

tensin system in patients with type 1 diabetes did not slow nephropathy progression but slowed the progression of retinopathy. These findings may stimulate the widespread use of blockers of the renin-angiotensin system in normotensive patients with type 1 diabetes and normoalbuminuria. However, a higher incidence of microalbuminuria in the losartan group, which had the best retinopathy outcome, raises concern about possible adverse renal effects of blockade of the renin-angiotensin system in these patients. Do we have to trade nephropathy for retinopathy? Further studies are warranted, but a closer look into the data in the study by Mauer et al. might help clarify this question. For instance, the renal outcomes of patients without retinopathy progression in each group should be compared. Until more data are available, we would think that blockade of the renin-angiotensin system in normotensive patients with type 1 diabetes and normoalbuminuria, even with angiotensin-converting-enzyme inhibitors, should not be generally recommended.

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**THE AUTHORS REPLY:** Although genetic predisposition to hypertension is associated with an increased risk of diabetic nephropathy in patients with type 1 diabetes, as Tamsma correctly points out, this does not mean that systemic hyperten-

sion is an important precondition for early mesangial expansion. In fact, earlier studies strongly suggested that hypertension in patients with type 1 diabetes is more likely the consequence than the cause of mesangial expansion.<sup>1</sup> Nevertheless, the results of the Renin-Angiotensin System Study (RASS) should not be extrapolated to the relatively uncommon circumstance of patients with diabetes, normoalbuminuria, normal or increased glomerular filtration rate, and systemic hypertension. The fact remains that the large majority of patients with diabetes and normoalbuminuria are normotensive, and renal benefits from blockade of the renin-angiotensin system could not be demonstrated in such patients. If precise early predictors of diabetic nephropathy become available, new studies including only patients at high risk would be warranted. In regard to the suggestion by Katavetin and Katavetin about patients without retinopathy progression, the RASS does not have sufficient power for this kind of subanalysis. We agree that further studies are warranted.

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1. Osterby R, Parving HH, Nyberg G, Hommel E, Mauer SM, Steffes MW. Morphology of diabetic glomerulopathy and relationship to hypertension. *Diabetes Metab* 1989;15:278-83.

## Rhabdomyolysis and Acute Kidney Injury

**TO THE EDITOR:** Bosch and colleagues (July 2 issue)<sup>1</sup> observe that although conventional hemodialysis filters do not remove myoglobin (molecular weight, 17.8 kD), hemodiafiltration with super-high-flux dialyzers may be effective.<sup>2</sup> We used a hemodialysis prescription with a super-high-flux dialyzer (HCO-1100, Gambro) that efficiently removed molecules of up to 60 kD. In two patients with rhabdomyolysis and acute kidney injury,

the mean serum myoglobin clearance with a single dialysis treatment was 59%.<sup>3</sup> A 4-hour dialysis treatment cleared myoglobin from the equivalent of 9 liters of extravascular fluid (twice the intravascular volume). The kinetics of myoglobin that we observed were similar to the kinetics of free light chains (25 to 50 kD).<sup>4</sup>

The experience gained in the use of super-high-flux dialysis to remove free light chains in myelo-

ma kidney (or cast nephropathy) should expedite the development of a randomized trial of the removal of myoglobin. A randomized, controlled trial of the use of super-high-flux dialysis to remove free light chains is under way.<sup>5</sup>

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1. Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. *N Engl J Med* 2009;361:62-72.
2. Ronco C. Extracorporeal therapies in acute rhabdomyolysis and myoglobin clearance. *Crit Care* 2005;9:141-2.
3. Hutchison CA, Harding S, Basnayake K, Bradwell AR, Cockwell P. Myoglobin removal by high cut-off hemodialysis: in-vivo studies. *J Am Soc Nephrol* 2007;18:250A. abstract.
4. Hutchison CA, Cockwell P, Reid S, et al. Efficient removal of immunoglobulin free light chains by hemodialysis for multiple myeloma: in vitro and in vivo studies. *J Am Soc Nephrol* 2007;18:886-95.
5. Hutchison CA, Cook M, Heyne N, et al. European trial of free light chain removal by extended haemodialysis in cast nephropathy (EuLITE): a randomised control trial. *Trials* 2008;9:55.

**TO THE EDITOR:** In their review article on rhabdomyolysis and acute kidney injury, Bosch et al. summarize the limited efficacy and prognostic impact of extracorporeal myoglobin removal by standard blood-purification techniques. New options are now possible given the availability of protein-permeable, high-cutoff filters in Europe (filing for approval by the U.S. Food and Drug Administration is in preparation). These filters are currently under investigation for elimination of nephrotoxic free light chains in cast nephropathy associated with multiple myeloma.<sup>1</sup> With an in vivo molecular cutoff at 45 kD, high-cutoff filters are effective in eliminating the 17-kD molecule myoglobin.<sup>2</sup> We have used high-cutoff hemodialysis for myoglobin removal in severe rhabdomyolysis. Myoglobin clearance with high-cutoff filters, corrected for membrane-surface area, is up to 20 times as high as myoglobin clearance with standard high-flux hemodialysis in intraindividual comparison. With the use of full-size, high-cutoff filters for 2.1 m<sup>2</sup> of membrane-surface area (Theralite, Gambro), myoglobin clearances in excess of 70 ml per minute can be obtained, resulting in a rapid and highly effective reduction of the plasma myoglobin concentration.

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1. Hutchison CA, Cook M, Heyne N, et al. European trial of free light chain removal by extended haemodialysis in cast nephropathy (EuLITE): a randomised control trial. *Trials* 2008;9:55.
2. Naka T, Jones D, Baldwin I, et al. Myoglobin clearance by super high-flux hemofiltration in a case of severe rhabdomyolysis: a case report. *Crit Care* 2005;9:R90-R95.

**THE AUTHORS REPLY:** Basnayake and colleagues comment on the potential use of extracorporeal removal of myoglobin with the use of super-high-flux dialysis membranes, and Heyne and colleagues suggest the use of high-cutoff membranes for this purpose. Although the experience with super-high-flux membranes or high-cutoff membranes may be encouraging, it is still limited. A number of questions about myoglobin metabolism, kinetics, and body distribution have not been answered, and these issues may complicate the application of the appropriate extracorporeal treatment in terms of frequency, duration, and intensity.<sup>1</sup> In addition, high-cutoff membranes with reported molecular-weight cutoff values of approximately 50 kD (100 kD in the article by Naka et al.<sup>2</sup>) may be associated with unwanted losses of albumin or other components that may be dangerous for the patient. We believe that although these techniques are promising, randomized, controlled clinical trials will be necessary before they can be recommended. Therefore, we would emphasize that since conventional dialysis or standard hemofiltration has not achieved clinically significant myoglobin removal,<sup>1,3</sup> and the experience with high-cutoff membranes or super-high-flux membranes is limited, at present, these techniques cannot be recommended for the preventive removal of myoglobin in rhabdomyolysis.

In Table 3 of our article, we recommend that volume replacement with normal saline solutions should be used for the prevention or treatment of rhabdomyolysis-induced acute kidney injury. The use of solutions containing bicarbonate is optional because their benefits have not been firmly demonstrated. Although slightly hypertonic bicarbon-

ate solutions have been used by some investigators and are commonly used in some countries as 1/6 M sodium bicarbonate (1.4% sodium bicarbonate),<sup>3</sup> we agree with others<sup>4,5</sup> that they should be isotonic or even slightly hypotonic. Since normal saline, commonly called isotonic saline is in fact slightly hypertonic (154 mmol per liter of sodium and chloride), the alternation with 100 mmol of bicarbonate in 1 liter of 5% dextrose is the most appropriate option if alkalinization is used. If 0.45% saline is to be used, it should be combined with 50 to 70 mmol of bicarbonate (rather than the 100 mmol listed in Table 3 of our article). As recommended in the text, volume repletion and alkalinization in patients with rhabdomyolysis should be monitored by the frequent measurement of levels of urine pH and serum bicarbonate, potassium, and calcium.

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1. Mikkelsen TS, Toft P. Prognostic value, kinetics and effect of CVVHDF on serum of the myoglobin and creatine kinase in critically ill patients with rhabdomyolysis. *Acta Anaesthesiol Scand* 2005;49:859-64.
2. Naka T, Jones D, Baldwin I, et al. Myoglobin clearance by super high-flux hemofiltration in a case of severe rhabdomyolysis: a case report. *Crit Care* 2005;9:R90-R95.
3. Peltonen S, Ahlström A, Kylävaio V, Honkanen E, Pettilä V. The effect of combining intermittent hemodiafiltration with forced alkaline diuresis on plasma myoglobin in rhabdomyolysis. *Acta Anaesthesiol Scand* 2007;51:553-8.
4. Sever MS, Vanholder R, Lameire N. Management of crush-related injuries after disasters. *N Engl J Med* 2006;354:1052-63.
5. Vanholder R, Sever MS, Ereik E, Lameire N. Rhabdomyolysis. *J Am Soc Nephrol* 2000;11:1553-61.

## Primary Care — Lifelines and Shortages

**TO THE EDITOR:** In their Perspective article (June 25 issue),<sup>1</sup> Bodenheimer et al. accurately depict our nation's intensifying primary care crisis. Although studies have found that increasing the number of primary care physicians leads to better and cheaper health care for their patients,<sup>2-4</sup> surveys also portray these doctors as physicians under siege.<sup>5</sup> One necessary reform is the equalization of compensation between general and specialty physicians.

Our U.S. system pays much more for procedures than for the medical management of illness. In my specialty of orthopedics, Medicare will approve a charge of approximately \$60 for my most common office visit but will permit a charge of over \$350 for carpal-tunnel-release surgery and over \$1,100 to fix a fractured hip. The carpal-tunnel procedure takes me as long as a simple office visit, whereas the hip surgery routinely requires the time of three patient visits. The great extent of these variations in reimbursement cannot be rationally justified.

Addressing these inequalities must be a part of any health care reform package. Our country cannot tolerate a reduced supply of primary care physicians and the corresponding decreased health of our citizenry. We specialists should be quite proud of the enormous contributions that we

make, but we cannot claim that our therapies are more important than the medical management of illnesses such as heart failure and diabetes. We need to view reimbursement from the vantage point of our primary care colleagues; specialty physicians have long opposed Medicare's relatively modest sustainable-growth cuts in reimbursement. Can we envision accepting a 60% cut? We would never willingly tolerate that level of compensation, but it is the current average for family physicians.<sup>6</sup> In a recent survey of primary care physicians, only 17% felt that their practices were "healthy and profitable."<sup>5</sup> Specialists should support reimbursement rates that close the gap among physicians and thereby improve the viability of primary care. Although new rates would come at a cost to specialists, the benefit to our patients' health must be our primary concern.

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1. Bodenheimer T, Grumbach K, Berenson RA. A lifeline for primary care. *N Engl J Med* 2009;360:2693-6.
2. Macinko S, Starfield B, Shi L. Quantifying the health benefits of primary care physician supply in the United States. *Int J Health Serv* 2007;37:111-26.
3. Starfield B, Shi L, Grover A, Macinko J. The effects of specialist supply on populations' health: assessing the evidence. *Health Aff (Millwood)* 2005;Suppl Web Exclusives:W5-97-W5-107.