Management of **Rheumatoid Arthritis** and its Complications

J. W. Hollingsworth

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RHEUMATOID ARTHRITIS
AND ITS COMPLICATIONS

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Preface

An earlier book, *Local and Systemic Complications of Rheumatoid Arthritis*, seems to have served a purpose for clinicians in bringing together a group of otherwise scattered observations. It also brought many invitations to speak to physicians in postgraduate sessions around the country. Those encounters, however, invariably led to broader discussions with physicians about the management of patients with rheumatoid arthritis.

This book is designed to provide a framework that may help the physician manage the rheumatoid patient. The first section deals with the general nature of rheumatoid arthritis and its diagnosis by clinical and laboratory parameters. Section II describes drugs and their actions, the principles of physical therapy and surgery, and ends with examples of how all of these measures may be used in individual patients. In Section III, management of individual joints and their local complications are discussed. Section IV updates much of the material in the earlier book on systemic manifestations of the disease. A last brief section centers on the rheumatoid patient who suffers from some other process or disease.

Primarily, this book is written to guide residents, fellows and general physicians in management of patients with a common and frustrating disease, rheumatoid arthritis. The book tends to avoid weighing all controversial problems, and relies heavily on extensive personal experience. I have taken positions on certain aspects of management, and undoubtedly some of those judgments will be proved incorrect as studies of rheumatoid arthritis move forward in the years to come.

JAMES W. HOLLINGSWORTH

Acknowledgments

My wife, Dorothy, contributed greatly to getting this book completed, but her contribution was not just the usual support and forebearance attributed to one's wife. She was involved in writing a book herself, with a deadline; her industry aroused my guilt, and I settled to work. The "his" and "hers" offices in the Hollingsworth house were indeed busy rooms in the first half of 1976.

Bobbi Kelley, my staff assistant, somehow fitted this manuscript into her already too full workday.

Patients have always been my most demanding teachers, and many of them came to mind as I was writing sections of this book. My fellows and colleagues over the years—Bill Burslem, Martha Dawson, Mike Catalano, John Huntwork, Roy Kaplan and Ron Saykaly—added to my education from patients, from the literature and from their own intellects.

Finally, the financial support of the Kentucky chapter of the Arthritis Foundation has allowed a busy departmental chairman to keep a small but active rheumatology group at the University of Kentucky.

Contents

SECTION I

GENERAL ASPECTS OF RHEUMATOID ARTHRITIS

Diagnosis and Clinical Course

Establishment of a firm diagnosis of rheumatoid arthritis eventually rests on the clinical evolution of a chronic, progressive, symmetric polyarthritis leading to joint destruction that is evident clinically and by radiographic examination. Until such a picture finally evolves (the definite or classic rheumatoid arthritis of the various epidemiologic survey techniques, as discussed under "Epidemiology"), the diagnosis must be considered somewhat tentative. Auxiliary evidence such as an elevated sedimentation rate, serum rheumatoid factor in significant titer or the finding of subcutaneous nodules enhances the security of the diagnosis. The classical monograph of Short, Bauer and Reynolds,[1] published in 1957, remains a benchmark for an understanding of the natural progress of the disease, although at the time their data were collected rheumatoid factor tests were unknown, and ankylosing spondylitis and psoriatic arthritis were considered variants of rheumatoid arthritis. Many other comprehensive reviews of large groups of patients, followed over long periods, have served to expand our knowledge of the natural course of rheumatoid arthritis.[2-5]

At a practical level, neither the physician nor the patient can postpone therapy until the disease reaches the classic stage in which diagnosis is essentially 100% certain. In the following sections it seems worthwhile to break the discussion into the time segments that generally present problems for the patient and the physician: the first 6 months, the first 2 years, and 2 or more years.

THE FIRST SIX MONTHS

Perhaps 80% of patients can be diagnosed and treated with reasonable certainty on the basis of observations made during the first 6 months.

Typical or usual course.—The typical patient is a youngish to middle-aged woman who begins to have fleeting arthralgic pains in the fingers, often accompanied by a mild sense of general fatigue. Within a 2–3-month period several proximal finger joints are definitely swollen, often symmetrically in the 2 hands. Metacarpophalangeal joints

may become involved early, and the wrists may be painful and swollen. Pain in the neck, shoulders and elbows is likely to occur. Involvements of toes, ankles and knees tends to be somewhat later than upper extremity involvement. During all this time, the usual pattern is one of fleeting and migrating pain and swelling that gradually evolves into persistent synovitis. Diffuse aching and stiffness, particularly in the morning and often described as muscular, is prominent. The firmness of diagnosis during this early phase is established by the degree of swelling and symmetry in the joint involvement, elevation of sedimentation rate and titer of latex or other tests for rheumatoid factor.

Acute-onset polyarthritis.—In about 10–20% of patients, the onset is much more acute, with generalized involvement of the joints described above. Often the patient will be incapacitated or nearly bedridden within 1 or 2 months of onset, with diffuse joint and muscular-type pain. Despite extensive and acute polyarthritis, even low-grade fever is rare. These patients usually end up in the hospital for diagnosis and treatment. Obviously, a definitive diagnosis is more difficult to establish in these patients, yet the need for therapeutic relief is great.

Still's disease-type onset in adults.—About 20% of children with rheumatoid arthritis have a disease characterized by high fever and a salmon-colored macular eruption. Joint disease is usually not prominent initially and may occur several weeks or months after the onset of the fever.[6] The rash may vary widely in its onset, permanence and prominence.[7] Since many of these children eventually have fairly characteristic arthritic deformities, this syndrome (often referred to as Still's disease) is felt to fall within the clinical spectrum of rheumatoid arthritis. Such an onset is seen sometimes in adults, usually in their teens and twenties, but sometimes even older.[8, 9] Occasional adult patients present with recurrence or recrudescence of the illness that began, but remitted, in childhood.

Diagnosis is difficult, and unless arthritis is relatively prominent these patients are likely to fall within the group of adult patients included in the familiar clinical grouping of prolonged "fever of unknown origin." Certainly, in some publications, inclusion of a febrile patient within the adult Still's disease category is relatively arbitrary.

Atypical articular onset.—Many patients present with unusual, often localized, inflammatory arthritis of 1 or 2 joints before the generalized process becomes evident. Almost every joint, even including the cricoarytenoid (see Section III) has been identified as the first to be involved. Painful toes present a diagnostic dilemma, and disease localized to toes and ankles for years has been described.[10] Patients

sometimes describe shoulder pain attributed to "bursitis" several months before a more generalized disease is present. More commonly, perhaps, one or both knees will swell before characteristic small joint involvement occurs.

Acute, intermittent arthritis of 1 or 2 joints is a rare mode of presentation, and diagnosis may be difficult and quite delayed. During the early descriptive phase of rheumatology, Hench and Rosenberg[11] reported, in 1944, a group of acute intermittent arthritics under the term "palindromic rheumatism." Late follow-up of patients with palindromic rheumatism reveals that about half go on to classic rheumatoid arthritis.

Prognosis within the first six months.—As discussed under "Epidemiology," the remission or cure rate depends considerably on what is accepted as *bona fide* rheumatoid arthritis. Short, Bauer and Reynolds[1] felt that about 20% of patients with the disease remit within the 1st year. There is also widespread agreement that those patients with the more acute onset, paradoxically, are more likely to remit or do relatively better than those with more classic disease. Short reviewed the prolonged remissions in the early series and found that all remissions occurred in patients with less than 5 years of disease.[12] No clinical or laboratory features, however, are sufficiently predictive to permit more than a general and very guarded prognosis to the individual patient. That remissions in the true disease do occur, however, is evidenced by recurrences, sometimes years later, of definite rheumatoid arthritis.

THE FIRST TWO YEARS

By the end of 2 years, clinical and laboratory features will have established a definitive diagnosis in all but a very few patients, perhaps fewer than 1%. Some indications of the natural history of the individual patient will emerge. Results of rheumatoid factor tests, which may vacillate between positive or negative in the 1st year, will stabilize permanently into seropositive or seronegative.

Although there is still some discussion of the significance of rheumatoid factor in prognosis, the bulk of opinion is that those patients who have negative results with conventional tests for IgM rheumatoid factor (latex, bentonite and sensitized sheep cell tests) will fare somewhat better. Certainly, some of the severe systemic rheumatoid complications are quite rare in the persistently seronegative patients. However, the seronegative patients, perhaps 20–30% of the group as a whole, are those who bear continued watching for a possible error in

diagnosis, as discussed under "Differential Diagnosis in More Chronic Arthritis."

During the first 2 years, there is such variation in the disease that it is often difficult to decide whether improvement follows therapeutic intervention or natural changes in severity. Although most remissions occur within the first 6–12 months, a few major remissions occur in the second year. Because of the natural tendency to fluctuating disease during the first 2 years, many experimental drug trials are done only in those patients with disease of longer duration.

AFTER TWO YEARS

The disease is established, and the therapeutic battle is joined, only rarely to be discontinued because of stable remission. Local articular problems reach proportions that may require surgical intervention. Systemic complications begin to occur and increase in frequency and severity with time as the disease worsens. A high titer of rheumatoid factor generally accompanies severe disease, whether concomitantly or causally (see Section IV).

In the late stages of disease certain patterns emerge clinically. Some patients seem to have most of their disease limited to the hands and feet. My colleague, Dr. Thomas Brower, professor of orthopedics at the University of Kentucky, often refers to the "wet" or "dry" rheumatoid. The "wet" rheumatoid is one with proliferative synovitis leading to effusions and destruction of bone and connective tissue. The "dry" rheumatoid, usually male, tends to have periarticular fibrosis and stiffening of joints without destructive hypermotility. Surgical procedures are likely to be less effective in patients with the "dry" form of the disease.

One hears much loose talk of the "old burned-out case" of rheumatoid arthritis. It often seems true that pain lessens with severe joint destruction, because the joints are so badly destroyed that pain sensation is somehow lost or diminished. Those "burned-out" patients usually have major serologic evidence of active inflammatory disease—high rheumatoid titers and excessive levels of immunoglobulins. True remissions at this late stage are rare. In general, then, the burned-out rheumatoid is subject to continued misfortune, like the central character in Graham Greene's novel, *A Burnt-Out Case*. Amyloidosis and Felty's syndrome tend to occur in these patients.

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Differential Diagnosis

GENERAL COMMENTS

The greatest error usually encountered is to make a diagnosis of rheumatoid arthritis too precipitously. If the patient indeed has rheumatoid arthritis, there is every reason to delay the final diagnosis, since it usually carries the specter of prolonged and progressive disease. In fact, missing some more treatable condition may cause actual harm to the patient. Some of the most bitter patients encountered in our clinic are those in whom some physician diagnosed rheumatoid arthritis, causing great mental anguish, and who subsequently were found to have some form of reversible illness.

The diagnosis of rheumatoid arthritis has major social consequences. Employability and insurability are very real practical considerations if the patient does have rheumatoid arthritis. We have encountered an extreme example of a young man who had a 3-week episode of a swollen, red, painful ankle at age 12, which resulted in hospitalization and a diagnosis of juvenile rheumatoid arthritis. As a young adult, he was denied permanent employment as a fireman on the basis of that illness, and only letters and examinations by three or four experienced rheumatologists (obtained at considerable expense) were able to reverse that early diagnosis. How much better it would have been simply to have used the designation "ankle pain and swelling, unknown cause" as the diagnosis in that early illness. Our tendency as physicians to want a firm diagnosis is ingrained in our training and our heritage. Perhaps one of the best features of the Weed problem-oriented record system is the ability to define problems at the real level of understanding, rather than in diagnostic terminology.

To be more practical, think negatively about rheumatoid arthritis as the diagnosis, and think positively of alternatives.

DIFFERENTIAL DIAGNOSIS WITHIN THE FIRST FEW MONTHS

Viral illnesses.—Many of the mild illnesses that are manifested by aches and pains for several months may well be virus infections of

various sorts. These illnesses perhaps account for the variations in prevalence rates detected in various epidemiologic surveys, as discussed under "Epidemiology." Two known viral illnesses, rubella and hepatitis, illustrate the fact that prolonged arthralgia and arthritis may be a prominent feature of viral diseases. The last great outbreak of German measles (rubella) occurred in the early to middle 1960s, and arthritis and arthralgia were prominent symptoms in a small percentage of adults (mostly women) who contracted the illness. In most patients, the arthritic manifestations lasted only a few weeks, but the joint manifestations were often identical with those of rheumatoid arthritis.[1,2] Symmetric finger joint enlargements, particularly of the proximal interphalangeal joints, were common. Some of the photographs of the hands in publications about that epidemic could be used as classic illustrations of early rheumatoid arthritis.[1] Live rubella vaccine may cause intermittent arthritis in women and children.[3,4]

Although arthralgia and arthritis have been recognized for many years as a feature of the prodromal symptoms of infectious hepatitis, the recent detection of the Australia antigen and antibodies has produced an outpouring of descriptions of the arthritis, including histology and attempts to identify the agent.[5,6] In chronic active "lupoid" hepatitis, joint complaints may persist.

Other viral arthritis has been described. Chickenpox and mumps occasionally leave one or two quite markedly inflamed joints.[7,8] The Australians have described a condition, perhaps caused by an arbovirus, in which arthritis is a prominent feature.[9] Episodes of arthritis, clinically thought to be viral in nature, have been described in New Guinea, Nigeria and among the Navajo Indians of this country.[10-12]

An epidemic of fever, skin rash and arthritis among children in Connecticut (Lyme arthritis) is the best example of a viral arthritis in the United States. The etiologic agent of that outbreak has still not been identified.[47]

These general observations have added much substance to the widely held belief that the basic etiology in rheumatoid arthritis is a persistent virus, as yet unidentified (see "Pathogenesis").

Psychogenic rheumatism.—Severely tense individuals may complain bitterly of musculoskeletal symptoms. This has been termed "psychogenic rheumatism." One often sees in practice young women, usually young mothers, who complain of joint pains without clinical or laboratory evidence of inflammatory disease. Usually all are thin, overworked in the care of small children and a bit bored and disenchanted with their lives. While many of these patients may have psychological problems, the symptoms tend to subside in a few months or