Contraceptives, pregnancy, and RA
A J Silman

Oral contraceptive use and pregnancy are associated with a good prognosis

Rheumatoid arthritis (RA) is a disease with a markedly greater incidence in women, suggesting perhaps the importance of sex hormones in disease susceptibility. Serum oestrogen levels are not, however, raised in women with RA, although in animal studies they have been shown possibly to be proinflammatory. It is against this background that the consistent observation that oral contraceptive (OC) use is probably protective for development of RA is, at first sight, surprising. One explanation might be that it is not the use of OCs themselves that is important but rather that their use is associated with delaying or reducing the likelihood of pregnancy. The latter has been shown to be important as the postpartum period is a time of increased risk of disease onset.

A separate question, however, emerges as to whether continuing OC use or subsequent pregnancy influences disease outcome in women who have already developed RA. This is an issue of practical relevance both to patients and their doctors but one that has received relatively little attention. The report in this issue by Drossaers et al on a cohort of young women with RA who were followed up to determine their radiographic and disability outcome, after OC use and pregnancy, is of interest. In brief, the authors showed that these factors had little influence on disease outcome 12 years later.

The size of the sample studied was relatively small, the confidence intervals wide, and the lack of significance in the differences seen may represent a lack of statistical power. There was evidence of “trends” towards less radiographic damage and reduced disability in women continuing to take OCs or who had further pregnancies. Thus, if their results have any clinical consequences, they suggest that women can be reassured about the lack of severe consequence of exposure either to OCs or pregnancy. It should be added that assembling cohorts of young women with RA, presenting during their fertile period, and following them up for the long period, with the low loss to follow up achieved by Drossaers et al, is a not insignificant achievement and is not easily repeated.

Women who continue to take OCs, however, are not a random sample of all young women with RA. They are likely to be sexually active and might thus be at the less severe end of the disease spectrum. By contrast, because of concerns about the consequences of pregnancy, including coping with a young infant, women with RA who have more severe disease may be selectively more likely to use OCs. We do not know which of these two potential biases is more likely.

Patients choosing OC use or pregnancy should not be dissuaded

Even more problematic for those contemplating studies in this area is the influence of disease activity and its treatment on the decision to become pregnant. It is likely, for the reasons stated above, that those who choose to become pregnant do have milder disease. It is interesting therefore to note in the data by Drossaers et al that in their cohort of all the patients who had a pregnancy, either before or after diagnosis, there was a suggestion that this group had milder disease. Pregnancy itself is associated with a strong likelihood of remission, with relapse post partum that might be related to breast feeding. In that latter study though, there was strong evidence of a selection effect, with women who were subsequently going to breast feed having less severe disease and an associated smaller likelihood of being given disease modifying treatment. This suggests that those women who choose to become pregnant, after the onset of RA have a milder disease and hence are at lower risk of a worse outcome. In support of this is the observation by Drossaers et al, that those women with three or more births after disease, were those with the best outcome.

This pregnancy behaviour would probably be reflected by an observational study of physical activity in RA. Thus, although it is clearly established that RA is associated with early work disability, those who choose to continue working are likely to do well long term—not that working is protective but that those who maintain their employment have self selected themselves for a better outcome.

When OCs were first introduced there was anxiety that they might be associated with a deterioration in disease activity. Changes in the constituents of currently used OCs with lower doses of hormones make it less likely that they would have any effect on disease. Is there any important message, therefore, from this study by Drossaers et al or were the conclusions entirely predictable? The answer is the former and the results are reassuring. The message is that if patients, once diagnosed, choose either to continue with OC use or to proceed to one or more pregnancies, they should not be dissuaded. They are likely to represent a group with a good prognosis.

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Author’s affiliations
A J Silman, ARC Epidemiology Unit, School of Epidemiology and Health Sciences, University of Manchester, Room 2.514, Stopford Building, Oxford Road, Manchester M13 9PT, UK

Correspondence to: Professor A J Silman; alan.silman@man.ac.uk

REFERENCES