adequacy; second, if a measure of urea removal were to be used, whether a simple urea reduction ratio is acceptable or whether a measure that incorporates a normalizing factor is necessary; and finally – whether the widespread use of *V* as this normalizing factor is valid. Jenkins' criticisms relate to the second point whereas our paper addressed the third.

Focusing solely on normalized urea clearance presents a flawed view of dialysis adequacy. There are many other facets. Middle molecule removal is important. Reanalysis of data from the HEMO study has demonstrated that retention of β_2 microglobulin was associated with increased mortality.[2] In addition to solute clearances, dialysis prescription encompasses other goals, including sodium and water, divalent ion and acid-base homeostasis. Dialysis hypotension is more likely to occur when dialysis session time is shortened, because of increased ultrafiltration rates, and failure to achieve adequate sodium removal with increased interdialytic weight gains.

Although we have criticized the appropriateness of the use of *Kt/V* in prescribing hemodialysis, we do believe that an assessment of the amount of dialysis delivered is vital, unless very long and/or very frequent dialysis sessions are employed. Normalized urea clearance, although not perfect, is a useful marker of adequacy, though we believe it could be used more astutely. Our paper proposes that the normalizing factor should reflect metabolic activity, as use of *V* may risk under-dialysis in women and small men. We suggest that this should be borne in mind while we continue to use *Kt/V*, and that the adequacy targets should be adjusted in these two groups.

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Lipid disorders in experimental chronic kidney disease: a role for SREBPs

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To the Editor: We have read with interest the article by Hai-Lu Zhao *et al.*[1] on fat redistribution and adipocyte transformation in uninephrectomized rats. Among numerous interesting findings, the authors demonstrate increased ectopic fat deposits in remnant kidneys and other solid organs of chronic kidney disease animals. The authors speculate on the possible mechanisms, taking into account increased lipid production. This hypothesis is strengthened by demonstrating that expression of HMG-CoA reductase, the rate-limiting enzyme in cholesterologenesis pathway, is increased in remnant kidneys.

We would like to confirm these results and highlight the potential role of sterol regulatory element-binding proteins (SREBPs) in the above-mentioned disturbances. SREBPs are nuclear transcription factors that are currently regarded as the major regulators of both cholesterologenesis and lipogenesis.

We have shown that both gene expression and protein abundance of SREBPs are increased in white adipose tissue[2] and livers[3] of chronic kidney disease rats. Moreover, increase in SREBP expression has been demonstrated in kidneys of diabetic mice[4] and in experimental age-related nephropathy,[5] where it has been clearly linked to lipid deposition in glomeruli, and consequently to mesangial expansion, glomerulosclerosis, and proteinuria.

These results complement the findings demonstrated by Zhao *et al.* as they bring us closer to elucidating the issue of altered lipid metabolism in the course of chronic kidney disease.[3]

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Response to 'Lipid disorders in experimental chronic kidney disease: a role for SREBPs'

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We thank Chmielewski *et al.* for drawing attention to the potential role of sterol regulatory element-binding

proteins (SREBPs) in the development of fat redistribution and adipocyte transformation associated with uninephrectomy-induced chronic renal impairment.[1] SREBPs are membrane-bound transcription factors that regulate multiple genes involved in cholesterol biosynthesis and uptake.[2] In our ongoing studies, we aim to define the correlations between SREBPs and fat dysfunction concomitant with the course of chronic kidney disease in uninephrectomized rats. Chmielewski *et al.* have demonstrated an increased gene expression and protein abundance of SREBPs in white adipose tissue[3] and livers[4] of 5/6 nephrectomized rats. Although these cross-sectional results complement our findings of fat dysfunction in uninephrectomized rats,[1] one has to be cautious in interpreting data from different nephrectomized experimental models. Renal failure model set up by 2/3, 5/6, or 7/8 nephrectomy might be different from the chronic kidney impairment induced by uninephrectomy in our study.[1] For example, our study demonstrated that the protein abundance of HMG-CoA reductase in the liver was similar among the three groups of rats with different lipid profiles.[1] As stated in our paper,[1] 'nephrectomy is a severe procedure that produces a myriad of effects on many systems, including the renin–angiotensin–aldosterone systems and the endocrine organs'. Indeed, the uninephrectomized rats also showed pancreatic β-cell deficit, insulin deficiency, and glucose intolerance.[5] All these data demonstrate that the kidney is one of the most important homeostatic organs.

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Paricalcitol and renin-angiotensin components in remnant kidneys

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To the Editor: A recent article demonstrated that 8-week paricalcitol treatment of 5/6 nephrectomized rats suppressed expression of several genes of the renin-angiotensin system (RAS) in the kidney at the mRNA level.[1] We recently performed a similar study,[2] and have now determined the RAS components from the kidneys with very different results.

In our experiment, rats were put on a 12-week paricalcitol (200 ng/kg) treatment period 15 weeks after 5/6 nephrectomy (NX). After 27 weeks of renal insufficiency, the mRNA values of almost all RAS components and connective tissue growth factor were different from sham-operated rats. However, no suppression of RAS genes between untreated and paricalcitol-treated NX rats was observed at the mRNA level (Table 1). In the study by Freundlich *et al.*,[1] the NX rats were put on paricalcitol (100 or 300 ng/kg) already 4 days after surgery. The subtotal NX produces a shock that undoubtedly alters gene expression in the remnant kidney, and it seems likely that these processes have not yet stabilized in 4 days. In our

Table 1 | No differences in RAS components between untreated and paricalcitol-treated NX rats (200 ng/kg thrice weekly)

	Sham (n=12)	NX (n=7)	NX+Paricalcitol (n=8)
Kidney mRNA using RT–PCR			
AT_{1a} receptor ($\times 10^4$/ng total RNA)	0.99 ± 0.04	0.83 ± 0.08*	0.80 ± 0.05*
AT_2 receptor ($\times 10^2$/ng total RNA)	0.76 ± 0.15	0.32 ± 0.06*	0.19 ± 0.03*
AT_4 receptor ($\times 10^3$/ng total RNA)	2.99 ± 0.21	3.76 ± 0.28*	3.90 ± 0.24*
Renin receptor ($\times 10^4$/ng total RNA)	2.31 ± 0.15	1.77 ± 0.11*	1.74 ± 0.08*
MAS oncogene ($\times 10^2$/ng total RNA)	4.80 ± 0.34	4.92 ± 0.48	4.77 ± 0.41
ACE ($\times 10^4$/ng total RNA)	0.98 ± 0.68	1.72 ± 0.21*	2.06 ± 0.20*
ACE2 ($\times 10^4$/ng total RNA)	1.10 ± 0.08	0.65 ± 0.14*	0.49 ± 0.09*
CTGF ($\times 10^4$/ng total RNA)	1.74 ± 0.11	2.76 ± 0.49*	2.84 ± 0.19*
Plasma renin activity (ng/ml/h)	24.3 ± 3.0	1.7 ± 1.0*	1.4 ± 0.7*

ACE, angiotensin-converting enzyme; CTGF, connective tissue growth factor; NX, 5/6 nephrectomy; RT–PCR, reverse transcription–polymerase chain reaction.
5/6 nephrectomy at the age of 8 weeks (study week 0), disease progression period 0–15 weeks, treatment period 15–27 weeks (12 weeks). Mean ± s.e.m., *$P<0.05$ compared with the sham group.