

# Managing Comorbidities in the Rheumatic Diseases: The New Reality



While we as rheumatologists are encouraged by recent advances in the therapy of several of our most challenging diseases, we are also keenly aware of important contributions in the recognition of comorbidities in the rheumatic diseases. These are no doubt intricately linked to and may have an impact on the quality of life and survival of our patients as much as the primary disease itself. So as we are now more able to manage the immediate manifestations of disease — pain, inflammation, disability — our attention turns to managing the comorbid conditions that accompany them.

Significant advances have been made not only in the epidemiologic description of comorbid conditions such as cardiovascular disease and glucocorticoid-induced osteoporosis, but also into their pathogenesis. Armed with this increasing body of knowledge, it is our hope that an even more comprehensive approach to patient care would result. Granted, this has always been the forte of the rheumatologist — care of the whole patient with multisystem disease. Now, the “multisystem” horizon has been broadened.

The report of Al-Herz, *et al* in the March issue of *The Journal*<sup>1</sup> sheds light on the practical challenges that lie ahead in the management of cardiovascular disease in systemic lupus erythematosus (SLE), and also sounds an alert regarding the management of comorbidities in general. This article provides a first examination into the recognition and screening of several cardiovascular risk factors in patients with SLE. Using the combined setting of a university-based tertiary referral clinic as well as several community-based private practices, the report surveys the extent to which known cardiac risk factors are documented and acted upon if abnormal in patients with SLE. In all, the results are enlightening. The authors demonstrate that hyperlipidemia occurred in 55% of subjects in whom measurements were made; however, lipids were measured in only 31% of subjects. Of those with abnormalities, only 36% had some sort of documented intervention, either diet, pharmacotherapy, or a referral for management. Other risk factors

such as the presence of nephritic syndrome, hypertension, and smoking received more attention in terms of screening. It could be argued, however, that knowledge of these particular risk factors would come about as a matter of routine care in SLE, not requiring the specific cognizance of cardiac risk. Thus, for those risk factors that require a specific awareness, screening maneuvers were not commonly performed.

We have appreciated that young women with SLE may be up to 50 times more likely to have a myocardial infarction than population-based controls<sup>2</sup> and several-fold more likely to be hospitalized for myocardial infarction, congestive heart failure, or stroke<sup>3</sup>, increases that are not fully accounted for by traditional Framingham risk factors<sup>4</sup>. The earlier observation that lupus sera was in itself atherogenic via immune complex-mediated mechanisms involving low density lipoprotein<sup>5</sup> has been recently augmented by findings that antibodies directed against high density lipoprotein and  $\beta_2$ -glycoprotein I may play a role in atherogenesis<sup>6</sup>. Although no therapy is available to address these latter mechanisms specifically, modification of known risk factors is presently possible.

It becomes apparent, however, that screening for cardiac risk factors, according to the report of Al-Herz, *et al*, is underutilized. One reason may be that physicians, including rheumatologists, may not be aware of the importance of cardiovascular disease in SLE. Indeed, the fact that the academic center performed much better in screening for risk factors than the private practices may reflect this. Also, the authors recognize that the prevalence of screening may be underestimated due to a failure of documentation. But given the known prevalence of ischemic cardiac disease in SLE, which may be as high as 82% in patients with nonspecific chest symptoms and 43% of asymptomatic women with SLE<sup>7</sup>, and an estimated incidence of myocardial infarction of 1.5% per year (strokes, 0.5% per year)<sup>8</sup>, the results of this study should prompt further evaluation into the state of management of these conditions.

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See Cardiovascular disease risk factor screening in SLE.  
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The article by Al-Herz, *et al* provides a first practice-based look at the state of care for cardiovascular comorbidity in SLE. Certainly, more data are required from a variety of settings to complete the picture, and just as with other comorbid conditions such as glucocorticoid-induced osteoporosis (GIOP), this information will help to develop strategies for intervention.

Even for GIOP, a condition that is well recognized and has been well described from both epidemiologic and mechanistic perspectives, the struggle continues to implement optimal care. A recently published study by Solomon and colleagues demonstrated that only 23% of patients taking longterm glucocorticoids had undergone bone densitometry testing in an academic rheumatology practice<sup>9</sup>. Other reports document the relatively infrequent use of anti-osteoporosis medications in those patients at risk<sup>10-14</sup>.

The problem of GIOP serves as a model by which we can learn the lessons of addressing the issue of comorbid conditions in patients with rheumatic diseases. The issue certainly has many dimensions, including recognition of the scope of the problem, elucidation of its pathophysiologic basis, the development of practice guidelines and dissemination of information to practitioners, continued practice-based quality monitoring, and even policy and legislative changes, all of which need to be addressed. This will continue to apply for all comorbid conditions, present and future, including cardiovascular disease in SLE and rheumatoid arthritis<sup>15-17</sup>, and malignancies in inflammatory myopathies<sup>18</sup> and perhaps SLE<sup>19</sup>.

With Al-Herz, *et al*'s article as a start, it is expected that more practice-based data such as the work of Bruce, *et al*<sup>20</sup> will continue to emerge to define the performance of practitioners over time and the areas in which interventions can be made to improve clinical management. Comparisons between private and academic practices as well as managed-care organizations will be necessary to examine the effect of delivery systems, which include the availability of technology and reimbursement for investigating these conditions. Such studies may also provide insights into physician awareness, and the need for continued education and dissemination of information.

While we do not have the full picture of all the modifiable factors involved in atherogenesis in SLE, data indicate that traditional risk factors are important and should be optimized<sup>4,21</sup>. Thus, vigilance regarding lipid levels, blood pressure, smoking cessation, regular exercise and weight control, glycemic control, and minimizing corticosteroid exposure should be maintained. In addition, management of homocysteine levels<sup>22</sup> should be strongly considered, as should appropriate monitoring and treatment of antiphospholipid antibody-related complications, all in addition to minimizing disease activity. At the same time, ongoing studies will no doubt shed further light on the relative impact of each of these interventions and define optimal treatment strategies.

Practice guidelines serve the broader purpose of defining the important factors within a disease entity, making updated evidence-based recommendations regarding treatment, and being a vehicle for dissemination of information, as exemplified by the American College of Rheumatology's guidelines for GIOP<sup>23</sup>. It is expected that similar documents will evolve for the other comorbid conditions that we encounter. It is also expected that studies into the practical implementation of such guidelines will be conducted, as practice patterns do not always reflect published recommendations; the reasons for this are not fully clear. Information needs to reach not only the rheumatologist but also other collaborating practitioners, including those in primary care. While not explicitly mentioned, the Al-Herz, *et al* study counted information obtained from both the rheumatologist and the patient's primary care/family doctor, whose information was made available to the specialist. This underscores the need for ongoing coordination both in screening and treating comorbid conditions, and ongoing education of physicians.

As information and guidelines evolve, we will be faced with issues of reimbursement and insurance coverage for the screening and treatment of these conditions. These will likely need to be augmented, calling for an increased dialogue with legislators and insurance payors. Bone densitometry screening in the US has been made much more accessible since the passage of the Bone Mass Measurement Act in 1997; we hope that a "Cardiac Screening Act" or "Malignancy Screening Act" for patients with rheumatic diseases will provide longterm benefits to patients and society in the future.

The problem of cardiovascular disease in SLE, as described by Urowitz, *et al*<sup>24</sup>, of the high incidence of myocardial infarction occurring in young, premenopausal women, is to say the least counterintuitive and alarming. The same may be said of any of the other comorbid conditions mentioned in this editorial. Although the epidemiology and biology of these problems have received much attention, evidence suggests that many questions, and indeed many barriers, still exist to providing the comprehensive patient care that we have all envisioned. At the same time, the work continues to overcome these barriers. We hope that the new reality will be the minimization of the effects of comorbidities on the lives of our patients.

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## REFERENCES

1. Al-Herz A, Ensworth S, Shojana K, Esdaile JM. Cardiovascular disease risk factor screening in systemic lupus erythematosus. *J Rheumatol* 2003;30:493-6.

2. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. *Am J Epidemiol* 1997;145:408-15.
3. Ward MM. Premature morbidity from cardiovascular and cerebrovascular diseases in women with systemic lupus erythematosus. *Arthritis Rheum* 1999;42:338-46.
4. Esdaile JM, Abrahamowicz M, Grodzicky T, et al. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. *Arthritis Rheum* 2001;44:2331-7.
5. Kabakov AE, Tertov VV, Saenko VA, Poverenny AM, Orekhov AN. The atherogenic effect of lupus sera: systemic lupus erythematosus-derived immune complexes stimulate the accumulation of cholesterol in cultured smooth muscle cells from human aorta. *Clin Immunol Immunopathol* 1992;63:214-20.
6. Delgado AJ, Ames PR, Donohue S, et al. Antibodies to high-density lipoprotein and beta 2-glycoprotein I are inversely correlated with paraoxonase activity in systemic lupus erythematosus and primary antiphospholipid syndrome. *Arthritis Rheum* 2002;46:2686-94.
7. Sun SS, Shiau YC, Tsai SC, Lin CC, Kao A, Lee CC. The role of technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography (SPECT) in the detection of cardiovascular involvement in systemic lupus erythematosus patients with non-specific chest complaints. *Rheumatology* 2001;40:1106-11.
8. Liang MH, Mandl LA, Costenbader K, Fox E, Karlson E. Atherosclerotic vascular disease in systemic lupus erythematosus. *J Natl Med Assoc* 2002;94:813-9.
9. Solomon DH, Katz JN, Jacobs JP, La Tourette AM, Coblyn J. Management of glucocorticoid-induced osteoporosis in patients with rheumatoid arthritis: Rates and predictors of care in an academic rheumatology practice. *Arthritis Rheum* 2002;46:3136-42.
10. Gudbjornsson B, Juliusson UI, Gudjonsson FV. Prevalence of long term steroid treatment and the frequency of decision making to prevent steroid induced osteoporosis in daily clinical practice. *Ann Rheum Dis* 2002;61:32-6.
11. Lee E, Zuckerman IH, Weiss SR. Patterns of pharmacotherapy and counseling for osteoporosis management in visits to US ambulatory care physicians by women. *Arch Intern Med* 2002;162:2362-6.
12. Ettlinger B, Chidambaran P, Pressman A. Prevalence and determinants of osteoporosis drug prescription among patients with high exposure to glucocorticoid drugs. *Am J Manag Care* 2001;7:597-605.
13. McDonald J, Stewart J, Urowitz MB, Gladman DD. Peripheral vascular disease in patients with systemic lupus erythematosus. *Ann Rheum Dis* 1992;51:56-60.
14. Kiebzak GM, Beinart GA, Perser K, Ambrose CG, Siff SJ, Heggenes MH. Undertreatment of osteoporosis in men with hip fracture. *Arch Intern Med* 2002;162:2217-22.
15. Wolfe F, Freundlich B, Straus WL. Increase in cardiovascular and cerebrovascular disease prevalence in rheumatoid arthritis. *J Rheumatol* 2003;30:36-40.
16. Goodson NJ, Wiles NJ, Lunt M, Barrett EM, Silman AJ, Symmons DP. Mortality in early inflammatory polyarthritis: cardiovascular mortality is increased in seropositive patients. *Arthritis Rheum* 2002;46:2010-9.
17. del Rincon ID, Williams K, Stern MP, Freeman GL, Escalante A. High incidence of cardiovascular events in a rheumatoid arthritis cohort not explained by traditional cardiac risk factors. *Arthritis Rheum* 2001;44:2737-45.
18. Hill CL, Zhang Y, Sigurgeirsson B, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet* 2001;357:96-100.
19. Bernatsky S, Clarke A, Ramsey-Goldman R. Malignancy and systemic lupus erythematosus. *Curr Rheumatol Rep* 2002;4:351-8.
20. Bruce IN, Gladman DD, Urowitz MB. Detection and modification of risk factors for coronary artery disease in patients with systemic lupus erythematosus: a quality improvement study. *Clin Exp Rheumatol* 1998;16:435-40.
21. Manzi S, Wasko MC. Getting to the heart of the matter in systemic lupus and rheumatoid arthritis. *Bull Rheum Dis* 2001;50:1-4.
22. Petri M, Roubenoff R, Dallal GE, Nadeau MR, Selhub J, Rosenberg IH. Plasma homocysteine as a risk factor for atherothrombotic events in systemic lupus erythematosus. *Lancet* 1996;348:1120-4.
23. American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. *Arthritis Rheum* 2001;44:1496-503.
24. Urowitz MB, Bookman AA, Koehler BE, Gordon DA, Smythe HA, Ogryzlo MA. The bimodal mortality pattern of systemic lupus erythematosus. *Am J Med* 1976;60:221-5.