Rheumatoid arthritis in the hands

Rhian Bevan
Kim Pearce
Rebecca Mills

Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disorder resulting from a T-cell-mediated immune response against soft tissues. Among the various joints affected, the hands are particularly susceptible, leading to joint destruction, deformity, significant disability and decreased quality of life for those affected. In the hands, RA predominantly affects the wrist joint and metacarpophalangeal (MCP) joints. In the early stages signs can be subtle, including joint pain and morning stiffness; however, as the disease progresses more severe symptoms and complications can occur, such as deformities of the hand and tendon ruptures. Significant advances in pharmacological treatments has meant there is less need for surgical intervention. With research still ongoing for pharmacological interventions, there are many promising treatments for RA.

Keywords Autoimmune; deformity; hand; rheumatoid athritis

Introduction

Rheumatoid arthritis (RA) is a common chronic inflammatory disorder. It is an immune-mediated multisystem disease primarily affecting synovial joints. Among the various joints affected, the hands are particularly susceptible, leading to joint destruction, deformity, significant disability and decreased quality of life for those affected. The most common initial presentation of rheumatoid arthritis is inflammatory arthritis of the metacarpophalangeal joints and wrist. This article explores the pathophysiology, symptoms, diagnosis, treatment, and management of rheumatoid arthritis in the hands.[1,2]

Genetic and environmental factors (aetiology)

The aetiology of RA is multifactorial and believed to result from a combination of genetic susceptibility and environmental triggers, as well as an abnormal immune response. Genetic factors include specific alleles of the HLA-DRB1 gene, which have been associated with increased risk. Environmental factors may include smoking, infections, and hormonal influences. Together, these factors contribute to the dysregulation of the immune system observed in RA and are summarized in Figure 1.[3]

Rhian Bevan ***BSc MBBCh MRCS PGDip Med Ed*** *is a Core Surgical Trainee in the Wessex Deanery currently working at University Hospitals Dorset, Dorset, UK. Conflicts of interest: none declared.*

Kim Pearce ***BSc BMBS PGCert Med Ed MRCS*** *is Trauma and Orthopaedic Registrar in the Wessex Deanery currently working at North Hampshire Hospitals, Hampshire, UK. Conflicts of interest: none declared.*

Rebecca Mills ***BMBCh MA (Oxon) FRCS (TR & Ortho)*** *is a Consultant Orthopaedic Surgeon at Dorset County Hospital, Dorset, UK. Conflicts of interest: none declared.*

Pathophysiology of rheumatoid arthritis in the hands

Overview

Rheumatoid arthritis (RA) is a chronic autoimmune disorder resulting from a T-cell-mediated immune response against soft tissues, in particular the synovial membrane, in addition to cartilage and bone.[4] The exact pathophysiological mechanisms of this autoimmune disease are unknown, however it is considered to involve both genetic and environmental contributors. The progressive immunological response involves both innate and adaptive immune activation with an initial non-specific inflammatory phase followed by an amplification phase of T-cell-mediated activation, leading to a state of persistent chronic inflammation.[4] Mononuclear cell destruction of tissues is believed to be the primary cellular mediator of tissue damage in RA in addition to IL-1 and TNF-alpha inflammatory cascades causing joint destruction. The resulting persistent inflammation causes synovial thickening, eventually leading to the destruction of cartilage and bone within joints.

Mechanisms of joint damage

In the hands, RA predominantly affects the wrist joint and metacarpophalangeal (MCP) joints. The inflammatory process involves numerous immune cells including T cells, B cells, and macrophages, which release cytokines and other inflammatory mediators. These substances contribute to the chronic inflammatory state and subsequent joint damage.[5]

Synovial hyperplasia: the synovium proliferates abnormally, leading to pannus formation. Pannus is an aggressive tissue that invades and erodes cartilage and bone.

Cartilage degradation: enzymes like matrix metalloproteinases (MMPs) break down cartilage, reducing joint function and causing pain.

Bone erosion: osteoclasts, activated by inflammatory cytokines, resorb bone tissue, leading to joint deformities.

Ligament and tendon damage: inflammation can weaken and rupture tendons and ligaments, contributing to joint instability and deformity.

Symptoms and clinical manifestations

Early symptoms

The early signs of RA in the hands can be subtle and may develop insidiously over several weeks or more rapidly over days. Joint pain is commonly the first symptom experienced by patients with persistent pain in the joints that can vary in intensity and may be accompanied by a feeling of warmth in the affected areas. Morning joint stiffness is one of the hallmark symptoms of RA, lasting for more that 30 minutes and worse on morning waking or after periods of inactivity. Additionally, the metacarpophalangeal

Summary of risk factors for rheumatoid arthritis

Environmental factors:

- Smoking
- Infectious agents – Parvovirus B19, Hepatitis C virus, Epstein-Barr virus
- Airborne agents – silica, inorganic/textile dust
- Microbiome – Periodontitis, *P. gingivalis,* Gut dysbiosis, *Prevotella* spp.
- Diet – red meat, sugar, sodium

Host factors:

- Genetic – HLA-DRB1, non-HLA genes (e.g. PTNP22)
- Immune-mediated – Type 1 diabetes, inflammatory bowel disease, vitiligo, alopecia areata
- Neuroendocrine – hypothalamic-pituitary-adrenal (HPA) axis activation, prolactin, aromatase, obesity, hyperlipidaemia
- Hormonal and reproductive – early menopause, puerperium, anti-oestrogens

Modified from Romão and Fonseca (2021).

Figure 1

joints, become swollen, tender, and warm to the touch. Polyarthropathy typically affects the hands and feet but may also affect large joints of the knees, ankles, cervical spine, shoulder, and elbows.[6]

Progressive symptoms

As RA progresses, more severe symptoms and complications may develop, reflecting the advancing underlying disease progress.

Deformities: characteristic finger deformities such as boutonnière deformity, flexion of the proximal interphalangeal (PIP) joint and hyperextension of the distal interphalangeal (DIP) joint (Figure 2) and swan-neck deformity, with hyperextension of the PIP joint and flexion of the DIP joint (Figure 3), may occur.

Rheumatoid nodules: firm subcutaneous lumps over olecranon, ulnar border and occasionally over the interphalangeal joints are the most common extra-articular manifestation of the disease, seen in 20% of patients and associated with positive serum rheumatoid factor (RF) and more aggressive disease. Rheumatoid nodules are demonstrated in Figure 4.[7]

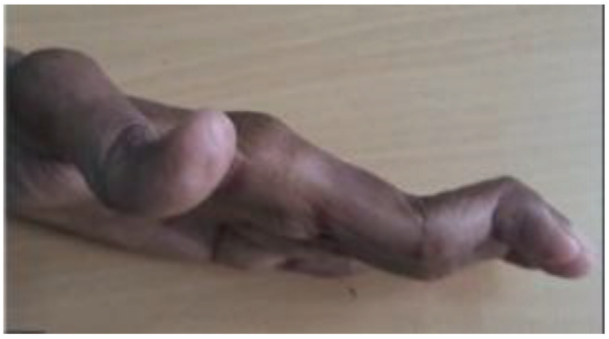

Figure 2 Ring finger demonstrating boutonnière deformity. This work © 2017 by Jagadeesan and Shenoy is licensed under Creative Commons Attribution 4.0 International.

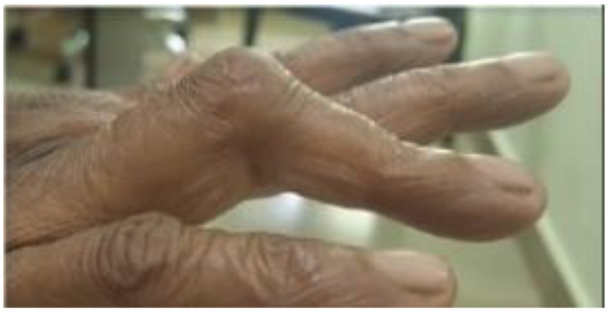

Figure 3 Index finger demonstrating swan-neck deformity. This work © 2017 by Jagadeesan and Shenoy is licensed under Creative Commons Attribution 4.0 International.

Reduced grip strength: inflammation and joint damage can lead to decreased strength and functionality in the hands.

Ulnar deviation: ulnar deviation of digits secondary to volar subluxation at the MCP joints leads to a characteristic ulnar drift. Persistent joint synovitis initiates a cascade of anatomical changes, which leads to tendon and ligamentous deformity in patients. Stretching of the sagittal fibres of the radial hood and associated volar plate stretching leads to the extensor tendons of the fingers subluxing ulnarly. Additionally, laxity in the collateral ligaments permits further ulna deviation, which leads to dysfunction of the ulnar intrinsic muscles, further worsening the deformity. Furthermore, there is radial deviation of the carpus bones resulting in ulnar migration of the flexor tendons.[4]

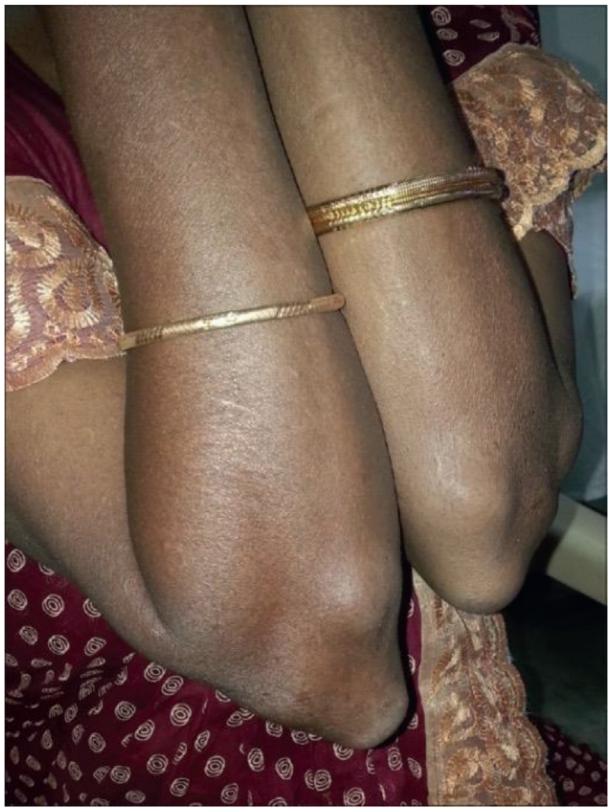

Figure 4 Rheumatoid nodules near elbow joints. This work © 2017 by Jagadeesan and Shenoy is licensed under Creative Commons Attribution 4.0 International.

Caput ulnae: deformity of the ulnar carpal ligaments from synovitis weakens the ligamentous support of the distal radioulnar joint (DRUJ), resulting in dorsal dislocation of the distal ulna with impaction of the ulna on the carpus and associated volar subluxation of the extensor carpi ulnaris tendon (ECU), which impedes its ability to stabilize the distal ulna, resulting in further dorsal dislocation.[8] Caput ulnae syndrome is illustrated in Figure 5.

Tendon ruptures: these are caused by invasive synovitis or tendon attrition on bone spurs.

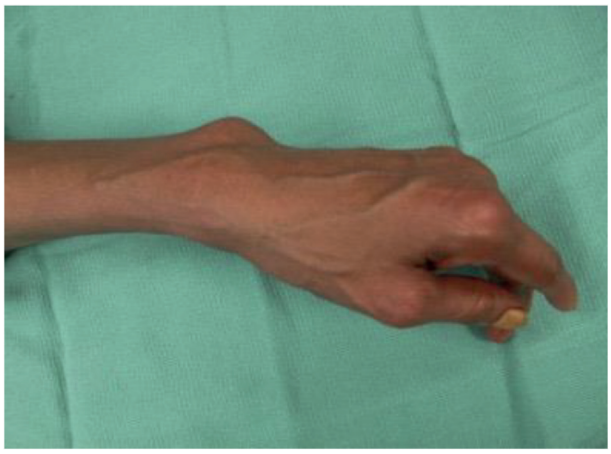

Figure 5 Caput ulnae syndrome. This work © 2017 by Jagadeesan and Shenoy is licensed under Creative Commons Attribution 4.0 International.

Mannerfelt syndrome – rupture of flexor pollicis longus (FPL) within the carpal tunnel commonly secondary to attrition on scaphoid bone spur or other carpal irregularities. FPL rupture subsequently increases the risk of further ruptures of flexor digitorum profundus (FDP) tendons to the fingers.

Vaughan-Jackson syndrome – progressive rupture of extensor tendons from ulnar to radial due to tendon attrition at the wrist due to DRUJ synovitis and instability.

Diagnosis of rheumatoid arthritis

Clinical evaluation

The diagnosis of RA involves a combination of clinical evaluation, laboratory tests, and imaging studies. The clinical evaluation focuses on a detailed patient history, including onset and duration of symptoms, family history of autoimmune diseases, and previous treatments, followed by a physical examination with assessment of joint swelling, tenderness, range of motion, and the presence of deformities or nodules.

Laboratory tests

Laboratory tests are crucial in supporting the diagnosis of RA

Rheumatoid factor (RF): an antibody present in approximately 70%–80% of patients with RA. However, it can also be found in other conditions and in some healthy individuals.

Anti-citrullinated protein antibody (ACPA): currently detected by cyclic citrullinated peptide (anti-CCP) assay and found in about 80% of people with RA. It has increased specificity for RA compared to RF and can provided additional information into RA subtypes and severity of disease.[5]

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP): indicators of inflammation, often elevated in RA; however, up to 40% of individuals with RA may have normal levels.[9]

Imaging studies

Imaging studies help diagnosis, assess the extent of joint damage, and monitor disease progression. Plain radiographs are used to detect joint erosion and deformities, as demonstrated in Figure 6. Signs demonstrated on radiographs include osteopenia with early periarticular osteopenia subsequently becoming more generalized as the disease progresses; joint space narrowing with initial joint space widening in the small joints of the hand as a result of initial joint effusion (however, with cartilage destruction joint spaces narrow); and periarticular erosions at intracapsular articular margins, which begin following the loss of cartilage at the joint and marginal erosions from hypertrophied synovium and granulation tissue.[6]

Ultrasound may be used to visualize soft tissue inflammation and early joint changes of specific joints. Magnetic resonance imaging (MRI) provides detailed images of soft tissue changes such as cartilaginous defects and osseous erosions. It is useful in the early detection of joint damage, able to detect synovial inflammatory changes and pannus formation before evidence on radiographs.

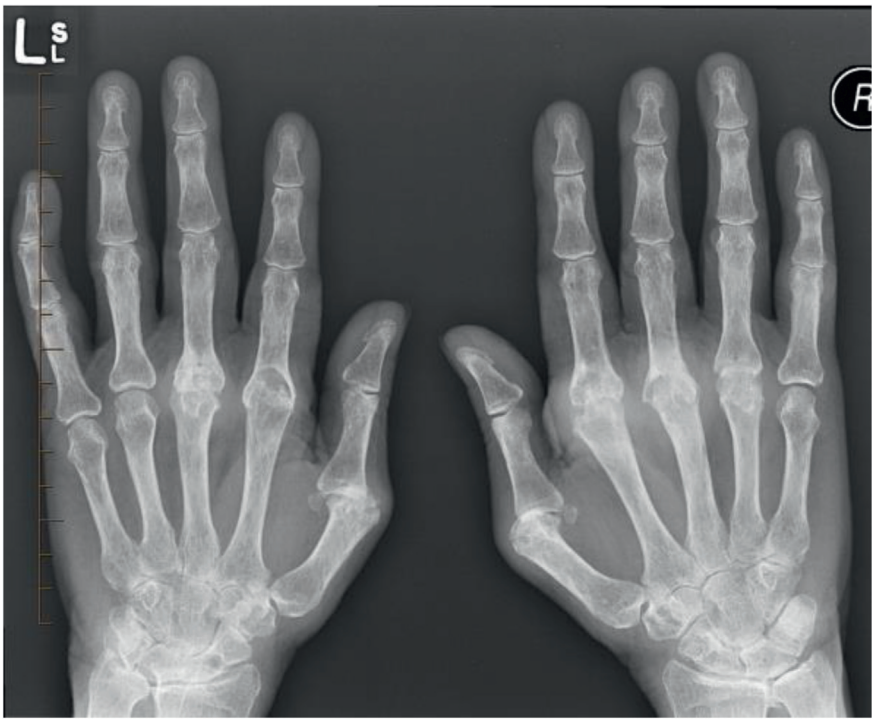

Figure 6 Plain radiograph of the hands demonstrating joint space narrowing, subluxation and periarticular osteopenia. Case courtesy of Dr Frank Gaillard, Radiopaedia.org, rID 2741.

Diagnostic criteria: 2010 rheumatoid arthritis classification criteria (American College of Rheumatology)

The 2010 rheumatoid arthritis classification criteria are a score-based algorithm criteria aimed at the classification of newly presenting patients with at least 1 joint with definite synovitis (swelling) that is not better explained by another disease pathology.[10]

A. Joint involvement: 1 large joint (0); 2–10 large joints (1), 1–3 small joints (2); 4–10 small joints (3); >10 joints (at least 1 small joint) (5)
B. Serology: Negative RF and negative ACPA (0); low positive RF or low positive ACPA (2); high positive RF or high positive ACPA (3)
C. Acute-phase reactants: Normal CRP and normal ESR (0); abnormal CRP or abnormal ESR (1)
D. Duration of symptoms: <6 weeks (0); >6 weeks (1)

A score equal to or greater than 6/10 is required for a patient to be classified as having RA.

Treatment and management

Pharmacological treatment

Significant advances in pharmacological treatment have led to a reduced need for surgical intervention, less severe deformities seen and increasingly less surgical experience in managing these deformities. The primary goal of RA treatment is to reduce systemic inflammation, relieve symptoms, prevent joint damage, and improve overall function achieved through disease remission or low disease activity if this cannot be achieved. Initial monotherapy with a conventional disease-modifying antirheumatic drug (cDMARD) to slow disease progression is increasingly preferred over the previous stepwise approach to pharmacological treatment. If remission or lower disease activity is not achieved on a single agent, combination therapy with additional DMARDs may be added. These may be used in conjunction with nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, which are used to relieve pain and improve function but do not prevent joint destruction.

Conventional disease-modifying anti-rheumatic drugs (cDMARDs)

Methotrexate: the most commonly used first-line DMARD. A folate analogue with anti-inflammatory properties through suppressing cell-mediated immunity and inhibiting IL-1 production. Once weekly oral preparation taken in conjunction with folic acid on remaining days.

Leflunomide: inhibits pyrimidine synthesis, providing an anti-inflammatory effect. Once daily oral preparation.

Sulfasalazine: exact mechanism not fully understood, but considered to inhibit various inflammatory molecules. Daily divided dose oral preparation.

Hydroxychloroquine: prevents activation of toll-like receptors (TLR) altering signalling pathways, inhibiting cytokine production, and reducing the inflammatory process. Single daily or divided dose oral preparation.

Biological and targeted synthetic DMARDs: target-specific components of the immune system. Recommended if there has

been an inadequate response to combination therapy with conventional DMARDs (BNF).

Tumour necrosis factor (TNF) alpha inhibitors/antagonists: inactivate the inappropriate or excessive activation of TNF-alpha signalling associated with chronic inflammation. Examples include etanercept, infliximab and adalimumab. Administered either subcutaneously or as intravenous infusion at weekly, alternate or multiple week intervals.

Interleukin-6 (IL-6) inhibitors/antagonists: tocilizumab and sarilumab.

T-cell activation inhibitors (CD80/86 inhibitor): abatacept.

B-cell depletion therapy (anti-CD20 drug): rituximab.

Janus kinase (JAK) inhibitors: a newer class of oral medications that inhibits the activity of one of more Janus kinase enzymes and signalling pathways involved in the inflammatory process, such as tofacitinib and baricitinib. Single daily or divided dose oral preparation.

Non-steroidal anti-Inflammatory drugs (NSAIDs) reduce acute inflammation, improving pain control and stiffness associated with RA. NSAIDs should be used at the lowest effective dose and stopped, if possible, when a satisfactory response to DMARDs is achieved.

Corticosteroids: potent anti-inflammatory drugs that can be used for short-term relief of severe symptoms or as bridging treatment to provide prompt symptomatic control when establishing DMARD treatment, which has a slow onset of action. Corticosteroids, such as prednisolone or methylprednisolone, are effective in relieving symptoms, however they have a considerable side effect profile, particularly when used long term.

Non-pharmacological treatment

In addition to medications, non-pharmacological treatments play a crucial role in managing RA in the hands, working synergistically to reach treatment aims and support a better quality of life. Physical therapy has a well-documented positive impact on patients with RA and consists of tailored exercises to maintain joint flexibility, strengthen muscles, and improve hand function. Occupational therapy uses techniques and assistive devices to aid in daily activities and reduce joint strain. These may include hand splints and supports to protect and align the joints, reducing pain and preventing deformities. Lifestyle modifications including dietary and nutritional support, individualized exercise programmes and smoking cessation can further improve overall health and reduce disease impact.[11]

Surgical interventions

When conservative treatments fail to provide adequate relief or prevent progression, surgical options may be considered.

Synovectomy: removal of inflamed synovial tissue to reduce pain and improve joint function.

Tendon reconstruction/transfer: usually direct repair is not feasible and tendon transfer is required to restore movement.

Joint replacement: in severe cases, replacing damaged joints with prosthetics to restore function and alleviate pain. This often requires careful re-balancing of the surrounding soft tissue structures to support the implant and prevent recurrent deformity.

Joint fusion: reducing pain in severely damaged joints or stabilizing joints where tendons have failed by fusing bones together.

It is important to recognize there may often be many different sites of deformity and pain within the hand, however the surgeon will work with the patient to consider what surgery could be considered to improve their hand function and quality of life. Often individuals with rheumatoid arthritis have adapted remarkably well to their significant hand deformities and wish to discuss the options available to them with the hand surgeon, providing an opportunity for shared decision making between patient and clinicians.

Rheumatologists retain the oversight of the patient's care when coordinating with the range of specialists involved in the care of RA and importantly medical management must be optimized prior to considering surgery, and the timing of any surgery therefore must be in collaboration with the patient's rheumatology team and treatment schedules. Consideration must be made to which treatments should be continued in the peri-operative phase and which need to be withheld, balancing the potential impact of a disease flare on quality of life with the risk of immunosuppression and increased risk of perioperative infection. Medications to be continued throughout surgery include DMARDs and select biologics (rituximab, belimumab and anifrolumab). Many biologics and JAK inhibitors, however, need to be withheld prior to surgery and have a post-surgical plan to restart once the surgical wound shows evidence of successful healing with suture or staples removed and no evidence of surgical or non-surgical site infection present.[12]

Living with rheumatoid arthritis in the hands

Daily living and coping strategies

Living with RA in the hands requires a multifaceted approach to manage symptom burden and maintain quality of life. Self-management programmes support patients to learn more about the condition and provide practical tips on how to manage everyday living. Energy conservation and goal setting exercises aim to pace activities to avoid fatigue, including taking regular breaks and prioritizing tasks. Additionally, joint protection techniques, such as using assistive devices or larger joints to carry objects, and adaptive equipment, the use of specially designed tools to make daily activities easier, such as jar openers, ergonomic handles, and button hooks, may reduce stress on affected joints. Techniques to manage pain in combination with medical therapy include utilizing heat and cold therapy and relaxation techniques.

Psychological support

The chronic nature of RA and its impact on hand function can lead to emotional and psychological challenges. Supportive strategies include counselling to address anxiety, depression, and

stress related to living with a chronic illness. These may be utilized alongside practices such as mindfulness, meditation, and yoga to manage stress and improve mental wellbeing. In addition, support groups can facilitate networking of individuals with RA to share experiences, advice, and emotional support.

Regular monitoring and follow-up

Regular monitoring and follow-up with healthcare providers are essential for managing RA effectively. Scheduled routine appointments with rheumatologists to monitor disease activity, adjust medications, and address any new symptoms or complications. The monitoring of disease activity and treatment response is supported by laboratory tests and imaging to periodically assess inflammation levels, monitor medication side effects, and detect joint damage early.

Research and future directions

Research in RA is ongoing, with several promising areas aimed at reducing the incidence of RA and slowing disease progression. Genetic research is focused on identifying genetic markers to predict disease risk and response to treatment. Ongoing research into the immunological processes causing RA are leading to the early development of new treatments including biological therapies that target specific pathways in the immune system with fewer side effects for patients.[13] Stem cell-based therapy research is exploring the potential of stem cells to stimulate regeneration of damaged tissues and modulate immune responses responsible for inflammation.[14] ◆

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Practice points

- Rheumatoid arthritis is a chronic autoimmune disorder resulting from a T-cell-mediated immune response against the synovium, cartilage, and bone. The progressive immunological response involves mononuclear cells, IL-1 and TNF alpha
- Medical management of RA aims to reduce systemic inflammation and prevent joint damage. DMARD monotherapy to achieve rapid disease remission is first-line treatment following diagnosis. Combination therapy is offered thereafter if the treatment target has not been achieved
- Advances in pharmacological management have significantly impacted the prognosis of RA and associated deformity in the hands leading to a decrease in surgical interventions
- Hand surgery, however, remains a key treatment option for the correction of deformity and functional impairment. Surgical options include synovectomy, tendon reconstruction and/or transfer, arthroplasty, and joint fusion