RHEUMATOLOGY ADVANCES IN PRACTICE

Rheumatology Advances in Practice 2020;0:1–9
doi:10.1093/rap/rkaa043

Review

BSR Spondyloarthritis Course, 27 February 2020. Spondyloarthritis: pathogenesis, diagnosis and management

Helena Marzo-Ortega [1,2], Ai Lyn Tan[1,2], Dennis McGonagle[1,2], David Pickles[1], Sayam Dubash [1,2], Claire Y. Vandevelde[1,2], Laura C. Coates [3], Stefan Siebert [4] and Philip S. Helliwell[1,2]

Abstract

High-quality continuous medical education is essential to maintain excellence in health-care delivery, upskilling professionals and improving patient outcomes. This is particularly relevant when addressing rare disease groups, such as the spondyloarthritides, a group of heterogeneous inflammatory conditions that affect joints and other organs, such as the skin, bowel and eye. Professional bodies, such as the British Society for Rheumatology (BSR), are well placed to deliver this type of education. In 2020, the BSR ran a dedicated SpA course aimed at rheumatology health-care professionals wishing to update their basic knowledge of SpA with a review of the latest advances in the field. Here, we summarize the proceedings of the meeting and discuss the value of such an initiative.

Key words: medical education, rheumatology, spondyloarthritis, axial spondyloarthritis, psoriatic arthritis, imaging, treatment, continuous medical education

Key messages

- Education in all aspects of spondyloarthritis remains a significant unmet need in rheumatology.
- A bespoke programme was developed, with a combination of lectures, practical workshops and case-based discussions.
- Ninety per cent of delegates rated the course as practice changing, confirming the impact of educational initiatives.

Introduction

The British Society for Rheumatology (BSR) is the UK's leading specialist medical society for rheumatology and musculoskeletal professionals, with a wide membership consisting of practising physicians, clinical and non-clinical academics and allied health professionals. One of the BSR remits is to support its members throughout their careers, allowing them to progress, collaborate and innovate so that they can deliver the best care for children and adults with rheumatic musculoskeletal diseases. To achieve this, BSR provides a wide range of high-quality courses to support the ongoing professional development of its membership.

In 2020, a group of physicians from the University of Leeds proposed a dedicated BSR sponsored SpA course. SpA is an umbrella term for a heterogeneous group of conditions that includes axial spondyloarthritis (axSpA), PsA, ReA and IBD-associated arthritis, which share a number of clinical and genetic characteristics. Despite a combined overall prevalence similar to that of RA, the study of SpA was historically neglected, largely

[1]NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, [3]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford and [4]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK

Submitted 18 June 2020; accepted: 3 August 2020

Correspondence to: Helena Marzo-Ortega, LIRMM, Second Floor, Chapel Allerton Hospital, Chapeltown Road, Leeds LS7 4SA, UK. E-mail: medhmo@leeds.ac.uk

REVIEW

owing to the lack of reliable diagnostic and classification criteria and the absence of efficacious therapies. Furthermore, awareness of SpA, particularly in its axial form, is variable and often poor among secondary and primary care clinicians in the UK [1, 2]. The advent of biologics and sensitive imaging techniques, such as US and MRI, at the turn of the 21st century allowed for a complete re-appraisal of these diseases, leading to significant, rapidly evolving advances in the knowledge of pathogenesis, diagnosis and treatment options. Yet, despite these changes, SpA remains a niche area of interest within rheumatology, with a limited number of dedicated specialists and researchers and with a general lack of specialist, tertiary clinics worldwide.

The 2020 BSR SpA Course offered rheumatology health-care professionals the opportunity to update their basic knowledge of SpA with a review of the latest advances in the field. The course was conceived as a 1-day combination of educational lectures, practical workshops and clinical case-based discussions facilitated by leading experts. Attendance was restricted to 30 delegates to allow for maximal interaction with the presenters and workshop participation. The purpose of this review is to summarize the key presentations from the 2020 BSR SpA Course and reflect on the value of this initiative based on the feedback provided by the attending delegates.

Lectures

Philip Helliwell: historical aspects

Professor Helliwell gave a brief summary of the recognition of SpA from the middle of the 20th century to the present time. The SpA concept was developed in Leeds by the rheumatologists Professor Verna Wright and Dr John Moll [3]. Although laboratory tests, such as RF, and X-ray imaging helped the synthesis and formulation of their ideas, the concept was largely based on careful clinical observation, and was contemporaneously supported by the discovery of HLA-B27 by Brewerton *et al.* [4] in London. Wright and colleagues noted the key linking feature to be inflammatory axial involvement and included in the spondyloarthritides AS (as the key central disorder), PsA, the arthritis associated with IBD, ReA and Behcet's syndrome (the last of these being removed in a later publication). Professor Wright built a large cohort of patients in the Rheumatology Regional Centre in Harrogate and in Leeds and passed this along to later researchers, such as Professor Helliwell. From these cohorts, refinements to classification were made. In terms of PsA, the need for a new study became apparent: the ClASsification Criteria for Psoriatic ARthritis (CASPAR) classification study [5]. At the same time, Professor Dennis McGonagle had the vision to see the importance of the enthesis in the pathogenesis of SpA and, together with Professor Michael Benjamin from Cardiff, formulated the concept of the synovio-entheseal complex [6]. Today, Leeds continues to lead research in the pathogenesis and treatment of SpA, truly reflecting its distinguished heritage.

Dennis McGonagle: pathogenesis and pathology in spondyloarthritis

Professor McGonagle summarized the pathogenesis of human SpA and explained how this was historically conceptualized in relationship to early sacroiliitis and a role of microbial triggers leading to an early synovitis with joint erosion. Over two decades, it was firmly established that the earliest lesion in axSpA was osteitis, typically in the subchondral bone adjacent to the fibrocartilage of the sacroiliac joints [7]. It emerged that the diffuse spinal involvement in SpA was also associated with diffuse peri-entheseal osteitis adjacent to the fibrocartilage anchorage points of different entheses. Likewise, enthesitis and adjacent osteitis formed the common denominator for inflammation in the peripheral skeleton and could be likened to SpA-like phenotypes, including arthritis mutilans and SAPHO syndrome. Both laboratory experimental studies and clinical trials have brought into focus that disease in rodents can be biomechanically driven [8] and that disease in humans can be targeted successfully by anti-cytokine therapy, including TNF, IL-17A and IL-23 targeting [9, 10], but the last of these worked only in the peripheral SpA form. Almost a decade ago, it was shown that the normal murine enthesis had a population of lymphocytes in the enthesis soft tissue that appeared to drive disease, but little was known about the enthesis in man.

The immunology of the normal human enthesis is now beginning to emerge, and both the peri-entheseal soft tissue adjacent to fibrocartilage and the underlying bone anchorage points have resident populations of immune cells in health. Both sites have resident myeloid cells that are capable of TNF and IL-23 production [11]. The sites also have resident ILC3 and gamma delta T cell populations that do not express IL-17 transcript in basal conditions but can be induced to do so. Of note, there are two major populations of gamma delta T cells in the spine, and one of these can produce IL-17A protein in an IL-23-independent manner [12]. The human spinal enthesis also has resident $CD4^+$ T cells, and ~2% of these can make IL-17A and are classical Th17 cells. Populations of $CD8^+$ T cells are also present at the enthesis, but with much lower inducible IL-17A production, although TNF is readily inducible. Thus, it is beginning to emerge that all of the cell types and cytokines that are players in SpA in the experimental setting are embedded in the normal enthesis. Studies of diseased tissue are urgently needed to characterize both peripheral and axial entheses better, in order to begin deciphering the emergent differential efficacy of therapies in these conditions. Another cardinal aspect of SpA pathogenesis is the presence of either subclinical or clinical gut involvement. Remarkably, many of the innate cell types, including gamma delta T cells and Mucosal-associated invariant T cells, might play important roles in both gut and skeletal homeostasis, although how this

gut–enthesis axis operates in SpA initiation and perpetuation remains largely unknown.

Philip Helliwell: clinical presentation and diagnosis of PsA

Professor Helliwell discussed the development of CASPAR classification criteria for PsA and helpful tips in diagnosing and distinguishing the condition. There is often confusion about the purpose of classification criteria, which are often used in the clinic as diagnostic criteria. In fact, in the case of the CASPAR classification criteria, there is evidence that these criteria do work well as diagnostic criteria [5], the exceptions being in the very early disease. It is also reassuring to know that the original Moll and Wright criteria [3] are incorporated within the new criteria. However, it might be time for a new set of criteria for two reasons: problems with the stem (inflammatory musculoskeletal disease), and the advent of new imaging, such as US.

In the clinic, there is usually no problem diagnosing PsA (80% of patients have psoriasis at disease onset), but difficulties in recognizing psoriasis and locating the disease in hidden areas sometimes mislead the assessor. Hallmark clinical features, such as dactylitis, enthesitis and axial involvement, are helpful pointers. Areas of uncertainty include DIP joint predominance and the possibility of nodal OA, chronic gout, which may present with dactylitis, and seronegative RA. Key radiological features, such as osteolysis and new bone formation, are not early features, although US can help if enthesitis is a marked feature. A key message was not to minimize the importance of PsA in terms of disability and poor quality of health; the patient may have oligoarthritis, a few entheseal tender points and a patch of psoriasis, but we know that the impact of the disease long term is just as bad as with RA, meaning that early aggressive treatment is recommended.

Helena Marzo-Ortega: clinical presentation and diagnosis of axSpA

There are many challenges in the diagnosis of SpA, because no specific diagnostic criteria exist, which has led to much confusion arising in recent years with the use of classification criteria in clinical practice. Dr Marzo-Ortega stressed that the diagnosis of axSpA should be based on the recognition of clinical symptoms, with laboratory and imaging features, taking into account any possible differential diagnosis. Classification criteria, in contrast, can be applied only once the diagnosis has been made. The characteristics of the different classification criteria were discussed (Fig. 1). The modified New York criteria developed in 1984 [13], for example, are highly specific for radiographic axSpA (r-axSpA), also known as AS. The subsequently developed Amor and ESSG criteria aim to classify the wider SpA group and incorporate features such as extra-articular manifestations. They allow for the recognition of an undifferentiated SpA subgroup but do not differentiate between the others (i.e. axSpA, PsA and peripheral SpA). The Assessment of SpondyloArthritis (ASAS) criteria were developed in 2009 [14], with the purpose of allowing the classification of two homogeneous groups (predominantly axial and predominantly peripheral), in an attempt to focus research efforts into these two main disease subsets.

In axSpA, the ASAS criteria allow for disease classification to be made according to the imaging arm or the clinical arm. The imaging arm has higher sensitivity and specificity because it is weighted towards imaging evidence of sacroiliitis, identified either by structural changes on plain radiographs (X-ray) or by the presence of active bone marrow oedema representative of inflammation on MRI. The criteria therefore allow for the identification of a non-radiographic subgroup, which can be identified either by inflammatory changes on MRI or by the presence of HLA-B27 and clinical features (clinical arm). However, there are many shortcomings with X-ray and MRI interpretation owing to the poor reliability of structural changes with the former and the low specificity of the latter. The recently published British Society of Spondyloarthritis (BRITSpA) guidelines in the interpretation of MRI in axSpA [15] were discussed, and different case scenarios were given to illustrate how to make a clinical diagnosis of axSpA and the correct utilization of available criteria.

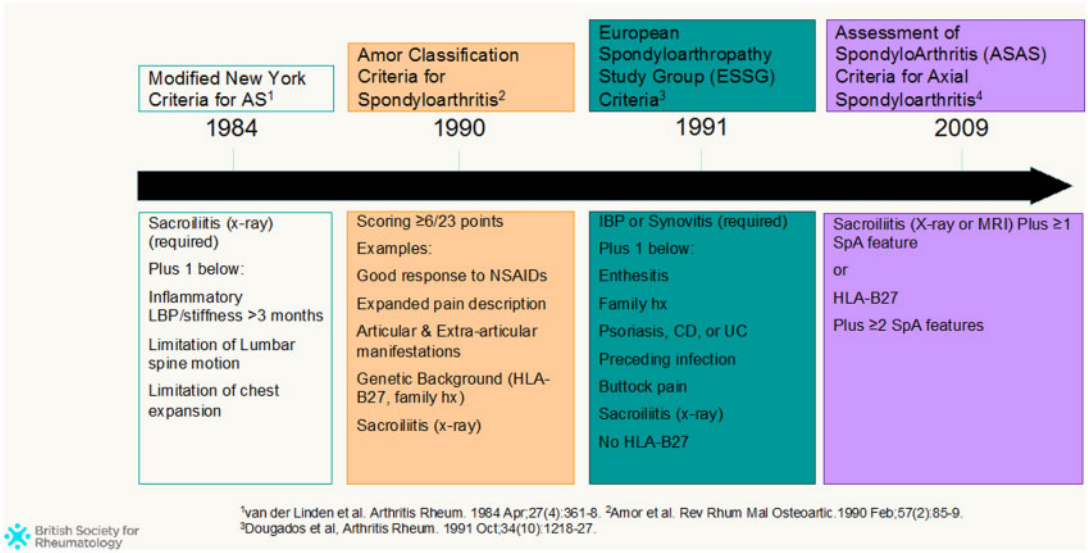
Ai Lyn Tan: imaging in SpA

Dr Tan highlighted the two main areas of application for imaging in SpA, namely in clinical practice and in the research setting [16–18]. The clinical use of imaging in SpA is supported by EULAR, who outlined its usefulness; in particular, the use of MRI and US [19]. The presentation focused on the research applications of MRI and US in SpA owing to their significant contributions to enhancing our understanding of the pathogenesis of SpA [20, 21].

Dr Tan showcased how complementary data from histology often improve the further understanding of the imaging findings. For example, in Achilles enthesis, histology helped explain the imaging observation of the precise distribution of new bone formation or enthesopathy and erosive changes and showed that the respective differential locations are related to the trabecular alignment within the calcaneum [22].

The digits are another good model for understanding the involvement of the enthesis in SpA owing to their relatively compact anatomy and close proximity with the nails and skin, all of which can be affected in PsA [23, 24]. High-resolution MRI and US with histology demonstrated that the pathological changes in the bones, tendons and nails all share a common anatomical link with various entheses that can therefore lead to diffuse inflammatory changes [25–29]. Functional enthesitis, which results from abnormal friction according to a pulley system, is well demonstrated in the extensor and flexor tendons of the digits on both MRI and US, which

Fig. 1 Historical look at the classification criteria for spondyloarthritis



IBP: inflammatory back pain; LBP: low back pain.

explains the diffuse swelling of dactylitis seen in PsA [25, 28, 30–32].

Imaging has therefore contributed significantly to the knowledge regarding the synovio-entheseal complex [33]. Dr Tan used the analogy of the parable of the blind people and an elephant to illustrate the appreciation of the sites of pathology in SpA, from the key anatomy, comprising the tendons/ligaments, synovium, joint capsule and bone, to the initial description of the enthesis, the interplay of these structures in the enthesis organ, and culminating in their synergistic roles in the synovio-entheseal complex [34–38] (Fig. 2).

Laura Coates: management of PsA

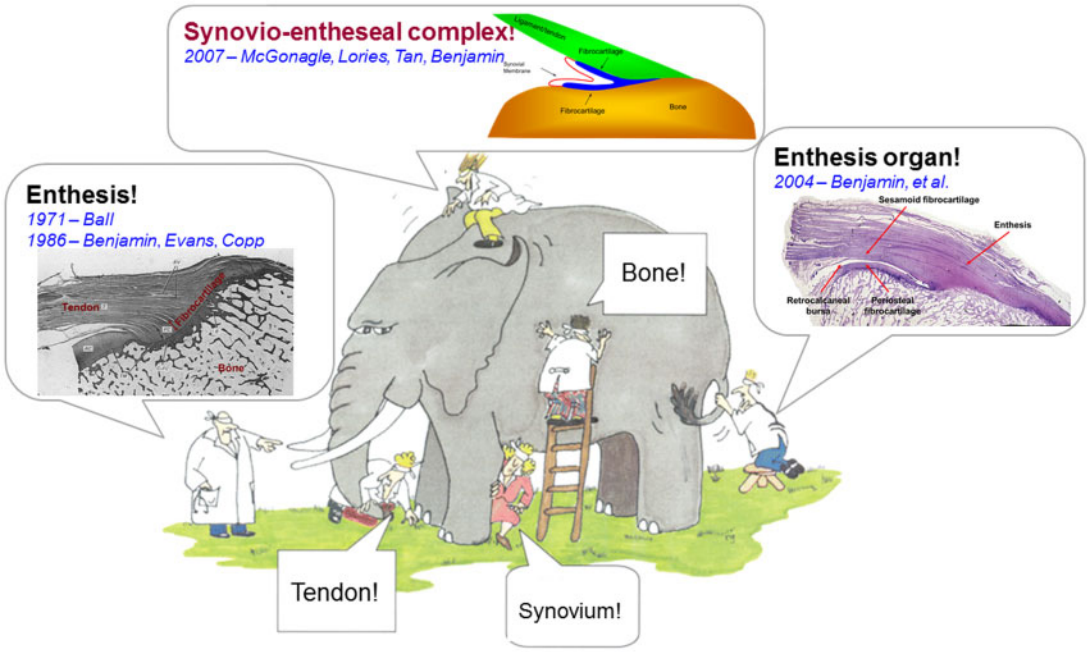
Dr Coates presented a brief update on the management of PsA. She opened by summarizing the overarching principles of treatment from the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines [39] and then talked through data on currently available therapies. She highlighted recent data on MTX, given the controversies over its evidence in PsA, in addition to data for other conventional systemic DMARDs. She discussed data for the currently available biologic and targeted synthetic DMARDs, including data from a new trial addressing the efficacy of secukinumab in axial PsA: the first large randomized controlled trial in axial PsA ever performed. She then showed recent data from new therapies in development for PsA, including bimekizumab, IL-23 inhibitors and selective Janus Kinase1 inhibitors.

Dr Coates then went on to discuss studies that might help to differentiate treatments in different domains of PsA. She summarized data from head-to-head trials in peripheral arthritis [40, 41] and enthesitis [42] before summarizing the strengths and weaknesses of the currently available targeted therapies. Finally she discussed the concept of treat to target in PsA, following the data from the tight control of inflammation in early psoriatic arthritis (TICOPA) trial [43] and international recommendations on the implementation of treat to target [44]. She highlighted the impact this can have in routine clinical practice and the availability of the GRAPPA app, which includes a minimal disease activity calculator in addition to a Psoriasis Area and Severity Index calculator, psoriatic arthritis impact of disease and psoriasis epidemiology screening tool. This is free to download and available in multiple languages.

Stefan Siebert: management of axSpA

Dr Siebert presented a brief update on the management of axSpA. He started by highlighting that management should be individualized and requires a multidisciplinary approach, with the primary goal of maximizing health-related quality of life. Key aspects of non-pharmacological management are education, exercise, physical therapy and smoking cessation. He covered the range of pharmacological treatment options available for axSpA. He highlighted the efficacy of NSAIDs for symptomatic improvement in axSpA and then discussed the controversy relating to the effect of high-dose NSAIDs on radiographic progression, with early studies suggesting a possible benefit, which was not confirmed in the subsequent ENRADAS trial [45].

Fig. 2 Evolution of the understanding of the synovio-entheseal complex



The blind people and the elephant analogy is used here to explain the conceptual understanding of the synovio-entheseal complex over the past decades. The basic structures (i.e. the tendon/ligament or joint capsule and bone), when put together, form the early description of the enthesis. The enthesis organ was later acknowledged owing to the function of the enthesis in close proximity to other structures, such as the fibrocartilage. More recently, with further advances in understanding of the pathogenesis of SpA, the interplay with the synovium that contributes synergistically to the inflammatory process of enthesitis led to the term synovio-entheseal complex [37, 38]. Adapted from a poem by John Godfrey Saxe (Cartoon originally copyrighted by the authors; G. Renee Guzlas, artist).

Dr Siebert then discussed the ASAS/EULAR and BSR treatment recommendations for biologic DMARDs in axSpA [46, 47]. He showed data indicating that both TNF and IL-17A inhibition were associated with reduced radiographic progression in the long term, with control of disease activity being the key factor. He also described the failure of IL-23 inhibition with both ustekinumab (p40) [48] and risankizumab (p19) [49] in axSpA and reminded the audience that SpA is characterized by inflammation at multiple tissue sites with differential responses to cytokine inhibitors [50]. He outlined factors, such as extra-articular manifestations, co-morbidities and cost, that can help to inform the choice of biologic in patients with axSpA in the absence of head-to-head studies. The final part of the talk described potential new therapies in development, including Janus Kinase1 inhibitors and other strategies to inhibit IL-17 signalling.

Workshops

Three workshops and a case-based facilitated discussion were held.

David Pickles: skin and nails

The workshop began with a brief overview on the prevalence of nail disease in PsA [51, 52] and its impact on patients' experience of pain and functional impairment, including a revision of the anatomy and physiology of the nail bed and matrix and the different pathologies that can arise from these structures. Delegates were introduced to the Nail Psoriasis Severity Index (NAPSI), a validated tool for the evaluation of nail psoriasis that is reproducible, objective and simple to use. Delegates learnt how to calculate the Psoriasis Area and Severity Index (PASI), the most widely used tool for the measurement of severity of skin psoriasis, whereby lesions are appraised for the grade of erythema, desquamation, induration and extent, in order to calculate the final score. PsA is a very heterogeneous disease; therefore, delegates were reminded of the need to quantify the different manifestations of disease regularly, in order to optimize treatment. Delegates were informed about various smartphone apps to assist with this task.

Sayam Dubash: the spine and dactylitis

Spinal mobility measurements or axial clinimetrics in SpA are performed in both clinical and research settings. These were discussed in detail, including practical methods and demonstration of measurements and calculations using the different BASMI definitions: the linear or 10-step, recommended by ASAS, and the original two-step method. Dactylitis is the pathognomonic

Table 1 Guidelines and recommendations for SpA in the last 5 years

Guidelines	Disease	Society	Year	Recommendations	Reference
EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update	PsA	EULAR	2019	Pharmacological management	[55]
2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis	SpA, RA, OA	EULAR	2018	Physical activity	[56]
EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis	AS, SpA, RA, OA	EULAR	2018	Pain management	[57]
BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics	axSpA	BSR	2017	Pharmacological management	[47]
2016 update of the ASAS–EULAR management recommendations for axial spondyloarthritis	axSpA	ASAS–EULAR	2016	Non-pharmacological and pharmacological treatment	[46]
EULAR recommendations for cardiovascular disease risk management in patients with RA and other forms of inflammatory joint disorders: 2015/2016 update	AS, PsA, RA	EULAR	2015–2016	Cardiovascular disease risk management	[58]
EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice	SpA	EULAR	2015	Imaging use	[19]
EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update	PsA	EULAR	2015	Pharmacological management	[59]
Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis	PsA	GRAPPA	2015	Pharmacological management	[39]
EULAR recommendations for patient education for people with inflammatory arthritis	AS, SpA, RA	EULAR	2015	Patient education	[60]

ASAS: Assessment of SpondyloArthritis; axSpA: axial spondyloarthritis; BSR: British Society for Rheumatology, BHPR: British Health Professionals in Rheumatology; GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis.

peripheral clinical lesion in SpA. A summary of the pathophysiology of dactylitis followed by a clinical discussion of differential diagnoses, including a hands-on experience with the dactylometer, was illustrated, leading to working through a case study to calculate the Leeds dactylitis index (LDI).

Claire Vandevelde: joints and enthesitis

The enthesitis workshop discussed the clinical difficulties in the recognition of enthesitis because these lesions are not generally associated with diffuse swelling and can also be hard to differentiate from OA- or FM-type pain. The role of imaging, and US in particular, as a clinical adjunct for diagnosis facilitation was also discussed. The ongoing difficulty in the evaluation of enthesitis was recognized.

Cased-based discussions

A series of real-life cases were presented, focusing on oligo-articular disease, axial involvement, co-morbidities and treatment failures. Each presentation consisted of a history, examination, laboratory tests and imaging, and each section was followed by questions for the audience with input from the specialist presenters, making the process interactive throughout. Before the meeting, delegates were encouraged to present their own difficult

or interesting cases, and one such presentation was made and discussed by the group.

Discussion

Continuing medical education refers to the need for those working in medical disciplines to maintain competence and learn about new and developing areas of their field to continue improving patient care. Offering health-care professionals high-quality continuous education leads to leveraging excellence in health-care performance. This education can be delivered in multiple formats, such as live conferences, written publications or via online programmes or electronic media. The advantages of investing in continuous education are many, but chiefly aim for highly skilled professionals and better patient outcomes. Nevertheless, there is no clear regulation of how this continuing medical education should be delivered, with the majority of provision being via the scientific meetings of professional bodies or funded by the pharmaceutical industry rather than through the National Health Service or dedicated educational courses.

The 2020 BSR SpA Course was put together to address an unmet demand for clinical education across the wide spectrum of SpA. The recently published National Institute of Health and Care Excellence (NICE) NG65 guideline for diagnosing and managing SpA [53] and related quality standards [54] aim to raise awareness of the features of SpA. These, together with other guidelines and recommendations published in recent years (Table 1), provide clear advice on what action to take when people with signs and symptoms first present in health-care settings and on the range of treatments available. Nevertheless, a recent survey showed that only half of rheumatology services in the UK have a dedicated SpA clinic [61].

In the BSR course, one-third of attending delegates were allied health professionals and primary care physicians, with the rest being rheumatology clinicians (consultants, trainees and specialty doctors), reflecting the interest in SpA education outside secondary care. Indeed, the majority of delegates (>90%) reported 'improving their knowledge' as the main reason for attending the course, with 70% reporting having attended other BSR educational meetings in the past. The overall level of satisfaction with the course (individual speaker quality, content) was very high (weighted average 4.3 of 5). One of the main comments was related to the value of understanding how the experts incorporate research or newly reported data into their clinical practice, with 94% of delegates reporting that attending the course would change the way they work.

Conclusions

The 2020 BSR SpA Course brought together UK clinical and academic experts in the SpA field with key presentations on the latest developments in pathogenesis, clinical challenges and treatment options in axSpA and PsA and with excellent feedback from attending delegates, who stated their willingness to attend similar courses in the future. The challenge remains how best to deliver and disseminate high-quality education in this rapidly evolving field. Specialist organizations, such as BSR or the more recently created British Society for Spondyloarthritis (BRITSpA), are ideally positioned to lead this challenge and educate UK-based rheumatology health-care professionals in the complexities of SpA.

Acknowledgements

H.M.-O., A.L.T., D.M., D.P., S.D., C.Y.V. and P.H. are supported by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre. L.C.C. is supported by the NIHR Oxford Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the (UK) National Health Service (NHS), the NIHR or the (UK) Department of Health.

Funding: No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: H.M.-O. has received research grants from Janssen, Novartis and consultancy fees/honoraria from Abbvie, Celgene, Eli-Lilly, Janssen, Novartis, Pfizer, Takeda and UCB. A.L.T. has received research grants from Abbvie, and honoraria for advisory boards and speaking from Abbvie, Lilly, Janssen, Novartis and Pfizer. C.Y.V. has received consultancy fees/honoraria from Abbvie, Celgene, Internis, Novartis and UCB. L.C.C. has received research grants from Abbvie, Celgene, Lilly, Novartis and Pfizer and consultancy fees/honoraria from Abbvie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Gilead, Janssen, Eli Lilly, Medac, Novartis, Pfizer and UCB. S.S. has received research grants, speaker or consultancy fees from AbbVie, BMS, Boehringer-Ingelheim, Celgene (now Amgen), GSK, Janssen, Novartis, Pfizer and UCB. The other authors have declared no conflicts of interest.

References

1 Mathieson HR, Merashli M, Gaffney K, Marzo-Ortega H, On behalf of BRITSpA (British Society for Spondyloarthritis). Poor awareness of inflammatory back pain and axial spondyloarthritis among secondary care specialists. Clin Rheumatol 2016;35:2627–8.

2 Jois RN, Macgregor AJ, Gaffney K. Recognition of inflammatory back pain and ankylosing spondylitis in primary care. Rheumatology (Oxford) 2008;47:1364–6.

3 Wright V, Moll JMH. Seronegative polyarthritis. Amsterdam: North Holland Publishing Co., 1976.

4 Brewerton DA, Hart FD, Nicholls A, *et al.* Ankylosing spondylitis and HL-A27. Lancet 1973;302:994–6.

5 Taylor W, Gladman D, Helliwell P *et al.* Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54: 2665–73.

6 Benjamin M, McGonagle D. The enthesis organ concept and its relevance to the spondyloarthropathies. Adv Exp Med Biol 2009;649:57–70.

7 Bennett AN, McGonagle D, O'Connor P *et al.* Severity of baseline magnetic resonance imaging-evident sacroiliitis and HLA-B27 status in early inflammatory back pain predict radiographically evident ankylosing spondylitis at eight years. Arthritis Rheum 2008;58:3413–8.

8 McGonagle D, Thomas RC, Schett G. Spondyloarthritis: may the force be with you? Ann Rheum Dis 2014;73: 321–3.

9 Dubash S, Bridgewood C, McGonagle D, Marzo-Ortega H. The advent of IL-17A blockade in ankylosing spondylitis: secukinumab, ixekizumab and beyond. Exp Rev Clin Immunol 2019;15:123–34.

10 Marzo-Ortega H, McGonagle D, O'Connor P, Emery P. Efficacy of etanercept in the treatment of the entheseal pathology in resistant spondylarthropathy: a clinical and magnetic resonance imaging study. Arthritis Rheum 2001;44:2112–7.

11 Bridgewood C, Sharif K, Sherlock J, Watad A, McGonagle D. Interleukin-23 pathway at the enthesis: The emerging story of enthesitis in spondyloarthropathy. Immunol Rev 2020;294:27–47.

12 Cuthbert RJ, Watad A, Fragkakis EM *et al.* Evidence that tissue resident human enthesis $\gamma\delta$T-cells can produce IL-17A independently of IL-23R transcript expression. Ann Rheum Dis 2019;78:1559–65.

13 van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.

14 Rudwaleit M, van der Heijde D, Landewé R *et al.* The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 2009;68:777–83.

15 Rusman T, John MB, van der Weijden MAC *et al.* Presence of active MRI lesions in patients suspected of non-radiographic axial spondyloarthritis with high disease activity and chance at conversion after a 6-month follow-up period. Clin Rheumatol 2020;39: 1521–9.

16 Tan AL, McGonagle D. The need for biological outcomes for biological drugs in psoriatic arthritis. J Rheumatol 2016;43:3–6.

17 Coates LC, Anderson RR, Fitzgerald O *et al.* Clues to the pathogenesis of psoriasis and psoriatic arthritis from imaging: a literature review. J Rheumatol 2008;35: 1438–42.

18 Braum LS, McGonagle D, Bruns A *et al.* Characterisation of hand small joints arthropathy using high-resolution MRI—limited discrimination between osteoarthritis and psoriatic arthritis. Eur Radiol 2013;23:1686–93.

19 Mandl P, Navarro-Compán V, Terslev L *et al.* EULAR recommendations for the use of imaging in the diagnosis and management of spondyloarthritis in clinical practice. Ann Rheum Dis 2015;74:1327–39.

20 Tan AL, McGonagle D. Imaging of seronegative spondyloarthritis. Best Pract Res Clin Rheumatol 2008; 22:1045–59.

21 Tan AL, McGonagle D. Psoriatic arthritis: correlation between imaging and pathology. Joint Bone Spine 2010; 77:206–11.

22 McGonagle D, Wakefield RJ, Tan AL *et al.* Distinct topography of erosion and new bone formation in Achilles tendon enthesitis: implications for understanding the link between inflammation and bone formation in spondylarthritis. Arthritis Rheum 2008;58:2694–9.

23 McGonagle D, Palmou Fontana N, Tan AL, Benjamin M. Nailing down the genetic and immunological basis for psoriatic disease. Dermatology 2010;221: 15–22.

24 Tan AL, Tanner SF, Waller ML *et al.* High-resolution [^{18}F]fluoride positron emission tomography of the distal interphalangeal joint in psoriatic arthritis—a bone–enthesis–nail complex. Rheumatology (Oxford) 2013;52: 898–904.

25 McGonagle D, Tan AL, Benjamin M. The nail as a musculoskeletal appendage—implications for an improved understanding of the link between psoriasis and arthritis. Dermatology 2009;218:97–102.

26 McGonagle D, Benjamin M, Tan AL. The pathogenesis of psoriatic arthritis and associated nail disease: not autoimmune after all? Curr Opin Rheumatol 2009;21: 340–7.

27 McGonagle D, Tan AL, Benjamin M. The biomechanical link between skin and joint disease in psoriasis and psoriatic arthritis: what every dermatologist needs to know. Ann Rheum Dis 2008;67:1–4.

28 Tan AL, Benjamin M, Toumi H *et al.* The relationship between the extensor tendon enthesis and the nail in distal interphalangeal joint disease in psoriatic arthritis—a high-resolution MRI and histological study. Rheumatology (Oxford) 2006;46:253–6.

29 McGonagle D, Hermann KG, Tan AL. Differentiation between osteoarthritis and psoriatic arthritis: implications for pathogenesis and treatment in the biologic therapy era. Rheumatology (Oxford) 2015;54:29–38.

30 McGonagle D, Tan AL, Watad A, Helliwell P. Pathophysiology, assessment and treatment of psoriatic dactylitis. Nat Rev Rheumatol 2019;15:113–22.

31 Tinazzi I, McGonagle D, Aydin SZ *et al.* 'Deep Koebner' phenomenon of the flexor tendon-associated accessory pulleys as a novel factor in tenosynovitis and dactylitis in psoriatic arthritis. Ann Rheum Dis 2018;77:922–5.

32 Girolimetto N, Macchioni P, Tinazzi I *et al.* Ultrasonographic evidence of predominance of acute extracapsular and chronic intrasynovial patterns in 100 cases of psoriatic hand dactylitis. J Rheumatol 2020;47: 227–33.

33 McGonagle D, Tan AL. The enthesis in psoriatic arthritis. Clin Exp Rheumatol 2015;33(5 Suppl 93):S36–9.

34 Benjamin M, Evans EJ, Copp L. The histology of tendon attachments to bone in man. J Anat 1986;149:89–100.

35 Ball J. Enthesopathy of rheumatoid and ankylosing spondylitis. Ann Rheum Dis 1971;30:213–23.

36 Benjamin M, Moriggl B, Brenner E *et al.* The "enthesis organ" concept: why enthesopathies may not present as focal insertional disorders. Arthritis Rheum 2004;50: 3306–13.

37 McGonagle D, Lories RJ, Tan AL, Benjamin M. The concept of a "synovio-entheseal complex" and its implications for understanding joint inflammation and damage in psoriatic arthritis and beyond. Arthritis Rheum 2007;56:2482–91.

38 McGonagle D, Aydin SZ, Tan AL. The synovio-entheseal complex and its role in tendon and capsular associated inflammation. J Rheumatol Suppl 2012;89: 11–4.

39 Coates LC, Kavanaugh A, Mease PJ *et al.* Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 treatment recommendations for psoriatic arthritis. Arthritis Rheumatol 2016;68:1060–71.

40 Mease PJ, Gladman DD, Collier DH *et al.* Etanercept and methotrexate as monotherapy or in combination for psoriatic arthritis: primary results from a randomized controlled phase III trial. Arthritis Rheumatol 2019;71: 1112–24.

41 Mease PJ, Smolen JS, Behrens F *et al.* Multicentre, randomised, open-label, assessor-blinded, parallel-group head-to-head comparison of the efficacy and safety of ixekizumab versus adalimumab in patients with psoriatic arthritis naive to biologic disease-modifying anti-rheumatic drugs: 24-week results. Ann Rheum Dis 2019;78 (suppl 2):A261.

42 Araujo EG, Englbrecht M, Hoepken S *et al.* Effects of ustekinumab versus tumor necrosis factor inhibition on enthesitis: results from the enthesial clearance in psoriatic arthritis (ECLIPSA) study. Semin Arthritis Rheum 2019;48:632–7.

43 Coates LC, Moverley AR, McParland L *et al.* Effect of tight control of inflammation in early psoriatic arthritis (TICOPA): a UK multicentre, open-label, randomised controlled trial. Lancet 2015;386:2489–98.

44 Smolen JS, Schöls M, Braun J *et al.* Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Ann Rheum Dis 2018;77:3–17.

45 Sieper J, Listing J, Poddubnyy D *et al.* Effect of continuous versus on-demand treatment of ankylosing spondylitis with diclofenac over 2 years on radiographic progression of the spine: results from a randomised multicentre trial (ENRADAS). Ann Rheum Dis 2016;75: 1438–43.

46 van der Heijde D, Ramiro S, Landewé R *et al.* 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis 2017;76: 978–91.

47 Hamilton L, Barkham N, Bhalla A *et al.* BSR and BHPR guideline for the treatment of axial spondyloarthritis (including ankylosing spondylitis) with biologics. Rheumatology (Oxford) 2017;56:313–6.

48 Deodhar A, Gensler LS, Sieper J *et al.* Three multicenter, randomized, double-blind, placebo-controlled studies evaluating the efficacy and safety of ustekinumab in axial spondyloarthritis. Arthritis Rheumatol 2019;71:258–70.

49 Baeten D, Østergaard M, Wei JC *et al.* Risankizumab, an IL-23 inhibitor, for ankylosing spondylitis: results of a randomised, double-blind, placebo-controlled, proof-of-concept, dose-finding phase 2 study. Ann Rheum Dis 2018;77:1295–302.

50 Siebert S, Millar NL, McInnes IB. Why did IL-23p19 inhibition fail in AS: a tale of tissues, trials or translation? Ann Rheum Dis 2019;78:1015–8.

51 Brazzelli V, Carugno A, Alborghetti A *et al.* Prevalence, severity and clinical features of psoriasis in fingernails and toenails in adult patients: Italian experience. J Eur Acad Dermatol Venereol 2012;26:1354–9.

52 Williamson L, Dalbeth N, Dockerty JL *et al.* Extended report: nail disease in psoriatic arthritis—clinically important, potentially treatable and often overlooked. Rheumatology (Oxford) 2004;43:790–4.

53 Spondyloarthritis in over 16s: diagnosis and management. NICE guideline [NG65]. National Institute of Health and Care Excellence; 2017. https://www.nice.org.uk/guidance/ng65 (24 August 2020, date last accessed).

54 Spondyloarthritis Quality standard [QS170]. National Institute of Health and Care Excellence, 2018. https://www.nice.org.uk/guidance/qs170 (24 August 2020, date last accessed).

55 Gossec L, Baraliakos X, Kerschbaumer A *et al.* EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020;79:700–12.

56 Rausch Osthoff AK, Niedermann K, Braun J *et al.* 2018 EULAR recommendations for physical activity in people with inflammatory arthritis and osteoarthritis. Ann Rheum Dis 2018;77:1251–60.

57 Geenen R, Overman CL, Christensen R *et al.* EULAR recommendations for the health professional's approach to pain management in inflammatory arthritis and osteoarthritis. Ann Rheum Dis 2018;75:797–807.

58 Agca R, Heslinga SC, Rollefstad S *et al.* EULAR recommendations for cardiovascular disease risk management in patients with rheumatoid arthritis and other forms of inflammatory joint disorders: 2015/2016 update. Ann Rheum Dis 2017;76:17–28.

59 Gossec L, Smolen JS, Ramiro S *et al.* European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2016;75: 499–510.

60 Zangi HA, Ndosi M, Adams J *et al.* EULAR recommendations for patient education for people with inflammatory arthritis. Ann Rheum Dis 2015;74:954–62.

61 Derakhshan MH, Pathak H, Cook D *et al.* Services for spondyloarthritis: a survey of patients and rheumatologists. Rheumatology (Oxford) 2018;57: 987–96.