

Management of Rheumatologic Disease in the Setting of the COVID-19 Pandemic

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Rural Provider Lecture Series
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Objectives

- Understand unique characteristics of patients with rheumatologic disease that increase their risk of infection
- Discuss changes in clinical management that may help to reduce risk of exposure to COVID-19
- Review Guidelines from the American College of Rheumatology for the management of rheumatic diseases in the setting of the COVID-19 pandemic
- Review recent data on COVID-19 infection in patients with rheumatic disease

High Risk Population

- Immunosuppressed due to medications
- Immunosuppressed due to underlying disease
 - Dysregulated innate and adaptive immune systems
- Stress shown to increase risk of flare of autoimmune disease
 - Global pandemic = Stress!
- More likely to require travel for medical treatment
 - clinic, pharmacy, infusion center
- Elderly
- Multiple co-morbidities (CVD, HTN, DM)

Treatment Goals:

- Prevent exposure to/infection with COVID-19
 - Patient
 - Provider/Health Care System
- Achieve or maintain low disease activity or remission
- Prevent flares
 - Flares increase:
 - Risk of infection
 - Requirement for steroids
 - Dose of DMARD/Biologic
 - Need for clinic visit or hospitalization

Prevention: Patient

- Patients should follow all CDC and Alaska State Department of Health Guidelines
- As Alaska “re-opens”, our patients should adopt these new measures slowly
 - Continue social/physical distancing
 - Limit public outings
 - Wear a mask in public
 - Work from home if possible



Prevention: Provider

- Provide patient education
 - Disease state, medications, signs/symptoms of flare
 - Online patient resources (ACR, Creaky Joints)
- Avoid disruption in treatment
 - Continue routine follow-up appointments via telemedicine
 - Ensure adequate refills of all chronic medications
 - Utilize medication mail-out systems
 - Reduce frequency of lab monitoring
- Discuss behavioral health concerns
 - Increased anxiety about risk of infection
 - Depression from lack of social interaction, financial stress
 - Substance abuse, physical abuse
- Treat co-morbidities

Lab monitoring

- When possible, routine lab monitoring (CBC, CMP) for high risk DMARDs, including methotrexate and leflunomide, should be continued in local clinics every 3 months.
- For patients who are unable to travel or when flight restrictions prevent lab processing, we recommend continuation of methotrexate and leflunomide for up to 4-5 months, but not more than 6 months, without lab monitoring in those who have had stable labs on these drugs for at least a year.
- Patients on infused biologics can have labs drawn in coordination with infusion appointments.

American College of Rheumatology

COVID-19 Clinical Guidance for Adult Patients with Rheumatic Diseases

- Developed March 26, 2020. Updated April 14, 2020
- Expert Opinion
 - Virtual panel of Rheumatologists and Infectious Disease Specialists
- Guidelines contain only statements that received a moderate (M) or high (H) level of consensus among panel members
- Guidelines are highly disease-, patient-, geography- and time-specific
- Not intended to replace clinical judgement
- Subject to change as new developments arise

Clinical Scenarios

1. Treatment of stable disease- no COVID
2. Treatment of stable disease- asymptomatic COVID exposure
3. Treatment of new or active disease – no COVID
4. Treatment of disease in the setting of confirmed COVID infection

Treatment of Stable Disease

- **In the absence of known COVID-19 infection, continue current medication therapy:**
 - NSAIDs
 - DMARDs
 - Biologics
 - Janus Kinase Inhibitors
 - Immunosuppressants
 - Corticosteroids

NSAIDs

- Conflicting data on the impact of Ibuprofen on COVID-19 disease severity related to ACE2 receptor upregulation. There is limited data on other NSAIDs.
- Patients who are on chronic NSAIDs may continue therapy.
 - NSAIDs are not associated with an increased risk of other infections and are safer to use for arthritis flares than steroids.
- Patients who are acutely ill should stop NSAIDs due to risk of gastritis and renal insufficiency.
- **In COVID patients with severe respiratory symptoms, NSAIDs should be stopped (M)**

Conventional Synthetic Disease Modifying Anti-Rheumatic Drugs (DMARDs)

- **Hydroxychloroquine (Plaquenil)**
- Sulfasalazine
- Methotrexate
- Leflunomide (Arava)

Hydroxychloroquine

- Standard arthritis dose: 200mg-400mg daily (5mg/kg or less)
- COVID-19 dose: **400mg BID on day 1**, then 200mg BID for 4 days
- NOT proven to prevent or treat COVID-19
 - Avoid false sense of security!
- Toxicity is dose dependent
 - Most patients on a stable arthritis dose of HCQ have a low risk of cardiac toxicity
 - Use caution in patients on other QTc prolonging drugs
 - Avoid in patients with prolonged QTc

Biologics



- Proteins derived from living cells
- Specifically target cytokines and cell surface proteins involved in the pathogenesis of autoimmune disease

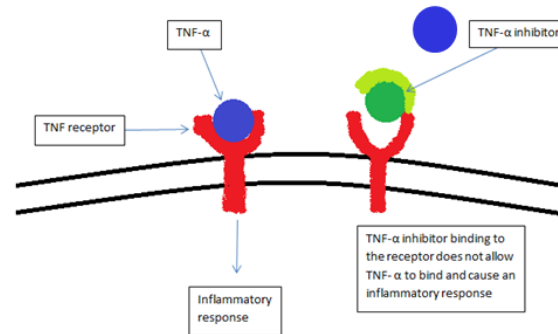
Cytokine Targeted Biologics

- **Anti-TNF**

- Etanercept (Enbrel)
- Adalimumab (Humira)
- Infliximab* (Remicade)
- Certolizumab (Cimzia)
- Golimumab

- **IL-1 Inhibitors**

- Anakinra (Kineret)
- Rilonacept
- Canakinumab



Sourced from Wikimedia, "TNF inhibitor"

- **Anti-IL6 receptor**

- Tocilizumab (Actemra)
- Sarilumab

- **Anti IL-12/IL-23**

- Ustekinumab (Stelara)

- **Anti-IL-17A**

- Secukinumab (Cosentyx)
- Ixekizumab

- **Anti-IL-17 receptor**

- Brodalumab

* Biosimilar (Renflexis) available at ANMC

Cell Targeted Biologics

B-Cell

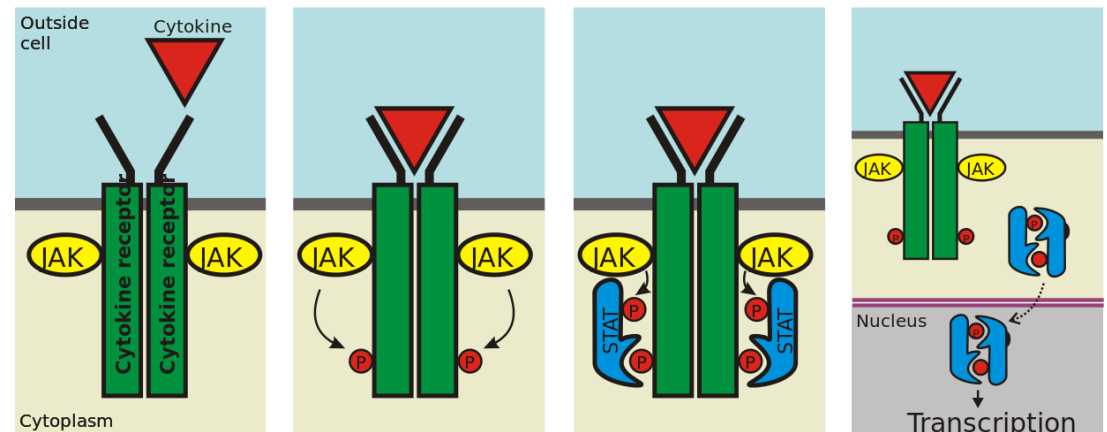
- Anti-CD20
 - **Rituximab (Rituxan)**
- B-Cell Growth Factor Inhibitor (Anti-Blys)
 - **Belimumab (Benlysta)**

T-Cell

- Co-stimulatory Molecule Inhibitor
 - **Abatacept (Orencia)**

Janus Kinase (JAK) Inhibitors

- JAK- intracellular protein that associates with and binds to cytokine and growth factor receptors
- **Tofacitinib (Xeljanz)** and **Baracitinib (Olumiant)**



sourced from Wikimedia "Jakstat pathway", diagram created by Peter Znamenkiy

Immunosuppressants

- Azathioprine
- Cyclosporine
- Cyclophosphamide
- Mycophenolate mofetile
- Tacrolimus

Corticosteroids

- Intra-articular steroids favored over systemic steroids in the setting of monoarticular flare
- Prednisone doses >6mg-10mg/day and especially at doses >20mg/day increase risk of infection and *should be avoided* if possible in RA, spondyloarthritis, psoriatic arthritis, and gout.
- Severe flares of lupus, vasculitis (including giant cell arteritis), myositis, interstitial lung disease and others may require high dose steroids and management should be directed by the patient's rheumatologist.
- Critically ill patients who are on chronic steroids (>5mg for 30+days or 20mg for 5+ days) will need stress dose steroids

1. Treatment of Stable Disease – No COVID

- In the absence of known COVID-19 infection, continue current medication therapy:
 - NSAIDs
 - DMARDs
 - Biologics
 - Janus Kinase Inhibitors
 - Immunosuppressants
 - Corticosteroids

2. Treatment of Stable Disease – asymptomatic COVID exposure

- In patients with stable rheumatic disease who are asymptomatic, but have been exposed to COVID-19:
 - HCQ, SSZ and NSAIDs may be continued (M/H)
 - Immunosuppressants, non-IL-6 biologics and Jak inhibitors should be stopped **temporarily** until COVID-19 testing is negative or after 14 day symptom-free period (M)
 - *Uncertainty among panel members regarding temporary hold of MTX and leflunomide*
 - In certain circumstances, IL-6 inhibitors may be continued (M)

3. Treatment of Active or New disease

- Inflammatory Arthritis:
 - For patients with active or newly diagnosed disease, conventional DMARDs may be started or switched. (M)
 - For patients with moderate to high disease activity despite conventional DMARD therapy, biologics may be started (H)
 - *Uncertainty about JAK inhibitors*
 - If indicated, low-dose glucocorticoids (10mg or less prednisone equivalent) or NSAIDs may be started. (M/H)
- Other Rheumatic Diseases:
 - In patients with systemic inflammatory or vital organ-threatening disease (ie. Lupus nephritis, vasculitis), high dose glucocorticoids or immunosuppressants may be initiated (M)

4. Active COVID-19 infection:

CONTINUE

- Hydroxychloroquine (Plaquenil) (M/H)
- Corticosteroids
- IL-6 inhibitors (select circumstances) (M)

STOP (M/H)

- Sulfasalazine, leflunomide, methotrexate
- Immunosuppressants
- Biologics
- Janus Kinase (JAK) inhibitors
- NSAIDs (in severe respiratory disease) (M)

Covid-19 in Immune-Mediated Inflammatory Diseases- Case Series from New York

Haberman, et al. 29 April 2020. NEJM

- Prospective Case Series, March 3- April 3, 2020
- 86 patients at NYU Langone Health Center, New York City.
 - 59 confirmed COVID, 27 highly suspicious for disease
 - RA, Psoriasis, Psoriatic Arthritis, Ankylosing Spondylitis, IBD, or related diseases
 - 76% on biologic or Jak inhibitor therapy
- 16% of patients required admission
 - Older age
 - Rheumatoid Arthritis
 - More co-morbidities (HTN, DM, COPD)
 - 79% were discharged, 2 still hospitalized, 1 required mechanical ventilation
 - One death
- **Infection rate similar to general NYC population**
- **Patients on biologics do not have a worse outcome**

COVID-19 Global Rheumatology Alliance

- **Our Mission:**

- *Our mission is to collect, analyze and disseminate information about COVID-19 and rheumatology to patients, physicians and other relevant groups to improve the care of patients with rheumatic disease.*

- **Our Vision:**

- *Bringing together the global rheumatology community to curate and disseminate accurate and comprehensive knowledge to advance rheumatology care in the COVID-19 pandemic.*

- <https://rheum-covid.org/>

- Secure, de-identified, international case reporting registry of patients with rheumatic disease who contract the COVID-19 virus

- ***Certain organizations and Tribal Councils may restrict enrollment of patients. Know your local rules before enrolling patients!***

COVID Testing

- Testing should be conducted based on state and local recommendations and test availability
- We are not currently preferentially testing asymptomatic patients on immunosuppressive therapy
- ***Patients on immunosuppressive therapy are still at high risk for OTHER infections that can be life threatening! Don't ignore symptoms if COVID-19 testing is negative.***

Online Rheumatology Resources

- ANTHC: <https://anthc.org/wp-content/uploads/2020/03/200318-COVID-19-Rheumatology-Recommendations-for-Patients.pdf>
 - *Patient handout with summary of Recommendations*
- American College of Rheumatology: <https://www.rheumatology.org/>
 - *Clinical Guidelines*
 - *Disease and Treatment handouts for patients*
- CreakyJoints: <https://creakyjoints.org/>
 - *COVID-19 support program for chronic disease patients and their families*

Rheumatology Consults

- Tiger Text:
 - “ANMC Rheumatology Consult”
 - Coverage from 8am-4:30pm
- Phone:
 - Internal Medicine Clinic (907) 729-1500
 - Rheumatology RN Case Manager (907) 729-2071
- Cerner, AFHCAN referrals

References

- American College of Rheumatology COVID-19 Clinical Guidance Task Force. (April 14, 2020). *COVID-19 Clinical Guidance for Adult Patients with Rheumatic Diseases*.
- West, S. (2019). *Rheumatology Secrets*. (4th Ed.). Philadelphia, PA: Elsevier
- Haberman, R. et al. (April 29 2020). *Correspondence: Covid-19 Immune Mediated Inflammatory Diseases—Case Series from New York*. Accessed online April 29, 2020 from www.NEJM.org. DOI: 10.1056/NEJMc2009567

THANK YOU!!