken to answer these questions and to determine in addition the rate of creatinine production.

Materials and methods. Seven azotemic patients and 3 normal subjects were utilized. The pertinent data are listed in Table I. All the patients had long standing chronic renal disease and documented azotemia for at least 3½ months preceding this study with stable plasma urea nitrogen (PUN) and creatinine clearance (C_{Cr}). All were free of complications and were not taking drugs. In 6 patients the daily urinary output exceeded 1500 ml.

TABLE I. Pertinent Clinical and Laboratory Data.

Case No.		Sex/Age (yr)	PUN (mg/100 ml)	P_{Cr}	Serum CO_2 (mEq/l)	C_{Cr} (ml/min)	B. Wt. (kg)	L. B. Wt. (kg)	Diagnosis
	Patients with azotemia								
1	M.P.	♀/42	42	7.9	23	6.4	56	52	*Chr. pyelonephritis (inactive)
2	J.V.D.	♂/58	47	6.7	20	15.9	84	70	†Chr. glomerulonephritis
3	"	/59	72	10.5	15	8.9	82	69	" "
4	S.K.	♀/51	66	7.1	18	10.5	57	55	*Polycystic kidney disease
5	D.R.	♂/43	73	11.8	20	6.6	73	67	*Chr. glomerulonephritis
6	E.B.	♂/48	87	12.4	23	5.5	78	71	* " "
7	"	/50	94	5.5	24	20.5	78	71	" "
8	E. McG.	♂/36	136	14.1	19	6.1	71	69	* " "
9	N.W.	♀/23	192	18.7	12	1.7	62	54	* " "
	Normal subjects								
10	C.H.	♀/49	7	1.2	23	109	76	63	
11	E.W.	♀/37	9	.9	24	88	52	48	
12	E. Wa.	♀/42	6	.8	23	96	61	56	

PUN = plasma urea nitrogen, P_{Cr} = plasma creatinine, Serum CO_2 = serum bicarbonate, C_{Cr} = endogenous creatinine clearance, B. Wt. = body weight, L. B. Wt. = lean body weight.

* Diagnosis verified by renal biopsy and/or autopsy.

† Diagnosis based on clinical evidence: 20 years previously acute glomerulonephritis (post-streptococcal), 5 years previously acute exacerbation.

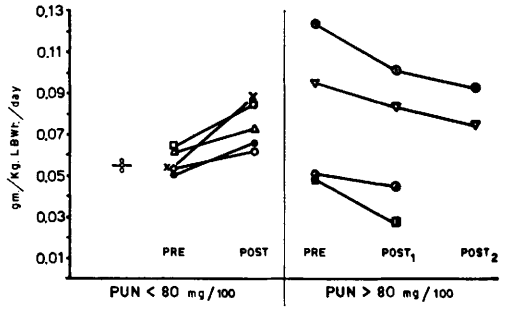

FIG. 1. Urea nitrogen production during pre- and postdialysis periods plotted against plasma urea nitrogen (PUN) predialysis.

Two patients (J.V.D. and E.B.) were studied on two separate occasions, the interval between each study being of 13 and 21 months, respectively.

The dietary regimen consisted of a low protein diet containing 0.5 to 0.7 g per day per kg of protein and constant amounts of carbohydrate and fat to make up a total of 25 to 38 calories per day per kg of body weight. The meals were prepared and weighed in the Metabolic Kitchen and eaten with insignificant remains. Appropriate aliquots of the meals served were pooled, frozen and later analyzed for nitrogen content. The equilibration period ranged from 12 to 26 days in the patients and from 13 to 19 days in the normal subjects. However, only the last 4 to 8 days were used for calculating urea nitrogen production. The patients with chronic azotemia were then subjected to hemodialysis and another dietary period of 5 to 8 days (including the day of dialysis) was obtained.

Hemodialysis was carried out with a disposable twin coil artificial kidney‡ for 6 hours, with bath changes at intervals of 2 hours. Aliquots of each bath were saved and analyzed for urea nitrogen. Two cases (No. 7 and 8) were subjected to a second hemodialysis 7 days after the first.

Throughout the study, urine was collected in 24-hour periods and analyzed on the Auto Analyzer§ by a modified diacetyl-carbamido reaction(5) for urea nitrogen, and by a modification of the Folin and Wu method(6) for creatinine. Blood samples collected twice weekly and before and after each dialysis, and aliquots of bath fluids (dialysate) were similarly analyzed for urea nitrogen. The nitrogen content of the dietary pools was determined by a modification of the micro-Kjeldahl technique of Conway(7).

Calculations. The daily rates of urea nitrogen and creatinine production were calculated according to Persike and Addis(8) by the formula:

$$\frac{\text{Urea nitrogen production}}{\text{Creatinine production}}\ (\text{g/day}) = \frac{\Delta\text{PUN}}{\Delta P_{Cr}}\ (\text{g/l/day}) \times \text{T.B.W.} + \frac{\text{urinary urea nitrogen}}{\text{urinary creatinine}}\ (\text{g/day}),$$

where P_{Cr} is plasma creatinine, and T.B.W. total body water estimated according to Thaysen(9).

Then urea nitrogen and creatinine production rates were related to lean body weight (L.B. Wt). The latter was estimated from the body surface area (S.A.) according to the nomogram of DuBois and DuBois and the formula(10): $47.1 \times \text{S.A.} - 20.7 = \text{L.B. Wt.}$

On the day of dialysis, on the assumption that urea is evenly distributed in body water and rapidly equilibrated between fluid compartments, T.B.W. was estimated as follows:

$$\frac{\text{Total urea nitrogen removed by dialysis (g)}}{\Delta\text{PUN pre- and postdialysis (g/l)}}.$$

Arguments in support of this formula have been given by Blakmore *et al*(11).

Results. The results are listed in Table II and Table III and illustrated in Fig. 1.

Normal subjects: Urea nitrogen production averaged 0.054 ± 0.002 S.D. g/day/kg/L.B. Wt and represented 55% of the dietary nitrogen. Creatinine production averaged 0.020 ± 0.002 S.D. g/day/kg/L.B. Wt, which nearly corresponds with the average of 0.023 g found in a larger series of normal subjects(12).

Patients with azotemia. Predialysis: Urea nitrogen in 7 cases (No. 1 through 6, and 9, Table II) was similar to that found in normal subjects, averaging 0.055 ± 0.006 S.D. g/day/kg/L.B. Wt. In the remaining 2 cases (No. 7 and No. 8, Table II) urea nitrogen production was markedly increased being 0.123 and 0.095 g/day/kg/L.B. Wt, respec-

‡ Travenol Laboratories, Morton Grove, Ill.

§ Technicon Instruments Corp., Chauncey, N. Y.

TABLE II. Urea Nitrogen Production.

Case No.		PUN (mg/100 ml)	Nitrogen intake (g/day) avg	Urinary urea nitrogen (g/day) avg	Urea nitrogen production (g/day/kg L.B. wt) avg
	Patients with azotemia				
1	Predialysis	42	4.7	2.9	.061
	Postdialysis	12-51*	4.6	1.8	.073
2	Pre	47	6.8	3.9	.054
	Post	23-64*	6.2	3.1	.088
3	Pre	72	7.7	3.9	.052
	Post	47-72*	7.7	3.2	.066
4	Pre	66	5.6	4.0	.064
	Post	19-79*	5.3	2.6	.086
5	Pre	73	5.3	3.5	.053
	Post	37-72*	4.5	2.1	.062
6	Pre	87	7.5	3.4	.049
	Post	43-44*	7.5	1.7	.026
7	Pre	94	9.0	8.0	.123
	Post	43-95*	9.7	4.5	.107
8	Pre	136	5.7	6.9	.095
	Post	92-113*	6.1	4.2	.085
9	Pre	192	5.9	2.6	.050
	Post	76-99*	5.9	1.0	.045
	Normal subjects				
10		7	6.3	3.5	.056
11		9	4.5	2.6	.054
12		6	5.4	3.1	.054

* Range during postdialysis period.

tively. Creatinine production (Table III) averaged 0.016 ± 0.004 S.D. g/day/kg/L.B. Wt, *i.e.*, slightly less than in normal subjects but the difference of the means was not significant ($P>0.05$).

Postdialysis: Two distinct types of changes in urea nitrogen production were noted. In 5 cases (No. 1 through 5, Table II) urea nitrogen production increased by 0.009 to 0.034 g/day/kg/L.B. Wt above control. In the other 4 cases (No. 6 through 9, Table II) urea nitrogen production decreased by 0.005 to 0.023 g/day/kg/L.B. Wt below control.

It is noteworthy (Fig. 1) that the sustained increase in urea nitrogen production occurred in the cases whose predialysis PUN ranged from 42 to 73 mg% and the decrease in those whose predialysis PUN ranged from 87 to 192 mg%. In 2 of these cases (No. 7 and 8, Table II) a second dialysis caused a further decrease in urea nitrogen production.

The average changes in creatinine production for the whole postdialysis period are

TABLE III. Creatinine Production.

Case No.		P_{cr} (mg/100 ml)	Urinary creatinine (g/day) avg	Creatinine production (g/day/kg L.B. wt) avg
Patients with azotemia				
1	Predialysis	7.9	.747	.014
	Postdialysis	3.0-8.9*	.522	.011
2	Pre	6.7	1.270	.018
	Post	3.9-8.1*	1.095	.016
3	Pre	10.5	1.327	.019
	Post	6.8-9.4*	1.121	.017
4	Pre	7.1	.796	.015
	Post	3.7-8.3*	.623	.012
5	Pre	11.8	1.169	.017
	Post	7.4-11.4*	.859	.013
6	Pre	12.4	.883	.013
	Post	7.9-11.7*	.562	.009
7	Pre	5.5	1.501	.022
	Post	3.4-6.1*	1.265	.020
8	Pre	14.1	1.237	.017
	Post	10.4-13.6*	.931	.017
9	Pre	18.7	.394	.010
	Post	10.6-14.8*	.197	.009
Normal subjects				
10		1.2	1.199	.019
11		.9	1.071	.022
12		.8	1.087	.020

* Range during postdialysis period.

listed in Table III. Creatinine production diminished in all but one case (No. 8, Table III) from a mean of 0.016 to a mean of 0.013 g/day/kg/L.B. Wt. This decrease was statistically significant ($p<0.001$).

Discussion. In the predialysis period the production of urea nitrogen in most of the patients with azotemia was similar to that found in normal subjects, and was less than the dietary nitrogen intake. This does not imply that these patients were in nitrogen balance since neither the non-urea nitrogen in the urine nor the fecal nitrogen was included in the calculations. In 2 cases (No. 7 and 8, Table II) urea nitrogen production equalled or exceeded nitrogen intake, suggesting an increased breakdown of endogenous protein. The reason for this is not apparent, since these 2 patients had stable PUN levels and had no evidence of blood loss, infection or any other cause of accelerated protein catabolism. It may be that the equilibration period was not prolonged enough to effect a decrease in urea nitrogen production from elevated to normal rates.

In the postdialysis period, 2 distinct patterns of urea nitrogen production were noted. An explanation for these divergent effects of hemodialysis is not apparent from the present data. If the rate of urea nitrogen production is considered as indicative of protein metabolism, the postdialysis changes suggest that hemodialysis accelerated protein breakdown in some of the cases but exerted a protein sparing effect in the others.

Although the mean predialysis rate of creatinine production in the azotemic patients was not significantly less than that found in normal subjects, 4 patients showed a creatinine production more than 2 standard deviations below the normal mean, supporting Goldman's(13) contention that creatinine production may be reduced in renal failure.

Summary. 1. The daily rate of urea nitrogen and creatinine production was determined in 7 patients with chronic stable azotemia and 3 normal subjects, maintained on a reduced protein intake. In addition, the effect of hemodialysis on urea nitrogen and creatinine production was observed in all the azotemic patients. 2. In 7 cases predialysis urea nitrogen production was similar to that found in normal subjects and averaged 55% of the nitrogen intake. In 2 cases urea nitrogen production was elevated, being equal to or exceeding the dietary nitrogen. The rate of creatinine production in the azotemic patients was slightly lower than that found in normal subjects. 3. Postdialysis urea nitrogen production increased significantly in 5 cases whose predialysis PUN ranged from 42 to 73 mg%, and decreased in 4 cases with predialysis PUN of 87 to 192 mg%. Creatinine production decreased in all but one case.

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