Accuracy of retrospective reports of infections during pregnancy

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ABSTRACT A large body of research suggests a relationship between maternal influenza and the development of schizophrenia in the adult offspring. Some researchers, however, have questioned this association. A study by Crow and Done (1992) asserts that prenatal exposure to influenza does not cause schizophrenia. The methodology employed by Crow and Done may account for their null findings. Crow and colleagues assessed influenza by asking mothers at the time of birth to recall influenza infections experienced during pregnancy. Such retrospective recall may bias reporting. We assessed influenza symptoms during pregnancy in a group of 136 mothers at the twenty-fifth week of pregnancy, and again one or two days after birth. We compared accounts of influenza at the twenty-fifth week to recollection of influenza after birth. Results suggest that mothers tend to under-report infections when recalling infections after birth. Retrospective assessment of influenza symptoms at birth may be an inaccurate method of assessing influenza during pregnancy.

Key words: schizophrenia, maternal influenza, second trimester, retrospective bias

We noted an elevated rate of schizophrenia among Helsinki residents exposed to the 1957 influenza epidemic during their second trimester of gestation (Mednick et al., 1988). Numerous independent studies, completed in a number of national settings, have replicated the results for the 1957 epidemic (Adams et al., 1993; Beckmann, 1993; Fahy et al., 1993; Kendell and Kemp, 1989; Kunugi et al., 1992; Machon and Mednick, 1994; O'Callaghan et al., 1991; Waddington et al., 1992; Welham et al., 1993). We reported that 86.7% of the Helsinki schizophrenia patients whose second trimester of gestation overlapped the influenza pandemic have an antenatal clinic record of a maternal upper respiratory infection (probably influenza but we had no serology confirmation). Only 20% of those exposed in the first or third trimesters have an antenatal clinic record of a maternal influenza infection. Obstetric nurses produced these records at frequent intervals during gestation at the time the pregnant

women attended the antenatal clinic in 1957–8 (Mednick et al., 1988).

We have also shown that over a period of 40 years in Denmark, across a series of influenza epidemics, unusually high levels of influenza in the population during the sixth month of gestation are followed by unusually high numbers of births of future schizophrenia patients (Barr et al., 1990). Numerous studies, in an assortment of national settings, replicate this finding for a variety of influenza epidemics (for example, Morris et al., 1993; Sham et al., 1992; Welham et al., 1993; Wright et al., 1995). The multiple replications support the hypothesis that a second-trimester maternal influenza infection increases risk for schizophrenia in the offspring.

Crow and Done (1992) reported a notable exception to these studies. They used data from the 1958 British Perinatal Mortality Study whose subjects were UK residents born in a week in March 1958, after the

1957 influenza epidemic. In this study, as a part of a larger questionnaire, mothers were asked at the time of delivery whether and when they had suffered an influenza infection during their pregnancy.

Crow and Done found no evidence of an elevation in rate of schizophrenia for those offspring whose mothers reported a second-trimester influenza infection. The Crow and Done study is notable because the investigators obtained maternal reports of influenza infections rather than only recording overlap of the period of gestation and the epidemic. In their study, however, 'infections were documented at the time of birth' (Crow and Done, 1992: 391). Crow and Done entitle their article 'prenatal exposure to influenza does not cause schizophrenia'.

The Crow and Done (1992) report has been criticized, however, because the rates of both maternal influenza and offspring schizophrenia seem unexpectedly low. Possible unreliability of maternal reports (obtained at the time of delivery) regarding earlier pregnancy events may contribute to the authors' failure to detect a significant relation. Perhaps women at that stressful period have other concerns demanding their attention.

We tested this possibility in the context of an ongoing Danish perinatal study of the neurointegrative functioning of a cohort of infants whose mothers suffered an influenza infection during their pregnancy. As a part of this perinatal study, we interviewed women in the eighteenth to twenty-fifth week of pregnancy regarding symptoms and timing of influenza infection (fever and persistent cough of at least two days duration) during their pregnancy in the period preceding the interview. For the purposes of the current study, we asked the same questions of a subgroup of these women again at the time of delivery.

The comparison of maternal reports of infections before the twenty-fifth week of gestation with maternal reports at the time of delivery provides a test of the reliability of maternal accounts of pregnancy-influenza infections at the time of delivery.

We assume that reports in close temporal proximity to the period of the infection are more accurate than those reported at birth. We chose to study maternal reports at the eighteenth to twenty-fifth weeks because that period covers a part of the second trimester. We also interviewed all the women in the perinatal study at that point in time. We hypothesized that at the time of delivery the women would, to a significant degree, under-report infection history relative to the report at the twenty-fifth week.

Methods

All women presenting for maternity care to the largest obstetric department in Copenhagen (Hvidovre Hospital) were asked to take part in the larger perinatal study. We interviewed pregnant women when they first presented for care. At each subsequent visit, we gave them a questionnaire to return to us at their next visit. The questionnaire contained a series of standard questions regarding any illnesses the women experienced during the pregnancy. The women were expected to visit the obstetric or midwife clinic at least five times during the pregnancy.

For purposes of this report, a group of 136 women who were interviewed in the eighteenth to the twenty-fifth week of pregnancy regarding fever and persistent cough were chosen to participate in this study. The 'influenza' questions from the interview were chosen for this study because they covered the end of the second trimester of the pregnancy. The women

Table 1: Comparison of fever and cough reports at time of delivery and at the 25th week of pregnancy

Table 1A.					Table 1B.				
Fever report after delivery					Cough report after delivery				
		Yes	No				Yes	No	
Fever report 25th week	Yes	12	12	24	Cough report 25th week	Yes	6	33	39
	No	2	110	112		No	8	89	97
		14	122	136			14	122	136

interviewed were unselected; their deliveries were a consecutive series beginning on 1 April 1993 and ending on 30 April 1993. One or two days after the delivery, we again asked the questions posed at the time of the twenty-fifth week of the pregnancy regarding infections.

Results and discussion

Table 1A compares the women's reports of fever at the time of delivery with their reports at the twenty-fifth week of pregnancy. As can be seen, of 24 women who reported a fever in the period preceding the twenty-fifth week of pregnancy, 12 (or 50%) failed to report this fever at the time of delivery. Table 1B compares the women's reports of a persistent cough at the time of delivery with their reports between the eighteenth and twenty-fifth weeks of pregnancy. As can be seen, of the 39 women who earlier reported a persistent cough, 33 (85%) failed to report this cough when questioned at the time of delivery. (Please note that these numbers of subjects are small.)

We found that at the time of delivery, a significant number of women failed to report illnesses they reported at a time in their pregnancy in closer temporal proximity to the illness. If we assume that we can generalize from women at delivery in Denmark in the month of April to similarly situated women in the UK in the month of March, these data would help explain the low number of reports of illness in the Crow and Done (1992) study. These data also suggest that a substantial number of the subjects Crow and Done considered to be unaffected controls could possibly have suffered a second-trimester influenza infection. Perhaps part of the reason Crow and Done did not find a relationship between adult schizophrenia and second-trimester maternal influenza was the unreliability of their assessment of the second-trimester maternal influenza.

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