Fall 2022, Volume 32, Number 3

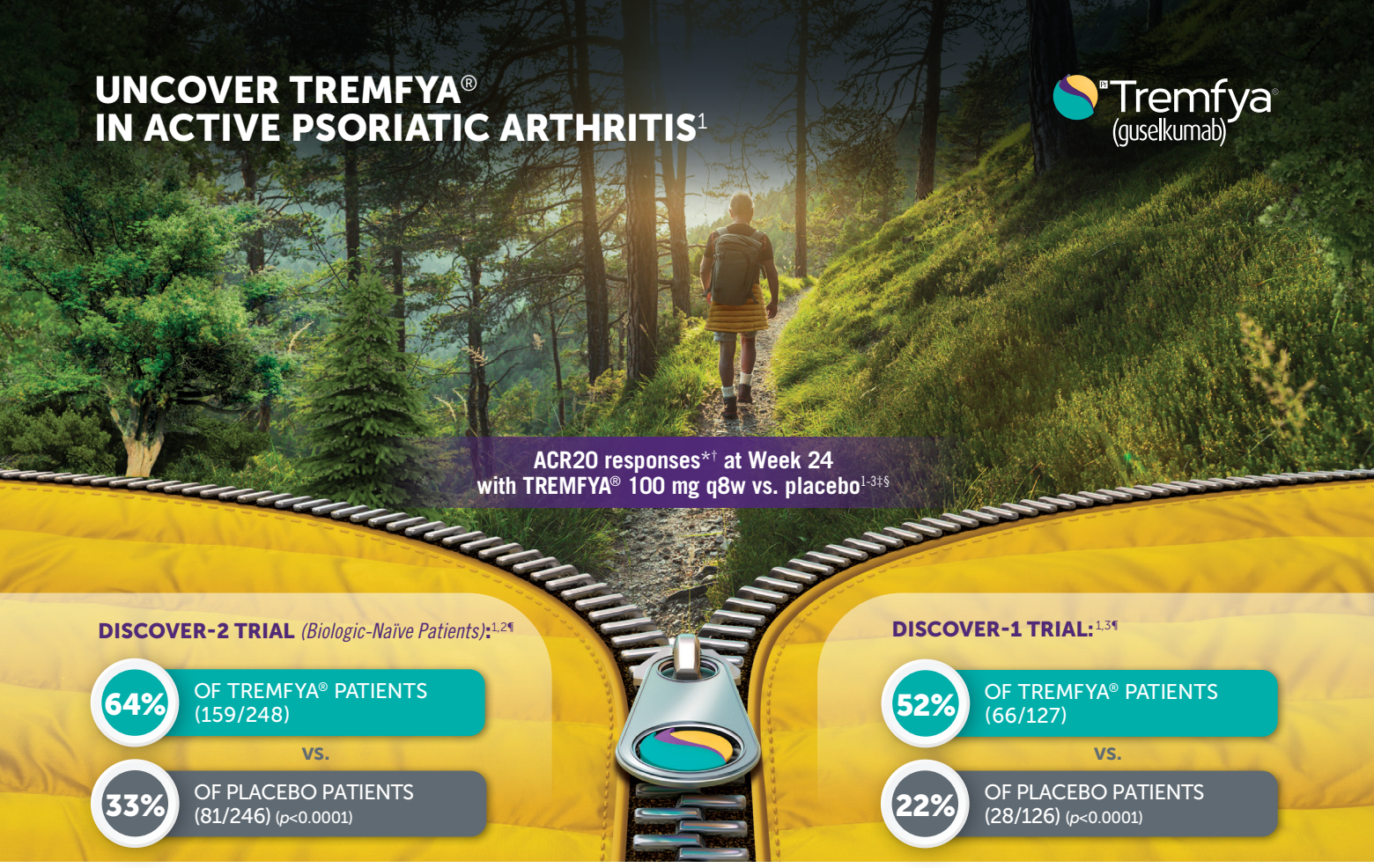
CRAJ SCR

The Journal of the Canadian Rheumatology Association

Spotlight on: Innovation in Rheumatology

UNCOVER TREMFYA®
IN ACTIVE PSORIATIC ARTHRITIS[1]

Tremfya® (guselkumab)



ACR20 responses*† at Week 24 with TREMFYA® 100 mg q8w vs. placebo[1-3‡§]

DISCOVER-2 TRIAL *(Biologic-Naïve Patients)*:[1,2¶]

64% OF TREMFYA® PATIENTS (159/248)

VS.

33% OF PLACEBO PATIENTS (81/246) (p<0.0001)

DISCOVER-1 TRIAL:[1,3¶]

52% OF TREMFYA® PATIENTS (66/127)

VS.

22% OF PLACEBO PATIENTS (28/126) (p<0.0001)

Demonstrated improvements in HAQ-DI and SF-36 PCS from baseline with TREMFYA® 100 mg q8w at Week 24 vs. placebo[1-3*†]

- Mean change in HAQ-DI score: -0.32 vs. -0.07 (DISCOVER-1) and -0.37 vs. -0.13 (DISCOVER-2) (p<0.001, both trials)
- Mean change in SF-36 PCS: 6.1 vs. 2.0 (DISCOVER-1; p<0.0001) and 7.4 vs. 3.4 (DISCOVER-2; p=0.011)

Indications and clinical use:

TREMFYA®/TREMFYA ONE-PRESS® (guselkumab injection) is indicated for the treatment of adult patients with active psoriatic arthritis. TREMFYA®/TREMFYA ONE-PRESS® can be used alone or in combination with a conventional disease-modifying antirheumatic drug (cDMARD) (e.g., methotrexate).

TREMFYA®/TREMFYA ONE-PRESS® is also indicated for the treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Relevant warnings and precautions:

- Do not initiate treatment in patients with any clinically important active infections until the infection resolves or is adequately treated
- Discontinue treatment if patient develops a serious infection or is not responding to standard therapy for infection
- Evaluate patients for tuberculosis infection prior to therapy and monitor for active tuberculosis during and after treatment
- Consider completion of all immunizations prior to treatment
- Concurrent use with live vaccines is not recommended
- Discontinue treatment in cases of serious hypersensitivity reactions, including anaphylaxis, urticaria and dyspnea, and institute appropriate therapy
- Women of childbearing potential should use adequate contraception
- Use during pregnancy only if clearly needed
- The benefits of breastfeeding should be considered along with the mother's clinical needs
- Effect on human fertility has not been evaluated
- Safety and efficacy in pediatric patients have not been evaluated
- Data in patients ≥65 years of age are limited

For more information:

Please consult the Product Monograph at www.janssen.com/canada/products for important information regarding adverse reactions, drug interactions, and dosing and administration that has not been discussed in this piece.

The Product Monograph is also available by calling 1-800-567-3331 or 1-800-387-8781.

HAQ-DI=Health Assessment Questionnaire-Disability Index; SF-36 PCS=Short Form (36-item) Physical Component Score; qw8=every 8 weeks; ACR20=American College of Rheumatology 20% improvement from baseline; TNFα=tumour necrosis factor alpha; CI=confidence interval.

* Patients with <5% improvement from baseline in both tender and swollen joint counts at Week 16 were qualified for early escape and were permitted to initiate or increase the dose of concomitant medications, including NSAIDs, oral corticosteroid, and cDMARD, and remained on the randomized study treatment. At Week 16, 19.0% and 3.1% (DISCOVER-1) and 15.4% and 5.2% (DISCOVER-2) of patients in the placebo and TREMFYA® 100 mg q8w groups, respectively, met early escape criteria.

† Patients with missing data at Week 24 were imputed as non-responders. Patients who initiated or increased the dose of cDMARD or oral corticosteroids over baseline, discontinued study or study medication, or initiated protocol-prohibited medications/therapies for PsA prior to Week 24 were considered treatment failures and non-responders. At Week 24, 16.7% and 5.5% (DISCOVER-1) and 6.9% and 4.8% (DISCOVER-2) of patients in the placebo and TREMFYA® 100 mg q8w groups, respectively, met treatment failure criteria.

‡ DISCOVER-2: Multicentre, double-blind, randomized, placebo-controlled phase 3 study in biologic-naïve adults with active psoriatic arthritis (PsA) (≥5 swollen joints, ≥5 tender joints, and a C-reactive protein [CRP] level of ≥0.6 mg/dL) who had inadequate response to standard therapies (e.g., conventional disease-modifying antirheumatic drugs [cDMARDs], apremilast, or nonsteroidal anti-inflammatory drugs [NSAIDs]), a diagnosis of PsA for ≥6 months, and a median duration of PsA of 4 years at baseline. Patients were randomly assigned to receive subcutaneous injections of TREMFYA® 100 mg at Weeks 0, 4, then q8w, or placebo. Primary endpoint was the percentage of patients achieving an ACR20 response at Week 24.

§ DISCOVER-1: Multicentre, double-blind, randomized, placebo-controlled phase 3 study in adults with active psoriatic arthritis (PsA) (≥3 swollen joints, ≥3 tender joints, and a CRP level of ≥0.3 mg/dL). Eligibility criteria also included inadequate response to standard therapies (e.g., cDMARDs, apremilast, or NSAIDs), a diagnosis of PsA for ≥6 months, and a median duration of PsA of 4 years at baseline. About 30% of study participants could have received one or two anti-TNFα agents. Patients were randomly assigned to receive subcutaneous injections of TREMFYA® 100 mg at Weeks 0, 4, then q8w, or placebo. Primary endpoint was the percentage of patients achieving an ACR20 response at Week 24.

¶ Treatment differences, 95% CIs and p-values were based on Cochran-Mantel-Haenszel test stratified by baseline non-biologic cDMARD and either prior CRP (<2.0, ≥2.0 mg/dL) (DISCOVER-2) or prior anti-TNFα agents (DISCOVER-1).

References: 1. TREMFYA®/TREMFYA ONE-PRESS® (guselkumab injection) Product Monograph. Janssen Inc. September 17, 2021. **2.** Mease PJ, Rahman R, Gottlieb AB, *et al.* Guselkumab in biologic-naïve patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomized, placebo-controlled phase 3 trial. Published online March 13, 2020 at https://doi.org/10.1016/S0140-6736(20)30263-4. **3.** Deodhar A, Helliwell PS, Boehncke W, *et al.* Guselkumab in patients with active psoriatic arthritis who were biologic-naïve or had previously received TNFα inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial. Published online March 13, 2020 at https://doi.org/10.1016/S0140-6736(20)30265-8.

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Rapamycin, mTOR, TNF Inhibition, RA, Longevity and Canadian Content: Putting the Puzzle Pieces Together

By Philip A. Baer, MDCM, FRCPC, FACR

Why do most continuing medical education (CME) presentations start with a patient case? Because science is more interesting when you can relate basic research to clinical innovations which will help your patient. This journey started with a message to call a patient of mine, a man with long-standing rheumatoid arthritis (RA) well-controlled on conventional disease-modifying antirheumatic drugs (DMARDs), as he wanted to discuss a new therapy he had read about online. What that therapy was, he wouldn't confide to my secretary.

It was a quiet day, so I returned his call. What could he have found? I was guessing cannabinoids, turmeric, noni juice, apple cider vinegar, bee venom or the like. No, he was interested in rapamycin (sirolimus). I told him I was familiar with it as an immunosuppressant and anti-rejection drug, but it was not approved for RA therapy. I did promise I would look into it further and let him know more at his next appointment.

I figured rapamycin might have been investigated in the past and failed in RA. True and false. A quick search found a EULAR (European Alliance of Associations for Rheumatology) abstract poster from 2018 reporting such a study (FRI 0063): "Rapamycin induces remission in patients with refractory rheumatoid arthritis" by H. Yao and colleagues.[1] Fifty RA patients treated with DMARDs for more than 6 months who did not achieve DAS-28 (Disease Activity Score in 28 joints) remission were enrolled and treated with rapamycin at a dose of 0.5 mg every 2 days for 24 weeks. Rapamycin treatment reduced RA disease activity and induced DAS-28 remission in 44.9% of active RA patients. Of course, there was no placebo group. I haven't seen anything since on the topic, other than an abstract on a similar study at the American College of Rheumatology (ACR) 2018 meeting.[2]

Other than reporting this back to the patient as promised, I thought that was the end of the matter. However, a few days later I received a financial news email I subscribe to from John Mauldin, a prolific and interesting writer. While he is generally gloomy on the financial future, he is very optimistic on advances in health care and biotechnology, particularly regarding extending the human lifespan. Not only was he discussing rapamycin, but also tumour necrosis factor (TNF) inhibition. The word for that is serendipity.

Dr. Erwin Gelfand and Dr. Philip Baer in Antarctica, in 2019.

Mr. Mauldin reported on a company called MyMD Pharmaceuticals[3] which he had invested in (MYMD on NASDAQ, if you want to take a flyer and are prepared to potentially lose your entire investment). "Their drug, MYMD-1 is a TNF-inhibitor. . . Unlike monoclonal anti-TNF antibodies, MYMD-1 is an orally administered synthesized version of a naturally occurring molecule found in plants." The company website indicates a molecular weight of 146 Daltons, the ability to cross the blood-brain barrier, and that "MYMD-1 selectively blocks TNF when it becomes overactivated in autoimmune diseases and cytokine storms, but does not block it from doing its normal job of being a first responder to any routine type of moderate infection." All very interesting if it pans out, but the drug is just now entering Phase 2, which many drugs do not survive.

Is the company studying their drug for RA? Not directly. Their trial is targeted to aging and specifically to reversing sarcopenia, which is of course a feature of uncontrolled RA. And that's where rapamycin comes in. Rapamycin is the gold-standard treatment for countering aging and increasing lifespan in mice. MYMD-1 markedly outperformed rapamycin in a mouse longevity study (in press apparently) performed by scientists at Johns Hopkins.[4]

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Rapamycin, mTOR, TNF Inhibition, RA, Longevity and Canadian Content: Putting the Puzzle Pieces Together *continued from page 3*

If you look online, you will find a lot of articles about off-label anti-aging therapies, with metformin and rapamycin most often touted. You can skip those, but I highly recommend a review by Dr. Daniel Sabatini, one of the leaders in research on rapamycin and its target mTOR.[5]

What will you learn? "Dr. Sabatini chose to investigate the molecular mechanism of rapamycin, a compound with antifungal, antitumour, and immunosuppressant properties. The decision was pivotal because Sabatini went on to discover the mechanistic target of rapamycin (mTOR) protein and signalling pathway, which serves as a central regulator of cell metabolism, growth, and proliferation."[6] Interesting naming to begin with: just like Lou Gehrig died of Lou Gehrig's disease, rapamycin's target mTOR happens to be named after rapamycin.

The mTOR protein turns out to be a central player in many cellular processes. "mTOR is the major regulator of growth in animals and is the key link between the availability of nutrients in the environment and the control of most anabolic and catabolic processes. Signalling of mTOR is deregulated in common diseases, like cancer and epilepsy, and mTORC1 (a complex containing mTOR) is a well-validated modulator of aging in multiple model organisms. There is significant excitement around using mTORC1 inhibitors to treat cancer and neurological disease and, potentially, to improve healthspan and lifespan." As Dr. Sabatini states, he never believed "the mTOR pathway would receive the recognition it has and eventually even be derided for 'doing everything'."

To bring this all home, the review figures show some of the molecules which interact with mTOR. These include some suggesting Canadian roots, such as RAPTOR (nothing to do with basketball; it is the Regulatory Associated Protein of mTOR) and CASTOR (our national symbol the beaver is Castor canadensis, but this is the Cytosolic Arginine Sensor for mTORC1). But rather than stretching for Canadian-themed content, Dr. Sabatini provides a real link, referencing research on rapamycin by Dr. Erwin Gelfand, a prolific immunologist, and a McGill graduate who was formerly on staff at the Hospital for Sick Children in Toronto. As you can see in the photo on page 3, I met Dr. Gelfand for the first time in Antarctica in 2019. Let me assure you, we did not spend our time talking about rapamycin.

Rapamycin for RA may be a dead end, but if my patient hadn't called me about it, I would never have learned any of the above!

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2022 CIORA Grant Award Recipients

By Janet Pope, MD, MPH, FRCPC

The Canadian Rheumatology Association (CRA) is pleased to announce that its granting division, the Canadian Initiative for Outcomes in Rheumatology cAre (CIORA), will be funding 4 two-year grants and 1 one-year grant for a total of $485,626 CDN to projects that will enhance access and innovation for rheumatology care. Additionally, the CRA will set aside $60,000 to fund the CRA (CIORA) Arthritis Society Clinician Investigator Award in 2023 (more details to follow).

Over the last 15 years, CIORA has funded 114 projects and provided almost $8.5M CDN in research funding since 2006.

CIORA's grant program supports sustainable projects related to:

- Academic clinical research initiatives related to all rheumatic diseases
- Clinical research initiatives for community rheumatologists related to all rheumatic diseases

Principal Investigator(s)	Title	Award
 **Vinet, E.**	Personalized therapy in lupus pregnancies.	**$114,000**
 **Boire, G.**  **Beausejour, M.**  **Feldman, D.**	Assessing the timeliness of referrals in rheumatology for chronic inflammatory arthritis from a centralized referral system.	**$111,074**
 **Abikhzer, G.**	Digital FDG PET/CT versus temporal artery biopsy and ultrasound for first-line diagnostic imaging of giant cell arteritis.	**$109,326**
 **Barber, C.**	Development and pilot of a shared-care model for rheumatoid arthritis leveraging an "on-demand" follow-up strategy.	**$109,796**
 **Gottheil, S.**	Reducing urgent care wait times in community rheumatology: A quality improvement project.	**$41,430**

A listing of all current and previous recipients is available at *rheum.ca/ciora*.

CRAF Update

By Ahmad M. Zbib, MD, CPHIMS-CA

We are pleased to announce that, as of July 13th, the Canada Revenue Agency has approved charitable status for the Canadian Rheumatology Association Foundation (CRAF). This is a significant milestone in our journey to establish the CRAF to help fund activities of the Canadian Rheumatology Association.

Stakeholder engagement remains a top priority for the CRAF. We continue to work closely with our members and partners as we activate the roll-out plan. Our priorities are to establish formal operational governance, documentation, and a foundation launch plan.

The main objective is to create an organization that allows us to build capacity to fund activities that are in line with the CRA mission, which is focused primarily on serving and representing rheumatologists so they can deliver the best care possible to their patients.

We continue to believe in building strong, synergistic partnerships with aligned charitable health and patient organizations so we can all better reach our collective goals.

We will continue to provide updates as we prepare for the soft launch this Fall and our public launch in the new year. For more information on how you might be able to support the CRAF, please contact Dr. Ahmad Zbib (by email: *executivedirector@crafoundation.ca* or by phone: 905-952-0698 extension 8.

"We are excited to be working on launching the new charitable organization, the Canadian Rheumatology Association Foundation (CRAF) which will focus on building sustainable sources of revenues to support and fund programs serving the rheumatology community."

- Dr. Ahmad Zbib
CEO, CRA

CIORA *continued from page 6*

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CIORA is issuing another call for grants in 2023!

CIORA Online Grant Application System opens on **January 23, 2023.**

Letter of Intent must be submitted by **February 20, 2023.**

CIORA Online Grant Application submission deadline is **March 31, 2023.**

Infographics to Facilitate the Diagnosis and Management of Giant Cell Arteritis and Gout by Emergency Physicians

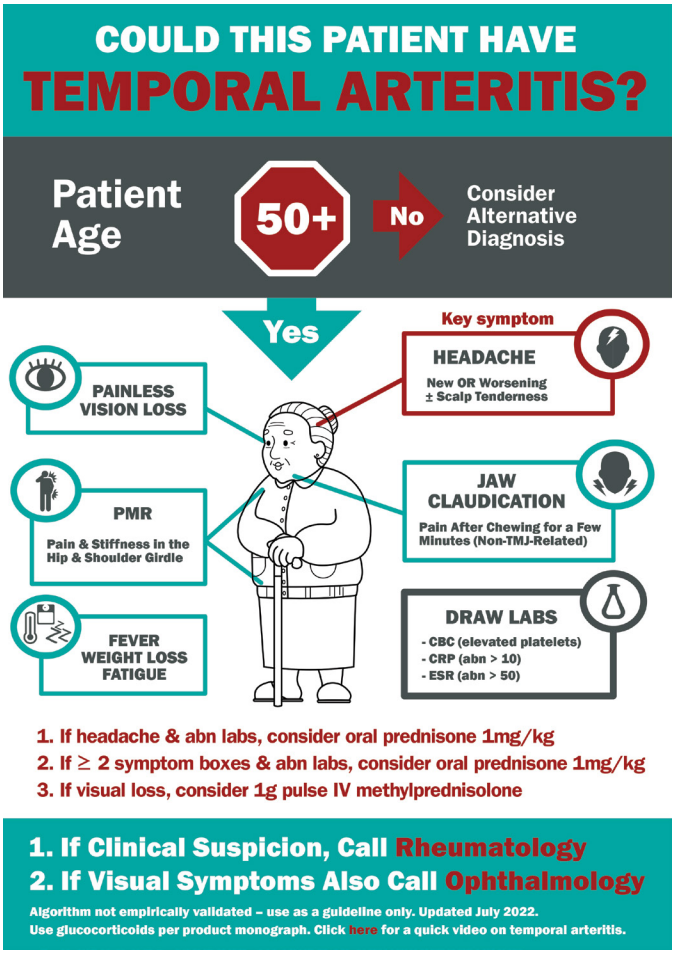
By Monish Ahluwalia, MSc; Sabrina Campbell, HBSc; Sangeeta Bajaj, MD, FRCPC; Raman Joshi, MD, FRCPC; Tripti Papneja, MD, FRCPC; and Vandana Ahluwalia, MD, FRCPC

Patients with rheumatologic complaints account for up to 8% of all emergency department visits.[1] Two diagnostic challenges of interest are giant cell arteritis (GCA) and gout. GCA is a medium-large vessel vasculitis with low prevalence, high morbidity, and variable presentation, making it a difficult diagnosis and one where patients often first present to the emergency department.[2,3] Models suggest that referrals for GCA could be better triaged to avoid unnecessary imaging, specialist referrals, and temporal artery biopsies.[4,5] Gout is a urate crystal arthropathy with increasing prevalence and increasing associated healthcare costs, yet still characterized by suboptimal treatment and patient outcomes.[6,7] Retrospective cohort analyses demonstrate that more than 30% of patients with a diagnosis of an acute gout flare may not receive anti-inflammatory medications and that medication errors in gout treatment are common.[8–11] Despite the importance of these diagnoses in clinical practice, much of the literature is not directed toward emergency physicians and additional educational resources are required.[2]

Unfortunately, continuing medical education for physicians is challenging due to overwhelming volumes of literature, time constraints, and imperfect information retention.[12] The awareness-to-adherence model describes that physicians who are regularly trying to implement knowledge into practice first require awareness, agreement, and intention.[13] To mitigate these barriers, infographics have been used to improve both exposure and knowledge.[12]

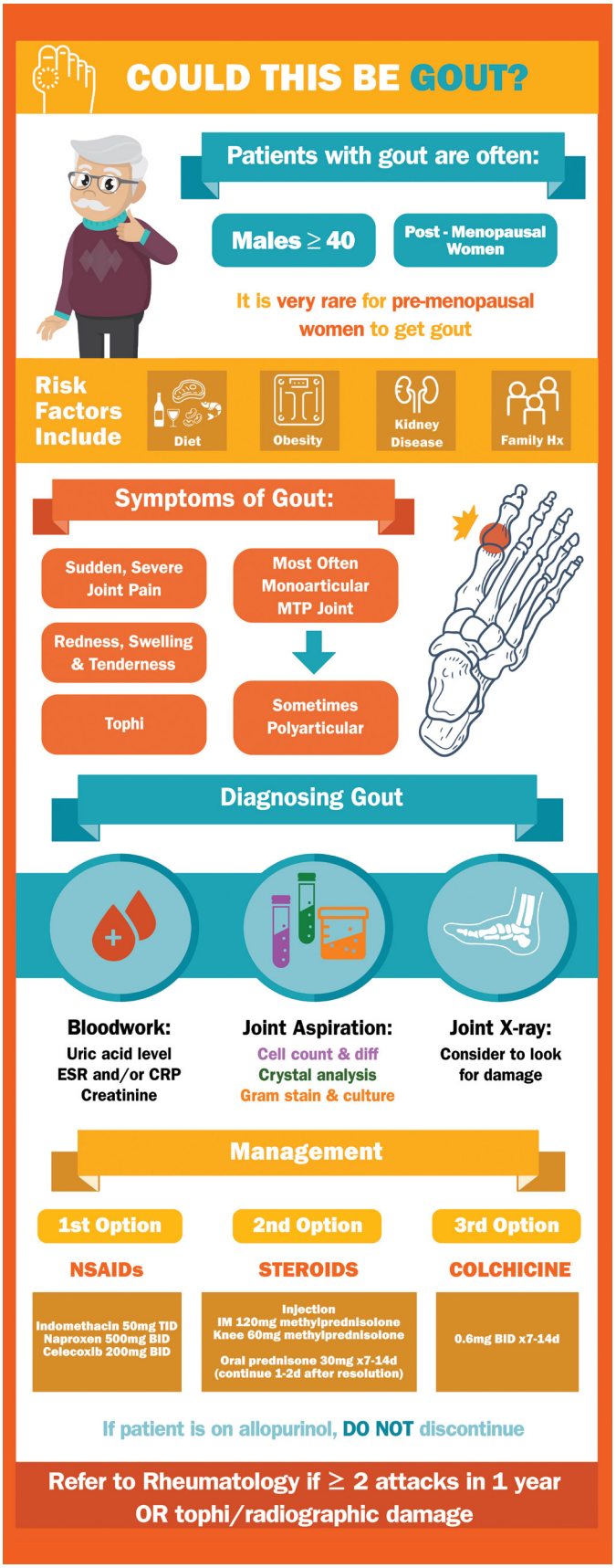
Infographics (or information graphics) are data visualizations that can convey large amounts of complex information succinctly and comprehensibly.[12,14] Infographics have been shown to be superior to text alone in terms of information retention due to a phenomenon known as the picture superiority effect – the idea that pictures are more likely to be remembered than words.[14,15] Compared to text-based resources, infographics are associated with higher reader preference, decreased cognitive load, and increased accessibility online and on mobile devices, which are preferred by emergency physicians.[12,16]

Thus, we created two infographics that illustrate the emergency diagnosis and management of GCA and gout. Our goal was to provide easily accessible and consumable



educational resources for emergency physicians (Figures 1 and 2). These serve as clinical diagnostic and management tools that providers can use on-the-job, while also being available as posters and educational tools for practicing physicians, medical trainees, and other healthcare professionals. If a rheumatologist receives a referral for one of these conditions, they may consider attaching the infographic in their letter back to the referring provider or posting the infographic on their clinic website to promote continuing education.

The GCA infographic was created using the 1990 and 2016 American College of Rheumatology (ACR) diagnostic



criteria and 2021 ACR and 2018 European League Against Rheumatism (EULAR) management recommendations.[17–20] The gout infographic was created using the 2020 ACR guidelines for gout management.[21] Each infographic was created in collaboration with four community rheumatologists to ensure accuracy and appropriateness, and reviewed with multiple community emergency physicians to ensure relevance. In addition, the GCA infographic is paired with a video synopsis by Dr. Joanne Jiang, a vasculitis fellow in Toronto, which can be found hyperlinked at *youtube.com/watch?v=7bcJQTRztX8*.

The infographics available in this article are to be used as a guideline only and may be re-distributed in their unmodified form in a non-commercial manner. Specifically, the algorithm proposed in the GCA infographic has not been empirically validated; however, future research will analyze its performance in classifying referrals from the emergency department.

Disclosure: The creation of these infographics was supported by F. Hoffmann-La Roche AG through an unrestricted educational grant.

The authors' full credentials are available in the online edition at *craj.ca*.

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Hire a Scribe. Get a Life!

By Vandana Ahluwalia, MD, FRCPC; Dilnoor Sidhu, MSc; Fallon Dennis; and Monish Ahluwalia, MSc

Electronic medical records (EMRs) have revolutionized medical care in Canada. Physicians are able to record clinical information legibly, and access laboratory reports, radiology reports, and hospital reports at the tips of their fingers. Despite this, EMRs are cumbersome as they were not designed by physicians, and still require significant data entry for optimal patient care. The need for data entry will only increase if value-based payments are to be implemented with standardized metrics. Unfortunately, the unintended consequences of EMRs have led to an increased physician-computer interaction (as opposed to physician-patient interaction), which is resulting in increased physician burnout. According to the 2021 Ontario Medical Association burnout task force report, the first recommendation was to "streamline and reduce required documentation and administrative work." In that report, the "use of medical scribes, particularly in relation to electronic medical documentation requirements," was recommended.[1] Despite the fact that scribes are commonly used in the United States, Canadian physicians have yet to adopt this model of care.

Three years ago, I hired a medical scribe. It was one of the best things I have done for my patients and my practice. A medical scribe is defined as "an unlicensed person hired to chart at the direction of a physician or practitioner, with the goal of allowing the physician to spend more time with the patient and have accurate documentation."[2] They can be pre-med students, post-grad students, or others without any science education.

The human scribe comes into the room with me (consented by the patient) and records the medical encounter including the history, physical examination, and the impression and plan. At the end of the day, we review all the notes in detail and ensure they are ready to be faxed to the referring physician.

With documentation being contemporaneous with the encounter, I have more face-to-face time with the patients, reduced clinic wait times, and have increased the number of patients seen per day. I still have enough energy, at the end of the day, to do the things I love to do at home.

Since 2021, I have hired and trained two more scribes for my rheumatology colleagues in our office. This has inspired me to create a Rheumatology Scribe Training Program to standardize the process. If we want this to be successful, more work needs to be done to understand the time and cost to hire, train, monitor and evaluate scribes for physician support in Canada. Insights gained by medical associations and government support will go a long way to making this a reality.

For a human scribe, sustainability is always the question. Although my scribe has been with me for 3 years, turnover typically occurs after 1-2 years. Virtual scribes that work remotely can improve the stability of this workforce, as more than one person may be available for support. Additionally, our Rheumatology Scribe Training Program hopes to make training a faster and easier process, so that the scribe is functional within 3 months. Artificial-intelligence-supported scribing may reduce turnover and decrease costs, but more work needs to be done to ensure accurate and flexible automated documentation of complex patient encounters.

In the end, scribes are not a replacement for EMR redesign, and we should continue to advocate for user interfaces that best suit physician needs. Until then, scribes can increase clinic productivity, reduce physician burnout, maintain patient satisfaction, and perhaps even increase career length. Hire a scribe! Get a life!

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Innovation to Improve Outcomes in Indigenous People at Risk of RA

By Hani El-Gabalawy, MD, FRCPC, FCAHS

Multiple studies from our Manitoba-based clinical research group, along with studies from several other groups in Canada, U.S., and Mexico, have demonstrated that many Indigenous North American (INA) populations have increased risk of developing seropositive rheumatoid arthritis (RA). In these populations, the prevalence of RA can be 2-3 times higher than that observed in most other populations, the disease is more severe and disabling, and the outcomes are often unfavourable, with an excess burden of morbidity and mortality. The basis for this involves a complex interaction between biological, environmental, sociocultural, and health care delivery variables which are notoriously difficult to untangle. This is a challenge that is in much need of innovation.

As such, an innovation agenda that aims to improve the outcomes of RA in INA people needs to take into account the unique challenges inherent in the design of clinical studies, as well as in the implementation and the scalability of the proposed interventions resulting from these studies. During my tenure as a Canadian Institute of Health Research (CIHR) Scientific Director, I became involved with a visionary and unique strategic initiative led by the Institute of Aboriginal People's Health entitled Pathways to Health Equity for Aboriginal Peoples (*cihr-irsc.gc.ca/e/47003.html*). At the time I became involved, the scope of this strategic (so called signature) initiative had already been determined to focus on the compelling challenges of mental wellness, diabetes/obesity, tuberculosis, and oral health. In hindsight, had I been able to engage with this initiative on the ground floor at its inception, perhaps RA would have been one of the chosen focus areas, but "this is history" to quote an old phrase.

Nevertheless, there was much to learn from the Pathways initiative about how to approach an innovation agenda for INA People. The initiative, which was firmly grounded in the principles of Community Based Participatory Research (*ethics.gc.ca/eng/tcps2-eptc2_2018_chapter9-chapitre9.html*), had several incremental phases where nascent ideas were first explored in various communities based on modest levels of funding, and successful research groups and ideas were then supported with larger funding envelopes to begin to address the implementation and the scalability of the projects. It seems to me that this is the appropriate "pathway" to accomplishing what we need to achieve for devastating diseases such as RA in INA.

The work of my own research group has focused on the prediction and prevention of RA in First Nations. We have been fortunate to receive uninterrupted CIHR funding for this program since 2005 through open competitions and strategic initiatives such as the Human Immunology Research Teams program. We have made important observations regarding the risk of developing RA in INA by longitudinally studying the at-risk first-degree relatives (FDR) of INA RA patients. For example, we have shown that development of anti-citrullinated protein antibodies (ACPA) is common in the FDR, but that this is far from being a one-way street leading to RA development (PMID 30861615). Indeed, a substantial proportion of ACPA+ FDR reverted back to a seronegative state, and those destined to develop RA exhibited unique glycosylation patterns of their ACPA (PMID 31067000) and specific proteomic features (PMID 32770634).

We are currently engaged in an exciting initiative where we aim to reduce the risk of future RA development using a combination of anti-inflammatory/immunomodulatory nutritional supplements. This is based on findings from a collagen-induced arthritis mouse model of RA development, where our group showed that a combination of vitamin D, omega-3, and curcumin supplements was highly effective in attenuating the onset of arthritis in this model, with the curcumin contributing the most to this effect (PMID 33494792). We have begun the long road to the clinical translation, evaluation, and implementation of this approach in INA individuals at risk for developing RA. We remain inspired by the sensible approach that was developed in the CIHR "Pathways" signature initiative.

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To Break or Not to Break (Again): Is That the Question?

By Raheem B. Kherani, BSc (Pharm), MD, FRCPC, MHPE; and Sonia Singh, MD, CCFP, MHSc

A 67-year-old woman with rheumatoid arthritis trips over the edge of a carpet and falls on her left side. She sustains a left hip fracture and is treated with a left hemiarthroplasty. She receives post-operative physical therapy and is starting to mobilize independently. What happens next? Is she at risk of another fracture? Is anything done to prevent the next fracture?

Fragility fractures occur spontaneously or following minor trauma such as coughing, sneezing, or falling from standing height. Individuals who sustain such a fracture are at a much higher risk of sustaining more fractures, leading to progressive disability, chronic pain, and decreased quality of life. Effective treatments can reduce future fracture risk by up to 50%, yet fewer than 20% of patients suffering from fragility fractures receive such treatments. This is the post-fracture osteoporosis care gap.

Systematic reviews support the Fracture Liaison Service (FLS) as the most effective model to close the care gap and improve patient care outcomes. A FLS has a dedicated coordinator who proactively identifies fracture patients, determines their future fracture risk, and facilitates appropriate osteoporosis treatments. FLS programs assess patients at the point of orthopedic care and seamlessly integrate secondary fracture prevention into the acute fracture experience. A FLS reduces overall healthcare costs by preventing expensive repeat fractures.

FLS-BC: Spreading FLS throughout British Columbia (BC) (*bccop.org/fls*) is a working group of the BC Coalition of Osteoporosis Physicians. Our goal is to spread the FLS model across BC. We work in collaboration with Osteoporosis Canada (*fls.osteoporosis.ca/*) and participate in FLS innovations in BC at a clinical, advocacy, and research level. Peace Arch and Chilliwack Hospitals have established FLS programs with the development of a FLS at Richmond Hospital. Finally, we are partnering with an FLS-Implementation Science Team (*msfhr.org/1/award/breaking-cycle-recurrent-fracture-scaling-secondary-fracture-prevention-program-fraser-health-inform*) to study how best to implement a FLS, in order to decrease repeat fractures and improve the quality of life for our patients.

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RheumTutor: An Invaluable Learning Resource

By Raj Carmona, MBBS, FRCPC

I had the great benefit of doing medical school in a resource-limited setting (University of the West Indies, Trinidad). Our ears became ECHOs, our eyes X-rays, and our fingertips ultrasounds. This deep appreciation for the value of clinical skills followed me into internal medicine and rheumatology training at McMaster. Dr. Sam Pillersdorf showed me my first four-finger joint examination technique, and Dr. Tulio Scocchia's weekly sessions sharpened our musculoskeletal (MSK) examination skills. Dr. Nader Khalidi taught me my first joint injections. It was during fellowship that Dr. Alf Cividino, who was the Medical Foundation 5 Director at the time, invited me to become involved in teaching within the MD program. The entire Division of Rheumatology had become heavily invested in undergraduate training, a strategy that provided early student exposure to rheumatology, and one that continues to pay dividends today. While our faculty were awesome teachers, I recognized the need for reliable audiovisual resources for MSK clinical skills teaching at both undergraduate and postgraduate levels.

With the acting prowess of fellows/residents at the time (Kim Legault, Arthur Lau, Brendan Flowers, and Andrew Duncan), the McMaster MSK Examination video series was created (2011-2012). This includes videos on examination of the hand/wrist, elbow, shoulder, back, hip, knee and ankle/foot. The benefit of these videos was immediately recognized, as students arrived at teaching sessions with a greater degree of preparedness. While these became part of the MD program curriculum, they were also quickly absorbed at various levels of training across a number of programs at McMaster. To provide open online access to the videos beyond McMaster, *RheumTutor.com* was launched in 2012. The response was humbling, with commendations from multiple faculty nationally and internationally, and formal requests from several institutions worldwide to use the videos and accompanying manual as part of their training programs.

Following the examination videos, multiple videos (23 and counting) teaching MSK injection techniques were created. Many of these are step-by-step instructional simulations, but several are actual procedures shot (pun intended) in clinic. To aid understanding, I drew surface anatomy illustrations for both examination and injection videos. The feedback on this artwork suggests that it is highly valued, maybe even legendary (oh humility, wherefore art thou?).

Back in 2012 (life is a blink!), YouTube could not handle larger file sizes. The videos were therefore hosted via Vimeo, with viewership recorded across more than 110 countries. Viewership exponentially increased with the more recent launch of the RheumTutor Channel on YouTube. To date, there have been over 2.9M views on YouTube, with over 14,500 subscribers and overwhelmingly positive feedback.

The hope for RheumTutor is to continue creating and providing high-yield resources. While it does not replace the teaching expertise of faculty and clinicians across the country, the hope is that it will continue to serve as an aid in teaching and learning, with the ultimate aim of improving patient care. I thank all those who have contributed and encouraged this endeavor along the way. Cheers from McMaster!

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UCAN CURE: Transforming Care and Optimizing Outcomes of Children Living with Arthritis

By Rae S. M. Yeung, MD, PhD, FRCPC; Alexander Mosoiu, PMP; and Susa Benseler, MD, PhD, FRCPC

Childhood arthritis — juvenile idiopathic arthritis (JIA) — is the most common chronic inflammatory musculoskeletal disease affecting more than 25,000 children in Canada. Many children with arthritis will continue to suffer from active disease as adults, and some will experience severe disability. One in three children with arthritis requires targeted biologic therapies — selected with limited guidance for the individual child and without a treatment end date. Biologic therapy can dramatically improve disease activity and prevent the progression of inflammatory injury to the joints. Some treatments such as the interleukin-1 inhibitors in children with systemic JIA[1] have been shown to change the biology of the disease and prevent disease chronicity when selected and started within an early window of opportunity.

The key challenge remains the clinical and biological heterogeneity of childhood arthritis.[2] The lack of good clinical and/or biomarker predictors hinders an evidence-based precision health approach. The result is our current trial-and-error approach, where biologics can often only be accessed after failing traditional therapies, resulting in critical delays in accessing effective drugs, exposure to unnecessary risks, and money wasted on ineffective treatments. This imposes not only health risks to the child, but also substantial economic burdens on patients, families, and society.

In 2017, the Canadian pediatric rheumatology community partnered with our Dutch colleagues to establish an international consortium focused on precision health in childhood arthritis. Our research program is rooted in the Canada-led Understanding Childhood Arthritis Network (UCAN) initiative, developed to enable national networks to not only capture clinical data from patients, families, and health care teams but collect biological specimens in a standardized way, supporting national and international collaborations in translational research. UCAN has become an international federation of research networks in childhood arthritis, with a unique focus on translational research. UCAN has built standardized international research platforms to support rapid translation of basic science findings to improve clinical care. Our Canadian and Dutch collaborative research initiatives (UCAN CANDU and UCAN CURE) capitalize on the recent, rapid pace of innovations in genomics medicine, eHealth tools and frameworks, and health economics.

Our research agenda was co-developed with children, families, and national family organizations including Cassie & Friends. Together, we have built an integrated and comprehensive precision medicine program, which is developing and delivering novel genomics-based tools to determine when and how specific biologic agents should be safely and effectively used and when they can be discontinued. We have a multi-pronged approach with a core focusing on biomarker science linked to molecular mechanisms, machine learning, economic modelling, and innovative integrated knowledge translation — achieved through the following thematic research programs:

Genomic Science Program

We are developing genomics-based predictive tools to determine when specific pharmaco-therapeutic agents should be safely and effectively used, thus improving outcomes, limiting risk, and reducing socioeconomic burden. Our innovative rapid detection biomarker-based tests for clinicians will help predict risk for long-term disability, enable rapid selection of targeted biologic therapies and help manage safe discontinuation of drugs.

Integrated Health Economics Analysis

We are developing a novel, updatable model of risks, benefits, and costs associated with genomics-based medicine for childhood arthritis. Together with families and pediatric rheumatologists across both countries, we are developing a standardized measurement framework and key performance indicators to measure clinical and economic outcomes; define preferences for the important risks and benefits affecting biologic-based treatment for children with JIA; and model clinical and health policy decisions.

Integrated Precision Medicine eHealth Platform

Our state-of-the-art eHealth platform has transformed patient engagement, joint decision making, and information sharing for the 21st century, supporting clinical management and encompassing the entire patient experience from eConsent to multi-directional information sharing between researchers, clinicians, policy-makers, patients and families, to the gamification of the research pipeline and early education of the future generation of genomic researchers.

Importantly, each of the three key activities is generating important data collection tools, measurement and value frameworks, and patient and physician preferences. These are leveraged and transferred to support multiple current and future research initiatives across the spectrum of childhood inflammatory and rare diseases. The im-

New Resources for People Living with Arthritis

By Trish Barbato, President and CEO, Arthritis Society Canada

In September we shine the spotlight on arthritis for Arthritis Awareness Month.

We launched our fiery new awareness campaign last September and have been working hard over the past 12 months to turn up the heat through all that we do. We recently awarded more than $1.2M to our inaugural Ignite Innovation Grants, invested in four Arthritis Ideators to help bring their innovations to those who need them most, and launched a new Social Impact program.

And while we've been raising the alarm about the seriousness of arthritis, we've developed new high-impact resources for people living with the disease. This includes our *Your Finances and Arthritis* web pages so that people are armed with important information on topics such as tax credits and benefits.

We've also launched a comprehensive *Pain Management Guide*. Both these resources can be accessed by scanning the respective QR codes to the right.

In addition to regularly adding new resources, we continue to offer our popular monthly Arthritis Talks webinars — which last year reached more than 107,000 people. And we're proud to be supporting a growing number of people through our free Arthritis Line, where people can have their questions answered by phone at 1.800.321.1433 or email at *info@arthritis.ca*.

Thank you for sharing our resources with your patients and continuing to shine a spotlight on arthritis every day.

Arthritis Pain Management Guide

Your Finances and Arthritis

UCAN CURE: Transforming Care and Optimizing Outcomes of Children Living with Arthritis

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pact of the added value has been multiplied in the current COVID pandemic, which has provided unique opportunities for our technologies and platforms to support virtual care in our rapidly changing healthcare system.

Our national funders, including the Canadian Institutes of Health Research (CIHR) and Genome Canada, together with the Stop Childhood Arthritis Initiative at The Arthritis Society, and Dutch partners in ZonMw and RheumaNetherlands have been key enablers of our work. The engagement and commitment of all pediatric rheumatology care providers across Canada and the Netherlands to the UCAN mission of real-life integration of innovative precision medicine strategies into care provision are continuing to transform the care of children with arthritis in Canada and around the world.

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EULAR 2022 Report

By Philip A. Baer, MDCM, FRCPC, FACR

Another pandemic year, another virtual European Alliance of Associations for Rheumatology (EULAR) meeting for me. This time, the meeting was hybrid in nature, with live sessions in Copenhagen. I thought I was fortunate to have an abstract accepted on the results of the ADAGIO study (POS0288) of patterns of methotrexate (MTX) de-escalation in Canadian patients initiating an advanced therapy for rheumatoid arthritis (RA). When this poster was then selected for a poster tour, that seemed even better. I recorded a 5-minute overview of the study and uploaded it to the EULAR portal without any difficulty — well, it took three takes to precisely squeeze all I wanted to say into the time allotted, but that was not unexpected. Finding out that I was needed for 3 minutes of live Q&A at 3:45 a.m. Toronto time was the shock. Fortunately, that was on the Saturday of the meeting, so I could catch up on lost sleep later that day. Having attended virtually, at least there was no jet lag to battle. The session was quite interesting, including another abstract on MTX discontinuation in similar patients (POS0286), and I was able to handle the questions that were lobbed my way.

This was the 75th anniversary of the first EULAR meeting, also held in Copenhagen, which was celebrated at the Opening Ceremony as well as throughout the conference, with an excellent session highlighting EULAR's past, present, and future. The conference platform had exceptional audio and video quality, both for live and pre-recorded sessions. Some sessions were not immediately available to virtual attendees, but the platform remained available until the end of July for review.

Parallel to the conference, there was the usual intense activity on Twitter, as well as daily updates from the RheumNow team led by Jack Cush. I especially enjoyed the 3 half-hour daily summary briefings moderated by Janet Pope and Hughes Allard-Chamard for Canadian rheumatologists. Janet had my favourite Tweet: "I was going to go to the session on fatigue in rheumatic diseases, but I was too tired!"

New EULAR guidelines on RA and axial spondyloarthritis (AxSpA) management were unveiled. The AxSpA guideline, in conjunction with the Assessment in Ankylosing Spondylitis (ASAS) working group, positioned the Ankylosing Spondylitis Disease Activity Score (ASDAS) as the primary measure of daily activity, approved of Janus Kinase (JAK) inhibitors as first-line therapy, and gave preference to interleukin-17 (IL-17) inhibitors in those with skin involvement, and to monoclonal antibodies to tumour necrosis factor (TNF) in those with uveitis.

The RA guideline panel included Canadian input from Janet Pope. The prior EULAR recommendation to use short-term glucocorticoids in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) was revisited, as it was not in accord with current American College of Rheumatology (ACR) guidelines. The new EULAR language says glucocorticoids are just "to be considered" in this scenario and emphasized they should be discontinued as rapidly as possible. The positioning of JAK inhibitors, previously listed as on par with biologics, was modifed in view of the ORAL-Surveillance trial. Now, JAK inhibitors "may be considered" as first-line advanced therapies, but pertinent risk factors for major adverse cardiovascular events (MACE), venous thromboembolic events (VTE) and malignancy must be taken into account. Data from the ongoing baricitinib safety studies, RA-BRIDGE and RA-BRANCH, may affect this advice once they are released.

An interesting presentation on the impact of guidelines by Professor L. Carmona confirmed that adherence to guidelines improved outcomes but showed that such adherence was low, even at Rheumatology Centres of Excellence.

Gender issues in rheumatic disease were prominently featured. The need for more studies was emphasized, as well as the availability of safe spaces and gender-specific support. I learned a new acronym, DEIB, referring to Diversity, Equity, Inclusion and Belonging, all of which are important considerations in patient care. OP0006 was a study with a gender lens, looking at exposure to silica as a risk factor for RA in women, and finding cleaning activities, dusty clothes laundering, and talcum powder handling as the main sources of exposure.

Looking at the abstracts more broadly, 619 covered all aspects of RA, 209 related to COVID-19, 112 to orphan diseases, with 74 on osteoarthritis (OA), 51 on osteoporosis, and 178 on psoriatic arthritis (PsA) treatment and clinical aspects. Futuristic technologies such as Machine Learning, Neural Networks, and Artificial Intelligence were commonly referenced. Long COVID and difficult-to-treat RA were topics of interest to me as well.

Other papers which caught my eye included the frequency of subclinical giant cell arteritis in PMR (OP0184), the NORDSTAR study of different treatment strategies in early RA (OP0058), and 2 studies on holding MTX after COVID-19 immunization (POS0259 and LB0003). I also noted POS0242 which showed that antimalarials increase drug retention in patients on biologics and JAK inhibitors.

Easy-to-remember trial names were PAISLEY (LB0004), a Phase 2 trial of deucravacitinib in systemic lupus erythematosus (SLE), and GLORIA, a pragmatic trial of low-dose prednisolone in RA patients over age 65 years.

Overall, this was another excellent EULAR conference in all aspects. Next year, the meeting will be held in Milan from May 31 to June 3. Will virtual attendance still be possible? No, according to EULAR's current plan.

Philip A. Baer, MDCM, FRCPC, FACR
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Poetry Inspired by the Injectable Steroid Shortage

By Philip A. Baer, MDCM, FRCPC, FACR; Rusty Goodman, MDCM, FRCPC; and Jane Purvis, MD, FRCPC

These are some funny, short poems, written in light of a recent shortage of Depo-Medrol® announced in the spring of 2022, to illustrate how much we were missing a trusted treatment for the local management of joint pain, which fortunately has now become available in the market again.

31 Vials of Depo

31 vials of Depo on the shelf,
31 vials of Depo.
If 1 of those vials should happen to fall,
Cancel that injection, make that call.

30 vials of Depo in the cupboard,
30 vials of Depo.
If 1 of those vials should happen to break,
A steroid holiday patients will take.

29 vials of Depo on the tray,
29 vials of Depo.
If 1 of those vials should happen to crack,
No needles today, cut me some slack.

28 vials of Depo in my hands,
28 vials of Depo.
If one of those vials should happen to spoil,
Take some time off, no need to toil.

27 vials of Depo in room one,
27 vials of Depo.
If one of those vials should be lost,
None on black market, regardless of cost.

The Night Before Clinic

Twas the night before clinic
And all through the pharms,
Not a Depo was present
First do no harms.

On Shoppers, On Rexall,
On Heritage and Ben's,
If the white stuff is missing
Empty syringes won't mend.

No Covid to blame,
For this tragic affair.
At a gaggle of swollen joints,
I despairingly stare.

I never did dream
That this day I would see.
I guess I'll go ortho,
And inject PRPs.

Roses are Red

Roses are red,
Violets are blue,
No Depo available,
No shots can I do.

Daffodils are yellow,
Daisies are white,
Without Depo-Medrol,
Office days are a fright.

Lavender's purple,
Spring grass is green,
This shortage of steroids,
Is the most annoying I have seen.

Depo at Hand

Do you need Depo at hand?

I do need it rheum, I am.
I do need, Depo in hand.

I would need it for a knee.
I would need it MCP.
I'd inject it pretty quick.
In a bursa I am slick.

Do I need it for a joint?
If no Depo, what's the point?

I do need it for RA.
I can use it in OA.
I can use it for the gout.
I'll inject it all about.

I do need my Depo quick
Kenalog won't do the trick.

Still's Got That Fever: Adult-onset Still's Disease in Fever of Unknown Origin

By Ming K. Li, BHSc; Calandra Li, MSc; Anas Makhzoum, MD; and Rohan Philip, MD

Abstract: *Still's Got That Fever* is a case report of a patient in her 60s, who presented with a 2-week history of fevers, diffuse arthralgias, and salmon-coloured rash. Given the rarity of this disease, it was almost 1 week into her admission before the diagnosis of adult-onset Still's Disease (AOSD) was made as the cause of her fever of unknown origin. This case highlights the Yamaguchi criteria, which are still the standard in making the diagnosis, which is a clinical one. Our patient underwent extensive investigations to rule out other infectious, malignant, and auto-immune causes. Furthermore, a life-threatening complication of AOSD that clinicians should be aware of is macrophage activation syndrome (MAS). The gold standard investigation to rule out MAS is bone marrow biopsy, which would show hemophagocytosis. Our patient did not develop MAS, was treated with steroids, and showed an immediate clinical response. We highlight other treatment options for AOSD based on disease severity, including methotrexate and biologics.

Key Points:

- Adult-onset Still's Disease (AOSD) is a rare inflammatory disease that is diagnosed clinically, with symptoms including high fevers, arthralgias, and a maculopapular rash.
- Investigations should include an infectious and inflammatory work-up, which typically shows an elevated ESR,[a] CRP,[b] and ferritin, but negative blood cultures, ANA,[c] and RF.[d]
- An important life-threatening complication rarely associated with AOSD is macrophage activation syndrome (MAS). It also presents with high fevers, high ferritin, and abnormal liver enzymes, but can progress to profound cytopenias and liver dysfunction. A bone marrow biopsy is the gold standard to rule out MAS.
- Steroids are the mainstay of treatment in patients with moderate disease (usually 0.5-1 mg/kg/day); however, pulse steroids, methotrexate, and biologic therapies may be considered for more severe-to-resistant disease.

Case Presentation:

A 64-year-old otherwise-healthy female presented with a 2-week history of recurrent fevers (max temperature 40.0°C), chills, bilateral otalgia, sore throat, generalized rash, migratory arthralgias and myalgias, and non-bloody diarrhea. Her exam on admission was pertinent for fever (38.8°C), 0.5 cm tender, mobile anterior cervical lymph nodes, and patches of pruritic rashes over the anterior trunk, and both thighs and arms. Over time, her ear pains and sore throat resolved, but she continued to have daily self-resolving fevers, arthralgias, and developed a salmon-coloured rash.

Her investigations revealed elevated ferritin, ESR, and CRP on day 5 of admission, with imaging evidence of inflammatory arthritis of the wrists, elbows, and knees. Her infectious work-up, including pan-cultures and CT,[e] revealed no source of infection, and her rheumatologic panel (ANA, ENA,[f] ANCAs,[g] rheumatoid factor, anti-CCP,[h] complement studies) were all normal. A bone marrow biopsy was normal. Clinically, she was diagnosed with Still's Disease, and was started on prednisone, which resulted in improvement of her symptoms and inflammatory markers. She was discharged in stable condition on prednisone with outpatient rheumatology follow-up. At her 8-week follow-up, her symptoms remained well-controlled and methotrexate was added as a steroid-sparing agent.

Clinical Manifestations

Patients with adult-onset Still's Disease (AOSD) present with a constellation of symptoms, the most common being severe arthralgias/arthritis, fevers, and subacute rashes.[1] It is a rare disease with an incidence of 1/625,000.[2] As seen with our patient, in about 70% of cases, patients present with a prodromal sore throat prior to manifestation of AOSD symptoms.[3] There is a bimodal age distribution (peaks between 15-25 and 36-46), although our patient was asymptomatic until her 60s, which is a late presentation compared to typical ages of onset.[1]

Fevers in AOSD are usually quotidian, >39˚C, with self-resolution within 2-4 hours.[4] A minority of patients (<20%) have double-quotidian fevers with a second fever spike during the day.[4] Patients tend to feel quite unwell during these febrile spikes. Given these fevers, many patients undergo a work-up for infectious causes which come back negative, and do not respond to antibiotics.

The joint involvement in AOSD may initially start with one or few joints, then most commonly progresses to become polyarticular, affecting both small and large joints.[5] Arthrocentesis usually reveals inflammatory arthritis. Our patient presented with bilateral knee, wrist, and elbow arthralgias. An arthrocentesis was not pursued given her improvement with steroids and our level of diagnostic certainty.

Rash in AOSD is very common, characteristically described as a salmon-coloured, non-pruritic rash usually present on the trunk, arms, or legs.[5] In some patients, this rash is only present during fevers.[4] Our patient indeed had a salmon-coloured rash, but it was quite pruritic, requiring potent topical lotions, and persisting during afebrile periods.

Diagnosis

AOSD is primarily a clinical diagnosis, and a broad differential should always be considered, given the non-specific constellation of symptoms. There is no investigation that confirms AOSD, but the clinical presentation and laboratory findings should be used in conjunction to make the diagnosis. It is usually a diagnosis of exclusion. The Yamaguchi criteria, first described in 1992, have a sensitivity of 96.2% and specificity of 92.1%.[2] A diagnosis of AOSD requires ≥5 criteria (≥2 major criteria) and no exclusion criteria. The criteria are shown in Table 1, with major criteria including fever ≥1 week, arthralgias ≥2 weeks, typical non-pruritic rash, and leukocytosis ≥10,000/mm^3.[2] Our patient met 3 major criteria and 3 minor criteria.

When suspecting AOSD, important investigations include CBC,[i] liver enzymes, ESR, CRP, ferritin, ANA, and RF.[4] An infectious work-up including pan-cultures should be conducted to rule out infectious diseases. As evidenced by our patient, patients commonly will have elevated leukocyte count, ferritin, ESR, and C-RP, but negative ANA and RF. There was no clinical evidence of any other rheumatological disease. Finally, her pan-CT showed no evidence of malignancy. Thus, she did not meet any of the exclusion criteria.

AOSD is typically not a life-threatening disease; however, a rare life-threatening complication of which physicians should be cognizant is macrophage activation syndrome (MAS). Such patients will have high fevers, elevated ferritin, and abnormal liver enzymes, and can deteriorate quickly. A bone marrow biopsy would show hemophagocytosis, and should be strongly considered, to rule out this life-threatening complication.[4] Our patient's biopsy was normal.

Treatment

Given that AOSD is quite rare, treatment is extrapolated from other autoimmune conditions such as rheumatoid arthritis and SLE. AOSD management depends on disease severity, with steroids being the mainstay of treatment.[6]

As there is no well-validated prognostication tool available for AOSD, treatment goals are targeted to control inflammatory signs, symptoms, and laboratory indices.[4] Mild-to-moderate disease, defined by non-disabling symptoms, may be initially treated with NSAIDs[j] and glucocorticoids. Depending on severity and individual patient assessment, initial doses of glucocorticoids, like prednisone, can range from 0.5 mg/kg/day to 1 mg/kg/day.

Moderate-to-severe disease, characterized by persistent debilitating symptoms, may require addition of a biologic agent, like anakinra, or other interleukin-1 inhibitors. Anakinra has shown efficacy as a monotherapy in early disease and in prevention of chronic arthritis and inflammation

Table 1:
Yamaguchi Criteria[2]

Major Criteria	Minor Criteria	Exclusion Criteria
Fever (39°C) lasting ≥ 1 week	Sore Throat	Infection
Arthralgia or arthritis lasting ≥ 2 weeks	Lymphadenopathy	Malignancy
Typical non-pruritic salmon-coloured rash	Splenomegaly	Other rheumatic disease (vasculitis)
Leukocytosis ≥10,000/mm^3 with 80% granulocytes	Abnormal liver enzymes	
	Negative ANA and RF	

later on.[7] At this stage, combination therapy with glucocorticoids may be needed for symptom control. Furthermore, DMARDs,[k] such as methotrexate, may be initiated after 2 weeks of symptom non-resolution, or as steroid-tapering adjuncts long-term. Methotrexate can be used for 3-6 months after discontinuing steroids.

Conclusion

Given its rarity and non-specific symptoms, AOSD is a systemic inflammatory disease that can be challenging to diagnose and treat. Its characteristic spiking fevers, arthritis, rash, and high ferritinemia can elude clinicians. This report highlights the importance of recognizing AOSD to initiate early therapy, and the room for additional research to optimize treatment options.

Glossary:

a. ESR: erythrocyte sedimentation rate
b. CRP: C-reactive protein
c. ANA: anti-nuclear antibodies
d. RF: rheumatoid factor
e. CT: computed tomography
f. ENA: extractable nuclear antigen
g. ANCA: antineutrophil cytoplasmic antibodies
h. anti-CCP: Anti–cyclic citrullinated peptide
i. CBC: complete blood count
j. NSAIDs: Non-steroidal anti-inflammatory drugs
k. DMARDs: Disease-modifying antirheumatic drugs

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Acknowledgements: The authors would like to acknowledge Dr. Melissa Sergi, Dr. Gregory Gaisano, and Dr. Vlad Dragan for their roles as part of the medical care team. We would like to thank our patient for providing consent for this case report.

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Appendix

Table 2:

Bloodwork Trends, by Day of Admission

	Day 3	Day 6*	Day 8	Day 9	Day 12	Day 13
Hb (g/L)	113	120	103	–	120	–
WBC (x 10^9/L)	4.5	5.4	9.4	–	11.3	–
Granulocyte %	80%	83%	92%	–	81%	–
Platelets (x 10^9/L)	242	183	186	–	371	–
ESR (mm/hour)	45	–	63	59	–	–
CRP (mg/L)	30.8	67.1	20	21.1	26	27.4
Ferritin (µg/mL)	6405	>16500	11323	6056	3102	2977

*Prednisone started on day 6 of admission

Patient Perspective: Cristina Montoya

At 22 years old, while living in my hometown of MedellÍn, Colombia, I was diagnosed with rheumatoid arthritis (RA) and Sjögren's Syndrome. It was my last year in the Nutrition and Dietetics undergraduate program. My RA was so aggressive that even lifting a piece of paper or typing became a painful chore. Within a year of diagnosis, I started to develop joint deformities, because the era of biologics was in its early stages and inaccessible to me for financial reasons. I was terrified of not being able to graduate as a nutritionist and dietitian with my peers. Thanks to a load of corticosteroids, I was able to reach the finish line.

I came to Canada in 2007 and thought the best way to adapt to a new country was to hide my pain and move on. There were no resources for new immigrants living with autoimmune diseases. I pushed through my first Canadian winter, worked tirelessly to validate my degree as a registered dietitian, and focused my efforts on helping seniors in long-term care homes. I wanted to feel normal without thinking about my disease. In 2015, I joined the Sjögren's Society of Canada and have continued to volunteer for this organization in some capacity since my first meeting. Unfortunately, Sjögren's has no clear treatment path, leaving patients feeling isolated and dismissed by many health care providers. In my dietetic practice and volunteer work with support groups across Canada, nine out of ten patients with Sjögren's suffer from xerostomia, dysphagia, and digestive issues affecting their quality of life.

Now, at 40, I am a proud mama of a whimsical 3-year-old boy and was honoured to present at this year's CRA Annual Scientific Meeting with the workshop "Beyond Dry Eyes and Dry Mouth: Managing Digestive Disorders in Patients with Sjögren's Syndrome." I was pleasantly surprised when my own rheumatologist attended the workshop and thanked me for sharing my personal and professional experience with Sjögren's.

Despite COVID-19 and another RA treatment failure, I managed to run a small 5-week group program for women living with Sjögren's called "Surviving Summer with Sjögren's." The program's roadmap included starting an anti-inflammatory way of eating, building balanced meals and snacks, implementing safe swallowing strategies, creating emergency food kits, self-care routines, and managing common digestive issues. The participants were also given access to an intuitive meal planner to help them make their own meal choices.

After 20 years of living with inflammatory rheumatic diseases, I am reminded that living with chronic conditions is a marathon, not a sprint. We must focus on what we can control. Self-advocacy, robust support systems, and collaboration with our health care providers are our most powerful tools to thrive with RA and Sjögren's. There are hardships, sad moments, and times when you feel like giving up; but then I look at all the meaningful connections I've made despite RA and Sjögren's — and even because of them.

Cristina Montoya, RD HCP
Registered Dietitian
Holistic Cannabis Practitioner
AHPA member
Arthritis Dietitian
www.arthritisdietitian.com
Oshawa, Ontario

The CRA's 2022 Distinguished Teacher-Educator: Dr. Stephen Aaron

What do you believe are the qualities of a good educator?

A good educator has the following qualities:

1. Listens to the student and decides what they may need to be better, and is a good coach.
2. Has a good grasp of his/her field, but at a conscious level; has a conceptual framework.
3. Can empathize with the student; knows when they are afraid, frustrated, tired.

From where do you think your passion for medical education stemmed?

My passion for medical education came from having good teachers. Over the years, there has been a change in emphasis from a focus on the teacher, to a focus on the learner. You hear less about "I told them that," to documenting that "they have looked after that." From syllabi to entrustable professional activities (EPAs).

What are some of the highlights and challenges you have experienced thus far in your career?

Highlights include leading the change from a traditional curriculum at the University of Alberta Medical School to a problem-based learning (PBL) curriculum; creating a clinical skills program for medical students; and being involved in building a new medical school and rheumatology program in Nepal.

What is your proudest accomplishment to date?

Getting a phone call from a student or resident who confidently diagnoses or treats a patient using physical exam tools or principles they learned from me.

Can you recall a teacher in your own past who inspired you and directed your own course into education?

Dr. A. M. Edwards (Buzz), who taught me during my first year of clinical clerkship; He cared about students and patients. He was immensely curious, and he was always having a wonderful time doing this.

More recently, you have been active in advancing arthritis care in Nepal and in First Nations communities. In Nepal you helped initiate the first training program in rheumatology. Can you tell us more about your work in Nepal as well as First Nations communities here in Canada?

In Nepal, they had only two rheumatologists, working at the same public hospital; we put together an entire resident training framework based upon the Royal College standards, recruited two Internal Medicine grads, and they have since graduated.

The clinics in the First Nations communities have been less sustainable; the problems there cannot be solved simply by moving the standard health care system to the reserve.

It is noted time and again that there is a disparity in access to quality healthcare for First Nations groups. Why does this gap in access continue to exist and what steps must be taken (by government and leaders) to eliminate this gap?

I'm not competent to give a good answer; the literature on health outcomes says that wealthy, well-educated patients do better no matter what disease you talk about. I suspect that unless you address education, poverty, and social inequity, nothing we do within the health care system itself will make a marked difference.

As a respected teacher-educator, what would your advice be to a prospective rheumatologist?

Make sure that you explore the breadth of rheumatology before you subspecialize. I see that many centres have very highly specialized clinics amongst which the rheumatology residents rotate; there is something to be said for being flexible enough to move on short notice from rheumatoid arthritis (RA) to systemic lupus erythematosus (SLE) to mechanical joint or tendon disease.

If you weren't a rheumatologist/teacher-educator, what other career path might you have chosen?
I might have been an architect or a mathematician.

If you had an extra hour in the day, how would you spend it?
I would spend more time in the garden.

You are marooned on a desert island, what book would you like to have on hand with you?
If Wikipedia were a book, I'd take that.

Stephen Aaron, MD, FRCPC
Professor,
Department of Medicine
Division of Rheumatology
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University of Alberta
Edmonton, Alberta

WELCOME TO THE RHEUM

Welcome to the following new CRA members:

Razan Al Yaarubi, Toronto, ON
Hafsah Al Azem, Calgary, AB
Fatema Alkhamees, Vancouver, BC
Kawthar Abduldaem Alsulami, Ottawa, ON
Shamma Alzaabi, Vancouver, BC
Jason An, Toronto, ON
Keltie Anderson, Saskatoon, SK
Megan Barber, Calgary, AB
Karen Beattie, Dundas, ON
Michael Buchanan, Prince George, BC
Glynis Byrne, Kingston, ON
Shane Cameron, Winnipeg, MB
Michael Catarino, Montreal, QC
Matthew Chan, Saskatoon, SK
Audrey-Anne Couture, Montreal, QC
Mojtaba Dabaghjamanesh, London, ON
Molly Dushnicky, Toronto, ON
Evelyne Gendron, Quebec, QC
Kaien Gu, Winnipeg, MB
Fares Kalache, Montreal, QC
Wassim Karkache, Ottawa, ON
Alexandra Kobza, Calgary, AB
John Krakovsky, London, ON
Andrew Kwan, Toronto, ON
Timothy Kwok, Markham, ON
Malcolm MacKenzie, Toronto, ON
Greta Mastrangelo, Toronto, ON
Haonan Mi, Thornhill, ON
Dalal Mohammad, Vancouver, BC
Anton Moshynskyy, Saskatoon, SK
Oscar Mwizerwa, Toronto, ON
Tripti P. Papneja, Brampton, ON
Gilda Parastandehchehr, Montreal, QC
Mary Purcell, Halifax, NS
Patricia Remalante Rayco, Toronto, ON
Micol Romano, London, ON
Cassandra Schulz, St. Mary's, ON
Teresa Semalulu, Hamilton, ON
Shreyasi Sharma, Saskatoon, SK
Hao Shen, Montreal, QC
Cheuk Hei (Keith) Tam, Richmond Hill, ON
Milica Tanic, Toronto, ON
Karine Toupin April, Ottawa, ON
Stefanie Wade, Vancouver, BC
Yanzhu Xu, Burnaby, BC
Alan Zhou, Scarborough, ON

Dr. Elizabeth Hazel

McGill Faculty Honour List

Dr. Elizabeth Hazel was nominated by the Department of Medicine for the prestigious McGill Faculty Honour List for Educational Excellence. The goal of this award is to recognize outstanding contributions to education in the Faculty of Medicine and Health Sciences, in the areas of teaching, educational leadership and innovation, faculty development, and research and scholarly activity.

She was honoured for her work in restructuring rheumatology resident curriculae and in advancing rheumatology education at the local and national levels, including her work in building a national rheumatology resident curriculum that meets the needs of today's learners.

Dr. Susan Humphrey-Murto

RCPSC Duncan Graham Award

Dr. Susan Humphrey-Murto received the Royal College of Physicians and Surgeons of Canada (RCPSC) Duncan Graham Award for recognition of outstanding contribution to medical education. Dr. Humphrey-Murto has engaged in and supported educational research throughout her career. Past positions include Deputy Registrar for the Medical Council of Canada and Co-Chair for the Education Research and Development Committee (RCPSC). She currently holds a Tier 2 Research Chair for medical education research from the University of Ottawa. She has published in the areas of performance-based assessment, rater bias, learner education handover, and the use of consensus group methods such as the Delphi in research. Through her roles as the Medical Education Fellowship Director and research supervisor, she has mentored many young scholars.

Dr. Sahil Koppikar

WCH Teacher/Educator Education Award

Dr. Sahil Koppikar received the Women's College Hospital (WCH) Teacher/Educator Education Award, which recognizes a healthcare professional who has demonstrated exceptional commitment to clinical teaching or to clinical supervision of students/learners at Women's College Hospital and the University of Toronto.

Dr. Koppikar is a Clinician-Teacher at Women's College Hospital, University of Toronto. He is also the Director of the Timmins Arthritis Program and Chair of the Northern Ontario Committee of the Ontario Rheumatology Association.

Dr. Alan Rosenberg

Saskatchewan Order of Merit

Dr. Alan Rosenberg is a recipient of the Saskatchewan Order of Merit, the province's highest honour. The award recognizes Dr. Rosenberg's contributions to pediatric and pediatric rheumatology care, research, and teaching. Dr. Rosenberg, a pediatric rheumatologist, is a University of Saskatchewan professor and Director of the Pediatric Rheumatic Disease Research Laboratory. He is co-founder of the Children's Health Foundation of Saskatchewan, which paved the way for the realization of Saskatchewan's Jim Pattison Children's Hospital. Recognizing the value of collaboration, he facilitates partnerships to improve child health, advance research, and inspire the next generation of care providers and scientists.

Dr. Dharini Mahendira

William Goldie Prize for Teaching

Congratulations to Dr. Dharini Mahendira on receiving the William Goldie Prize for Teaching. This prize is awarded to a member of the Department of Medicine at the University of Toronto who has made a contribution of notable merit to the training of physicians through teaching. The Goldie Prize is considered one of the highest teaching awards for early-to-mid-career faculty at the University of Toronto.

Dr. Mahendira is a Clinician Teacher at St. Michael's Hospital, University of Toronto, who has been recognized both locally and nationally for her excellence in teaching and education. Her contributions to several CRA educational initiatives include co-leading the post-graduate medical education sub-committee and the National Rheumatology Residents Curriculum.

AWARDS, APPOINTMENTS, AND ACCOLADES

The *CRAJ* would like to recognize the contributions of its readers to the medical field and their local communities. To have any such awards, appointments, or accolades announced in an upcoming issue, please send recipient names, pertinent details, and a brief account of these honours to *JyotiP@sta.ca*. Picture submissions are greatly encouraged.

Survey Results: CRA Choosing Wisely — Ordering RF & ACPA Tests and Monitoring DMARDs

This issue's Joint Count survey, in collaboration with the CRA Choosing Wisely submcommittee, aimed to better understand when rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) tests are ordered, and how disease-modifying anti-rheumatic drugs (DMARDs) are monitored. The CRA Choosing Wisely subcommittee (at the time of this writing) plans to publish new statements regarding the ordering of RF and ACPA tests, as well as the monitoring of DMARDs this fall (these statements are shown in the box below). The survey was sent to members of the CRA (603 members), and a total of 68 responses were received.

The first question of the survey queried members about how often they monitored lab work in a stable patient with inflammatory arthritis on non-biologic disease-modifying anti-rheumatic drug therapy. Most (approximately 70%) indicated every three months, while 18% said every 2 months; 9% said less often than every 3 months; and only 3% said every month. One respondent commented that the question was too vague, and that patients' comorbidities would also need to be taken into account.

The next question asked members about what tests they monitor for patients on methotrexate therapy. Responses are shown in Chart 1. A complete blood count (CBC) and alanine aminotransferase (ALT) were almost universal. Overall, there seems to be a lot of variability in what tests are ordered and how often. It should be noted that some provinces, such as Ontario, limit the ordering of aspartate aminotransferase (AST) to GI specialists. As well, with the current health human resources crisis affecting laboratory medicine, physicians have been requested to review their routine lab ordering protocols, especially for non-specific tests such as ESR.

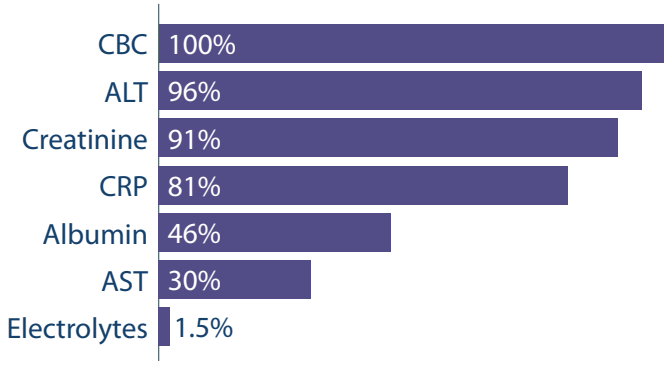
For the next question, only 26% of survey respondents were aware that the symptoms located in the metatarsophalangeal (MTP) joints are not part of the EULAR definition of clinically suspicious arthralgia (CSA) at risk of developing rheumatoid arthritis (RA). The EULAR definition of CSA includes symptoms of new joint pain, pain in metacarpophalangeal (MCP) joints, morning stiffness >60 minutes, most severe symptoms in the morning, presence of 1st-degree relative with RA, difficulty making a fist and positive MCP squeeze test.

Regarding the last question, the results reflected that only about a quarter of respondents were aware that among individuals with clinically significant arthralgia with positive RF and ACPA, 30-60% will never develop RA (for more information visit *rheum.ca/resources/choosing-wisely)*.

The CRA would love to hear your reflections. For any feedback on the survey, please reach out to Mona Bosinceanu at *mbosinceanu@rheum.ca.* For further information, visit *choosingwiselycanada.org* or *rheum.ca/resources/choosing-wsely/.*

The CRA Choosing Wisely Subcommittee would like to thank the CW working group: Maryam Obaidalla (Ontario); Bindu Nair (Saskatchewan); Nicole Beckett (Nova Scotia) Nicolas Richard (Quebec); Zachary Shaff (Nova Scotia) Nadia Lucia (Alberta); and Shirley Lake (Ontario)

Chart 1: In a patient on methotrexate therapy, the lab tests that I monitor on a regular basis include (choose all that apply):



CBC, complete blood count; ALT, alanine aminotransferase; CRP, C-reactive protein; AST, aspartate aminotransferase

Two New Choosing Wisely Statements:

RF & ACPA Tests:

Do not order Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibody (ACPA) tests unless patients have clinically suspicious arthralgia (CSA*) or arthritis on exam.

DMARD Monitoring:

Do not order labs for drug toxicity monitoring (i.e., CBC, liver enzymes, creatinine) more often than every 8-12 weeks for patients on a stable dose of non-biologic disease modifying anti-rheumatic drugs (DMARDs), in patients without comorbidities or (baseline) lab abnormalities.

*EULAR defined characteristics defining Clinically Suspect Arthralgia at risk for RA

NS

Update from Nova Scotia

By Volodko Bakowsky, MD, FRCPC

Boom! That is the sound of the seismic changes that have recently unfolded in rheumatology in Nova Scotia.

After a long and distinguished career, Dr. John Hanly has retired from clinical care as of July 1st, 2022. He and his wife Noreen plan on splitting their time between Halifax and Ireland.

More people than ever are moving to our province, further straining our bulging wait lists. If there are any rheumatologists that would enjoy smelling the sea air and stretching their housing dollars here in Nova Scotia, please let me know.

Dr. John Hanly

Dr. Alex Legge

The daunting task of attempting to fill his shoes falls on the indomitable Dr. Alex Legge, who has joined the division in a major research position after completing a year-long research fellowship at the University of British Columbia (UBC) under the supervision of Dr. Diane Lacaille.

Halifax rheumatologists have created CRA Executive "bookends" as Dr. Evelyn Sutton is now Past-President and Dr. Trudy Taylor is newly established as Vice-President.

Dr. Julie Mongeau completed her residency in rheumatology one year ago and has set up a practice in Truro, Nova Scotia. She is currently expecting her first child.

Dr. Janet Roberts had a baby boy, Henry, and is finishing up her maternity leave while starting an MPH program at Harvard. She will return to clinical care at the end of the summer.

In association with the QEII Health Sciences Foundation, a fully funded 4-million-dollar endowment has been created for a Research Chair in Rheumatology. Recruitment into the position will be starting soon.

Dr. Janet Roberts and her son Henry.

Volodko Bakowsky, MD, FRCPC
Interim Division Head/Chief,
Associate Professor,
Division of Rheumatology, Department of Medicine
Dalhousie University, Halifax, Nova Scotia

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- Severe infections such as sepsis, tuberculosis and opportunistic infections
- Moderate or severe (NYHA class III/IV) congestive heart failure

MOST SERIOUS WARNINGS AND PRECAUTIONS:

Infections:

- Serious infections leading to hospitalization or death, including sepsis, tuberculosis (TB), invasive fungal, and other opportunistic infections, have been observed with the use of TNF antagonists including golimumab. Administration of SIMPONI® should be discontinued if a patient develops a serious infection or sepsis. Treatment with SIMPONI® should not be initiated in patients with active infections including chronic or localized infections.
- Physicians should exercise caution when considering the use of SIMPONI® in patients with a history of recurring or latent infections, including TB, or with underlying conditions, which may predispose patients to infections, who have resided in regions where TB and invasive fungal infections such as histoplasmosis, coccidioidomycosis, or blastomycosis are endemic.
- Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation) has been observed in patients receiving TNF-blocking agents, including golimumab. Tuberculosis may be due to reactivation of latent tuberculosis infection or to new infection.
- Before starting treatment with SIMPONI®, all patients should be evaluated for both active and latent tuberculosis.
- If latent tuberculosis is diagnosed, treatment for latent tuberculosis should be started with anti-tuberculosis therapy before initiation of SIMPONI®.
- Physicians should monitor patients receiving SIMPONI® for signs and symptoms of active tuberculosis, including patients who tested negative for latent tuberculosis infection.

Malignancy:

- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which golimumab is a member.

OTHER RELEVANT WARNINGS AND PRECAUTIONS:

- Risk of hepatitis B virus reactivation
- Risk of malignancies

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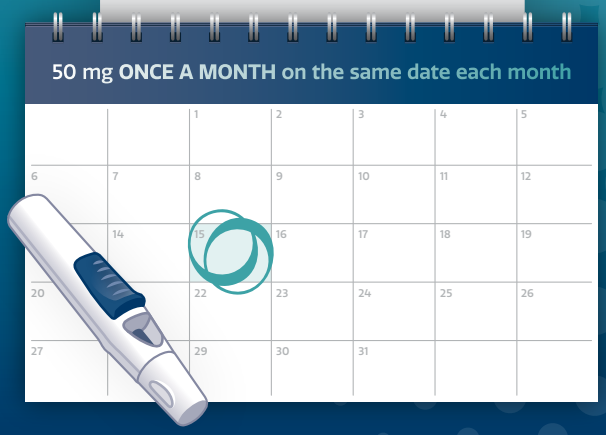

- Risk of worsening or new onset of congestive heart failure
- Risk of infection with concurrent use of anakinra, abatacept or other biologics; concurrent use is not recommended
- Risk of hematologic reactions
- Risk of hypersensitivity reactions
- Risk of latex sensitivity
- Risk of clinical infections, including disseminated infections, with live vaccines and therapeutic infectious agents; concurrent use is not recommended
- Risk of autoimmunity
- May cause immunosuppression; may affect host defences against infections and malignancies
- Potential for medication errors
- Risk of new onset or exacerbation of CNS demyelinating disorders
- Risk of infection in peri-operative patients
- Adequate contraception must be used to prevent pregnancy in women of childbearing potential for at least 6 months after last treatment
- Not to breastfeed during and for at least 6 months after treatment with SIMPONI®
- Use with caution in patients with impaired hepatic function
- May have a minor influence on the ability to drive due to dizziness following administration

FOR MORE INFORMATION:
Please consult the product monograph at www.janssen.com/canada/products for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The product monograph is also available by calling 1-800-387-8781.

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* across combined indications.

PsA = psoriatic arthritis | AS = ankylosing spondylitis | RA = rheumatoid arthritis | nr-Ax SpA = non-radiographic axial spondyloarthritis | MTX = methotrexate | CRP = C-reactive protein | MRI = magnetic resonance imaging | NSAIDS = nonsteroidal anti-inflammatory drugs

Reference:
1. SIMPONI® Product Monograph. Janssen Inc. June 20, 2019.

Janssen Inc. | 19 Green Belt Drive | Toronto, ON | M3C 1L9
www.janssen.com/canada | CP-203649E

RHEUMATOID ARTHRITIS

PrXELJANZ®/PrXELJANZ® XR, in combination with methotrexate (MTX), is indicated for reducing the signs and symptoms of rheumatoid arthritis (RA) in adult patients with moderately to severely active RA who have had an inadequate response to MTX and to one or more disease-modifying anti-rheumatic drugs (DMARDs). In cases of intolerance to MTX and other DMARDs, physicians may consider the use of XELJANZ/XELJANZ XR (tofacitinib) as monotherapy.

Use of XELJANZ/XELJANZ XR in combination with biological DMARDs (bDMARDs) or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.

For more information:

Please consult the Product Monograph at http://pfizer.ca/pm/en/XELJANZ.pdf and an Important Safety Information Advisory available at https://recalls-rappels.canada.ca/en/alert-recall/xeljanzxeljanz-xr-tofacitinib-risk-major-adverse cardiovascular-events-malignancy for important information relating to contraindications, warnings, precautions, adverse reactions, interactions, dosing, and conditions of clinical use, which have not been discussed in this piece. The Product Monograph is also available by calling 1-800-463-6001.

* Please see the Product Monograph for complete dosing information

References: 1. Pfizer Canada ULC. XELJANZ/XELJANZ XR Product Monograph. **2.** Health Canada. XELJANZ XR Notice of Compliance information.

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PrXELJANZ® XR
(tofacitinib citrate)