Time to pregnancy and occupational exposure to pesticides in fruit growers in The Netherlands

Johan de Cock, Karolien Westveer, Dick Heederik, Egbert te Velde, Roel van Kooij

Abstract

***Objectives*—Although pesticides are regularly used in agriculture, relatively little is known about possible adverse health effects, especially reproductive effects, due to occupational exposure. This explorative study investigates the relation between exposure of the fruit grower to pesticides and fecundability (probability of pregnancy) in a population of fruit growers.**

***Methods*—The analysis is based on self reported data and includes 91 pregnancies during 1978–1990 of 43 couples. Cox' proportional hazards model was used to analyse time to pregnancy after correction for gravidity and consultation with a physician for fertility problems.**

***Results and conclusions*—Application of pesticides solely by the owner was associated with a long time to pregnancy, resulting in a fecundability ratio of 0·46 (95% confidence interval (95% CI) 0·28–0·77). Similarly a low spraying velocity (⩽ 1·5 hectares/h) resulted in a fecundability ratio of 0·47 (95% CI 0·29–0·76) and is associated with the use of older spraying techniques and tractors without a cabin. These factors were assumed to cause high exposure, which was confirmed by exposure measurements in the field. The effect of high exposure was mainly apparent if the couple had intended to become pregnant in the period from March-November (fecundability ratio 0·42, 95% CI 0·20-0·92). This is the period in which pesticides are applied. Out of the spraying season the effect of a high exposure was absent (fecundability ratio 0·82, 95% CI 0·33–2·02). In the high exposure group 28% of the pregnancies had been preceded by consulting a physician because of fertility problems, compared with 8% in the low exposure group. These findings indicate that an adverse effect of exposure to pesticides on fecundability is likely.**

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Based on some case reports, physicians of the Academic University Hospital of Utrecht in the Netherlands suspected a link between use of pesticides and infertility among men who visited the fertility unit of the clinic. These indications were not substantiated by the scientific literature. Baird *et al* suggested the use of time to pregnancy as a simple measure in epidemiological studies to find the effects of environmental exposures on fecundability.[1] According to Zielhuis *et al* valid data on time to pregnancy can be provided by a face to face interview.[2] Time to pregnancy is the number of non-contraceptive cycles that it takes a couple to conceive, or the number of menstrual cycles expressed in months. The fecundability of a couple, the probability of conception for each menstrual cycle, is estimated by the inverse of time to pregnancy. Fecundability is dependent on many different biological processes, including gametogenesis, transport of germ cells, fertilisation, transport of the embryo, implantation, and early survival of the foetus. Toxic substances may interfere with these processes through a range of different mechanisms.[3 4] Therefore, time to pregnancy is a good measure to take when no specific hypothesis can be formulated. It can be used to study reproductive effects in men. Furthermore, small effects within the normal individual variation may be discovered, and an additional advantage is that data on time to pregnancy can be obtained by a simple questionnaire.[5] So far, mostly semen analysis has been used to examine the effect of specific agents on male fertility.[6 7] Most studies on pesticides describe toxicological effects on spermatogenesis of dibromochloropropane (DBCP)[8-11] and to a lesser degree a related compound ethylenedibromide (EDB).[12] The recognition that exposure to pesticides may be significant for workers in agriculture, and that possibly a relation exists that effects human reproduction is more recent.[13] Only a few epidemiological studies refer to reproductive effects of pesticides currently used in this industry. In a study in floriculture,[14] the fungicide captan was used as a marker of exposure in a study on the prevalence of adverse reproductive outcomes in a population exposed to pesticides. Wyrobek *et al* found that the insecticide carbaryl affected spermatogenesis of exposed production workers.[15] The evidence, however, can not be seen as conclusive, as the proportion of abnormal sperm cells was inversely related to the duration of exposure. In animal studies carbaryl as well as benomyl,[16] maneb, zineb, and thiram[17] reduced the reproductive capacity and caused histopathological changes in the gonads. These pesticides are frequently used in fruit growing. For many other pesticides, no information is available on possible reproductive effects. The lack of data about complex exposures in agriculture and possible inconsistencies between animal studies and human epidemiological data gave rise to an explorative epidemiological study. In this study the relation between time to pregnancy of the wives of fruit growers and occupational exposure to pesticides of the man is investigated. The fruit growing industry was selected, because this study could be incorporated into an ongoing exposure study.

Materials and methods

STUDY POPULATION

The study population consisted of 447 fruit growers out of around 3000 members of the Dutch National Fruit Growers' Organisation who participated in a research program on exposure to pesticides and were willing to participate in follow up studies. In the first phase a postal questionnaire was sent to all fruit growers to gather basic information about the population, the farms, tasks performed, and use of pesticides. Out of this population a selection was made of all the couples with children of 12 years of age or younger. Thus, the data concern 91 pregnancies that occurred between 1978 and 1990. This period was chosen, as a compromise between limited recall time and large number of pregnancies. Existing data suggest that a recall period up to about 10 years does not seriously affect the reliability of the time to pregnancy data.[18] Exclusion criteria were the occurrence of pregnancies despite contraceptive use, no contraceptive use preceding the intention to become pregnant, and time to pregnancy exceeding 24 months.[19] Thereby, all data on time to pregnancies are assumed to be comparable with respect to the explicit intention of all couples to become pregnant.

DATA COLLECTION

Wives of fruit growers were personally interviewed on time taken to conceive in the period of 1978–1990 by two female researchers and two female research assistants. The questionnaire was based on the questionnaire used by Baird and colleagues. A pretest of this questionnaire among eight farmer's wives, led us to delete a question about frequency of coitus, because it was experienced as inconvenient by the interviewee. Moreover, the validity of this question was expected to be low, because it is known that frequency of coitus in the past is measured with low precision and answers are subject to social expectations.[20] Time to pregnancy was asked for by a direct question, and calculated from the date of birth, the length of gestation, and the date at which contraceptive use stopped. In the analyses the direct question on time to pregnancy was used. The questions were asked backward in time, starting with the most recent event—that is, date of birth, and the most recent pregnancy. Information was obtained on possible confounding factors such as age, contraceptive method, nursing preceding the pregnancy in question, smoking habits, alcohol consumption of the husband and consultation with a physician for fertility problems. To ascertain possible exposure of the wife of the fruit grower, information was obtained about farm work and occupation. Information on farm characteristics and use of pesticides in 1989 was available from the postal questionnaire. The participating farms were sent an additional questionnaire to collect information on changes that had occurred in working conditions during the 1975–1990 period in type of fruit grown, farm size, spraying equipment used and time spent applying pesticides by the fruit grower himself. These data roughly reflect the working conditions, which indicate exposure of the male to pesticides.

From a separate field study of exposure in the same population, data were available on dermal and respiratory exposure during application of pesticides. From May-October 1990, exposure to four commonly used fungicides has been measured on 149 fruit farms from the initial study population of 447 fruit growers. Data on the most frequently used fungicide captan have been used as a marker, to study factors influencing exposure during application. Dermal exposure was measured with circular skin pads made of α-cellulose (diameter 2·5 cm), placed on the back of the neck, forehead, arm, and both wrists. Respiratory exposure of inspirable pesticide particles was measured by personal air sampling in the breathing zone[21] on a glass-fibre filter (diameter 2·5 cm), connected to a portable pump device with a flow of 1·96 l/min. The analysis of captan was performed with high performance liquid chromatography (HPLC) with a c18 reversed phase column, connected to a UV absorbence detector (wavelength 210 nm). A mixture of acetonitrile (55%) and water (45%) was used as eluent (unpublished data).

STATISTICAL ANALYSIS

All analyses were performed with statistical analysis system software (SAS). Survival analysis was used to study the relation between exposure of the fruit grower and time to pregnancy of the couple. In univariate analyses of time to pregnancy and the independent variables, Kaplan-Meier curves were calculated with Proc LIFETEST. For multivariate analysis, the Cox proportional hazards model was used.[22] In the PHREG SAS procedure,[23] the fecundability ratio is calculated as e^{β}, representing the fecundability of the exposed group relative to the referent group. To account for the occurrence of ties, because time to pregnancy is expressed in months, exact maximum likelihood estimates were calculated.

Survival curves and fecundability ratios were calculated for potential confounding factors. The strength of the relation with time to pregnancy was used as a criterion to add the variables in a multivariate proportional hazards model.[24] A physician's visit for fertility problems is considered to be a confounding factor,[1] because the more highly exposed couples might tend to visit a physician more often and consultation may influence fecundability through altered sexual behaviour or medication. This factor may also be considered to be an effect variable. Therefore, analyses both adjusted and unadjusted for this variable were carried out. The effect of single exposure variables was estimated, uncorrected and corrected for the set of potential confounding variables. Ordinal and interval variables were included in the analysis as dichotomous variables, with categories divided at the median to increase statistical power. Exposure variables of the man that had a significant relation to time to pregnancy, and had no or low mutual correlation were considered in one multivariate model.

Results

POPULATION

From the selected group of 91 couples, 59 were willing to participate and have been interviewed. After inspection of the data, 10 couples from the initial group did not meet the criteria for participation, as their children were either over 12 years of age or had been adopted. For 10 non-responding couples, the subject of fertility was the main reason not to participate. The other non-respondents mentioned motivations beyond the study subject, such as pressure of work. Together, the remaining 59 couples had 133 pregnancies during the 1978–1990 period. A reliable time to pregnancy could not be calculated in all cases. The following pregnancies have been excluded: 12 pregnancies in spite of contraceptive use at the time of conception, 28 pregnancies from women who did not use any contraceptive method, and one pregnancy that took over 24 months to conceive. The final analysis includes 91 pregnancies of 43 couples. Table 1 presents relevant characteristics of the pregnancies. In 65% of the pregnancies women conceived within three months. The most frequently used contraceptives were oral contraceptives (53%) and condoms (29%), roughly reflecting Dutch contraceptive use. In 61% of the cases the data concerned the first or second pregnancy.

Table 1 Characteristics of study population (91 pregnancies)

Characteristic	*No*	*(%)*
Time to pregnancy (months):		
1	32	35
2–3	27	30
4–6	20	22
7–12	9	10
≥13	3	3
Age of woman (y):		
20–24	19	21
25–29	47	52
30–34	20	22
>34	5	5
Contraceptive use:		
Oral contraceptive	48	53
Condom	26	29
Timing of intercourse	9	10
Intrauterine device	4	4
No use of contraceptive*	4	4
Gravidity (No of pregnancies):		
1	25	28
2	30	33
3	23	25
≥4	13	14
Recent nursing, preceding pregnancy	9	10
Visit to a physician for fertility problems†	15	16
Current smokers	42	46

* Time to pregnancy started after birth of preceding pregnancy.
† Woman's visit to a physician preceding most recent, or earlier pregnancy.

ANALYSIS

Of the potential confounding variables, gravidity, expressed as the number of pregnancies (fecundability ratio 1·24, 95% CI 1·04–1·47) and visit to a physician for fertility problems (fecundability ratio 0·36, 95% CI 0·20–0·66) showed a strong relation with time to pregnancy. We found no significant relation for the use of an intrauterine device and oral contraceptives with time to pregnancy. A high gravidity is associated with a shorter time to pregnancy, which is reflected by a fecundability ratio of 1·24. Consultation of a physician is associated with an extended time to pregnancy.

In table 2 survival analyses are presented and show a significant relation for several farm characteristics with time to pregnancy. Results presented are unadjusted, as well as adjusted for confounding variables. The use of a modern "cross current" airblast sprayer is related to a shorter time to pregnancy. A low spraying velocity, expressed as the crop area sprayed/h (≤ 1·5 hectares/h), application of pesticides carried out solely by the farm owner, a low number of spraying days/y, and a small crop area are related to a longer time to pregnancy. In a multivariate analysis with spraying velocity and application solely by the

Table 2 Survival analyses of 91 pregnancies with one exposure variable unadjusted and after adjustment for consultation and gravidity

Variable	*Fecundability ratio: (95% CI)*	*P value*
Unadjusted:		
Cross current airblast sprayer	1·73 (1·10–2·72)	0·02
Spraying velocity ≤ 1·5 hectares/h	0·49 (0·31–0·78)	< 0·01
Application solely by owner	0·64 (0·40–1·02)	0·06
Crop area ≤ 10 hectares	0·61 (0·40–0·93)	0·02
Spraying days ≤ 15 days/y	0·44 (0·24–0·83)	0·01
Adjusted for consultation and gravidity:		
Cross current airblast sprayer	1·48 (0·94–2·34)	0·09
Spraying velocity ≤ 1·5 hectares/h	0·53 (0·33–0·85)	< 0·01
Application solely by owner	0·55 (0·34–0·88)	0·01
Crop area ≤ 10 hectares	0·59 (0·38–0·90)	0·02
Spraying days ≤ 15 days/y	0·48 (0·25–0·91)	0·02

Table 3 Multivariate survival analysis of 91 pregnancies for spraying velocity and application solely by the farmer

Variable	*Fecundability ratio: (95% CI)*	*P value*
Consultation	0·39 (0·21–0·71)	< 0·01
Gravidity	1·38 (1·11–1·69)	< 0·01
Spraying velocity	0·47 (0·29–0·76)	< 0·01
Application solely by owner	0·46 (0·28–0·77)	< 0·01

Table 4 Farm characteristics of each exposure group (n = 43 farms)

Farm characteristic	*High exposure*	*Low exposure*
Spraying velocity (hectares/h)	≤1·5	>1·5
No of farms	19	24
Traditional growing system (%)	37	13
Modern equipment (%)	11	50
Knapsack sprayer (%)	37	13
Cabin on tractor (%)	32	71
Application solely by owner (%)	63	71
Mean (SD):		
Spraying velocity (hectares/h)	1·0 (0·4)	2·5 (1·6)
Crop area (hectares)	7·9 (6·9)	12·4 (4·0)
Spraying days (1975)	28 (18)	38 (26)
Spraying days (1990)	38 (26)	39 (17)

Table 5 Differences in dermal and respiratory exposure for different spraying equipment

	No cabin on tractor			*Cabin on tractor*				*Old type airblast sprayer, without a cabin*			*Modern cross current airblast sprayer with a cabin*			
	n	*AM*	*GSD*	*n*	*AM*	*GSD*	*P value*	*n*	*AM*	*GSD*	*n*	*AM*	*GSD*	*P value*
Respiratory exposure (mg/m³)	23	0·06	4·1	23	0·10	7·2	0·60	16	0·06	3·4	9	0·11	6·4	0·85
Dermal exposure, forehead + neck (mg/(m².h))	17	7·06	2·9	10	0·50	1·9	< 0·01	11	7·35	3·4	4	0·57	1·9	0·01
Dermal exposure, wrists + arm (mg/(m².h))	22	16·14	3·2	18	4·08	3·6	< 0·01	15	11·82	3·1	7	3·98	3·7	0·01

The exposure data are log normally distributed. AM = arithmetic mean; GSD = geometric standard deviation; P value: *t* test on log transformed data.

owner showed a fecundability ratio of 0·47 and 0·46 (P < 0·01) respectively, and the significance level increased compared with the univariate analyses (table 3). This suggests that both of these variables are independent determinants of exposure. No additional exposure variables were put into the model because of multicollinearity.

In table 4 the population is divided into categories of spraying velocity. A low spraying velocity represents less frequent use of the modern spraying technique, more frequent use of engine driven knapsack sprayers, less use of tractor cabins, a longer spraying time for each spraying and a small crop area. There is a striking increase in number of spraying days in the 1975–1990 period in the low compared with the high spraying velocity group where this number was stable. Because of the strong relations of spraying velocity with these variables, a low spraying velocity is interpreted as relatively intensive contact to pesticides (high exposure group) and a high spraying velocity as relatively less intensive contact (low exposure group).

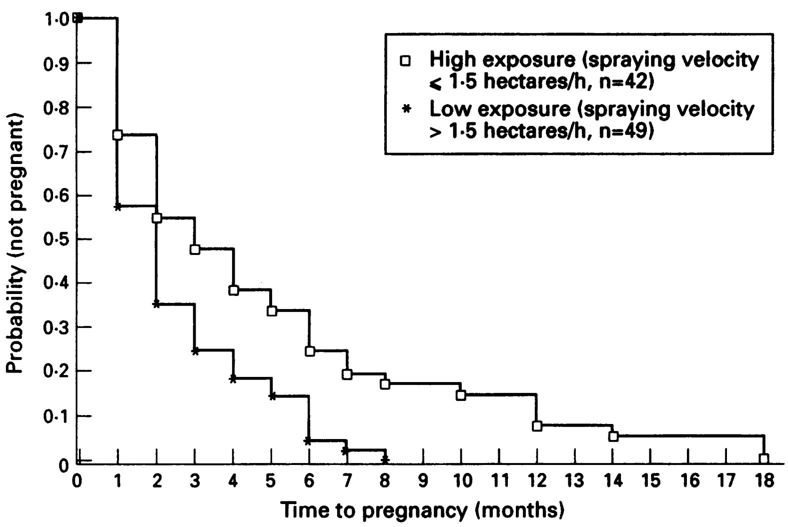

Figure 1 Kaplan-Meier curve of time to pregnancy (n = 91) by exposure category.

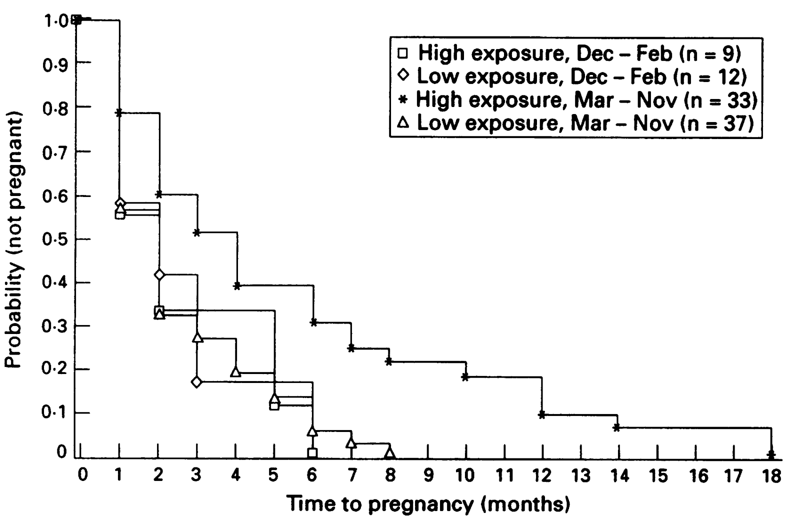

Figure 2 Kaplan-Meier curve of time to pregnancy (n = 91) for exposure category and time of year that couple intended to become pregnant.

Some of the underlying variables of spraying velocity were studied in a separate exposure study. The effect of a cabin on dermal exposure was confirmed by exposure measurements during applications of captan. In table 5, the effect of a tractor cabin and the use of an "old type" of airblast sprayer on exposure is compared with the use of a modern cross current airblast sprayer. No differences in respiratory exposure were found for cabin use and type of airblast sprayer. Significantly lower dermal exposure of the forehead and back of the neck and of the wrists and arm was found among users of modern equipment and users of a cabin. The magnitude of the difference in dermal exposure found varied from three to 14. Exposure data were log normally distributed, therefore the geometric SD is given. Large geometric SDs (table 5) are not unusual for occupational exposure measurements.[25] Figure 1 shows the crude effect of exposure on time to pregnancy. As application of pesticides is a seasonal activity, the period of the year when the couple tried to conceive was included in the analysis. The spraying season is defined as the period of March up to and including November. The population is broken down into four categories according to exposure level and season. Figure 2 shows the survival curve for each category. Highly exposed farmers, who tried to conceive during the spraying season, show a time to pregnancy twice as long as the other categories. Only highly exposed farmers who tried to conceive during the spraying season (33 pregnancies) show a significantly decreased fecundability ratio (0·42, 95% CI 0·20–0·92). Out of the spraying season the effect of a high exposure was absent (fecundability ratio 0·82, 95% CI 0·33–2·02).

Thus far, a visit to a physician for fertility problems was considered to be a confounding factor in the analysis. It could also be regarded as a possible effect of exposure, and may therefore have resulted in overcorrection in the previous analyses. In the high exposure group 28% of the pregnancies were preceded by a visit to a physician for fertility problems compared to 8% in the low exposure group. An analysis without this confounding variable resulted in a stronger association between the exposure variables and time to pregnancy. The fecundability ratio for spraying velocity decreased from 0·47 (95% CI 0·29–0·76) to 0·42 (95% CI 0·26–0·67).

All pregnancies have been assumed to be independent: however, theoretically pregnancies from the same couple are dependent—that is, women with a long time to pregnancy might have a long time to pregnancy for all subsequent pregnancies as well. Thus, a subset of the first pregnancies (n = 25) of every couple was analysed. A similar negative effect of exposure on fecundability was shown. The fecundability ratio was 0·33 (95% CI 0·12–0·93). Because the gravidity of these pregnancies was equal to one, this confounding variable was not included in this analysis.

Discussion

Crude analyses showed that the following indices of exposure were related to differences in time to pregnancy: the type of sprayer used (old or modern), spraying velocity, application solely by the farm owner, crop area, and frequency of sprayings a year. After adjustment for confounders in a multivariate analysis the strongest relation remained with the application of pesticides by the owner of the farm and spraying velocity. These two variables seemed to be independent indicators of exposure. Application of pesticides solely by the farm owner most probably leads to a longer duration of contact with pesticides each season, compared with farmers who share this task with other individuals. Spraying velocity is assumed to be a good indicator of intensity of exposure, because it probably leads to a more intensive contact with pesticides. Working conditions, such as the use of less modern equipment associated with a low spraying velocity, result in a higher exposure. A low spraying velocity mainly occurred on small farms. This category showed an increase in number of spraying days in the 1975–1990 period, without keeping step with the use of modern equipment. A higher spraying velocity, however, which may result in a lower exposure, does not necessarily imply a lower overall use of pesticides. These farms generally have a larger crop area and a higher crop density, and thus consume larger amounts of pesticides. It is, however, reasonable to assume a lower personal exposure here, due to the differences in working conditions during the application of pesticides.

It is unlikely that qualitative differences in pesticide exposure exist within this population, for instance because different pesticides are used. On all farms the main crops grown were apples and pears, and fruit growers generally rely on the annual publication by the Dutch National Fruit Growers' Organisation of recommendations on pesticide use. These detailed recommendations comprise the use of specific pesticides, dosage, and frequency of use for each crop.

The exposure variables such as application of pesticides by the farm owner and spraying velocity are directly related to the exposure of the applicator. Usually mixing, loading, and applying of pesticides is a task exclusively of the men. The women often participate in tasks involved with the crop such as bending, pruning, thinning, and harvesting, which may result in exposure as well. Also contact with contaminated clothing or contamination of the home may be a source of exposure. Thus, it cannot be ruled out that part of the effect is mediated by exposure of the wife. The seasonal effect found supports the relation between intensity of exposure to pesticides and fecundability. A seasonal effect also suggests that the decrease in fecundability is reversible.

Attempts were made to validate the qualitative indices of exposure. It could be shown that some of the underlying factors that determine spraying velocity like the use of a tractor cabin or use of an old airblast sprayer were related to a higher dermal exposure. Exposure measurements during the application of the fungicide captan showed that use of a cabin on the tractor and use of modern equipment indeed resulted in a lower dermal exposure but no difference in respiratory exposure. This supports the validity of the exposure indices used. The exposure data cannot be interpreted as quantitative measures of exposure dose, because exposure to pesticides was restricted to application of only one pesticide. It was impossible to validate the variable spraying velocity, because spraying velocity also represents other application techniques such as use of a knapsack sprayer and the frequency of spraying days each year, for which no exposure measurements were available. Furthermore, other tasks for which no exposure measurements were available, like pruning and thinning may add greatly to the total exposure dose of farm workers. It is important to note that captan was used here as a marker of exposure to pesticides in general. In a study of Restrepo and coworkers, captan was also used as a marker of exposure in a study on the prevalence of adverse reproductive outcomes in a population exposed to pesticides.[14] In their study only respiratory exposure was taken into account. A striking difference is that the exposure data in our study suggest that the dermal route may play a predominant part in determining exposure dose. On the other hand it is important to realise that to use one component as a marker of exposure for a large variety of different pesticides, which may result in mixed exposures, is beset with problems. The importance of the exposure route depends on the physical and chemical properties of a chemical. Also, respiratory exposure normally stops directly after the job has been finished, whereas dermal uptake may continue, depending on the hygienic behaviour of the worker. And, moreover, exposure of the skin will not be uniformly distributed over the body surface.[26]

ALTERNATIVE EXPLANATIONS

A differentiation in spraying velocity and related factors such as farm size, possibly runs parallel with socioeconomic status, which could be a confounding variable.[1] The chance that this could have an effect in the same order of magnitude as the effect of spraying velocity is not plausible, especially because fruit growers form a relatively homogeneous socio-economic population. Another possible explanation is a higher degree of participation of the wife in farm work resulting in exposure when in the orchard. For both exposure categories the type of work performed by the wives is the same. On the larger farms more work is to be done, but generally more workers are hired. Unfortunately, no information is available on time spent on the farm by the wives, so a definite answer cannot be given. A direct relation to pesticide exposure of the man is more plausible, although a combination of both is still possible. Finally, it is unlikely that the increased time to pregnancy of couples trying to conceive during the spraying season is due to indirect effects such as high work load, stress, or a decreased frequency of sexual intercourse, because time to pregnancy was not increased in the farmers with a low exposure.

QUALITY OF DATA

Both the exposure and effect variables are retrospective, self reported data. We assume the validity of the fecundability data to be high because the respondents were generally convinced by their own answers. A high validity of fecundability data from face to face interviews is supported by a study of Zielhuis *et al.*[2] Another supporting argument is the coherence of the expected relations between time to pregnancy and confounding factors.[27] For instance the relation between time to pregnancy and gravidity[26] and a visit to a physician for fertility problems.[1] A lower fecundability was also found for older women and for recent nursing, but because of the small numbers, these variables were not taken into account in the analyses. An important explanation for the absence of an effect of smoking and alcohol consumption is probably the absence of extremely heavy smokers and drinkers.[19] The exposure data apply to the 1989 situation, whereas pregnancies concern the 1978–1990 period. In general, information from publications for crop protection and spraying calendars shows a stable use of pesticides, but changes in working conditions have occurred during the 1975–1990 period. The number of tractor cabins has been increased and the cross current airblast sprayer was introduced in 1982. Possible misclassification of older pregnancies will have resulted in a dilution of the observed effect.

Moreover, the use of crude exposure variables can only mask the effect by non-differential misclassification.[28] Differential misclassification is not probable because data on exposure and time to pregnancy were collected independently. Both the respondent and the interviewer were uninformed about actual exposure levels.

SELECTION BIAS

Non-respondents who were not willing to participate form a potential source of bias. Underlying motivations could have been objection because of personal convictions (taboo, intimacy) or personal experiences with reproductive problems. The couples with reproductive problems (n = 10) form a systematic source of bias, dependent on the exposure resulting in either a stronger or weaker effect. Given the strong relation and the small number of non-respondents, it does not seem plausible that this bias will affect the conclusions. Another important potential source of bias may be caused inherently by the method of calculating time to pregnancy. This excludes infertility, which may cause a serious underestimation of the effects of pesticide exposure on reproduction.

CONCLUDING REMARKS

The results indicate that a negative effect of exposure to pesticides on fecundability is present. The exposure variables used, globally indicate the real personal exposure dose. It is impossible to draw conclusions about specific pesticides responsible for the effect, or about the underlying mechanism. Further research in fruit growing is concentrating on the measurements of quality and quantity of exposure to pesticides, not only during application of pesticides, but also during other tasks performed in the orchards. Probably, the role of the skin as an exposure route of pesticides is underestimated. Because of lack of knowledge concerning the uptake of chemicals through human skin, a reliable estimation of the internal dose is hardly possible. Besides, in contrast with respiratory exposure, validated methods to measure dermal exposure are not yet available. Although the threshold limit value TLV for captan of 5 mg/m^3 for the air borne concentration[29] has not been exceeded for fruit growers, one can doubt if TLV's for pesticide exposure through the respiratory route only (when available) will safeguard occupationally exposed workers in agriculture.

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