

## Expert reviews in clinical immunology

### How Can Primary Care Physicians Enhance the Early Diagnosis of Rheumatic Diseases?

#### 1. *Importance of Primary Care in Identifying Inflammatory Rheumatic Diseases*

Primary care is key to the early diagnosis and ongoing care of people with inflammatory rheumatic diseases. Primary care is usually the first point of call for health problems and is the setting where most health care occurs. Indeed, in the UK >90% of all patient contacts occur in primary care, with most encounters being with a general practitioner (GP).

Musculoskeletal disorders represent a significant proportion of primary care consultations, with up to 20% of adults seeking help from their GP every year for such problems [1]. Most consultations are managed exclusively in the community, with no need for onward referral to specialist services. Whilst this is often appropriate for common conditions like low back pain and osteoarthritis, patients with suspected inflammatory arthritis may need alternative care pathways to optimise outcomes.

#### 2. *Benefits of Early Diagnosis of Inflammatory Arthritis*

For rheumatoid arthritis (RA), which represents the commonest form of inflammatory arthritis, there is a substantial evidence base that early diagnosis and prompt treatment with disease-modifying anti-rheumatic drugs (DMARDs) improves patient outcomes. This has led to the concept of a “window-of-opportunity” with the first few months of symptom onset representing a pathologically distinct phase of RA, during which outcomes are more effectively modulated by treatment [2]. Although less well established, there is growing evidence that similar benefits of early treatment are seen in other forms of inflammatory arthritis, for example psoriatic arthritis [3].

#### 3. *Challenges in Identifying Inflammatory Arthritis*

In England and Wales, the benefits of early diagnosis and treatment have led to a Quality Standard from the National Institute for Health and Care Excellence (NICE) that patients with suspected persistent synovitis are referred by GPs to specialists within 3-working days of presentation. A recent national audit has, however, demonstrated that this standard is met in only 17% of patients, with one-quarter waiting >3 months for referral [4]. For GPs, the challenge is to identify patients who potentially have an inflammatory arthritis from those who do not, at an early stage of their illness and refer them for urgent specialist review. This is seldom straight-forward for several reasons.

Firstly, incident inflammatory arthritis is rare. The estimated annual incidence of RA lies between 15-40 cases per 100,000 adults [5,6]. Therefore, the average full-time GP will only encounter approximately one new case of RA annually. Compare this to the daily workload, where joint pain is a common occurrence, and the challenges faced by GPs in correctly identifying and referring new-onset inflammatory arthritis become apparent.

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Secondly, patients with inflammatory arthritis may not present with classical “text-book” features. If a middle-aged female presents with bilateral, symmetrical small joint swelling and early morning stiffness, GPs can rapidly identify a potential inflammatory arthritis and refer onto specialist services. However, many patients have non-specific symptoms in the early phases of their disease, such as numbness and weakness [7], or present in an atypical manner, such as a palindromic arthritis. These atypical and non-specific presentations can delay GP recognition and referral.

Thirdly, patients commonly report symptoms suggestive of an inflammatory arthritis in the absence of such a condition. This was highlighted in a recent survey by Hider et al, who sent a self-completion questionnaire to >10,000 patients consulting their GPs for musculoskeletal and non-musculoskeletal complaints [8]. Although symptoms suspicious of inflammatory arthritis were more frequent in patients consulting their GP for musculoskeletal problems, 75%, 37% and 64% of patients consulting their GPs for non-musculoskeletal issues also reported joint pain, swelling and stiffness, respectively.

### *4. How Do GPs Decide Who to Refer?*

At a time when primary care is increasingly under pressure to avoid unnecessarily referrals to specialists, how does a GP decide who needs specialist review? One strategy GPs commonly employ to “identify” patients with new-onset RA is to perform a rheumatoid factor (RF) test in those with suspicious clinical features. This practice was highlighted in a GP survey performed by our research group at Keele University, which had responses from 1,388 GPs about the challenges they face in diagnosing and referring RA patients (the RA Questionnaire (RA-QUEST) study; unpublished data). Of those GPs surveyed, 74% said they would request investigations to inform their referral decision in a patient in whom they suspected RA, with 95% of those requesting investigations stating they would perform an RF-test.

Such widespread use of RF testing in primary care, where the pre-test probability of RA is low, is not however supported by research evidence. In an analysis of the Clinical Practice Research Datalink (a large, UK, primary care consultation database) Miller et al reported that the sensitivity of RF was low at 57.8%, with a poor negative likelihood ratio of 0.5 (95% CI 0.4-0.5) [9]. In this analysis, a negative RF test is also associated with a longer referral delay (the median referral time was 67 days in those with a negative RF test vs. 22 days in those with a positive RF test). Negative results may, therefore be falsely reassuring to physicians and can lead to significant delays in diagnosis and treatment.

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### 5. *How Can We Support GPs to Improve the Early Diagnosis of Inflammatory Rheumatic Diseases?*

The lack of rheumatology training at under and post-graduate level is well documented, and despite repeated calls to address this imbalance the amount of rheumatology teaching in the curriculum has remained unchanged for 20 years [10,11]. There is emerging evidence, however, that targeted education can improve referrals of suspected inflammatory arthritis patients. A systematic review of strategies to reduce delays in the diagnosis/treatment of inflammatory arthritis patients, identified 8 studies of methods to improve primary care provider knowledge [12]. These spanned workshops, joint consultations with rheumatologists, tele-clinics, and educational material. All studies reported some success in improving knowledge and ability in detecting inflammatory arthritis and/or quality of the referral process. Since this review was published the benefits of a targeted education program in increasing referral rates in simulated patients with an axial/peripheral spondyloarthritis has also been demonstrated [13]. In this study, the proportion of GPs that would refer a simulated patient with features of an axial spondyloarthritis increased from 6% to 77% following the educational intervention.

Another strategy is to develop decision aids that GPs could use in patients with arthralgia to identify those at high-risk for progression to an inflammatory arthritis requiring urgent referral. A recent Dutch study demonstrated that rheumatologists have good accuracy at identifying patients with arthralgia that are likely to develop RA [14]. The subjective nature of their assessment, which is experiential, has led to a European League Against Rheumatology (EULAR) task-force developing a points-based definition for patients with arthralgia suspicious for progression to RA [15]. Seven parameters were included in their definition, comprising (1) symptom duration <1 year, (2) symptoms in metacarpophalangeal (MCP) joints, (3) morning stiffness duration  $\geq 60$  minutes, (4) most severe symptoms in early morning, (5) first-degree relative with RA, (6) difficulty with making a fist, and (7) positive squeeze test of MCP joints. The presence of  $\geq 3$  parameters had a 90% sensitivity for identifying patients that experts would classify as being at high-risk of progression to RA; the presence of  $\geq 4$  parameters had a specificity  $>90\%$ . As this definition was derived for use in secondary care, the taskforce agreed further research would be needed to assess its applicability to primary care. Such research is urgently needed.

Finally, breaking down primary-secondary care boundaries and improving access to rapid specialist opinions in patients with suspected new-onset inflammatory arthritis is likely to be important. The RA-QUEST study suggests this represents a significant issue, with 62% of surveyed GPs reporting no access to “early arthritis clinics” (which streamline the referral process offering urgent appointments to patients with persistent synovitis), and 25% rating their ease of access to rheumatology as being  $\leq 5$  out of 10. This is despite evidence that the

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presence of early inflammatory arthritis clinics increasing the chances of a patients with new-onset inflammatory arthritis being seen within 3-weeks of referral [4].

### 6. Conclusion

Whilst primary care is key to the early specialist review of patients with inflammatory rheumatic conditions, the low incidence of these diseases and high-volume of non-inflammatory musculoskeletal pathologies, creates challenges in identifying such patients. An increased focus is needed on GP education around rheumatic diseases, with a particular focus on equipping them with the confidence to identify patients with a new-onset inflammatory arthritis based on clinical features, alongside the development of decision aids suitable for community healthcare professionals. These initiatives need to be aligned with improving access to secondary care advice and services, with an increased uptake of early arthritis clinics and co-creating referral pathways for other inflammatory rheumatic conditions with service users, primary care physicians, and hospital specialists. This will provide the opportunity to both improve patient outcomes and nest high-quality research at the interface between primary and secondary care. Primary and secondary care clinicians have highly complementary skill-sets – now is the time to work more closely together to ensure we can improve outcomes for patients with inflammatory rheumatic diseases.

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### References

- [1] Jordan KP, Kadam UT, Hayward R, et al. Annual consultation prevalence of regional musculoskeletal problems in primary care: an observational study. *BMC Musculoskelet. Disord.* [Internet]. 2010;11:144. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medc&NEWS=N&AN=20598124>.
- [2] Raza K. The Michael Mason prize: early rheumatoid arthritis--the window narrows. *Rheumatology (Oxford).* [Internet]. 2010;49:406–410. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=19955223>.
- [3] Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann. Rheum. Dis.* [Internet]. 2015;74:1045–1050. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=24525911>.
- [4] Ledingham JM, Snowden N, Rivett A, et al. Achievement of NICE quality standards for

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- patients with new presentation of inflammatory arthritis: observations from the National Clinical Audit for Rheumatoid and Early Inflammatory Arthritis. *Rheumatology (Oxford)*. [Internet]. 2017;56:223–230. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=27694337>.
- [5] Rodriguez LAG, Tolosa LB, Ruigomez A, et al. Rheumatoid arthritis in UK primary care: incidence and prior morbidity. *Scand. J. Rheumatol.* [Internet]. 2009;38:173–177. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=19117247>.
- [6] Humphreys JH, Verstappen SMM, Hyrich KL, et al. The incidence of rheumatoid arthritis in the UK: comparisons using the 2010 ACR/EULAR classification criteria and the 1987 ACR classification criteria. Results from the Norfolk Arthritis Register. *Ann. Rheum. Dis.* [Internet]. 2013;72:1315–1320. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=22945499>.
- [7] Stack RJ, van Tuyl LHD, Sloots M, et al. Symptom complexes in patients with seropositive arthralgia and in patients newly diagnosed with rheumatoid arthritis: a qualitative exploration of symptom development. *Rheumatology (Oxford)*. [Internet]. 2014;53:1646–1653. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=24729397>.
- [8] Hider SL, Muller S, Prior J, et al. SAT0708 Symptoms indicative of inflammatory arthritis are common in the primary care population: findings from the symptoms in persons at risk of rheumatoid arthritis survey. *Ann. Rheum. Dis.* [Internet]. 2017;76:1043 LP-1043. Available from: [http://ard.bmj.com/content/76/Suppl\\_2/1043.1.abstract](http://ard.bmj.com/content/76/Suppl_2/1043.1.abstract).
- [9] Miller A, Nightingale AL, Sammon CJ, et al. O8. Negative Rheumatoid Factor in Primary Care Delays Referral of Patients with Rheumatoid Arthritis. *Rheumatology* [Internet]. 2014;53:i29–i29. Available from: <http://dx.doi.org/10.1093/rheumatology/keu086.002>.
- [10] Hosie GA. Teaching rheumatology in primary care. *Ann. Rheum. Dis.* [Internet]. 2000;59:500–503. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=10873956>.
- [11] Lanyon P, Pope D, Croft P. Rheumatology education and management skills in general practice: a national study of trainees. *Ann. Rheum. Dis.* [Internet]. 1995;54:735–739. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=7495345>.
- [12] Villeneuve E, Nam JL, Bell MJ, et al. A systematic literature review of strategies promoting early referral and reducing delays in the diagnosis and management of inflammatory arthritis. *Ann. Rheum. Dis.* [Internet]. 2013;72:13–22. Available from: <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med8&NEWS=N&AN=22532640>.
- [13] van Onna M, Gorter S, Maiburg B, et al. Education improves referral of patients suspected of having spondyloarthritis by general practitioners: a study with

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unannounced standardised patients in daily practice. RMD open [Internet].

2015;1:e000152. Available from:

<http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=prem&NEWS=N&AN=26535152>.

- [14] van Steenbergen HW, van der Helm-van Mil AHM. Clinical expertise and its accuracy in differentiating arthralgia patients at risk for rheumatoid arthritis from other patients presenting with joint symptoms. *Rheumatology* [Internet]. 2016;55:1140–1141. Available from: <http://dx.doi.org/10.1093/rheumatology/kev431>.
- [15] van Steenbergen HW, Aletaha D, Beart-van de Voorde LJJ, et al. EULAR definition of arthralgia suspicious for progression to rheumatoid arthritis. *Ann. Rheum. Dis.* [Internet]. 2017;76:491 LP-496. Available from: <http://ard.bmj.com/content/76/3/491.abstract>.