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# Time to pregnancy and paternal exposure to pesticides in preliminary results from Danish and French studies

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Several studies on animals have shown that long-term exposure to high doses of pesticides leads to changes in spermatogenesis and causes urogenital malformations (1). For humans, Whorton (1) found, in 1988, lower fertility levels and sterility among agricultural workers exposed to dibromochloropropane (DBCP) on the banana plantations of Costa Rica. The semen analysis showed clear changes in sperm characteristics (2). Very few epidemiologic studies have investigated the effects of pesticide use on human fertility. Ratcliffe et al (3) found changes in sperm characteristics among Indian agricultural workers exposed to ethylene dibromide (a pesticide used in papaya production), and, in 1994, de Cook (4) found a correlation between the pesticide spraying season and the time taken by couples to conceive a child in The Netherlands. We studied the effects of pesticide use on male fertility by carrying out a retrospective epidemiologic study to assess the relationship between pesticide exposure and the time required to conceive a child (time to pregnancy). This study was carried out in 2 European countries as part of a European research network (Asclepios). In Denmark, we studied agricultural workers who used conventional farming methods, organic farmers, and greenhouse workers. In France, we studied vineyard workers and workers in jobs connected with agriculture.

## Material and methods

In Denmark, we enrolled a random sample of conventional farmers and all organic farmers in part of the country (Jutland), altogether 1146 men. Furthermore, we identified 899 male greenhouse workers exposed to pesticides, from a list of members in the Danish Gardeners' Union. Accordingly, we included 2 exposed groups, conventional farmers and greenhouse workers. The reference group consisted of organic and conventional farmers who were not exposed to pesticides during the year before the birth of their youngest child. In France, we used the annual medical examination given to workers as part of the national health insurance system (Securité Sociale). Over 3 months the participating health physicians approached all 1326 agricultural workers of Alsace (vineyard and other rural workers) and asked them to participate in the study. The exposed group was composed of workers

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4 The Asclepios project on occupational hazards to male reproductive capability is a biomedical research project of the European Union that was carried out in 14 European centers in 1993—1998. The project was coordinated by The Steno Institute of Public Health, University of Aarhus Denmark, and it included the following researchers: Belgium, Gent (P Kiss, A Mahmoud, M Vanhoorne, H Verstraelen); Denmark, Aarhus (A Abell, JP Bonde, SB Larsen, G Danscher, E Ernst, H Kolstad), Copenhagen (A Giwercman); England, London (A Dale, M Joffe, N Shah); Finland, Helsinki (M-L Lindbohm, H Taskinen, M Sallmen), Turku (J Lähdetie); France, Paris (P Jouannet, P Thonneau), Strasbourg (A Clavert); Germany, Erlangen (KH Schaller, W Zschiesche); Italy, Brescia (P Apostoli, S Porru), Milano (L Bisanti), Pietrasanta (L Lastrucci), Rome (M Spanò); The Netherlands, Nijmegen (N Roeleveld, H Thuis, GA Zielhuis), Zeist (W de Kort); Poland, Lodz (K Sitarek).

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having used pesticides the year before the birth of their last child. The controls comprised workers from Alsace who were not exposed to pesticides during the year before the birth of their youngest child.

Data were collected using a questionnaire developed by an expert working group of the Asclepios project and included social demographic characteristics of the couple, their medical and surgical histories, the presence of particular risk factors for infertility among the man or the woman (smoking, tubal or testicular disease), and the method of contraception used before conception of the last child. The key question phrased was "How long did it take your wife to become pregnant?" The participants were classified as to their exposure to pesticides the year before the most recent child was born (yes;no). In Denmark, data were collected by telephone interviews between October 1995 and May 1996, while, in France, all male workers of the Alsace region (February to April 1996) provided the same data with the help of a physician in relation to their annual medical visit. The response rate was 84% for the agricultural workers, 80% for the greenhouse workers, and 74% for the vineyard workers. We excluded men who had never married, men with no children or with a wife less than 6 months pregnant, and cases of last pregnancy due to failure of birth control. In Denmark we also excluded men who had not worked in agriculture during the year before the birth of their youngest child. Consequently the analysis included the following numbers of pregnancies at risk and not at risk from paternal exposure to pesticides: 326 at risk and 123 not at risk for the agricultural workers, 121 at risk for the greenhouse workers, and 142 at risk and 220 not at risk for the vineyard workers. The ratio between the fecundability for pregnancies at risk and not at risk were computed using a discrete analogue of the Cox regression with adjustment for several potential confounding variables (age, smoking, parity, most recently used form of contraception).

## Results

The ratio of the adjusted fecundability in pregnancies at risk and not at risk did not differ from unity in any of the 3 study groups. The adjusted fecundability ratios were as follows: 1.09 (95% CI 0.82—1.43) for the agricultural workers, 0.83 (95% CI 0.69—1.18) for the greenhouse workers (in comparison with pregnancies not at risk among the vineyard workers), and 1.17 (95% CI 0.89—1.55) for the vineyard workers.

## Discussion

The preliminary results of this large epidemiologic study (N = 2353), carried out in 2 European countries using different designs (exposed and unexposed groups identified on the basis of a sample of workers in France and directly on the basis of known exposure to pesticides in Denmark) does not demonstrate any significant difference in the time taken for the partners of pesticide-exposed and unexposed workers to become pregnant. In both countries, smoking by the woman and first pregnancy were associated with a longer time to conception. In The Netherlands, de Cock et al (3) found that the effect of pesticide exposure was only significant if couples were attempting to conceive during the spraying season and pesticides were being applied by the farmer himself. Work conditions, such as the use of less modern equipment with a low spraying velocity may result in very high levels of exposure. One limitation of our study was the lack of exact exposure measurements. It is difficult to determine the level of exposure to pesticides in each of the 3 exposed groups because many compounds are in use. Mixing men exposed only slightly or moderately or highly to pesticides in the "exposed group" may result in an underestimate of the correlation between exposure and time to pregnancy (4)). In our analysis we studied the relation between time to pregnancy and pesticide exposure after adjustment for several potential confounding factors. Smoking by the woman and primiparity were correlated with time to pregnancy, and the effect of these 2 factors on fertility has been known for some time (5, 6). The fact that the same effect was found for these risk factors in all 3 pesticide-exposed groups is consistent with the overall validity of the study.

In conclusion, the preliminary results of this study found no effect of pesticide exposure on fertility among men in the 3 European pesticide-exposed groups studied. Further studies using complementary reproductive indicators (time to pregnancy, semen analysis, pregnancy outcome), and accurate assessment of exposure are warranted on this topic.

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