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PESTICIDE EXPOSURE AND BIRTHWEIGHT: AN EPIDEMIOLOGICAL STUDY IN CENTRAL POLAND

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Abstract. The aim of this study was to evaluate the influence of maternal exposure to pesticides in the 1st and 2nd trimesters of pregnancy on infant birthweight in a population of Polish farmers. The subjects were women who delivered in 25 maternity hospitals in the region of Łódź (Central Poland), including 117 women who delivered infants with low birthweight (LBW) and 377 infants with birthweight ≥2500 g delivered on randomly selected 70 days between 31 January 1998 and 30 June 2001. A questionnaire on maternal demographic and anthropometric characteristics as well as the occurrence of several occupational hazards, including pesticide use and involvement in heavy physical work on the farm in each of pregnancy trimesters, was administered by a physician 1-2 days after delivery. The pesticides used most frequently included: phenoxyacetic acid derivatives, organophosphates, ureas, triazines, synthetic pyrethroids and N-phenylamides (anilides). Infants born to women exposed to pesticides in 1st or 2nd trimester had birthweight lower by 189 g than that of infants of the non-exposed women. When adjusted for pregnancy duration, the women exposed to pesticides were found to deliver infants with birthweight lower by about 100 g ($p = 0.067$) than that of infants of the non-exposed women. After adjusting for the variables that may have impact on pregnancy duration, we noted that mothers exposed to pesticides, on average delivered half a week earlier than those non-exposed. Our results indicate that maternal exposure to pesticides may contribute to a slight reduction in the duration of pregnancy. A slower pace of fetal development, corresponding to the small-for-gestational-age effect, was observed, but the increment in the risk was of borderline significance.

Key words:
Pesticide, Birthweight, Low birthweight, Pregnancy duration

INTRODUCTION

Adverse reproductive outcomes postulated to result from exposure to pesticides include both pre- and post-conception events. The pre-conception events consist in the changes in reproductive hormone profile [1] and subfecundity [2,3,4], whereas the post-conception events include early [5] and late fetal loss [6], congenital malformations [7] and childhood malignancy [8]. Although each of these outcomes has been examined in several studies, the results have not been consistent even for the most frequently investigated outcomes such as birth defects [7] or early fetal loss [5]. Apart from problems related to exposure assessment and health outcome measurements, the influence of genetic susceptibility may be one of the reasons for the lack of consistency [9].

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No consensus has either been reached with regard to the less often examined outcomes, particularly the risk of small-for-gestational-age (SGA) birth [6,10–13] and preterm delivery (PD) [6,11,14]. It has been well recognized that in the absence of chronic maternal and fetal disease, birthweight is affected by the duration of pregnancy, infant's sex, socio-economic variables (education, marital status) and intrauterine exposure to tobacco smoke. Less known is whether some environmental factors, including maternal exposure to pesticides may contribute to SGA birth or PD. The problem is important as farmers in general, compared to non-farmers, have more favorable birth characteristics, including lower rates of SGA infants [6], which may obscure the potential risk factors inherent in farmers' jobs. The aim of the present study was to evaluate the association between maternal exposure to pesticides during pregnancy and infant birthweight in a population of Polish farmers.

MATERIALS AND METHODS

Study population

Between 31 January 1998 and 31 December 2000, 389 women who delivered on randomly selected 70 days in 25 district maternity hospitals covering rural population of the Łódź region were approached about our project. Originally, the authors intended to investigate the prevalence of established risk factors for poor pregnancy outcomes in the rural areas of the region. For these reasons a random sample of deliveries in this area was selected. The high prevalence of exposure to pesticides made us put forward a hypothesis of its potential association with low birthweight (LBW), which by definition includes infants with weight at delivery below 2500g. To further explore this association, a case-control design was applied. As the number of LBW cases registered in those hospitals was small [12], we decided to extend the enrollment of mothers of LBW infants in two maternity hospitals (Radomsko, Opoczno) for another six months. Apart from the Radomsko and Opoczno districts, where all cases delivered between 1 January 2001 and 30 June 2001 were considered, the selection of random sample of LBW cases took place between 31 January 1998 and 31 December 2000, therefore the sample was population-based. Such differences in case recruitment in two subpopulations should not influence the study results as long as an analysis stratified by region is applied. Eventually, the study population comprised mothers of 117 LBW infants and 377 infants with birthweight ≥2500 g.

Only the women who were involved in farming activities for seven days or more during pregnancy were considered in the project. The study population was rather homogeneous in terms of the socioeconomic status, age and nutrition habits. It was limited to uncomplicated pregnancies, and mothers with such diseases as diabetes, hypertension, infectious diseases and other pathologies increasing the risk of intrauterine growth retardation or preterm birth were excluded from the study. All the examined women received prenatal medical care at local maternity units and it is unlikely that major maternal or fetal pathology remained unrecognized.

Interview

A questionnaire on maternal demographic and anthropometric characteristics (weight and height, prepregnancy weight), job history, chronic diseases during pregnancy (e.g., hypertension, diabetes), smoking and reproductive history (spontaneous and elective terminations, stillbirths and live births, the number, duration, birthweight and sex of each infant) was administered by a physician 1-2 days after delivery. The questionnaire addressed the occurrence of several occupational hazards, including the use of pesticides in each of pregnancy trimesters and the involvement in heavy physical work (frequent lifting of loads >5 kg) on the farm.

Confirmation of pesticide exposure

Within 6–12 months after delivery, an interviewer with a background in pest control products visited the 49 husbands of women (51.6%) who reported pesticide use on their farms during pregnancy. The aim of such visit was to elicit information on the trade names of pesticides and the exact timing and duration of exposure. Active ingredients were identified using the database on pesticides registered

in Poland and classified by their chemical groups [15]. Exposure assessment was intended to identify both occupational (direct) and residential (indirect) exposure resulting from the use of pesticides on a given farm during the study period.

Statistical analysis

To analyze the quantitative differences (pregnancy duration and birthweight at a given pregnancy duration) between mothers exposed and non-exposed to pesticides, multiple linear regression was used. Logistic regression model was applied to evaluate the impact of pesticide exposure on the risk of LBW. All regression models were fitted using STATA software. The model included pesticide exposure as well as other variables known to affect birthweight: infant sex, maternal prepregnancy weight, height, smoking during pregnancy, calendar year of birth and involvement in fieldwork.

To evaluate the association between exposure to specific pesticides and birthweight, the expected values of infant birthweight were calculated and compared with the actual ones. As the number of women reporting the use of specific pesticides was small, only the main variable that had impact on birthweight in this project, the place of residence, was taken into account.

RESULTS

Occupational risk factors of LBW

In the univariate analysis, the women reporting pesticide use on their farms were characterized by an elevated risk of LBW (Table 1). Similar effect was observed in smokers and women engaged in heavy physical work (data not presented in tables).

In the multivariate analysis, after controlling for maternal age, marital status, prepregnancy maternal weight, parity, maternal smoking, physical work during pregnancy and place of residence, only a slight increase in the risk of LBW associated with pesticide exposure could be observed. The place of residence was included in the model, for the cases and controls were recruited from different source populations with different prevalence of pesticide exposure.

After controlling for pesticide use and engagement in physical work, the season of the year the conception took place, did not influence the infant's birthweight and thus was not included in the multivariate analysis.

Pesticide exposure

Ninety-five women (19.3%) reported pesticide exposure in 1st or 2nd trimester of pregnancy (Table 2). Most of the mothers (83.7%) who reported pesticide exposure during 1st trimester had a similar experience in the 2nd one.

As mentioned above, half of the women who after delivery reported some pesticide exposure were later visited by an interviewer in order to validate this information. The confirmation rate was 85.7% and no significant differences were found between the groups of women classified according to the timing of exposure or the LBW status. The husbands of women who did not report pesticide use in pregnancy were not approached by the interviewer for validating such reports. Most of these women worked on small farms and they used no pesticides at all.

The pesticides used most frequently included: phenoxyacetic acid derivatives, organophosphates, ureas, triazines, synthetic pyrethroids and N-phenylamides (anilides) (Table 3).

Table 1. Pesticide exposure in 1st or 2nd pregnancy trimester and the risk of LBW

	LBW(-) N = 377		LBW(+) N = 117		Crude OR 95%CI	Adjusted* OR 95%CI
	N	%	n	%		
No	333	88.3	66	56.4	Reference group	Reference group
Yes	44	11.7	51	43.6	**5.84 (3.61–9.47)**	1.29 (0.63–2.65)

* Adjusted for maternal age, marital status, prepregnancy maternal weight, parity, maternal smoking, physical work during pregnancy and place of residence.

Table 2. Validation of self-reported exposure to pesticides

Pesticide exposure	N (total)	Farm visited		Confirmation of maternal report of exposure	
		n	%	n_1	%
Trimester 1 (+)	92	49	53.3	42	85.7
Trimester 2 (+)	80	38	47.5	33	86.9
Trimesters 1 or 2 (+)	95	49	51.6	42	85.7

Women exposed to pesticides were more often engaged in heavy physical work in the field (61.0%), compared to those non-exposed (26.3%) ($p < 0.001$). This is an important finding which has confirmed the need to regard heavy physical work as a negative confounder when analysing the risk of LBW.

Pesticide exposure and birthweight

As the majority of exposed women (83.6%) experienced pesticide exposure in the 1st and 2nd trimesters, we have decided to combine these two groups. After adjusting for the variables that may have impact on birthweight, we found that the infants born to women exposed to

Table 3. Pesticides by chemical group of active ingredients or trade name of pesticide

Chemical group/trade name of pesticide	Type	Number of exposed	Rate per 100 subjects
Classification by chemical groups			
Phenoxyacetic acid derivatives	H	24	57.1
Organophosphates	I, A	14	33.3
Ureas	H	7	16.7
Triazines	H	7	16.7
Synthetic pyrethroids	I, A	6	14.3
N-phenylamides (anilides)	F	6	14.3
Triazoles	F	5	11.9
Fenazaquin	A,I	4	9.5
Inorganics (copper)	F	3	7.1
Carbamates	F,H,	3	7.1
Aryloxyphenoxypropionic acids	H	2	4.8
Amides	H,I	2	4.8
Dithiocarbamates	F	1	2.4
Unclassified pesticides			
Bensultap	I	2	4.8
Dithianon	F	2	4.8
Dodine	F	1	2.4
Chlorothalonil	F	1	2.4
Captan	H	1	2.4
Isoxaflutole	H	1	2.4

A – acaricide; F– fungicide; H – herbicide; I – insecticide.
Rate per 100 subjects was used as exposure may result from more than one pesticide.

pesticides in 1st or 2nd trimester had birthweight lower by 189g ($p<0.01$) than the infants of those non-exposed (Table 4).

To investigate the possible association between maternal exposure to pesticides and infant birthweight, a linear model was developed. After adjusting for the variables that may have influence on pregnancy duration, we noted that mothers exposed to pesticides on average delivered half a week earlier than those non-exposed ($p = 0.05$) (Table 4).

To further investigate the influence of maternal pesticide exposure on the pace of fetal development (the risk of SGA infant) a linear model was constructed in which pesticide exposure was related to birthweight, taking into account pregnancy duration and the set of variables specified above. The women exposed to pesticides delivered infants with birthweight lower by about 100g ($p = 0.067$) than that of infants of the non-exposed subjects. As adjustment was made for pregnancy duration, this outcome did not result from a shortened duration of pregnancy in the exposed group (Table 4).

The comparison between birthweight of infants born to women exposed to specific pesticides and the expected birthweight values based on respective data for the non-exposed women, did not yield any significant difference. Values lower than expected were found for: organophosphates, triazines, synthetic pyrethroids and phenoxyacetic acid derivatives (Table 5).

Similar approach was used to analyze the relationship between exposure to specific pesticides and pregnancy duration (Table 6). Mothers exposed to organophosphates and triazines had a slightly shorter pregnancy duration than those non-exposed .

Table 4. Birthweight and pesticide exposure in 1st or 2nd trimester of pregnancy

Variables	Birthweight (g)		Pregnancy duration (weeks)		Birthweight at given pregnancy duration (g)	
	Coefficient*	P	Coefficient**	P	Coefficient*	P
Pesticide exposure in 1st or 2nd trimester (ref.– non-exposed group)	-189	**<0.01**	-0.53	**0.052**	-103	0.067
Place of residence: Radomsko, Opoczno (ref. – other examined populations)	-747	**<0.001**	-1.7	**<0.001**	-475	**<0.001**
Marital status – single (ref. – married or divorced)	-80	0.540	-0.43	0.401	-12	0.907
Smoking (no. of cigarettes)	-271	**<0.001**	-0.48	0.060	-194	**<0.001**
Maternal age (years) (continuous variable)	-5,5	0.368	-0.05	**0.035**	2,5	0.604
Previous pregnancies:						
one	136	**0.048**	0.17	0.523	109	**0.044**
two	95	0.256	-0.12	0.713	114	0.083
three or more (ref. – primiparous)	163	0.097	0.02	0.964	160	**0.038**
Prepregnancy maternal weight (kg) (continuous variable)	8,7	**<0.001**	0.01	0.368	7,5	**<0.001**
Heavy physical work: frequent lifting of loads > 5 kg (ref. – lifting loads below 5 kg)	-56	0.440	0.03	0.912	-61	0.285
Pregnancy duration (continuous variable)	–	–	–	–	162	**<0.001**

All coefficients are from multiple linear regression models.
* Weight difference for categorical variables, change per unit for continuous variables.
** Difference in pregnancy duration for categorical variables, change per unit for continuous variables.

Table 5. Observed and expected birthweight of infants delivered by women exposed to specific pesticides in 1st or 2nd trimester of pregnancy

Chemical group of pesticide	Birthweight (g)				P
	Observed		Expected*	Difference	
	Mean	SD			
Phenoxyacetic acid derivatives	2711	752	2746	-35	0.822
Organophosphates	2561	669	2810	-249	0.187
Ureas	3210	643	3156	54	0.832
Triazines	2442	815	2701	-259	0.433
N-phenylamides (anilides)	3428	789	3457	-29	0.932
Synthetic pyrethroids	3303	316	3457	-154	0.286
Others	2973	641	2847	127	0.416
No exposure	3265	687	–	–	Reference

* Based on the place of residence.

Table 6. Observed and expected pregnancy duration in women exposed to specific pesticides in 1st or 2nd trimester of pregnancy

Chemical group of pesticide	Pregnancy duration (weeks)				P**
	Observed		Expected*	Difference	
	Mean	SD			
Phenoxyacetic acid derivatives	38	2.5	38	0	0.846
Organophosphates	37	2.4	38	-1	0.367
Ureas	39	1.5	39	0	0.866
Triazines	36	3.8	38	-2	0.177
N-phenylamides (anilides)	39	2.1	39	0	0.825
Synthetic pyrethroids	39	0.6	39	0	0.451
Others	39	1.5	38	1	0.037
No exposure	39	2	–	–	Reference

* Based on the place of residence.
** For difference between birthweight value for the infants of women exposed to given pesticides and non-exposed adjusted for the place of residence.

DISCUSSION

Consistency with the findings of other studies

The present study revealed that maternal pesticide exposure during 1st or 2nd trimester of pregnancy produced a small but statistically significant effect on infant birthweight. The two main factors that influence birthweight are the pace of intrauterine growth and pregnancy duration. Further analysis revealed that in our study both the explanations seem to be likely.

Only a few reports addressed the risk of preterm delivery in farmers or other populations occupationally exposed to pesticides [6,14]. Rastrepo et al. [14] reported an increased risk of prematurity for women exposed during pregnancy to pesticides in floriculture greenhouses, compared to those who delivered before they commenced working under such exposure. No attempt was made to evaluate the pesticide-specific risk of the reported pregnancy outcomes

In Norway, Kristensen [6]. found that grain farmers were at a higher risk of midpregnancy delivery (21–24 week gestation) than the non-grain farmers. The risk referred particularly to seasons with poor harvest quality. However, in

general, a lower proportion of preterm births was found among farmers' offspring as compared with respective data for non-farmers.

Two reports indicated an increased risk of SGA in relation to maternal exposure [10,11]. A case-control study in 29 hospitals in Shanghai, China, covered 75 756 infants with birthweights of ≥1000g. For women exposed to pesticides during pregnancy, the risk of having an SGA infant was approximately three times higher after adjusting for infant's sex, fetal number, birth defects, maternal chronic illness and pre-eclampsia. Since the prevalence of maternal smoking was very low in the Chinese population, this variable was not included in the analysis. Owing to the limited number of exposed cases (N = 16), no subdivisions regarding specific chemicals or exposure time were made [11].

Based on the US National Natality Survey and National Fetal Mortality Survey, the risk of SGA infant was somewhat elevated with maternal pesticide exposure at home, OR = 1.5 95% CI (1.1–2.0), and to a lesser extent at work, OR = 1.2 95% CI (0.6–2.3). An elevated risk of delivering an infant with very low birthweight was found in the group of women reporting pesticide exposure at work OR = 2.4 95% CI (1.1–5.0) [10].

Two other studies [6,12] found a decreased risk of SGA in the occupations labeled as "agriculture" or "farmer". In Scotland, an analysis of 252 147 live births documented a slightly decreased risk of SGA (≤5th gestation-specific birthweight percentile) which varied little with the mother's and father's occupation, including agriculture [12]. Similarly, the comparison of almost 200 000 births to farmers with those to non-farmers, that was conducted in Norway in the period of 1967–1989, revealed fewer SGA births among farmers when adjusted for the year of birth, maternal age and geographical region [6].

Male preconceptual exposure to pesticides was postulated as a risk factor for poor pregnancy outcome in their partners. In the population identified by the Canadian Census of Agriculture, preterm delivery was strongly related to the use of some herbicides (atrazine, 2,4-dichlorophenoxybutyric acid) in the preconception period [13]. Although pesticide exposure was assessed for the male partners, the authors did not exclude a possibility that the reported associations could have been due to maternal exposure as well. No association was found between the farm use of pesticides in the preconception period and the risk of SGA.

Reliability of pesticide exposure assessment

Our study consisted in a retrospective assessment of relationship between pesticide exposure and adverse pregnancy outcomes and, therefore, was subject to some limitations typical of this study design. However, we have undertaken several steps to obtain valid assessments. For as much as 50% of mothers reporting pesticide exposure, we managed to verify the information about exposure by inquiring the persons directly involved in pesticide application. These persons, most often their husbands, were encouraged to recall the details of exposure using leaflets issued by pesticide manufacturers and labels from empty containers. The women living on farms are rarely involved, especially during pregnancy, in the mixing of chemicals, loading and cleanup of equipment and disposal of empty containers. However, they may be present on the field during the application of pesticides, take care of the clothing worn by the applicators and be subject to re-entry exposure while entering the field after spraying. We did not attempt to reproduce in detail the field activities of the pregnant woman; however, her involvement in fieldwork during specific pregnancy period was ascertained.

Although biological monitoring seems to be the optimal method to assess individual exposure to pesticides, such an approach is possible only in prospective cohort studies. This method has not as yet been introduced to retrospective assessment but it has been strongly recommended for this kind od study [16]. However, according to a recent postulate "biological monitoring may not be suitable when the nature of the work makes it difficult to pinpoint a priori which exposures among a broad range of possible contaminants are more likely than others" [16].

The validity of retrospective assessment of pesticide exposure, in spite of some limitations, is quite reassuring. The results of the US National Cancer Institute project indicate that the data obtained via a standardized ques-

tionnaire may be reasonable indicators of occupational exposure if biomarker data are not available [17,18]. The rationale for this is that the farmer's use of pesticides is based on the specific needs related to the occurrence of pests. The farmer carefully selects the pesticide most likely to be effective, buys it, keeps the records of purchase, mixes and applies the pesticide and finally evaluates its effectiveness. All these activities tend to reinforce his memory [17].

We did not exclude the possibility of exposure misclassification bias due to the retrospective assessment. However, this usually tends to contribute to underestimating the actual risk rather than overestimating it. Thus, if we document a significant excess even in a relatively small sample, it is rather unlikely that it results from the bias in exposure evaluation.

Recall bias

As the exposure variables were obtained through an interview, the recall bias is plausible. Mothers whose infants had a lower birthweight than that expected for a given duration of pregnancy may have recalled their activities in pregnancy more thoroughly than mothers of non-LBW infants. However, as the confirmation rate of pesticide exposure was similar in women who delivered LBW and non-LBW infants, we do not think this might be the case in this particular study.

Combined exposure effects

The size of the population for whom we managed to determine the trade names of the pesticides used was inadequate to undertake an analysis of birthweight/pregnancy duration by the type of pesticide. However, in the case of organophosphates and synthetic pyrethroids there was some tendency towards lower birthweight values in the exposed women. The women exposed to the first two groups of chemicals were also found to have a slightly shorter pregnancy duration. This observation should be discussed in the light of the data from the Ontario study where paternal exposure to triazines during the preconception period was associated with an increased risk of preterm delivery [10]. In view of these results and our own findings, it seems that both paternal and maternal exposure to triazines may increase the risk of preterm delivery, though the actual mechanism is difficult to establish. Unfortunately, the design of the present study did not make it possible to differentiate the role of paternal exposure to pesticide in the preconception period and maternal exposure in 1st trimester of pregnancy. In further studies much more effort should be made to consider both the types of exposure.

One of the largest study group was that exposed to phenoxyacetic acid derivatives. No increased risk of shortened pregnancy duration and decreased birthweight was found in this group. However, the reported exposure was due to methylchlorophenoxyacetic acid and 2,4-D but not to 2,4,5-trichlorophenoxyacetic acid (*TCPA* 2,4,5-T)

Potential confounding factors

We did adjust for the well-recognized factors that affect birthweight such as maternal age, marital status, prepregnancy weight, smoking, parity and physical work in the field. After controlling for several potential confounders, we noted a significant effect of maternal exposure to pesticides during 1st or 2nd trimester of pregnancy on infant birthweight. Further analyses indicated that the observed effect might be related both to the shortening of pregnancy duration and a slower pace of fetal development corresponding to the SGA effect.

The season of the year the conception took place was strongly correlated with the use of pesticides and engagement in physical work. After allowing for these relationships, we did not find a significant influence of this variable on infant birthweight, hence it was not included in the multivariate analyses.

Due to the active recruitment of cases in two centers which worked in the area characterized by a high frequency of pesticide use, the place of residence was considered as a confounding factor and was allowed for in the analysis. Additional analyses performed after exclusion of the actively recruited cases confirmed the same course of association, i.e., a negative effect on infant birthweight, pregnancy duration and birthweight at a given pregnancy duration (data available from the authors).

CONCLUSIONS

Our results indicate that maternal exposure to pesticides may contribute to a slight reduction in birthweight, mostly due to the shortening of pregnancy duration. A lower pace of fetal development, corresponding to the SGA effect, could also be observed, but the increment in the risk was of borderline significance.

An attempt was made to evaluate the relationship between pesticide-specific exposure and birthweight. Preliminary results indicate that exposure to triazines and organophosphates may be related to a lower birthweight.

REFERENCES

1. Padungtod C, Lasley BL, Christiani DC, Ryan LM, Xu X. *Reproductive hormone profile among pesticide factory workers*. JOEM 1998; 40: 1038–47.
2. Fuortes L, Clark MK, Kirchner HL, Smith EM. *Association between female infertility and agriculture work history.* Am J Ind Med 1997; 31: 445–51.
3. Kristensen P. *Pesticides and reproduction*. Epidemiology 1999; 10: 103–5
4. Curtis KM, Savitz DA, Weinberg CR, Arbuckle TE. *The effect of pesticide exposure on time to pregnancy*. Epidemiology 1999; 10: 112–7.
5. Arbuckle TE, Lin Z, Mery LS. *An explanatory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population*. Environ Health Perspect 2001; 109: 851–7.
6. Kristensen P, Irgens LM, Andersen A, Bye AS, Sundheim L. *Gestational age, birth weight, and perinatal death among births to Norwegian farmers. 1967–1991.* Am J Epidemiol 1997; 146: 329–38.
7. Garcia AM. *Occupational exposure to pesticides and congenital malformations. A review of mechanisms, methods, and results*. Am J Ind Med 1998; 33: 232–40.
8. Kristensen P, Andersen A, Irgens LM, Bye AS, Sundheim L. *Cancer in offspring of parents engaged in agricultural activities in Norway: Incidence and risk factors in the farm environment*. Int J Cancer 1996; 65: 39–50.
9. Au WW, Sierra-Torres CH, Cajas-Salazar N, Shipp BK, Legator MS. *Cytogenetic effects from exposure to mixed pesticides and the influence from genetic susceptibility*. Environ Health Perspect 1999; 107: 501–5.
10. Savitz D, Whelan E, Kleckner RC. *Self-reported exposure to pesticides and radiation related to pregnancy outcome – results from National Natality and Fetal Mortality Surveys.* Public Health Reports 1989; 104: 473–7.
11. Zhang J, Cai W, Lee DJ. *Occupational hazards and pregnancy outcomes*. Am J Ind Med 1992; 21: 397–408.
12. San Jose S, Roman E, Beral V. *Low birthweight and preterm delivery, Scotland, 1981–84: effect of parent's occupation.* Lancet 1991; 338: 431–8.
13. Savitz D, Arbuckle T, Kaczor D, Curtis KM. *Male exposure and pregnancy outcome*. Am J Epidemiol 1997; 146:1025–36.
14. Rastrepo M, Munoz N, Day NE, Parra JE, de Romero L, Nguyen-Dinh X. *Prevalence of adverse reproductive outcomes in a population occupationally exposed to pesticides in Colombia*. Scand J Work Environ Health 1990; 16: 232–8.
15. Tordoir WF, Maroni M, He F, editors. *Health Surveillance of Pesticide Workers. A Manual for Occupational Health Professionals.* Amsterdam: Elsevier; 1994.
16. Cooper S, Burau K, Sweeney A, Robison T, Smith MA, Symanski E, et al. *Prenatal exposure to pesticides: a feasibility study among migrant and seasonal farmworkers*. Am J Ind Med 2001; 40: 578–85.
17. Blair A, Zahm SH. *Patterns of pesticide use among farmers: implications for epidemiological research.* Epidemiology 1992; 4: 55–62.
18. Hernandez-Valero M, Bondy M, Spitz MR, Zahn SH. *Evaluation of Mexican American migrant farmworker work practices and organochlorine pesticide metabolites*. Am J Ind Med 2001; 40: 554–60.