Because infusion nurses actively participate in rheumatoid arthritis (RA) patient care, they can provide clinical pearls that promote patient safety and outcomes. Four patient case studies are presented to illustrate nursing strategies for comprehensive management of patients with RA. Assil Saleh, MD, MPH, began with describing information that should be shared with rheumatologists, particularly for infusion clinics not directly affiliated with prescribing rheumatologists.

**Dr Saleh:** Most infusion clinics understand the importance of reporting rare serious adverse effects. However, subtle changes, such as gradual decreases in blood cell counts or hints of patient intolerance to infusions, should be reported to rheumatologists. Questions by patients or family members and counseling provided by nurses should be shared with rheumatologists because this information provides insight into whether patients are tolerating infusions, both physically and psychosocially. Patient concerns about safety or efficacy can affect future compliance with therapy. Timely documentation, including thorough nursing notes and laboratory results, is imperative, especially for detecting life-threatening toxicities.

**Ms Ruffing:** Often, nursing documentation focuses on infusions and not on patient concerns or education provided. When nurses share counseling information, rheumatologists can verify or expand this information.

**CASE 1: INITIAL TREATMENT OPTIONS FOR NEWLY DIAGNOSED PATIENT**

A 25-year-old female, new to rheumatology, presented with the following symptoms: C-reactive protein (CRP), 2.7 mg/dL; erythrocyte sedimentation rate (ESR), 51 mm/hr; rheumatoid factor, 223 IU/mL; bilateral swollen, tender wrists, metacarpophalangeal (MCP), and metatarsophalangeal joints; and morning stiffness of 2 hours. She is married, works full-time, has a 2-year-old son, and wants more children.

A diagnosis of RA was confirmed. Her insurance copayment is 20%, and she has a fear of injections. When counseling this patient about initial treatment options, what advantages and disadvantages would be discussed about the following disease-modifying antirheumatic drugs (DMARDs): methotrexate (MTX); an injectable tumor necrosis factor-α (TNF-α) blocker; or an infusible biologic, specifically infliximab, rituximab, or abatacept?

**DISCUSSION**

**Ms Ruffing:** Occasionally, rheumatologists recommend TNF-α blocker therapy and request nurses to help patients select the most suitable agent. Because this patient wants more children, MTX may not be an option. However, her fear of needles suggests MTX would be best. Her high activity level and costly copayment should also be considered.

**Ms Daul:** Counseling should include explanations about the lifelong commitment associated with DMARD therapy and about therapy effectiveness as supported by clinical data. Patients should understand that agents can be changed if ineffective or if intolerance occurs, especially as newer agents become US Food and Drug Administration approved.
The infusion schedule associated with biologics can interfere with this patient’s full-time work schedule. Infliximab may be administered every 8 weeks over 2 or more hours. However, clinical data recommend its use with MTX, and it may be given as often as every 4 weeks.\(^1\) Abatacept may suit her active lifestyle because it is administered over 30 minutes every 4 weeks post-induction.\(^2\) Rituximab tends to be reserved for treatment failure with another biologic, and it is also recommended with MTX concomitantly.\(^3\)

**Ms Dexter:** Abatacept offers the advantage of effective clinical data as monotherapy. Patient autonomy is always important when making therapy decisions.

**Ms Dilliard:** Infliximab prescribing information (PI) reports no evidence of toxicity in animal reproductive studies (pregnancy category B) whereas abatacept and rituximab PIs report inconclusive data (pregnancy category C).\(^1-3\) Infliximab has some pregnancy safety data available in off-label clinical studies.\(^4\)

**Ms Ruffing:** If a patient becomes pregnant while on a biologic, the manufacturer should be notified for data collection purposes. In my experience, some patients, who did not enter pregnancy-associated remission, opted to restart biologic therapy in their third trimester, and their infants were born healthy. In some patients who did enter pregnancy-associated remission, RA symptoms exacerbated dramatically post-pregnancy, requiring almost immediate resumption of biologics. After the prolonged drug holiday associated with pregnancy, the risk of infusion reactions could be increased.

**Ms Dexter:** Infliximab may be restarted at maintenance doses if the drug holiday is 3 months or less. In my experience, abatacept was restarted at maintenance dosing in one patient after pregnancy. She resumed therapy without incident, and her symptoms improved approximately after her third infusion.

**Ms Ruffing:** Could the autoinjectors available with injectable TNF-\(\alpha\) blockers alleviate her fear of needles?

**Ms Grace:** Because she has family support, her husband could be trained in injectable administration, especially if her fear of needles involves self-injecting. However, her 20% copayment could make therapy expensive.

**Ms Ruffing:** Copayment assistance patient assistance programs could be an option. These programs tend to cover 1 year of therapy, which may be beneficial if she becomes pregnant.

**Ms Dilliard:** In my experience, one unintentional pregnancy resulted in congenital cancer. It is not certain if this cancer was coincidence or caused by the biologic. This emphasizes the importance of reporting pregnancy outcomes and of counseling patients about pregnancy avoidance. Pregnancy should be postponed for at least 3 months postinfusion. Patients can also determine during this 3-month hiatus if they are able to tolerate RA symptoms without biologic treatment.

**Ms Dolan:** When patients initiate biologics, nurses should introduce the relationship as a long-term mutual partnership, letting patients know their best interests are fundamental. For this patient, her best interest may be delaying pregnancy until her symptoms are controlled. She should also be informed that pregnancy is occasionally, but not absolutely, associated with RA remission.

**Ms Grace:** The CORRONA (Consortium of Rheumatology Researchers of North America, Inc.) database may provide relevant information because its goal is to improve care of patients with RA through national aggregate data collection and analysis.

**Ms Dolan:** A list of databases could be helpful to infusion nurses (Table).

**Ms Neuberger:** Because this patient is early in disease progression, aggressive treatment is critical, and delaying pregnancy seems advisable.

**Ms Dolan:** This patient should understand that biologic therapy is a lifelong commitment, and although therapy can be interrupted, maximal benefit may be impacted. In essence, this case addresses the issue of balancing quality of life with benefits of treatment. Infusion nurses should provide patients with broad unbiased information and allow patients to make therapy decisions.

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**Table. Internet Database Resources for Rheumatoid Arthritis**

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<thead>
<tr>
<th>Database</th>
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<tr>
<td>CORRONA Data Collection Program</td>
<td><a href="http://www.corrona.org">http://www.corrona.org</a></td>
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<tr>
<td>OTIS Rheumatoid Arthritis in Pregnancy Research Study</td>
<td><a href="http://www.otispregnancy.org/otis_study_ra.asp">http://www.otispregnancy.org/otis_study_ra.asp</a></td>
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<td>Rheumatology Nurses Society</td>
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CORRONA = Consortium of Rheumatology Researchers of North America, Inc.  
OTIS = Organization of Teratology Information Specialists.
Ms Daul: Nurses should educate patients, respect their choices, and work with the parameters set by patients.

Ms Grace: It would be informative to determine if pregnancy-associated remission is related to symptoms only or if joint destruction stops progressing.

Ms Daul: Because radiographic studies are contraindicated during pregnancy, the effect of pregnancy on joint destruction may not be fully understood.

Ms Ruffing: Radiographic studies would be the best indication of remission versus CRP, ESR, or inflammation assessment.

CASE 2: INFUSIBLE BIOLOGIC IN A PATIENT WITH FAILURE TO METHOTREXATE

A 45-year-old female on MTX for 6 years presented with worsening RA. Radiographs showed new MCP erosions. Her inflammatory markers and liver function tests (LFTs) were elevated. MTX was discontinued, and after discussing biologic options, she was referred to the infusion clinic for initiation of infliximab.

What would be the role of the infusion nurse in prescreening, drug administration, patient monitoring, psychological support, patient education, and care plan collaboration?

Ms Daul: Because her LFTs are elevated, lifestyle questions should be asked, such as alcohol and drug use. Screening for hepatitis should be performed, including taking a health history that accounts for body piercings and tattoos.

Ms Ruffing: In addition to tuberculin skin testing (PPD), would you test for hepatitis B (HBV)?

Ms Daul: If not already ruled out, HBV serology markers should be checked.

Ms Grace: Concomitant medications that affect LFTs should be reviewed, such as statins. Her LFT response to MTX discontinuation should also be assessed.

Ms Dolan: Because infliximab is recommended to be given with MTX, collaboration with the rheumatologist concerning the treatment plan would be indicated.

Ms Ruffing: Asking the patient would be appropriate because she may know whether MTX will be restarted, potentially at a lower dose. LFT elevation secondary to MTX may respond to dose reduction or holding MTX therapy until LFTs return to normal.

Ms Daul: Insurance companies may deny payment for infliximab if not given concurrently with MTX. Carefully documenting the reason why MTX is held should avoid this denial.

Ms Grace: Physicians may switch MTX to another immunosuppressant, such as azathioprine.

Ms Dilliard: In my experience, patients with RA who have hepatitis C have received infliximab plus an immunosuppressant other than MTX. More recently, newer biologics as monotherapy have offered other options for patients with RA who have liver disease. When required, the benefits of concomitant therapy should be emphasized to patients. Leflunomide would not be optional as an alternate to MTX because it may also elevate LFTs.

Ms Ruffing: In this case, prescreening determined the patient was PPD negative and HBV negative. MTX was restarted at lower dose, and appropriate counseling was completed. Would screening differ at subsequent biologic infusion visits?

Ms Dexter: Although most education occurs at the first visit, re-education would occur at subsequent visits. Assessment about side effects and response to therapy would occur at every visit.

Ms Dilliard: Education would include reporting subjective infusion-related side effects, such as pain at the intravenous (IV) site. Verbal and written discharge instructions would be provided.

Ms Ruffing: Regarding drug administration, is there any special information that may be helpful to infusion nurses?

Ms Dexter: When calculating infliximab doses (ie, 3 mg/kg), common practice is to round up (ie, 367 mg becomes 370 mg). If the dose is 305 mg, some clinics may round down or consult the physician. My clinic tends to be aggressive and generally always rounds up, except to avoid wasting excessive amounts. Because vial size is 100 mg, 305 mg would be rounded down to 300 mg. However, 309 mg would be rounded up to 400 mg.

Ms Daul: Because the approved dosing range for RA is 3 to 10 mg/kg, doses can probably be safely rounded up.

Ms Ruffing: If the 10 mg/kg range is reached, then caution when rounding would be required.

Ms Dilliard: Outside pharmacies may ship the number of vials based on the patient’s weight and dose. For example, if the dose is calculated to be 301 mg, the pharmacy will ship 4 100-mg vials, and dose should be
rounded up for reimbursement purposes.

**Ms Dolan:** In my clinic, physicians write orders already rounded up.

**Ms Daul:** We receive a weight-based order, such as 3 mg/kg, and then we calculate the dose after weighing the patient.

**Ms Dexter:** Occasionally, physicians will base the dose on the vial size, such as “increase to 400 mg,” and not focus on the actual mg/kg dose.

**Ms Dolan:** Teaching hospitals may have more uniformity in prescribing because select attending physicians train residents. When nurses calculate doses, is this dose communicated to the physician?

**Ms Dexter:** The dose is documented in the patients’ charts, and physicians usually dictate the final dose in their progress notes.

**Ms Dilliard:** If patients gain weight, dose adjustment may be required. Generally, if weight gain is 30 lbs or more, an additional vial is necessary, and insurance approval should be obtained.

**Ms Ruffing:** If the biologic is not prepared by the pharmacy, complete patient-specific labeling of the final product is necessary to ensure patient safety.

**Ms Dilliard:** Because several biologics are now available, labeling and safety precautions are essential. Supplemental identifiers, such as color-coded arm bands for patients on specific biologics, improve monitoring and patient safety.

**Ms Ruffing:** Patient safety is a major initiative of JCAHO (Joint Commission on the Accreditation of Healthcare Organizations).

**Ms Dolan:** When infusing infliximab, slowing infusion rates can significantly reduce infusion reactions, which is another method to improve patient safety.

**Ms Dexter:** Titrating infusion rates of infliximab to higher or maximum rates improves patient tolerance and avoids infusion reactions.

**Ms Grace:** Flowchart documentation of initial rates and subsequent rate increases is useful. If a reaction occurs, the infusion amount and rate can be determined. SOAP (subjective, objective, assessment, and plan) notes are also useful because patients’ perspectives can be assessed.

**Ms Dexter:** Because pretreatment protocols vary among infusion clinics, are there any important facts to know?

**Ms Dolan:** Given that there is no standard of care, nurses should realize that physician preferences are based on practice experience. If one clinic pretreats and another does not, neither clinic should be considered wrong.

**Ms Grace:** Pretreatment preferences could be physician-specific, drug-specific, or even patient-specific.

**Ms Daul:** When administering infliximab, infusing via piggyback into a primary IV is a safer administration method.

**Ms Dilliard:** Smaller infusion clinics, particularly those in physicians’ offices, may not have standard protocols that define appropriate administration methods.

**Ms Ruffing:** In larger clinics, initial protocols are often based on clinical trial methods. Clinical practice may dictate revisions to initial protocols, such as pre-medication choices.

**Ms Grace:** Standard protocols should allow for appropriate deviations based on physician preference or patient refusal. Treatment regimens are often patient-specific, which emphasizes the need for flexible protocols.

**Ms Ruffing:** If premedications are refused, patients should understand the associated consequences, such as delayed fever reactions.

**Ms Dolan:** Treatment regimens can be written as guidelines, which do not translate into mandatory procedure.

**Ms Daul:** Pharmaceutical manufacturers have disclaimers about information as “recommendations.” Clinical expertise should dictate practice.

### CASE 3: MANAGEMENT OF AN INFUSION REACTION TO A BIOLOGIC

A 71-year-old retired male with a 12-year history of RA visited the infusion clinic for his regularly scheduled infliximab, which he had received without incident for 4 years. No abnormalities were noted during the prescreening and patient history assessment. Approximately 10 minutes into the infusion, he experienced dizziness, diaphoresis, and chest tightness. How should this reaction be managed? Should the infusion be stopped or slowed down?

### DISCUSSION

**Group:** The infusion should be stopped.

**Ms Ruffing:** This reaction demonstrates the safety of infusing via IV piggyback because the primary IV can still be infused. Assuming this infusion center did
not premedicate the patient, what medications would you use post-reaction?

**Ms Daul:** I would administer diphenhydramine 25 to 50 mg IV, acetaminophen oral, and hydrocortisone 100 mg IV or its corticosteroid equivalent as per standard protocol orders, then notify the physician. Diphenhydramine treats the immediate reaction, acetaminophen keeps the patient comfortable, and a corticosteroid protects from further delayed reactions.

**Ms Dexter:** My clinic administers methylprednisolone 40 mg IV. **Ms Dilliard:** My clinic may order hydrocortisone IV instead of methylprednisolone IV. Diphenhydramine, methylprednisone, and hydrocortisone are not compatible with many biologics. Therefore, if emergency medications are required because of an infusion reaction, complete flushing of the IV line is required before and after administration of emergency medications. Alternately, using a primary solution, such as normal saline, with the biologic infused as a piggyback alleviates incompatibility issues and allows for easier flushing of the IV line.

**Ms Daul:** Administering infliximab and rituximab using a piggyback is part of our protocol for these 2 agents. However, because no infusion reactions have yet been observed in my clinic, abatacept is administered as a primary IV. If a reaction occurs, nurses are instructed to stop the abatacept and start an infusion of normal saline. With any of these described methods, patients will receive a residual amount of biologic as left in tubing, thus caution is needed.

**Ms Dexter:** Because the patient received infliximab safely for 4 years without premedications, it seems that premedications would not have prevented the reaction at this particular visit. Also, there are no obvious prescreening questions that may have predicted the reaction.

**Ms Ruffing:** The importance of monitoring at every infusion visit is emphasized, regardless of the number of infusions received. In this case, should the infliximab be changed to an alternate biologic?

**Ms Dexter:** Perhaps starting a premedication regimen would be more appropriate before making the decision to discontinue infliximab.

**Ms Daul:** Checking flow sheets and SOAP notes would help determine if anything differed at this visit versus previous visits. Often, the rate of administration may cause infusion reactions. This patient may not have been rate-titrated because past infusions were tolerated. Rate titration at future infusions could be attempted.

**Ms Dilliard:** Occasionally, reactions may start as very subtle symptoms, such as minor tingling or coughing, which patients should be instructed to report.

**Ms Daul:** Nursing also should observe patients for minor changes in appearance, such as flushing.

### CASE 4: WORSENING RA IN A PATIENT RECEIVING BIOLOGIC THERAPY

A 33-year-old male with a 10-year history of RA presented with new-onset lack of response to injectable etanercept after 6 years of therapy. Symptoms included worsening erosions, elevated CRP and ESR, and painful swollen MCPs and wrists. Biologic therapy was changed to abatacept. After 12 weeks of infusions, the patient complains of persistent pain in his hands. What counseling should the infusion nurse provide?

**DISCUSSION**

**Ms Dexter:** In clinical trials, abatacept may take from 15 days to 6 months before clinical response to therapy is evident. The physician should also be notified of the pain symptoms. Short-term oral corticosteroid therapy may alleviate pain symptoms.

**Ms Daul:** Compliance with other concomitant RA medications should be reviewed. Perhaps the patient is not taking his corticosteroid or non-steroidal anti-inflammatory drug as prescribed. Once pain and other RA symptoms improve, concomitant therapies could potentially be discontinued or changed to as-needed frequencies.

**Ms Ruffing:** This case illustrates the impact of patient expectations. In actuality, although the patient still had painful MCPs, MCPs were no longer swollen at 12 weeks. His CRP was normal, his ESR was declining, and his morning stiffness was absent. MCP pain may have been caused by his new erosions, which are not reversible. Pain management would probably be more appropriate for this patient.

### CONCLUDING DISCUSSION

**Ms Ruffing:** Are there any other issues to discuss in conclusion of this program?

**Ms Dexter:** Rheumatology workload is increasing because infusions are now being administered in clinics to more than just rheumatology patients. Time management strategies have become challenging.

**Ms Daul:** Subspecialties, such as gynecology and endocrinology, may also refer patients to rheumatology clinics for infusion therapies.
Ms Neuberger: Because infusion therapies seem to be the trend for more conditions, facilities will have to expand their resources to ensure patient safety.

Ms Daul: According to the Infusion Nurses Society, a safe nurse-to-patient ratio for complex biologic therapies is 3 to 1.

Ms Grace: Because reimbursement may be less for rheumatology versus other departments, institutional allocation of resources may be less for rheumatology.

Ms Daul: Although RA disease progression and disability have decreased with the advent of biologics, reimbursement disparities may decrease the use of biologics.

Ms Dolan: In local settings, trending disabilities may justify requests for more resources.

Ms Neuberger: In larger teaching settings, resources may be more readily available because the reputation of the institution is vulnerable. More profitable departments, such as cardiology, will support smaller departments, such as rheumatology. One potential mechanism to justify resources could be the provision of published studies that demonstrate the role of biologics in slowing RA progression and improving patient quality of life.5-12

Group: The future of RA therapies is promising and continues to grow. Research includes new indications and subcutaneous routes for current biologics, in addition to oral biologics and tyrosine kinase inhibitors. Investigational monoclonal antibodies and pegylated TNF-α therapies are also in clinical trials.

REFERENCES