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Time to pregnancy among female greenhouse workers

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Objectives This study examined the possibility that work in greenhouses with potential exposure to pesticides entails a risk for reduced fecundity in terms of increased time to pregnancy.

Methods Among 1767 female members of the Danish Gardeners Trade Union, telephone interview data were obtained on the 492 most recent pregnancies of women employed when they stopped contraception to get a child (the starting time). The pregnancies were classified according to job characteristics at the starting time. The ratio between the likelihood of pregnancy during a month for the exposed persons versus the referents (the fecundability ratio) was estimated by discrete proportional hazards regression.

Results The adjusted fecundability ratio for workers in flower greenhouses versus other union members was 1.11 [95% confidence interval (95% CI) 0.90—1.36]. Among workers in flower greenhouses the handling of cultures many hours per week, the spraying of pesticides, and the nonuse of gloves was related to reduced fecundability [adjusted fecundability ratio 0.69 (95% CI 0.47—1.03), 0.78 (95% CI 0.59—1.06), and 0.67 (95% CI 0.46—0.98), respectively].

Conclusions The findings suggest that female workers in flower greenhouses may have reduced fecundability and that exposure to pesticides may be part of the causal chain. Additional studies of fertility among women working in greenhouses are highly warranted.

Key terms fecundability, fertility, greenhouses, pesticides.

During the past 2 decades it has become evident that occupational exposure to certain pesticides damages testicular function (1—4). With respect to women most interest has been directed towards possible developmental toxicity in the form of spontaneous abortion, birth defects, and still birth (5), whereas only few studies have examined the reproductive toxicity of pesticides among women (6). Methodological limitations such as inaccurate assessments of the type, quantity, and timing of exposure are typical of earlier studies (6).

Time to pregnancy is the number of months it takes a couple to obtain a pregnancy after the discontinuation of contraception. This measure of fecundity has been used in several studies dealing with reproductive toxicity in the workplace (7—9). A study of fruit growers in The Netherlands indicated an increase in time to pregnancy after a seasonal increase in pesticide exposure of the male partner (10). In a multicenter study in France and Denmark no differences in time to pregnancy were found between pesticide-exposed male farmers and greenhouse workers and unexposed referents (11). A Canadian farm study included information on pesticide exposure for both husband and wife. No strong or consistent pattern of associations of pesticide exposure with time to pregnancy was found. However during exposure intervals in which women participated in pesticide activities, 6 of 13 pesticide exposure categories were associated with a decrease in fecundability (12). To our knowledge, the time-to-pregnancy values of the couples for which only the woman was exposed to pesticides have never been published.

In Denmark about 4000 women are occupationally exposed to pesticides in gardening. They are mainly exposed from the manual handling of cultures with pesticide residuals on the surface (called re-entry activity), but the spraying of pesticides may also contribute exposure. The use of pesticides is highest in greenhouses with flower production and lowest in greenhouses with the production of vegetables and outdoor gardening. The most used pesticides are insecticides, fungicides, and growth regulators, whereas herbicides are not used in greenhouses. Dermal exposure to pesticides is highly correlated with

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manual contact with pesticide-treated plants (13, 14). Women typically perform the tasks involving the most plant contact (eg, nip cutting). Flower production in Denmark mainly uses pot cultures, which probably involve less exposure to pesticides than the production of cut flowers.

The purpose of this study was to examine whether work in greenhouses associated with dermal exposure to pesticides entails a risk for reduced fecundity among women.

Subjects and methods

Population

We studied female members of the gardeners' trade union in the 2 Danish regions with the highest density of greenhouses. Some 90—95% of Danish gardeners are members of the union. Our study population was identified in January 1995, and it included all female greenhouse or plant nursery workers aged 25—45 years with union membership during at least part of the previous 5 years. Altogether 1767 women were identified by name and address (figure 1).

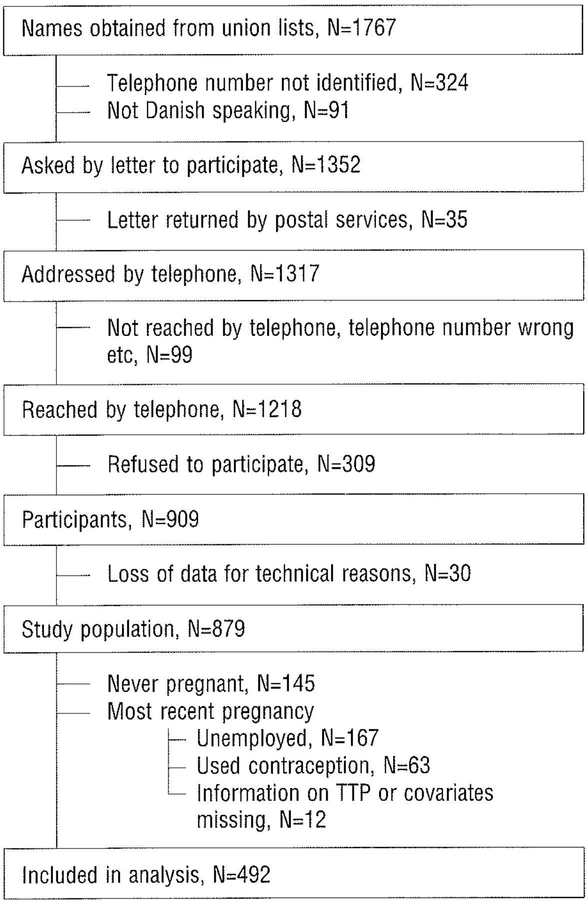

Figure 1. Selection of the study population. (TTP = time to pregnancy)

Questionnaire

A standardized questionnaire for a population-based survey of time to pregnancy was developed in the European Study on Infertility and Subfertility (15). The same questionnaire was used in the present investigation. A detailed description of the European study has been given elsewhere (15).

Data collection

The data were collected in a telephone interview during 1995 to 1996. The questionnaire data included reproductive history, time to pregnancy (for up to 4 pregnancies), as well as occupational and other exposures at the time when the couple started having unprotected intercourse to become pregnant (the starting time). For women not using contraception after a delivery, the starting time was defined by the return of menstruation. The key question on fecundity was phrased "How many months did it take you to become pregnant? That is, for how many months were you having sexual intercourse without doing anything to avoid a pregnancy?" As pregnancies we included all recognized pregnancies, but not induced abortions.

Exposure assessments

The potential exposure to pesticides was characterized by the following variables:

Manual handling of cultures (hours per week): "How many hours per week did you have your hands in contact with plants or soil treated with pesticides?" The answers were dichotomized to at least 20 hours per week, yes;no.

Use of gloves: "Did you use gloves when handling pesticide-treated cultures?" (always;sometimes;never).

Application of pesticides: "Did you spray pesticides?" (yes;no).

The preceding variables were combined into an aggregated measure of working without gloves more than 20 hours per week or spraying (yes;no).

Study group

The most recent pregnancies were classified according to the job characteristic at the starting time as follows: (i) workers in flower greenhouses (N=253) (table 1) and (ii) a reference group, other members of the gardeners' union (N=239). The reference group included persons who were not gardeners at the starting time (N=198) or who worked in greenhouses not using pesticides (N=9) or who worked in greenhouses producing vegetables (N=13) or in outdoor gardening (N=8) or who worked in other gardener's jobs (N=11). The reference jobs were not associated with any significant occupational exposure to pesticides.

In addition we defined the indices of higher exposure for workers in flower greenhouses as follows: (i) manual handling of cultures at least 20 hours per week (N=220), (ii) not using gloves (N=213), (iii) applying pesticides (N=82), (iv) a combination of manual handling of cultures at least 20 hours a week, not using gloves and applying pesticides or handling cultures without using gloves more than 20 hours a week or applying pesticides (N=202).

Among those reached by telephone, 74.6% (909 of 1218) participated (figure 1). The age, number of children, and childlessness did not differ much between the respondents and the nonrespondents (table 2). At the time of the interview the workers in flower greenhouses were younger than the reference group of other union members, and a high percentage of workers in flower greenhouses had their most recent pregnancy after 1990. The workers in flower greenhouses differed in life-style from the reference group of union members; they smoked less, had a lower caffeine intake but used oral contraception more frequently. In the group of workers in flower greenhouses the high exposure group, defined by the aggregated information on exposure, had a high percentage of primipara pregnancies and a higher percentage of smokers than the low exposure group (table 3).

Statistical analyses

The time-to-pregnancy distributions were examined in the various groups. We compared exposed workers in flower greenhouses with other union members and with subgroups of workers in flower greenhouses according to exposure. The analyses were performed for the first and the most recent pregnancy, only including a pregnancy if no contraception was used. Persons who were unemployed at the starting time were excluded.

Table 1. Number of greenhouse workers by the exposure variables. Figures in bold indicate high exposure in the aggregated exposure classification.

Manual handling of cultures	Not spraying	Spraying	All
<20 hours per week			
Wore gloves	3	**2**	5
Did not wear gloves	20	**8**	28
≥20 hours per week			
Wore gloves	28	**7**	35
Did not wear gloves	**120**	**65**	185
All	171	82	253

Table 2. Characteristics of the participants and nonparticipants.

	Age (years)		Number of children		No children	
	Mean[a]	SD	Mean	Range	N	%
Participants (N=879)	34.3	6.6	1.6	0—8	157	18
Nonparticipants (N=309)	36.9	8.5	1.8	0—5	69	22

[a] The mean ages were calculated from rounded ages.

Table 3. Characteristics of the study population.[a]

	Exposed workers in greenhouses (N=253)[b]		Other members of the gardeners' union (N=239)[c]		Workers in greenhouses			
					High exposure[d, e] (N=202)		Low exposure[d, f] (N=51)	
	N	%	N	%	N	%	N	%
Mother's age, at interview								
<30 years	76	30	39	16	65	32	11	22
30—34 years	106	42	76	32	86	43	20	20
35—40 years	39	16	35	15	32	16	7	14
≥40 years	32	13	88	37	19	9	13	26
Mother's age, 1st child								
<20 years	16	6	34	14	13	6	3	6
20—29 years	212	84	187	79	167	83	45	88
≥30 years	25	10	15	6	22	11	3	6
Year of most recent pregnancy								
Before 1970	1	0	16	7	-	0	1	2
1970—1979	14	6	71	30	7	4	7	14
1980—1989	45	18	96	41	36	18	9	18
1990	193	76	54	21	159	79	34	67
Education above compulsory level	228	90	200	84	186	92	42	82
Most recent pregnancy								
Oral contraception within 2 months	112	45	90	38	92	46	21	41
Father smoker	116	46	154	65	98	49	18	35
Mother smoker	103	41	122	51	86	43	17	33
Primipara	68	27	54	23	63	31	5	10
>500 mg of caffeine/day	111	44	129	54	88	44	23	45

[a] Only participants for whom the most recent pregnancy was included in the analysis. [b] Mean number of live children 1.7, SD 0.8.
[c] Mean number of live children 1.8, SD (0.7). [d] Aggregated indicator of exposure: at least 20 hours per week of manually handling cultures without gloves or applying pesticides. [e] Mean number of live children 1.6, SD 0.8. [f] Mean number of live children 1.9, SD 0.6.

Table 4. Percentage of women pregnant at 6 and 12 months, the unadjusted and adjusted[a] fecundability ratios and the most recent pregnancy.

	Number of pregnancies	Percentage of women pregnant within 6 months	Percentage of women pregnant within 12 month	Unadjusted fecundability ratio	95% CI[b]	Adjusted fecundability ratio	95% CI[c]
Members of the gardeners' trade union							
Other union members	239	75.3	85.4	1.00		1.00	
Workers in flower greenhouses	253	78.7	85.4	1.04	0.86— 1.27	1.11	0.90—1.36
Workers in greenhouses							
<20 hours of contact with cultures	33	84.8	93.9	1.00		1.00	
≥20 hours of contact with cultures	220	77.7	84.1	0.64	0.43—0.94	0.69	0.47—1.03
Workers in greenhouses							
Always using gloves when in contact with plants	40	80.0	95.0	1.00		1.00	
Sometimes using gloves when in contact with plants	57	82.5	86.0	0.82	0.54—1.26	0.78	0.50—1.21
Never using gloves when in contact with plants	156	76.9	82.7	0.73	0.51—1.06	0.67	0.46—0.98
Workers in greenhouses							
Not spraying pesticides	171	81.3	88.3	1.00		1.00	
Spraying pesticides	82	73.2	79.3	0.75	0.56—1.00	0.78	0.59—1.06
Workers in greenhouses							
Low exposure (see table 2)	51	86.3	96.1	1.00		1.00	
High exposure (see table 2)	202	76.7	82.7	0.58	0.42—0.80	0.64	0.45—0.90

[a] Adjusted by maternal smoking, paternal smoking, maternal age when child born, parity, education, caffeine consumption, and oral contraception.
[b] For the unadjusted fecundability ratio.
[c] For the adusted fecuntability ratio.

Table 5. Unadjusted fecundability ratios for potential confounding variables, most recent pregnancy.

Variable	Fecundability ratio	95% CI
Female smoking (yes;no)	0.80	0.66—0.97
Male smoking (yes;no)	1.09	0.90—1.32
Education above compulsory level (yes;no)	0.99	0.74—1.31
Female age, ≥30 years (yes;no)	0.68	0.55—0.86
>500 mg caffeine per day (yes;no)	0.98	0.80—1.19
Female primipara (yes;no)	0.54	0.43—0.70

Adjusted hazard ratios were calculated for indicators of the pesticide exposure variables and confounding variables by proportional hazards regression (16). Confounders were defined by the characteristics at the starting time. As potential confounders we included maternal cigarette smoking (yes;no), paternal cigarette smoking (yes;no), mothers' age (<29 years; ≥30 years), caffeine consumption (<499 mg; ≥500 mg per day) mother's education above compulsory level (yes;no), parity (primipara; others), and oral contraception within the last 2 months before the starting time (yes; no). The proportional risk assumption was verified for all the variables included in the model with the exception of use of oral contraception. Persons who used oral contraception within 2 months before the starting time had a low probability of conceiving during the first months and higher probability in later months. Therefore the regression analyses were stratified on the use of oral contraception. We used the SAS (Statistical Analysis System) procedure PHREG (with the options STRATA oral contraception, and EXACT to handle ties). The data were censored at 13 months. The analyses were restricted to persons who achieved a pregnancy. Therefore the fecundability was conditional on pregnancy and not on the true probability of pregnancy in 1 menstrual cycle.

Results

Among the workers in flower greenhouses, 27.7% achieved a pregnancy during the first month compared with 31.0% among the reference union members. Table 4 shows the percentage achieving a pregnancy during the first 6 and 12 months.

In the proportional hazards regression analysis (table 4), the adjusted fecundability ratio for the workers in flower greenhouses compared with the other union members was 1.11 [95% confidence interval (95% CI) 0.90—1.36].

In analyses only including the workers in flower greenhouses handling cultures many hours per week, spraying, and no use of gloves were related to reduced fecundability (table 4). The fecundability ratio was respectively 0.69 (95% CI 0.47—1.03), 0.78 (95% CI 0.59—1.06), and 0.67 (95% CI 0.46—0.98). And the fecundability ratio of the aggregated exposure variable was 0.64 (95% CI 0.45—0.90).

Fecundability ratios in the same range were found in analyses involving the first pregnancy, with the exception that the fecundability among the other union members was slightly lower than in the analysis of the most recent pregnancy.

In table 5 the unadjusted fecundability ratios are shown for the potential confounders included in the model.

Discussion

We found no difference in the fecundability ratio between exposed workers in flower greenhouses and other gardener union members. But for workers in flower greenhouses only the fecundability was decreased among the women doing tasks supposedly entailing a higher dermal exposure to pesticides.

Pregnancies were excluded from the analysis due to birth control failure more often than among other gardener union members (14.3%) than among workers in flower greenhouses (7.9%). Highly fecund couples are more likely to have birth control failure, and as a consequence they were excluded from the study (17). Thus the fecundability in the reference group may have been biased towards values that were too low and therefore resulted in a bias in the risk estimate towards the null hypothesis. There were no big differences in the rates of induced abortions between the exposed workers in flower greenhouses and the other gardener union members.

We expected the other members of the gardeners' union to be a proper comparison group for the workers in flower greenhouses, but most of the other union members were not working in gardener jobs when they received their most recent child. They worked in factories, as cleaners, in public service taking care of children or old people or in offices.

The group of other union members included 41 women working as gardeners when they received their most recent child. They may have been exposed to pesticides although the exposure was probably low. Therefore the analysis comparing the exposed workers in flower greenhouses and the other gardener union members was also performed with the exclusion of those with other gardener jobs. This procedure did not change the fecundability ratio estimates.

Differential participation of pesticide-exposed women with reduced fertility would bias the results. In the introduction letter we did not specify explicitly that pesticides and time to pregnancy would be studied. The letter was kept in general terms about an investigation of occupation and reproductive health. In addition, the differences in fecundability were seen within the group of greenhouse workers, all exposed to pesticides, and with no knowledge of the exposure classification used in the study.

As we analyzed time to pregnancy conditional on pregnancy, women who had never achieved a pregnancy were not included. If pesticide exposure reduces fecundability, analyses of time to pregnancy may underestimate the effect.

Since low parity may be due to low fecundity, we analyzed data with and without controlling for parity. This procedure did not give rise to substantial differences in the fecundability ratios between the exposed workers in flower greenhouses and the other union members. For the greenhouse workers the fecundability ratio of the aggregated exposure variable declined to 0.59 (95% CI 0.40—0.81), but no substantial changes were seen in relation to the variables including only 1 determinant of exposure. By including parity in the model, we might have blurred an effect of pesticide exposure. But the analysis of the first pregnancy fecundability ratios were in the same range as those presented in table 4.

As an additional analysis we compared the time to pregnancy in our study (exposed workers in flower greenhouses and other union members) to a random sample of the Danish population. The population sample data were collected in 1991 by personal interview, using the same questionnaire as in this study. With the use of the same criteria for exclusion for the population sample, the exposed workers in flower greenhouses and the other union members compared with the population sample had a fecundability ratio of 0.84 (95% CI 0.73—0.97). This is an indication of lower fecundability among all gardener union members in comparison with a random population sample.

The main limitation of our study was the crude exposure assessment based on several indirect indicators of exposure and a lack of documentation of the exposure. As dermal exposure is by far the most important (13, 14, 18), it seems reasonable to assume that the number of hours in contact with plants reflects the level of exposure. At least 20 hours per week was chosen as an indicator of at least half-time dermal contact to cultures. The use of gloves when re-entry activities are performed can only be expected to lower exposure if used correctly, and for sprayers the incorrect use of gloves may in fact increase dermal exposure (19). The use of gloves when re-entry activities are performed has become more widespread during recent years, and the awareness of risks associated with improper use may have increased. Thus it is reasonable to assume that the use of gloves during re-entry activities does decrease exposure. As the use of gloves has increased during recent years, the result achieved in the analysis of the use of gloves may have, in part, been a consequence of time trend bias (20). No exposure data exist to handle this potential bias.

Hoekstra et al (18) found that, compared with re-entry activities, spraying doubled the exposure per workhour. In this study the mean spraying time per week among sprayers was 5.5 (SD 8.0, median 2) hours. Thus we expected exposure from spraying activities to contribute less to the total exposure than exposure from re-entry activities. This assumption may be in accordance with the lower fecundability among the exposed persons classified according to the use of gloves than among the exposed persons classified according to the application of pesticides. The misclassification achieved by the use of proxy variables, and the fact that workers are exposed in several ways, would probably bias the results towards the null hypothesis. Part-time work may be related to family size, and part-time workers are also less likely to be highly exposed. Therefore the analysis of hours per week manually handling cultures and the aggregated exposure measure were restricted to full-time workers (75%). The fecundability ratio of manual handling was 0.55 (95% CI 0.33—0.92), and the fecundability ratio of aggregated exposure remained almost unchanged 0.63 (95% CI 0.40—0.99).

Most of the pregnancies among the exposed occurred after 1990. Thus the findings in the study can probably not be explained by earlier high exposure, unless pesticides accumulate in the body or have an irreversible effect. Some organochlorides such as lindane and endosulfane have been used in greenhouses within the last few years, and they tend to interfere with the homeostasis of reproductive hormones. Disruption of endocrine regulation may interfere with many of the biological processes involved before a pregnancy is recognized (21, 22).

The fungicide thiram and the insecticide amitraz in animal testing block ovulation. And the fungicides carbendazin and benomyl interfere with spindle formation, effects that, in humans, may decrease fecundity (23).

In conclusion our findings indicate that exposure to pesticides among women working in flower greenhouses may lead to reduced fecundity. Additional studies of fecundity among women working in greenhouses are highly warranted. Efforts to achieve measurements of exposure would add to the reliability of the results.

Acknowledgments

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References

1. Whorton MD, Foliart DE. Mutagenicity, carcinogenicity and reproductive effects of dibromochloropropane (DBCP). Mutat Res 1983;123:13—30.
2. Wyrobek AJ, Watchmaker G, Gordon L, Wong K, Moore D, Whorton D. Sperm shape abnormalities in carbaryl-exposed employees. Environ Health Perspect 1981;40:255—65.
3. Glass RI, Lyness RN, Mengle DC, Powell KE, Kahn E. Sperm count depression in pesticide applicators exposed to dibromochloropropane. Am J Epidemiol 1979;109:346—51.
4. Cohn WJ, Boylan JJ, Blanke RV, Fariss MW, Howell JR, Guzelian PS. Treatment of chlordecone (kepone) toxicity with cholestyramine. N Engl J Med 1978;298:243—8.
5. Nurminen T. Maternal pesticide exposure and pregnancy outcome. J Occup Environ Med 1995;37:935—40.
6. Fuortes L, Clark MK, Kirchner HL, Smith EM. Association between female infertility and agricultural work history. Am J Ind Med 1997;31:445—51.
7. Rowland AS, Baird DD, Weinberg CR, Shore DL, Shy CM, Wilcox AJ. Reduced fertility among women employed as dental assistants exposed to high levels of nitrous oxide. N Engl J Med 1992;327:993—7.
8. Schaumburg I, Olsen J. Time to pregnancy among Danish pharmacy assistants. Scand J Work Environ Health 1989; 15:222—6.
9. Bisanti L, Olsen J, Basso O, Thonneau P, Karmaus W. Shift work and subfecundity: a European multicenter study. J Occup Environ Med 1996;38:352—8.
10. de Cock J, Westveer K, Heederik D, de Velde E, van Kooij R. Time to pregnancy and occupational exposure to pesticides in fruit growers in The Netherlands. Occup Environ Med 1994;51:693—9.
11. Thonneau P, Abell A, Larsen SB, Bonde JP, Clavert A, Ducot B, et al. Effects of pesticide exposure on time to pregnancy: results of a multicenter study in France and Denmark. Am J Epidemiol. In press.
12. Curtis KM, Savitz DA, Weinberg CR, Arbuckle TE. The effect of pesticide exposure on time to pregnancy. Epidemiology 1999;10:112—7.
13. Brouwer DH, Brouwer R, Mik DG, Maas LC, Van Hemmen JJ. Pesticides in the cultivation of carnations in greenhouses: part 1 — exposure and concomitant health risk. Am Ind Hyg Assoc J 1992;53:575—81.
14. Brouwer R, Brouwer DH, Tijssen SCHA, Van Hemmen JJ. Pesticides in the cultivation of carnations in greenhouses: part 2 — relationship between foliar Residues and exposures. Am Ind Hyg Assoc J 1992;53:582—7.
15. Bolumar F, Olsen J, Boldsen J. Smoking reduces fecundity: a European multicenter study on infertility and subfertility. Am J Epidemiol 1996;146:578—87.
16. Allison P.D. Survival analysis using the SAS system: a practical guide. Cary (NC): SAS Institue Inc, 1995.
17. Baird DD, Weinberg CR, Schwingl P, Wilcox AJ. Selection bias associated with contraceptive practice in time-to-pregnancy studies. Ann N Y Acad 1994;feb.18:154—64.
18. Hoekstra EJ, Kiefer M, Tepper A. Monitoring of exposure to benomyl in nursery workers. J Occup Environ Med 1996;38:775—81.
19. Kangas J, Laitinen S, Jauhiainen A, Savolainen K. Exposure of sprayers and plant handlers to mevinphos in Finnish greenhouses. Am Ind Hyg Assoc J 1993;54:150—7.
20. Weinberg CR, Baird DD, Rowland AS. Pitfalls inherent in retrospective time-to-event studies: the example of time to pregnancy. Stat Med 1993;12:867—79.
21. Baird DD, Wilcox AJ. Effects of occupational exposures on the fertility of couples. Occup Med 1986;1:361—74.
22. Cummings AM. Toxicological mechanisms of implantation failure. Fund Appl Toxical 1990;15:571—9.
23. Sipes IG, McQueen A, Gandolfi AJ. Comprehensive toxicology. In: Boekelheide K, Chapin RE, Hoyer PB, Harris C, editors. Oxford: Elsevier Science Ltd, 1997:249—328.

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