

Difficult-to-treat rheumatoid arthritis

György Nagy 

Division of Rheumatology and Clinical Immunology, Department of Internal Medicine and Oncology,
Semmelweis University, Budapest, Hungary

Rheumatoid arthritis (RA) remains a complex systemic disease, with a significant subset of patients reaching a “difficult-to-treat” (D2T) state characterized by persistent inflammation despite conventional and biological DMARD therapies. This presentation explores the multi-faceted nature of D2T RA, emphasizing that it is not merely a failure of pharmacological intervention but a complex psycho-neuro-immunological state. Key contributing factors include multi-morbidity (such as cardiovascular and lung disease), non-inflammatory conditions like fibromyalgia and depression, and behavioral factors including medication non-adher-

ence and poor coping strategies. Recent research highlights the critical role of central nervous system (CNS) involvement, where altered brain connectivity and “morbid adaptation” – marked by hopelessness and cognitive rigidity – contribute to poor outcomes. Advanced imaging and transcriptomic analyses suggest that controlling peripheral inflammation alone is often insufficient, necessitating the consideration of central mechanisms.

Ultimately, the management of D2T RA requires a shift toward a multidisciplinary approach and personalized, patient-tailored treatment strategies.

Why we develop autoimmunity

Yehuda Shoenfeld 

Department of Medicine B and Center for Autoimmune Diseases Chaim
Sheba Medical Center, Tel-Hashomer, Israel