

## Pregnancy outcome among women in a Swedish rubber plant

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AXELSSON O, EDLING C, ANDERSSON L. Pregnancy outcome among women in a Swedish rubber plant. *Scand j work environ health* 9 (1983): suppl. 2, 79-83. Suspicions of reproductive disturbances among women in a tirebuilding department was the reason for this study, encompassing 42 women, 30 of whom provided a total of 84 pregnancies out of which 21 were exposed to the tirebuilding process. Nine of the 21 exposed pregnancies had an unfavorable outcome (threatening abortion, spontaneous abortion or malformation) versus only seven of the remaining 63 nonexposed pregnancies, a difference which remained significant also when various risk indicators like age, smoking, pregnancy order, and calendar year were taken into account. In contrast to earlier observations, there was no difference in thioether excretion in the urine (as potentially indicative of the skin absorption of rubber chemicals) between women working in the tirebuilding department and a reference group. It remains unclear however whether the observed cluster was causally related to occupational exposures or not, but, together with other observations, this report may contribute to the elucidation of possible reproductive disturbances in the rubber industry.

**Key terms:** abortion, epidemiologic study, malformation, rubber industry, thioethers, women workers.

The concerns about reproductive health hazards from industrial exposures have increased over the past few years, making both workers and managements rather alert about such effects in their own proximity. Rumors and anxiety, eg, with regard to spontaneous abortions, are consequently quite commonplace and usually require some sort of evaluation of the immediate circumstances at the particular plant involved. Such evaluations tend to be questionable from the viewpoint of epidemiologic research, however, since difficulties arise in the interpretation of causality if a cluster is finally identified among workers with a particular exposure, ie, the cluster might be a random phenomenon, which is confirmed in the study that is initiated. On the other hand causal mechanisms might very well have been involved also, and the only choice, therefore, seems to be to undertake an evaluation

even if some rumors or preliminary observations are at hand and disturb the possibility of finally obtaining a more conclusive view as to causality. However, if a cluster is verified, it might be reported for consideration in view of other epidemiologic and toxicologic experience and might also be taken as a clue for further studies, either in similar industrial settings or for the prospective follow-up of the workers in the same plant.

The present study is rather much an example of the situation alluded to since it was initiated by some ill-defined rumors about "too many abortions" among a few women in the tirebuilding department of a big rubber plant in Sweden. The work conditions in this department can be characterized as rather automated, two-shift work with a permanent night shift. The tirebuilding process required a standing position, and the handling of the uncured rubber gave rise to skin contact with the somewhat sticky, uncured rubber material, a situation suggesting a potential, percutaneous route of exposure to various rubber chemicals. The hands of the workers remained quite clean however,

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but nevertheless absorption might have taken place through the skin. No noticeable levels of air pollution were present in this department.

## Subjects and methods

Only the women working in the tirebuilding department during the spring of 1981 were available for the study. Since some of their pregnancies had occurred during employment in this department and others during periods of work in other departments of the rubber factory, during work elsewhere, or at home as a housewife, it was possible to create a contrast between exposed and nonexposed pregnancies occurring between 1958 and 1980. Thus the pregnancies in the respective groups could be compared regarding outcome – spontaneous abortions, threatening abortions, and malformations being grouped together as abnormal outcomes, whereas extrauterine pregnancies and legal abortions in this situation were subsumed into the category of normal pregnancy outcome. Information about pregnancies was obtained through standardized interviews undertaken by the industrial physician, an experienced gynecologist. (It might be added that, in Sweden, the industrial physician has a rather neutral position between the employer and the employees.) The interview also covered smoking habits, alcohol consumption, and the use of drugs as being potential determinants of the pregnancy outcome [cf Harlap & Shiono (5), Himmelberger et al (6), Kline et al (8)]. The information about exposure status during pregnancy was obtained in this way. For two of the pregnancies there was some hesitation as to the exposure conditions, and therefore both were considered nonexposed.

A recent Finnish study has revealed increased concentrations of thioethers among women in a similar work situation, seemingly due to skin absorption of rubber chemicals (7). Therefore urinary samples were taken at the end of the week, and analyses were made for thioethers according to the method of van Doorn et al (3). Samples were also obtained from another department, where various rubber products were handled but no skin contact with uncured rubber occurred.

In the statistical analyses, stratification

was applied in which smoking and pregnancy order were primarily supposed to be rather strong determinants of pregnancy outcome. To some extent this stratification was also expected to take care of associated confounding, say, from the use of alcohol and age, respectively. Also the Miettinen confounder score technique (12) was applied however, the scoring being based on a linear multiple regression function [cf Anderson et al (1)]. Furthermore the Mantel-Haenszel procedures were utilized (9), and the confidence intervals were calculated by the test-based approximative method (11). The standardized rate ratios were obtained according to the principles delineated by Miettinen (10).

## Results

Forty-two women in the department were interviewed and 30 of them had been pregnant. There had been 84 pregnancies, 21 of which (among 13 women) had been exposed and the remaining 63 of which were nonexposed. Out of all the pregnancies 16 were abnormal according to the criteria applied, nine of them having been exposed

**Table 1.** Distribution of exposure and outcome of pregnancy among women in the tirebuilding department of a rubber plant.

| Type of outcome             | Exposed during pregnancy | Non-exposed during pregnancy |
|-----------------------------|--------------------------|------------------------------|
| Threatening abortions       | 4                        | 2                            |
| Abortions                   | 4                        | 2                            |
| Malformations               | 1                        | 3                            |
| Total abnormal outcomes     | 9                        | 7                            |
| Total number of pregnancies | 21                       | 63                           |

**Table 2.** Exposure to smoking and the distribution of abnormal pregnancy outcomes of women in the tirebuilding department of a rubber plant.

|                   | Exposed during pregnancy | Non-exposed during pregnancy |
|-------------------|--------------------------|------------------------------|
| Smokers           |                          |                              |
| Abnormal outcomes | 4                        | 4                            |
| Normal outcomes   | 0                        | 32                           |
| Nonsmokers        |                          |                              |
| Abnormal outcomes | 5                        | 3                            |
| Normal outcomes   | 12                       | 24                           |
| Total             | 21                       | 63                           |

and seven nonexposed (table 1). Eight of the sixteen abnormal pregnancies occurred to smokers, but there was no report of any noticeable use of alcohol or drugs (table 2).

Table 3 shows the material by stratification on order of pregnancy and smoking. The exposed pregnancies ended up with an abnormal outcome more than four times as often as the nonexposed ones. When other determinants of an unfavorable outcome are accounted for by stratification on the confounder score, built up on calendar year, age at delivery, pregnancy order, and smoking, the rate ratio is

**Table 3.** Pregnancy outcome among tire builders; exposure refers to employment in tire building during pregnancy. Cases are threatening abortions, abortions, and malformations.

| Pregnancy order                      | Non-exposed during pregnancy | Exposed during pregnancy |
|--------------------------------------|------------------------------|--------------------------|
| First                                |                              |                          |
| Smokers                              |                              |                          |
| Cases                                | 1                            | 2                        |
| Normals                              | 11                           | 0                        |
| Total                                | 12                           | 2                        |
| Nonsmokers                           |                              |                          |
| Cases                                | 2                            | 0                        |
| Normals                              | 11                           | 3                        |
| Total                                | 13                           | 3                        |
| Second                               |                              |                          |
| Smokers                              |                              |                          |
| Cases                                | 2                            | 0                        |
| Normals                              | 6                            | 0                        |
| Total                                | 8                            | 0                        |
| Nonsmokers                           |                              |                          |
| Cases                                | 0                            | 2                        |
| Normals                              | 8                            | 4                        |
| Total                                | 8                            | 6                        |
| Third                                |                              |                          |
| Smokers                              |                              |                          |
| Cases                                | 1                            | 2                        |
| Normals                              | 15                           | 0                        |
| Total                                | 16                           | 2                        |
| Nonsmokers                           |                              |                          |
| Cases                                | 1                            | 3                        |
| Normals                              | 5                            | 5                        |
| Total                                | 6                            | 8                        |
| Total                                |                              |                          |
| Smokers                              |                              |                          |
| Cases                                | 4                            | 4                        |
| Normals                              | 32                           | 0                        |
| Total                                | 36                           | 4                        |
| Nonsmokers                           |                              |                          |
| Cases                                | 3                            | 5                        |
| Normals                              | 24                           | 12                       |
| Total                                | 27                           | 17                       |
| Standardized rate ratio <sup>a</sup> | 1.0                          | 4.3                      |
| Mantel-Haenszel $\chi^2$ (1) = 10.97 |                              |                          |
| Mantel-Haenszel rate ratio           |                              |                          |
| Point estimate                       | 1.0                          | 4.7                      |
| 95 % confidence interval             | 1.0                          | 1.8–11.7                 |

<sup>a</sup> With the exposed as the standard.

somewhat reduced however, namely, to 2.9 with a 95 % confidence interval of 1.2–6.6, as shown in table 4.

The urinary samples did not show any differences in thioether excretion between tire builders and the reference group, nor were the findings with regard to smoking consistent between the groups (table 5).

## Discussion

The design of this study, as based on currently employed women, might imply some selection bias, since women with unsuccessful pregnancies tend to continue

**Table 4.** Pregnancy outcome among tire builders by stratification on a confounder score.<sup>a</sup> Cases are threatening abortions, abortions, and malformations. (No information obtained from the two top strata, which are shown for completeness, however.)

| Confounder score                     | Cases/pregnancies |          |
|--------------------------------------|-------------------|----------|
|                                      | Non-exposure      | Exposure |
| –0.0923– –0.0137                     | 0/7               | 0/0      |
| > –0.0137– 0.0649                    | 2/13              | 0/0      |
| > 0.0649– 0.1435                     | 2/19              | 3/9      |
| > 0.1435– 0.2221                     | 1/15              | 2/7      |
| > 0.2221– 0.3007                     | 3/9               | 4/5      |
| Total                                | 7/63              | 9/21     |
| Standardized rate ratio <sup>b</sup> | 1.0               | 2.9      |
| Mantel-Haenszel $\chi^2$ (1) = 6.50  |                   |          |
| Mantel-Haenszel rate ratio           |                   |          |
| Point estimate                       | 1.0               | 2.9      |
| 95% confidence interval              | 1.0               | 1.2–6.6  |

<sup>a</sup> According to  $Y_{Ab/Normal} = -3.95 + 0.81 \ln(\text{calendar year}) + 0.19 \ln(\text{age}) - 0.02 (\text{pregnancy order}) + 0.11 (\text{smoking})$ .

<sup>b</sup> With the exposed as the standard.

**Table 5.** Thioether (SH) concentrations in urine – Means and ranges.

|                                   | Number of persons | $\mu\text{mol SH/ mmol creatinine}$ |           |
|-----------------------------------|-------------------|-------------------------------------|-----------|
|                                   |                   | Mean                                | Range     |
| Tire builders, total group        | 33                | 35.6                                |           |
| Smokers                           | 17                | 43.1                                | 27.5–75.0 |
| Nonsmokers                        | 16                | 27.7                                | 12.5–44.3 |
| Component department, total group | 30                | 41.4                                |           |
| Smokers                           | 14                | 39.9                                | 23.7–52.0 |
| Nonsmokers                        | 15                | 42.7                                | 13.8–87.1 |
| External reference group          | 17                | 35.0                                | ..        |

work, whereas women giving birth quite often, at least temporarily, quit work. Selective forces might also go in another direction, however, since those having abortions but wanting a child might leave the department, especially when suspicions arise that the work conditions might have had unfavorable effects. Although there is no general impression of any selection in this group of women workers, such phenomena might nevertheless have taken place.

Another aspect of concern is the possibility of recall bias in a study based on interviews. However, the rate of abnormal pregnancies among the nonexposed was about the average for the general population, or 11 %, a level which speaks against any serious bias since a false overclassification of abnormal pregnancies to the exposed group through a recall bias mechanism would have created a corresponding deficit among the nonexposed [cf Axelson (2)].

Another problem of validity in a study of this type might be the general comparability of the exposed and nonexposed pregnancies, even though the effects of the various, recognized confounders have been reasonably well controlled. Thus there might be ill-defined risk factors which are operating differently among the exposed and nonexposed pregnancies, say, general stress in occupational work versus housewife work, work in a standing position, etc. Such factors could perhaps be at least part of the explanation for the differences observed; 8 out of the 12 threatening and spontaneous abortions occurred among the exposed pregnancies. It is worth noticing also that the pregnancy order appeared to be a rather weak and negative confounder, as reflected in the coefficient of the confounder score function (contrary to the preliminary judgement that was made in this respect).

The rubber industry is thought to represent a potentially hazardous environment through the many chemicals involved in the production and has seemingly resulted in disorders like eczemas, bronchitis, and tumors among the employees. It is reasonable therefore to suspect reproductive hazards also to occur, but, until now, few studies of reproductive disturbances have been con-

ducted in the rubber industry. Furthermore, since a recent Finnish study from the rubber industry revealed an increased urinary concentration of thioethers among women in the belt department, there might be percutaneous exposure to alkylating agents in this type of job, which could mean a reproductive hazard. On the other hand there was no indication of increased thioethers in the present study, but the method of analysis (3) may have been suboptimal and has been subject to improvements (4). Moreover the qualities of the tires have changed over time, along with the chemicals involved, and currently obtained urinary samples are not likely to be representative for the whole period covered by this study. It may also finally be noted that smoking might have reinforced an effect of exposure since all the four exposed pregnancies of smokers were unsuccessful.

In summary, this study represents a situation in which a routine evaluation seemed necessary because of rumors of reproductive disturbances and because chemical risks could be suspected to be operating. It remains unclear however whether the identified cluster of abnormal pregnancies represents the manifestation of a chemical hazard, whether it is a random phenomenon, or whether it relates to some other circumstances, say, general work stress and work in a standing position. In any case it seems reasonable to suggest further studies of reproductive hazards in the rubber industry.

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