Session # 1: September 27\textsuperscript{th}, 2016

- Introduction and discussion of session objectives
- Diagnosis of inflammatory arthritis with emphasis on RA and PsA
- The need for new models of care
- Who and when to refer to secondary care
- Overview of DMARDs and Biologic drug use with emphasis on the role of primary care in sharing the care
- Examination of the hands
Following this section of the talk, participants should be able to:

- Identify signs and symptoms that may indicate RA
- Obtain pertinent history and perform appropriate physical/laboratory/imaging exams in order to diagnose RA more quickly and more accurately
- Appreciate the potential ramifications of delayed diagnosis and treatment
- Recognize when to refer a patient to a rheumatology colleague, & what information to include in a referral
The Mission of the Ontario Rheumatology Association is to represent Ontario Rheumatologists and promote their pursuit of excellence in Arthritis care in Ontario through Leadership, Advocacy, Education, and Communications.
## Current Burden of Arthritis in Canada

<table>
<thead>
<tr>
<th>Section</th>
<th>Osteoarthritis (OA)</th>
<th>Rheumatoid Arthritis (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Living with arthritis</strong></td>
<td>2010 – 1 in 8</td>
<td>2010 – 1 in 136</td>
</tr>
<tr>
<td>By 2040</td>
<td>1 in 4</td>
<td>1 in 68</td>
</tr>
<tr>
<td><strong>Direct health care costs</strong></td>
<td>$12.6 billion in 2010</td>
<td></td>
</tr>
<tr>
<td>For both OA and RA</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Loss of productivity</strong></td>
<td>$17.3 billion</td>
<td>$3.3 billion</td>
</tr>
<tr>
<td>(1.0% CA GDP in 2010)</td>
<td>(0.2% CA GDP in 2010)</td>
<td></td>
</tr>
</tbody>
</table>
Arthritis, is the leading cause of disability in Canada

Top ten causes of disability among men and women aged 15 years and over, 2001

<table>
<thead>
<tr>
<th>Condition</th>
<th>Men (%)</th>
<th>Women (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrine, nutritional, metabolic disorders</td>
<td>5.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Other MSK</td>
<td>1.9</td>
<td>5.0</td>
</tr>
<tr>
<td>Sight disorders</td>
<td>3.8</td>
<td>5.4</td>
</tr>
<tr>
<td>Respiratory disorders &amp; asthma</td>
<td>4.8</td>
<td>6.1</td>
</tr>
<tr>
<td>Hearing disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other disorders of the nervous system</td>
<td>5.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Heart conditions or heart disease</td>
<td>8.2</td>
<td>10.1</td>
</tr>
<tr>
<td>Upper &amp; lower limb MSK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back &amp; spine MSK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>16.8</td>
<td>23.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30.7</td>
</tr>
</tbody>
</table>

Source: Public Health Agency of Canada, Life with Arthritis in Canada, 2010
Geographic Distribution of Rheumatologists

Number of Rheumatologists by Province/Territory in Canada in 2014
as reported by Canadian Medical Association

Population (thousands) 2011

- 36.5 - 45
  - 1,500 - 4,000
- 45 - 200
  - 4,000 - 8,000
- 200 - 650
  - 8,000 - 13,678.7
- 850 - 1,500

1 cm = 250 km

Source: ORA Models of Care
Putting patients 1st...improved outcomes through a shared-care management model

Patient focused
Evidence-based
Quality-driven
Shared accountability
Optimal use of existing resources
Coordinated services
Outcome measurement
Better patient experiences

Value for Health Care Dollars
Variation in Care: Prescribing Practices at Baseline

Variation in Patient Outcomes: Proportion of Patients in Remission at Followup
PURPOSE:
Establishment of a framework for the development of high quality models of care that are evidence informed & reinforced by best practices.

TARGET USERS:
Health policy decision-makers and system planners; rheumatologists, allied health providers and other primary care providers; and, people living with arthritis.

Report Web Launch April 2014: www.arthritisalliance.ca
The Arthritis Alliance of Canada (AAC) is very pleased to support and make the Inflammatory Arthritis Care Path Toolkit available. This toolkit is designed to assist care providers and patients through the continuum of care, and it is intended to help design and improve care for patients with inflammatory arthritis. The toolkit was a collaborative project designed to assist professionals as they assist adult patients through the continuum of care, with supporting tools.

The Toolkit is intended to be an educational tool and a useful resource for care providers, patients and other stakeholders. It is not a substitute for qualified and competent advice or the exercise of professional and clinical judgment. This Care Path is intended for use with adult patients, the age of majority and older. The Inflammatory Arthritis Care Path is not recommended for use in paediatric patients.
Diagnosis and Referral
Do you find it difficult to distinguish mechanical from inflammatory arthritis?

What questions would you ask your patients in order to make the distinction?
Let’s meet a patient with joint pain...
Ask the Right Questions to Distinguish Mechanical from Inflammatory Pain

Key questions:

- Where exactly does it hurt and for how long?
- When does it hurt most (i.e., with activity, at rest, both)?
- Do you suffer from morning stiffness lasting for more than 30 minutes?
- Is pain improved upon movement?
- Have you seen any swelling? Where?
Ask some other questions

Key questions:

- Pain /10
- Function
Discriminating Inflammatory from Non-inflammatory Joint Pain

Use clues from the patient’s history and exam to generate a differential diagnosis:

<table>
<thead>
<tr>
<th>Feature</th>
<th>Inflammatory</th>
<th>Non-inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint pain</td>
<td>Usually improves with activity</td>
<td>Usually worsens with activity</td>
</tr>
<tr>
<td>Joint swelling</td>
<td>Soft tissue</td>
<td>Bony</td>
</tr>
<tr>
<td>Joint deformity</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Local erythema</td>
<td>Sometimes</td>
<td>Absent</td>
</tr>
<tr>
<td>Local warmth</td>
<td>Frequent</td>
<td>Absent</td>
</tr>
<tr>
<td>Morning stiffness</td>
<td>&gt; 30 minutes</td>
<td>&lt; 30 minutes</td>
</tr>
<tr>
<td>Systemic symptoms</td>
<td>Common, especially fatigue</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Patterns of Joint Involvement

What does each of these images indicate? Why?

Early RA

Late RA

Osteoarthritis

Psoriatic arthritis

Figures courtesy of Dr. H.L. Averns. Reprinted with permission.
Important Considerations in RA Assessment

Clinical suspicion of RA is supported by the presence of ANY of the following:

- ≥ 3 swollen joints
- MTP/MCP involvement
  - Positive squeeze test
- Morning stiffness ≥ 30 mins

Inflammatory Features Suggesting Diagnosis Other than RA

<table>
<thead>
<tr>
<th>System</th>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Mucosal ulcers</td>
</tr>
<tr>
<td></td>
<td>Photosensitivity</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
</tr>
<tr>
<td></td>
<td>Skin rashes</td>
</tr>
<tr>
<td>Eye</td>
<td>Uveitis</td>
</tr>
<tr>
<td>Bowel</td>
<td>Inflammatory bowel disease</td>
</tr>
<tr>
<td></td>
<td>Infectious diarrhea</td>
</tr>
<tr>
<td>Other</td>
<td>Raynaud’s</td>
</tr>
<tr>
<td></td>
<td>Urethritis – new sexual partners?</td>
</tr>
<tr>
<td></td>
<td>Self-limiting post-viral symptoms</td>
</tr>
</tbody>
</table>

# Diagnostic Laboratory and Imaging Tests

**Recommended for initial evaluation of RA**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>Often increased</td>
</tr>
<tr>
<td>ESR</td>
<td>Often increased to &gt; 30 mm/hr</td>
</tr>
<tr>
<td>Hemoglobin/ hematocrit</td>
<td>May be decreased</td>
</tr>
<tr>
<td>Liver function</td>
<td>Normal or slightly elevated alkaline phosphatase</td>
</tr>
<tr>
<td>Platelets</td>
<td>Usually increased</td>
</tr>
<tr>
<td>WBC</td>
<td>May be increased – usually non contributory</td>
</tr>
<tr>
<td>Radiographic findings of involved joints</td>
<td>May be normal or show osteopenia or erosions near joint spaces in early disease</td>
</tr>
</tbody>
</table>

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Time for a blood test quiz........
Auto-antibodies: RF and Anti-CCP

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity(^1) (% of RA patients who are positive)</th>
<th>Specificity(^1) (% of non-RA patients who are negative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF</td>
<td>~60-65%</td>
<td>~80%</td>
</tr>
<tr>
<td>Anti-CCP</td>
<td>~68%</td>
<td>~95%</td>
</tr>
</tbody>
</table>

- Even when these tests are negative, the patient may still have RA\(^1\)
- Anti-CCP is highly specific for RA, but may also be found in other types of inflammatory arthritis\(^2\)
- Both RF and anti-CCP seropositivity are associated with more severe disease\(^2\)

When should a patient be referred to a rheumatologist?

Why is referral important?
Brief Delay of Therapy Affects Radiographic Outcomes

Important Considerations for Referral

- > 12 weeks delay in treatment results in a missed opportunity to improve long-term outcomes\(^1\)
- RF positivity, raised acute phase response, and erosions on x-ray are associated with poor outcomes\(^1\)
- Ongoing/untreated systemic inflammation is associated with increased comorbidities (cardiovascular disease, cancer) in patients with RA\(^2,3\)

- Corticosteroids should generally be avoided without a confirmed diagnosis of RA\(^1\)

# Referral Information Needed by Rheumatologist

- Reason for consultation
- Duration of symptoms
- Duration of morning stiffness
- Limitation of daily/work activities
- Involved joints
- Laboratory tests
  - RF
  - CRP
  - ESR

Therapeutic Management
Therapeutic Management – Learning Objectives

Following this section of the talk, participants should be able to:

- Appreciate the fundamental concepts that guide RA treatment
- Specify the key components of the CRA RA treatment algorithm
- Evaluate appropriate usage of glucocorticoids
- Differentiate biologic and non-biologic DMARDs used to treat RA
- Describe common measures of disease activity
Your patient has significant joint involvement and you suspect RA; however, she is reluctant to see a rheumatologist.

What would you say to her?
Management of RA: Fundamental Concept

Tight control of inflammation improves outcomes and requires structured protocols and regular review.

Figure reproduced from Smolen JS et al. *Ann Rheum Dis* 2009;68:159-62.
CRA Guidelines: Initial Treatment of RA

Diagnosis of RA

Aim for goal of remission (or LDA when not possible)

Assess disease activity and prognostic features

Start DMARD as soon as possible

DMARD monotherapy: MTX unless CI

DMARD combination therapy: with MTX unless CI

Inadequate response

Switch DMARD

Proceed to biologic therapy

In certain situations:
1. DMARD CI
2. HDA + poor prognostic factors (esp early disease)

Inadequate response = not reaching target by 3 to 6 months

Non-biologic DMARDs

Most commonly used DMARDs

- Methotrexate
- Sulfasalazine (Salazopyrin®)
- Hydroxychloroquine (Plaquenil®)
- Leflunomide (Arava®)
- Tofacitinib (Xeljanz®)
- Gold (Myochrisine®)

Double and triple combinations regimens are also available

Roughly 2/3 of patients initially respond to non-biologic DMARD monotherapy (approximately 60% reduction in pain, swelling and stiffness)

Combination DMARDs may offer an advantage for some patients
Biologic Agents Used in RA and their Mechanisms of Action

- Biologics are large, complex proteins grown through biological processes using living cells (from mice, humans, or microorganisms)

- They reduce inflammation by blocking key molecules involved in the pathogenesis of RA

## Biologic Options for RA

<table>
<thead>
<tr>
<th>Mechanism of action</th>
<th>Name</th>
<th>Trade name</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Adalimumab</strong>¹</td>
<td>Humira</td>
<td>SC</td>
</tr>
<tr>
<td>Inhibits tumour necrosis factor</td>
<td><strong>Certolizumab pegol</strong>¹</td>
<td>Cimzia</td>
<td>SC</td>
</tr>
<tr>
<td></td>
<td><strong>Etanercept</strong>¹</td>
<td>Enbrel</td>
<td>SC</td>
</tr>
<tr>
<td></td>
<td><strong>Golimumab</strong>¹</td>
<td>Simponi</td>
<td>SC</td>
</tr>
<tr>
<td></td>
<td><strong>Golimumab</strong>¹</td>
<td>Simponi IV</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td><strong>Infliximab</strong>¹,²</td>
<td>Remicade Inflectra</td>
<td>IV</td>
</tr>
<tr>
<td>Inhibits interleukin-6</td>
<td><strong>Tocilizumab</strong>²</td>
<td>Actemra</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td><strong>Anakinra</strong></td>
<td>Kineret</td>
<td>SC</td>
</tr>
<tr>
<td>Inhibits interleukin-1</td>
<td><strong>Abatacept</strong>¹</td>
<td>Orenacia</td>
<td>IV</td>
</tr>
<tr>
<td>Inhibits T cell activation</td>
<td><strong>Abatacept</strong>¹</td>
<td>Orenacia</td>
<td>SC</td>
</tr>
<tr>
<td>Depletes B cells</td>
<td><strong>Rituximab</strong>²</td>
<td>Rituxan</td>
<td>IV</td>
</tr>
</tbody>
</table>

*Maintenance frequency except for rituximab

Full reference list provided in the slide notes.
Evaluating Disease Activity: Functional and Joint Assessments

What we do here....

## Evaluating Disease Activity: Key Composite Disease Activity Measures

<table>
<thead>
<tr>
<th>Measure (score range)</th>
<th>Assessments included</th>
<th>Scores for disease activity levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>High</td>
</tr>
<tr>
<td>CDAI (0 – 76)</td>
<td>TJC, SJC, PGA,* PhGA</td>
<td>&gt;22</td>
</tr>
<tr>
<td>DAS28 (0 – 9.4)</td>
<td>TJC, SJC, ESR, PGA†</td>
<td>&gt;5.1</td>
</tr>
<tr>
<td>SDAI (0.1 – 86)</td>
<td>TJC, SJC, PGA,* PhGA, CRP</td>
<td>&gt;26</td>
</tr>
</tbody>
</table>

- The goal of treatment is remission

Adapted from Bykerk VP, et al. *J Rheumatol* 2011;38:2095-104.

*On a scale of 0 to 10 cm; †On a scale of 0 to 100 mm
Summary

- Minimizing cumulative inflammation has the potential to reduce or prevent joint damage and disability.

- Once RA is confirmed, the CRA recommends starting DMARD therapy as early as possible.
  - Several biologic and non-biologic DMARDs are currently available.
  - DMARD therapy should be switched if response is inadequate.
  - Glucocorticoids should be used sparingly and only under specific circumstances.
The PCP’s Role in Ongoing Management

We will discuss this next time!
The PCP’s Role in Ongoing Management – Learning Objectives

Following this section of the talk, participants should be able to:

- List vaccinations required by RA patients before and during immunosuppressive therapy
- Recognize the importance of careful pregnancy planning and management in women with RA
- Manage infections in patients with RA on immunosuppressive therapy
- Assess the need for perioperative management of drug therapy in patients with RA
## Non-biologic DMARDs

<table>
<thead>
<tr>
<th>PRODUCT</th>
<th>Dose</th>
<th>Time to onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate (po or sc)</td>
<td>Up to 25 mg per week</td>
<td>4 to 6 weeks</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>200 to 400 mg QD</td>
<td>4 to 12 weeks</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>1 g BID to QID</td>
<td>5 to 10 weeks</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>10 to 20 mg daily</td>
<td>4 to 12 weeks</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>2.5 to 5 mg/kg/d 2 intakes</td>
<td>6 to 12 weeks</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50 to 150 mg QD</td>
<td>6 to 12 weeks</td>
</tr>
<tr>
<td>Gold salts (i.m.)</td>
<td>25-50 mg q2-4 weeks</td>
<td>3 to 6 months</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>5 mg twice daily</td>
<td>2 to 12 weeks</td>
</tr>
</tbody>
</table>
## Live Vaccines: Must Not be Given During Anti-TNFα Therapy

<table>
<thead>
<tr>
<th>Live vaccines</th>
<th>Suggested alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral live polio vaccine (OPV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Inactivated polio vaccine (IPV)</td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td></td>
</tr>
<tr>
<td>Live typhoid vaccine</td>
<td>Inactivated vaccine (but only 70% protective)</td>
</tr>
<tr>
<td>Chickenpox/shingles (Varicella)</td>
<td></td>
</tr>
<tr>
<td>Bacillus Calmette-Guérin (BCG)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>Must not be given to patient OR household contacts  
<sup>b</sup>Must not be given to patients; household contacts OK

*If the patient is travelling to an endemic region, please consult your travel/ID expert for further management information*

Step 4 Shared Care
Value Through Collaborative Care

Shared care – Stable patients
- Treat-to-target
- Monitoring
- Adherence
- Patient support
- Education

Multiple patient touch-points between specialist visits

Sharing of information between primary care, specialist and other providers

Care plan support, education, disease management tools

Cross-referral back to specialist as needed
Annual one-on-one medication review with your pharmacist for all medications
• Rx and over-the-counter (OTCs)
• Publicly funded for eligible Ontarians

Requirements
• 3+ chronic medications
• OHIP card

Follow-up visits also available if needed
Standard template that patients can take to their pharmacists

April 2015

Dr. Mary J Bell, Division of Rheumatology
M1-401 – 2075 Bayview Avenue
Toronto, ON, Canada
M4N 2M5 Tel 416 480-4580 Fax 416 480-4233

Dear Pharmacist:

I am kindly referring to your care, ______________________ (patient name), who has been diagnosed with a chronic rheumatic disease and is on multiple medications.

I have discussed with ______________________ (patient name) the importance of having a complete MedsCheck with a pharmacist. Please book my patient an appointment with you to receive:

☐ MedsCheck Review
☐ MedsCheck Follow-up (subsequent to referral request)
☐ MedsCheck Annual Review

Once you have completed the MedsCheck, please FAX (416 480-4233) back to me the following information:
  • Complete list of prescription medication filled or refilled in the past 3 months
  • A copy of the “MedsCheck” encounter form
  • Any additional information related to my patient’s medications

If you have any questions or would like to discuss any specific health related issues regarding my patient, I would welcome your call at 416 480-4580

I look forward to working collaboratively with you to ensure that our patients receive excellent care and the best health outcomes to manage their chronic rheumatic conditions.

Thank you for your cooperation.
Yours very truly,

Mary J Bell, M.D., FRCP
ORCR
Ontario Rheumatology Association
Standard template that Rheumatologists can give to their patients about MedsCheck

April 2016

Dr. Mary J Bell, Division of Rheumatology
M1-401 - 2075 Bayview Avenue
Toronto, ON, Canada
M4N 3M6 Tel 416.480.4580 Fax 416.480.4239

Dear _________(Patient/Name)

You have been diagnosed with a chronic rheumatic condition which may require you to take a number of different medications.

As part of your rheumatology care, I am referring you to book an appointment with your Pharmacist to provide you with a complete MedsCheck. The MedsCheck is a free consultation service provided by any community pharmacist in Ontario.

During your Medscheck appoint you will be able to review your prescriptions, any over-the-counter and alternative medications you are taking and how they may be interacting with each other. At the end of the private one-on-one interaction with the pharmacist, you will receive:

- A complete and accurate medication list (including over the counter medications, and vitamins)
- Medication adherence support for your medications
- Suggestions for managing adverse events that you may experience
- Support to help avoid and/or manage drug interactions you may experience

Upon completion of the MedsCheck session, your pharmacist will send me a follow up note. Together we will work collaboratively to ensure that you continue to receive excellent care and the best health outcomes to manage your chronic rheumatic condition.

Should you have any questions please do not hesitate to contact me at any time.

Yours very truly,

Mary J Bell, MD, FRCPA

OR A Models of Care