**The Natural History of Rheumatoid Arthritis**

[Deane KD](https://www.ncbi.nlm.nih.gov/pubmed/?term=Deane%20KD%5BAuthor%5D&cauthor=true&cauthor_uid=31196652)1, [Holers VM](https://www.ncbi.nlm.nih.gov/pubmed/?term=Holers%20VM%5BAuthor%5D&cauthor=true&cauthor_uid=31196652)2. [Clin Ther.](https://www.ncbi.nlm.nih.gov/pubmed/31196652) 2019 Jul;41(7):1256-1269. doi: 10.1016/j.clinthera.2019.04.028. Epub 2019 Jun 10.

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Abstract

PURPOSE:

This article reviews the phases of rheumatoid arthritis (RA) development in terms of the evolution of disease, with a focus on events that occur before the first appearance of clinically apparent inflammatory arthritis. This presynovitis period is defined in individuals who eventually develop classified RA as the pre-RA phase. We include additional discussion of the relevance of this model of RA development to the concept of disease prevention.

METHODS:

The information provided in this review was identified through searches of the medical literature through MEDLINE and a review of references from published manuscripts as well as information obtained by the authors through attendance at various conferences and working groups related to pre-RA.

FINDINGS:

It is now well established that RA develops in a series of phases. The first of these phases is believed to be the presence of genetic and/or environmental risk factors for RA in the absence of detectable systemic autoimmunity in the blood. After this phase, autoimmunity may be detectable through a variety of means (eg, autoantibodies, autoreactive cells) in peripheral blood; in addition, there is emerging evidence that perhaps initiation and early propagation of RA-related autoimmunity may occur at mucosal sites. The presence of autoimmunity detectable in the blood through serologic or other testing is followed in most individuals by a propagation phase that is characterized by an expansion of autoimmunity, inflammation, and symptoms. This transition may be associated with similar or different genetic and environmental factors that initially triggered autoimmunity, as well as continued mucosal inflammation and local RA-related autoantibody production. Eventually, clinically detectable inflammatory arthritis develops that can be classified as RA.

IMPLICATIONS:

Understanding the phases of RA development are critical to the development of preventive strategies for this disease.