GUEST Editorial

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The Golden Era of Treatment in Rheumatology

This is the eighth of a 12-part series: This year we're focusing on the phenomenal progress that the medical community has made in the 30 years of Federal Practitioner's *existence. Each month we'll feature an editorial written by one of our Editorial Advisory Association members, reminding us how much has changed in their particular medical field over the past 30 years. This month's focus is rheumatology.*

Remember back in 1983 when gold was all the rage? A huge Brinks robbery in London that year resulted in the loss of £26 million of gold bullion. A British rock group called Spandau Ballet released a hit single named "Gold." The price of gold ended the year at $382.40 per ounce. And who could forget the release that year of the important tome in rheumatology, *Modern Aspects of Gold Therapy*?[1] Thirty years ago, gold therapy was considered one of the mainline therapies for rheumatoid arthritis (RA) (both oral and injectable). Undeniably, much has changed in the last 30 years in both the diagnosis and treatment of rheumatology.

CHANGES IN DIAGNOSIS

For years, serology in rheumatology was centered on the presence of rheumatoid factor (RF) in the serum of many patients with RA. When the American Rheumatism Association (forerunner of the current American College of Rheumatology [ACR]) introduced its diagnostic criteria for RA in 1987, the presence of RF was among the 7 diagnostic criteria.[2] However, many studies documented the lack of sensitivity and specificity of RF in the diagnosis of RA.

Recognizing that RA was a chronically destructive disease led rheumatologists to seek new and better criteria for its diagnosis, with the emphasis on starting treatment earlier to avoid the erosions that inevitably ensued in the joints of those who had the disorder. The most significant breakthrough was the description of anti-citrillunated peptide antibodies (ACPAs) and the development of a commercial assay for this test in the early part of the 21st century. In 2010, this led to the revision of the ACR diagnostic guidelines for RA, and ACPAs were included as a criterion for early diagnosis.[3] The other major change in the diagnosis of RA was the increasing adoption of musculoskeletal ultrasound by rheumatologists. This enabled earlier documentation of erosive changes in RA, leading to earlier treatment of patients with RA with a goal to stop the progression of the disease earlier in its course.

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If only there had been similar breakthroughs in the diagnostic criteria for other important autoimmune diseases, such as systemic erythematosus (SLE), systemic sclerosis, spondyloarthropathies, cryoglobulinemic vasculitis, and Sjogren's syndrome! As an example, the 1982 revised criteria for the diagnosis of SLE has not significantly changed in 30 years, with only a minor update in 1997.[4,5] Additionally, the lack of specificity of antinuclear antibodies (ANAs) in the diagnosis of rheumatic diseases, including lupus, has been known for over 30 years! The identification of the hepatitis C virus (HCV) and the development of a commercial assay to detect antibodies to it in the early 1990s led to the recognition of the important role of HCV in vasculitis and even Sjogren's syndrome. The development of vasculitis antibody panels for antinuclear cytoplasmic antibodies was an important addition to the understanding of vasculitis, but vasculitis still remains a poorly understood disease apart from a few risk factors such as hepatitis B and HCV. The refinement of testing for ANAs has led to significant increases in sensitivity, but not necessarily specificity,

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for the diagnosis of SLE and other autoimmune disorders, with no "gold standard" in terms of diagnostic testing for these patients.

CHANGES IN TREATMENT

The 1990s marked a time of unprecedented excitement in the treatment of RA, with the introduction of the first monoclonal antibody directed against tumor necrosis factor-alpha (TNF-α). These drugs were developed in the 1980s in response to a developing awareness of cytokines as proinflammatory agents, especially the role of TNF-α in the inflammatory cascade. This development was especially noteworthy, because these drugs not only significantly increased the armamentarium for the treatment of autoimmune diseases, albeit at a substantial cost, but also were the first new drugs developed specifically for the treatment of RA since prior drugs had largely been adapted from other usages in oncology and dermatology.

The wave of excitement that accompanied the introduction of etanercept would soon produce other biologics in the late 20th century and early 21st century—infliximab, adalimumab, certolizumab, tocilizumab, and abatacept (among others)—along with ever expanding indications for these drugs, such as ankylosing spondylitis, psoriatic arthropathy, and Crohn's disease, to name a few. Furthermore, the 1980s and 1990s saw an increase in the number of pediatric rheumatologists, due in large part to the increasing numbers of treatments available to children with autoimmune diseases.

However, the standard treatments of the 1980s became passé due to the increased efficacy of the new treatments, as well as recognition of the toxicities of the older ones. Thus, drugs such as gold, sulfasalazine, and penicillamine went into the historical records as drugs that were no longer being produced in large quantities, if at all, due to their being replaced by the biologic drugs. Even promising new nonsteroidal antiinflammatory drugs such as celecoxib and rofecoxib were shown to have unacceptable adverse effects (AEs). Only methotrexate, a drug widely used in the 1980s, is still being used as a disease-modifying antirheumatic drug today. Even the standard drugs for treatment of diseases like gout are changing, with rasburicase and febuxostat leading the charge.

One footnote to this story, which shows how these diseases are still poorly understood, is the continuing use of steroids, which is one of the most commonly used classes of drugs in rheumatology, and their effects in these diseases. One wistfully looks at the ongoing list of AEs from steroids, which makes them anything but "golden" drugs, and wishes that the treatment for rheumatic diseases could somehow avoid them. Yet, the fact remains that steroids are and will continue to be used in the suppression of autoimmunity, based on their potent and widespread effects on the human immune system.

Thus, rheumatology has matured into a full-blown science, riding on the heels of immunology and the explosion of the immune system modulators. The golden era of treatment in rheumatology still seems to be blooming, with an ever increasing arsenal of immunomodulators, providing new hope for those afflicted with the disease common to all mankind—arthritis. One hopes that the "golden years" of rheumatology lie yet ahead of us. ●

Author disclosure

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