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RHEUMATOLOGY NURSE NEWSLETTER

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

LEARNING OBJECTIVES

- Assess the value of attending international rheumatology conferences to meet professional development goals
- Translate EULAR recommendations for management and treatment of cardiovascular risk into clinical practice
- Based upon data from the SCEPTRE trial, discuss with all new RA patients of child-bearing age the risks associated with the use of biologic therapies during conception and pregnancy
- Determine sound reasoning to help RA patients overcome objections to beginning an exercise program

STATEMENT OF EDUCATIONAL NEED

Attendance at international rheumatology meetings allows healthcare providers who manage patients with rheumatic diseases to keep up with the latest information related to the diagnosis and treatment of a spectrum of conditions. New data allows attendees to get insight into their personal practices and potentially make changes in overall patient care.

Because nurses often serve as the glue in the management of rheumatoid arthritis (RA), as well as other rheumatic conditions, it is vital that they keep an eye on developing trends and receive detailed analyses from their colleagues based upon key data presented at these meetings.

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Kori Anne Dewing, MN, ARNP, has disclosed the following relevant financial relationships that have occurred within the past 12 months: UCB/C; Wyeth, Amgen, Inc./SB.

Nicole M. Furfaro, MSN, ARNP, has disclosed the following relevant financial relationships that have occurred within the past 12 months: Abbott Laboratories, Amgen Inc., Wyeth, Hoffman-La Roche Inc./A; Genentech, Inc., Biogen Idec, Inc., Pfizer, Inc., UCB/A, SB; Abbott Laboratories, Bristol-Myers Squibb Company/SB.

Joyce M. Kortan, RN, has disclosed the following relevant financial relationships that have occurred within the past 12 months: Centocor/A; Amgen, Inc., Wyeth, Hoffman-LaRoche, Novartis, Genentech, Inc., Bristol-Myers Squibb, Mitsubishi Tanabe Pharma Corporation/SB.

Ann Marie MacIsaac, MAPM, MSN, NP, APRN-BC, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

Off-label and/or investigational use of the following products will be discussed within the literature of this enduring activity: tocilizumab, CP-690

CONTENT AND VALIDATION TEAM

Scott Kober, Medical Writer, Institute for Continuing Healthcare Education, has disclosed that he does not have any relevant financial relationships specific to the subject matter of the content of the activity.

Karen Thomas, Accreditation and Compliance Specialist, Institute for Continuing Healthcare Education, has disclosed that she does not have any relevant financial relationships specific to the subject matter of the content of the activity.

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

Any relationships faculty members have with commercial entities have been reviewed and any potential conflict(s) have been resolved.

EULAR 2009

THE IMPORTANCE OF NEW DATA FOR TODAY'S RHEUMATOLOGY NURSE

The European League Against Rheumatism (EULAR) is the European equivalent to the American College of Rheumatology, representing the interests of patients and healthcare professionals throughout Europe. EULAR's stated goals are to stimulate, promote, and support the research, prevention, treatment, and rehabilitation of rheumatic diseases. The annual EULAR conference, which began in 2000, attracts more than 13,000 attendees from more than 110 countries. Less than 8% of conference attendees practice in the United States.

This year's conference, held June 10-13 in Copenhagen, Denmark, involved more than 2,800 accepted abstracts either as oral presentations or in poster format. While EULAR is primarily a physician-based conference, much of the information presented this year should be of interest to U.S.-based rheumatology nurses.

In this issue of *Rheumatology Nurse*, we'll take a look at some of the most important studies presented at EULAR 2009 and get analyses from practicing rheumatology nurses on the direct impact these results may have on daily nursing practice now and in the future. Information in this issue will focus on four general areas:

- Biologic therapy in RA
- Comorbidities of RA
- Safety of biologic agents and long-term registry data
- Miscellaneous information

BIOLOGIC THERAPY IN RA

TNF Inhibitors

While TNF inhibitors have certainly built a solid foothold in the treatment and management of RA, their specific role and the timing of their administration continues to be debated. With the recent approval by the U.S. Food and Drug Administration (FDA) of two new TNF inhibitors (golimumab and certolizumab pegol), the decision of what agent to use and when to use it has become even more complex.

A series of studies were presented at EULAR 2009 in an attempt to clarify some of the key clinical questions surrounding the use of TNF inhibitors.

In the first, an observational study from Northeast Italy enrolled 570 patients with high-disease activity (DAS28>5.1). Patients were treated with manufacturer-recommended doses of adalimumab, etanercept, or infliximab in combination with methotrexate. Leflunomide was added after 12 weeks in patients who had not achieved remission, defined as DAS28<2.6. Some patients were switched between TNF inhibitors during their course of treatment.¹

Results showed that remission was significantly more likely to occur in patients initially treated with etanercept compared to adalimumab or infliximab. Overall, remission was achieved in 62.2% of all patients and was equally likely to occur in patients who were switched to a second or third TNF inhibitor due to lack of durable response to previous TNF inhibitors as

it was in patients given only one TNF inhibitor. Age <40 years was the only independent factor found to have an impact on the likelihood of remission.¹

Additional data was also presented from the COMET trial (combination of methotrexate and etanercept in active early rheumatoid arthritis), which is evaluating the efficacy of etanercept used both as monotherapy and in combination with methotrexate. In line with previously published data from COMET, new information presented at EULAR showed that the consistent use of etanercept plus methotrexate for a 2-year period led to significantly higher rates of clinical remission than patients treated with methotrexate alone (57% vs. 35%).²

Rates of radiographic nonprogression were also significantly higher in the combination therapy group. Patients who were switched from methotrexate monotherapy to etanercept combination therapy, or vice versa, 1 year after the start of the study also demonstrated significantly higher rates of clinical remission after 2 years compared to patients on methotrexate monotherapy throughout the course of the study.²

A final study evaluated the efficacy of golimumab, a subcutaneous TNF inhibitor approved by the FDA in April 2009 for the treatment of moderate-to-severe RA. The study compared ACR50 response rates of patients randomized to receive intravenous infusions of golimumab 2 mg/kg or 5 mg/kg (both with and without methotrexate) or placebo plus methotrexate.³

Results did not demonstrate that ACR50 response rates were significantly increased in any of the five treatment arms at 14 weeks. However, significantly more patients in both golimumab plus methotrexate groups attained ACR50 responses at week 24 compared to individuals in the placebo arm (see Table 1).³

TABLE 1 EULAR GOLIMUMAB DATA

	ACR50 WEEK 14	ACR 50 WEEK 24
PLACEBO + METHOTREXATE	13.2%	9.3%
GOLIMUMAB 2 MG/KG + MONOTHERAPY	12.5%	8.6%
GOLIMUMAB 4 MG/KG + MONOTHERAPY	19.4%	11.6%
GOLIMUMAB 2 MG/KG + METHOTREXATE	21.7%	18.6%
GOLIMUMAB 4 MG/KG + METHOTREXATE	21.1%	25.0%

WHY YOU SHOULD CARE

Joyce Kortan: Data surrounding the use of TNF inhibitors for the treatment of RA is complicated, especially with the recent FDA approval of two new agents. The data highlighted here gives further credence to the widely accepted view that combination therapy—where a TNF inhibitor is administered along with a second, non-biologic agent (usually methotrexate)—usually leads to the best patient outcomes.

As rheumatology nurses, we are often asked by patients how their team of providers decided which biologic agent to recommend to them. It is our duty to be aware of the science that supports the efficacy of each agent, as well as any relevant drug safety issues. Being nurse educators means that we should be able to anticipate some of these common questions and have the information handy (or know where to find it easily) that will allow us to educate our patients for the betterment of their long-term health.

TABLE 2 EULAR CP-690 DATA

	CP-690 1 MG BID	CP-690 5 MG BID	CP-690 10 MG BID	CP-690 15 MG BID	ADA	PLACEBO
ACR20	35%	63%	75%	75%	47%	29%
ACR50	15%	41%	49%	54%	25%	12%
ACR70	7%	12%	25%	28%	4%	5%
DAS28<2.6 (REMISSION)	9%	24%	34%	40%	4%	7%
ADVERSE EVENTS LEADING TO WITHDRAWAL	19%	6%	5%	5%	15%	22%

TABLE 3 EULAR TOCILIZUMAB DATA

	PLACEBO + MTX	TOCILIZUMAB 4 MG/KG + MTX	TOCILIZUMAB 8 MG/KG + MTX
ACR20	25%	47%	56%
ACR50	10%	29%	36%
ACR70	4%	16%	20%
DAS28<2.6 (REMISSION)	8%	30%	47%
ADVERSE EVENTS LEADING TO WITHDRAWAL	2.3%	7.0%	8.0%
MALIGNANCIES PER 100 PATIENT YEARS	0.78	3.34	0.86

WHY YOU SHOULD CARE

Joyce Kortan: Researchers in rheumatology continue to search for a therapeutic approach that better controls disease activity, improves symptoms, allows patients to regain a normal lifestyle, and slows joint damage. As rheumatology nurses, it is important to recognize that there are many different pathways under investigation and to prepare ourselves for the possible introduction of some of these new agents in the future. If and when any of these agents under investigation receive approval from the FDA, our patients will undoubtedly ask us about them.

A number of nursing professionals work in centers that either participate in clinical trials or actively enroll patients in trials run by other sites. Because of the amount of interest in developing improved agents to better manage patients with RA, a wealth of opportunities are available for nurses who have an interest in being involved in clinical research. At the very least, nurses have the ability take an active role in identifying patients who may be suitable candidates for clinical trials and providing them with guidance they may need to get more information.

Novel Therapeutic Approaches

Despite strides that have been made in the treatment of RA since the introduction of biologic therapies approximately a decade ago, unmet needs persist. Specifically, patients continue to suffer reduced life expectancy, uncontrolled fatigue, and persistent pain.

Data on a diverse number of new approaches focusing on unique therapeutic targets were discussed at EULAR 2009, including those that target interleukin-6 (IL-6), IL-17, JAK enzymes, the GM-CSF receptor, and transforming growth factor beta-activated kinase 1. Many of these compounds remain in early-stage clinical trials, while two—tocilizumab and CP-690—have moved into later-stage development.

CP-690

CP-690 is an oral, selective, potent inhibitor of the JAK family of enzymes, which are involved in numerous inflammatory and autoimmune diseases, including RA. Trial results from a phase 2B study presented at EULAR demonstrated that higher doses of CP-690 (5, 10, and 20 mg) taken twice daily resulted in high percentages of ACR20/50/70 response and DAS28 remission at 12 weeks.⁶

Interestingly, this trial not only used a placebo control, but also evaluated patients taking adalimumab (ADA) monotherapy. Response rates were generally higher in patients taking higher doses of CP-690 compared to both placebo and adalimumab. Common adverse events in the CP-690 group included urinary tract infections, diarrhea, bronchitis, and headache. However, rates of adverse events were similar in all treatment groups (see Table 2).⁶

Tocilizumab

Tocilizumab is a humanized monoclonal antibody that inhibits the activity of the IL-6 cytokine. IL-6 is a pro-inflammatory mediator whose inhibition is thought to potentially reduce joint inflammation, prevent long-term damage, improve quality of life, and relieve certain systemic effects of RA.

Phase 3 data from the LITHE trial presented at EULAR showed that RA patients with an inadequate response to methotrexate significantly improved compared to placebo when administered both low-dose (4 mg/kg) and high-dose tocilizumab (8 mg/kg) in combination with methotrexate every 4 weeks.⁴

ACR20/50/70 responses and DAS28 scores measured 1 year following the start of treatment were best in the 8 mg/kg group. However, adverse events, including serious infections, grade 3/4 neutropenia, and malignancies were all higher in the tocilizumab groups compared to placebo (see Table 3).⁵



COMORBIDITIES OF RA

CARDIOVASCULAR DISEASE

Cardiovascular (CV) disease is the leading cause of death among patients with RA, so appropriate management and treatment is of paramount importance for healthcare providers. To help develop evidence-based recommendations for the management of CV risk, a multidisciplinary steering committee was formed, comprising 18 members from 9 European countries. Rheumatologists, cardiologists, internists, and epidemiologists were all represented on the committee.⁸

At EULAR 2009, this committee presented its 9 recommendations.⁸

1. RA should be considered as a high-risk condition for CV disease. This also applies to ankylosing spondylitis (AS) and psoriatic arthritis (PsA), although the evidence is more limited. The increased risk appears to be due to both an increased prevalence of traditional risk factors and the inflammatory burden.
2. Adequate control of disease activity is necessary to lower the CV risk (best evidence for TNF inhibitor treatment and MTX treatment).
3. CV risk assessment using national guidelines is recommended for all RA patients on an annual basis and should be considered for all AS and PsA patients on an annual basis. Risk assessments should be repeated when anti-rheumatic treatment has been changed (in absence of national guidelines, the Systematic Coronary Risk Evaluation [SCORE] function model is advised).
4. Risk score models should be adapted for RA patients by introducing a 1.5 multiplication factor that should be used when a RA patient meets 2 of the following 3 criteria:
 - a. Disease duration of more than 10 years
 - b. Rheumatoid Factor or anti-cyclic citrullinated peptide antibody positivity
 - c. Presence of certain extra-articular manifestations.
5. TC/HDL cholesterol should be used when the SCORE model is used.
6. Intervention with lipid-lowering agents and antihypertensive drugs should be carried out according to national guidelines.
7. Statins, ACE-inhibitors, and/or AT-II blockers are preferred treatment options due to their potential pleiotropic effects.
8. The role of COXIBs and most NSAIDs regarding the CV risk is not well established and needs further investigation. Hence, they should be prescribed cautiously.
9. Corticosteroids: Use the lowest dose possible.

In addition to these 9 evidence-based recommendations, the committee also recommended that rheumatologists consider a yearly assessment of individual patients' CV risk profile, using the EULAR recommendations as guidance.

A companion study based upon data from a Swedish registry further emphasized the importance of managing CV risk factors in patients with RA. The study evaluated 7,653 patients with newly-diagnosed RA (<18 months of symptoms) and looked at the rates of hospitalization and death as a result of myocardial infarction (MI), along with all-cause mortality.⁸

Prior to diagnosis of RA, no elevated risk of MI was apparent. However, within a year of diagnosis, measurable increases in the risk of hospitalization and death as a result of MI were noted; these risks increased over the course of 10 years. In all, the risk

of hospitalization as a result of MI nearly doubled within 10 years of the diagnosis of RA while the risk of death as a result of MI was also increased, although not to as excessive of a degree.⁸

NEUROLOGIC DISORDERS

Rare but troubling reports have previously surfaced indicating an association between the use of TNF inhibitors and worsening symptoms of multiple sclerosis. A study by Fernández-Espartero et al sought to shed additional light on this possible association, as well as a possible association between TNF inhibitors, demyelinating disease, and optic neuritis.⁹

This study evaluated 9,256 patients with rheumatic disease taken from the Spanish BIOBADASER, a national drug registry established in 2001 to gauge the long-term

safety of biologic therapies. Through September 2008, 49 patients were identified with new-onset neurologic signs and symptoms. In 82% of those cases, neurologic symptoms appeared after patients were prescribed their first TNF inhibitor.⁹

Of the 49 patients with new-onset neurologic signs, 9 had confirmed cases of demyelinating disease, 5 had confirmed cases of optic neuritis, and 1 had a confirmed case of multiple sclerosis. The majority of cases were related to the use of etanercept, while some occurred in patients prescribed infliximab. There were no cases related to the use of adalimumab.

While the authors noted that the rate of multiple sclerosis in rheumatic patients taking TNF inhibitors was consistent with population controls, the prevalence of optic neuritis was higher than expected.⁹

WHY YOU SHOULD CARE

Ann Marie MacIsaac: Nurses in the United States are keenly aware of the impact of cardiovascular health on the overall well-being of the general population. Data from the Framingham Heart Study, as well as other long-term clinical trials, have been incorporated into nursing curriculum for many years. Regardless of the therapeutic focus, discussions about cardiovascular comorbidities are a staple of many continuing education activities because of the impact they have across disease states.

While it is unfortunate that the nursing community was not represented on the EULAR steering committee that developed the 9 evidence-based recommendations related to the management of CV risk in patients with rheumatic conditions, it should not detract from nurses' attention to the recommendations, as they provide a worthy challenge for all rheumatology practices. While individually, each recommendation follows well-accepted

practice patterns, the implementation of all 9 of these recommendations into clinical practice will not happen overnight. However, rheumatology nurses can play a pivotal role in propelling their acceptance forward.

Taking the time and effort (about 30-40 minutes) to obtain a thorough story from your patients before initiating any kind of therapy is always beneficial for all parties involved. Patience and careful attention to detail are vital to decrease the potential risk of under-reporting significant symptoms or misunderstanding questions. Using simple screening questions may not be enough, especially in individuals with sensory deficits. This is especially important for elderly patients. It is important that patients hear, understand, and are given adequate time to respond to inquiries. Additionally, be sure to remember that older patients may speak in indirect functional terms that can indicate underlying changes in their health status. For example, "I have not been able to get out to bingo" may indicate the onset of new cardiovascular symptoms such as

dyspnea, lower extremity edema, or worsening fatigue.

In today's fast-paced healthcare climate, it is easy for details to be lost, or perhaps more importantly, be perceived by the patient to be unimportant. Consequently, subtle or intermittent changes, especially related to neurological functioning, may be ignored or go unreported by the patient. It is incumbent of nursing professionals to be an advocate for their patients so that these details do not fall into a black hole and negatively impact clinical decisions.

Admittedly, it will require a significant commitment of time and resources to implement a program that ensures improved patient safety while also enabling your patients to become informed and involved healthcare consumers. I encourage you to be creative in looking at ways that capture the essence of the parameters outlined in the EULAR 2009 cardiovascular recommendations while remaining cognizant that it is the whole picture that is important.

LONG-TERM DRUG SAFETY & REGISTRY DATA

INTERNATIONAL REGISTRIES

One of the strengths of the annual EULAR conference is the insight evident in results from various national RA registries. In 2009, long-term clinical data was presented from RABBIT, the German biologics registry, as well as QUEST-RA, a multinational registry.^{10,11}

Data from the RABBIT trial compared statistics from RA patients in 1994 to those in 2007. Documented changes related to treatment among RA patients in that time period included the following:¹⁰

- Methotrexate use increased from 45% to 59%
- NSAID use decreased from 61% to 38%
- Biologic use increased from 0% (no biologics were available in 1994) to 17%
- DAS28 scores decreased from an average of 4.0 to an average of 3.4. This change was especially notable in patients with early RA.

Documented changes related to patient care among RA patients in that time period included the following:

- Inpatient patient rehabilitation as a result of RA decreased from 15% to 5%
- Hospitalizations as a result of RA decreased from 27% to 13%
- Total joint replacements decreased from 5.5% to 2.6%
- Any joint surgery decreased from 19% to 7.5%

Further trends in RA treatment were presented from the QUEST-RA database, a collection of data from 7,568 patients in 30 countries. This database demonstrated the following in patients who had taken at least one DMARD during the course of their RA treatment:¹¹

- 83% had taken or were taking methotrexate
- 70% had taken or were taking prednisone
- 22% had taken or were taking leflunomide
- 23% had taken a biologic DMARD at some point in their treatment
- 17% were currently taking a biologic

DAS28 scores in those countries with a high percentage of patients treated with DMARDs were typically among the lowest. While it was noted that trends to introduce DMARDs earlier into the course of therapy for RA patients were promising, patients remain undertreated in many countries.



WHY YOU SHOULD CARE

Nicole Furfaro: Global trends related to the treatment of RA patients are fascinating. RA is an expensive condition to manage because of treatment costs, emotional costs to the individual, and direct medical costs to society in the form of disability. With the addition of biologic agents to our medication armamentarium and shift in treatment approach from "wait and see" to early, aggressive therapy, we should all be looking for evidence of improvement in RA disease severity. Assessing the true value of biologic therapy remains challenging, although as more data is released showing its overall efficacy in reducing disease progression as well as direct medical costs, the use of biologic therapy earlier in the disease process may be justified.



A final, more specific registry review from Denmark looked at reduction in radiographic joint destruction among RA patients treated first with conventional DMARDs and then later with a TNF inhibitor (infliximab, etanercept, or adalimumab). Two years after the introduction of a TNF inhibitor, 65% of patients remained on their initial TNF inhibitor, 22% were on a different TNF inhibitor, and 13% were no longer using a TNF inhibitor.¹²

Hand and wrist X-rays of patients were taken 2 years before the start of treatment with a TNF inhibitor, at the start of treatment, and approximately 2 years after the start of treatment. Radiographic evaluations showed that the progression rate was reduced by 65% during the 2 years after the initiation of TNF inhibitor therapy compared to the 2 years prior to TNF inhibitor therapy. Additionally, while 68% of patients demonstrated radiographic progression following traditional DMARD therapy, only 45% progressed following TNF inhibitor therapy.¹²

DRUG SAFETY DURING PREGNANCY

Data on the relationship between exposure to TNF inhibitors and birth defects has been historically sparse. In a study by Snoeckx et al, all medically-confirmed cases of pregnancy in patients exposed to infliximab through August 2008 were collected and analyzed. Information came from Johnson & Johnson's Benefit Risk

Management Worldwide Safety Database (SCEPTRE).¹³

The purpose of the trial was to determine whether a causal relationship exists between the use of infliximab, a Pregnancy Category B drug, and VATER (vertebral effects, atresia, tracheoesophageal fistula/esophageal atresia, and renal defects). VATER is typically noted in newborns with more than 3 of these individual anomalies.¹³

In this trial, 723 cases of maternal exposure to infliximab during pregnancy were noted. The majority of women were taking infliximab for treatment of either Crohn's disease (73%) or RA (9%). Seventy-four percent (522 of 723) of all women delivered live births; the remaining cases ended either due to stillbirth, spontaneous termination/intrauterine death, induced/elective termination, or unspecified termination.¹³

Of the 522 live births, 73% (388 of 522) resulted in a healthy child. Premature delivery was noted in 53 cases (10%) while at least one adverse event (excluding congenital abnormalities or malformations) was apparent in 34 live births (7%).¹³

Importantly, while individual adverse events were noted in a significant number of live births, none of the offspring exposed to infliximab in utero met the criteria for VATER association. The authors cautioned, however, that data remains limited on the use of TNF inhibitors during pregnancy and that infliximab should only be given to pregnant women if clearly necessary.¹³

WHY YOU SHOULD CARE

Nicole Furfaro: Since many of our RA patients are of child-bearing age, questions related to drug safety often come up during pre-pregnancy planning discussions. After explaining that there is little robust clinical trial data related to the effects of most biologic agents during pregnancy, I generally go on record recommending against use of biologics during pregnancy. This is an obvious recommendation for agents such as methotrexate, which is known to have teratogenic effects, as well as leflunomide, which requires a lengthy washout period before attempts at conception.

Occasionally, I will see a pregnant patient who has been exposed to one or more DMARDs, and in those cases, I refer the patient to studies that may answer her questions about RA and pregnancy. The Web site of the Organization of Teratology Information Specialists (www.otispregnancy.org/hm/) is a good source that provides drug-specific information on the impact of various agents in pregnant women.

OTHER DATA OF INTEREST TO RHEUMATOLOGY NURSES

RA

Nursing Care Around the Globe

In many ways, the role of the rheumatology nurse in Europe is underdeveloped compared to the United States. For starters, there is no equivalent to a nurse practitioner or physician assistant in most European countries. Traditionally, rheumatology nurses have served primarily as rheumatologists' assistants, carrying out clinical procedures and helping perform clinical trials. Recently, however, progress is being made to involve nurses more in monitoring disease progression and teaching and counseling patients.

A study presented at EULAR by Koksvik et al examined the effectiveness of nurse-led care in a rheumatology outpatient clinic by comparing patient satisfaction and disease progression in individuals managed by a rheumatology nurse to those managed by a physician. Sixty-eight patients were included in the study—35 in the nurse-led group and 33 in the physician group. The majority of patients (56%) had been diagnosed with RA. Outcomes were measured via a patient satisfaction questionnaire and DAS-28 scores.¹⁴

At 2-year follow-up, patients in the nurse-led care group were significantly more satisfied on all patient satisfaction subscales compared to those in the physician-managed group. DAS-28 scores did not change significantly in either group and no significant differences were apparent in this measure between the groups.¹⁴



WHY YOU SHOULD CARE

Kori Anne Dewing: The American Nurses Association defines nursing as the "protection, promotion, and optimization of health and abilities, prevention of illness and injury, alleviation of suffering through the diagnosis and treatment of human response, and advocacy in the care of individuals, families, communities, and populations."

As a rheumatology nurse, I try to incorporate these values into my daily practice. I am so proud when I see results from studies like this that support and recognize the great work my colleagues do every day! While this study was performed in Norway, where they don't have the equivalent of a nurse practitioner, it reinforces the value of using specially trained rheumatology nurses to provide competent care and successfully manage patients with rheumatologic conditions.

As the shortage of practicing rheumatologists in the U.S. deepens, nurses are being called upon in increasingly greater numbers to manage patients with rheumatic disease. However, nurses and nurse practitioners are trained as generalists and require significant post graduate training to handle the gamut of rheumatologic conditions. Fortunately, a number of educational resources are available to nurses who are new to rheumatology.

The Association of Rheumatology Health Professionals has developed a comprehensive, self-paced online training program and related in-person skills training course (www.rheumatology.org/arhp/index.asp). An online course is also available from the Royal College of Nursing demonstrating methods that may be used to perform a DAS-28 joint count (www.rcn.org.uk/development/communities/rcn_forum_communities/rheumatology/resources/das_28_joint_assessment). Additional training is available through the Rheumatology Nurses Society, which recently held its second annual meeting for rheumatology nurses.

WHY YOU SHOULD CARE

Kori Anne Dewing: It has only been within the last few years that biologic agents have been studied and approved for use in children. Because their bodies are growing, children cannot be thought of as “little adults,” and medications may act differently and pose increased risks. Therefore, studies specifically performed in pediatric populations, such as the two studies noted here, are important to demonstrate both efficacy and safety.

It is important to note that in August 2009, the FDA sent out an alert based upon post-marketing data related to the increased risk of developing lymphoma and other malignancies in children and adolescents treated with TNF inhibitors. Black box warnings for these agents were updated to reflect this risk. Although it is encouraging that biologic agents have demonstrated efficacy in patients with JIA, these and other associated risks must be noted. As nurses, it is our responsibility to report any unexpected or serious events associated with the use of drugs to the FDA’s MedWatch Program (www.accessdata.fda.gov/scripts/medwatch/).

Juvenile Inflammatory Arthritis

For patients with juvenile idiopathic arthritis (JIA), management can often be complicated after failure with traditional DMARDs, including methotrexate. Two studies presented at EULAR looked at the efficacy of various biologic therapies in this patient population.

In the first, a small Portuguese study followed 24 patients with juvenile idiopathic arthritis who initiated biologic therapy at a mean age of approximately 15 years and maintained treatment for approximately 3 years. The majority of patients received etanercept as a first-line biologic, while others received either infliximab or anakinra.¹⁵

Three months after the start of treatment, all disease parameters were significantly reduced, with a 91% reduction in active joint count and a 47% decrease in erythrocyte sedimentation rate. The majority of patients (75%) remained on their initial therapy while 25% switched to a second biologic at a mean of 22 months due to loss of efficacy.¹⁵

For the 75% of patients who did not switch biologic therapy up to 7 years after its initiation, overall response rates were sustained.¹⁵

The second study looked at 50 young patients (mean age=6.57 years) with either systemic JIA or poly/oligoarthritis who had previously received methotrexate + cyclosporine. These patients were administered rituximab once a week for 4 consecutive weeks. Patients could receive up to three courses of 4-week treatment. Overall efficacy was measured by DAS28 scores.¹⁶

After each course of treatment, DAS28 scores were significantly improved, with 52% of patients treated with three courses of therapy reaching remission. Infusion reactions were noted in 36% of patients during the first course of therapy, 31% during the second course, and 27% during the third course. Neutropenia was present in 16% of cases (see Table 4).

TABLE 4 EULAR JIA DATA

	PRETREATMENT	1 COURSE OF THERAPY	2 COURSES OF THERAPY	3 COURSES OF THERAPY
DAS28<2.8 (REMISSION)	NA	NA	38%	52%
DAS28<3.2 (LOW DISEASE ACTIVITY)	0%	20%	30%	13%
DAS28< 5.1 (MODERATE DISEASE ACTIVITY)	16%	52%	14%	9%
DAS28>5.1 (HIGH DISEASE ACTIVITY)	84%	28%	18%	26%

WHY YOU SHOULD CARE



Kori Anne Dewing: Newly diagnosed patients with rheumatoid arthritis are always surprised when I tell them that they should be exercising. They are fearful that exercise will further damage their injured and painful joints. But when I explain the need to build the strength of muscles surrounding the affected joints, maintain flexibility, and improve cardiovascular health, they begin to understand its importance. It is hard to convince anyone to start an exercise program, but the data from this EULAR study, as well as other previous findings, can be used to help motivate our patients.

Exercise can help alleviate sleep problems, reduce fatigue, manage stress, and enable patients to maintain a healthy weight. It also helps to reduce cardiovascular disease, the No. 1 cause of death in patients with rheumatoid arthritis. Best of all, it is a low-cost mechanism that can be used to improve the quality of life of our patients.

Lifestyle Management

Despite mounting evidence to the contrary, many RA patients continue to think that regular exercise will cause additional damage to their joints. To help provide more ammunition for healthcare providers to counter this belief, a study by Baillet et al thoroughly evaluated all literature published or presented between 2003 and June 2008 that compared outcomes of RA patients on an exercise regimen to those patients on nonaerobic interventions.¹⁷

The study evaluated 28 randomized controlled trials that enrolled 2,534 patients. These trials included patients involved in dynamic exercise programs (8 studies), strengthening exercises (2 studies), cardiovascular fitness (8 studies), and plain aerobic exercises (10 studies). Parameters evaluated included quality of life, as well as functional, clinical, and radiologic outcomes.¹⁷

Results demonstrated that all forms of exercise, independent of the type of exercise protocol, significantly improved quality of life, Health Assessment Questionnaire function, and joint count. Furthermore, radiologic damage and pain were both significantly decreased. DAS-28 scores at 6 and 12 months were not significantly different between the exercise and nonaerobic groups.

Exercise protocols performed in a supervised environment (eg, a gym) were slightly more beneficial than home-based protocols, although both led to significantly better outcomes compared to nonaerobic patients.

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THE ABC'S OF CLINICAL TRIALS

UNDERSTANDING AND EVALUATING THE IMPORTANCE OF DATA PRESENTED IN A CLINICAL TRIAL, WHETHER IN PRINT FORMAT OR PRESENTED AT A LIVE MEETING, CAN BE A DAUNTING TASK FOR A NEW NURSE.

Thousands of trial reports are printed in the medical literature each month, and choosing which ones to read, much less use to make any future adjustments in patient management and treatment, can be time-consuming. However, familiarizing yourself with the basic structure of a clinical trial and the standard vocabulary common to the medical literature may help get you started.

Published results of today's clinical trials follow a standard, industry-accepted format known as introduction, methods, results, and discussion (IMRAD) that was initially developed in the 17th century, but only popularized in the last 75 years.¹ IMRAD includes the following components:²

INTRODUCTION

A brief summation of what is known about the topic to date. This section explains why the authors performed the trial in the first place.

METHODS

Details on how the trial was conducted. Who was enrolled? What was being tested or measured? How was this testing or measurement conducted?

RESULTS

Details on the findings of the study.

DISCUSSION

Analysis by the study authors on the meaning of the results. This often includes a concluding paragraph or two at the end of the section.

Many clinical trials also include an introductory abstract, which summarizes these sections in truncated format. These abstracts often serve as a good place to start when deciding whether you want to read the full study.³

Here are some other common terms you may come across when reading clinical trials:⁴

BLINDED TRIAL

A blinded trial is one in which patients are not told which intervention arm of the trial they are included in. In a double-blinded trial, clinicians are also unaware of which arm individual patients have been assigned.

INCLUSION/EXCLUSION CRITERIA

Clinical trials are designed to test patients who fit a certain medical profile.

Inclusion/exclusion criteria of a clinical trial may include specific medications, conditions, patient demographics, and medical history that are allowed and not allowed for enrollment into the trial.

EFFICACY

The ability of a drug or treatment regimen to produce a result. The U.S. Food and Drug Administration (FDA) mandates that phase II clinical trials gauge a drug's efficacy while phase III clinical trials confirm it.

PHASE I TRIALS

Phase I trials determine the metabolism and pharmacologic action of drugs in humans and side effects associated with increasing doses. Phase I trials often include healthy participants.

PHASE II TRIALS

Phase II trials are controlled clinical studies conducted to evaluate the effectiveness of a drug for a particular indication or indications in patients with the disease or condition under study and to determine common short-term side effects and risks.

PHASE III TRIALS

Phase III trials are intended to gather additional information to evaluate the overall risk-benefit relationship of the drug and provide an adequate basis for physician labeling. These are often large trials that enroll hundreds of patients.

PHASE IV TRIALS

Phase IV trials are post-marketing studies used to delineate information such as a drug's risks, benefits, and optimal course of use.

PLACEBO

An inactive pill, liquid, or powder that has no treatment value. In many clinical trials, experimental therapies are compared to placebo therapy to determine their overall efficacy.

RANDOMIZED TRIAL

A study in which patients are assigned, by chance, to one of two or more interventions. Placebos may sometimes be used in a randomized trial as one of the interventions.

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ACTIVITY LEARNING ASSESSMENT & EVALUATION FORM

ACTIVITY INSTRUCTIONS & CRITERIA FOR SUCCESS

Continuing Nursing Education contact hours are offered to all activity participants. To successfully complete this activity and obtain a Certificate of Contact Hours awarded, 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 70% of the learning assessment questions. A Certificate of Contact Hours awarded will be forwarded via regular mail within 2 to 3 weeks of submission. All forms must be received by October 15, 2011, to be eligible for CE credits.

- Please fax both sides of this evaluation to ICHE at (215) 592-9085, *OR*
- Please complete the evaluation online by going to www.iche.edu and clicking on **Enduring Materials**.

NAME _____

DEGREE/CERTIFICATION _____

ACTIVITY POST-TEST QUESTIONS

Please circle the letter that matches the correct response to each question below.

- Which one of the following statements about the annual EULAR conference is true?
 - The majority of meeting attendees practice in the United States
 - EULAR has been the leading rheumatology meeting in the world since the mid-1970s
 - Data presented at EULAR has significant relevance for all healthcare professionals who treat rheumatic conditions regardless of the location of their practice
 - EULAR primarily caters to bench scientists interested in the molecular basis of rheumatic diseases
- Which of the following is not under investigation as a potential therapeutic target for the treatment of RA?
 - IL-6
 - FOXA1
 - The GM-CSF receptor
 - JAK enzymes
- Evidence-based recommendations for the treatment of cardiovascular (CV) disease among patients with RA presented at EULAR 2009 included which of the following?
 - Intervention with lipid-lowering agents and antihypertensive drugs should be carried out according to national guidelines
 - RA should be considered as a high-risk condition for CV disease
 - Adequate control of disease activity is necessary to lower the CV risk
 - All of the above
- Since the introduction of biologic therapy approximately a decade ago, which of the following therapeutic trends among patients with RA have become apparent?
 - The use of NSAIDs has increased
 - DAS-28 scores have decreased, especially among patients with early RA
 - Hospitalizations as a result of RA have increased
 - The use of methotrexate has decreased
- Based upon data presented at EULAR, which of the following DMARDs used to treat RA can be safely used in pregnant women?
 - Methotrexate
 - Leflunomide
 - Infliximab
 - None of the above
- In a Swedish registry study presented at EULAR, measurable increases in rates of hospitalization and death due to CV disease were apparent within what time period after the diagnosis of RA?
 - Three months after diagnosis
 - One year after diagnosis
 - Two years after diagnosis
 - Five years after diagnosis
- A robust trial by Baillet et al presented at EULAR investigating the effect of exercise on patients with RA demonstrated which of the following results?
 - All forms of exercise significantly improved patients' quality of life
 - All forms of exercise significantly decreased radiologic damage and pain
 - All forms of exercise significantly improved DAS-28 scores
 - A and B only
 - All of the above
- The XYZ trial enrolled 4,000 patients from 56 centers in 8 countries throughout North America to test a new drug for the treatment of RA. Based largely upon the results of this trial, company ABC presented its final submission to the FDA to consider approval of this new drug. The XYZ trial is a good example of a clinical study performed during which research phase?
 - Phase I
 - Phase II
 - Phase III
 - Phase IV
- Clinical trials published in peer-review academic journals typically follow which of the following formats?
 - Introduction, Methods, Results, and Discussion
 - Hypothesis, Methods, Results, and Conclusion
 - Introduction, Demographics, Results, and Conclusion
 - Hypothesis, Demographics, Findings, and Conclusion
- According to data from the QUEST-RA database, RA patients were most likely to have taken which of the following DMARDs during the course of their treatment?
 - Infliximab
 - Rituximab
 - Prednisone
 - Methotrexate

The learning objectives designed for this activity (listed below), can help me strive toward:	Nothing at this time	Reinforcement of current practices	Moderate Improvement	Significant Improvement		
1. Assess the value of attending international rheumatology conferences to meet professional development goals	1	2	3	4		
2. Translate EULAR recommendations for management and treatment of cardiovascular risk into clinical practice	1	2	3	4		
3. Based upon data from the SCEPTRE trial, discuss with all new RA patients of child-bearing age the risks associated with the use of biologic therapies during conception and pregnancy	1	2	3	4		
4. Determine sound reasoning to help RA patients overcome objections to beginning an exercise program	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 provides 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. How often do you review new data presented at major rheumatology meetings or published in peer-reviewed journals?
- Once a week or more
 - About once a month
 - A few times a year
 - Never
7. Do you ever make changes to your daily practice based upon new data presented at major rheumatology meetings or published in peer-reviewed journals?
- Yes
 - No
8. The following is the primary barrier to implementing change at my facility:
- Lack of knowledge regarding evidence-based strategies
 - Misperceptions of or negative attitudes about research and evidence-based care
 - Demanding patient workloads
 - Fears about practicing differently from peers

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MY MOST Memorable PATIENT...

BY JOYCE KORTAN



In 1991, I left my hospital to work in a rheumatology clinic. At the time, I barely had a rudimentary knowledge of rheumatic diseases. Within months of starting my new job, I met Sheila. Like me, Sheila was a nurse and worked at a nearby hospital. Like me, before she stepped foot into the rheumatology clinic for the first time, she knew very little about rheumatoid arthritis (RA).



On the day we met, Sheila was in so much pain that she could barely walk. During our first conversation, she told me, "You hear of rheumatism, but you have no idea the impact the disease has on your life." She went on to tell me she desperately needed our help because she couldn't afford to lose her job. Unfortunately, though, her disease was very aggressive, and it proved difficult to successfully manage Sheila's disability and pain.

Sheila was a frequent visitor to our clinic, and she actively participated in discussions with me and our rheumatologist regarding her treatment plan. The more I learned about RA, the more comfortable I felt introducing my suggestions into our discussions. Sheila was determined to work with us to manage and control her disease and to maximize her quality of life.

However, when we first broached the possibility of introducing biologic therapy into her treatment regimen, Sheila was hesitant. She expressed significant concern about potential side effects, and I distinctly remember sitting down with her to review the clinical evidence, emphasizing the

various pros and cons of biologic therapy. Eventually, she agreed to give biologics a try, knowing that she needed aggressive therapy to stay on top of her condition and remain in the workforce.

Unfortunately, Sheila's disease continued to progress despite her and our best efforts. Our rheumatologist regularly switched biologic agents in an effort to control her RA, with limited success. And yet, despite increasing levels of pain and disability, Sheila continued to work in her hospital. During one of her regular visits to our clinic, I asked her, "How are you able to draw up medications for patients?" Her response? "I do what I can do," she said. "I have good co-workers."

Shortly after she turned 60, our rheumatologist advised Sheila to see a hand surgeon, who suggested that she undergo immediate surgery. Sheila, fearful that the surgery would cause her to lose her job, refused. Eight years later, Sheila finally did retire from her nursing career. She never had the surgery.

Sheila loves to garden and care for her grandchildren and still attempts to do as much as she can. She recently ruptured a tendon in her hand, which has further

complicated her daily lifestyle. The damage to her joints is irreversible (her hands are shown in the image on the left).

Sheila and I often talk about how healthcare providers do a good job taking care of others, but when it comes to our own care, we can often be stubborn and short-sighted. She recently told me that, looking back, she regrets not having the hand surgery.

"It may have provided more function in my hands today," she said. "I just didn't want to take away time from my family or work to have the surgery. I pushed myself very hard and didn't think about the long-term effects of my decisions."

I am doing everything I can to help Sheila maintain a reasonable quality of life. At our last visit, I provided her with a video on gardening with RA and I'm anxious to see if the adaptive tools suggested in the video will be helpful.

The relationships we develop with our patients are priceless. Every time I see Sheila, I am reminded of the daily challenges our RA patients face. Even with aggressive therapy in the era of biologics, some of our patients just will not respond and will progress to worse stages of disease or even permanent disability. There are still unmet needs in the treatment of RA, which is why I am always encouraged that significant research into new therapeutic options continues. Patients like Sheila will always be a challenge for me, but she is a great reminder of how much our patients need the support of the nursing community.



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