

The Future of Rheumatoid Arthritis and Hand Surgery - Combining Evolutionary Pharmacology and Surgical Technique

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Abstract: Rheumatoid arthritis is a systemic autoimmune disease of uncertain aetiology, which is characterized primarily by synovial inflammation with secondary skeletal destructions.

Rheumatoid Arthritis is diagnosed by the presence of four of the seven diagnostic criteria, defined by The American College of Rheumatology.

Approximately half a million adults in the United Kingdom suffer from rheumatoid arthritis with an age prevalence between the second and fourth decades of life; annually approximately 20,000 new cases are diagnosed.

The management of Rheumatoid Arthritis is complex; in the initial phase of the disease it primarily depends on pharmacological management. With disease progression, surgical input to correct deformity comes to play an increasingly important role. The treatment of this condition is also intimately coupled with input from both the occupational therapists and physiotherapy.

Keywords: Rheumatoid arthritis, hand, arthropathy, sinovitis, inflammation.

Rheumatoid arthritis is a systemic, autoimmune disease of uncertain aetiology, which is characterized primarily by synovial inflammation with secondary skeletal destructions [1].

It is a chronic disease that challenges individuals psychosocially as well as physically, causing a great deal of stress to those living with this pathology [2, 3]. The stress resulting from the inability to perform simple day to day tasks independently, the associated discomfort and the insult to patient's aesthetic sensibilities result in high levels of depression in this group; at approximately 20% it is twice that of the general population [4]. It is well recognised that occupation, including paid employment has a large influence on personal well being and society as a whole [5-8].

Coming from the Greek rheuma- ("ρευμα-" meaning flux) and -toid ("-τοειδής" meaning form) [9] it describes a condition where synovial and articular tissues are focal target structures; the immunologic disorder frequently affects disparate visceral organs such as the heart, pericardium, and lungs [1].

This article aims to discuss and summarise the current perspective of Rheumatoid Arthritis in terms of epidemiology and pathophysiology as well as considering any new ideas in management of this condition.

RHEUMATOID ARTHRITIS: DIAGNOSIS, CLASSIFICATION, EPIDEMIOLOGY AND GENETIC BACKGROUND

Diagnosis & Classification

Rheumatoid arthritis is a term that describes a condition where synovial and articular tissues are focal target structures. This immunologic disorder frequently affects various visceral organs such as the heart, pericardium, and lungs [1].

Numerous combinations of clinical findings exist and have been named after the person to first describe them. These eponymous forms of Rheumatoid arthritis include Adult Stills Syndrome, Felty's, Sjogren's as well as Caplan's Syndrome [10] (Table 1).

Juvenile Rheumatoid Arthritis (JRA) usually occurs before the age of sixteen; symptoms may start as early as six months old [11, 12].

Eponymous syndromes of JRA include: Polyarthritic-systemic Juvenile Chronic Arthritis (JCA), Polyarthritic-non-systemic seronegative JCA, Polyarthritic-non-systemic seropositive JCA, Oligoarthritis I and finally Oligoarthritis II [10] (Table 2).

Clinically Rheumatoid Arthritis is diagnosed by the presence of four of the seven diagnostic criteria, defined by The American College of Rheumatology [13] (Table 3).

Morning stiffness lasting over one hour, symmetrical arthritis, arthritis affecting three or more joint areas and arthritis of the hand joints must be present for at least six weeks before rheumatoid arthritis can be diagnosed [13].

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Table 1. The Different Types of Juvenile Syndromic Rheumatoid Arthritis and their Clinical Signs

Eponymous Juvenile Rheumatoid Arthritis	Associated Clinical Signs
Polyarthritic-systemic Juvenile Chronic Arthritis (JCA)	Early childhood with fever, sometimes severe organ manifestations
Polyarthritic-non-systemic seronegative JCA	Largest group
Polyarthritic-non-systemic seropositive JCA	Mainly girls in late childhood, Anti-nuclear antibodies positive in 77%
Oligoarthritis I ("early type")	Mainly girls, Chronic Iridocyclitis, ANA positive
Oligoarthritis II ("late type")	Mainly boys, fewer joints (esp. knee), Sacroiliitis, HLA-B27 positive, may develop Ankylosing Spondylitis

Table 2. The Different Types of Adult Syndromic Rheumatoid Arthritis and their Clinical Signs

Eponymous Rheumatoid Arthritis	Associated Clinical Signs
Adult Still's Syndrome	Chronic Polyarthritits, Hepatomegaly, Splenomegaly, Lymphadenopathy, Leucocytosis, Iridocyclitis, Polyserositis
Felty's Syndrome	Seropositive RA, Splenomegaly, Lymphadenopathy, Leucopaenia, Granulocytopenia, Thrombocytopenia
Sjogren's Syndrome	Xerophthalmia, Xerostomia, Sicca Syndrome (1ry&2ry)
Caplan's Syndrome	Pneumoconiosis, RA

Table 3. The American College of Rheumatology Diagnostic Criteria for Rheumatoid Arthritis

Diagnostic Criteria for Rheumatoid Arthritis	
1	Morning stiffness
2	Symmetrical Arthritis
3	Arthritis of Hand Joints
4	Arthritis of tree or more joints
5	Rheumatoid nodules
6	Serum Rheumatoid Factor positive
7	Typical radiological changes in the hands and feet

Haematological investigation includes base line inflammatory markers, in addition to the rheumatoid factor. This however is only helpful in seropositive patients. Anticyclic citrullinated peptide antibody is highly specific for the disease and is particularly useful both in the diagnosis and prognosis of patients who are seronegative, for the rheumatoid factor [14].

Radiologically, Steinbrocker published his findings of the radiographic stages of Rheumatoid Arthritis in a mixed,

clinical-radiographic classification in 1949 [15]. This is based on the combination of radiological staging with clinical findings; it includes stage I where osteoporosis without erosions is seen, stage II where osteoporosis, slight narrowing of the joint space or subchondral bone destruction is evident; stage III with osteoporosis, destruction of the articular cartilage and extensive bone destruction is prevalent and finally stage IV which includes osseous ankylosis in existing osteoporosis and severe bone destruction.

In 1975 Larsen's grading of radiographic signs included six grades that ranged from Grade 0 with "Definitely no pathologic findings" to Grade V which denotes "Mutilating joint destruction" [16] (Table 4).

Table 4. Radiological Grading System for Rheumatoid Arthritis

Grade	Radiographic Signs by Larsen
0	Definitely no pathologic findings
I	Unspecific pathological findings
II	Mild, but certain destructive lesions
III	Moderate destructive lesions
IV	Severe destructive lesions
V	Mutilating joint destruction

More recently Simmen and Huber (1994) differentiated three basic types of Rheumatoid Arthritis on a functional basis, reliant on a primarily surgical point of view. Type I is the Ankylosing subtype, type II is Rheumatoid Arthritis with secondary osteoarthritis and finally type III which is Rheumatoid Arthritis with disintegration [17].

Epidemiology

Currently there are almost half a million adults in the United Kingdom suffering from rheumatoid arthritis [18]. There is age prevalence between the second and fourth decades of life, in the adult variant of the disease [1].

Annually approximately 20,000 new cases are diagnosed [19]; women are affected three times more commonly than men [18].

One in seven patients will give up their employment within one year of diagnosis [20], and up to 25 percent of working people with rheumatoid arthritis lose their jobs within five years; three quarters of these are for reasons directly related to their condition [21].

The prevalence of Rheumatoid Arthritis in children is difficult to estimate because of differences in nomenclature and the heterogeneity of the diseases and the subtypes encompassed under this heading [22].

Genetic Background and Pathophysiology

The most well established genetic link is with HLA-DR4 [23]. However, this is not consistent across all studied cohorts and there are many other newly defined associations, including polymorphisms in PTPN22 and PADI4 [24].

IgM or IgG rheumatoid factors are present in more than 70% of affected patients, rendering them seropositive [25].

The exact aetiology of Rheumatoid Arthritis remains unknown but a model whereby repeated exposure to environmental agents is coupled with a genetic predisposition to autoimmune responses appears to be reasonable [26].

Of the numerous environmental factors proposed to contribute to Rheumatoid Arthritis, tobacco smoking is perhaps the best defined. Smoking exposure has a dose response relationship with Rheumatoid Arthritis risk [27-29].

Rheumatoid Arthritis usually begins with the proliferation of synovial macrophages and fibroblasts after a triggering incident, possibly autoimmune or infectious [30].

Matrix Metalloproteinases are produced by the rheumatoid synovium; these enzymes break down all components of connective tissue. This process is followed by the release of cytokines from macrophages; including tumour necrosis factor alpha, in addition to numerous Interleukins that degrade bone, cartilage, ligament and tendons [26]. Over time, bone erosion and irreversible joint damage can occur, leading to permanent disability [31].

RHEUMATOID ARTHRITIS: CONSERVATIVE AND SURGICAL MANAGEMENT

The management of Rheumatoid Arthritis is complex; in the initial phase of the disease it primarily depends on pharmacological management.

With disease progression, surgical input to correct deformity comes to play an increasingly important role, especially in women, who require significantly higher numbers of joint replacements than men [32]. The treatment of this condition is also intimately coupled with input from both the occupational therapists and physiotherapy.

The 'rheumatoid hand' is one of the earliest presentations of Rheumatoid Arthritis, and the progression of its pathology can be unpredictable [33].

It is this complexity of the disease and the resulting, devastating deformities that demand that such patients are managed in a coordinated MDT setting [34]. The ultimate aim when dealing with Rheumatoid Arthritis is to induce complete remission. If remission is unable to be achieved, treatment is aimed at controlling disease activity and slowing the rate of joint damage [35].

Medical

Pharmacological treatment of patients with any inflammatory arthritis includes primarily the use of non-steroidal anti-inflammatory medication and cyclo-oxygenase-2 selective inhibitors. These drugs bring about both anti-inflammatory, as well as analgesic effects. There is however, no scientific proof that they prevent joint damage [36-38].

It is becoming increasingly evident that a 'critical period' may exist, during which - with aggressive medical intervention - the disease process of Rheumatoid Arthritis may be reversed [39]. This has resulted in disease modifying antirheumatic drugs being used much earlier in the fight against Rheumatoid Arthritis, rather than when the pathology has progressed further, as previously indicated [39].

Methotrexate treatment for example, has been shown to delay the diagnosis of Rheumatoid Arthritis and retarding radiographic joint damage [39].

Methotrexate remains the most commonly used, as well as most effective monotherapy; it is the recommended standard of comparison for new medications [40].

Biologic agents, such as TNF alpha-antagonists, have also been added to the resources available against Rheumatoid Arthritis. Individuals with no or poor response may be offered biologic agents, with a different mechanism of action: Most recently Tocilizumab. It is an IL-6 receptor inhibitor, which shows swift and significant efficacy in the battle against Rheumatoid Arthritis. This has been proven by satisfactory remission rates, in addition to a favourable safety profile [40].

It has been shown that patients started on disease modifying antirheumatic drug therapy early, exhibit reduced radiographic joint damage. They also experience greater preservation of function, when compared to patients whose treatment had been delayed [39-41].

Hence, current recommendations stipulate that patients who are most likely to develop disabling rheumatoid arthritis should start disease modifying antirheumatic drugs therapy the earliest possible [42].

Occupational Therapy

The aim of splinting in Rheumatoid Arthritis is to provide rest, anatomical and functional support for deformed joints [43, 45, 50-52]; to decrease inflammation, the subsequent swelling and resulting pain [43, 48, 53, 54] during flare ups of the condition [44-49, 54-56].

There is however little evidence to validate the effectiveness of resting splints. Therapists concur that resting splints have a place in the overall management of the Rheumatoid Arthritis patient, especially during exacerbations [44]. Resting periods of up to three weeks have been proven to be beneficial, longer periods on the other hand may result in joint stiffness [48].

Spoorenberg (1994) [57] concluded that resting splints were not popular with patients and that only 17% of his study cohort wore their splints regularly; mainly due to discomfort, size and difficulty with the application.

Occupational therapists are therefore encouraged to consider their patient's individual needs, in order to increase compliance and to provide the most comfortable and effective aids possible [46].

Physio Therapy

Van den Ende *et al.*, proved that dynamic exercise therapy is effective in increasing muscle strength, with out affecting pain levels or disease activity [58].

Two more recent studies [59, 60] show that exercise does not cause exacerbation of the disease in the short term; long term effects, however, are still unknown.

Weight reduction for Rheumatoid Arthritis patients, who are overweight or obese, limits impact on weight bearing joints and improves risk factors for cardiovascular disease. Weight control plays an important role in the general disease management [61].

Surgery

In 2001 Gordon *et al.*, concluded, in a study extending over a ten year period, that patients with Rheumatoid

Arthritis exhibited a deterioration of radiographs and function despite regular Disease Modifying Anti Rheumatoid Drug treatment and apparent clinical containment. There was a steady requirement for surgical intervention with time [62].

As mentioned previously, more effective and efficient medical options are utilised, earlier on in the treatment of the affected joint. This results in more restricted pathology and slower joint deterioration. Therefore, surgeons have observed that the rate of rheumatoid hand surgery has been decreasing in the developed world, where costly therapies are more readily available [63].

Surgical intervention is typically used when conservative therapy is unable to limit the disease evolution towards joint instability. Surgical intervention should be considered, especially when the instability is associated with uncontrollable pain and loss of function [64].

Rheumatoid hand interventions can be categorized into prophylactic and therapeutic surgical procedures:

Prophylactic procedures include the removal of inflammatory synovial tissue before synovial hypertrophy stretches the ligamentous support around joints, which can cause a tendon imbalance, or before synovial tissue invades into tendons, causing tendon rupture, or before it destroys the articular cartilage [64].

Once the joints are destroyed or the tendons are ruptured, surgical options may be considered:

Wrist

Rectifying wrist deformities is often vital to prevent and correct hand deformities [65]. Arthrodesis of the wrist offers an important possibility in the surgical management of rheumatoid disease. In patients with well-preserved midcarpal joints, a limited (radiolunate) fusion will preserve some wrist motion [66-68].

The Swanson Silastic wrist arthroplasty is an option that conserves movement, however careful case selection is vital. Arthroplasty is indicated only in patients with long term, dormant disease with a very low work demand and insufficient bone stock to allow a total wrist arthroplasty with a metal on plastic design [69-74].

Extensor Tendons

Tenosynovitis of the extensors is a relatively early finding in rheumatoid disease. Mechanical abrasion by dorsal wrist osteophytes may cause rupture of these structures. Ischemia from pannus or direct invasion may also result in erosion of extensor tendons [75]. Dorsal tenosynovectomy is recommended for tenosynovitis that has resisted six months of medical management [76-78].

Flexor Tendons

'Mannerfelt lesion' is responsible for flexor pollicis longus rupture. This is the most common flexor tendon rupture in the rheumatoid hand and results from tendon erosion by direct friction against the scaphoid bone [79].

Flexor digitorum profundus and superficialis ruptures are usually due to direct synovial infiltration of the tendons [80] and attrition ruptures are unusual [81]. Flexor Digitorum Profundus tenosynovitis usually manifests as carpal tunnel syndrome or

trigger digits. In such cases the carpal tunnel may be decompressed. For trigger fingers, the A1 pulley should not be released, as it may be the only remaining supporting structure for the metacarpo-phalangeal joint. If synovectomy is not sufficient, then excising a slip of the Flexor Digitorum Superficialis could solve the restriction, by thinning the tendon.

MP Joints

Early disease of the MP joints can be addressed by synovectomy, which alleviates pain [82].

With extensive metacarpo phalangeal joint pathology, replacement arthroplasty may be indicated. Silicone arthroplasty of these joints is commonly performed, unlike with the wrist and in the thumb CMC joint where silicone arthroplasty has fallen out of favor [83-85].

Recurrent ulnar drift (31%), implant fracture (26%) and silicone synovitis represent possible complications of silicone joint replacements [86-90].

Finger Joints

Early synovectomy, to avoid the progressive synovitis that ultimately displaces and infiltrates the extensor mechanism is indicated. It is the preferred treatment, to conserve as much joint function as possible [91, 92].

Frozen PIP joints only respond to fusion or arthroplasty [93].

Thumb

Metacarpophalangeal joint synovectomy is indicated early on and may be combined with extensor mechanism modification such as Extensor Pollicis Longus rerouting or Extensor Pollicis Brevis advancement [94].

The recommended surgical treatment for mild to moderate swan-neck deformities is implant hemiarthroplasty. When there is advanced deformity, resection arthroplasty, combined with volar tenodesis of the joint may be performed. An alternative option to this is joint fusion, with release of the fascia of the first dorsal interosseous muscle [95].

Arthrodesis is recommended for moderate deformities, when the metacarpophalangeal joint is totally destroyed but the remainder of the thumb ray is only minimally involved. If destructive changes are evident at either the carpometacarpal or interphalangeal levels, metacarpophalangeal arthroplasty is preferred.

Allotransplant: The Future?

Iglesias *et al.* recently propose to perform an allotransplant of the osteomyotendinous structures in patients with Rheumatoid Arthritis, by comparing them to trauma patients, that receive allotransplants coupled with immunosuppressant medication, to ensure the graft's survival [96].

The basis for their hypothesis is that between 1998 and 2009, 42 hand and three arm allotransplants in 33 patients have been performed worldwide; after a follow-up from 17 to 120 months, 25 of these transplants are still viable [97].

Iglesias also drew on the similarity between the medication used by both the trauma patients on immunosuppressants and the rheumatoid patients.

Both groups of patients are often treated with non-steroidal drugs, corticosteroids, Methotrexate, Azathioprine, and monoclonal antibodies [98-101].

They set out to prove the feasibility of their hypothesis by operating on ten cadavers; the average operative time was approximately 20 hours.

Their approach specified the preservation of the recipient's skin flap and sensory nerves, to render the graft, psychologically more acceptable and functionally superior, for the patient [96].

DISCUSSION

A recent study, by Amy K Alderman, found that 70% of rheumatologists consider hand surgeons deficient in understanding the medical options available for Rheumatoid Arthritis, while 73.6% of surgeons believe rheumatologists have insufficient knowledge of the surgical options for the rheumatoid hand [102].

Mc Ewen and Chung KC had already confirmed with their preceding studies, that surgical outcomes research is limited for physicians managing RA hand deformities [103,104].

It has therefore been proven, that both rheumatologists and hand surgeons have minimal interdisciplinary training, restricted interdisciplinary communication regarding clinical management and disagree significantly on the timing and indications for hand surgery [102].

Clinical pathways, with a multidisciplinary approach in mind, that include hand surgeons, rheumatologists and occupational therapists, are useful clinics that are more convenient for patients and more successful in targeted disease management [102,103].

CONCLUSION

The diagnosis and management of Rheumatoid Arthritis is a fast evolving field and it is important to keep up to date with the latest information.

One important step is to prevent a disarticulated approach, when managing a patient. Early involvement of all specialists and a coordinated treatment plan in an MDT setting is vital to successfully deal with the signs and symptoms of a Rheumatoid Arthritis patient.

As mentioned above, the current recommendations are that patients should start disease modifying antirheumatic treatment at the earliest possible opportunity to delay the degeneration of joint integrity.

The decision for surgical intervention must be based on its overall ability to address the patient's primary wishes and needs. Although there have been tremendous advances in the surgical armamentarium, the role of specific procedures has many areas of uncertainty and controversy.

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CONFLICT OF INTEREST

None declared.

REFERENCES

- [1] Charles HT. Grabb and Smith's Plastic Surgery. 6th ed. 2007; 92: pp. 889-90.
- [2] Katz PP. The stresses of rheumatoid arthritis: appraisals of perceived impact and coping efficacy. *Arth Care Res* 1998; 11: 9-22.
- [3] Mahat G. Perceived stressors and coping strategies. *J Adv Nurs* 1997; 25: 1144-50.
- [4] Creed F. Psychological disorders in rheumatoid arthritis: a growing consensus. *Ann Rheum Dis* 1990; 49: 808-12.
- [5] Yerxa EJ. Occupational therapy's role in creating a future climate of caring. *Am J Occup Ther* 1980; 34: 529.
- [6] Rogers J. The study of human occupation. In: Keilhofner G. Ed. *Health through occupation: theory and practice in occupational therapy*. Philadelphia: FA Davis 1983.
- [7] Keilhofner G, Ed. *Health through occupation*. Baltimore: Williams and Wilkins 1985.
- [8] MacKinnon J, Noh S, Miller W. Occupation as a mediator of depression in people with rheumatoid arthritis. *J Occup Sci* 1998; 2(5): 82-92.
- [9] *Rheumatoid Arthritis* In: *Dorland's medical dictionary*. 28th ed. Philadelphia: WB. Saunders Company 1994.
- [10] Symmons D, Turner G, Webb R, *et al*. The prevalence of rheumatoid arthritis in the United Kingdom: new estimates for a new century. *Rheumatology* 2002; 41(7): 793-800.
- [11] Wiles N, Symmons DPM, Harrison B, *et al*. Estimating the incidence of rheumatoid arthritis – Trying to hit a moving target? *Arthritis Rheum* 1999; 42(7): 1339-46.
- [12] Barrett EM, Scott DG, Wiles NJ, Symmons DP. The impact of rheumatoid arthritis on employment status in the early years of disease: a UK community-based study. *Rheumatol* 2000; 39(12): 1403-9.
- [13] Young A, Dixey J, Kulinskaya E, *et al*. Which patients stop working because of rheumatoid arthritis? Results of five years' follow up in 732 patients from the Early RA Study (ERAS). *Ann Rheum Dis* 2002; 61(4): 335-40.
- [14] Manners PJ, Bower C. Worldwide prevalence of juvenile arthritis: why does it vary so much? *J Rheumatol* 2002; 29: 1520-30. *study*. *Rheumatology (Oxford)* 2001; 40: 1256-61.
- [15] Lingg G, Schmitt R. Rheumatoid arthritis. In: Schmitt R, Lanz U, Buchberger W Eds. *Diagnostic imaging of the hand*. Germany: Thieme 2004; pp. 418-29.
- [16] Prince FH, Otten MH, van Suijlekom-Smit LW. Diagnosis and management of juvenile idiopathic arthritis. *BMJ* 2010; 3; 341: c6434.
- [17] Ruperto N, Lovell DJ, Quartier P, *et al*. Paediatric Rheumatology International Trials Organization and the Pediatric Rheumatology Collaborative Study Group. Long-term safety and efficacy of abatacept in children with juvenile idiopathic arthritis. *Arthritis Rheum* 2010; 62(6): 1792-802.
- [18] Arnett FC, Edworthy SM, Bloch DA, *et al*. The American Rheumatism Association 1987. Revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988; 31: 315-24.
- [19] Quinn MA, Gough AK, Green MJ, *et al*. Anti-CCP antibodies measured at disease onset help identify seronegative rheumatoid arthritis and predict radiological and functional outcome. *Rheumatology (Oxford)* 2006; 45: 478-80.
- [20] Streinbrocker O, Traeger GH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. *J Am Med Assoc* 1949; 140: 659-62.
- [21] Larsen A, Dale K, Eek J. Radiographic evaluation of rheumatoid arthritis and related conditions by standard reference films. *Acta Radiol Diagn* 1975; 16: 393.
- [22] Simmen BR, Huber H. The wrist joint in chronic polyarthritis—a new classification based on the type of destruction in relation to the natural course and the consequences for surgical therapy. *Handchir Mikrochir Plast Chir* 1994; 26: 182-9.
- [23] De Rosa MC, Giardina B, Bianchi C, *et al*. Modeling the ternary complex TCR-VBeta/CollagenII (261-273)/HLA-DR4 associated with rheumatoid arthritis. *PLoS One* 2010 14; 5(7): e11550.
- [24] de Vries N, Tijssen H, van Riel PL, van de Putte LB. Reshaping the shared epitope hypothesis: HLA-associated risk for rheumatoid arthritis is encoded by amino acid substitutions at positions 67-74 of the HLA-DRb1 molecule. *Arthritis Rheum* 2002; 46: 921-8.
- [25] Panay GS. Developments in the immunology of rheumatoid arthritis, a personal perspective. *Rheumatology* 2011; 50(5): 815-7.

- [26] Ngian GS. Rheumatoid arthritis. *Aust Fam Physician* 2010; 39: 626-8.
- [27] Costenbader KH, Feskanich D, Mandl LA, Karlson EW. Smoking intensity, duration, and cessation, and the risk of rheumatoid arthritis in women. *Am J Med* 2006; 119(6): 503.e1-9.
- [28] Albano S, Santana-Sahagun E, Weisman M. Cigarette smoking and rheumatoid arthritis. *Semin Arthritis Rheum* 2001; 31(3): 146-59.
- [29] Criswell L, Saag K, Mikuls T, *et al.* Smoking interacts with genetic risk factors in the development of rheumatoid arthritis among older Caucasian women. *Ann Rheum Dis* 2006; 65: 1163-7.
- [30] Rindfleisch JA, Muller D. Diagnosis and management of rheumatoid arthritis. *Am Fam Physician* 2005; 72(6): 1037-47.
- [31] Kevin CC, Sandra V. Kotsis Outcomes of hand surgery in the patient with rheumatoid arthritis. *Curr Opin Rheumatol* 2010; 22: 336-41.
- [32] Burke FD, Miranda SM, Owen VM, Bradley MJ, Sinha S. Rheumatoid hand surgery: differentiating perceptions amongst surgeons, rheumatologists and therapists in the UK. *J Hand Surg Eur* 2011; 36(8): 632-41.
- [33] Pincus T, Marcum SB, Callahan LF. Long term drug therapy for rheumatoid arthritis in seven rheumatology private practices: II. Second line drugs and prednisone. *J Rheumatol* 1992; 19: 1885-94.
- [34] Patrick G, Jean W, Hugh J, Terence G. A10 Year Prospective Follow up of Patients with Rheumatoid Arthritis 1986-96. *J Rheumatol* 2001; 28: 2409-15.
- [35] American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. *Arthritis Rheum* 2002; 46(2): 328-46.
- [36] SIGN. Management of early rheumatoid arthritis: A national clinical guideline. SIGN Publication No. 48, December 2000.
- [37] Combe B, Landewé R, Lukas C, *et al.* EULAR recommendations for the management of early arthritis: Report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCI-SIT). *Ann Rheum Dis* 2007; 66: 34-45.
- [38] Luqmani R, Hennell S, Estrach C, *et al.* British Society for Rheumatology and British Health Professionals in Rheumatology Guideline for the management of rheumatoid arthritis. *Rheumatology* 2006; 1-16.
- [39] van Dongen H, van Aken J, Lard LR, *et al.* Efficacy of methotrexate treatment in patients with probable rheumatoid arthritis: A double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2007; 56(5): 1424-32.
- [40] Lard LR, Visser H, Speyer I, *et al.* Early versus delayed treatment in patients with recent-onset rheumatoid arthritis: comparison of two cohorts who received different treatment strategies. *Am J Med* 2001; 111: 446-51.
- [41] Van Aken J, van Dongen H, le Cessie S, *et al.* Comparison of long term outcome of patients with rheumatoid arthritis presenting with undifferentiated arthritis or with rheumatoid arthritis: An observational cohort study. *Ann Rheum Dis* 2006; 65: 20-5.
- [42] Symmons DPM, Silman AJ. Aspects of early arthritis. What determines the evolution of early undifferentiated arthritis and rheumatoid arthritis? An update from the Norfolk Arthritis Register. *Arthr Res Ther* 2006; 8(4): 214.
- [43] Melvin J. In: *Rheumatic disease in the adult and child: occupational therapy and rehabilitation*. 3rd ed. Philadelphia: FA Davis 1989.
- [44] Phillips C. The therapist's management of patients with rheumatoid arthritis. In: Hunter JM, Mackin EJ, Callahan AD, Eds. *Rehabilitation of the hand, surgery and therapy*. 4th ed. St. Louis: Mosby 1995.
- [45] Falconer J. Hand splinting in rheumatoid arthritis. A perspective on current knowledge and directions for research. *Arth Care Res* 1991; 4(2): 81-6.
- [46] Callinan N, Mathiowetz V. Soft versus hard resting splints in rheumatoid arthritis: pain relief, preference and compliance? *Am J Occ Ther* 1995; 50(5): 347-53.
- [47] Melvin J. Orthotic treatment of the hand: what's new? *Bull Rheum Dis* 1995; 44(4): 5-8.
- [48] Gault S, Spyker J. Beneficial effects of immobilisation of joints in rheumatoid and related arthritides: a splint study using sequential analysis. *Arthr Rheum* 1969; 12(1): 34-44.
- [49] Bexon C, Greenstock M. *The splinting handbook*. Nottingham Rehabilitation 1994.
- [50] Jones G, Francis H, Grimner K, Browne C, Rowell W. Ancillary services in rheumatology. *Pract Ess Rheumatol* 1997; 166: 434-9.
- [51] Keitel W. Occupational therapy, splinting and aids in the rheumatic diseases. *Rheumatol Eur* 1997; 26(2): 60-3.
- [52] Hicks J, Leonard J, Nelson V, Esquenazi A. Prosthetics/ orthotics and assistive devices: orthotic management of selected disorders. *Arch Phys Med Rehab* 1989; 70: 5210-7.
- [53] Feinberg J, Brandt K. Use of resting splints by patients with rheumatoid arthritis. *Am J Occup Ther* 1981; 35(3): 173-8.
- [54] Phillips C. Rehabilitation of the patient with rheumatoid hand involvement. *Phys Ther* 1989; 69(12): 1091-9.
- [55] Malcus Johnson P, Sandkvist G, Eberhard K, Liang B, Herrlin K. The usefulness of nocturnal resting splints in the treatment of ulnar deviation of the rheumatoid hand. *Clin Rheumatol* 1992; 11(1): 72-5.
- [56] Spoorenberg A, Boers M, Van der Linden S. Wrist splints in rheumatoid arthritis: what do we know about efficacy and compliance? *Arthritis Care Res* 1994; 7(2): 55-7.
- [57] de Jong Z, Munneke M, Zwinderman AH, *et al.* Is a long-term high intensity exercise program effective and safe in patients with rheumatoid arthritis? Results of a randomized controlled trial. *Arthritis Rheum* 2003; 48(9): 2415-24.
- [58] Stenström CH, Minor MA. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid arthritis. *Arthritis Rheumatism* 2003; 49(3): 428-34.
- [59] Han A, Judd MG, Robinson VA, *et al.* Tai chi for treating rheumatoid arthritis. *Cochrane Database Syst Rev* 2004; 3.
- [60] Luqmani R, Hennell S, Estrach C, *et al.* British Society for Rheumatology and British Health Professionals in Rheumatology Guideline for the management of rheumatoid arthritis. *Rheumatology* 2006; 1-16.
- [61] Anderson RJ. Controversy in the surgical treatment of the rheumatoid hand. *Hand Clin* 2011; 27/1(21-25): 0749-12.
- [62] Chung KC, Kotsis SV. Outcomes of hand surgery in arthritis patients. *Curr Opin Rheumatol* 2010; 22: 336-41.
- [63] Neumann DA, Bielefeld T. The Carpometacarpal Joint of the Thumb: stability, deformity, and therapeutic intervention. *J Orthop Sports Phys Ther* 2003; 33(7): 386-99.
- [64] Shapiro JS. The wrist in rheumatoid arthritis. *Hand Clin* 12: 477.
- [65] Chamay A, Della Santa D, Vilaseca A. Radiolunate arthrodesis, factor of stability for the rheumatoid wrist. *Ann Chir Main* 1983; 2: 5.
- [66] Linscheid RL, Dobyns JH. Radiolunate arthrodesis. *J Hand Surg* 1985; 10A: 821.
- [67] Chamay A, Della Santa D. Radiolunate arthrodesis in rheumatoid wrist (21 cases). *Ann Hand Surg* 1991; 10: 197.
- [68] Goodman MJ, Millender LH, Nalebuff ED, Phillips CA. Arthroplasty of the rheumatoid wrist with silicone rubber: an early evaluation. *J Hand Surg Am* 1980; 5: 114-21.
- [69] Vicar AJ, Burton RI. Surgical management of the rheumatoid wrist - fusion or arthroplasty. *J Hand Surg* 1986 11A: 790.
- [70] Fatti JF, Palmer AK, Mosher JF. The long-term results of Swanson silicone rubber interpositional wrist arthroplasty. *J Hand Surg* 1986; 11A: 166.
- [71] Comstock CP, Louis DS, Eckenrode JF. Silicone wrist implant: long-term follow-up study. *J Hand Surg* 1988; 13: 201.
- [72] Jolly SL, Ferlic DC, Clayton ML, Dennis DA, Stringer EA. Swanson silicone arthroplasty of the wrist in rheumatoid arthritis: A long-term follow-up. *J Hand Surg* 1992; 17A: 14.
- [73] Brase DW, Millender LR. Failure of silicone rubber wrist arthroplasty in rheumatoid arthritis. *J Hand Surg* 1986; 11A: 175.
- [74] Wilson RL, DeVito MC. Extensor tendon problems in rheumatoid arthritis. *Hand Clin* 1996; 12: 551.
- [75] Millender LH, Nalebuff EA. Preventive surgery - tenosynovectomy and synovectomy. *Orthop Clin North Am* 1975; 6: 765.
- [76] Wynn Parry CB, Stanley JK. Synovectomy of the hand. *Br J Rheumatol* 1993; 32: 1089.
- [77] Ryu J, Saito S, Honda T, Yamamoto K. Risk factors and prophylactic tenosynovectomy for extensor tendon ruptures in the rheumatoid hand. *J Hand Surg* 1998; 23B: 658.
- [78] Mannerfelt L, Norman O. Attrition ruptures of flexor tendons in rheumatoid arthritis caused by bony spurs in the carpal tunnel. A clinical and radiological study. *J Bone Joint Surg* 1969; 51B: 270.
- [79] Ferlic DC. Rheumatoid flexor tenosynovitis and rupture. *Hand Clin* 1996; 12: 561.

- [80] Yang SS, Kalainov DM, Weiland AJ. Fracture of the hook of the hamate with rupture of the flexor tendons of the small finger in a rheumatoid patient: a case report. *J Hand Surg* 1996; 21A: 916.
- [81] Ellison MR, Kelly KJ, Flatt AE. The results of surgical synovectomy of the digital joints in rheumatoid disease. *J Bone Joint Surg* 1971; 53A: 1041.
- [82] Gellman H, Stetson W, Brumfield RH Jr., Costigan W, Kuschner SH. Silastic metacarpophalangeal joint arthroplasty in patients with rheumatoid arthritis. *Clin Orthop Rel Res* 1997; 342: 16.
- [83] Mannerfelt LG, Anderson K. Silastic arthroplasty of the metacarpophalangeal joint in rheumatoid arthritis. *J Bone Joint Surg* 1975; 57A: 484.
- [84] Blair WF, Shurr DG, Buckwalter JA. Metacarpophalangeal implant arthroplasty with a Silastic spacer. *J Bone Joint Surg Am* 1984; 66(3): 365-70.
- [85] Vahvanen V, Viljakka T. Silicone rubber implant arthroplasty of the metacarpophalangeal joint in rheumatoid arthritis: a follow-up study of 32 patients. *J Hand Surg* 1986; 11A: 333.
- [86] Beckenbaugh RD, Dobyns JH, Linscheid RL, Bryan RS. Review and analysis of silicone-rubber metacarpophalangeal implants. *J Bone Joint Surg* 1976; 58: 483.
- [87] Derkash RS, Niebauer JJ Jr., Lane CS. Long-term follow-up of metacarpal phalangeal arthroplasty with silicone Dacron prostheses. *J Hand Surg* 1986; 11A: 553.
- [88] Kirschenbaum D, Schneider LH, Adams DC, Cody RP. Arthroplasty of the metacarpophalangeal joints with use of silicone-rubber implants in patients who have rheumatoid arthritis. *J Bone Joint Surg* 1993; 75A: 3.
- [89] Foliart DE. Swanson silicone finger joint implants: a review of the literature regarding long-term complications. *J Hand Surg* 1995; 20A: 445.
- [90] Ansell B, Harrison S. A five year follow-up of synovectomy of the proximal interphalangeal joint in rheumatoid arthritis. *Hand* 1975; 7: 34.
- [91] Kiefhaber TR, Strickland JW. Soft tissue reconstruction for rheumatoid swan-neck and boutonniere deformities longterm results. *J Hand Surg* 1993; 18A: 984.
- [92] Swanson AB, Maupin BK, Gajjar NV, Swanson GD. Flexible implant arthroplasty in the proximal interphalangeal joint of the hand. *J Hand Surg* 1985; 10A: 796.
- [93] Terrono A, Millender LH. Surgical treatment of the boutonniere rheumatoid thumb deformity. *Hand Clin* 1989; 5(2): 239.
- [94] Nalebuff EA. The rheumatoid hand. Reflections on metacarpophalangeal arthroplasty. *Clin Orthop* 1984; 182: 150.
- [95] Iglesias M, Butrón P, Santander-Flores S, *et al.* Surgical technique in cadaveric donors for partial hand allotransplant in patients with rheumatoid arthritis. *Transplant Proc* 2010; 42: 2389-94.
- [96] Hand + Transplant. International Registry on Hand and Composite Tissue Transplantation. IRHCTT [serial on internet]. 2011 October 24. Available from: <http://www.handregistry.com>
- [97] American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. *Arthritis Rheum* 2002; 46: 328.
- [98] Diaz-Jouanen E, Abud-Mendoza C, Garza-Elizondo MA, *et al.* Recomendaciones para el tratamiento médico de la artritis reumatoide. *Rev Invest Clin* 2005; 57: 725.
- [99] Fonseca JE, Santos MJ, Canhão H, *et al.* Interleukin-6 as a key player in systemic inflammation and joint destruction. *Autoimmun Rev* 2009; 8: 538.
- [100] Imazeki I, Saito H, Hasegawa M, *et al.* IL-6 functions in cynomolgus monkeys blocked by a humanized antibody to human IL-6 receptor. *Int J Immunopharmacol* 1998; 20: 345.
- [101] Alderman AK, Ubel PA, Kim HM, Fox DA, Chung KC. Management of the Rheumatoid Hand: consensus and controversy among rheumatologists and hand surgeons. *J Rheumatol* 2003; 30: 7.
- [102] McEwen C. Multicenter evaluation of synovectomy in the treatment of rheumatoid arthritis. Report of results at the end of five years. *J Rheumatol* 1988; 15: 765-9.
- [103] Chung KC, Kowalski CP, Kim HM, Kazmers IS. Patient outcomes following Swanson silastic metacarpophalangeal joint arthroplasty in the rheumatoid hand: a systematic overview. *J Rheumatol* 2000; 27: 1395-402.
- [104] Rymer MM, Summers D, Soper P. Development of clinical pathways for stroke management: an example from Saint Luke's Hospital, Kansas City. *Clin Geriatr Med* 1999; 15: 741-64.

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