mesothelial cells," but, to our knowledge, these authors never employed immunohistochemical analysis in any of their published papers on peritoneal biopsy morphology. Immunohistochemistry is absolutely necessary to distinguish the different fibroblastic subpopulations in the peritoneal tissue before and during peritoneal dialysis (PD). In a recent and ulterior study [3], we have further confirmed the existence of a fibroblast subpopulation derived from the mesothelium in patients undergoing PD.

RAFAEL SELGAS, JOSÉ JIMENEZ-HEFFERNAN, and MANUEL LÓPEZ-CABRERA
Madrid, Spain

Correspondence to Rafael Selgas, Diego de León 62, E-28006 Madrid, Spain.
E-mail: rselgas.hlpr@salud.madrid.org

REFERENCES

1. WILLIAMS JD, CRAIG KJ, Von RUHLAND C, *et al*: The natural course of peritoneal membrane biology during peritoneal dialysis. *Kidney Int* 64(Suppl 88):S43–S49, 2003
2. YAÑEZ-MO M, LARA-PEZZI E, SELGAS R, *et al*: Peritoneal dialysis and epithelial-to-mesenchymal transition of mesothelial cells. *N Engl J Med* 348:403–413, 2003
3. JIMÉNEZ-HEFFERNAN JA, AGUILERA A, AROEIRA L, *et al*: Immunohistochemical characterization of fibroblasts subpopulations in normal peritoneal tissue and in peritoneal dialysis-induced fibrosis. *Virchows Arch* 2004 (Epub ahead of print)

Reply from the Authors

Dr. Selgas and his colleagues suggest in their letter that our recently published review [1] was unreasonably critical of their paper in the *New England Journal of Medicine* [2] and was based on personal rather than scientific opinion. In fact, our review was fully referenced, including the statements used in the critique of Dr. Selgas' paper. We believe that there is data available in the scientific literature that they have chosen not to consider, and we indicated this in our publication. Furthermore, we indicated that their presentation of peritoneal morphology is in contrast to that with which we are familiar.

With regard to our relationship to the Peritoneal Biopsy Registry, we wish to make it clear that the opinions expressed in the review are solely those of the named authors. We do acknowledge the donation of peritoneal tissue by all the centers listed at the end of our review, and we apologize for any confusion caused. The opinions of the authors are based on the experience gained by examination of this collection of biopsies.

JOHN D. WILLIAMS, KATHRINE J. CRAIG, CHRIS VON RUHLAND, NICHOLAS TOPLEY, and GERAINT T. WILLIAMS
Wales, United Kingdom

Correspondence to John D. Williams, Institute of Nephrology, UWCM, Cardiff CF14 4XN, Wales, United Kingdom.
E-mail: williamsjd4@cf.ac.uk

REFERENCES

1. WILLIAMS JD, CRAIG KJ, RUHLAND C, *et al*: The natural course of peritoneal membrane biology during peritoneal dialysis. *Kidney Int* 64(Suppl 88):S43–S49, 2003
2. YANEZ-MO M, LARA-PEZZI E, SELGAS R, *et al*: Peritoneal dialysis and epithelial to mesenchymal transition of mesothelial cells. *N Engl J Med* 348:403–413, 2003

A catalog of gene expression in the developing kidney

To the Editor: In a recent paper, Schwab et al [1] provided an extensive description of gene expression during mouse nephrogenesis by coupling microarrays and robust target microamplification techniques. In addition to other evidences of kidney stepwise organogenesis in the rat [2], this work established very useful baselines for further investigations of mouse nephrogenesis. However, one should emphasize that gene regulation only represents the first step of tissue differentiation that should be complemented by studies at the protein level. We have recently described ontogeny patterns of proximal tubule (PT) transporters during mouse and human nephrogenesis, showing that PT maturation was essentially achieved at the initiation of glomerular filtration [3]. The comparison of data obtained by real-time polymerase chain reaction (PCR) and immunoblotting in mouse embryonic kidneys clearly shows that divergent ontogeny patterns can be observed at the mRNA and protein levels (Fig. 1). Additional differences may also arise from post-translational modifications, such as complex N-glycosylation, which may also be regulated during ontogeny and plays a significant role in protein maturation [3]. In conclusion, gene expression analyses represent a powerful tool to identify and compare pathways involved in regular and mutant embryogenesis [4]. However, the complexity of post-transcriptional regulations should be considered when integrating the factors involved in differentiation and organogenesis cascades.

FRANÇOIS JOURET, HUGUETTE DEBAIX, and OLIVIER DEVUYST
Brussels, Belgium

Correspondence to Olivier Devuyst, Division of Nephrology, Université catholique de Louvain Medical School, B-1200 Brussels, Belgium.
E-mail: devuyst@nefr.ucl.ac.be

REFERENCES

1. SCHWAB K, PATTERSON LT, ARONOW BJ, *et al*: A catalogue of gene expression in the developing kidney. *Kidney Int* 64:1588–1604, 2003
2. STUART RO, BUSH KT, NIGAM SK, *et al*: Changes in global gene expression patterns during development and maturation of the rat kidney. *Proc Natl Acad Sci USA* 98:5649–5654, 2001
3. JOURET F, IGARASHI T, GOFFLOT F, *et al*: Comparative ontogeny, processing, and segmental distribution of the renal chloride channel, ClC-5. *Kidney Int* 65:198–208, 2004
4. REINKE V: Functional exploration of the *C. elegans* genome using DNA microarrays. *Nat Genet* 32(Suppl):541–546, 2002

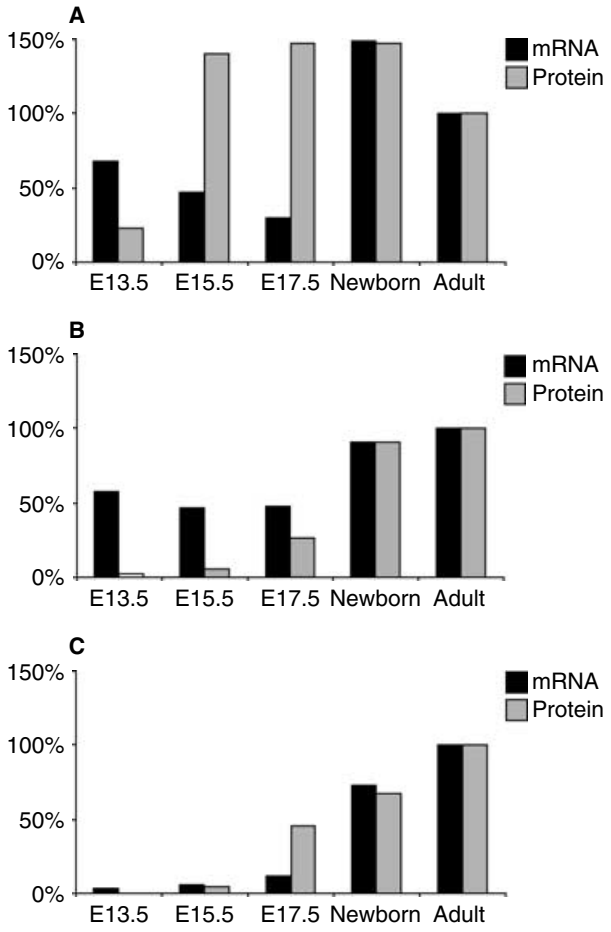

Fig. 1. Comparative ontogeny of the chloride channel ClC-5, the E1 subunit of the vacuolar H^+-ATPase, and the water channel AQP1 in mouse kidney. Quantitative real-time PCR results (*A* to *C*, black bar) and densitometry analyses of immunoblots (A to C, grey bar) of ClC-5 (A), H^+-ATPase E1 subunit (B), and AQP1 (C) expression in embryonic (E13.5, E15.5, E17.5), neonatal, and adult mouse kidneys. Real-time PCR analyses were performed by adjusting ClC-5, H^+-ATPase E1 subunit, and AQP1 mRNA levels to GAPDH at each stage, and comparing the relative changes in expression during ontogeny to the adult level (taken as 100%). Ratio = $(E_{target})^{\Delta Ct(Adult\text{-}sample)}/(E_{GAPDH})^{\Delta Ct(Adult\text{-}sample)}$. The analyses were performed in duplicate on pooled samples from an average of 12 embryos, from 4 different litters. Densitometry analyses of specific immunoreactive bands were performed with a Hewlett Packard Scanjet model IVC using the NIH Image V1.60 software. Optical densities were normalized to β-actin density in the corresponding sample. All immunoblots were at least performed in duplicate. The early (E13.5) induction of ClC-5 mRNA transcription was followed by a decrease during late nephrogenesis, whereas ClC-5 protein expression was stable from E14.5 until birth (A). For the E1 subunit of the H^+-ATPase, its stable mRNA expression during nephrogenesis contrasted with a late (E16.5) and progressive detection of the protein (B). Finally, AQP1 mRNA detection was paralleled by a progressive protein expression and maturation (N-glycosylation) during late ontogeny (C). The ontogeny of these three transporters mostly expressed in the proximal tubule of the nephron illustrates that significant differences can be observed between mRNA and protein expression patterns during nephrogenesis. The data have been compiled and adapted from [3].

Urea space and body water

To the Editor: PICARD program investigators reported larger kinetic urea distribution volumes (V_{urea}) than anthropometric body water (TBW) in acute renal failure (ARF) patients [1]. They now find larger $^{[13C]}$urea-measured V_{urea} than both D_2O-measured and anthropometric TBW [2]. TBW measured by D_2O (38.3 L) was close to anthropometric estimates (38.3 and 39.3 L); the correlation between them and isotopic TBW were highly significant (Ps $\leq$ 0.01). Thus, anthropometric methods estimated TBW reasonably well, as they were designed to do. V_{urea} (51.0 L), however, was higher (about 30%) than TBW and correlated weakly or not at all with TBW (Ps $\geq$ 0.04). Bioimpedance estimated that volumes were between V_{urea} and TBW.

These findings are interesting, stimulating, and informative because HEMO Study investigators report higher anthropometric TBW (about 20%) than kinetic V_{urea} in chronic renal failure (CRF) patients [3]. Thus, V_{urea} appears much higher than TBW in ARF, but much lower than TBW in CRF. What happens to V_{urea} in CRF patients who become ill, or ARF patients who become chronic?

What should clinicians with good estimates of TBW—thought to equal V_{urea} until very recently—do? Should they increase prescribed Kt by 30% in ARF, but reduce it by 20% in CRF to achieve comparable Kt/V_{urea}? Or should nephrologists who treat dialysis patients rejoin the ranks of other clinicians who use less ambiguous body size measures, such as body surface area or body weight [4], to judge physiologic functions and to prescribe treatments?

EDMUND G. LOWRIE
Concord, Massachusetts

Correspondence to Edmund G. Lowrie, 21 Edmonds Road, Concord, MA 01742.
E-mail: edlowrie@prodigy.net

REFERENCES

1. KANAGASUNDRAM NS, GREENE T, LARIVE AB, *et al*: Prescribing an equilibrated intermittent hemodialysis dose in intensive care unit acute renal failure. *Kidney Int* 64:2298–2310, 2003
2. IKIZLER TA, SEZER MT, FLAKOLL P, *et al*: Urea space and total body water measurements by stable isotopes in patients with acute renal failure. *Kidney Int* 65:725–732, 2004
3. DAUGIRDAS JT, GREENE T, DEPNER TA, *et al*: Anthropometrically estimated total body water volumes are larger than modeled urea volume in chronic hemodialysis patients: Effects of age, race, and gender. *Kidney Int* 64:1108–1119, 2003
4. LOWRIE EG, LI Z, OFSTHUN N, LAZARUS JM: Body size, dialysis dose and death risk relationships among hemodialysis patients. *Kidney Int* 62:1891–1897, 2002