

Additional
Information

NOTICE: This is the author's version of a work that was accepted for publication in *Manual Therapy*. Changes resulting from the publishing process, such as peer review, editing, corrections, structural formatting, and other quality control mechanisms may not be reflected in this document. Changes may have been made to this work since it was submitted for publication. A definitive version was subsequently published in *Manual Therapy*, Vol. 18, Issue 6, (2013). doi: <http://dx.doi.org/10.1016/j.math.2013.01.006>

1 **Professional Issue.**

2 **Physiotherapy co-management of rheumatoid arthritis:**

3 **Identification of red flags, significance to clinical practice**

4 **and management pathways.**

5 Andrew M Briggs^{1*} BSc(Physiotherapy)Hons, PhD, NH&MRC Research Fellow

6 Robyn E Fary^{1,2} BAppSc(Physiotherapy), GradDipManipTherapy, PhD, Lecturer

7 Helen Slater^{1,2} BAppSc(Physiotherapy), GradDipAdvManipTherapy, PhD, FACP, Associate

8 Professor

9 Sonia Ranelli^{1,2} BSc(Physiotherapy), PhD, Lecturer

10 Madelynn Chan³ MBBS, FRACP, Rheumatologist

11
12 ¹ Curtin Health Innovation Research Institute, Curtin University, Australia.

13 ² School of Physiotherapy, Curtin University, Australia

14 ³ Department of Rheumatology, Royal Perth Hospital, Australia

15
16 **Corresponding Author*

17 Curtin Health Innovation Research Institute (CHIRI), Curtin University

18 GPO Box U1987, Perth, WA 6845

19 Australia.

20 Email: A.Briggs@curtin.edu.au

21 Tel: + 61 8 9266 9953

22 Fax: +61 8 9266 3699

ACKNOWLEDGEMENTS

Dr Andrew Briggs is supported, in part, by a Fellowship awarded by the Australian National Health and Medical Research Council. Jason Chua, project officer, is acknowledged for supporting the development of this paper.

Professional Issue.

Physiotherapy co-management of rheumatoid arthritis:

Identification of red flags, significance to clinical practice

and management pathways.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease. Physiotherapy interventions for people with RA are predominantly targeted at ameliorating disability resulting from articular and peri-articular manifestations of the disease and providing advice and education to improve functional capacity and quality of life. To ensure safe and effective care, it is critical that physiotherapists are able to identify potentially serious articular and peri-articular manifestations of RA, such as instability of the cervical spine. Additionally, as primary contact professionals, it is essential that physiotherapists are aware of the potentially serious extra-articular manifestations of RA. This paper provides an overview of the practice-relevant manifestations associated with RA that might warrant further investigation by a medical practitioner (red flags), their relevance to physiotherapy practice, and recommended management pathways.

Key words: rheumatoid arthritis; red flags; safety; physiotherapy.

Word count: 1,954

INTRODUCTION

23

24 Rheumatoid arthritis (RA) is a systemic, autoimmune, inflammatory condition that affects
25 multiple tissues and organs in the body, in particular the synovial joints and peri-articular
26 tissues. It is the most common of the inflammatory joint diseases. RA is associated with
27 significant pain, functional impairments and co-morbid health conditions (Kvien, 2004). In
28 recognition of the substantial health, psychosocial and community impacts imposed by RA, this
29 condition is recognised as a National Health Priority Area in Australia and current health
30 policies address the need to optimise health service delivery (Department of Health (Western
31 Australia), 2009; National Health Priority Action Council, 2006). The systemic and progressive
32 nature of the condition and associated co-morbidities (Briggs et al., 2009) also contribute to
33 premature mortality (Myasoedova et al., 2010), particularly in individuals who experience
34 extra-articular (EA) manifestations associated with the disease. In order to ensure safe and
35 effective patient care, clinicians working in primary care need to be able to readily identify
36 manifestations which may contribute to morbidity and mortality and influence prognosis.

37

38 Physiotherapy represents a critical component of the overall management for patients with
39 RA, as substantiated by a strong evidence base, and reflected in clinical practice guidelines
40 (Bell et al., 1998; Ottawa Panel, 2004a; Ottawa Panel, 2004b; Li et al., 2006a; Li et al., 2006b;
41 Forestier et al., 2009; Royal Australian College of General Practitioners, 2009; Hurkmans et al.,
42 2011). Recent data suggest that the physiotherapy workforce needs professional development
43 in the safe and effective delivery of clinical physiotherapy services. In particular, the ability of
44 physiotherapists to identify the presence of *red flags* in patients with RA and implement
45 appropriate on-referral was highlighted as an essential skill required for safe and effective care
46 (Briggs et al., 2012; Fary et al., 2012). Red flags have been defined as the “clinical indicators of
47 possible serious underlying conditions requiring further medical intervention” (Hunter New

48 England NSW Health, 2005, p.1) and “...manifestations that suggest that physician referral may
49 be warranted” (Leerar et al., 2007, p. 42). The broader definitions of red flags may equally be
50 attributed to those serious physical findings whose management is outside the scope of
51 physiotherapy practice, e.g. visual disturbances related to scleritis. This professional issue
52 article is written within the context of this broader definition. The aim of this paper is to
53 provide an overview of articular, peri-articular and EA red flags associated with RA and
54 highlight specifically what clinicians need to *look* and *listen* for in practice, and the practice
55 implications.

56

57

RHEUMATOID ARTHRITIS

58 Although there is no cure for RA, early identification and initiation of appropriate therapies are
59 important to arrest the progression of symptoms and improve longer-term outcomes (Finckh
60 et al., 2006; van der Linden et al., 2010). Physiotherapists need to be able to: (i) recognise signs
61 and symptoms (musculoskeletal and other body systems) that at pre-diagnosis suggest RA, and
62 (ii) identify any serious disease or medical condition associated with RA that may lead to
63 irreversible damage or premature death (Beattie et al., 2011).

64

65 The following sections outline the articular, peri-articular and EA red flags associated with RA
66 that are relevant to contemporary clinical practice.

67

Articular and peri-articular red flags in RA

69 Early recognition of the articular and peri-articular features of RA that may indicate disease-
70 specific severity and that require on-referral is important for the primary care clinician, as
71 these have implications for patient safety and best-practice care (Table 1).

72

73 The typical disease course of RA involves chronic low-grade inflammation with periodic flares
74 which may present as articular or peri-articular manifestations (Prete et al., 2011).

75 Inflammatory mediators contribute to the progressive destruction of joint tissue in the
76 absence of disease-modifying treatment (Tarner et al., 2005). Chronic synovial inflammation,
77 bone erosion, and cartilage destruction within the joint may lead to joint instability in both
78 appendicular and axial skeletons.

79

80 Up to 86% of people with RA have involvement of the cervical spine (Mukerji and Todd, 2011),
81 of whom 17-85% will progress to cervical spine instability (Wolfs et al., 2009). Furthermore,
82 neurological deterioration is almost inevitable in patients with RA treated conservatively for
83 cervical spine instability associated with myelopathy (Wolfs et al., 2009). The presence of
84 cervical spine instability in RA also leads to a higher mortality rate (Paus et al., 2008;
85 Wasserman et al., 2011). Recognising the potential association between RA and joint
86 instability and identifying risk is particularly critical in the cervical spine, where instability and
87 subluxation (particularly in the upper cervical spine) can have catastrophic consequences
88 leading to sudden, unexpected death (Neva et al., 2006; Paus et al., 2008; Wasserman et al.,
89 2011) or quadriplegia (Neva et al., 2006) due to compromise of the spinal cord and/or brain
90 stem. Significantly, while a range of signs and symptoms are indicative of cervical spine
91 involvement (Table 1), a large proportion of cervical instabilities are asymptomatic (Collins et
92 al., 1991; Neva et al., 2006) highlighting the need for clinical vigilance in patients with RA.

93 Moreover, the severity of cervical instability has been associated with the severity of RA
94 activity in peripheral joints (Hirano et al., 2012) and a long duration of disease (Neva et al.,
95 2006), further highlighting the need for clinical vigilance in this context. A recent survey of
96 Australian physiotherapists indicated that only 64.4% of respondents would test for cranio-
97 cervical instability when treating the upper cervical spine of patients with RA (Osmotherly and

98 Rivett, 2011). A clinical case on upper cervical spine instability in RA is published in this issue of
99 Manual Therapy (Slater et al. 2013).

100

101 Instability also occurs in peripheral joints and may require splinting or surgical stabilisation to
102 reduce symptoms and improve function.

103

104 Commonly occurring peri-articular conditions associated with RA include: tenosynovitis (often
105 the first sign of inflammatory joint disease (Hmamouchi et al., 2011)) and tendon rupture;
106 boutonnière deformity, swan neck deformity and carpal tunnel syndrome in the hand, and
107 hallux valgus, medial longitudinal arch flattening and claw toe in the foot (Table 1). Notably,
108 early evidence of hand deformities is a reliable indicator of more severe disease (Johnsson and
109 Eberhardt, 2009), highlighting the importance of early recognition and appropriate
110 intervention or on-referral.

111

112 **Practice points**

113 Assessing and monitoring disease severity is an important clinical skill. Tools to assist clinicians
114 have recently been identified and could readily form part of best evidence practice including
115 communication with the RA team or GP (Anderson et al., 2012).

116 Risk/benefit analysis: recommend screening for signs and symptoms of RA prior to
117 implementing management, especially in the upper cervical spine: on-refer if in doubt.

118 Increased vigilance in using manual techniques in the cervical spine if suspicion of instability
119 especially C1/C2.

120

121

INSERT TABLE 1 HERE

122 **Extra-articular red flags in RA**

123 As RA is a systemic, autoimmune disease, multiple organs and systems may also be affected.
124 Understanding the implications of systemic disease involvement means that physiotherapy
125 management can be better informed and contraindications to management are identified at
126 an early stage, ensuring safe and effective patient care (Table 2).

127

128 Extra-articular features are largely influenced by inflammatory mediators associated with the
129 disease process (Hochberg et al., 2008) and have a significant influence on prognosis (Turesson
130 et al., 2002; Prete et al., 2011). For example, in a recent review on the epidemiology of EA
131 features in patients with RA, based on studies with RA cohorts of greater than 100 patients,
132 Prete et al. 2011 reported an overall incidence of 28% (19.8% non-severe form and 8.3%
133 severe forms). The authors reported a greater incidence in northern European countries and
134 among smokers, highlighting the role of environmental and genetic factors in their aetiology.
135 Severe EA features may occur in individuals with recently diagnosed RA (Turesson et al., 1999).

136

137 Most EA features are an expression of rheumatoid vasculitis, occurring as a consequence of
138 chronic inflammation, causing organ-specific manifestations, usually in the cutaneous (Figure
139 1) and neurological systems (Genta et al., 2006), but may also occur in other systems (Table 2),
140 such as the visual system (Figure 2). Drug-induced conditions associated with RA are also
141 significant, for example glucocorticoid-induced osteoporosis and diabetes mellitus, and the
142 increased susceptibility to cancer and infections as a consequence of immunosuppressive
143 agents. Table 2 provides an overview of practice-relevant EA features and co-morbidities,
144 adapted from Young and Koduri (2007) and Prete et al. (2011).

145

146 While a large volume of studies have been undertaken to characterise the epidemiology of EA
147 manifestations of RA, comparability between studies is limited due to substantial sampling

148 differences, the absence of a standard classification system for these manifestations (Turesson
149 and Jacobsson, 2004; Young and Koduri, 2007; Prete et al., 2011) and the complexity in
150 distinguishing these manifestations from co-morbid conditions associated with drug therapies
151 and disease duration (Young and Koduri, 2007; Prete et al., 2011).

152

153

INSERT TABLE 2 HERE

154

INSERT FIGURE 1 AND FIGURE 2 HERE

155

156

Practice points

157

A thorough patient history and physical examination are critical in patients with RA (see
158 Castrejón et al., 2012).

159

Identification of EA features requires a thorough clinical assessment, including screening for
160 other systemic signs (e.g.; dyspnoea, skin lesions, itchy eyes), in conjunction with screening for
161 articular and peri-articular features (e.g. Figures 1-2).

162

Cardiac, neurological and pulmonary manifestations have the potential to cause disability and
163 may require modification of physiotherapy management. Reduced cardiac, pulmonary and
164 neuromuscular performance may lead to fatigue, dyspnoea and reduced capacity to engage in
165 aerobic and strengthening exercise and perform functional tasks.

166

EA features require a broad consideration of management and may indicate the need for on-
167 referral. Referral communications should highlight key aspects of a patient's medical history
168 that suggest RA (see Jack et al. 2012).

169

170

Assessing and monitoring disease activity

171

The use of screening tools in clinical practice may alert the clinician to the presence of an

172

inflammatory joint condition and assist in identifying red flags and recognising the implications

173 for physiotherapy management. Current recommendations for clinically-appropriate tools to
174 measure RA disease activity are available (Anderson et al., 2012). A self-administered early
175 inflammatory arthritis detection tool has also been developed for use in primary care (Bell et
176 al., 2010). Although the psychometric and scoring properties of the instrument are yet to be
177 established, use of the 11-item instrument in physiotherapy practice may help alert the
178 clinician to possible RA or other inflammatory joint disease. Further, use of the gait, arms, legs
179 and spine (GALS) locomotor screening examination for RA (recently tested for use among
180 physiotherapists) has high specificity, suggesting utility as a physical screening test in primary
181 care settings (Beattie et al., 2011).

182

183 While this review is focussed on red flags, psychological co-morbidities (such as depression and
184 anxiety) commonly associated with pain and impaired function as a consequence of chronic
185 and progressive diseases such as RA (McKnight-Eily et al., 2009) should be screened for and
186 on –referral is recommended when appropriate.

187

188

SUMMARY

189 RA is a chronic, progressive and serious systemic condition, potentially causing death. Timely
190 identification of potentially serious articular, peri-articular and EA manifestations of RA is
191 imperative to ensure safe and effective patient care and enhances the role of the
192 physiotherapist as part of an interdisciplinary health professional team. Timely on-referral of
193 patients to a general practitioner, rheumatologist or orthopaedic surgeon can minimise delays
194 in accessing appropriate care and optimising patient outcomes.

195

196

197

ACKNOWLEDGEMENTS

198

199

REFERENCES

200 Anderson J, Caplan L, Yazdany J, Robbins ML, Neogi T, Michaud K, et al. Rheumatoid arthritis
201 disease activity measures: American College of Rheumatology recommendations for
202 use in clinical practice. *Arthritis Care Res* 2012;64(5):640-7.

203 Beattie KA, MacIntyre NJ, Pierobon J, Coombs J, Horobetz D, Petric A, et al. The sensitivity,
204 specificity and reliability of the GALS (gait, arms, legs and spine) examination when
205 used by physiotherapists and physiotherapy students to detect rheumatoid arthritis.
206 *Physiotherapy* 2011;97(3):196-202.

207 Bell MJ, Lineker SC, Wilkins AL, Goldsmith CH, Badley EM. A randomized controlled trial to
208 evaluate the efficacy of community based physical therapy in the treatment of people
209 with rheumatoid arthritis. *J Rheumatol* 1998;25(2):231-7.

210 Bell MJ, Tavares R, Guillemin F, Bykerk VP, Tugwell P, Wells GA. Development of a self-
211 administered early inflammatory arthritis detection tool. *BMC Musculoskel Disord*
212 2010;11:50.

213 Briggs AM, March L, Lassere M, Reid C, Henderson L, Murphy B, et al. Baseline comorbidities in
214 a population-based cohort of rheumatoid arthritis patients receiving biological
215 therapy: data from the Australian rheumatology association database. *Int J Rheumatol*
216 2009;86:1481.

217 Briggs AM, Fary RE, Slater H, Bragge P, Chua J, Keen HI, et al. Disease-specific knowledge and
218 clinical skills required by community-based physiotherapists to co-manage patients
219 with rheumatoid arthritis. *Arthritis Care Res* 2012;64(10):1514-26.

220 Castrejón I, McCollum L, Tanriover MD, Pincus T. Importance of patient history and physical
221 examination in rheumatoid arthritis compared to other chronic diseases: Results of a
222 physician survey. *Arthritis Care Res* 2012;64(8):1250-5.

223 Collins DN, Barnes CL, FitzRandolph RL. Cervical spine instability in rheumatoid patients having
224 total hip or knee arthroplasty. *Clin Orthop Relat Res* 1991;(272):127-35.

225 Department of Health (Western Australia). *Inflammatory Arthritis Model of Care*, Perth: Health
226 Networks Branch, 2009.

227 Fary RE, Slater H, Chua J, Briggs AM. Translating policy into practice for community-
228 based management of rheumatoid arthritis: Targeting professional development
229 needs among physiotherapists. *Int J Rheumatol* 2012; doi:10.1155/2012/240689.

230 Finckh A, Liang MH, van Herckenrode CM, de Pablo P. Long-term impact of early treatment on
231 radiographic progression in rheumatoid arthritis: A meta-analysis. *Arthritis Rheum*
232 2006;55(6):864-72.

233 Forestier R, Andre-Vert J, Guillez P, Coudeyre E, Lefevre-Colau MM, Combe B, et al. Non-drug
234 treatment (excluding surgery) in rheumatoid arthritis: clinical practice guidelines. *Joint
235 Bone Spine* 2009;76(6):691-8.

236 Genta MS, Genta RM, Gabay C. Systemic rheumatoid vasculitis: a review. *Seminars Arthritis
237 Rheum* 2006;36(2):88-98.

238 Hirano K, Imagama S, Oishi Y, Kanayama Y, Ito Z, Wakao N, et al. Progression of cervical
239 instabilities in patients with rheumatoid arthritis 5.7 years after their first lower limb
240 arthroplasty. *Mod Rheumatol* 2012;22(5):743-9.

241 Hmamouchi I, Bahiri R, Srfi N, Aktaou S, Abouqal R, Hajjaj-Hassouni N. A comparison of
242 ultrasound and clinical examination in the detection of flexor tenosynovitis in early
243 arthritis. *BMC Musculoskel Disord* 2011;12:91.

244 Hochberg MC, Johnston SS, John AK. The incidence and prevalence of extra-articular and
245 systemic manifestations in a cohort of newly-diagnosed patients with rheumatoid
246 arthritis between 1999 and 2006. *Curr Med Res Opin* 2008;24(2):469-80.

247 Hunter New England NSW Health. Pain matters - medical practice guidelines, New Lambton:
248 Hunter Integrated Pain Service, 2005.

249 Hurkmans EJ, van der Giesen FJ, Bloo H, Boonman DCG, van der Esch M, Fluit M, et al.
250 Physiotherapy in rheumatoid arthritis: Development of a practice guideline. *Acta*
251 *Rheumatol Port* 2011;36(2):146-58.

252 Jack C, Hazel E, Bernatsky S. Something's missing here: a look at the quality of rheumatology
253 referral letters. *Rheumatol Int* 2012;32(4):1083-5.

254 Johnsson PM, Eberhardt K. Hand deformities are important signs of disease severity in patients
255 with early rheumatoid arthritis. *Rheumatology (Oxford)* 2009;48(11):1398-401.

256 Kvien TK. Epidemiology and burden of illness of rheumatoid arthritis. *Pharmacoeconomics*
257 2004;22(2):1-12.

258 Leerar PJ, Boissonnault W, Domholdt E, Roddey T. Documentation of red flags by physical
259 therapists for patients with low back pain. *J Man Manip Ther* 2007;15(1):42-9.

260 Li LC, Davis AM, Lineker SC, Coyte PC, Bombardier C. Effectiveness of the primary therapist
261 model for rheumatoid arthritis rehabilitation: A randomized controlled trial. *Arthritis*
262 *Rheum* 2006a;55(1):42-52.

263 Li LC, Maetzel A, Davis AM, Lineker SC, Bombardier C, Coyte PC. Primary therapist model for
264 patients referred for rheumatoid arthritis rehabilitation: A cost-effectiveness analysis.
265 *Arthritis Care Res* 2006b;55(3):402-10.

266 McKnight-Eily LR, Elam-Evans LD, Strine TW, Zack MM, Perry GS, Presley-Cantrell L, et al.
267 Activity limitation, chronic disease, and comorbid serious psychological distress in US
268 adults - BRFSS 2007. *Int J Public Health* 2009;54:111-9.

269 Mukerji N, Todd NV. Cervical myelopathy in rheumatoid arthritis. *Neurol Res Int* 2011; 153628.

270 Myasoedova E, Davis JM, 3rd, Crowson CS, Gabriel SE. Epidemiology of rheumatoid arthritis:
271 rheumatoid arthritis and mortality. *Curr Rheumatol Rep* 2010;12(5):379-85.

272 National Health Priority Action Council. National Service Improvement Framework for
273 Osteoarthritis, Rheumatoid Arthritis and Osteoporosis, Canberra: Australian
274 Government Department of Health and Ageing, 2006.

275 Neva MH, Hakkinen A, Makinen H, Hannonen P, Kauppi M, Sokka T. High prevalence of
276 asymptomatic cervical spine subluxation in patients with rheumatoid arthritis waiting
277 for orthopaedic surgery. *Ann Rheum Dis* 2006;65(7):884-8.

278 Osmotherly PG, Rivett DA. Knowledge and use of craniovertebral instability testing by
279 Australian physiotherapists. *Man Ther* 2011;16(4):357-63.

280 Ottawa Panel. Ottawa panel evidence-based clinical practice guidelines for therapeutic
281 exercises in the management of rheumatoid arthritis in adults. *Phys Ther*
282 2004b;84(10):934-72.

283 Ottawa Panel. Ottawa panel evidence-based clinical practice guidelines for electrotherapy and
284 thermotherapy interventions in the management of rheumatoid arthritis in adults.
285 *Phys Ther* 2004a;84(11):1016-43.

286 Paus AC, Steen H, Roislien J, Mowinckel P, Teigland J. High mortality rate in rheumatoid
287 arthritis with subluxation of the cervical spine: a cohort study of operated and
288 nonoperated patients. *Spine* 2008;33(21):2278-83.

289 Prete M, Racanelli V, Digiglio L, Vacca A, Dammacco F, Perosa F. Extra-articular manifestations
290 of rheumatoid arthritis: An update. *Autoimmun Rev* 2011;11(2):123-31.

291 Royal Australian College of General Practitioners. Clinical guideline for the diagnosis and
292 management of early rheumatoid arthritis, Melbourne: RACGP, 2009.

293 Slater H, Briggs AM, Fary RE, Wellman C, Chan M. Upper cervical instability associated with
294 rheumatoid arthritis: what to 'know' and what to 'do'. *Man Ther* 2013

295 Tarner IH, Harle P, Muller-Ladner U, Gay RE, Gay S. The different stages of synovitis: acute vs
296 chronic, early vs late and non-erosive vs erosive. *Best Pract Res Clin Rheumatol*
297 2005;19(1):19-35.

298 Turesson C, Jacobsson L, Bergstrom U. Extra-articular rheumatoid arthritis: prevalence and
299 mortality. *Rheumatology* 1999;38(7):668-74.

300 Turesson C, Jacobsson L, Bergstrom U, Truedsson L, Sturfelt G. Predictors of extra-articular
301 manifestations in rheumatoid arthritis. *Scand J Rheumatol* 2000;29(6):358-64.

302 Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL. Occurrence of extraarticular
303 disease manifestations is associated with excess mortality in a community based
304 cohort of patients with rheumatoid arthritis. *J Rheumatol* 2002;29(1):62-7.

305 Turesson C, Jacobsson LTH. Epidemiology of extra-articular manifestations in rheumatoid
306 arthritis. *Scand JRheumatol* 2004;33(2):65-72.

307 van der Linden MP, le Cessie S, Raza K, van der Woude D, Knevel R, Huizinga TW, et al. Long-
308 term impact of delay in assessment of patients with early arthritis. *Arthritis Rheum*
309 2010;62(12):3537-46.

310 Wasserman BR, Moskovich R, Razi AE. Rheumatoid arthritis of the cervical spine: clinical
311 considerations. *Bull NYU Hosp Jt Dis* 2011;69(2):136-48.

312 Wolfs JF, Kloppenburg M, Fehlings MG, van Tulder MW, Boers M, Peul WC. Neurologic
313 outcome of surgical and conservative treatment of rheumatoid cervical spine
314 subluxation: a systematic review. *Arthritis Rheum* 2009;61(12):1743-52.

315 Young A, Koduri G. Extra-articular manifestations and complications of rheumatoid arthritis.
316 *Best Pract Res Clin Rheumatol* 2007;21(5):907-27.

317

318

319

Table 1 Articular and peri-articular manifestations associated with rheumatoid arthritis, representing potential red flags

Articular and peri-articular manifestations	<i>Listening for: reports of</i>	<i>Looking for: examination and findings</i>
Cervical spine instability	Pain at the back of the head and/or neck. Sensory and motor changes in the upper limbs. Vertebro-basilar artery insufficiency symptoms. Lips and tongue sensory disturbance. Symptoms of spinal cord compromise, including possible lower limb symptoms such as gait disturbances.	Thorough subjective and physical examination including comprehensive neurological examination; view computed tomography/magnetic resonance images to ascertain cervical cord compromise, especially C1/C2; Babinski/Hoffman sign, clonus, reflexes, sensation. (see Slater et al. 2013)
Tenosynovitis	Swollen, painful tendons. Pain on resisted movement/load.	Crepitus on movement; warmth; evidence of swelling.
Tendon rupture and/or joint dislocations of the hand/wrist or foot/ankle joints	Loss of function; deformity	Rupture: loss of tendon function, joint instability and tendon discontinuity. Discordance between active and passive joint movement. Dislocation: lack of synovial joint congruity in active and passive movement.
Boutonnière deformity	Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist.	Combination of flexion of proximal IP joint and hyperextension of distal IP joint.
Swan neck deformity	Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist.	Limitation of active flexion of the proximal IP joint. IP joint instability. Combination of flexion at MCP joint, hyperextension of the proximal IP joint and flexion of the distal IP joint.

Carpal tunnel syndrome	Pain and/or sensory disturbance in the hand in the median nerve distribution; wasting or weakness with gripping; dropping things; symptoms worse at night; shaking the hand helps.	Sensory and motor examination of relevant peripheral median nerve distribution (negate differential spinal root compression that may mimic carpal tunnel involvement). Positive Phalen's and Tinel's tests. Screen for diabetes, thyroidism, B12 deficiency. Weakness or wasting in abductor pollicis brevis.
Hallux valgus, medial longitudinal arch flattening and claw toe	Pain in the foot. Reports of increased disability with gait and weight-bearing.	Postural and alignment changes in the foot, including: medial deviation of the first metatarsal and lateral deviation of the hallux. Pattern of dorsiflexion at MTP joint combined with plantar flexion at PIP and DIP joints for claw toes.
Synovitis-driven rotator cuff and/or glenohumeral symptoms	Shoulder girdle pain (e.g.; impingement or lateral shoulder pain) not mechanically-patterned and not responding consistently to therapy (e.g. tendon unloading).	Pattern of movement dysfunction (control or impairment of range) consistent with subjective complaint; warmth; crepitus; check for rotator cuff rupture. Partial or no response to simple analgesia.
Secondary osteoarthritis	Pattern of symptoms mechanically-patterned (i.e.; stimulus-response coupled: hurts and pain eases when resting), non-inflammatory joint degeneration.	Age-dependent. Longer RA disease duration and/or chronic synovitis. Insidious onset. Responds to simple analgesia. Bony tenderness on palpation. Bony enlargement. Crepitus with movement. No palpable warmth (difficult if patient also has a flare). Loss of joint space, osteophytes, subchondral cysts on plain X-ray.

Abbreviations: MCP – metacarpophalangeal; IP – interphalangeal; MTP – metatarsophalangeal; PIP – proximal interphalangeal; DIP – distal interphalangeal

Table 2 Practice-relevant extra-articular manifestations and co-morbidities associated with rheumatoid arthritis, by body system, representing potential red flags.

Body system	Extra-articular manifestation	What to look for	Co-morbidities/complications	What to look for
Skin	Rheumatoid nodules	Single or multiple subcutaneous nodules, >5mm diameter. Usually painless and on extensor surfaces.		
	Major cutaneous vasculitis ^a	Petechiae/purpura (red or purple skin lesions which do not blanch on pressure). Leg ulcers and peripheral gangrene (Figure 1).		
Pulmonary	Bronchiolitis obliterans organizing pneumonia (BOOP)	Dry cough, dyspnoea, wheezing, crackles on auscultation.		
	Pleuritis ^a	Sharp chest pain with deep breathing, coughing, sneezing.		
Cardiovascular	Interstitial lung disease ^a	Dyspnoea, cough.		
	Pericarditis ^a	Chest pain, dyspnoea Palpitations.		
	Vasculitis ^a	Signs of ischaemia or necrosis in affected organs/tissues.		
Neurological	Mononeuritis multiplex ^a Peripheral neuropathy ^a	Acute sensory and/or motor neuropathy, occurring as a result of vasculitis,		

	Cervical myelopathy ^b	compression, or diabetes. Neck pain, upper limb pain, sensory and motor changes in upper limbs, gait disturbances.		
Visual	Sjögren's syndrome	Dry eyes and mouth. Skin, nose and vaginal dryness also present.		
	Episcleritis, scleritis ^a , retinal vasculitis ^a	'Red eye', eye pain, photophobia, decreased visual acuity, dry/itchy eye (Figure 2).		
Haematological	Felty's syndrome ^{a, c}	Frequent bacterial infections, fever, weight loss, fatigue, splenomegaly.		
Metabolic/Endocrine			Osteoporosis Steroid-induced diabetes mellitus	Minimal trauma fracture, height loss. Skin thinning, painful peripheral neuropathy.

^a Severe manifestations are classified according to the Malmö criteria (Turesson et al., 2000; Turesson & Jacobsson, 2004)

^b occurs as a consequence of subluxation of cervical spine joints due to instability of the cervical spine, especially the upper cervical spine (refer to Table 1)

^c defined as chronic polyarthritis, neutropenia and splenomegaly

CAPTIONS TO ILLUSTRATIONS

Figure 1: Example of cutaneous vasculitis of the lower extremities



Figure 2: Example of RA-associated episcleritis of the right eye, termed 'red eye'



Figure 1: Example of cutaneous vasculitis of the lower extremities. The lesions do not blanch when pressure is applied. Reproduced through a licence agreement with DermNet NZ (<http://dermnetnz.org/>).

Figure 2: Example of RA-associated episcleritis of the right eye, termed 'red eye'. Reproduced through a licence agreement with Science Photo, UK (www.sciencephoto.com).