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Spontaneous abortions among rubber workers and congenital malformations in their offspring

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Iiro Kilpikari, MD,² Harri Vainio, MD¹

LINDBOHM M-L, HEMMINKI K, KYRÖNEN P, KILPIKARI I, VAINIO H. Spontaneous abortions among rubber workers and congenital malformations in their offspring. *Scand j work environ health* 9 (1983): suppl 2, 85-90. Spontaneous abortions of hospitalized women and congenital malformations were analyzed among rubber workers to investigate the possibility of an association between reproductive problems and chemical exposures in the rubber industry. Information on workers was obtained from the membership register of the Union of Rubber and Leather Workers and from the personnel register of a rubber factory. The frequencies of spontaneous abortions did not appreciably differ when the pregnancies occurred during Union membership or during employment in the factory as compared with the pregnancies occurring before or after that time. A case-referent study concerning the association between different exposures and spontaneous abortions showed that the odds ratio for factory workers exposed to rubber chemicals was increased in the footwear department. A corresponding risk was not observed in the tire department. The contradictory observations may be explained by concomitant exposure to solvents in the footwear department or by other nonoccupational factors. The possible association between congenital malformations and exposures in the rubber and leather industries was studied by the case-referent technique. No significant increase in the risk for malformations was observed in any branch of employment. However, the numbers of malformations were rather small.

Key terms: register data, reproductive hazards, rubber chemicals, tire and footwear manufacturing.

Postzygotic exposure to genotoxic or cytotoxic chemicals may induce cell death or dysfunction in the developing embryo; this phenomenon may lead to spontaneous abortion or malformations in the offspring. Prezygotic exposure to mutagenic chemicals may damage germ cells and produce similar end effects (6). Reproductive problems associated with chemical exposure may also appear as infertility, low birth weight, or infant mortality. At present, monitoring industrial populations for spontaneous abortions has been recommended as one of the most promising surveillance systems for

reproductive impairment and mutagenesis (3).

The aim of this investigation was to analyze spontaneous abortions of hospitalized women and congenital malformations among rubber workers. The information on pregnancy outcome was obtained from the hospital discharge register and from the Finnish Register of Congenital Malformations, respectively. Rubber workers were identified from two sources: (i) the membership files of the Union of Rubber and Leather Workers and (ii) records of the personnel of a rubber factory.

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Material and methods

The Finnish National Board of Health maintains a computerized hospital discharge register that includes all patients discharged from hospitals. We collected

information from the register on patients treated for spontaneous abortions [International Classification of Diseases, eighth revision (ICD-8) codes 643 and 645; women with diagnosis 645 treated for induced or spontaneous abortion in the four preceding months were removed], induced abortions (ICD-8 codes 640–642), and deliveries (ICD-8 codes 650–662) from 1973 to 1977. Information on malformations was obtained from the Finnish Register of Congenital Malformations. The reproductive data were linked by the personal identification code to the membership register of the Union of Rubber and Leather Workers from the year 1980 and to the data on the members who resigned between 1975 and 1980, the latter having been collected from a file of member cards. The Union had about 10,000 female members, and the unionization of labor in the rubber and leather industry was high, estimated at 95 % by the Union officials. For all members we obtained information on the chapter to which the member belonged, the branch of employment of the chapter, the date when the member joined the Union, and, for members who had resigned, the date of resignation.

The women were considered exposed if they joined the Union no later than 2.5 months after conception or if they did not resign before the sixth week of pregnancy. Those members who did not conform

to these criteria formed a reference group.

For more specific information on exposure the data of the hospital discharge register in 1973–1976 were linked to the personnel register of a rubber factory. This plant had about 450 women working in the tire-manufacturing department and 1,000 women in the footwear-manufacturing department. Information on occupation was collected by the industrial health staff. Only those women who had worked in the factory during the first or second month of pregnancy were included as exposed workers. The reference group was formed from those rubber workers who had worked at the factory but not at the same stage of pregnancy.

To investigate the effect of different exposures at the factory, a case-referent study was performed. Two random referents who had given birth to a child were selected for every case of spontaneous abortion from among the workers in both departments.

The number of spontaneous abortions was related to the number of pregnancies (births + induced abortions + spontaneous abortions, ie, the rate of spontaneous abortions) and to the number of births (ie, the ratio of spontaneous abortions). Two different proportions for spontaneous abortions were calculated because of the large number of induced abortions in Finland. The rate is likely to underestimate the true frequency, and the ratio is likely to over-

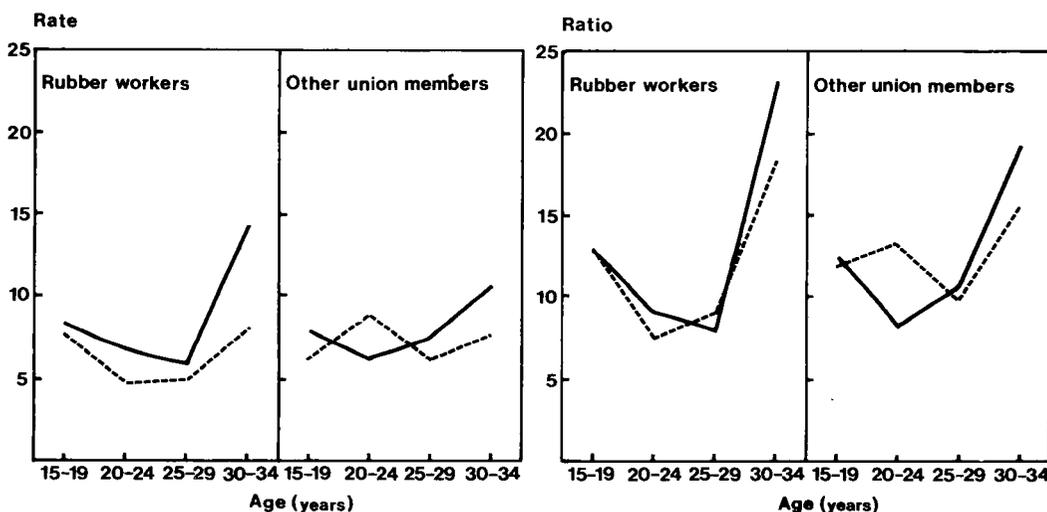


Fig 1. Rate and ratio of spontaneous abortions during membership (—) and before or after membership (---) among the members of the Union of Rubber and Leather Workers in 1973–1977.

estimate it. Statistical significance was determined by the chi-square test or by the Fisher's "exact" test.

A case-referent study was also performed to determine the occurrence of congenital malformations in children of the members of the Union. Two referent mothers with normal births were chosen from the hospital register for each case mother. The date of the delivery (+ 1.5 years) and the chapter to which the member belonged were matched. For one case mother only one referent was available. The estimates of relative risks (odds ratios) and their confidence limits were calculated according to the method of conditional maximum likelihood (2).

The reliability and accuracy of the hospital discharge register and the Finnish Register of Congenital Malformations has been described elsewhere (4, 9).

Results

During 1973–1977, 41 spontaneous abortions had occurred among rubber workers who had been hospitalized. The rate and ratio among the workers in the age groups 15 to 34 years were 7.4 and 10.3, respectively. Both frequencies were as high as the corresponding frequencies for all other members of the same union.

The comparison between rubber workers and other members of the same union may be biased by regional differences in the availability and use of hospital services or in the treatment of patients. Therefore we compared the frequencies of spontaneous abortions taking place during union membership with those occurring before or after membership. The rate of spontaneous abortions was systematically, but rather slightly, higher in all age groups during union membership when compared with the rate before or after membership (fig 1). The ratio was higher for all but one age group (20–24 years). Among other union members the rate and ratio of spontaneous abortions were higher during membership than before or after membership in all age groups except the 20- to 24-year one.

Further studies were carried out with the employees of a large Finnish rubber factory producing tires and rubber footwear. The frequencies of spontaneous

Table 1. Rate and ratio of spontaneous abortions among the workers of a rubber factory (women aged 15 to 34 years) in 1973–1976.

Group	Spontaneous abortions		
	Number	Rate	Ratio
Rubber workers employed during pregnancy	20	6.8	9.3
Tire department	8	6.6	9.8
Footwear department	12	6.9	9.1
Rubber workers not employed during pregnancy	19	7.8	12.8

abortions were slightly lower for the rubber workers employed during pregnancy than for those not employed during pregnancy (table 1). The women in the tire department had an equally high rate and ratio of spontaneous abortions as the women in the footwear department.

To investigate the possibility of an association between spontaneous abortions and different occupational exposures during the first two months of pregnancy, a case-referent study was performed among the factory workers. The cases and the referents were the most commonly exposed to rubber chemicals through the skin as they were handling uncured rubber. Other exposures included solvents and rubber fumes originating from hot rubber during calendaring and curing. The odds ratio for women exposed to rubber chemicals in the footwear department was significantly increased when compared with that of nonexposed women of the same department (table 2). The odds ratio was increased among both women under and over 25 years of age. The subject series included only one woman with two spontaneous abortions during 1973–1977. No increase could be observed among the women exposed to rubber chemicals in the tire department or among those exposed to other chemicals (solvents or rubber fumes) in the tire and the footwear department.

The possibility of an association between congenital malformations and occupational exposures in the rubber and leather industries was also studied among the members of the same union with a case-referent design. During 1973–1977, 48 infants with one or more malformations

Table 2. Odds ratios^a of spontaneous abortion for exposure to rubber chemicals and other chemicals (solvents and rubber fumes) among the workers of a rubber factory in 1973–1976.

Department	Number of pregnancies	Number of exposed cases	Odds ratio	Significance ^b
Tire				
Rubber chemical exposure	21	5	0.7	NS
Other chemical exposure	10	4	2.7	NS
Footwear				
Rubber chemical exposure	33	11	10.3	p < 0.01
Other chemical exposure	29	2	1.3	NS

^a Exposed vs nonexposed.

^b Fisher's "exact" test, NS = not significant.

Table 3. Relative risks for malformation in children of the members of the Union of Rubber and Leather Workers in 1973–1977.

Branch of employment	Number of triplets	Number of exposed mothers ^a		Relative risk	95% confidence limits
		Cases	Referents		
Rubber industry	7	3	10	0.4	0.1–2.1
Shoe industry	15	10	19	1.1	0.3–4.1
Leather and leather products industry	12	7	15	0.9	0.3–3.0
Sections with mixed industry	13	7	12	1.5	0.3–7.5

^a Exposed = member of the Union during the first three months of pregnancy.

Table 4. Malformation diagnoses of children of the rubber workers in the Union of Rubber and Leather Workers according to membership during pregnancy.

ICD-8 code ^a	Type of malformation
<i>Member during pregnancy</i>	
746 + 759.30	Congenital anomaly of the heart and Down's syndrome
749	Cleft palate and lip
755.50	Manus vara
<i>Nonmember during pregnancy</i>	
740.99	Anencephalus
748.60 + 752.29 + 756.80	Pulmonary hypoplasia, hypospadias and other malformations of muscle, tendon and fascia
752.40 + 755.61	Hydrocele testis and preluxation of hip
755.00	Polydactyly
755.61	Preluxation of hip

^a International Classification of Diseases, eighth revision.

were born among the members of the union. Twenty-nine of the case mothers had belonged to the union during the first three months of pregnancy. The average age at delivery was rather similar for the mothers of the malformed children (25.6 years) and the mothers of the matched referents (24.1 years). The relative risks

did not differ significantly from unity for any branch of employment (table 3). The rubber workers' relative risk for having a malformed child was 0.4, with 95 % confidence limits of 0.1 to 2.1. Table 4 gives the distribution of the recorded malformation diagnoses of the children of the rubber workers. The types of malformations in three children of women who had been union members during pregnancy were Down's syndrome with congenital anomaly of the heart, cleft lip and palate, and manus vara. The defects noted were mainly major malformations among the cases and the referents.

Discussion

So far two studies have been performed on reproductive hazards among rubber workers in addition to ours. In Sweden Axelson et al confirmed, on the basis of a cluster of reproductive problems, an increase in complications of pregnancy (miscarriages, threatened abortions and malformations) among exposed tire builders (1). The result persisted after gravidity and smoking were controlled for. In our study the rate

of spontaneous abortions was not elevated among the factory workers in the tire department. We had, however, no information on threatened miscarriages. On the other hand, our results were similar to those of a study concerning the workers of another Swedish rubber factory, where no difference was found in the observed and expected numbers of miscarriages, perinatal deaths, or malformations (7).

No information was available in this study on the earlier reproductive history of the women or on smoking and use of alcohol or drugs during pregnancy. The use of rubber workers who were non-members or not employed during their pregnancy as a reference group probably reduced the effect of these confounding factors. On the other hand we had no information on whether the women in the reference group were homemakers or worked elsewhere during their pregnancy. The reference group was "non-exposed" only in reference to rubber work.

The more specific investigation of the possible effects of different exposures in the rubber factory indicated that the exposure to rubber chemicals in the footwear department was associated with an increase in spontaneous abortions. As the result was not confirmed in the tire department, it might be explained by other factors in the work environment. Yet, according to information obtained from the health staff of the factory, exposure to rubber chemicals is likely to be aggravated by concomitant exposure to solvents in the footwear department, an occurrence which may explain the finding. In addition differences in reproductive history or life-style factors may have biased the result. However there is no reason to believe that these factors and exposure would correlate, nor is there evidence that they were strong confounders.

Although no elevated frequencies of spontaneous abortions were observed, we have earlier shown that, among rubber workers, short periods of employment associate with significantly higher frequencies of spontaneous abortions than longer periods of employment (5). This finding indicates some selection among rubber workers, as is caused by the "healthy worker effect" in occupational mortality studies. On the basis of our data

we were unable to conclude whether the reason for this phenomenon was occupational or nonoccupational.

The present study also included an analysis of congenital malformations in children of the members of the Union of Rubber and Leather Workers. No significant increase in the risk for malformations was observed in any branch of employment. The numbers of malformations were small, and thus only very high risks could be excluded. In addition the register of malformations is incomplete, as it has been estimated that about 30 to 40 % of the cases are missing (9).

The results of this study refer to spontaneous abortions recorded in a hospital register, and thus they cannot be generalized to concern abortions occurring in the very first weeks of pregnancy. The number of spontaneous abortions with chromosome anomalies was probably larger among the pregnancies missed as compared with those detected, as the number of chromosome anomalies decreases as pregnancy proceeds (8).

The results of this study indicate a need for further studies. The contradictory observations among workers exposed to rubber chemicals in the footwear and tire department suggest a role for solvents in the etiology of spontaneous abortions. The effect may depend on solvents as such or on an increased absorption of other chemicals mediated by solvent exposure. Such possibilities need to be investigated in detail.

Acknowledgments

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