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Prevention and cure of rheumatoid arthritis: Is it possible?

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Advances in treatment of rheumatoid arthritis have made it possible to profoundly influence signs and symptoms as well as the course of joint destruction in inflammatory arthritis. Earlier and more efficient treatment appears to significantly improve the prognosis of this disease. Despite these advances, cure (the absence of signs and symptoms without further treatment) is still relatively rare, observable in, at most, 20% of the patients. Remission (or a state of very low disease activity), however, has been observed with intense and individually tailored treatment in up to 75% of patients. The use of structured assessments followed by individual modification of the intensity of treatment aiming for remission leads to better clinical responses and radiological outcomes. It remains to be seen whether earlier and more aggressive treatment of patients with not yet 'fully established' rheumatoid arthritis may succeed in preventing at least some of them from progressing to destructive arthritis.

Spectrum of rheumatoid arthritis and initial assessment of inflammatory arthritis

The term 'rheumatoid arthritis' (RA) describes a spectrum of diseases which, in their more severe forms, may lead to several outcomes (related to each other) that substantially influence important aspects of the afflicted individuals' lives: the disease(s) are associated with pain, stiffness, fatigue, impairment to perform everyday tasks, disability, loss of gainful work (paid or unpaid) or employment, loss of quality of life and even premature death [1–4]. Given these possible sequelae, it is evident that it is the most important goal of treatment to substantially influence the course of disease and thus to avoid or at least delay these outcomes. Observations on patient cohorts as well as advances in genetic knowledge have provided insights in the variability in the course of the disease as well as the factors

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contributing to more favourable as well as severe outcomes and/or responses to treatment [5–12]. From these studies, it has become clear that there are subsets of patients, particularly those with lower inflammatory activity, negative rheumatoid factor or anti-citrullinated peptide-antibodies (ACPAs) and/or absence of genetic risk factors [13–15], that do comparatively well even without aggressive treatment, whereas another group of individuals will have progressive disabling disease with high risk of joint destruction and substantial and rapid loss of quality of life. Therefore, it seems necessary, particularly in the very early periods of the disease, when the usual 'classification criteria' are not applicable, to apply some kind of risk assessment in order to estimate the likelihood of a given patient to develop RA. One of these risk-assessment strategies incorporating the type of clinical involvement, sex, age and autoantibodies has been recently proposed and validated independently [16,17]. However, these scores allow the correct classification of only about 70% of early-arthritis patients–a considerable amount of uncertainty remains, particularly in the light of having to decide to start possibly harmful treatments. Nevertheless, it has been clearly demonstrated that the time frame within which these decisions should be made is rather short [18–27]. Most rheumatologists defined 'early' arthritis as a disease with no more than a 3-month duration of symptoms [28].

Cure and prevention

Conceptually, 'cure' of a disease means that, after a period of 'absence of health' the affected individual regains full health [29] without continuous treatment. RA is regarded as a chronic inflammatory disease whose causes are still unknown but appear to be multifactorial with genetic, environmental, nutritional, behavioural and social factors contributing and accumulating their impacts on any given susceptible individual over a period of time until the disease emerges with its first symptoms. Thereafter, RA progresses with cumulative damage to joints and, sometimes, soft tissue and internal organs. In this framework, 'cure' appears to be a very ambitious goal with relatively low probability of ever occurring. 'Prevention', however, has several stages: 'primary prevention' refers to methods designed to avoid the occurrence of disease or impairment (e.g., the provision of a balanced diet to avoid malnutrition or immunisations to avert infections and their sequelae); 'secondary prevention' (sometimes referred to as 'intervention prevention') is usually directed at those identified within the targeted population as 'at risk' and thus refers to early diagnosis and treatment to shorten illness episodes and to limit disease sequelae; tertiary prevention involves both the treatment of the identified problem or disease and restoration of the individual to a full state of functioning within the targeted population [30]. Definitions of both secondary and tertiary prevention imply that some limited amount of impairment might remain and, thus, are the more likely scenarios when discussing outcomes of interventions in (rheumatoid) arthritis. Moreover, as the bulk of the literature on RA implies, even if only minimal disease activity is reached (frequently referred to as 'remission') most patients appear to be in need of at least some amount of treatment [31]. This article focusses on secondary and tertiary prevention, because primary prevention (i.e., risk avoidance or modification of lifestyle, social, economic or environmental factors) is beyond its scope.

Remission

Because, in RA, 'cure' according to the definition given above is regarded to be rare, several definitions of 'remission' (a state of minimal disease activity assumed to be close to cure, albeit under treatment) have been put forward [32–36]. However, even patients with RA in remission have been shown to show substantial progression of radiographic damage and synovitis detectable by magnetic resonance imaging (MRI) and ultrasound [37–39].

Evidence for effectiveness of treatment

The currently available drugs (disease-modifying anti-rheumatic drugs (DMARDs), including glucocorticoids) have been shown in numerous studies to effectively reduce signs and symptoms of RA and to be able, in the longer term, to prevent or at least significantly slow down the joint destruction that is the hallmark of the disease. This effectiveness exists for biological and non-biological drugs