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Time to pregnancy among the wives of Finnish greenhouse workers

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Objectives This study investigated the possibility of men's work in greenhouses and their exposure to pesticides being associated with reduced fertility.

Methods A study on time to pregnancy was conducted among the families of Finnish male greenhouse employers and employees. Exposure to pesticides was assessed on the basis of questionnaire information and data gathered from the enterprises. Fecundability density ratios (FDR) for occupational exposure were calculated with discrete proportional hazards regression analyses.

Results After three mailings, 578 (43%) couples participated. Fecundability was suggestively decreased for exposed greenhouse workers who were inefficiently protected, with FDR values of 0.67 [95% confidence interval (95% CI) 0.33–1.35], 0.92 [95% CI 0.45–1.88] and 0.77 [95% CI 0.46–1.29] for high exposure, moderate exposure and low exposure, respectively, as compared with unexposed greenhouse workers. The exposed men who efficiently used personal protective equipment were as fertile as the unexposed greenhouse workers. Exposure to pyrethroids (FDR 0.40, 95% CI 0.19–0.85) was related to decreased fecundability. Suggestive associations were observed for organophosphates (FDR 0.70, 95% CI 0.42–1.17) and carbamates (FDR 0.55, 95% CI 0.27–1.11).

Conclusions The findings of the study provide limited support for the hypothesis that exposure to pesticides is associated with reduced fertility. The findings for pyrethroids, organophosphates, and carbamates can serve as a basis for a hypothesis for future studies.

Key terms fecundability, male exposure, pregnancy delay, reproductive health.

One of the first agents observed to be hazardous for male reproduction in humans was the nematocide DBCP (dibromochloropropane) (1). Some other pesticides [ie, 2,4-dichlorophenoxyacetic acid (2,4-D), ethylene dibromide (EDB), chlordecone (KeponeTM), and carbaryl] have also been shown to cause adverse effects on semen quality (2–3). A Dutch study observed decreased fecundability among highly exposed fruit growers as compared with that of workers with low exposure (4), but three other studies found no association between exposure to pesticide and male fecundability (5–7). All in all, data on

the effects of pesticide exposure on male fertility are scarce and difficult to compare due to exposure heterogeneity.

About 7000 permanent workers and 12 000 temporary workers are employed in greenhouses in Finland. About 40% of the employees are men. The pesticides mainly used in Finnish greenhouses are herbicides and insecticides. Typical examples are carbamates (benomyl and thiophanate-methyl), dithiocarbamates (mancozeb and thiram), organochlorine compounds (dienochlor, dicofol, endosulfan, lindane), and sulfur (8–9). More

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than half of the insecticides are organophosphates (dimethoate, dichlorvos, mevinphos, sulfotep). Carbamates (aldicarb, pirimicarb), pyrethroids (deltamethrin, permethrin), and nicotine are also used to control insects.

Pesticide concentrations in the air often exceed the occupational exposure limits in greenhouses when fumigated (10). Most insecticides, such as organophosphates, carbamates, and organochlorines, penetrate the skin easily. Most of the exposure occurs via the skin, depending on the application method (11). Some pesticides degrade on the leaves into more toxic compounds with even a stronger penetration capacity through the skin than their parent compounds. Workers are exposed to pesticides via inhalation during applications and to pesticide residues through the skin when they handle treated plants.

The aim of our study was to investigate whether the work of men in greenhouses and exposure to pesticides are associated with decreased fertility. Time to pregnancy was used as the measure of fertility (12). Valid data on time to pregnancy at a group level can be derived retrospectively, with a recall time of 14 years or more (13).

Subjects and methods

A study on time to pregnancy was conducted among Finnish male greenhouse employers and employees. The employers and employees who had been working in greenhouses at least one month in 1980–1990 were included. Data on male employees were collected from the files of the LEL Employment Pension Fund. All employees working in agriculture are insured under LEL. Data on greenhouse companies were obtained from employers' associations (1247 enterprises). Data on the identification codes of male employers and male family members, cultivated plants, and the pesticides used for each plant were collected with a questionnaire from the enterprises. The participation rate was 54% in that inquiry. Due to missing information on male employers or family members the data covered only 478 male employers. Altogether data were obtained on 14 733 employees and 419 employers who were born in 1930–1971 and were 19 to 50 years of age during the study period, 1980–1990.

Data on marital status, the wives of greenhouse workers and employers, and the addresses of the couples were collected from the Finnish Population Register Centre. The study was restricted to men in their first marriage at the time of the inquiry (May 1994). The men in their first marriage numbered 3622 among the employees and 303 among the employers. The pregnancies of the wives were identified from the nationwide database on medically diagnosed pregnancies in 1973–1990.

The database includes information on all births, spontaneous abortions, and induced abortions retrieved from the Hospital Discharge Register and records of hospital polyclinics (outpatient clinics) in Finland (14). The number of wives having pregnancies was 2328, and the total number of pregnancies was 4734. Altogether 86% of the pregnancies were births, 9% were spontaneous abortions, 4% were induced abortions, and 0.6% were extrauterine pregnancies.

The inclusion criteria for couples and pregnancies were as follows: (i) the couple had to be married within 5 months after the estimated conception date of the pregnancy (376 exclusions), (ii) the couple had to have either a birth or a spontaneous abortion during the study period, 1980–1990 (349 exclusions), (iii) the wife had to be 18–39 years of age in the third month of the pregnancy (11 exclusions), (iv) the wife could not have had more than two pregnancies ending in spontaneous abortion in 1973–1990 (7 exclusions), and (v) the pregnancy should have started after the husband's entry into greenhouse work (180 exclusions). The study pregnancy was defined as the first eligible pregnancy (either a birth or a spontaneous abortion) during the study period. A total of 1407 couples met these criteria. In addition 72 couples were excluded because of a different address of the man and wife or the missing address of the couple.

Data on time to pregnancy and related factors were asked in questionnaires at two stages in 1994 to 1995. Data inquiry took place 4 to 15 years after the studied pregnancies. At the first stage, separate questionnaires were sent to 1335 men (1225 workers and 110 employers) and their wives to obtain data on the pregnancies, work histories, and personal habits. The potential confounders were selected on the basis of a priori knowledge on their association with fertility. The men were asked about their work history in greenhouses since 1975. There were detailed questions about the application of pesticides in the work area, the spraying of pesticides or work with the treated plants, the names of the pesticides used (the questionnaire included a list of the most common pesticides used in Finland), and the use of personal protective equipment. The men were asked to record these work conditions for each work period when necessary. Histories of the occurrence of solvents, welding work, exhausts, metal dusts or fumes, tobacco smoke, and work temperatures of 30°C or more were requested from both spouses. The wives were asked about their work history, work in greenhouses, pregnancy history, and the time required to get pregnant for each pregnancy that ended in a birth or a spontaneous abortion. The couples were asked about their possible fertility problems and medical consultations for such problems.

A total of 578 (43.3%) couples participated after two reminders. Two of the participants did not report the

study pregnancy, three had missing information on the dates of the pregnancies, and one refused further contact. Short-time workers (less than a year of work in greenhouses; participation rate 39%) were less willing to participate, as compared with employers (58%) or those who had worked for at least a year (53%). Women who had experienced a spontaneous abortion were more passive (39%) than women with a birth as the study pregnancy (44%). In addition women with at least three pregnancies in the register (39%) were less willing to participate than women with no more than two registered pregnancies (46%). In addition to the 578 families, also 37 men (2.8%) and 75 wives (5.6%) participated in the first stage of the study only.

Another inquiry was restricted to the 572 families who participated in the first phase of the study. A second questionnaire was sent to wives to obtain detailed information on the time to pregnancy preceding the selected study pregnancy. Those who did not use any contraception at the time of conception were asked: "Did you get pregnant during the first menstrual cycle that occurred after you started sexual intercourse without contraception? During the second cycle? If not: How many cycles (or months) did it take to get pregnant? ____ (years) ____ months." The wives were asked about their last contraceptive method, the consumption of coffee and alcohol, and smoking habits preceding the pregnancy. Information on work and the occurrence or handling of pesticides or solvents at work was also requested.

Altogether 489 (85.5%) wives participated in the second inquiry. Missing or contradictory information on time to pregnancy was complemented with phone calls (N=8) or questionnaires (N=13). The pregnancy was due to contraceptive failure in the case of 24 women. Only two (0.4%) of the remaining women could not determine their time to pregnancy. Eight couples were excluded because of the wife's hormonal treatment for infertility or the study pregnancy had started through in vitro fertilization. The study was restricted to couples (N=588) with information on time to pregnancy from either the second (N=456) or the first (N=132) inquiry. In 522 (88.8%) cases, also the man participated.

Exposure assessment

Exposure and the use of protective equipment were assessed for the beginning of the time-to-pregnancy period. The date when the time to pregnancy started was calculated using the dates from the medical records and the length of time to pregnancy allowing 80 days for spermatogenesis. An experienced occupational hygienist conducted the exposure assessment of male greenhouse workers without knowledge of the time to pregnancy. Exposure assessment was made for all the work-tasks within the 12-month period following the onset of

time to pregnancy, regardless of the length of time to pregnancy. Only the assessment for jobs during the time to pregnancy was used in the analyses, however. Exposure assessment was based on the following information: (i) questionnaire data, (ii) data on cultivated plants and used pesticides as reported by the employers, and (iii) results of previous studies on exposure conditions in Finnish greenhouses (9). The calendar months with pesticide exposure were taken into account in the assessment to reduce the misclassification of exposure. Male exposure to other occupational factors and female exposure were defined on the basis of the questionnaire information.

Both the likelihood and the level of exposure were assessed for exposure to pesticides in general. A greenhouse worker was classified as unexposed if he did not report any pesticide application or handling of treated plants. Workers were ranked as potentially exposed if their employers had offered information about pesticide applications in the company. The men who reported the application of pesticides or the handling of treated plants were regarded as exposed.

Exposure was rated as high if a person had applied pesticides at least once a week or had worked with treated plants on 3 days a week. The exposure was considered moderate if pesticides were applied two to three times a month or the treated plants were handled on 1 or 2 days a week. If a worker had sprayed pesticides only once a month or had worked with treated plants less than once a week, his exposure was considered low. In the analyses, potential exposure (N=5) was included in the low-exposure category. Use of protective equipment was efficient if a worker reported wearing appropriate protection whenever being in contact with pesticides or their residues. Protection was inefficient if a person did not use any protection or he wore protective equipment only sometimes or only during some tasks when exposure was possible. The exposure groups were decided before the data analysis was carried out.

Pesticides were classified into 11 categories: 1–6 = insecticides: organophosphorous compounds, organochlorines, carbamates, nicotine, pyrethroids, organotin compounds (only 4 exposed workers); 7–9 = fungicides (bentimidazoles, dithiocarbamates, other fungicides); 10 = herbicides (all in the same group), and 11 = plant growth regulators (all in the same group).

A total of 210 (36%) men worked in greenhouses or gardens during the time to pregnancy, and 143 (24%) were assessed as exposed to pesticides. Exposure was defined as high for 50 men, moderate for 28 men, and low for 65 men. Exposure could not be assessed for 8 men. Altogether 15 highly exposed men, and 11 and 32 men in the moderate and low exposure groups, respectively, did not use protective equipment efficiently. The association of male exposure to pesticides and

Table 1. Time to pregnancy (TTP) distributions and unadjusted fecundability density ratios (FDR) according to men's work in greenhouses or gardens and potential confounders—21 proportional hazards models.^a (95% CI = 95% confidence interval)

	Time to pregnancy								FDR	95% CI
	1-2 months		3-6 months		7-12 months		>12 months			
	N	%	N	%	N	%	N	%		
Male factors										
Participation										
No (only wife participated)	46	69.7	15	22.7	3	4.6	2	3.0	1.0	Reference
Yes (both couples participated)	293	56.1	143	27.4	40	7.7	46	8.8	0.69	0.53–0.92
Work in greenhouses or gardens										
Yes	112	53.3	54	25.7	18	8.6	26	12.4	0.81	0.57–1.01
No (men in other occupations or unemployed)	227	60.1	104	27.5	25	6.6	22	5.8	1.0	Reference
Work in greenhouses or gardens										
Yes ^b	112	53.3	54	25.7	18	8.6	26	12.4	0.84	0.62–1.15
Exposure to pesticides (use of protective equipment not considered)										
Not exposed	31	52.5	15	25.4	8	13.6	5	8.5	1.0	Reference
Low exposure	32	49.2	18	27.7	4	6.2	11	16.9	0.84	0.57–1.24
Moderate exposure	15	53.6	9	32.1	2	7.1	2	7.1	1.11	0.69–1.80
High exposure	29	58.0	9	18.0	4	8.0	8	16.0	0.92	0.61–1.39
Unknown	5	62.5	3	37.5	–	0	–	0	1.69	0.78–3.66
Work in greenhouses or gardens										
Yes ^b	112	53.3	54	25.7	18	8.6	26	12.4	0.81	0.60–1.08
Exposure to pesticides (use of protective equipment considered)										
Not exposed	31	52.5	15	25.4	8	13.6	5	8.5	1.0	Reference
Exposed – no efficient protection										
Low exposure	18	56.3	6	18.9	1	3.1	7	21.9	0.82	0.50–1.32
Moderate exposure	6	54.6	4	36.4	–	0	1	9.1	1.15	0.57–2.31
High exposure	7	46.7	4	26.7	–	0	4	26.7	0.69	0.36–1.32
Exposed – protected efficiently										
Low exposure	14	42.4	12	36.4	3	9.1	4	12.1	0.87	0.55–1.38
Moderate exposure	9	52.9	5	29.4	2	11.8	1	5.9	1.09	0.61–1.93
High exposure	22	62.9	5	14.3	4	11.4	4	11.4	1.05	0.67–1.65
Unknown	5	62.5	3	37.5	–	0	–	0	1.67	0.75–3.71
Age at the beginning of TTP										
<21 years	12	35.3	12	35.3	5	14.7	5	14.7	0.68	0.51–0.89
21–29 years	261	60.0	119	27.4	30	6.9	25	5.8	1.0	Reference
30–44 years	66	55.5	27	22.7	8	6.7	18	18.2	0.73	0.58–0.92
Smoking										
Nonsmokers	99	57.9	53	30.0	9	5.3	10	5.9	1.0	Reference
Smokers										
1–14 cigarettes/day	56	61.5	21	23.1	9	9.9	5	5.5	1.00	0.76–1.31
≥15 cigarettes/day	46	41.8	40	36.4	12	10.9	12	10.9	0.72	0.55–0.93
Ex-smokers	36	59.0	10	16.4	4	6.6	11	18.0	0.73	0.53–1.01
Alcohol										
Nonusers	64	60.4	30	28.3	7	6.6	5	4.7	1.0	Reference
Users										
≤6 drinks/week	118	57.0	51	24.6	20	9.7	18	9.7	0.84	0.65–1.08
≥7 drinks/week	22	40.0	20	36.4	5	9.1	8	14.6	0.63	0.44–0.90
Temperatures of ≥30°C at work										
0 hours/week	219	56.7	111	28.8	26	6.7	30	7.8	1.0	Reference
≤2 hours/week	13	50.0	7	26.9	3	11.5	3	11.5	0.82	0.53–1.26
≥3 hours/week	31	47.0	16	24.2	9	13.9	10	15.2	0.72	0.54–0.96
Female factors										
Age at the beginning of TTP										
<21 years	44	51.7	27	31.8	6	7.1	8	9.4	0.86	0.67–1.11
21–29 years	258	59.6	115	26.6	31	7.2	29	6.7	1.00	Reference
30–38 years	37	52.9	16	22.9	6	8.6	11	15.7	0.74	0.56–0.97
Study pregnancy										
Birth	316	58.1	146	26.8	40	7.4	42	7.7	1.0	Reference
Spontaneous abortion	23	52.3	12	27.3	3	6.8	6	13.6	0.82	0.58–1.14
Pregnancy order										
1st pregnancy	199	54.7	111	30.5	25	6.9	29	8.0	0.96	0.80–1.15
2nd and later pregnancies	139	62.1	48	21.4	18	8.0	19	8.5	1.0	Reference

(continued)

Table 1. Continued

	Time to pregnancy								FDR	95% CI
	1-2 months		3-6 months		7-12 months		>12 months			
	N	%	N	%	N	%	N	%		
No previous births	212	54.4	118	30.3	29	7.4	31	8.0	0.92	0.76–1.10
Previous spontaneous abortion	16	43.2	11	29.7	5	13.5	5	13.5	0.70	0.46–1.06
Previous spontaneous abortion or extrauterine pregnancy	20	44.4	13	28.9	6	13.3	6	13.3	0.69	0.47–1.00
Last method of contraception										
Pill	69	46.3	54	36.2	19	12.8	7	4.7	1.17	0.90–1.52
Intrauterine device	24	63.2	5	13.2	1	2.6	8	21.1	1.00	0.66–1.52
Condom, rhythm method and other unsafe method	103	67.3	34	22.2	5	3.3	11	7.2	1.53	1.17–1.99
None	36	46.8	19	24.7	10	13.0	12	15.6	1.0	Reference
Marital status at the beginning of TTP										
Unmarried	62	46.3	49	36.6	9	6.7	14	10.5	1.0	Reference
Married	277	61.0	109	24.0	34	7.5	34	7.5	1.24	1.01–1.53
Smoking										
Nonsmokers	262	60.9	108	25.1	27	6.3	33	7.7	1.0	Reference
Smokers										
1–4 cigarettes/day	11	47.8	7	30.4	2	8.7	3	13.0	0.75	0.48–1.16
≥5 cigarettes/day	46	43.4	37	34.9	13	12.3	10	9.4	0.76	0.60–0.96
Coffee consumption										
≤4 cups/day	184	57.0	92	28.5	25	7.7	22	6.8	1.0	Reference
>4 cups/day	66	49.6	38	28.6	11	8.3	18	13.5	0.78	0.63–0.98
Coffee consumption and smoking										
Coffee ≤4 cups/day										
Nonsmokers + smokers of 1–4 cigarettes/day	161	59.9	74	27.5	18	6.7	16	6.0	1.0	Reference
Smokers of ≥5 cigarettes/day	23	42.6	18	33.3	7	13.0	6	11.1	0.63	0.49–0.82
Coffee >4 cups/day										
Nonsmokers or smokers of ≥5 cigarettes/day	46	52.3	20	22.7	8	9.1	14	15.9	0.69	0.53–0.90
Smokers of ≥5 cigarettes/day	20	44.4	18	40.0	3	6.7	4	8.9	1.23	0.83–1.84
Alcohol										
Nonusers	129	63.2	49	24.0	14	6.9	12	5.9	1.0	Reference
Users										
≤2 or unknown drinks/week	161	55.3	83	28.5	22	7.6	25	8.6	0.85	0.70–1.03
≥3 drinks/week	22	42.3	17	32.7	4	7.7	9	17.3	0.61	0.44–0.86
Employment and greenhouse or garden work										
Not employed	59	71.1	19	22.9	2	2.4	3	3.6	1.0	Reference
Employed	191	51.2	111	29.8	34	9.1	37	9.9	0.61	0.47–0.80
In a greenhouse or garden	16	53.3	11	36.7	2	6.7	1	3.3	1.20	0.88–1.64
Sprayed pesticides herself	7	43.8	3	18.8	1	6.3	5	31.3	0.48	0.25–0.94

^a A category of missing information was included in the model when necessary.

^b Reference: men from other occupations or unemployed men.

fertility was assessed for the 58 inefficiently protected and 85 efficiently protected workers with exposure, compared with 59 greenhouse or garden workers without any exposure.

Statistical analysis

Time-to-pregnancy data were analyzed with a discrete proportional hazards regression analysis (15) using the SAS PHREG procedure and EXACT handling of ties (SAS Institute, Cary, NC, USA). Time-to-pregnancy categories of more than 13 cycles were combined into one category to exclude the possible effects of medical treatment for infertility, and because of the sparseness of the data beyond this point. The outcome parameter is

a hazard ratio. Since pregnancy is a desired outcome, we used the phrase “fecundability density ratio” (FDR) in place of hazard ratio (16). FDR values below unity reflect reduced fertility.

The covariates were selected for the final model on the basis of the association with fecundability (FDR ≤0.7 or FDR ≥1.4 or P-value <0.1). The selection was performed starting with female age and reproductive factors, followed by personal habits, occupational factors, and male factors. Covariates for male age, smoking, use of alcohol, and exposure to temperatures of 30°C or more were not associated with fecundability in the multivariate models and were thus not included in the final model. It was checked that their inclusion in the model did not change the findings for male pesticide

exposure. An interaction variable for female coffee use and smoking was included in the final model on the basis of a recent finding (17).

Results

The distributions and unadjusted FDR values are presented in table 1 (on pages 88 & 89). Among the female factors, older age, no contraceptive use preceding time to pregnancy, smoking, consumption of coffee and alcohol, employment, and spraying pesticides were associated with prolonged time to pregnancy. Among the male factors, older age, smoking, consumption of alcohol, and work in temperatures of 30°C or more were

Table 2. Adjusted fecundability density ratio (FDR) by exposure to pesticides—proportional hazards model.^a (95% CI = 95% confidence interval, TTP = time to pregnancy)

	N	FDR	95% CI
Male factors			
Participation ^b			
Yes	522	0.75	0.50–1.12
Work at greenhouses or gardens ^c	210	0.86	0.62–1.19
Exposure to pesticides			
No efficient protection			
Low exposure	32	0.77	0.46–1.29
Medium exposure	11	0.92	0.45–1.88
High exposure	15	0.67	0.33–1.35
Protected efficiently			
Low exposure	33	0.82	0.51–1.34
Medium exposure	17	1.15	0.63–2.11
High exposure	35	0.94	0.58–1.52
Unknown	8	2.00	0.86–4.64
Not exposed	59	1.0	Reference
Female factors			
Married at the beginning of TTP	454	1.33	1.06–1.68
Age ≥30 years	70	0.67	0.49–0.92
First pregnancy	364	0.88	0.71–1.09
Last method of contraception ^d			
No	77	0.74	0.54–0.99
Condom, rhythm method, and other unsafe method	153	1.33	1.06–1.68
Smoking			
1–4 cigarettes/day	23	0.70	0.45–1.11
≥5 cigarettes/day	106	0.68	0.50–0.91
Coffee >4 cups/day			
Nonsmokers + smokers of 1–4 cigarettes/day	88	0.75	0.57–0.99
Smokers of ≥5 cigarettes/day	45	1.42	0.93–2.18
Alcohol			
≤2 or unknown drinks/week	291	0.82	0.67–1.01
≥3 drinks/week	52	0.66	0.46–0.96
Employment ^e			
Employed	373	0.69	0.52–0.91
Work in greenhouses or gardens	69	1.19	0.85–1.68
Sprayed pesticides herself	16	0.51	0.26–1.01

^a A category of missing information was included in the model when necessary.

^b Reference: only wife participated.

^c Reference: no work in greenhouses or gardens.

^d Reference: intrauterine device, pills.

^e Reference: not employed.

related to lower fertility. The families in which both couples participated in the study were less fertile than those in which only the wife participated. The wife's participation in the second inquiry was related to reduced fertility (crude FDR 0.78, 95% confidence interval (95% CI) 0.63–0.96).

The prevalence of men working in greenhouses or gardens decreased over time—55%, 32%, and 17% of the men working in that branch in 1979–1984, 1985–1987, and 1988–1989, respectively. Fecundability was slightly decreased for greenhouse and garden workers as compared with that of men from other occupations or unemployed men (unadjusted FDR 0.81, 95% CI 0.57–1.01) when pesticide exposure was not considered (table 1, on pages 88 & 89).

Fecundability was slightly decreased for the exposed greenhouse workers who were inefficiently protected [adjusted FDR 0.67 (95% CI 0.33–1.35), 0.92 (95% CI 0.45–1.88) and 0.77 (95% CI 0.46–1.29) for high exposure, moderate exposure and low exposure, respectively] as compared with that of the unexposed greenhouse workers (table 2). The exposed men who used personal protective equipment efficiently were as fertile as the unexposed greenhouse workers.

Subgroup analyses were conducted for wives' participation in the second inquiry and for background variables that showed differences in participation rates (table 3 on page 91). The results were essentially unchanged among the men who had worked in greenhouses for at least 4 months during the study period, among the pregnancies ending in births, and according to the wives' participation. Male exposure to pesticides was associated with decreased fecundability among primiparous families [FDR 0.31 (95% CI 0.10–0.99) and 0.43 (95% CI 0.22–0.81) for high and lower exposure, respectively]. However, male exposure to pesticides was not related to fecundability among parous wives.

Fertility was examined according to the type of pesticides used (table 4 on page 92). Exposure to pyrethroids (FDR 0.40, 95% CI 0.19–0.85) was related to decreased fecundability. Suggestive associations were observed for organophosphates (FDR 0.70, 95% CI 0.42–1.17) and carbamates (FDR 0.55, 95% CI 0.27–1.11).

Discussion

Fecundability was suggestively reduced among the exposed men without efficient personal protection as compared with that of the unexposed greenhouse workers. The exposed men who wore personal protective equipment efficiently were as fertile as the unexposed workers. The main result was based on only 15 highly

Table 3. Adjusted fecundability density ratios (FDR) for men's exposure to pesticides with modifications of the basic model—five proportional hazards regression models.^a (95% CI = 95% confidence interval).

	FDR	95% CI	Modification
Model 1			Only employers and workers who had worked at least 4 months in greenhouses or gardens (N=311)
Exposure to pesticides			
Not efficiently protected			
Low-to-moderate exposure	0.93	0.54–1.60	
High exposure	0.73	0.31–1.71	
Protected efficiently	1.07	0.66–1.71	
Model 2			Restricted to pregnancies ending in births (N=544)
Exposure to pesticides			
Not efficiently protected			
Low-to-moderate exposure	0.83	0.52–1.32	
High exposure	0.57	0.27–1.22	
Protected efficiently	0.85	0.57–1.26	
Model 3			Restricted to primiparous women (N=391)
Work in greenhouses or gardens	1.35	0.85–2.15	
Exposure to pesticides			
Not efficiently protected			
Low-to-moderate exposure	0.43	0.22–0.81	
High exposure	0.31	0.10–0.99	
Protected efficiently	0.59	0.34–1.01	
Model 4			Restricted to women with previous children (N=197)
Work in greenhouses or gardens	0.61	0.36–1.02	
Exposure to pesticides			
Not efficiently protected			
Low-to-moderate exposure	1.24	0.58–2.64	
High exposure	1.48	0.53–4.08	
Protected efficiently	1.32	0.71–2.47	
Model 5			Wife participated in the second stage of the inquiry (N=456)
Exposure to pesticides			
Not efficiently protected			
Low-to-moderate exposure	0.86	0.52–1.42	
High exposure	0.59	0.28–1.25	
Protected efficiently	0.83	0.55–1.26	

^a Adjusted for male participation, female age, previous pregnancies, last contraceptive method, marital status, smoking, interaction between drinking coffee and smoking, use of alcohol, employment, work in greenhouses or gardens, spraying of pesticides, and missing information.

exposed men; this low number, together with the low participation rate, weakens the conclusions drawn from this study.

Our findings are in accordance with the observations of two Dutch studies (4, 18). In the first study, fertility was reduced in the families of exposed fruit growers (4). In the other study (18), male exposure to pesticides was related to reduced fertilization capacity. However, exposure to pesticides was associated with an improved implantation rate in the same in vitro fertilization data (19). Other studies do not suggest an association between male exposure and fecundability (5–7).

Our study was a synthetic prospective study conditional on pregnancy (20). The first time to pregnancy after the husband's entry into greenhouse work was followed. This design has two major advantages. First, the selected time to pregnancy is the most likely to have occurred during male exposure. This point is essential if short-time workers are considered. Second, the design

is less prone to the so-called time trend bias, which may be prominent in retrospective studies on time to pregnancy, if the exposure under study has changed over calendar time (21–22). The potential for time-trend bias and truncation bias was also reduced since the comparisons were made among the greenhouse workers. The prevalence of greenhouse or garden work declined during the study period. Therefore, the suggestive finding of decreased fecundability observed for male work in greenhouses overestimates the true association. However, there was no clear time trend in the prevalence of pesticide exposure within the greenhouse workers, and the findings for male pesticide exposure are more reliable. In addition, the potential for the confounding effect of work at high temperatures or humidity was reduced because of the comparison within the greenhouse workers.

The strengths of the exposure assessment were as follows: (i) data on male exposure were collected

Table 4. Adjusted fecundability density ratios (FDR) by the type of pesticide exposure—10 proportional hazards models.^a (95% CI = 95% confidence interval)

Type of pesticide	N	FDR	95% CI
Organophosphates			
Not protected efficiently	32	0.70	0.42–1.17
Protected efficiently	66	0.92	0.61–1.39
Organochlorines			
Not protected efficiently	15	1.04	0.54–2.02
Protected efficiently	40	1.09	0.70–1.70
Carbamates			
Not protected efficiently	15	0.55	0.27–1.11
Protected efficiently	38	1.04	0.65–1.66
Nicotine			
Not protected efficiently	10	1.16	0.53–2.54
Protected efficiently	18	0.84	0.47–1.52
Pyrethroids			
Not protected efficiently	15	0.40	0.19–0.85
Protected efficiently	31	1.02	0.62–1.66
Benzimidazoles			
Not protected efficiently	22	0.87	0.49–1.53
Protected efficiently	46	0.97	0.62–1.52
Dithiocarbamates			
Not protected efficiently	11	1.68	0.80–3.54
Protected efficiently	23	0.73	0.42–1.28
Miscellaneous fungicides			
Not protected efficiently	26	0.70	0.40–1.20
Protected efficiently	52	1.10	0.71–1.70
Herbicides			
Not protected efficiently	11	0.67	0.31–1.48
Protected efficiently	17	0.67	0.36–1.26
Plant growth regulators			
All ^b	16	0.92	0.51–1.65

^a Adjusted for male participation, female age, previous pregnancies, last contraceptive method, marital status, smoking, interaction between drinking coffee and smoking, use of alcohol, employment, work in greenhouses or gardens, spraying of pesticides, and missing information.

^b All = 3 persons not protected efficiently and 13 persons protected efficiently.

independently of the studied outcome, (ii) exposure assessment was conducted by an experienced occupational hygienist without knowledge of the time to pregnancy, and (iii) seasonal variation in the use of pesticides was considered. The shortcomings were as follows: (i) exposure assessment was based mainly on self-reports of the work conditions and exposure and (ii) no specific data on occupational hygiene measurements from the companies or biomonitoring of the workers were available. Proper protective clothing is effective in decreasing the exposure of workers during and after applications (11). The finding that the association was enhanced among those who did not use personal protection efficiently makes the results more plausible.

It is difficult to attribute the possible risk to any specific pesticide. Simultaneous exposure to several types of pesticides was prevalent in our data. In addition, only few workers were exposed to individual pesticides or were highly exposed to different types of pesticides.

Therefore, only the findings of any exposure to the types of pesticides are presented.

Many Finnish greenhouses are family enterprises. Therefore, also a proportion of the wives was exposed to pesticides. Our findings, adjusted for male exposure, suggest that heavy female exposure, characterized by the women spraying pesticides, may be associated with reduced fertility. The finding is in accordance with that of a recent Danish study (23) in which female flower greenhouse workers handling treated cultures, spraying pesticides, and working without gloves had reduced fecundability.

The main shortcoming of our study was the low participation rate (43%). Participation was related to job seniority and the number of pregnancies in the medical records. The main comparison was made between exposed and unexposed greenhouse workers. Among them the participation was slightly higher (49%) because long-time workers and employers were overrepresented in these groups. The findings were virtually unchanged in the analysis that was restricted to more permanent workers. This observation is not suggestive of selection bias.

Separate questionnaires were sent to the men and their wives. The couples were not aware that the focus was on the first time to pregnancy after the husband's entry into greenhouse work. In the first questionnaire, we collected detailed information on up to five work periods in greenhouses. Information on time to pregnancy for all the pregnancies ending in births or spontaneous abortions was collected independently from the wives. The eligible study pregnancy was defined on the basis of medical records, work pension information, and data collected from the employers. It does not seem plausible that the couples could connect the husband's exposure status or the use of efficient protection and the time taken to conceive. Because of these methodological aspects, we believe that the potential for response bias is rather low.

Men's exposure to pesticides was associated with reduced fertility among primiparous wives, whereas among parous wives the association was towards improved fertility. It is not likely that response bias alone could cause such a big difference in the findings. It has been suggested that one should always use the subset of first-time pregnancies in a separate analysis when estimating the exposure-effect association (24). If the effect measure among primiparous women differs much from the overall measure, bias related to selection forces may well be the explanation. This may have been the case in our study as well. However, it is difficult to assess the direction of this potential bias because the first period of time to pregnancy after the husband's entry into greenhouse work was followed.

The wives who responded to the first inquiry but not to the second (data on time to pregnancy from the first inquiry) were more fertile than those responding to both inquiries. The association between pesticide exposure and fertility was, however, similar in both phases of the study. This observation does not suggest selection bias in relation to the studied association. However, this finding is an indication of the poor comparability of differently collected data on time to pregnancy (25–27).

The findings of our study provide limited support for the hypothesis that men's work in greenhouses and exposure to pesticides are associated with reduced fertility. The findings on the exposure to pyrethroids, carbamates, and organophosphates can serve as a basis for a hypothesis for future studies.

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