Pregnancy and its effect on the risk of developing rheumatoid arthritis

Given the predominance of women over men in the occurrence of rheumatoid arthritis (RA), the well established ameliorating effect of pregnancy on the course of the disease1-3 seems to be paradoxical. More than 75% of pregnant patients with RA improve, starting in the first or second trimester with maximum improvement in the third trimester of pregnancy. Some weeks to months after delivery, however, a disease flare up will be experienced by more than 90% of these patients. The hypothesis from these observations that female hormones may modulate the course of RA is enhanced by the protective effect of oral contraceptive use on disease development.4-6 It is thus relevant to ask whether pregnancy also influences the development of RA.

Earlier studies on the relation between parity and RA are contradictory. A large population study in the United States reported an increased rate of RA among parous women above the age of 45 years compared with nulliparous women,7 whereas in a population study in the United Kingdom nulliparous women had more arthritis than the multiparous in all age groups from 35 to 65.8 These studies, however, did not distinguish between parity preceding and following the onset of RA. Kay and Bach,9 25 years ago, were the first to make the distinction between pregnancies occurring before and after the onset of RA in a controlled study, reporting subfertility both before and after the development of RA. The subfertility seemed to be mainly due to an increased rate of nulliparity before disease onset among the patients with RA. Three recent studies looking at the effect of pregnancy history on the development of RA have confirmed these findings.5 10 11 They found that women who developed RA were more often nulliparous before symptom onset than controls, indicating either that nulliparity might be a risk factor for the development of RA, or, conversely, that parity might be protective against RA. A possible 'dose-effect' relation between pregnancy experience and the risk of RA was not found: the mean family size among parous women being similar in cases and controls. An alternative interpretation for the difference is that subfertility is an early feature of RA, though preceding the onset of symptoms. In one of these studies the preventive effect of pregnancy was significantly associated with the age at first pregnancy.11 The younger the women were at their first pregnancy the more they seemed to be protected against the development of RA. The association between parity or age at first pregnancy and the risk of RA has not been confirmed in a preliminary report of a prospective study of nurses in the United States.12 In this study, however, half of the cases had been classified as probable RA, a very uncertain disease status which has therefore been abandoned in the new 1987 revised American Rheumatism Association criteria for the classification of RA.13

Despite the favourable effect of parity there is a suggestion that RA is precipitated by pregnancy as the onset seems to cluster in the postpartum period.14-16 On the other hand, several studies have shown that the risk of developing RA during pregnancy is reduced.5 14 16 17 Del Junco found that the nearly fivefold increased risk of RA in the 12 months postpartum was counterbalanced by a decreased risk during pregnancy,16 illustrating that pregnancy only postponed the onset of RA. Some caution has to be used in interpreting data on the development of RA in the peripartum period, however, as there may be a tendency among patients to relate the onset of their symptoms to a previous critical life event. This would apply particularly when the event (child birth) requires increased physical demands and the period before that (pregnancy) had probably suppressed mild symptoms already existing.

In contrast with the possible protective effect of pregnancy on the development of RA, pregnancies with an adverse outcome have been proposed as a risk factor in the causation of RA.18 A group of mainly black American patients with RA was found to have a spontaneous abortion ratio higher than that of a comparison group before onset of their disease,19 and an increased rate of stillbirth before disease onset was found in a small number of British patients with RA compared with their unaffected relatives.20 Subsequent larger studies, however, have not confirmed these reports.6-11 21

Summarising the epidemiological data on pregnancy and RA compiled so far we may conclude that (a) pregnancy has an ameliorating effect on RA; (b) patients with RA are more commonly nulliparous before disease onset than are controls, but when they have children before symptom onset their family size is similar to that among controls; (c) there is a suggestion that having the first pregnancy at a young age will decrease the risk of developing RA; (d) pregnancy possibly postpones RA onset to the postpartum period; (e) it is unlikely that poor pregnancy outcome is a risk factor in rheumatoid arthritis.

Many biological mechanisms for the ameliorating effect of
Oral contraception and its possible protection against rheumatoid arthritis

Despite many epidemiological studies conducted in the search for environmental influences on rheumatoid arthritis (RA) we have few clues to possible risk factors. High hopes were raised following the publication of the Royal College of General Practitioners’ oral contraception study, which provided evidence for a protection against RA among oral contraceptive users.1 Many subsequent studies have been initiated to question this finding. A dozen years and numerous conflicting publications later we still seem to have no clear answer to the question whether oral contraceptive use protects against RA or not.1-13 The earlier studies had methodological problems, zealously discussed in international reports.1-16 Despite methodological improvements recent studies continue to fuel the controversy. To date seven studies have shown a reduction of RA of about 50% by oral contraceptive use,1-7 whereas five studies reported no effect of oral contraceptive use on the development of RA8-12 and one was inconclusive.13 In March 1989 a special


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