The Role of the Advanced Practice Nurse in Rheumatology IV Infusion Therapy

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Objectives

* Define outpatient NP role in Rheumatology practice
* Discuss monitoring of biologic therapies in outpatient practice
* Discuss infusion reactions and treatments
* Case studies
From the United States Rheumatology Workforce: Supply and Demand 2005-2025 Report, it states there is currently a critical shortage of rheumatologists in the United States, which is only expected to worsen as the U.S. population ages and the number of persons with a rheumatic disease increases. Establishing a collaborative rheumatology practice between a rheumatologist and a nurse practitioner (NP), physician assistant (PA) or other rheumatology clinicians have been identified as one solution to the critical shortage of rheumatologists, while maintaining accessible, high quality care for rheumatology patients. Nurse practitioners, physician assistants and other rheumatology clinicians receive little training in their educational programs. Therefore, there is a need to provide readily available, timely, and standardized training in the diagnosis and management of rheumatic diseases while entering into collaborative practice with rheumatologists.

What role does a NP have in Rheumatology?

- Majority: RA
- Others: Dermatomyositis/ PM, Lupus, Scleroderma, PsA, Inflammatory arthritis, Inflammatory eye disease, Gout
- Sub-specialty training in vasculitis: GPA/MPA, Takayasu’s, PMR/GCA
- Screening for Biologic infusions
- Urgent calls from infusion center- management of infusion reactions
- Management of care is a collaborate effort with MD/CNP

What types of patients do we see?

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Infusion Room

What are the approved biologics for RA?

- Actemra
- Cimzia
- Enbrel
- Humira
- Kineret
- Ocrevus
- Remicade
- Rituxan
- Simponi
- Xeljanz
Considerations before starting biologic therapy

- **Hepatitis Screening**
  - Hepatitis B: Rare reactivation of hepatitis B has occurred in chronic carriers of the virus; evaluate all patients prior to initiation and during treatment in patients at risk for hepatitis B infection.

- **Malignancy Screening**
  - Confirm up to date age appropriate cancer screening is complete.
  - Malignancy: Use may affect defenses against malignancies; impact on the development and course of malignancies is not fully defined. An increased risk of lymphoma has been noted in clinical trials.

- **Tuberculosis**
  - Patients should be evaluated for latent tuberculosis infection with a tuberculin skin test prior to starting therapy. Treatment of latent tuberculosis should be initiated before therapy is started. Some patients who tested negative prior to therapy have developed active infection; monitor for signs and symptoms of tuberculosis in all patients.

Considerations before starting biologic therapy

- **Infections**: Serious and potentially fatal infections have been reported including bacterial sepsis and tuberculosis.

- **Vaccination update**: All vaccines should be brought up-to-date before starting anti-TNF therapy. Immunosuppressed patients should not receive live vaccines.
  - [https://www.clevelandclinicmeded.com/online/specialties/rheumatology.htm](https://www.clevelandclinicmeded.com/online/specialties/rheumatology.htm)

- **Pregnancy test**: Anti-TNF therapy has not been studied in pregnancy. Use of these therapies during pregnancy should be avoided.

- **Nervous system disorders (demyelinating disease)** such as Multiple Sclerosis, seizures, or inflammation of the nerves of the eyes have occurred in rare cases. Symptoms include numbness or tingling, problems with vision, weakness in arms and legs, and dizziness.

- **Congestive Heart Failure**: Recent ECHO or exam to rule out signs/symptoms of CHF: administration of anti-TNF agents has been linked to worsening or new onset CHF.

FDA website
Considerations before starting biologic therapy

**Biologics: Patient Assessment**

- Allergies?
- Congestive Heart Failure?
- Neurologic disorders, cancer, infection?
- Vaccination with attenuated live-virus products?
- Recent/anticipated surgery?
- Pregnancy, nursing, childbearing age?
- Residence/travel to foreign country?
- History of TB, histoplasmosis, herpes zoster?

*Data from J. Infusion Nursing Stone 2003*

**Contraindications to the use of biologic DMARDs**

- Infectious disease and/or pneumonitis
- Hematologic and oncologic: prior lymphoproliferative disease diagnosed and/or treated in the past 5 years
- Cardiac: moderate to severe heart failure (NYHA Class III-IV)
- Liver: Acute hepatitis B or C; chronic hepatitis B or C for those with significant liver injury
- Neuro: MS or demyelinating disorders
- Preoperative infectious risk: Recommendations to hold medication for > 1 week before/after surgery.

*American College of Rheumatology 2008 Recommendations for the Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis*
**PRE MEDICATION**

- **Infliximab**: Premedication with antihistamines (H₁-antagonist +/- H₂-antagonist), acetaminophen, and/or corticosteroids may be considered to prevent and/or manage infusion-related reactions.

- **Abatacept**: No pre medication required but ➔ Anaphylaxis/hypersensitivity reactions: Rare cases of hypersensitivity, anaphylaxis, or anaphylactoid reactions have been reported; medication for the treatment of hypersensitivity reactions should be available for immediate use.

- **Tocilizumab**: No pre medication required but ➔ Anaphylaxis/hypersensitivity reactions: May cause hypersensitivity, anaphylaxis, or anaphylactoid reactions (fatalities have been reported); hypersensitivity reactions have occurred in patients who were premedicated, in patients with and without a prior history of hypersensitivity, and as early as the first infusion. Stop infusion and permanently discontinue treatment in patients who develop a hypersensitivity reaction to tocilizumab. Medications for the treatment of hypersensitivity reactions should be available for immediate use.

- **Rituximab**: Acetaminophen and an antihistamine is recommended for all indications. For patients with RA, premedication with methylprednisolone 100 mg I.V. (or equivalent) is recommended 30 minutes prior to each dose. Infusion reactions: [U.S. Boxed Warning]: Severe (occasionally fatal) infusion-related reactions have been reported, usually with the first infusion; fatalities have been reported within 24 hours of infusion; monitor closely during infusion; discontinue with grades 3 or 4 infusion reactions.
An infusion reaction includes any signs or symptoms experienced by a patient during the infusion of pharmacologic or biologic agents or any events occurring on the first day of drug administration. Infusion reactions can be acute (occurring within two hours of infusion) or delayed (occurring up to 14 days after an infusion). The most common indicators are rash, flushing, change in blood pressure, or a "tickle in the throat."

Infusion reactions can happen with **ANY biologic infusion**

**Management of a mild infusion reaction**

- Most infusion reactions are mild with symptoms such as headache, nausea, or dizziness.
  - Stopping the infusion of the drug is usually sufficient to treat mild reactions.
- Most of the time allow at least 30 min and then resume at a slower rate

**Managing a moderate infusion reaction**

- Further signs of an infusion reaction include URI type symptoms (itchy throat), HIVES, chills, nausea, joint aches, fever, FLUSHING and fatigue.
- Stopping the infusion is indicated for approximately 30 min
- Consider adding medication to treat the symptoms: usually 25-50 mg of diphenhydramine, 500-650 mg acetaminophen, or a dose of hydrocortisone pushed via the IV.
- Be sure to observe that symptoms are improving before resuming
Severe infusion reactions are rare but have been observed on several instances with a variety of biologic treatments:

- hypo or hypertension (a 40 mm degree difference in blood pressure)
- Angioedema
- Wheezing
- stridor
- treatment is the same (IV diphenhydramine, IV solumedrol, IV fluids) with care to maintain the airway and the possible use of oxygen or epinephrine to treat anaphylaxis
- INFUSION MUST BE STOPPED, NOT ADVISABLE IN THE OUTPATIENT SETTING TO RECHALLENGE

Case Example:

- 36 yo female with RA
- Medications: Pred 15mg/d, MTX 20 mg/wk and infliximab 3mg/kg.
- Had 1 infusions of infliximab so far and states felt ok but was itchy during the infusion
- She is here today for her 2nd infusion
- What types of pre meds do you order?
A. Acetaminophen 1 gm
B. Acetaminophen 650 mg + diphenhydramine 50mg
C. IV solomedrol 125 mg
D. No pre meds needed

Case #1

**You gave Acetaminophen 650 mg + diphenhydramine 50mg**

**Patient in 20 mins into infusion and again feels some “itching”**

**The nurse pages you and tells you the patient is itchy but seems fine and is having lunch**

**What do you do?**
Case 1

A. Tell the nurse to call you back in anything changes
B. Tell the nurse to give another 25mg of diphenhydramine
C. Go fully evaluate the patient
D. This is a severe reaction and you should stop the infusion

Results

* Upon fully evaluating the patient, you see she is covered in hives.
* You stop the infusion
* Give bolus of fluids and IV solumedrol 100 mg IVP
* Symptoms resolve quickly but infusion not restarted.
* Real-life senerio → patient was rechallenged 2 weeks later with premeds of IV solumedrol 100mg, acetaminophen 650 mg and diphenhydramine 50 mg.
  * She severely reacted within 10 min of starting the infusion and was transported to the ED
  * Biologic therapy was changed at next cycle and she is doing well now
Case 2

* RA- Rheumatoid arthritis. **Onset 9/04. (+) RA. Weakly (+) CCP.**


IV Abatacept

* Patient in for IV abatacept after being seen by Tiffany Clark, CNP. 4th infusion of abatacept

* Pre medicated: No premedications ordered.

* Is this the correct premedication regime?

A. yes
B. no
Patient complains of itching of arms and back. Redness and hives noted on forearms, posterior chest, and cheeks. Abatacept discontinued (75% was infused). Tiffany Clark, CNP paged and came to see patient. Patient also stated that "chest feels a little congested and tight."

- Benadryl 50 mg PO and Tylenol 1000 mg PO given per order. Instructed to observe patient for thirty minutes. SAO2 noted to be 94% with a heart rate of 104. IV Normal Saline infusing at 50 ml/hr.

**What next?**

- Would you do anything differently beside acetaminophen, benadryl, fluids and observe?

- Discussion
* Within the next 15 minutes → Patient skin color pale, warm and dry, closing eyes but remains responsive. Chair reclined back to lower head.
* Oxygen applied at 4 liters / nasal cannula.
* BP checked manually 110/60.
* Solumedrol 60 mg IV given per order.
* SAO2 noted to be 89%, oxygen increased to 6 liters / nasal cannula.
* 15 min later - BP rising, patient more responsive, skin pink, breathing better, transferred to ED.
* No further abatacept infusion

**Take Home Message**

Infusion reactions can happen ANYTIME with ANY MEDICATION
Conclusion

- **Prompt intervention is important** and may prevent a more serious reaction.
- Evaluation by medical team needed every time at bedside
- Watch carefully for signs of hives/flushing - patients may be sleeping or covered up - during checks be sure to fully evaluate patient
- Facilitate communication well with the patient in order to recognize a reaction early and distinguish it from anxiety, hunger, pain, or other distress.
- A serious reaction can be life threatening - have emergency care in infusion suite and be prepared
- Re-challenging: a decision to try the drug again must be made on a case-by-case basis.