

Initial Release Date: December 15, 2008
CE Available Until: December 15, 2010

CE-Certified

RHEUMATOLOGY NURSE NEWSLETTER

Issue 4, Winter 2008

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Practical information and tools you can apply to your everyday practice!

LEARNING OBJECTIVES

Upon completion of this activity, participants will be able to do the following:

- Describe the genesis of the American College of Rheumatology's (ACR's) recently published treatment recommendations and the methods used to develop overall recommendations
- Explain the role of nonbiologic and biologic disease-modifying antirheumatic drugs (DMARDs) as prescribed within the ACR's recommendations for patients with early rheumatoid arthritis (RA) and those with intermediate or longer-duration RA
- Identify hurdles that have historically prevented the widespread acceptance of published healthcare recommendations at individual treatment centers ■

STATEMENT OF EDUCATIONAL NEED

In June 2008, the ACR published updated recommendations for the use of nonbiologic

and biologic DMARDs in patients with RA. These were the first recommendations for nonbiologic DMARDs since 2002 and the first recommendations ever for biologic DMARDs. While they are not intended to replace the independent judgment of healthcare practitioners, the intent of these recommendations was to standardize clinical practice by providing evidence-based guidelines for the treatment of patients with RA.

Historically, the implementation of RA guidelines in the United States has been hampered by a number of factors, including lack of agreement with individual recommendations. The ACR's expert panel attempted to minimize barriers to implementation through the use of a structured review process shown to have a high degree of validity. Rheumatology nurses must familiarize themselves with these recommendations, as well as the logic behind them, to improve the quality of overall patient care.

This activity is designed for rheumatology nurses, rheumatology advanced practice nurses, and infusion nurses. ■

INTRODUCTION

Rheumatology Nurse is a CE-certified newsletter series designed for nurses who manage patients with RA **by** nurses who understand firsthand the complexities and challenges of managing patients with RA.

Each newsletter contains practical information and tools you can apply to your everyday practice! ■



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Nicole M. Furfaro, MSN, ARNP, is the nurse planner for this activity.

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THE 2008 ACR RECOMMENDATIONS

What Do Nurses

Treatment options for rheumatoid arthritis (RA) have expanded dramatically in the past decade to include both nonbiologic disease-modifying antirheumatic drugs (DMARDs) and newer biologic agents. Earlier this year, after reevaluating its 2002 treatment guidelines, the American College of Rheumatology (ACR) released updated recommendations for the use of nonbiologic and biologic DMARDs in RA.¹ The 2008 ACR recommendations address 5 key areas of RA assessment and treatment:

- Indications for DMARD use
- Screening for tuberculosis (TB) prior to biologic DMARD therapy
- Safety monitoring
- Assessing clinical response
- Factoring cost and patient preference in the selection of biologic DMARDs

The 2008 recommendations were developed using a Research and Development/University of California, Los Angeles (RAND/UCLA) Appropriateness Method.² Unlike other guideline-development methods (eg, the Delphi method), the RAND/UCLA process is not designed to force expert consensus. While devising the most recent ACR guidelines, if no agreement was reached among the expert panel based on the available evidence, no recommendation was made. As a result, several pertinent questions—in particular, questions about switching therapy—are left unanswered within the guidelines. Additionally, while the recommendations address a variety of individual clinical decision points, they do not provide a comprehensive algorithm or longitudinal road map for use by healthcare providers.³ ■

Need to Know?

INDICATIONS FOR DMARD USE

According to the guidelines, the ACR expert panel supports initial therapy with methotrexate or leflunomide monotherapy for almost all patients, regardless of disease duration, disease activity, or clinical features. However, the recommendations move quickly toward more aggressive therapy, particularly for patients with unfavorable baseline characteristics. For example, first-line biologic therapy is recommended for patients with high disease activity or poor prognostic features, such as radiographic evidence of erosions or elevated rheumatoid factor (RF) level, anti-cyclic citrullinated peptide (anti-CCP) antibody level, erythrocyte sedimentation rate (ESR), or C-reactive protein (CRP) level.





Specific treatment recommendations are stratified according to the average disease duration in reviewed clinical studies: <6 months, or early disease; 6–24 months, or intermediate disease duration; and >24 months, or longer disease duration. For biologic DMARD use, disease duration is further broken down into ≤3 months or 3–6 months. In addition to disease duration, treatment recommendations

are also influenced by disease activity and the presence of poor prognostic indicators.

In the 2008 recommendations, biologic therapy is not recommended for patients with early RA who have low or moderate disease activity. However, anti-tumor necrosis factor-alpha (TNF-α) agents are indicated as an option to be used interchangeably in combination with methotrexate as first-line therapy in

patients with early RA who have high disease activity. In addition, anti-TNF-α agents are recommended for patients with intermediate- and longer-duration RA who have failed to respond adequately to methotrexate therapy. ■

CONTRAINDICATIONS TO DMARD THERAPY

After reviewing the potential adverse events associated with DMARD therapy, the ACR panel developed a list of contraindications to guide the use of each class of DMARDs. Specifically, the ACR recommendations discourage treatment with methotrexate, leflunomide, or biologic DMARDs in patients who have active bacterial infections, although these agents can be started shortly after infections have been fully resolved or successfully treated. Methotrexate, leflunomide, or biologic DMARDs are also discouraged in patients who have herpes zoster infection, hepatitis B or C, or active, latent, or suspected TB. Consequently, it is important to test for hepatitis and TB exposure before initiation of therapy or on an as-needed basis in high-risk individuals.

The ACR recommendations also caution against the use of methotrexate, leflunomide, or minocycline among patients who are planning to get pregnant and throughout the duration of pregnancy and breastfeeding. Additionally, patients with a history of heart failure or lymphoma, or with multiple sclerosis or demyelinating disorders, are discouraged from being prescribed anti-TNF-α agents.

In patients with hematologic and oncologic contraindications (white blood cell count <3000/mm³), the recommendations state that neither leflunomide nor methotrexate should be used. In addition, patients with a platelet count <50,000/mL³ should avoid therapy with leflunomide, methotrexate, and sulfasalazine.

TABLE 1
Recommendations for Vaccinations in Patients With RA Receiving Nonbiologic and Biologic DMARDs

Therapeutic Agents*	Pneumococcus†	Influenza‡	Hepatitis B§	Avoid Live Vaccinations
Hydroxychloroquine		X		
Leflunomide	X	X	X	
Methotrexate	X	X	X	
Minocycline		X		
Sulfasalazine	X	X		
All biologic agents	X	X	X	X

*Therapies are listed alphabetically; X=recommended.

†Vaccination should be considered according to recommendations of the Centers for Disease Control and Prevention (CDC), which includes all patients with chronic illness, active malignancy, immunosuppression/use of immunosuppressive drugs, diabetes mellitus, pregnancy, and chronic lung disease, independent of when RA drugs are initiated. The CDC also recommends a 1-time pneumococcal revaccination after 5 years for persons with the previously listed conditions. For persons aged ≥65 years, 1-time revaccination is recommended if they were vaccinated ≥5 years previously and were <65 years old at the time of primary vaccination.

‡Vaccination should be considered according to recommendations of the CDC, which includes all patients with chronic illness, active malignancy, immunosuppression/use of immunosuppressive drugs, diabetes mellitus, pregnancy, and chronic lung disease, independent of when RA drugs are initiated.

§If hepatitis risk factors are present (eg, intravenous drug abuse, multiple sex partners in the previous 6 months, healthcare personnel).

DMARD=disease-modifying antirheumatic drug, RA=rheumatoid arthritis.

Additional recommendations for patients with cancer include the following:

- Leflunomide and methotrexate are contraindicated in patients with a history of abnormal blood counts
- Leflunomide, methotrexate, and anti-TNF- α agents are contraindicated in patients with lymphoma that has been diagnosed or treated within the past 5 years
- For all other types of cancer, the ACR did not provide any specific recommendations for the use of nonbiologic or biologic DMARDs

The ACR recommendations also address the risk of perioperative infection in patients taking biologic DMARDs for RA. In general, biologic therapy should be withheld during the perioperative period, which is defined as at least 1 week before and 1 week after surgery. However, optimal management of perioperative risk depends both on the half-life of the biologic

agent (eg, a longer withdrawal period is recommended for agents with longer half-lives) and the inherent infectious risk of the surgical procedure (eg, there is less concern regarding patients undergoing minor surgeries). ■

TUBERCULOSIS SCREENING

Biologic DMARD therapy is contraindicated in patients who have a history of active or latent TB, severe upper respiratory tract infection, or nonhealing skin ulcers. Therefore, before initiating biologic DMARD therapy, all patients should be assessed for potential TB risk factors and undergo a TB skin test, regardless of previous TB surveillance. As recommended by the Centers for Disease Control and Prevention, patients with latent TB infection should be treated with daily isoniazid for 9 months, and treatment should be managed by a clinician with expertise in TB. ■

SAFETY MONITORING

Ongoing risk surveillance and safety monitoring are important features of the 2008 recommendations. For example, the ACR recommendations encourage preventive immunizations (Table 1). In particular, influenza and pneumococcal vaccine status should be updated before starting RA therapy, and live vaccines (eg, varicella-zoster vaccine, oral polio, and rabies) are contraindicated during biologic therapy. Hepatitis B and C screening is also recommended for high-risk patients.

When starting or resuming DMARD therapy, baseline tests should include a complete blood count, liver transaminase levels, and serum creatinine levels. Elevated liver transaminase levels (≥ 2 times higher than normal) are a contraindication to treatment with methotrexate, leflunomide, and sulfasalazine (Table 2). Patients receiving these DMARDs should undergo repeated testing every 2 to 4 weeks for 3 months after the initiation of treatment or dose escalation and routinely monitored at regular intervals thereafter.

TABLE 2
Recommendations for Baseline Evaluation for Patients Starting, Resuming, or Increasing the Dose of Nonbiologic and Biologic DMARDs¹

Therapeutic Agents*	CBC	Liver Transaminases	Creatinine	Hepatitis B and C Testing [†]	Ophthalmologic Examination [‡]
Hydroxychloroquine	X	X	X		X
Leflunomide	X	X	X	X	
Methotrexate	X	X	X	X	
Minocycline	X	X	X		
Sulfasalazine	X	X	X		
All biologic agents	X	X	X		

*Therapies are listed alphabetically; X=recommended test.

[†]If hepatitis risk factors are present (eg, intravenous drug abuse, multiple sex partners in the previous 6 months, healthcare personnel). Evaluation might include tests for hepatitis B surface antigen, hepatitis B antibodies, and/or hepatitis C antibodies.

[‡]Ophthalmologic examination is recommended within the first year of treatment. For patients in higher-risk categories (eg, liver disease, concomitant renal disease, and age ≥ 60 years), the American College of Ophthalmology recommends an annual follow-up eye examination.

CBC=complete blood count, DMARD=disease-modifying antirheumatic drug.



TABLE 3
Instruments for Measuring Disease Activity in RA¹

Instrument	Threshold of Disease Activity		
	Low	Moderate	High
Disease Activity Score in 28 Joints	≤3.2	3.2 to ≤5.1	>5.1
Simplified Disease Activity Index	≤11	11 to ≤26	>26
Clinical Disease Activity Index	≤10	10 to ≤22	>22
Rheumatoid Arthritis Disease Activity Index	<2	2.2 to ≤4.9	>4.9
Patient Activity Scale (PAS) or PASII	<1.9	1.9 to ≤5.3	>5.3
Routine Assessment Patient Index Data	<6	6 to ≤12	>12

Patients starting hydroxychloroquine should have a complete ophthalmologic examination, with retinal examination through a dilated pupil and central field sensitivity testing, within the first year of treatment. Ophthalmologic examinations should be repeated annually for high-risk patients and every 5 years for low-risk patients. ■

ASSESSING RESPONSE

According to the ACR expert panel, clear definitions of disease activity are required to guide evidence-based therapeutic choices. Indeed, the algorithms for each clinical decision point contain branches related to disease activity. Rather than mandating the use of any specific measures of disease activity, the panel encouraged individual healthcare providers to incorporate any 1 of the 6 measures that have been widely used in clinical studies of RA (Table 3). ■

PATIENT PREFERENCES

In reviewing data related to biologic DMARD therapy, the ACR asked the expert panel to consider the role of

cost in clinical decision making. As a result, the new recommendations include an alternative treatment pathway for patients who have cost or insurance limitations. In an editorial accompanying the publication of the ACR recommendations, the authors suggest that the alternative pathway is “presumably suboptimal” and write, “...the fact that such a modification is needed is a sad commentary on our broken healthcare system.”²³ However, it should be noted that less costly options may improve long-term adherence to DMARD therapy among patients with financial limitations to optimal care (see Hurdles to Guideline Implementation). ■

SUMMARY

The 2008 ACR recommendations reflect the importance of early aggressive therapy in minimizing long-term joint damage and disability among patients with RA. At the same time, the guidelines leave ample room for healthcare providers to apply their own judgment in treating individual patients. Because of the lack of definitive clinical evidence to support one approach over another, decisions about switching to

or adding alternative DMARDs are not addressed by the current recommendations. Future updates may expand to fill these treatment gaps, as well as venture into newer aspects of patient care, such as tailoring therapy to specific biomarkers of treatment response. ■



THE 2008 ACR RECOMMENDATIONS

Past
Present
Future

In 1996, the ACR first published clinical guidelines for the management and treatment of RA. In that year, the ACR released 2 clinical guidelines that addressed the management of RA and the monitoring of RA drug therapy, respectively, and were developed by an expert consensus of 12 rheumatologists and primary care practitioners.^{4,5} The 1996 guidelines suggested initiating treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or steroids, and reserved DMARD use only for patients with persistent active disease despite an initial trial of NSAID and/or steroid therapy.

In 2002, the ACR updated and consolidated their consensus recommendations into a single set of clinical guidelines for the management of RA.⁶ The 2002 update emphasized the importance of early and aggressive treatment, and recommended the initiation of DMARD therapy in patients with RA within 3 months of diagnosis. In 2005, the ACR released an addendum to the 2002 guidelines alerting healthcare providers to the potential cardiovascular risks associated with prolonged use of cyclooxygenase-2 (COX-2) selective NSAIDs.

Another milestone in RA recommendations was reached in 2006, when the ACR released quality measures for several rheumatic diseases, including RA.⁷ Although quality measures are not formal guidelines, they define the minimum quality standards for the assessment and treatment of RA and preview changing paradigms in RA care.

The 2006 ACR quality standards for RA include the following instructions:

- If a patient has a confirmed diagnosis of RA, a measure of each of the following should be documented within 3 months of diagnosis and at least annually thereafter: joint examination, functional status assessment, acute-phase reactant, measurement of pain, physician global assessment, and patient global assessment



- If a patient has an established diagnosis of RA, the patient should be treated with a DMARD unless contraindication to DMARD, inactive disease, or patient refusal is documented
- If a patient with RA is being treated with a DMARD and there is evidence of increased disease activity or progression of bony damage over a 6-month period, then one of the following should be done unless the patient refuses or contraindications are present:
 - Change DMARD dose or route of administration
 - Change DMARD
 - Add an additional DMARD
 - Start or increase dose of glucocorticoids
 - Provide local glucocorticoid injection(s)

For the 2008 update, the ACR refined its methodology and focus. For example, the ACR transitioned from the relatively

informal consensus method to the more rigorous, evidence-based RAND/UCLA Method of developing clinical recommendations. Although the 1996 and 2002 publications are referred to as “guidelines,” the ACR has adopted “recommendations” to describe the 2008 release.¹

In addition to introducing biologic agents for the first time, the 2008 ACR recommendations also focus on the appropriate use of just 10 agents: 5 nonbiologic DMARDs (hydroxychloroquine, leflunomide, methotrexate, minocycline, and sulfasalazine) and 5 biologic DMARDs (abatacept, adalimumab, etanercept, infliximab, and rituximab). Additional DMARDs were not included for 1 of 3 reasons:

- They were not subjected to a systematic review of the literature due to their infrequent use (eg, anakinra, which is used in <5% of RA patients)

- They are associated with a high incidence of adverse events
- They were reviewed but not recommended for patients who were set to start or resume treatment with DMARDs (anakinra, azathioprine, cyclosporine, and organic gold)

Unlike earlier guidelines, information on the use of glucocorticoids, NSAIDs, and other analgesics is not included in the 2008 recommendations.¹ Future ACR guidelines may address some of the gaps in the 2008 recommendations, particularly those related to the optimal timing and options for switching among DMARD therapies. ■

ACR Recommendations: Past, Present, and Future

Year	1996 ^{4,5}	2002 ⁶	2008 ¹
Key features	First ACR guidelines	First guideline to emphasize the importance of early and aggressive treatment	First recommendations to include biologic DMARD therapy
Initial therapy	NSAIDs or local or systemic steroid therapy	Nonbiologic DMARD within 3 months of RA diagnosis	Anti-TNF therapy in combination with MTX in patients with early RA, high disease activity, and poor prognostic features
Other recommendations	DMARDs are reserved only for patients with active disease despite NSAID and/or steroid therapy	Repetitive flares, unacceptable disease activity, or progressive joint damage requires changes to the DMARD regimen	Use of nonbiologic DMARDs and/or biologic DMARDs depends on disease duration, severity, and clinical features
Development process	Informal consensus	Informal consensus	RAND/UCLA Method

ACR=American College of Rheumatology, DMARD=disease-modifying antirheumatic drug, MTX=methotrexate, NSAID=nonsteroidal anti-inflammatory drug, RA=rheumatoid arthritis, RAND/UCLA=Research and Development/University of California, Los Angeles, TNF=tumor necrosis factor.

Hurdles to Guideline Implementation

Evidence-based guidelines can have a rapid and dramatic effect on clinical practice. In Sweden, the 1998 publication and dissemination of national guidelines promoting the benefits of early intervention with DMARDs in patients with RA was followed quickly by a statistically significant increase in nationwide DMARD use ($P < 0.0001$).⁸ In the United States, widespread implementation of ACR guidelines has been hampered by poor adherence to specific recommendations. Unfortunately, poor adherence to effective therapy can lead to poorer outcomes among patients with RA.

One recent trial examined adherence to the 2002 ACR guidelines, particularly the recommendations regarding patient assessment. Among 313 patient visits to one large academic rheumatology center in Canada, tender joints, swollen joints, and pain were assessed in the majority of visits (95%, 95%, and 69%, respectively), but functional assessment, morning stiffness, and fatigue were not routinely reported (48%, 46%, and 33%, respectively).⁹ Although the study was not designed to evaluate the reasons for nonadherence, the study authors hypothesized that some physicians disagreed with the importance of certain assessment criteria and, therefore, did not embrace those criteria in their own practices. Given the move from the consensus-based methodology of the 2002 guidelines to the evidence-based approach of the 2008 update, healthcare providers may be more willing to embrace and implement the latest recommendations.

In another recent trial set at a large academic medical center in Boston,

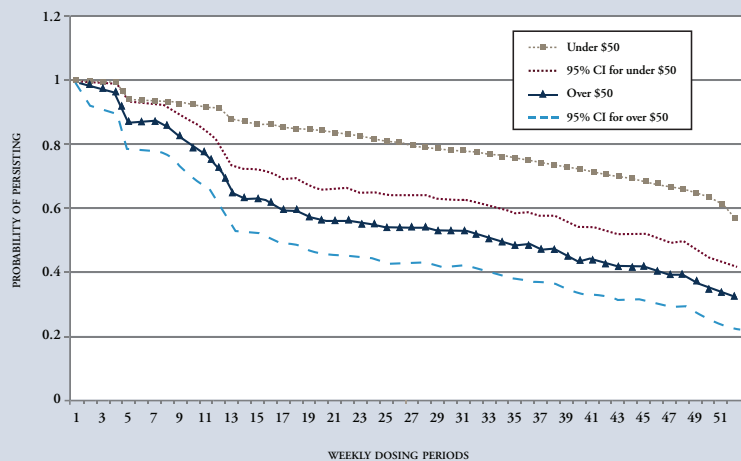
researchers measured adherence to 3 quality indicators in RA: treatment with a DMARD, appropriate baseline laboratory testing among patients with a new DMARD prescription, and follow-up monitoring for drug safety.¹⁰ Adherence to these quality indicators was 97%, 50%, and 60%, respectively. Although adherence to the first quality initiative (DMARD use) was high, these findings suggest that significant gaps in optimal care remain, even within modern treatment centers. The study authors suggested that improving treatment protocols—for example, by adopting automated reminder systems—might improve adherence to quality indicators.

Increasing healthcare costs have a dramatic and detrimental effect on adherence to biologic therapy. In one study, researchers examined the relationship between out-of-pocket (OOP) costs and adherence among 2285 patients who were treated with etanercept or adalimumab between

2002 and 2004. The probability that a patient maintained therapy through the first year of treatment dropped from 57% among patients with OOP costs less than \$50 per week to 32% for patients whose medication cost more than \$50 per week ($P < 0.001$) (Figure 1). Overall, each \$5.50 increase in weekly OOP cost translated to approximately 1 week of lost therapy in the first year.¹¹ The 2008 ACR recommendations suggest alternate treatment pathways for patients with cost or insurance limitations.

Given the cost and toxicity associated with newer treatments for RA, it is important to assess whether patients truly failed adequate trials of standard therapy. Healthcare providers should address potential adherence issues with patients and, if necessary, negotiate with patients to develop a tailored regimen that will improve the likelihood of adherence.¹² ■

FIGURE 1
Medication Adherence Drops With Increasing OOP Costs



Expert Insight

**Jeffrey R. Curtis,
MD, MPH**



For an inside view of clinical issues, Jeffrey R. Curtis, MD, MPH, a member of the ACR Core Expert Panel that developed the 2008 recommendations, provided insight in a recent one-on-one interview into the process by which the recommendations were reached as well as their clinical applicability. Dr. Curtis is assistant professor in the Division of Immunology and Rheumatology at the University of Alabama at Birmingham.

1 QUESTION 1

Can you describe the methods used for the development and scope of the 2008 ACR recommendations and some of the limitations of the recommendations?

Dr. Curtis: The ACR recommendations were developed using the RAND/UCLA Method, a structured process that has been shown to have high validity. In contrast to previous efforts in developing recommendations and guidelines that were predominantly consensus based, the process for this endeavor started with a systematic literature review and was as evidence based as possible. These recommendations are not meant to represent cookbook medicine and are not intended to eclipse clinical decision making or supplant an individual nurse's assessment about the right approach for any given patient.

The scope of the recommendations is extensive, but some things are missing. For example, we're generally silent on switching drugs. In other words, at what point should you give up on a certain therapy and change to another? Those are incredibly relevant scenarios, but they weren't addressed because there's little evidence to support one approach compared with another. If someone is not doing well on certain medicine, you're going to change them, but *when* you should change them, and *what* you should change them to, is frankly not very evidence based. Although there are certain domains where consensus might be acceptable, the task force panel elected to stay away from contentious issues where there's no evidence and best practice is completely up to the discretion of the clinician.

The guidelines also don't cover every drug. For example, some physicians use parenteral gold. Even though it has a number of side effects associated with it, some people can do quite well on it. Some of those older drugs, or ones that are less commonly used, such as azathioprine, are not addressed in the guidelines. ■

2 QUESTION 2

What are some of the current issues involved in documenting a patient's response to treatment?

Dr. Curtis: This area reflects one of the key recommendations made by the panel: you should measure how well the patient is doing. When we're thinking about hypertension, we measure blood pressure. When we're thinking about hyperlipidemia, we measure cholesterol. For heart failure, we have ejection fraction. For almost all domains of medical care, something is measured in a quantitative way. For RA, we have disease activity, measured in one of a variety of ways. However, there is a substantial amount of resistance by physicians to measuring and documenting disease activity.

The panel was very careful not to be prescriptive about what is the best way to measure disease activity, and some of the methods are based on logistic factors. For example, do you have laboratory data available at the time that you assess patients? In most scenarios, the answer is no. That means that some of the traditional measures used in clinical trials, such as a disease activity score, aren't going to be available for decision making at point of

care, when the patient is in your office. But it is recommended to measure and document something, because otherwise you're not going to know if the patient is getting better.

The fear and the pushback are twofold. First, doctors say, "I do just as well if I don't measure anything because my gestalt is sufficient to know the right thing to do." The panel did not endorse that approach. Even if all you're doing is measuring and recording a visual analog scale about how well the patient is doing, that at least is something you can compare and trend over time.

Second, doctors fear that if you document something, insurance companies could use that against you. For example, if you're not documenting that there's been enough of a change to warrant continued use of an expensive therapy, the insurance company could disallow the patient continued access to that therapy. I am aware that a number of insurance companies are starting to do that. They want an assessment, as often as every 3 to 6 months, about whether the patient is doing well on the therapies that the insurance is paying for, and you have to document that. If you don't, patients no longer are allowed to receive the medication. ■

QUESTION 3

How does that work, because the trend line can't continue to show improvement forever?

Dr. Curtis: It doesn't have to be continued improvement, because obviously they'll hit a plateau, but they have to show that the patient is doing well on therapy, whatever "well" means. That is part of the pushback.

Once you start to measure something, parameters can be set on what it means to be doing well, regardless of the 10 different ways you could potentially document patient response. That's really the fear. ■

QUESTION 4

In the treatment algorithms, some of the decision points hinge on patient prognosis. Can you describe how healthcare providers should assess prognosis?

Dr. Curtis: Some features of disease activity tell us how the patient is doing today, and others are predictive markers for how they might do in the future. There is some correlation, but prognosis is typically a separate assessment than disease activity. Some blood tests, including elevated levels of rheumatoid factor or anti-CCP antibody, and evidence of erosions on x-ray are markers of poor prognosis. You probably want to be more aggressive with these patients because they are more likely to have disability and damage in the future. A number of recommendations are predicated on whether or not the patient has any of these markers of poor prognosis.

Another factor is disease duration; the recommendations are stratified according to how long the patient has had RA. One of the critical challenges in our field relates to the substantial waiting times to see a rheumatologist. The triage system most often followed in the United States is often not effective for getting people with new-onset RA with active synovitis to be seen by an arthritis specialist for assessment. Additionally, the musculoskeletal examination is a sometimes neglected

part of medical training, so some primary care physicians may not feel that they have the expertise to recognize synovitis. However, underscoring the importance of early diagnosis and treatment, there is accumulating evidence for a "window of opportunity" during which some of the treatments that we might offer could prevent irreversible damage if patients were treated more appropriately and more aggressively. ■

QUESTION 5

What kinds of tools can be effective for implementing these treatment recommendations?

Dr. Curtis: Our standard of care for many patients is to start them on methotrexate and increase the dose over time. But that may not be aggressive enough for patients who have some of these bad prognostic features. You may want to be as aggressive as you possibly can, within some cost constraints, for these folks. Allied healthcare providers have a great deal of importance—even beyond their roles in other areas—in helping to implement a standardized approach to assessing and risk stratifying patients. That may mean developing a protocol within a rheumatology practice.

For example, the Tight Control of Rheumatoid Arthritis (TICORA) trial may be a helpful model for protocol development. The "tight control" idea is borrowed from diabetes, where we follow hemoglobin A1C levels, and a change is made in treatment if patients are not at goal.¹³ In this way, a treatment protocol

allows a more standardized approach to managing patients. Rheumatology practices can say, "Let's think about what our goals are, and if we're not at goal, then we need to change something." Overall, that could improve patient care. ■

QUESTION 6

What other evidence gaps do you hope will be filled in time for the next revision of the recommendations?

Dr. Curtis: My hope is that when these recommendations are revised in the future, we will have the evidence to know what should be done after the initial selection of treatment has been made. The recommendations we have today address only the first several steps in disease management. The next wave of research may fill in what should be next, after those steps perhaps do not sufficiently address an individual patient's evolving situation.

Another dominant area of research is identifying biomarkers or genetic predictors of response that would allow us to tailor certain therapies to individual patients. Oncology has done that for a few types of cancer; for example, for estrogen receptor (ER)-positive cancers, they might select a certain medication, but ER-negative disease might require a different medication. The next wave of research will be integrating biomarker or genetic prognostic features into treatment decisions, and ultimately, within recommendations and guidelines. Many research groups are spending tremendous resources on this. It's a challenging field, but it has tremendous promise for us as we manage patients in the next decade. ■

QUESTION 7

What other steps can rheumatology nurses take to improve overall patient care?

Dr. Curtis: Nurses should think of these patients as immunosuppressed and consider vaccinations. Everyone should get an influenza vaccination every year and should be up to date on pneumococcal vaccine. Although it is somewhat controversial, patients should be considered for the live herpes zoster vaccine based upon the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) recommendations.

Beyond vaccination, it's important to consider other health maintenance issues. Patients rarely come in to a rheumatology clinic to talk about whether they had their colonoscopy, mammography, bone density tests, and cardiovascular risk assessment. Most of the focus is on short-term toxicities, monitoring blood counts and liver enzyme tests, and perhaps eye exams for people on hydroxychloroquine. Other long-term preventive services tend to be overlooked. Some rheumatologists say, "I don't have time to think about that, that's the job of primary care." But primary care may or may not do that, and primary care providers may see the patient less often than the arthritis specialist does. Nurses can play a key role in managing these hugely important health issues and making sure that screening and other preventive measures are up to date. ■

REFERENCES

1. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
2. Fitch K, Bernstein SJ, Aguilar MD, et al. *The RAND/UCLA Appropriateness Method User's Manual*. Santa Monica, Calif.: RAND Corporation; 2001.
3. Bathon JM, Cohen SB. The 2008 American College of Rheumatology recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis: where the rubber meets the road. *Arthritis Rheum.* 2008;59(6):757-759.
4. American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. Guidelines for the management of rheumatoid arthritis. *Arthritis Rheum.* 1996;39(5):713-722.
5. American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. Guidelines for monitoring drug therapy in rheumatoid arthritis. *Arthritis Rheum.* 1996;39(5):723-731.
6. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum.* 2002;46(2):328-346.
7. American College of Rheumatology. American College of Rheumatology's starter set of measures for quality in the care for rheumatic and musculoskeletal diseases, February 2006. <http://www.rheumatology.org/practice/qmc/starterset0206.asp>. Accessed October 17, 2008.
8. Carli C, Bridges JF, Ask J, Lindblad S; for the Swedish Rheumatoid Arthritis Register. Charting the possible impact of national guidelines on the management of rheumatoid arthritis. *Scand J Rheumatol.* 2008;37(3):188-193.
9. Kitamura CR, Rohekar G, Bykerk VP, Carrette S. Are the 2002 American College of Rheumatology guidelines for the management of rheumatoid arthritis being followed in Canada's largest academic rheumatology center? *J Rheumatol.* 2007;34(11):2183-2192.
10. Agnew-Blais JC, Coblyn JS, Katz JN, Anderson RJ, Mehta J, Solomon DH. Measuring quality of care for rheumatic diseases using an electronic medical record. *Ann Rheum Dis.* 2008 May 29. [Epub ahead of print]
11. Curkendall S, Patel V, Gleason M, Campbell RS, Zagari M, Dubois R. Compliance with biologic therapies for rheumatoid arthritis: do patient out-of-pocket payments matter? *Arthritis Rheum.* 2008;59(10):1519-1526.
12. Harrold LR, Andrade SE. Medication adherence of patients with selected rheumatic conditions: a systematic review of the literature. *Semin Arthritis Rheum.* 2008 Mar 11. [Epub ahead of print]
13. Grigor C, Capell H, Stirling A, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. *Lancet.* 2004;364:263-269.

ACTIVITY LEARNING ASSESSMENT

Request for Credit & Evaluation Form

*Name**Degree/Certification**Activity Instructions & Criteria for Success*

Complimentary CE credit is offered to all activity participants. To successfully complete this activity and obtain a Statement of Credit, the learner is required to read the entire newsletter, complete the post-test, and complete the activity evaluation form. Learners are required to correctly answer 80% of the post-test questions. Statements of Credit will be forwarded via regular mail within 4 to 6 weeks. **All forms must be received by December 15, 2010 to be eligible for CE credits.**

Activity Post-Test Questions (Please circle the letter that matches the correct response to each question below)

1. According to the 2008 ACR recommendations, which of the following are appropriate first-line treatment options for newly diagnosed RA patients with low disease activity and no poor prognostic indicators?
 - a. Methotrexate or leflunomide monotherapy
 - b. Methotrexate in combination with an anti-TNF- α agent
 - c. Leflunomide in combination with an anti-TNF- α agent
 - d. Any of the above would be appropriate choices in this patient subset
2. According to the 2008 ACR recommendations, which of the following are appropriate first-line treatment options for newly diagnosed RA patients with high disease activity, poor prognostic indicators, and no cost or insurance limitations?
 - a. Methotrexate or leflunomide monotherapy
 - b. Methotrexate in combination with an anti-TNF- α agent
 - c. Anti-TNF- α agent monotherapy
 - d. Both A and B would be appropriate choices in this patient subset
3. Which of the following patients would be contraindicated to receive a DMARD according to the 2008 ACR recommendations?
 - a. A 60-year-old woman with diabetes
 - b. A 35-year-old man with HIV
 - c. A 55-year-old woman with suspected tuberculosis
 - d. A 48-year-old man with a history of alcohol abuse
4. According to the 2008 ACR recommendations, at what point should healthcare providers consider switching anti-TNF- α agents?
 - a. After a lack of response for a period of 2 months
 - b. After a lack of response for a period of 3 months
 - c. After a lack of response for a period of 4 or more months
 - d. The ACR recommendations do not address the appropriate timing for switching therapies
5. In 2006, the ACR published quality standards for RA that included which of the following instructions?
 - a. If a patient has an established diagnosis of RA, the patient should always be treated with a DMARD
 - b. If a patient has a confirmed diagnosis of RA, a physician global assessment should be performed at least annually
 - c. If a patient has a confirmed diagnosis of RA, joint examination and functional status assessment should be performed once every 3 years
 - d. If a patient has an established diagnosis of RA, the patient should never be permitted to refuse treatment
6. Which of the following disease activity measures was identified by the ACR panel as the clear preferred choice that should be used by providers to guide evidence-based therapeutic choices?
 - a. Disease Activity Score in 28 Joints (DAS-28)
 - b. Clinical Disease Activity Index (CDAI)
 - c. Simplified Disease Activity Index (SDAI)
 - d. No preference was identified by the ACR panel
7. According to a recent study, adherence was highest to which of the following RA quality indicators at one Boston academic medical center?
 - a. Treatment with a DMARD
 - b. Appropriate baseline laboratory testing among patients with a new DMARD prescription
 - c. Follow-up monitoring for drug safety
 - d. There was no significant difference found in adherence to any of these quality indicators
8. How was the process behind the development of the 2008 ACR recommendations different from those processes used for previous recommendations in 1996 and 2002?
 - a. The 2008 recommendations were developed using informal consensus, while previous guidelines used a structured, peer-reviewed process
 - b. Nurses were included on the ACR panel for the first time in 2008
 - c. The 2008 recommendations were developed using a structured, peer-reviewed process, while previous guidelines used informal consensus
 - d. There was no significant difference in the development process in 2008 compared with previous years
9. According to the 2008 ACR recommendations, how frequently should high-risk RA patients get an ophthalmic examination?
 - a. Every 6 months
 - b. Every year
 - c. Every 2–3 years
 - d. Every 5 years
10. Which of the following has been offered as rationale for the importance of regularly measuring disease activity in patients with RA?
 - a. As with other medical conditions (eg, heart disease, hypertension), it is important to have a qualitative measure of a patient's disease progression
 - b. Insurance companies are beginning to balk at paying for treatment without evidence of a regular qualitative assessment
 - c. Trusting an individual provider's "gestalt" is insufficient if used as the only means by which to assess disease activity
 - d. All of the above

The learning objectives designed for this activity (listed below), can help me strive toward: 1=Nothing as of yet—learning objectives were not met; 2=Reinforcement of competency and/or performance; 3=Moderate improvement of competency and/or performance; or 4=Significant improvement of competency and/or performance

	Not Met	Reinforcement	Moderate Improvement	Significant Improvement
1. Describe the genesis of the American College of Rheumatology's (ACR's) recently published treatment recommendations and the methods used to develop overall recommendations	1	2	3	4
2. Explain the role of nonbiologic and biologic disease-modifying antirheumatic drugs (DMARDs) as prescribed within the ACR's recommendations for patients with early rheumatoid arthritis (RA) and those with intermediate or longer-duration RA	1	2	3	4
3. Identify hurdles that have historically prevented the widespread acceptance of published healthcare recommendations at individual treatment centers	1	2	3	4

Please indicate the extent of your agreement with the following statements:

	Strongly Disagree		Not Sure		Strongly Agree	
1. The information presented in this newsletter was pertinent to my professional needs	1	2	3	4	5	6
2. The content of this newsletter contributes valuable information that will assist me in improving patient outcomes	1	2	3	4	5	6
3. Based on my experience, I would recommend future newsletters to my colleagues	1	2	3	4	5	6
4. Were you able to locate information about faculty disclosure at the beginning of the newsletter?	YES				NO	
5. Did you perceive any bias or commercial influence in the newsletter? If so, your help in identifying it is appreciated: _____	YES				NO	
6. As a result of reading this activity, I intend to assist in implementing change at my facility	YES				NO	

If you answered **YES**, please explain: _____

7. The following is the primary barrier to implementing change at my facility:
- a. Lack of knowledge regarding evidence-based strategies
 - b. Misperceptions of or negative attitudes about research and evidence-based care
 - c. Demanding patient workloads
 - d. Fears about practicing differently from peers

8. Based upon the information presented in this educational activity, which of the following statements best reflects your understanding of RA?
- a. I have learned everything I need to learn about RA
 - b. I would like to learn more about RA

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Q & A

**NICOLE M. FURFARO,
MSN, ARNP**



Nicole M. Furfaro, MSN, ARNP, is a nurse practitioner in rheumatology and internal medicine at Seattle Rheumatology Associates in Seattle, Washington.

1. Why did you initially choose to specialize in RA?

Rheumatology appealed to me because of the opportunity to work with people of a variety of ages, conditions, and situations. Patients develop a long-term relationship with their nurse, and that feeling of really helping out when someone needs education, support, or just a shoulder to cry on is something that I valued in becoming a nurse in the first place. What keeps me in rheumatology? I started in rheumatology before the advent of biologics and have had the enjoyment and satisfaction of seeing people come in being pushed in a wheelchair and walking up to give me a hug after a couple of months of treatment. There is nothing like being “thanked” for doing your job.

2. Besides a regular paycheck, what keeps you motivated as a nursing professional?

It's definitely NOT the paycheck. I truly love my job. I see being able to go to work and help people cope with the confusion, loss, and adjustments they must make after being diagnosed with a chronic illness as a privilege. I am constantly motivated by the education being sent in nurses' direction, by attending meetings, and by feeling like we are finally being recognized for the dedicated, educated professionals we are.

3. What is the biggest frustration about your job?

So many patients, so little time... Seriously, I get frustrated at the huge amount of paperwork I have to complete for each patient I see. It seems like I spend as much time documenting a visit, requesting prior authorizations on medications, and filling out forms as I do in face-to-face patient time. If I had a magic wand that would automatically complete my charts and fill out forms, work would be so much simpler.

4. Can you recall a particularly rewarding patient interaction that occurred in the last 12 months?

A patient was referred for evaluation of fibromyalgia. She had seen her physician several times with diffuse musculoskeletal pain and fatigue with morning stiffness. Because she had a negative rheumatoid factor and no obvious joint swelling, she was given the diagnosis of fibromyalgia. By the time she presented in our office (6 weeks later, unfortunately), she had developed swelling in the metacarpophalangeal joints of the hand and a large knee effusion. Her sedimentation rate elevated to almost 80. She “knew something was wrong” but didn't question her primary

care physician. Educating her regarding RA, the potential for effective treatment, and how to deal with morning stiffness and medications was so rewarding. She cried in relief of having hope. She came back for a follow-up after starting methotrexate and prednisone and expressed absolute joy at having found our office.

5. What makes you hopeful about significant improvements to the overall treatment of patients with RA in the next 5 years?

The explosion of new targeted therapies is so exciting! We have never been able to offer patients so many options in treating their RA. As understanding of the immune system deepens and more therapies come to the market, we are able to better treat toward disease remission or at least significantly affect the progression of joint damage.

6. In what area do you find that the majority of new nursing graduates specifically need to develop their skills?

Without a doubt, intravenous (IV) skills. In training—which is hospital based—patients' IVs are generally started and maintained by an IV team. Once in clinical practice, though, nurses need to become adept at IV starts, specific medication administration, and patient education regarding the use of RA medications and immunosuppressants. New graduates are spending so much time just getting comfortable with the role of being a nurse that skill development and gaining specific knowledge about disease states are difficult tasks. The more that experienced nurses can step in and help direct new nurses toward solid resources, nonbiased information, and training workshops, the better off our patients and profession will be.

7. What is the single biggest thing you wish the general public understood about your job?

That nurses give care differently than physicians. It is not that physicians are “smarter” than nurses, but rather that they possess specialized training on how to diagnose and treat physical illness. Nurses, on the other hand, are educated to view the whole person and complement healthcare. They are specialists in treating the individual's response to illness. We are trained to look at how the individual's illness affects a patient socially, emotionally, psychologically, and physically. We also must possess medical knowledge at a different level, just as physicians must possess the ability to assess the psychological impact of disease. Nurses are professionals with a specific set of skills that make them indispensable to the delivery of good medical care.



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Supported by educational grants from **Genentech, Inc.** and **Biogen Idec Inc.**



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