

# Why are rheumatologists treating lupus nephritis?

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A consensus document was published in 2006 that codified definitions of the various renal responses and nonresponses to therapy in patients with nephritis secondary to systemic lupus erythematosus.<sup>1</sup> This document was well researched and provided a sound approach to defining measures of kidney function and response criteria for lupus nephritis. What was especially interesting about this publication was that the chair of the consensus group was a rheumatologist and the document itself was published in *Arthritis and Rheumatism*. Furthermore, the first authors on the majority of articles used as the evidence base for this paper were rheumatologists.<sup>1</sup> Of the 21 clinical trials of renal disease in lupus that were listed in the evidence table, 13 were published in internal medicine, pediatric or pheresis journals, 5 in rheumatology journals, and just 2 in nephrology journals.

How did this transfer of ‘ownership’ of lupus nephritis to rheumatologists happen? There are two possible reasons. Either rheumatologists hijacked lupus nephritis as part of their overall management of systemic lupus erythematosus, or, more likely, nephrologists lost interest in this disease because they became occupied elsewhere, such as with making hemodialysis rounds four times a month. In either case, the fact that renal biopsies can now be performed by interventional radiology might have been a contributing factor. Previously, renal biopsy was under the aegis of the nephrology community, so a kidney doctor had to be involved at least to the extent of agreeing to perform the biopsy, and possibly in following up with diagnosis and therapy. Now, however, the rheumatologist (or even internist) can, at many centers, request renal biopsy without the intercession of the nephrology service. Thus, lupus nephritis can be diagnosed and treated by the rheumatologist alone.

Whichever of the above two scenarios is responsible, ownership of lupus nephritis by rheumatologists becomes a self-fulfilling prophecy as rheumatologists become more empowered and confident in the management of this renal disease,

and many nephrologists are perhaps beginning to feel progressively more uncomfortable in dealing with lupus. Management of lupus nephritis does not belong to nephrologists or rheumatologists, however, but to physicians who understand this condition. Nevertheless, there are still insights that nephrologists can provide that will improve diagnosis and treatment.

It is hoped that, with years of training and practice, the nephrologist has special insight into the diagnosis and treatment of glomerulonephritis. What follows are some examples of issues of which nephrologists are more likely than rheumatologists to be aware, and of which they can contribute their knowledge as subspecialists to the management of lupus.

First, in microscopic urinalysis, lots of red blood cells and red cell casts per high-power field are not necessarily worse than a few red blood cells and red cell casts. The pseudo-Addis-count assumption that more red cells and casts reflect a more severe form of disease is common among rheumatologists, and in a tightly regulated urinalysis laboratory this might be the case. In real life, however, the number of cells or casts can be affected by the duration of centrifuge time and how vigorously the pellet at the bottom of the centrifuge tube is resuspended into the supernatant. Furthermore, nephrologists are aware from their experience with, for example, IgA nephropathy, that even more-benign processes than the development of lupus nephritis (such as mesangial proliferation) can be associated with red cells and red cell casts in the urine, but this does not necessarily mean that the patient needs to be treated with antiproliferative agents.

Second, severe proliferative nephritis takes time to heal. Nephrologists are aware from their management of diseases such as postinfectious glomerulonephritis that severely inflamed glomeruli or tubules can take many weeks or months to heal. It is not rare for a patient to remain on dialysis for several months before signs of renal improvement become apparent and dialysis can be withdrawn. Lack of awareness of this fact

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Received 5 November 2006

Accepted 12 January 2007

www.nature.com/clinicalpractice  
doi:10.1038/ncpneph0489

can lead to spiraling empiricism, whereby immunosuppressive therapy is inappropriately intensified when the serum creatinine level does not start to improve within, say, the first week. The consequence of this approach could be increased susceptibility to septic complications, which are an important cause of morbidity and mortality in active lupus. It is likely that, in the subset of patients with acute renal failure secondary to lupus that does show rapid improvement in renal function, the component that is improving is the associated acute tubular necrosis. This concept is another that many rheumatologists could not be expected to know.

Third, there are other causes of increased creatinine levels in patients with lupus nephritis. Clinicians other than nephrologists might be unaware that several processes (not necessarily related to nephritis) can affect renal function at the same time. For example, a patient with severe peripheral edema might be vigorously diuresed, with a consequent increase in serum creatinine concentration. If the patient is also receiving a corticosteroid, the serum urea might also be elevated as a result of both the contraction of plasma volume and the stimulation of protein catabolism via the urea disposal pathway. Neither the increased creatinine nor increased urea levels necessarily reflect a worsening of renal parenchymal disease, however. Other causes of increased serum creatinine concentration that are unrelated to worsening or unresolving glomerulonephritis include associated acute tubular necrosis (discussed above), administration of co-trimoxazole as prophylaxis for *Pneumocystis jiroveci* pneumonia, and concurrent treatment with NSAIDs. Finally, coadministration of angiotensin-converting-enzyme inhibitors or angiotensin-receptor blockers with diuretics can also lead to intrarenal hypoperfusion and a hemodynamically induced decrease in renal function.

Fourth, the completeness of a 24 h urine collection is judged by total creatinine excretion, not by urine volume. It is well-recognized by nephrologists that 24 h urine volume usually reflects daily solute and water intake. This measure cannot, therefore, be used as a reliable indicator of the completeness of collection. If the patient's serum creatinine level is in steady state, the total

creatinine excretion is a better marker of the accuracy of the urine collection. I have witnessed patients receive more-intensified immunotherapy because they had a 50% increase in proteinuria, when the total creatinine excretion had increased by the same proportion, reflecting an overcollection. Similarly, 24 h urine collections can underestimate or overestimate creatinine clearance if not performed properly.

Finally, good planning for renal replacement therapy might be more important than intensifying immunosuppression for a patient with advanced chronic renal disease. A patient with stage 4 or 5 chronic kidney disease as a result of previous damage from lupus nephritis might not warrant another round of aggressive immunosuppressive therapy to 'save' the kidneys in the face of a renal-limited flare of the disease. The 'cost' of increased immunosuppression must be weighed against the chances of achieving significant return of renal function or keeping a patient off dialysis for a few more months. In some cases it might be better to plan for a controlled transition to dialysis instead. Nephrologists who also have experience in managing renal transplant recipients may be particularly adept in handling immunosuppressive agents—in particular, in knowing when the risk of further therapy outweighs the potential benefit.

What should be done, then, to improve the management of lupus nephritis? Program directors must ensure that nephrology trainees receive core training in the diagnosis and treatment of this disease. Such training should include systematic reviews of the literature as part of the curriculum, and experience in the management of acute and chronic manifestations of lupus nephritis. It would be preferable for nephrologists to work together with other specialists, especially rheumatologists, in the management of this multisystem disease, as this integrative approach may help us to learn from each other, and, most importantly, improve patient care.

#### Reference

- 1 Renal Disease Subcommittee of the American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Response Criteria (2006) The American College of Rheumatology response criteria for proliferative and membranous renal disease in systemic lupus erythematosus clinical trials. *Arthritis Rheum* **54**: 421–432

#### Competing interests

The author declared she has no competing interests.