

## A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO UPDATES IN RHEUMATOLOGY

some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

### READING 1 – VACCINATION OF PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

**Wong PK, Bagga H, Barrett C, Hanrahan P, Johnson D, Katrib A, Leder K, Marabani M, Pentony P, Riordan J, White R, Young L. A practical approach to vaccination of patients with autoimmune inflammatory rheumatic diseases in Australia. Intern Med J. 2017 Jan 19. [Epub ahead of print] PubMed PMID: 28101910.**

**DOI: 10.1111/imj.13371. [Payment required]**

Author information:

Wong PK(1), Bagga H(2), Barrett C(3), Hanrahan P(4), Johnson D(5) et al.

(1)Mid-North Coast Arthritis Clinic, Coffs Harbour and UNSW Rural Clinical School, Coffs Harbour, NSW. (2) Mid-North Coast Arthritis Clinic, Coffs Harbour, NSW. (3)Redcliffe Hospital, Redcliffe, QLD, Redcliffe Northside Rheumatology, Redcliffe, QLD. (4)Private Rheumatology practice, South Perth, WA and Faculty of Medicine, University of Western Australia, WA. (5)Department of General Medicine and Infectious Diseases, Austin Health, Heidelberg, VIC. et al.

#### ABSTRACT

Autoimmune inflammatory rheumatic diseases (AIIRD) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are often complicated by infection, which results in significant morbidity and mortality. The increased risk of infection is probably due to a combination of immunosuppressive effects of the AIIRD, comorbidities, and the use of immunosuppressive conventional synthetic disease modifying anti-rheumatic drugs (DMARDs) and more recently, targeted synthetic DMARDs and biologic DMARDs which block specific pro-inflammatory enzymes, cytokines or cell types. The use of these various DMARDs has revolutionized the treatment of AIIRD. This has led to a marked improvement in quality of life for AIIRD patients, who often now travel for prolonged periods. Many infections are preventable with vaccination. However, as protective immune responses induced by vaccination may be impaired by immunosuppression, where possible, vaccination may need to be performed prior to initiation of immunosuppression. Vaccination status should also be reviewed when planning overseas travel. Limited data regarding vaccine efficacy in patients with AIIRD makes prescriptive guidelines difficult. However, a vaccination history should be part of the initial work-up in all AIIRD patients. Those caring for AIIRD patients should regularly consider vaccination to prevent infection within the practicalities of routine clinical practice.

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### READING 2 – SELECTED MANAGEMENT OF COMORBIDITIES AND RISK FACTORS OF CHRONIC INFLAMMATORY RHEUMATIC DISEASE

**Gossec L, Baillet A, Dadoun S, Daien C, Berenbaum F, Dernis E, Fayet F, Hudry C, Mezieres M, Pouplin S, Richez C, Saraux A, Savel C, Senbel E, Soubrier M, Sparsa L, Wendling D, Dougados M. Collection and management of selected comorbidities and their risk factors in chronic inflammatory rheumatic diseases in daily practice in France. Joint Bone Spine. 2016;83(5):501–9. PubMed PMID: 27369644.**

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Author information:

Gossec L(1), Baillet A(2), Dadoun S(3), Daien C(4), Berenbaum F(5), Dernis E et al.

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## ABSTRACT

**INTRODUCTION:** In chronic inflammatory rheumatic diseases (CIRDs), comorbidities such as cardiovascular disease and infections are sub-optimally managed. EULAR recently developed points to consider to collect and report comorbidities. The objective of this present study was to develop a pragmatic guide to collect, report and propose management recommendations for comorbidities, from a rheumatologist perspective.

**METHODS:** The collection and reporting of comorbidities and risk factors was adapted from the EULAR points to consider. To develop management recommendations, the process comprised (1) systematic literature reviews by 3 fellows and (2) a 2-day consensus process involving 110 experts (rheumatologists and health professionals). Votes of agreement (Likert 1-5 where 5 indicates full agreement) were obtained.

**RESULTS:** The six selected comorbidities were ischemic cardiovascular diseases, malignancies, infections, diverticulitis, osteoporosis and depression. The literature review retrieved 97 articles or websites, mostly developed for the general population. The consensus process led to reporting presence of comorbidities, current treatment, risk factors (e.g. hypertension), screening (e.g. mammography) and prevention (e.g. vaccination). Management recommendations include physical examination (e.g. blood pressure or lymph node examination), prescribing screening procedures, and interpreting results to refer in a timely manner to appropriate other health professionals. Agreement was high (mean±standard deviation, 4.37±0.33).

**CONCLUSIONS:** Using an evidence-based approach followed by expert consensus, this initiative furthers the dissemination in France of the EULAR points to consider, and clearly defines what part of the management of comorbidities is potentially within the remit of rheumatologists. This initiative should facilitate systematic management of patients with CIRDs.

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## READING 3 – AIMS OF PRESENT DAY GOUT TREATMENT

**Keenan RT. Limitations of the current standards of care for treating gout and crystal deposition in the primary care setting: A review. Clin Ther. 2017;39:430–41. PubMed PMID: 28089200.**

**DOI: 10.1016/j.clinthera.2016.12.011. [Free full text]**

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## ABSTRACT

**PURPOSE:** This article outlines several important issues regarding the management of patients with gout. The topics discussed include best practices for gout based on the most current guidelines, opportunities for improving gout management, and current and emerging therapies for gout.

**METHODS:** [PubMed and Google Scholar databases] were search for all articles and trials published before 2016, using the key terms [hyperuricemia, gout, tophi, joint erosion, joint damage, treatment guidelines, American College of Rheumatology (ACR), European League Against Rheumatism (EULAR), flare, comorbidity, epidemiology, adherence, serum uric acid (sUA), monosodium urate (MSU), <6 mg/dL, MSU crystal formation, as well as individual drug names and classes of treatments of interest (allopurinol, febuxostat, colchicine, non-steroidal anti-inflammatories (NSAIDs)]. Studies were selected that presented data on gout treatment, including drugs under development, and on the management of gout from both the physician and patient perspectives. The reference lists of identified articles were searched manually for additional publications.

**FINDINGS:** Gout, a progressive debilitating form of inflammatory arthritis, is caused by factors that elevate serum uric acid (sUA) levels, leading to hyperuricemia. Continued elevated sUA can result in monosodium urate crystal deposition in joints

and soft tissues, causing acute and chronic inflammation. Crystal deposition can lead to chronic gout, with an increased number of flares, tophi development, and structural joint damage. The aims of gout treatment are to reduce the sUA level to <6 mg/dL, to inhibit the formation of new crystals, and to promote the dissolution of existing crystals. Gout is often poorly managed for several reasons, including a lack of adherence to treatment guidelines by health care providers, patients' poor adherence to therapy, and differences between a provider's and patient's perspectives regarding treatment.

**IMPLICATIONS:** Patients need to be educated about their diagnosis and management of the disease, such as the importance of compliance with long-term treatment. Gout treatment may also be confounded by contraindications to current standards of therapy and the limitations of current treatment paradigms. Recently approved medications, as well as drugs under development, may provide new ways for reaching the sUA target and also "curing" the disease.

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#### READING 4 – EULAR 2016 RECOMMENDATIONS FOR TREATMENT OF GOUT

**Richette P, Doherty M, Pascual E, Barskova V, Becce F, Castañeda-Sanabria J, Coyfish M, Guillo S, Jansen TL, Janssens H, Lioté F, Mallen C, Nuki G, Perez-Ruiz F, Pimentao J, Punzi L, Pywell T, So A, Tausche AK, Uhlig T, Zavada J, Zhang W, Tubach F, Bardin T. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis*. 2017;76:29–42. PubMed PMID: 27457514.**

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Richette P(1), Doherty M(2), Pascual E(3), Barskova V(4), Becce F(5), Castañeda-Sanabria J, et al.

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#### ABSTRACT

**BACKGROUND:** New drugs and new evidence concerning the use of established treatments have become available since the publication of the first European League Against Rheumatism (EULAR) recommendations for the management of gout, in 2006. This situation has prompted a systematic review and update of the 2006 recommendations. **METHODS:** The EULAR task force consisted of 15 rheumatologists, 1 radiologist, 2 general practitioners, 1 research fellow, 2 patients and 3 experts in epidemiology/methodology from 12 European countries. A systematic review of the literature concerning all aspects of gout treatments was performed. Subsequently, recommendations were formulated by use of a Delphi consensus approach.

**RESULTS:** Three overarching principles and 11 key recommendations were generated. For the treatment of flare, colchicine, non-steroidal anti-inflammatory drugs (NSAIDs), oral or intra-articular steroids or a combination are recommended. In patients with frequent flare and contraindications to colchicine, NSAIDs and corticosteroids, an interleukin-1 blocker should be considered. In addition to education and a non-pharmacological management approach, urate-lowering therapy (ULT) should be considered from the first presentation of the disease, and serum uric acid (SUA) levels should be maintained at <6 mg/dL (360 µmol/L) and <5 mg/dL (300 µmol/L) in those with severe gout. Allopurinol is recommended as first-line ULT and its dosage should be adjusted according to renal function. If the SUA target cannot be achieved with allopurinol, then febuxostat, a uricosuric or combining a xanthine oxidase inhibitor with a uricosuric should be considered. For patients with refractory gout, pegloticase is recommended.

**CONCLUSIONS:** These recommendations aim to inform physicians and patients about the non-pharmacological and pharmacological treatments for gout and to provide the best strategies to achieve the predefined urate target to cure the disease.

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## READING 5 – PRAGMATIC USE OF ULTRASOUND IN MANAGEMENT OF RHEUMATOID ARTHRITIS FROM DIAGNOSIS TO REMISSION

**D'Agostino MA, Terslev L, Wakefield R, Østergaard M, Balint P, Naredo E, Iagnocco A, Backhaus M, Grassi W, Emery P. Novel algorithms for the pragmatic use of ultrasound in the management of patients with rheumatoid arthritis: from diagnosis to remission. *Ann Rheum Dis.* 2016;75:1902–8. PubMed PMID: 27553213.**

**DOI: 10.1136/annrheumdis-2016-209646. [Payment required]**

### Author information:

D'Agostino MA(1), Terslev L(2), Wakefield R(3), Østergaard M(2), Balint P(4), Naredo E(5), Iagnocco A, et al. (1)Rheumatology Department, APHP, Hôpital Ambroise Paré, Boulogne-Billancourt, France INSERM U1173, Laboratoire d'Excellence INFLAMEX, UFR Simone Veil, Versailles-Saint-Quentin University, Saint-Quentin en Yvelines, France Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Chapel Allerton Hospital, Leeds, UK. (2)Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark. (3)Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Chapel Allerton Hospital, Leeds, UK NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, UK. (4)Third Rheumatology Department, National Institute of Rheumatology and Physiotherapy, Budapest, Hungary. (5)Department of Rheumatology, Hospital General Universitario Gregorio Marañón and Universidad Complutense, Madrid, Spain, et al.

### ABSTRACT

The absence of specific guidance on how to use ultrasound (US) to diagnose and manage patients with inflammatory arthritis, especially with rheumatoid arthritis (RA) has hindered the optimal utilisation of US in clinical practice, potentially limiting its benefits for patient outcomes. In view of this, a group of musculoskeletal US experts formed a working group to consider how this unmet need could be satisfied and to produce guidance (additional to European League against Rheumatism (EULAR) imaging recommendations) to support clinicians in their daily clinical work. This paper describes this process and its outcome, namely five novel algorithms, which identify when US could be used. They are designed to aid diagnosis, to inform assessment of treatment response/disease monitoring and to evaluate stable disease state or remission in patients with suspected or established RA, by providing a pragmatic template for using US at certain time points of the RA management. A research agenda has also been defined for answering unmet clinical needs.

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## READING 6 – PROSPECTIVE EVALUATION OF IMPLEMENTING A PATIENT-INITIATED REVIEW SYSTEM FOR PEOPLE WITH RHEUMATOID ARTHRITIS

**Goodwin VA, Paudyal P, Perry MG, Day N, Hawton A, Gericke C, Ukoumunne OC, Byng R. Implementing a patient-initiated review system for people with rheumatoid arthritis: a prospective, comparative service evaluation. *J Eval Clin Pract.* 2016;22:439–45. PubMed PMID: 26762900.**

**DOI: 10.1111/jep.12505. [Payment required]**

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Goodwin VA(1), Paudyal P(2), Perry MG(3), Day N(3), Hawton A(1), Gericke C(4), Ukoumunne OC(1), Byng R(5).

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## ABSTRACT

**RATIONALE, AIMS AND OBJECTIVES:** The management of rheumatoid arthritis (RA) usually entails regular hospital reviews with a specialist often when the patient is well rather than during a period of exacerbation. An alternative approach where patients initiate appointments when they need them can improve patient satisfaction and resource use whilst being safe. This service evaluation reports a system-wide implementation of a patient-initiated review appointment system called Direct Access (DA) for people with RA. The aim was to establish the impact on patient satisfaction of the new system versus usual care as well as evaluate the implementation processes.

**METHODS:** As all patients could not start on the new system at once, in order to manage the implementation, patients were randomly allocated to DA or to usual care. Instead of regular follow-up appointments, DA comprised an education session and access to a nurse-led telephone advice line where appointments could be accessed within two weeks. Usual care comprised routine follow-ups with the specialist. Data were collected on patient satisfaction, service use and outcomes of any contact to the advice line.

**RESULTS:** Three hundred and eleven patients with RA were assessed as being suitable for DA. In terms of patient satisfaction, between-group differences were found in favour of DA for accessibility and convenience, ease of contacting the nurse and overall satisfaction with the service. Self-reported visits to the general practitioner were also significantly lower. DA resulted in a greater number of telephone contacts (incidence rate ratio = 1.69; 95% confidence interval 1.07 to 2.68). Hospital costs of the two different service models were similar. Mean waiting time for an appointment was 10.8 days.

**CONCLUSION:** This service evaluation found that DA could be implemented and it demonstrated patient benefit in a real-world setting. Further research establishing the broader cost-consequences across the whole patient pathway would add to our findings. © 2016 John Wiley & Sons, Ltd. DOI: 10.1111/jep.12505 PMID: 26762900 [PubMed - indexed for MEDLINE]

## READING 7 – INTERPLAY OF RHEUMATOID ARTHRITIS, AGEING, AND COMORBIDITIES

**van Onna M, Boonen A. The challenging interplay between rheumatoid arthritis, ageing and comorbidities. BMC Musculoskelet Disord. 2016;17:184. Review. PubMed PMID: 27118031; PubMed Central PMCID: PMC4845363.**

**DOI: 10.1186/s12891-016-1038-3. [Free full text]**

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## ABSTRACT

**BACKGROUND:** The incidence of rheumatoid arthritis (RA) is expected to increase over the next 10 years in the European Union because of the increasing proportion of elderly people. As both RA and ageing are associated with emerging comorbidities such as cardiovascular disease, malignancies and osteoporosis, these factors will have a profound effect on the management of RA. In addition, both increasing age and comorbidities may independently alter commonly used RA-specific outcome measures.

**DISCUSSION:** Age-related decline in immune cell functions (immunosenescence), such as a decrease in T-cell function, may contribute to the development of RA, as well as comorbidity. The chronic immune stimulation that occurs in RA may also lead to premature ageing and comorbidity. The interplay between RA, ageing and (emerging) comorbidities is interesting but complex. Cardiovascular disease, lung disease, malignancies, bone and muscle wasting and neuropsychiatric disease all occur more frequently in RA patients as compared to the general population. It is unclear how RA should be managed in 'today's world of multiple comorbidities'. Evidence that treatment of RA improves comorbidities is currently lacking, although some promising indirect observations are available. On the other hand, there is limited evidence that medication



regularly prescribed for comorbidities, such as statins, might improve RA disease activity. Both ageing and comorbidity have an independent effect on commonly used outcome measures in the RA field, such as the Health Assessment Questionnaire (HAQ) and the clinical disease activity index (CDAI). Prospective studies, that also account for the presence of comorbidity in (elderly) RA patients are therefore urgently needed. To address gaps in knowledge, future research should focus on the complex interdependencies between RA, ageing and comorbidity. In addition, these findings should be integrated into daily clinical practice by developing and testing integrated and coordinated health care services. Adaptation of management recommendations is likely required. The elderly RA patient who also deals with (emerging) comorbidities presents a unique challenge to treating clinicians. A paradigm shift from disease-centered to goal-oriented approach is needed to develop adequate health care services for these patients.

## READING 8 – ASIA PACIFIC LEAGUE OF ASSOCIATIONS FOR RHEUMATOLOGY 2015 TREATMENT RECOMMENDATIONS FOR RHEUMATOID ARTHRITIS

**Lau CS, Chia F, Harrison A, Hsieh TY, Jain R, Jung SM, Kishimoto M, Kumar A, Leong KP, Li Z, Lichauco JJ, Louthrenoo W, Luo SF, Nash P, Ng CT, Park SH, Suryana BP, Suwannalai P, Wijaya LK, Yamamoto K, Yang Y, Yeap SS; Asia Pacific League of Associations for Rheumatology. APLAR rheumatoid arthritis treatment recommendations. *Int J Rheum Dis.* 2015;18:685–713. Review. Erratum in: *Int J Rheum Dis.* 2015;18:917. PubMed PMID: 26334449.**

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### ABSTRACT

**AIMS:** Rheumatoid arthritis is a chronic inflammatory condition that affects approximately 1% of the world's population. There are a wide number of guidelines and recommendations available to support the treatment of rheumatoid arthritis; however, the evidence used for these guidelines is predominantly based on studies in Caucasian subjects and may not be relevant for rheumatoid arthritis patients in the Asia-Pacific region. Therefore, the Asia Pacific League of Associations for Rheumatology established a Steering Committee in 2013 to address this issue.

**MATERIALS AND METHODS:** The AGREE II instrument and the ADAPTE Collaboration framework were applied to systematically identify, appraise, synthesize, and adapt international rheumatoid arthritis guidelines for use in the Asia-Pacific region. **RESULTS:** Forty rheumatoid arthritis treatment recommendations, based on evidence and expert opinion, were drafted and are presented in this report.

**CONCLUSION:** The Asia Pacific of Associations for Rheumatology rheumatoid arthritis treatment recommendations are intended to serve as a reference for best practice management of rheumatoid arthritis in Asia-Pacific, focusing on local issues to ensure the delivery of basic care for these patients, and to improve their outcomes. In addition, the document will serve as a reference for national rheumatology associations in Asia-Pacific for developing guidelines in their respective countries.

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**READING 9 – EFFECT OF TIGHT CONTROL OF INFLAMMATION IN EARLY PSORIATIC ARTHRITIS — UK MULTICENTRE OPEN-LABEL RANDOMISED CONTROLLED TRIAL**

**Coates LC, Moverley AR, McParland L, Brown S, Navarro-Coy N, O'Dwyer JL, Meads DM, Emery P, Conaghan PG, Helliwell PS. Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. Lancet. 2015;386:2489–98. PubMed PMID: 26433318; PubMed Central PMCID: PMC4920221.**

**DOI: 10.1016/S0140-6736(15)00347-5 [Free full text]**

Author information:

Coates LC(1), Moverley AR(1), McParland L(2), Brown S(2), Navarro-Coy N(3), O'Dwyer JL(4), Meads DM(4), Emery P(1), Conaghan PG(1), Helliwell PS(5).

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### ABSTRACT

**BACKGROUND:** Early intervention and tight control of inflammation optimise outcomes in rheumatoid arthritis but these approaches have not yet been studied in psoriatic arthritis. We aimed to assess the effect of tight control on early psoriatic arthritis using a treat-to-target approach. **METHODS:** For this open-label multicentre randomised controlled trial, adult patients (aged  $\geq 18$  years) with early psoriatic arthritis ( $< 24$  months symptom duration), who had not previously received treatment with any disease-modifying anti-rheumatic drugs, were enrolled from eight secondary care rheumatology centres in the UK. Enrolled patients were randomly assigned in a 1:1 ratio to receive either tight control (with review every 4 weeks and with escalation of treatment if minimal disease activity criteria not met) or standard care (standard therapy according to the treating clinician, with review every 12 weeks) for 48 weeks. Randomisation was done by minimisation incorporating a random element, to ensure treatment groups were balanced for randomising centre and pattern of arthritis (oligoarticular vs polyarticular). The randomisation procedure was done through a central 24-h automated telephone system based at the Leeds Institute of Clinical Trials Research (Leeds, UK). This was an open-label study in which patients and clinicians were aware of treatment group assignment. Clinical outcomes were recorded by a masked assessor every 12 weeks. The primary outcome was the proportion of patients achieving an American College of Rheumatology (ACR) 20% (ACR20) response at 48 weeks, analysed by intention to treat with multiple imputation for missing ACR components. Cost-effectiveness was also assessed. This trial is registered with ClinicalTrials.gov, number NCT01106079, and the ISCRCTN registry, number ISCRCTN30147736.

**FINDINGS:** Between May 28, 2008, and March 21, 2012, 206 eligible patients were enrolled and randomly assigned to receive tight control ( $n=101$ ) or standard care ( $n=105$ ). In the intention-to-treat patient population, the odds of achieving an ACR20 response at 48 weeks were higher in the tight control group than in the standard care group (odds ratio 1.91, 95% CI 1.03–3.55;  $p=0.0392$ ). Serious adverse events were reported by 20 (10%) patients (25 events in 14 [14%] patients in the tight control group and eight events in six [6%] patients in the standard care group) during the course of the study. No unexpected serious adverse events or deaths occurred.

**INTERPRETATION:** Tight control of psoriatic arthritis disease activity through a treat-to-target approach significantly improves joint outcomes for newly diagnosed patients, with no unexpected serious adverse events reported.

**FUNDING:** Arthritis Research UK and Pfizer. Copyright © 2015 Elsevier Ltd. All rights reserved.

**READING 10 – ACUTE ANTERIOR UVEITIS AND SPONDYLOARTHRITIS**

**Khan MA, Haroon M, Rosenbaum JT. Acute Anterior Uveitis and Spondyloarthritis: More than meets the eye. Curr Rheumatol Rep. 2015;17:59. Review. PubMed PMID: 26233598.**

**DOI: 10.1007/s11926-015-0536-x. [Payment required]**

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### ABSTRACT

Ankylosing spondylitis (AS) and related forms of spondyloarthritis (SpA) are associated with some extra-articular features, and the most common symptomatic association is with acute anterior uveitis (AAU). Thus, approximately 40 % of patients with AS will experience a sudden onset of a unilateral anterior uveitis sometime during the course of their disease. Patients with AAU, especially those who are HLA-B27 positive, should be questioned about inflammatory low back pain and also evaluated for other clinical features of SpA. Since a prolonged delay in diagnosis is common among SpA patients and occurrence of AAU may be the reason for their first interaction with medical care, occurrence of AAU presents a unique opportunity for identifying such undiagnosed SpA patients. Therefore, a novel evidence-based algorithm called Dublin Uveitis Evaluation Tool (DUET) has been proposed to guide ophthalmologists and primary care physicians to refer appropriate AAU patients to rheumatologists. In a large two-phase study, approximately 40 % of patients presenting with idiopathic AAU were noted to have undiagnosed SpA, and DUET algorithm was noted to have excellent sensitivity (96 %) and specificity (97 %). It has a positive likelihood ratio (LR) 41.5 and negative LR 0.03. In most instances, the eye inflammation responds well to corticosteroid and mydriatic eye drops and without the need for additional therapy. Use of oral corticosteroids is reserved for patients, especially with associated chronic inflammatory bowel disease or psoriatic arthritis presenting with bilateral, chronic, anterior, and/or intermediate uveitis, and this treatment is rarely needed for more than a couple of weeks. A very small percentage may be more refractory to such treatment and require potential novel therapies, including the use of tumor necrosis factor blockers.