Rheumatoid arthritis: An overview

Angela DeLaura

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A Thesis Submitted to the Faculty of
The College of Fine and Applied Arts
In Candidacy for the Degree of
MASTER OF FINE ARTS

RHEUMATOID ARTHRITIS: AN OVERVIEW

By

Angela DeLaura

August 1, 1989
September 7, 1989

Without doubt,

This thesis is one of the most accurate presentations of subject matter ever submitted in the Masters' Program of Medical Illustration.

The bibliography is outstanding!

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ACKNOWLEDGEMENTS

This thesis is dedicated to my friends, faculty committee members, and family, especially my father, for his continuous support, encouragement, and devotion.

All illustrations contained within this paper are by the author and are intended to be integral to the written component of the research. They are included at the end of the appropriate chapters.
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Chapter I.

INTRODUCTION

Goals of the Study

The purpose of this thesis is to conceive and create a series of medical illustrations which reflects a descriptive overview of Rheumatoid Arthritis (RA). Five specific areas of the disease are investigated: 1.) History, definitions, variants, statistics, 2.) Morphology, 3.) Etiology and pathogenesis, 4.) Clinical course, and 5.) Treatment.

The written component of the thesis integrates the technical literature with the visual material, to provide a more complete understanding of the origins, current research models, and implications of this crippling disease.

Five specific goals are designed to guide the research and illustration process:

1. Maintain conceptual and anatomical accuracy through-out; maintain aesthetic criteria as it correlates to complex medical information.

2. Visually communicate the essentials of RA via a comparison, when possible, to a normal or non-diseased state.

3. Develop appropriate icons to depict recurring anatomical structures, i.e., the body, hand, and generic joint, as primary loci of disease.

4. Create images with and without the benefit of direct observation; critically use available resource material to expand a vocabulary of medical images.
5. Offer the reader generalized information on RA, further education and awareness and the central role a patient can play in his own health care.

**History and Development of Medical Illustration**

Medical illustration, an ancient profession, is inextricably linked to the development of direct observational techniques that brought medical practice out of the dark ages of superstition and mistaken adherence to unproven theory.

The foundations of modern medical science are usually traced back to two great Italian anatomists: Andreas Versalius and Leonardo da Vinci. Versalius, whose masterpiece of 1543, *De Humani Corporis Fabrica* (O'Malley and Saunders, 1950), is principally remembered for its stunning wood block illustrations produced in Titian's workshop. Prior to Versalius and da Vinci, medical texts were largely unillustrated, and those plates that did accompany the text were usually copied from earlier works, with no reference to the actual dissection of human bodies (Jansen, 1962). Versalius and his artists, along with da Vinci, however, strictly adhered to the visual facts that they could establish through direct observation of cadavers. In so doing, they demonstrated both the value of original research and the need for accuracy for effective visual communication in medical science. Thereafter, during the
16th through 19th centuries, the roles of the artist/illustrator and scientist/physician grew dramatically through the consequent discoveries of the world and of man himself in nature.

The modern profession of medical and scientific illustration has far out-grown the Renaissance notions of artists embellishing a textbook. Max Brodell, in 1911, migrated from Germany to begin the first school in the United States at Johns Hopkins University, where the program continues today. With the rise of new technologies and information of the 20th and 21st centuries, medical illustrators now must meet the challenges of the communications industry for the bio-medical sciences.

The ability to visually interpret information clearly, concisely, and correctly with technical skills and creativity, is the process by which art and science is truly represented as a single expression.
Chapter II.
OVERVIEW OF RHEUMATOLOGY

History and Development

Arthritis is one of the oldest known diseases. Studies on prehistoric skeletons indicates early close association in "homo sapiens" (Smith and Jones, 1910). It is a general term used when the joints themselves are the major seat of the rheumatic disease. The earliest known example of multiple arthritis in a fossil vertebrate is in the skeleton of a platycarpus (a large swimming reptile), which lived about 100,000,000 years ago. This now resides in the Museum of Natural History at the University of Kansas (Murphy, 1943). Chronic arthritis of the spine was present in the Ape Man of 2,000,000 years ago as well as in our ancestors, the Java and Lansing men of 500,000 years ago, and the Egyptian mummies dating to 8,000 B.C. (Osgood, 1948). The Romans built extensive baths throughout their empire because of the prevalence of the disease (Jansen, 1962).

Rheumatism is derived from the Greek work "rhumatismos" which designated mucus (catarrhah) as an evil humor which was thought to flow from the brain to the joints and other portions, producing pain (Hormell, 1940). Since many other studies (Ragan, 1948; Mikkelsen, 1976) have shown that an alteration of an important constituent of the joint mucin
(the mucopoly-saccharide: hyaluronic acid) actually occurs in at least some of the 'rheumatic diseases', the term at long last may be somewhat appropriate.

The term 'rheumatism' was probably introduced by Galen in medieval times (Copeman, 1969), but it was Baillou (1583-1658) who first used the word in its modern sense to designate it as a form of acute polyarthritis which has no connection to gout (Baillou, 1643). He was also the first to regard rheumatism as a clinical entity. (Copeman, 1969) Today the term 'rheumatic diseases' or 'rheumatology' is used to cover a large variety of diseases including rheumatic fever, bursitis, arthritis, gout and other conditions. They are induced by aging, hereditary and environmental factors such as physical, chemical, infective, metabolic and immunologic. These in turn, produce signs and symptoms referable to the musculoskeletal system and connective tissue, which cause somatic pain, stiffness and inflammation. Obviously, the term 'rheumatoid diseases' has little pathological meaning, but it does provide a system of classifying several poorly understood diseases and disorders.

Rheumatoid arthritis (RA) then, is one such condition or group of conditions. It was first recognized as a separate disease entity in 1800 by Landre-Beauvais, with a pathology distinct from gout (Copeman, 1964). However, Virchow in 1863 called all forms of chronic arthritis "arthritis deformans" and Charrot also believed they were the
more or less the same disease: 'rheumatisme articulaire chronique" (Charot, 1889). By 1906, Bannatyne had successfully further distinguished RA from osteoarthritis (Copeman, 1964).

The 'renaissance of rheumatology' began shortly after World War II, when numbers of young physicians who had been trained in Army Arthritis centers returned to civilian practice (Copeman, 1969). Due to the founding of the Arthritis and Rheumatism Foundation (1948), the discovery of the effects of cortisone on arthritic inflammation (1949), and the establishment of the National Institute of Arthritis and Metabolic Diseases (1953), tremendous impetus and focus was given to RA. The same remarkable growth trend has been noted in many other countries throughout the world.

Definitions of Rheumatoid Arthritis

Rheumatoid arthritis then, is a major member of a group of inflammatory system connective tissue diseases ("collagen diseases"), which includes rheumatic fever, disseminated lupus erythematosus, polyarthritis, scleroderma, and possibly other conditions (Lichenstein, 1975). Duthie, a foremost rheumatologist, defines RA as a "subacute or chronic, non-suppurative, inflammatory polyarthritis affecting mainly the peripheral synovial joints, normally in a symmetric fashion, running a prolonged course of exacerbations and
remissions, and accompanied by signs of systemic disturbance such as anemia, weight loss and a raised erythrocyte sedimentation rate" (Duthie, 1969).

Other generalized manifestations include: age of onset at the third to fourth decade, world wide prevalence of three-percent, affecting females to males (3:1 ratio), usual presence of rheumatoid factor (RF), infiltration of lymphocytes and plasma cells, x-ray findings with erosions and osteoporsis, subcutaneous nodules (present in 20%), and end-stage bony or fibrosis ankylosis, and, or amyloidosis (Huskisson, 1987; Ghadially, 1985; Berens and Lin, 1979).

Variants of Rheumatoid Arthritis

Two varieties of RA merit brief descriptions: Juvenile Rheumatoid Arthritis (JRA) and Felty's syndrome.

Juvenile RA, or Still's disease is an uncommon, crippling disease of children which primarily involves the joints and cervical spine along with enlargement of lymph nodes, liver and spleen. Children usually test positive for rheumatoid factor (RF). The peak incidence is between the ages of one and three years (Robbins and Kumar, 1987); however the sixteenth birthday is usually considered the upper age limit for juvenile onset (Calabro, 1979). Unlike the classic form of RA, 50% of all patients experience complete remission (Hollander, 1980).
Felty's syndrome comprises the triad of polyarthritis (inflammation of several joints together); leukopenia (abnormal reduction in number of WBC's in blood); and splenomegaly (enlargement of the spleen). This disease occurs in patients between forty-five and sixty-five years of age although has onset many years before detection of the splenomegaly (Zvavilfler, 1985). It presents the manifestations of systemic rheumatoid disease, i.e., high titers of RF in the serum and subcutaneous nodules, however, in these patients the hematologic problems often predominate the clinical picture. Felty's accounts for less than five-percent of all cases coming to medical attention (Mitchel, 1985).

Epidemiology

According to latest estimates derived from numerous surveys published (Arthritis Foundation, 1985), there are over 20,100,000 people suffering from some form of arthritis or related disease in the United States; RA specifically affects over 2,400,000. The distribution prevalence of three-percent of the population is worldwide with a consistent female to male ratio of three to one (Hollander, 1980).

Although arthritis cripples a large number of persons each year, it kills relatively few. There is no other group
of diseases which causes so much suffering by so many for so long. Because of the tendency to cripple without killing, arthritis and rheumatism belong at the very top of the list of chronic diseases from the standpoint of social and economic importance. National Health Survey figures showed that 26% of the people with rheumatic disease were at least partially handicapped, and about 10% were grossly disabled. Arthritis and rheumatism result in 27,000,000 lost work days yearly, second only to heart disease as the cause of chronic limitation of ability to work (Report of National Arthritis Commission, 1985; Hollander, 1980).

Classification System

Most cases of arthritis (Hench, et.al., 1948) fall into one of five groups:

Group I: cases caused by a specific infectious microorganism

Group II: cases that are possibly infectious but of unproven etiology

*Group III: cases representing degenerative forms of joint disease

Group IV: cases in which arthritis results from direct trauma to the joint

Group V: cases of metabolic arthritis (i.e. gout)

In 1963, the American Rheumatism Association (ARA) approved the terminology of this classification system and is recommended for general use (Blumberg, Bunim, et.al., 1964).
Group III (degenerative forms of joint disease) will be the major topic of discussion for this paper.

See Figure 1. Title Panel: Rheumatoid Arthritis
RHEUMATOID ARTHRITIS

1. Title Panel: Rheumatoid Arthritis

Scale: 1" = 2.6"
Rheumatoid arthritis is a systemic disease that can cause significant damage to many organs, although its most destructive effects are seen in the joints. Classically, it is characterized by bilateral symmetric joint involvement, which principally affects the small joints of the hands, feet and wrist, large joints of the shoulder, hip joints, elbow, temporomandibular joint, and sometimes the joints of the vertebral column. See Figure 2. Primary Disease Sites in the Body.

Non-articular manifestations (Huskisson and Hail, 1987) occur in the peri-articular soft tissues, i.e. subcutaneous nodules, tenosynovitis around hands or wrists, bursitis, synovial cysts, and muscle wasting. Major organs including the heart, lung, spleen, eyes, and skin are also target sites although not as common for disease activity. Vasculitis (inflammation of the blood vessels), neuropathy (compression and carpal tunnel syndrome), and osteoporosis and bone fractures also have been shown correlative to RA.

Clinicians and radiologists alike have focused particularly on the hands and wrists in RA because of the early joint involvement, their functional importance, the
fairly characteristic appearance of the disease at these sites, and the ease with which high-quality radiographs of these thin body parts are obtained (Genant, 1979).

The most common sites of early involvement include the ulnar styloid, the first through third metacarpophalangeal joints (Berens and Lin, 1969); see Figure 2. **Sites in the Hands.** This schematic representation of the hand illustrates the most frequent sites of early erosion in RA.

Articular erosions are a form of bone resorption along the surface of subchondral compact bone. These erosions are usually preceded by soft-tissue swelling. Erosions generally begin at the joint margin in the region of the synovial reflection where the cartilage ends and the capsule inserts in the "bare" areas (Martel, 1968). Here, as pannus develops and erodes local cartilage, the underlying cortical and deeper cancellous bone becomes rarefied and indistinct, and later focally destroyed, thereby producing the initial 'surface erosion' (Genant, 1979). See: Differential Diagnosis: Radiology.

**Subcutaneous Nodules**

Rheumatiod subcutaneous nodules eventually develop in about one-quarter to one-third of patients (Robbins and Kumar, 1987), and are often the hallmark of the moderate or severe stage (Boyle, 1984). These granulomas occur in
subcutaneous tissue and tendon, and may also be found in internal organs such as the heart, lung, and spleen (Huskisson and Hail, 1987). They are firm, nontender, oval or rounded masses varying in size from millet seed-like to up to 2cm in diameter (Robbins and Kumar, 1987). Excision is the only useful treatment and is usually at least temporarily successful for the more common nodule; recurances are very common (Decker and Plotz, 1979).

They have characteristic histological features (Dieppe, Bacon, et.al., 1986): a central area of neurosis is surrounded by mononuclear cells, the macrophages align with their long axes pointing to the center of the lesion, and outer layer of fibrous tissue.

Superficial nodules occur over pressure areas, the most common sites being the ulnar border just below the elbow and over the Achilles tendon. Small nodules are found only by careful examination, and are usually hard and attached to the underlying periosteum. High titers of serum IgM rheumatoid factor are nearly always found in nodular disease and is therefore, diagnostically important (Dieppe, Bacon, et.al., 1986).

Stages of Rheumatoid Arthritis

Descriptions of the progressive nature of RA slightly vary within the literature. The American Rheumatoid
Association (ARA) in 1981, revised the classification of the anatomical stages of the disease; this standardization of nomenclature is designed to categorically define specific phases and thereby facilitate disease diagnosis and management. Noted rheumatologists (McCarthy, Duthie, Ghadially, Copeman, etc.) have also sought to generalize the essential morphological changes.

For purposes of simplification, the following stages condense and exemplify the disease's four main stages:

**Stage I (Early)**

The process begins as a non-specific inflammatory synovitis characterized by swelling and hypertrophy of the synoviocytes and the underlying connective tissues. Soft-tissue swelling, thickening of the affected joint capsule(s) and slight osteoporosis maybe seen. However, there is no major damage upon X-ray examination.

**Stage II (Moderate)**

In this phase, there is X-ray evidence of osteoporosis, with or without slight sub-chondral bone destruction; slight articular cartilage destruction may be present due to the inflamed synovial tissue (pannus) which has begun to grow into the joint cavity across the cartilage. X-ray evidence will show narrowing of the joint spaces due to cartilage loss, creating limitation of joint mobility. No joint deformities are present, however, adjacent muscle atrophy may occur. Extra-articular soft tissue lesions, i.e. nodules, teno-synovitis may be present.

Pannus is essentially a sheet of fibrovascular granulation tissue arising from the perichondral synovial membrane. It is very firmly attached to the surface of the articular cartilage. It presents a shaggy surface because of the small villous projections and adhesions (stretching across from the opposite joint face) torn during opening the joint (Ghadially, 1983).
Stage III (Severe)

The pannus of synovium having destroyed the articular cartilage now partially fills the joint cavity, and the erosions have begun into the sub-chondral bone. X-ray evidence will show cartilage and bone destruction, in addition to osteoporosis. Joint deformity, i.e. subluxation, ulnar deviation or hypertension may be present, however without fibrous or bony ankylosis. There is extensive muscle atrophy and extra-articular soft-tissue lesions, i.e. nodules and teno-synovitis may be present.

Stage IV (Terminal)

In the final stage of the disease, the inflammatory process will subside and fibrous or bony ankylosis of the joint will end its functional life. All other criteria of Stage III may also be present.

Despite the fact that early and late changes in the joint are well recognized, this chronic disease shows such variations in severity and progression, that it is often difficult or impossible to distinguish from pathological examination alone the sequence of earlier RA from the heavy overlay of secondary osteoporosis after the inflammatory reaction has subsided (Lichtenstein, 1975), or whether the disease has been present for a few months or many years (Robbins and Kumar, 1987). Additionally, a number of changes can occur simultaneously.

Figure 3. Stages of Rheumatoid Arthritis compares a healthy synovial joint to that of the progressive destruction within the joint capsule: synovial inflammation, pannus formation, and subluxation with bone erosion.
Primary Disease Sites in the Body

1. Temporomandibular joints
2. Shoulders
3. Vertebral column
4. Elbows
5. Wrists
6. Small joints of the hand
7. Hips
8. Knees
9. Ankles
10. Small joints of the foot

Sites in the Hand

Scale: 1" = 2.7"
Chapter IV.
ETIOLOGY AND PATHOGENESIS

Theoretical Origins

Almost all definitions of RA emphasize its chronic and inflammatory nature. These characteristics are immediately evident on examining the swollen, red, and tender joints of affected patients and on sampling the fluids that both the joints (See: Differential Diagnosis: Synovialysis). The inflammatory response is considered to be a biological adaptation to protect the host from a hostile environment; a prerequisite is that this response be accomplished without significant injury to the host's own tissue. Therefore, the inflammation in RA must be considered inappropriate.

What causes this disease and what mechanism(s) facilitate their introduction into the host? Despite advances in our understanding of the immunologic processes leading to articular inflammation and the biochemistry of connective tissue destruction, the cause of this malady remains an enigma. It is still not clear whether RA is one disease with multiple etiologies or a symptom complex produced by a single causative factor.

Over the years, many theories have been considered and discarded; therefore the brief discussion that follows will be limited only to current hypotheses.
Evidence implicating a specific infectious pathogen is still lacking; researchers have yet to find any bacterial or viral particles in rheumatoid tissue that would persist as a stimulus to rheumatoid factor (RF), a unique antibody. However, much interest has focused on Epstein-Barr Virus (EBV) in connection with RA. Antibodies directed against an EBV antigen have been found in the serum of 65-93% of cases of RA. It is still not known whether EBV injection is an etiologic or coincidental factor.

Perhaps there is malfunction of the immune system at some point, i.e. RF producing B and T lymphocytes are not removed from the circulation during the development of the immune system. Another possible explanation could come from genetic origins, i.e., there is a significant association of RA with tissue type HLA-DR4, which has been reported by Griffin, et.al., 1984.

However, the "immune-complex theory", which holds that there is a local and perpetual immune reaction, is considered to be the most attractive hypothesis for this disease and is currently widely accepted as causative.

Pathogenesis

Cellular and Immunological Mechanisms

Although the basic cause of RA is not yet defined, the mechanisms leading to the various pathological effects are
better understood. Rheumatoid arthritis arises from the results of abnormal and detrimental immune system activity within the body. There is some original and presently unexplained impetus that results in the formation of what is known as "rheumatoid factor" (RF), which leads to the misplaced immune response. Despite extensive research, the basic cause of the disease remains unknown.

Overall, a synovitis is first seen, followed by a proliferation of the inflamed tissue into the joint cavity. The inflammation gradually spreads across the articular cartilage and into the underlying bone. Eventually, inflammation subsides, but scar tissue remains. The scar tissue, plus the interaction of muscles, tendons and ligaments with the inflamed joints themselves, leads to the deformation of the infected areas. The result is the destruction of various joints of the body, especially the small joints of the tarsals, carpals, and phalanges (Ghadially, 1985; Hough and Sokoloff, 1985; Utsinger, Zvaifler, et.al., 1985).

For purposes of simplification, five stages of pathogenesis will be considered:

1. initiation of synovitis (presumably by some etiological RF carried to the joint via the circulation)

2. subsequent immunological events that perpetuate the primary inflammatory response in the synovium

3. the transition reaction into pannus formation
4. cartilage and bone destruction, subluxation, ulnar deviation, nodules, and tenosynovitis

5. fibrous, bony ankylosis

In the initiation stage of RA, an unknown impetus leads to the formation of rheumatoid factor (RF), by the coordinated efforts of T and B lymphocytes. RF is a group of antibodies whose specificity is for a class of molecules that naturally occurs in the body: Immunoglobin G (IgG). In general RF is specific for the Fc or constant region of the IgG molecules; this region is found in all IgG molecules. The exact antigenic sites in the Fc section of the IgG molecule have been analyzed and areas in both the Ch2 and Ch3 region of all subclasses (IgG1, IgG2, IgG4, and to a lesser extent IgG3) have been identified as the exact antigenic sites (Kooperman and Schrohenloher, 1985). Thus, beneficial, naturally-occurring antibody is the target for RF. RF's themselves are typically IgM proteins, although RF can also occur as any of the other classes of immunoglobins (IgG, IgD, IgA, IgE). In general, circulating RF is usually IgM, while both RF/IgM and RF/IgG are seen in the synovium (Ghadially, 1985; Hough and Sokoloff, 1985; Utsinger, Zvaifler, et.al., 1985).

Any of these bindings (RF to IgG) is viewed by the body as an immune complex. In general, the presence of immune complexes in blood vessels cause platelets and basophils to release vasoactive amines, which causes complement to be
fixed and activation of the Hageman factor (Robbins, 1987; Roitt, Brostoff, et.al., 1985). Vasoactive amines leads to increased vascular permeability, leading to edema and allowing the immune complexes to deposit in between the endothelial cells. Products of complement fixation, C3a and C5a, also increase vascular permeability (C5a is a chemotactic factor for neutrophils). Ordinarily, the neutrophils attach to the antigen-antibody complexes via cell surface receptors and phagoctyzes and remove the immune complexes. Neutrophils, however, have great difficulty in phagocytosing the immune complexes that have deposited in the tissue. The result is "frustrated phagocytosis" in which the neutrophils release their enzyme-containing granules into the blood stream and onto the endothelium, causing local tissue damage. Platelets also form microthrombi between the cells, leading to tissue injury (Robbins, 1987; Roitt, Brostoff, et.al., 1985). Therefore, a peristance of immune complexes results and a Type III Hypersensitivity (Immune Complex Disease) develops (Hough and Sokoloff, 1985; Robbins, 1987; Roitt, Brostoff, et.al., 1985; Utsinger, Zvaifler, et.al., 1985). It is also thought that the existence of circulating RF preceeds synovial involvement (Zvaifler, 1985).

Synovitis results when the attempt to clear immune complexes occurs in the synovial tissue of a joint. It is not clear why the small joints of the hands and feet are the "favored soil" for the disease; possibly RF is in some way
tissue-specific (Roitt, Brostoff, et al., 1985). Also, it is not known whether vasculitis must always precede synovitis, but damaged blood vessels in or around the synovium would allow all the necessary components of inflammation, (i.e., the immune complexes, complement, circulating IgG, neutrophils, RF specific B and T cells, serum proteins, etc.) to pass easily into the synovium (Ghadially, 1985). Once in the synovium, RF-specific B cells continue to produce RF, via the influence of lymphokines produced by RF-specific T cells. Immune complexes of all varieties (RF/IgM-IgG, RF IgG-IgG) form in the synovium and in the synovial fluid. These immune complexes attach to the surface of the synovium and the frustrated phagocytosis of the neutrophils results in a "rain" of destructive enzymes and free oxygen radicals onto the surface of the synovium (Robbins, 1987; Roitt, Brostoff, et al., 1985). The destructive molecules are released from the lysozomes of the neutrophils, which include neutral proteases that can digest basement membranes, collagen, elastin, and cartilage. These enzymes can also cleave the C3 and C5 molecules of the complement system, furthering the generation of C3a and C5a; furthermore, kallikrein is also released, leading to the formation of bradykinin, a pain mediator (Robbins, 1987).

In the next stages of the disease, pannus, or granulation tissue forms in the synovium. Lymphokines from the RF-specific T cells cause proliferation of the
synoviocytes, more RF-specific B and T cells, fibroblasts, and blood vessels. The result is that the synovium greatly increases in thickness with its lining cells becoming elongated and arranged in a palisade fashion. Also, fibrin is deposited onto the synovial surface, forming a thick cap in some places, and also in the matrix of the synovium. Beneath the palisade layer are up to twenty layers of synoviocytes, sometimes including giant multinucleated cells. Foci of necrosis do occur, as well as desquamation (Ghadially, 1985). B and T lymphocytes tend to concentrate in compact foci around blood vessels. T cells, however, also migrate throughout the synovial tissue and fluid, while B cells and plasma cells are relatively immobile, and form the bulk of the lymphocytes within the granulation tissue (Boyle, 1984; Ghadially, 1985; Robbins, 1987; Utsinger, Zvaifler, et al., 1985).

Once the articular cartilage is covered with pannus, the inflammatory process erodes the cartilage. The destruction is most noticeable at the cartilage-pannus junction, resulting in a "chewed" appearance (Hough and Sokologg, 1985). As subchondral granulation forms, the adjacent chondrocytes become necrotic and the articular cartilage disappears. Using immunohistological techniques, immune complexes and collagenases have been demonstrated in pannus in these areas. Also, prostaglandins, which are involved in several aspects of the inflammatory process, have been
produced when pannus is cultured *in vitro* (Zvaifler, 1985). Once collagen has been destroyed, the damage to the articular cartilage is irreversible (Boyle, 1984; Ghadially, 1985; Zvaifler, 1985).

Ultimately, erosions begin to appear in the subchondral bone. Since the subchondral granulation tissue is continuous with granulation tissue in the synovium, there is massive inflammation of the surrounding tissues. Osteoclastic bone resorption occurs and normal vascular foramina become enlarged; the bone weakens and the bone marrow also may become inflamed (Ghadially, 1985; Robbins, 1987). Eventually, the inflammation subsides, perhaps because most of the pannus has been replaced by scar tissue and that there are no cells left to "feed" the infection.

Subluxation results from the result of muscle action over the altered surfaces and weakened synovial capsules and ligaments. Tendon contractures and ruptures also can add to the macroscopic disfigurement and destruction.

Finally fibrosis and in extreme cases bony ankylosis fuse the joints (Boyle, 1984; Hough and Sokoloff, 1985). Tendons and ligaments, which are near to the synovial capsules in small joints may also be similarly damaged.

**Pathological Features**

**Serositis and Vasculitis**

The three main pathological features of RA are
serositis, nodules and vasculitis. Subcutaneous nodules are discussed in the Morphology section, therefore, a brief description of vasculitis and serositis completes the clinical profile.

Vasculitis affects a small proportion of patients with RA. Inflammation of the walls of small blood vessels may result in a number of different pathological features. The most common lesions occur around the nails and may appear transiently during the phases of active disease. More persistent vasculitis may result in peripheral ulceration and even gangrene; characteristic vasculitic ulcers are very painful (Dieppe, Bacon, et al., 1986).

Serositis, the inflammation of a serous membrane, manifests itself in the synovial tissue, tendon sheath, and bursa, causing synovitis, tendonitis, and bursitis. Synovitis in RA has features of both chronic and acute inflammation; it is usually painful, particularly on motion, and is characterized by a fluctuating swelling due to effusion within the synovial sac (Ghadially, 1985). Synovitis may be visualized directly by either arthroscopy or at arthrotomy.

Tendonitis and bursitis may also cause destruction and deformity, leading to joint subluxation, laxity of periarticular tissues and tendon rupture. Tendonitis is the inflammation of the tendon and tendon muscle attachments. Bursitis affects the bursa, the fluid filled cavity located within the tissue where friction would otherwise develop.
Together, these two manifestations are associated with the development of a characteristic set of clinical deformities: ulnar drift of the fingers, Swan Neck deformities, loss of finger extension/flexion, and wrist subluxation. (Boyle, 1984) Figure 4. Normal Joint Architecture, Rheumatoid Synovitis illustrates the contrasting changes that may occur within the RA joint architecture. Such severe features of the disease may warrant surgical intervention, should drug therapy prove ineffective. (See: Treatment, Surgery).
Normal Joint Architecture

Rheumatoid Synovitis

- Bursect
- Tendon
- Synovial sheath of tendon
- Synovial membrane
- Synovial cavity
- Articular cartilage
- Joint capsule
- Muscle

4. Normal Joint Architecture, Rheumatoid Synovitis

Scale: 1" = 2.0"
Chapter V.
CLINICAL COURSE

General Description

Although RA is basically a symmetric polyarticular arthritis, the joint involvement may be connected with constitutional symptoms such as weakness, malaise, weight loss, and low grade fever. Many of these conditions result from the release of IL-1 upon activation of macrophages under the influence of T cells (Robbins and Kumar, 1987).

The arthritis first begins with aching and stiffness in the joints, particularly in the morning. Although the small joints of the hand are usually affected first, other joints become involved in most cases and sometimes virtually all the joints of the body are affected. (See Fig 2. Primary Disease Sites in the Body, Sites in the Hand). As the disease advances the joints become enlarged, motion is limited, and complete ankylosis may occur. The fingers may become completely immobilized in a claw-like position, and in advanced cases ulnar deviation may result. At this stage of the disease, anemia is common. Vasculitis may give rise to chronic leg ulcers, and may even cause infarctions in the brain, heart, or intestines.
Classification Criteria

The American Rheumatoid Association (1983) has developed four categories to classify degrees of RA: classic, definite, probable, and possible:

**Classic** RA requires seven of the following criteria; in criteria 1 through 5, the joint signs or symptoms must be continuous for at least six weeks; criteria 2 through 6 must be observed by a physician:

1. Morning stiffness.
2. Pain on motion or tenderness in at least one joint.
3. Swelling of soft tissue in at least one joint.
4. Swelling of at least one other joint.
5. Symmetrical joint swelling.
7. Roentgenographic changes typical of RA (must include at least bony decalcification localized to involved joints).
8. Positive agglutination test (demonstration of rheumatoid factor).
9. Poor mucin precipitate from synovial fluid (synovianalysis).
10. Characteristic histologic changes in the synovium with three or more of the following:
   a) marked villous hypertrophy
   b) proliferation of synovial cells with palisading
   c) marked infiltration of chronic inflammatory cells (lymphocytes or plasma cells)
   d) deposition of compact fibrin on surface or interstitially
   e) foci of necrosis
11. Characteristic histologic changes in nodules showing foci with central zones of cell necrosis, surrounded by a palisade of proliferated mononuclear and chronic inflammatory cell infiltration.

**Definite** RA diagnosis requires five of the above criteria; in criteria 1 through 5, the joint signs or symptoms must be continuous for at least six weeks.

**Probable** RA diagnosis requires three of the above criteria; in at least one of criteria 1 through 5, the joint signs or symptoms must be continuous for at least six weeks.

**Possible** RA diagnosis requires two of the following criteria; total duration of joint symptoms must be at least three months:

a) Morning stiffness
b) Tenderness or pain on motion for at least three weeks
c) History of observation of swelling
d) Subcutaneous nodules
e) Elevated sedimentation rate

**Classification of Functional Activity in RA**

**Class I:** Complete functional capacity with ability to carry on all usual duties without handicaps.

**Class II:** Functional capacity adequate to conduct normal activities despite handicap of discomfort or limited mobility of one or more joints.

**Class III:** Functional capacity adequate to perform few or none of the duties of usual occupation or of self-care.

**Class IV:** Total or almost total incapacitation, with patient bedridden or confined to wheelchair, able to perform little or no self-care.
Clinical Prognosis

Our knowledge of the course of RA comes from many longitudinal investigations of the disease carried out during the past fifty years. Notable among the early studies (Duthie, Brown, et.al., 1964) in Scotland, whose patients with advanced RA were admitted to tertiary care centers. Other studies have dealt with defined populations who were either hospitalized or nonhospitalized. Based on results of several other major studies, (Mitchell, 1985) makes the following observations regarding the clinical outcome:

1. A poorer prognosis is likely in patients who are seropositive for rheumatoid factor.

2. Patients with radiographic evidence of erosions at diagnosis have a poorer prognosis.

3. Advanced age at study entry was the most powerful predictor of eventual functional disability.

4. Women tend to have more chronic and disabling disease than men.

5. Extra-articular manifestations of disease, i.e. subcutaneous nodules and vasculitis correlate with a more severe course.

6. Delay in treatment and poor initial response to treatment have been cited as pointing to a poor outcome.

However, (Masi, Maldonado-Crocco, et.al., 1986), observe features that may predict a favorable prognosis and clinical course. These include disease of short duration, less swollen upper extremity joints in the early course of the
disease, initial asymmetric joint involvement, acute onset under the age of thirty, favorable response to treatment, male sex, and black race.

Clinical Prognosis Over Time

The clinical course of RA is highly variable. After approximately ten years, the disease in about half of the patients becomes stabilized or may even regress. Most of the remainder pursue a chronic, remitting, relapsing course. After fifteen to twenty years, approximately ten-percent of patients become permanently and severely crippled. Additionally, RA is an important cause of reactive amyloidosis. This complication develops in five to ten percent of these patients, particularly those with protracted severe disease.

Clinical Remissions

Due to the significant number of regressions and remissions in patients with RA, (Pinals, Masi, and the ARA Subcommittee, 1981), established the criteria for clinical remission. For RA to be considered in remission, five or more of the following requirements must be fulfilled for at least two consecutive months:

1. Duration of morning stiffness not exceeding fifteen minutes
2. No fatigue
3. No joint pain (by history)
4. No joint tenderness or pain on motion
5. No soft tissue swelling in joints or tendon sheaths
6. Erythrocyte sedimentation rate (Westergren method) less than 30mm/hour for a female or 20mm/hour for a male.

To be considered for this designation, a patient must have met the ARA criteria for classic or definite RA some time in the past.

The purpose of these criteria is to encourage uniformity in definition and use of the term 'remission'. The authors do not attempt to define a total absence of all articular and extra-articular inflammation and immunologic activity related to RA.

These criteria are based on data provided by sixty-five rheumatologists on 275 RA patients considered to be in complete remission and 269 patients considered to be in partial remission or to have the disease. The majority of patients entering the study had received "remission-inducing" drugs. Although the inclusion of spontaneous remission was actively solicited, few such patients were identified. This may indicate that natural remissions are rare or that such patients are lost to follow-up by rheumatologists.
**Differential Diagnosis**

**General Descriptions**

Prognosis and therapy can only follow with precise diagnosis, i.e., skillful history taking (symptoms) and physical examination (signs), with subsequent laboratory testing, radiology, and a surgical team if indicated.

The purpose of the history and the physical examination, (McCarty, 1979) is to classify a patient's problem into broad categories which represent the primary nature of the disease. Common symptoms include: stiffness, pain, weakness, fatigue and emotional depression; common signs include: swelling, tenderness localized over afflicted joints, heat and erythema, and bony spurs. Signs and symptoms, combined with laboratory investigations, (i.e., synovianalysis, radiography, and rheumatoid factor positivity), are critical in diagnosis of RA. Two specific aspects of differential diagnosis will be discussed in detail: synovianalysis and radiography.

**Synovianalysis**

Paracelsus called joint fluid 'synovia' (like egg). Synovial fluid (synovia) then, is a clear, sticky liquid that is similar to egg white. The synovium is the tissue lining the joint space containing the synovia, terminating at the margin of the articular cartilage, and supported by the dense
fibrous joint capsule. It is richly supplied with blood vessels and lymphatics. Synovia is secreted by the synoviocytes (synovial lining cells). These are normally arranged in layers one to three cells thick, embedded in ground substance but with no basement membrane. The synovium is therefore not a true membrane, but a modified tissue space (Rodman, Beneck, et.al., 1966).

Much information about various arthritic diseases and the systemic rheumatic diseases with prominent joint involvement can be obtained by 'synovianalysis', a term coined to indicate an analogy with urinalysis. Test types include routine and special studies (Hollander, Jessar, et.al., 1961). Routine synovianalysis consists of gross and microscopic examination to assay: color, "mucin" clot, viscosity, clarity, WBC concentrations, and differential leukocyte count (Dorland's Illustrated Medical Encyclopedia, 1988). The analysis of joint fluid is an office or bedside procedure; its function is to divide a given fluid into one of five groups:

Group I. normal
Group II. non-inflammatory (Traumatic arthritis, osteoarthritis)
Group III. inflammatory-immunologic (Systemic lupus erythematosus, RA, and Reiter's syndrome)
Group IV. inflammatory-crystalline (Gout, pseudo-gout)
Group V. inflammatory-infectious (Acute bacterial arthritis, tuberculous arthritis)

Synovia may be easily obtained from the joints by
needling, a procedure known as **arthocentesis**, (puncture of joint followed by a withdrawal of fluid, usually be suction through the puncture needle, or puncture and aspiration of a joint). Aspiration of joints has been used for differential diagnosis in arthritis as well as provide a means for effective local treatment in intra-articular corticosteroid therapy (Ghadially, 1983).

Figure 5. illustrates via comparison the normal and rheumatoid synovial joint analysis as would be expected upon gross and microscopic examination:

**Normal Synovialysis (Group I)**

- **appearance**: straw-colored
- **mucin clot**: good
- **leukocytes per ml.**: <200 (<25%)
- **viscosity**: very high
- **other features**: sugar is 90% of serum level

**Rheumatoid Synovialysis (Group III-inflammatory-immunologic)**

- **appearance**: cloudy, light yellow
- **mucin clot**: poor
- **leukocytes per ml.**: 8,000–20,000 (60–75%)
- **viscosity**: low
- **other features**: low compliment, slightly low sugar

The above values represent combined data from various reports (Ghadially, 1985).

**Radiology**

The gross pathologic processes appearing in the musculoskeletal system in RA are often demonstrable by radiologic examination. A specific radiologic diagnosis is
most often possible, but more importantly, the detection, evaluation, and assessment of the structural joint abnormalities can be achieved.

A good radiographic image is essential for the accurate assessment of subtle skeletal abnormalities. High resolution magnification radiology (i.e. fine-detail) has proven particularly valuable in the evaluation of arthritic and metabolic bone disorders (Jacobs, 1973; Genant, 1979). High resolution magnification is achieved by optical magnification of fine-grain film or by direct radiographic magnification (used for thicker body parts of the central skeleton) (Wicke, 1987). Optical magnification is well established and proven in the clinical assessment of RA, for they are often of a better contrast, higher resolution and less background noise. In a controlled study, fine-detail radiography in patients with RA significantly improved detection of early erosive disease. Assessment of soft-tissue swelling was only modestly improved with high-resolution radiography in patients with early or minimal RA. These results are of particular importance in view of the prognostic significance of the presence of erosive disease in the initial examination. When pronounced changes were initially present, the disease tended to run a rapid course, indicating the early need for more aggressive therapy (Mall, Genant, et. al., 1981).

In RA, the foremost destruction is to the articular and
periarticular structures. Any synovial joint of the body may be involved, but especially the small joints of the hands, wrists, knees, and feet. The process may begin asymmetrically, which in time becomes relatively symmetric. Radiologic manifestations that reflect these gross pathologic changes in RA are seen in three distinct areas: 1) periarticular soft-tissue, 2) the interosseous cartilage space, and 3) the sub-chondral bone (McCarthy, 1979).

Soft tissue swelling develops early in the disease and invariably precedes cartilaginous changes. Swelling results form the accumulation of joint fluid, synovial proliferation, and periarticular edema. Radiographically, symmetric uniform swelling around the joints is easily detected in the small joints of the hands and wrist. Slight, regional osteoporosis may be present in the periarticular regions which contain trabecular bone, (Doi, Genant, et.al., 1976), producing an irregular, patchy demineralization; the dominant hand may be more affected than the non-dominant (Johnson, Hench, et.al., 1973).

Articular erosions are the most distinctive radiologic manifestation of RA, and their radiographic appearance provides an important parameter for disease activity, assessment, and therapy. Erosions begin at the joint margins where pannus also develops and erodes local cartilage. Together, initial surface erosion results in a characteristic "dot-dashed" or serrated appearance of the cortical line
Narrowing of the interosseous space reflects cartilage loss. Such narrowing is almost invariably uniform in a given joint, perhaps reflecting the greater importance of enzymatic degradation of cartilage rather than direct erosion by 'pannus'. This involvement is recognized by the simple loss of distance that separates the articular ends of the bone when viewed tangentially (Jacobs, 1973). A false interpretation of narrowing of cartilage may result from oblique projections (Johnson, Vaughan, et al., 1973). In early disease, a comparison of the interosseous space with that of an adjacent or contralaterally involved joint(s) is essential.

In late disease, the interosseous space may be quite irregularly narrowed or widened as a result of the advanced destruction and fragmentation of sub-chondral bone, and even the damage to the supporting capsule, ligaments and tendons. Osteoporosis is replaced by a uniform demineralization, disease, immobilization, and in some cases, corticosteroid therapy can contribute to this generalized state. Subluxation or eventual dislocation may take place. Bony ankylosis (abnormal joint fixation), although not prominent in adult RA does develop in approximately ten-percent of cases of advanced disease; it primarily involves the small peripheral joints, especially the carpals and the tarsals (Mall, Genant, et al., 1981). Figure 6. Normal Bone Anatomy; Rheumatoid Bone Anatomy illustrates some of the radiographic
features found in later stage of RA as compared to a normal hand. Note the subluxation of the interphalangeal joint of the thumb, loss of interosseus space in the metacarpophalangeal joints, with ulnar deviation and subluxation.

Clearly then, radiology is a significant imaging technique in the diagnosis and management of RA. It correlates gross anatomical structures, (i.e., periarticular soft-tissue, interosseous cartilage space, and sub-chondral bone) with density variations of two-dimensional images. Radiographic data provides a permanent record not only of destructive joint changes, but also of the reversal of bony erosions and joint space narrowing; it represents good evidence that a given therapeutic agent is effective (McCarthy, 1979).
5. Normal Joint, Rheumatoid Synovial Joint

Scale: 1" = 2.6"
6. Normal Bone Anatomy, Rheumatoid Bone Anatomy

Scale: 1" = 2.6"
Chapter VI.
TREATMENT

General Descriptions

This section will briefly discuss and review some of the basic modalities that may be used for the initial and total management of RA. These include a hierarchy of therapies used in the disease, roughly in the order of their risk-benefit ratio:

1. patient education
2. physical therapy
3. salicylates
4. non steroidal anti-inflammatory drugs (NSAIDs)
5. slow acting anti-inflammatory drugs (SAARDs)
6. cytotoxic drugs
7. steroids
8. intra-articular therapy
9. surgery

Education

Without question, the single most important element in the management of rheumatoid disease is education of the patient. Most patients have only a vague notion of RA and are unaware of the tendency for their symptoms to remit and exacerbate spontaneously. Intense anxiety and depression is commonly found. Additionally, the average patient is often unaware of the critical role he himself must play. The
relief of symptoms, preservation of joint function, and a reasonable lifestyle are three realistic goals that should be discussed and coordinated between the patient and the physician (Lightfoot, 1979).

**Physical Therapy**

Rheumatoid synovitis (early stage) is a chronic, inflammatory destructive process which, if unchecked, proceeds to fibrosis of periarticular soft-tissue, limitation of movement, destruction of articular structures, with ultimate malalignment, subluxation, and complete loss of joint function. Thus, physical therapy is intended to 1) maintain the range of motion, 2) prevent disuse atrophy of muscle, 3) minimize deformity, 4) provide adequate systemic rest, and 5) minimize excessive articular trauma, i.e., provide local rest. The elements of such a therapy program should be initiated as soon as the diagnosis is made and should be monitored by the primary physician (Huskisson, 1987; Flatt, 1984).

**Salicylates, NSAIDs, and SAARDs**

Since most arthritic diseases are characterized by inflammation causing tissue injury and loss of function, drug therapy is directed therefore towards limiting the
inflammatory process and its consequences. Several major
categories of antirheumatic drugs are generally recognized;
they differ substantially in their characteristics, mode of
action and clinical effects.

The history of the anti-inflammatory effects of the
NSAIDs, (non-steroidal anti-inflammatory drugs), began
centuries ago with the use of salicylates by Pliny for gout
(Gross, 1948). But it was not until 1964 that aspirin was
shown conclusively to be effective in RA. Fremont-Smith and
Bayles showed decreased ring size, increased range of motion,
and increased grip strength in most of the RA patients whom
they treated (Fremont-Smith and Bayles, 1965). Their
findings have been confirmed, and extended by
placebo-controlled studies using aspirin in doses of 4.0
g/day or more (Broadman, 1967; Calabro, 1970).

Clinically, aspirin and other NSAIDs are effective
analgesics. The action of salicylates is generally
considered to be peripheral in contrast with the central
action of narcotics. They can suppress the induction of
chemically induced pain, i.e. bradykinin, but do not block
the transmission or perception of painful stimuli.
Gastro-intestinal bleeding and peptic ulcers are possible
side effect requiring decrease or discontinuation of dosage.
Standard dose of aspirin therefore, depends to some extent on
the therapeutic goals.

The non steroidal anti-inflammatory drugs (NSAIDs) are
agents that reduce the signs and symptoms of established inflammation within the first few days of administration. Examples include aspirin, phenylbutazone, indomethacin, ibuprofen, fenoprofen, naproxen, and tolmetin. They may be effective only while blood levels of the drug are sustained; withdrawal of a NSAID is soon followed by recurrance of the signs and symptoms of inflammation, although moderated, chronic inflammatory arthritis often is not completely suppressed by an NSAID, and damage to joints continues to occur during NSAID administration.

**Slow acting antirheumatoid drugs (SAARDs),** also called remission-inducing drugs (RIDs), are a diverse group of compounds that share a common pattern of clinical response. Administration of one of these drugs does not result in any immediate therapeutic benefit, but after weeks or months; the onset of clinical improvement may be detected. With continued administration this may eventually result in complete suppression of some or all disease manifestations. However, if drug administration is then discontinued, disease symptoms gradually recur. During a remission induced by a SAARD, damage to joints and other tissues probably stops, although it resumes after the drug has been discontinued. Examples of SAARDs include the organic gold compounds, anti-malarial drugs, antimetabolites, alkylating agents, d-penicillamine, and levamisole. It is noteworthy to mention that all were developed for other indications and then
applied to the treatment of rheumatic diseases as an afterthought. Some SAARDs suppress immune responses, and others have no generally accepted effects on the immune system.

**Corticosteroids**

The corticosteroids themselves have some characteristics of NSAIDs in that they rapidly moderate established inflammation and do not prevent the progression of joint damage. On the other hand, high doses of prednisone have prolonged effects on immunoglobulin synthesis, and the appearance of some drug effects may even be delayed, as in treatment of vasculitis or nephritis (Paulus and Furst, 1985).

The administration of immunosuppressive drugs to patients with rheumatic diseases, begun in the last quarter century, has increased to such an extent that it has now passed from the investigational to the routine. Additionally, more recent immunostimulation therapy has equally been tested and advocated. Thus, we have now extended our concepts to speak of 'immunoregulatory' drugs in the management of RA. However, the advantages and disadvantages of each drug needs to be considered individually against the background of the specific degree of the disease.
Surgery

There are four major types of operations currently used on the joints of patients with rheumatoid arthritis: synovectomy, arthroplasty, osteotomy, and arthrodesis. Synovectomy is the excision of a synovial membrane, as of the lining the capsule of the knee joint or of the synovial sheath of a tendon. Arthroplasty is any operation which reconstitutes a joint. Osteotomy involves the surgical cutting of a bone near to a joint but outside the joint capsule. Arthrodesis involves the surgical fixation of a joint by a procedure designed to accomplish fusion of the joint by a promoting the proliferation of bone cells, also called artificial ankylosis (Mowat, 1979). See Figure 7. The Arthritic Hand.

Synovectomy, or the removal of part or all of the synovial lining/membrane of a joint was first used in rheumatoid arthritis in 1887 by Schiiller following its beneficial effect in tuberculosis. However, synovectomy was only undertaken in significant numbers of patients from the mid-1950's, following promising results when tried in a variety of joints (Copeman, 1964). At present, the operation is only considered of value when performed on finger joints, the wrist, elbow and knee joints (Chase, 1983).

The synovial membranes surrounding the extensor tendons at the wrist when involved in rheumatoid arthritis, pose a
threat to the continuing integrity of the extensors. The extensors pass through tunnels beneath the extensor retinaculum at the wrist, and at this point tendon direction changes, creating a need for a pulley-like mechanism. Tendon gliding within the tunnels is assured by the existence of the synovium. The inflammation of this synovium in rheumatoid disease causes swelling, thickening and invasion of the tendons by inflammatory cells (Scott, 1984).

Clinically, the synovial swelling is evident as it protrudes both proximal and distal to the extensor retinaculum. Drug therapy and immobilization may be adequate to control dorsal tenosynovitis but if it is progressive despite non-surgical efforts, synovectomy should be recommended (Chase, 1983).

An example of this condition was surgically observed in a thirty-eight year-old woman with a five-year history of rheumatoid arthritis. She had pain over the extensor surface of her wrist and marked swelling limited to the extensor tendon area for an area three centimeters distal to the extensor retinaculum at the wrist. The mass was boggy and cystic to palpation, and on pressure one could detect transmission to the area beneath the retinaculum and proximal to it in the forearm. Because of her pain and the probable threat to the integrity of her extensor tendons, extensor synovectomy was decided upon (See Figure 8. Synovectomy).
The procedure was begun with a lazy-S shaped incision on the dorsum of the hand and wrist, extending proximal and distal to the extensor retinaculum. The extrasynovial extensor retinaculum was incised at the ulnar border and the retinaculum was reflected radially. By cutting the partition between the tunnels close to the bone, the retinaculum was lifted like a blanket across the wrist. As much of the hypertrophic synovium as possible was excised, being careful not to injure the already weakened extensor tendons. The flap of the extensor retinaculum was replaced beneath the tendons and the wound was closed. Considerable bow-stringing of the extensors after this procedure can be anticipated, however a small sacrifice to save the extensor tendons from progressive destruction, stretching and rupture. However, it must be emphasized that synovectomy produces predictable results in terms of relief of pain and swelling for periods of three to five years.

A second example of another type of operation used on patients with RA is tendon transfer. Tendon transfers are useful in restoring functions of the hand because of paralysis produced by disease or trauma (Milford, 1988). Rheumatoid synovitis involving the synovium around the extensor tendons at the wrist, if left unchecked, may ultimately result in destruction of the extensor tendons. Rupture of extensor tendons is more common than flexor tendon rupture (Mowat, 1979). Rupture or attenuation and stretching
of the extensor tendons leaves the patient unable to extend the metacarpophalangeal joint and robs him of extension strength at the interphalangeal joint levels. Diseased and attenuated tendons are not repairable by repair without reinforcement. The best method to restore extension capability is by tendon transfer. Occasionally, one may use a tendon graft to bridge the area of the weakness in the extensor, however, it is generally more satisfactory to hook the distal end of the ruptured tendon into a functioning, intact extensor by transfer. (See: Figure 9. Tendon Transfer).

A fifty-eight year old man with RA with multiple joint involvement was directly observed in surgery. He had developed progressive weakness in extension of the long, ring, and little fingers of the right hand and developed a finger drop deformity in these fingers. However, he had excellent strength in the extensor indicis and a transfer of the extensors of the ulnar three fingers to the indicis was selected for treatment.

Surgical exploration of the dorsum of the hand revealed and undiseased, intact extensor digitorum tendon to the index finger as well as a normal extensor indicis. A side-to-side juncture of the distal ends of the extensor digitorum tendons of the long and ring fingers, as well as the tendon of the extensor digiti minimi, to the extensor digitorum to the index finger was performed while the three dropped digits
were held in extension. Post-operatively, the hand was splinted with the fingers in extension at the metacarpophalangeal joints and neutral position for the interphalangeal joints. After a period of six weeks of splinting, it was predicted that complete extension would not be restored to the long, ring and little fingers, however the function would be greatly improved. Independent extension of the index finger would remain undisturbed.

It must be remembered that the goal of surgery is fourfold: 1) relieve pain, 2) improve and or restore function, 3) inhibit progression of disease, and 4) improve cosmesis (Milford, 1988). When combined with patient assessment, surgical, and technical considerations, it usually becomes evident when a patient should be referred for surgical treatment versus other forms of therapy.
Surgical Procedures

THE ARTHRITIC HAND

Lee Milford, M.D.

From the seventh edition of
CAMPBELL'S OPERATIVE ORTHOPAEDICS

Third Edition
SYNOVECTOMY
Extensor Tendons at the Wrist

1. Hypertrophied synovial sheaths
2. Incision of extensor retinaculum
3. Complete removal of synovial sheaths
4. Removal of retinaculum

Scale: 1" = 3.2"
TENDON TRANSFER
Rupture of Extensor Tendons

Scale: 1" = 3.2"
Chapter VII.

CONCLUSIONS

There now exists a remarkable quantity of information on this topic. Ample fossil evidence and early writings attest to its long standing and close association with 'homo sapiens'. Our current understanding of RA has enabled rheumatologists from around the world to define and develop systems of classification as well as isolate specific variants of the disease.

The morphology and its stages have been thoroughly identified, both macroscopically and histologically, however, the middle phases are at times difficult to clinically distinguish.

Intense research has clarified many of the basic pathological processes involved in RA, although its theoretical origins and causes are least understood, despite recent advances in immunology and biochemistry related to connective tissue destruction.

Standards of diagnosis and management have grown and improved enormously, now offering the patient a broad spectrum of therapeutic modalities. However, we still have no or little concept of curative treatment or prevention, a goal which seems unlikely to be achieved for some years to come.
Although much data is now available about the cause epidemiology, pathogenesis, clinical course, and treatment, their relationship to one another is not clear. Once these answers are known, it will explain why rheumatoid arthritis is so common (affecting as many as 1% of all adults), present in almost all populations, persistent (lasting years to decades), intimately associated with a unique antibody (rheumatoid factor), and why it has its particular genetic constitution (a locus related to HLA-DR4). It is hoped that the answers will allow us to understand the reasons for remissions, exacerbations, and the bilateral symmetry of the arthritis, but more importantly, it should explain the foremost question, namely, why is rheumatoid arthritis a disease of the joints?
APPENDIX I

DESCRIPTION OF ILLUSTRATIONS

General Considerations

The following information corresponds to general guidelines used in the execution of the illustrations:

1. Materials and Methods:
   Varies within each illustration; see specific plates for complete production descriptions.

2. Presentation Factors
   a. Matting includes a 3" border on all colors are of neutral values which are included within the illustration.
   b. Mounting includes in laying illustrations into matte boards; all are backed with 1/4" foam-core.
   c. Framing is with 3/8" high-chrome mylar film (Letraset).
   d. Exhibition installation of each illustration is wired from the back and secured with gaffers tape and staples.

3. Typography Specifications
   All type is either by transfer or Leroy lettering system.
   a. Titles (excluding Frontis piece) are set in Microstyle light or bold in various point sizes.
   b. Leroy lettering system in upper/lower case in sizes from 8-18 point.
   c. Leader lines hand ruled, either dotted or dashed.

4. Ratio and Proportions
   All illustrations are sized for 8 1/2"x11", 11"x14", used in similar and or different orientations or multiples of a single format.

5. Resource Materials
   Includes direct observation, anatomy textbooks, models, X-rays, and photographs.
Figure 1. Title Panel: Rheumatoid Arthritis

Intent of the Illustration: To present the title of the Thesis in graphic way which acts as a directory for the color scheme of the art work, matting, and typography. Each of the horizontal strips correlates to an illustration in the order in which they are exhibited.

Materials and Methods: Materials include only the actual papers and matte boards used in the exhibit; they are glued and then laminated to foam-core. Complete title was set in Microstyle Bold (72 pt.), and converted to "Chromatec" transfer.
Intent of the Illustration: To present the major disease sites in the body by use of number positions keyed to a list of locations; to represent disease sites in the hand by specifically coloring areas on the bones to emphasize their important position in origin. Both hand and body is on a raised thickness to increase dimensionality.

Materials and Methods: Materials include Stratmore illustration board, Stratmore plate bristol, Winsor-Newton water colors, and foam-core. Methods include airbrush of background, figure, and contour of hand; bones are rendered in water colors and gouche. Finally presentation of hand is color-enhanced color xerox.
Figure 3. Stages of Rheumatoid Arthritis

Intent of the Illustration: To compare a normal synovial joint to the progressive stages of the disease, by emphasizing internal changes within the joint capsule relational to compact and spongy bone. The four joints are raised off the surface to increase dimensionality.

Materials and Methods: Materials include gradated Pan-tone paper, Stratmore bristol, India ink and Winsor-Newton water colors. Original ink work done 200% larger; final presentation is a black and white photostat with color enhanced airbrushed areas to indicate changes of the synovial fluid.
Intent of the Illustration: To contrast the anatomy of the normal architecture to three of the pathological features of rheumatoid serositis.

Materials and Methods: Materials include warm and cool gradated Pan-Tone papers, India ink and Berol color pencils. Identical positioning of joint and surrounding structures changes only according to the specific pathology.
Figure 5. Normal Joint, Rheumatoid Synovial Joint

Intent of the Illustration: To compare a normal synovial joint to a diseased synovial joint via values assayed for in synovianalysis.

Materials and Methods: Materials include Stratmore Plate Bristol, India ink and Winsor-Newton watercolors. Original art work done at 150% larger; final presentation is a black and white photostat with color-enhanced airbrushed areas in the joint spaces and syringe.
**Figure 6. Normal Bone Anatomy, Rheumatoid Bone Anatomy**

**Intent of the Illustration:** To contrast via background reversal, the normal hand position and anatomy to that of a rheumatoid hand. Emphasis in the RA hand illustrates some of the classic radiographic features commonly found in the later stages of the disease.

**Materials and Methods:** Materials include graduated Pan-tone paper for the rheumatoid hand and Stratmore bristol for the normal hand. Both hands (bones) are airbrushed; labelling is with LeRoy lettering; title set at 36pt., executed and exhibited at 100%.
Intent of the Illustration: To illustrate a combination of morphological features, i.e. swelling, deformity, subluxation, rendered in a non-schematic style, to suggest the "classic" RA hand which would require surgical intervention; to layout and design a corresponding book title with appropriate credits.

Materials and Methods: Materials include Stratmore Watercolor board, Winsor-Newton water colors, matte board and transfer type (Baskerville in various point sizes). The hand is hand painted; the background is airbrushed; scale is actual size to a typical hand.
Intent of the Illustration: To illustrate the surgical procedure 'synovectomy', i.e., the removal of diseased synovial membranes located in the dorsum of the hand; to communicate the basic surgical steps by including essential anatomical landmarks and techniques used with involvement of the extensor tendons.

Materials and Methods: Materials include carbon dust, India ink, colored pencil and pastel on video media paper. Lettering is with Leroy; title is set in Microstyle 36 point; executed and exhibited actual size.
Figure 9. Tendon Transfer: Rupture of Extensor Tendons

Intent of the Illustration: To illustrate the surgical procedure 'tendon transfer', i.e., relocation of diseased tendon(s) into an intact tendon via transfer; to illustrate the basic steps of the procedure and to emphasize the before and after of the technique.

Materials and Methods: Materials include carbon dust, India ink, colored pencil and pastel on video media paper. Lettering is with Leroy; title is set in Microstyle 36 point; executed and exhibited actual size.
APPENDIX II
JOURNALS, AGENCIES, ORGANIZATIONS

Principle Rheumatological Journals in English

Acta Rheumatalogica Scandinavica
Annals of Rheumatic Diseases
Arthritis and Rheumatism
Bulletin of Rheumatic Diseases
Journal of Rheumatology

Selected Government and Voluntary Agencies

Arthritis and Rheumatism Council in Great Britain
American Rheumatism Association (ARA)
Arthritis Foundation (U.S.)
Australian Rheumatism Council
Canadian Arthritis and Rheumatism Society
National Arthritis Commission
National Institute of Arthritis and Metabolic Diseases (DHEW)

National and World Organizations

European League Against Rheumatism (EULAR)
La Ligue Internationale contre le Rheumatisme (aka International League Against Rheumatology (ILAR)
Pan-American League Against Rheumatism (PANLAR)
Southeast Asia and Pacific Area League Against Rheumatism (SEAPAL)
World Health Organization (WHO)
BIBLIOGRAPHY


