Spontaneous abortions among dental assistants, factory workers, painters, and gardening workers: a follow up study

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SUMMARY This investigation was conducted to test the hypothesis that exposure of pregnant women to chemicals increases the risk of spontaneous abortion. The chemical risk factors under study to which dental assistants, factory workers, painters, and gardening workers were exposed were nitrous oxide, inorganic mercury, organic solvents, and pesticides. The study was carried out within the Danish county of Funen. It included all dental assistants employed in private or public dentistry. A comparable reference group was made up by employees less exposed to chemicals. Further study groups included all women painters within the county, women factory workers from selected factories, and about 50% of the women gardening workers within the county. Shop assistants and packers formed their control group. Information was obtained through a postal questionnaire study in May 1980 and from hospital records. Only among factory workers and painters was the odds ratio of spontaneous abortion found to be significantly increased. Neither among these women nor among dental assistants and gardening workers, however, was the reported exposure to any single chemical during pregnancy associated with a significantly increased odds ratio of spontaneous abortion.

The widespread occupational use of chemicals, the susceptibility of the rapidly dividing germ cells and the developing fetus, the few restrictions imposed when new chemicals are introduced in industry, and our lack of knowledge emphasise the importance of examining the effect of occupational chemical exposure on human reproduction.

Organic solvents constitute a category of substances used extensively in industry, and nitrous oxide is a commonly used anaesthetic. In vitro and in vivo studies in animals indicate that these chemicals may have embryotoxic or fetotoxic effects.¹ Halogenated organic solvents are chemically related to anaesthetic gases, and epidemiological investigations suggest that an occupational environment involving anaesthetics may influence the reproductive capacity of operating room personnel.¹⁻³

A high risk of malformations of the central nervous system among children of mothers exposed to organic solvents during the first trimester of pregnancy has been found.⁴ It has been suggested

that these findings were due to information bias,⁵ and they were not confirmed when the exposure status was based on more objective but less precise occupational titles.⁶ No effect on the risk of spontaneous abortions was seen in studies among laboratory workers exposed to organic solvents.⁷⁻⁸

Dental assistants exposed to nitrous oxide during pregnancy and wives of exposed dentists were shown to have a high risk of spontaneous abortions and the risk increased with the intensity of exposure.⁹ Nevertheless, the reply rates were below 74%.

Both organic and inorganic mercury have been shown to be embryotoxic in studies on animals,¹⁻¹⁰ but only exposure of pregnant women to methylmercury is known to carry excess risk to the fetus.¹ Occupationally low exposure to inorganic mercury has, however, been shown to induce aneuploidy.¹¹ Inorganic mercury poisoning may lead to abortions.¹²

Studies in animals have shown that pesticides as a group are embryotoxic only at high doses.¹³ Heavy exposure of men to DBCP was associated with

infertility due to azospermia or oligospermia,¹⁴ and low sperm counts have been found in those less exposed to DBCP.¹⁵ A Danish study found that the risk of male or female infertility was not associated either with occupations involving pesticide application or with specific pesticide exposure at work.¹⁶ It has been suggested in a register study that women working in agriculture may be at higher risk of spontaneous abortions compared with all women,¹⁷ but the method used was imprecise.

Carcinogens must be considered a hazard to the developing embryo if they cross the placental barrier.¹

The present study investigates different female occupations and occupational chemical exposures as risk factors for spontaneous abortions. The exposures are nitrous oxide and inorganic mercury by dental assistants, organic solvents by factory workers and painters, and pesticides by gardening workers. The risk of spontaneous abortion is estimated using data from a questionnaire and hospital register.

Subjects and methods

QUESTIONNAIRE STUDY

The investigation is based on data from a historical prospective study of women representing 12 selected occupations within the Danish county of Funen (population about 430 000). The eligibility of subjects to the study and the collection of questionnaire data have been previously described in detail.⁸ Data were collected covering the women's entire reproductive life before May 1980.

Study subjects

This investigation deals with 10 of the 12 occupations. Dental assistants worked in private dental clinics or in dental schoolservices. Many of these were exposed to nitrous oxide and according to the heads of the clinics often worked in poorly ventilated clinics. Furthermore, exposure to inorganic mercury in amalgam by inhalation or skin contact was common. Their control group were employees less exposed to chemicals at work and included physiotherapists, occupational therapists, office workers, and technical assistants and designers. The study group and the controls were comparable with respect both to work postures and movements during a day. A few office workers, however, who handled parcels in post offices and physiotherapists who treated patients were probably exposed to greater physical strain than were the study group.

Factory workers were predominantly exposed to organic solvents in the rubber, plastics, machines, and tin industries. Painters were all exposed to organic

solvents and may also have been exposed to potential teratogens such as phthalic acid esters¹⁸ and potential mutagens such as epoxies¹ in waterbased paints. Most of the painting work was done indoors. Sometimes protective equipment was used.

Many gardening workers were exposed to pesticides and most work was done in greenhouses. The exposure by spraying was probably intense, but only skilled gardeners were authorised to spray and they made up only 9% of the group. Indoors the unskilled gardeners might be indirectly exposed on the day after the spraying. Their controls were shop assistants from larger supermarkets and packers from a packing warehouse for vegetables who were less exposed to chemicals at work, and who were considered to be of similar socioeconomic status to the gardeners, painters, and factory workers. Furthermore the factory workers and the reference group were comparable both for work postures which were either sitting or standing for a long time and for physical strain, since minor subgroups among all these workers undertook heavy lifting. The gardening workers and the painters, however, probably changed work postures more frequently than did the control group.

Sampling

Within the county there are 24 clinics for the dental schoolservice and 194 private dental clinics, including clinics closed down after 1973. All dental schoolservice clinics and 186 private clinics helped in the study. Five clinics refused to submit the information on the assistants who had left work (about 15 women). Sampling of the reference group of employees has been described previously.⁸ One hospital and one factory did not supply the information on employees who had left work (about 10 women) and two women refused from the start to be included in the study.

The criteria for entrance into the study of a factory were size and direct or indirect exposure of many female factory workers to organic solvents as reported by the factory inspectors. All six factories who were asked to help in the study complied. The painters were selected from every local division of the trade union. The gardening workers were members of the Odense division of a trade union that includes about 50% of the members within the county. Of 24 supermarkets who were asked to help in the study, 19, covering 91% of the employees, complied. Five supermarkets did not submit the information on shop assistants no longer employed (about 60 women). From three of the largest supermarkets the information on formerly employed shop assistants was not given until these had agreed to enter the study, and 305 of the 317 women agreed. The

packing warehouse for vegetables in Odense also participated in the study as a reference group. The information on packers who had left the job, however, was missing for about 10 women. In summary, owing to insufficient information from the participating employers, about 110 women, covering less than 2% of the subjects eligible for the study, were not included. Table 1 presents the response rates among the occupational groups.

Table 1 Response rates to postal questionnaires

Group of women	Questionnaires sent	Replies received	
	No	No	%
Dental assistants	772	728	94
Reference group employees	1571	1431	91
Factory workers	1431	1203	85
Gardening workers	965	853	88
Painters	81	76	94
Reference group workers	1034	914	88

We have previously described the methods of analysis of the questionnaire data, the calculation of the spontaneous abortion rate, and the odds ratio (OR), the risk estimate of spontaneous abortion.⁸

HOSPITAL STUDY

A description of the hospital data and the methods of analysis has been given.⁸ Respondents and non-respondents to the questionnaire were all examined for abortions and births that occurred in the county of Funen. All women except 11 dental assistants provided their civil identification number which ensured complete follow up in the hospital data.

Results

QUESTIONNAIRE STUDY

Table 2 shows the crude odds ratios of spontaneous abortion by occupation using questionnaire data only; these tend to be increased for factory workers, painters, and outdoor gardening workers. Only factory workers, however, had a statistically significant increased OR of 1.9 ($p < 0.05$). Controlling for gravidity, pregnancy order, and the woman's age at pregnancy using a logistic regression model did not change any of the ORs substantially, except the OR of 2.0 for painters, which increased to 2.9 and became borderline statistically significant.

Table 3 shows the ORs for spontaneous abortion within selected groups according to whether the women reported exposure to chemicals or not. Women who did not know whether they were exposed and those who did not reply were regarded as not exposed. Overall, 5% of women did not know whether they were exposed and 15% did not reply.

Table 2 Odds ratio of self reported spontaneous abortion among women who worked in chemically exposed occupations during pregnancy compared with women who worked in a reference occupation during pregnancy (95% confidence interval)

Occupation	Pregnancy No	Spontaneous abortions		Births No	Odds ratio	
		No	%		Crude	Controlled*
Reference group, employees	843	84	10.0	759	1.0	1.0
Dental assistants, private clinics	259	29	11.2	230	1.1 (0.7-1.8)	1.0 (0.6-1.6)
Dental assistants, dental schoolservice	93	9	9.7	84	1.0 (0.4-2.0)	0.9 (0.4-2.0)
Reference group workers	337	24	7.1	313	1.0	1.0
Factory workers	357	46	12.9	311	1.9 (1.1-3.4)	1.7 (1.0-2.9)
Painters	38	5	13.2	33	2.0 (0.6-5.8)	2.9 (1.0-8.8)
Gardening workers, indoor	102	8	7.8	94	1.1 (0.4-2.7)	0.9 (0.4-2.2)
Gardening workers, outdoor	18	2	11.1	16	1.6 (0.2-7.6)	1.3 (0.2-7.1)

*Controlled for gravidity, pregnancy order, and age by logistic regression model.

Women in most of the exposure categories had no increased risk of spontaneous abortion. None of the raised crude ORs were statistically significant. Subsequent analyses using logistic regression to control for the possible effects of gravidity,

pregnancy order, and age at pregnancy showed essentially the same results.

HOSPITAL STUDY

The crude ORs of spontaneous abortions among the

Table 3 Odds ratio of self reported spontaneous abortion among women occupationally exposed to a specific chemical during pregnancy compared with women not exposed to that chemical (95% confidence interval)

Occupation	Exposed to	Pregnancies No	Spontaneous abortions No	Odds ratio	
				Crude	Controlled*
Dental assistants, private clinics	Organic solvents:				
	Yes	57	4	0.5	0.4
	No	202	25	(0.1-1.7)	(0.1-1.2)
Dental assistants, dental schoolservice	Yes	7	0	0	0
	No	86	9	(0.0-7.1)	-
Factory workers	Yes	105	12	0.8	0.7
	No	252	34	(0.4-1.7)	(0.3-1.5)
Painters	Yes	35	5	-	-
	No	3	0	(0.1-)	-
Dental assistants, private clinics	Nitrous oxide:				
	Yes	179	19	0.8	0.9
	No	80	10	(0.3-2.1)	(0.4-2.1)
Dental assistants, dental schoolservice	Yes	76	6	0.4	0.3
	No	17	3	(0.1-2.8)	(0.0-1.8)
Dental assistants, private clinics	Inorganic mercury:				
	Yes	218	21	0.4	0.5
	No	41	8	(0.2-1.3)	(0.2-1.4)
Dental assistants, dental schoolservice	Yes	68	8	3.2	2.6
	No	25	1	(0.4-147.8)	(0.2-31.2)
Gardening workers indoor	Pesticides:				
	Yes	64	6	1.9	2.0
	No	38	2	(0.3-19.7)	(0.3-11.8)
Gardening workers, outdoor	Yes	8	0	0	0
	No	10	2	(0.0-6.6)	-
Dental assistants, private clinics	Colourants, aromatic nitrocompounds, or vinylchloride:				
	Yes	14	1	0.6	
	No	245	28	(0.0-4.3)	
Dental assistants, dental schoolservice	Yes	10	2	2.7	
	No	83	7	(0.2-17.8)	
Factory workers	Yes	13	1	0.6	
	No	344	45	(0.0-3.9)	
Painters	Yes	2	0	0	
	No	36	5	(0.0-37.9)	
Factory workers	Corrosive agents:				
	Yes	7	1	1.1	
	No	350	45	(0.0-9.6)	
Factory workers	Other potential mutagens:				
	Yes	3	1	3.4	
	No	354	45	(0.1-66.9)	
Dental assistants, private clinics	Acrylamide				
	Yes	3	1	4.1	
	No	256	28	(0.1-79.9)	

*Controlled for gravidity, pregnancy order, and age by logistic regression model.

respondents to the questionnaire tend to be increased only for factory workers but this increase is not statistically significant ($p>0.05$) (table 4). The table shows a trend toward higher rates of spontaneous abortions among the non-respondents in the questionnaire study in comparison with the respondents, except among painters and gardening workers where the opposite is found. None of the differences, however, were significant ($p>0.05$). For respondents and non-respondents together the ORs are essentially unchanged. But when the ORs are adjusted for age at pregnancy the OR for factory workers increases from 1.3 to 1.4 which is just statistically significant ($p<0.05$).

The seeking of care at spontaneous abortion is estimated by ORs of self reported versus hospital

abortions (table 5). All groups have raised ORs except dental assistants and painters.

The crude ORs of self reported spontaneous abortions analysed by the woman's occupational title at inclusion in the study is for dental assistants 1.0 (0.8-1.2) and for gardening workers 1.1 (0.8-1.6) and are similar to the crude ORs in table 2. The corresponding ORs for factory workers 1.3 (1.0-1.8) and for painters 0.7 (0.4-1.4) are lower than the ORs in table 2. Control for age at pregnancy left ORs unchanged.

Discussion.

This is one of the first studies of the risk of spontaneous abortion among women exposed to

Table 4 Odds ratio of hospital registered spontaneous abortion in the exposed occupations compared with the reference group among respondents and non-respondents (95% confidence interval)

Occupation	Pregnancies No	Spontaneous abortions		Odds ratio	
		No	%	Crude	Controlled*
<i>Respondents:</i>					
Reference group employees	921	95	10.3	1.0	1.0
Dental assistants	429	49	11.4	1.1 (0.7-1.7)	1.0 (0.7-1.5)
Reference group workers	445	45	10.1	1.0	1.0
Factory workers	817	105	12.9	1.3 (0.9-1.9)	1.3 (0.9-1.9)
Painters	48	5	10.4	1.0 (0.4-3.3)	1.1 (0.4-2.9)
Gardening workers	518	59	11.4	1.1 (0.7-1.9)	1.2 (0.8-1.8)
<i>Non respondents:</i>					
Reference group employees	67	11	16.4		
Dental assistants	20	3	15.0		
Reference group workers	44	6	13.6		
Factory workers	129	23	17.8		
Painters	6	0	0		
Gardening workers	56	4	7.1		
<i>Total:</i>					
Reference group employees	988	106	10.7	1.0	1.0
Dental assistants	449	52	11.6	1.1 (0.7-1.7)	1.2 (0.8-1.7)
Reference group workers	489	51	10.4	1.0	1.0
Factory workers	946	128	13.5	1.3 (0.9-1.9)	1.4 (1.0-1.9)
Painters	54	5	9.3	0.9 (0.3-2.3)	1.4 (0.4-2.5)
Gardening workers	574	63	11.0	1.1 (0.6-1.9)	1.1 (0.7-1.6)

*Controlled for age.

painting work, gardening work, inorganic mercury in dentistry, and organic solvents in factories.

The data do not indicate a general increased risk of spontaneous abortions among dental assistants or gardening workers. In none of the categories of dental clinics or gardening work are women at an enhanced risk of spontaneous abortion. The negative findings are probably not due to raised risk among controls, since their rates of hospital abortions 10.7% and 10.4% are below the rate of 12% in the Danish population.¹⁸ The risk of spontaneous abortion among factory workers was, on the other hand, significantly raised. In addition to the chemical exposure, however, these women are exposed to noise at work or two shift work. Noise was found embryotoxic in animal studies¹⁸⁻¹⁹ and was associated with infertility in women.¹⁸ Shiftwork has been shown to increase the risk of spontaneous abortions.⁷ The OR was statistically significantly increased among painters, though the sample size was small (table 2). Nevertheless, there is probably information bias among painters and the results were not confirmed by the hospital data and the second set of self reported data (tables 4 and 5).

The information on chemical exposure is not precise, and the intensity and time of exposure in the pregnancy is unknown. The exposure specific ORs below 1 indicate, however, that the exposures probably do not increase the risk of spontaneous abortion, or that only minor subgroups might run a high risk. The negative findings by exposure to organic solvents are similar to those in two studies among laboratory employees.^{7,8} The exposure specific increased ORs are inexactly estimated owing to the small number of observations. In conclusion, therefore, it cannot be ruled out that some occupational processes involving extensive exposure of women may be dangerous to the embryo.

Bias related to non-response

The statistically insignificant selection of non-respondents was probably due to their small number. The selection among painters, gardening workers, and their controls tend to exaggerate the ORs among the respondents. Correction of the bias hardly reduced the ORs, probably because the non-respondents were few. The higher spontaneous abortions rate among non-respondent factory

Table 5 Odds ratio of self reported spontaneous abortions compared with hospital registered spontaneous abortions among respondents

Occupations	Pregnancies No	Spontaneous abortions		Odds ratio Crude
		No	%	
<i>Self reported:</i>				
Reference group employees	1329	167	12.6	1.3 (1.0-1.7)
Dental assistants	569	69	12.1	1.1 (0.6-1.9)
Reference group workers	621	78	12.6	1.3 (0.8-2.0)
Factory workers	1204	192	15.9	1.3 (1.0-1.7)
Painters	65	6	9.2	0.9 (0.6-1.4)
Gardening workers	741	103	13.9	1.3 (0.9-1.8)
<i>Hospital registered:</i>				
Reference group employees	921	95	10.3	
Dental assistants	429	49	11.4	
Reference group workers	445	45	10.1	
Factory workers	817	105	12.9	
Painters	48	5	10.4	
Gardening workers	518	59	11.4	

The fewer hospital registered pregnancies compared with self reported pregnancies is due to two factors: only pregnancies registered at the hospitals within the county of Funen are included and the register period is one year shorter, 1973 to mid-1980, than the period of self reported pregnancies, 1972 to mid-1980.

workers than among respondents was unexpected and may reflect that they do not connect the risk of spontaneous abortion with the exposures at work. The uniform selection among the non-respondent factory workers and control imply non-bias.

Bias of questionnaire information or of hospital data

The significantly increased OR of self reported versus hospital spontaneous abortions among controls but not among dental assistants, indicates negative information bias. Similar findings were seen in a study of laboratory workers⁸ and in both investigations a medical insight in the study groups may lead to their seeking more frequent care, especially for early abortions, than controls. This would bias the hospital data towards too high ORs of spontaneous abortions. The corresponding ORs are 1.3 within all other occupations (except in painters, whose numbers were few) which do not suggest bias either of self reported or of hospital data.

Discrepancies between different self reported data

The higher ORs in table 2 of factory workers and painters compared with the ORs analysed by the woman's occupational title could reflect that relatively many index women were not working in the risk occupation while pregnant. ORs in the latter analysis and ORs assessed by hospital data may then be underestimated. The findings indicate that occupational rather than social factors contribute to the increased ORs in the two study groups.

Bias related to induced abortions

The rate of induced abortion estimated by hospital data among respondent dental assistants is 10.1% (48 of 477 pregnancies) and similar to controls' 9.5% (97/1018). The rates among factory workers 18.9% (191/1008) and painters 15.8% (9/57) are slightly raised compared with controls' 13.7% (72/527), signifying that the ORs assessed by hospital data are a little overestimated. Among gardening workers the rate 12.6% (75/593) is lower than among controls, and therefore OR is slightly underestimated.

Induced abortions were sought in the hospital register only when the respondents reported at least one pregnancy after 1972, but they were sought among all non-respondents. Therefore the induced abortions were not included in the analysis of non-response bias.

Whether the association found between factory

work, especially painting work, and spontaneous abortion is of an aetiological nature ought to be further examined.

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