REPORT ON WOMEN PHARMACEUTICAL WORKERS AND ADVERSE REPRODUCTIVE OUTCOMES

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16. Abstract (Limit: 200 words)

A reproductive history survey of past and current female employees of pharmaceutical laboratories (SIC-2934) was conducted using a retrospective cohort study design. A total of 191 laboratory workers and 318 comparisons participated in telephone interviews. A panel of physicians classified responses into categories of congenital malformation, perinatal illness, normal physiologic variant, and normal. Age and parity groups were used as strata when making comparisons on reproductive outcome between laboratory and administrative workers. Women who had previously worked in the laboratory reported significantly greater proportions of malformations during the early 1970s than did comparisons. Specifically, the proportion of infants born with malformations to mothers who worked in the laboratory at the estimated date of conception was significantly different from the proportion of comparisons. The proportion of miscarriages, and differences in birth weight were not significantly different. The authors conclude that there was a significantly higher proportion of congenital malformations among children born to women employed in the laboratory area of a pharmaceutical research facility. The cluster was limited in time and results may have been biased by social and economic traits. In addition, the study was not a randomly selected population, but rather a self reported cluster of miscarriages and stillbirths.

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Abstract

In response to a complaint of increased frequency of perinatal deaths among children of women working in a research laboratory, NIOSH conducted a telephone survey of the reproductive history of 191 women laboratory workers, including former employees, and 318 women employed in the administrative areas of the same company. A panel of physicians classified the responses into categories of congenital malformation, perinatal illness, normal physiologic variant, and normal. Miscarriages and stillbirths did not differ significantly between groups but congenital malformations alone and congenital malformations combined with perinatal illnesses were significantly more common among laboratory workers. When stratified by age, by parity, or by race, the positive association with work area (odds ratios between 1.76 and 1.95) persisted, but was not statistically significant. Malformations and perinatal illnesses appear to have been concentrated in the early 1970's.

The only exposure common to the laboratory as a whole was organic solvents, taken as a group. This study is consistent with others which have shown an increased reproductive risk among laboratory workers and workers exposed to solvents, but, since the population was essentially self-selected through a reported cluster, some caution is appropriate in drawing conclusions from these data.

I. INTRODUCTION

In 1976, three women employed in the laboratories of the Research & Development unit of a pharmaceutical company became concerned about 9 perinatal deaths among 23 pregnancies of women who worked there and requested that a health hazard evaluation be conducted by the National Institute for Occupational Safety and Health (NIOSH).

NIOSH conducted an initial walk-through survey at the company on April 21, 1976. The Research and Development unit was composed of several laboratories which used many organic chemicals and solvents for the development and testing of various drugs such as tranquilizers, contraceptives, antihistamines, antibiotics, hypoglycemics, cortico-steroids, and anti-metabolites. Some of these reagents are known or suspect carcinogens [See Table 1]; others, such as N,N-dimethyl acetamide and some of the drugs present are thought to be embryotoxins, teratogens or mutagens[1,2].

In 1976, the company employed about 250 women as laboratory technicians, research scientists, clerks, secretaries, and administrative personnel. The Administrative area and the Research and Development area of the company were located in the two separate sides of the largest building, a U-shaped facility with one walkway connecting the two sides. There were two additional buildings which housed the rest of the research workers, those working in Product Development and Virology; workers from the Product Development and Virology Units were not included in the study.

The company had occupied this location since 1955 and had made no major structural changes in the buildings since construction. A phosgene spill occurred in 1974; both areas of the main building had to be evacuated. The hood exhaust ventilation plenums located on the roof were found to be too close to the fresh air intake; the company subsequently installed an activated charcoal filter system to prevent recurrence of similar problems.

In 1976 and 1977 the company provided preliminary data to NIOSH indicating an unsuccessful pregnancy rate of 25% for women working in the Research and Development area as compared to 10.8% for those in administration; these rates, however, were based on small numbers. Further data supplied by the company were presumed to be incomplete because they included only those women known by the company to have been pregnant. Since terminated employees were not included and many pregnant women quit work to raise a family, these data probably underestimated the number of pregnancies.

The affected women worked in different areas of the building. Of the many suspect chemicals used within the worksite, only solvents (as a class) were sufficiently prevalent to constitute a plausible explanation for the cluster.[1] A literature review revealed several epidemiological and experimental reports indicating an association between solvent exposure during pregnancy and adverse reproductive outcomes, notably among women working in laboratories.

In 1968, Kucera[3] published the first report suggesting an association between maternal exposure to solvents and damage to the fetus. Since then, other studies have reported statistically significant increased incidences of congenital malformations[4,5], perinatal deaths[6], spontaneous abortions[7], and chromatid breaks[8] among laboratory workers, pharmaceutical company workers, and women who were exposed to solvents during pregnancy.

The following factors prompted NIOSH to conduct a full scale epidemiological study of reproductive outcomes among the female employees: 1) the preliminary data provided by the company, 2) the presence of hazardous substances in the work areas, and 3) the apparent high level of concern among company employees.

II. METHODS

A. Study Design and Data Collection:

A reproductive history survey of past and current female employees was conducted using a retrospective cohort study design. Our hypotheses were that employment in the Research and Development laboratory areas was associated with an increased risk of adverse reproductive outcomes at any time after the employment and that such employment was associated with an increased risk of adverse reproductive outcomes if the pregnancy coincided with the employment.

Company personnel records of all female employees who worked during the period from 1/1/62 to 6/8/77 were used for selection of a study population. The group studied:

- worked 6 months or more (to exclude short term workers);
- worked in the building which housed the R&D and Administrative divisions;
- worked between January 1, 1968 and June 8, 1977 (to maximize recall of events during the last 10 years);
- were in childbearing age during their period of employment. Specifically, they:

  were over 18 years old at the end of employment (or the end of the study period if still employed); and

  were under 45 years old at the beginning of the study period (or when first employed if hired after the start of the study period).

709 women met the requirements for inclusion. (Figure 1.) 23% (166/709) of the women worked in the laboratory area and will be referred to as the exposed group. 70% (499/709) were clerical or administrative workers, employed in the administrative wing and not significantly exposed to the laboratory environment; employees in the administrative building were selected as an internal comparison group. 6% (44/709) of the women had worked in both buildings and were classified as exposed.

Efforts were made to locate and contact all members of the study group. About 2/3 (468/709) of the women no longer worked at the company at the start of the study. Tracing them was difficult both because they changed last names when they married, divorced, and/or re-married; and because they were usually listed under their spouses' names in such important location sources as the telephone directory. Ultimately, 578 of the 709 women (82%) were located and contacted; 6 (1%) were deceased; and 125 (18%) could not be contacted. A total of 513 (72%) of the 709 women completed interviews.

Environmental insults to germ cells, embryo, or fetus can result in congenital malformations, low birthweight, spontaneous fetal loss, altered sex ratio, stillbirth or late fetal death, and developmental disability or disease[9]. This study was designed to look for all of these potential endpoints because of the possibility that one outcome might mask another, as when fetuses with chromosomal anomalies such as trisomy or triploidy sustain a high spontaneous fetal loss rate.

The questionnaire was designed to elicit demographic data and work, reproductive, and general health and medical histories for each subject and her spouse*. Women with at least 3 years experience as professional interviewers were trained to conduct the interview and complete the questionnaire. Most interviewing was done by telephone, which has been shown to be highly successful and cost-effective in obtaining an excellent response rate in urban areas[10,11]. For the few respondents who lived in the Philadelphia, Pennsylvania area, and had no phone or an unlisted phone number, an attempt was made to conduct the interview in person.

*Questionnaire available on Request

Before the women were interviewed, both NIOSH and the pharmaceutical company sent each woman an introductory letter which explained the purpose of the study. Interviewing began on August 15, 1979 and continued through April, 1980, although the majority of the interviews were completed within 3 months of the beginning date. The few women who were difficult-to-trace primarily accounted for the extended period of interviewing. Pregnancies ending as late as August 14, 1979 were eligible for inclusion. Of the 578 eligible women contacted, 513 (89%) completed an interview; 60 (10%) refused interviews; and 5 (1%) consented to interviews, but the actual interview could not be completed by the end of the study period.

B. Statistical Methods:

Estimated date of conception was calculated for each pregnancy by subtracting 9 months from the date of each live or still birth, 4 months from the date of each miscarriage, or 3 months from the date of each abortion. These events were compared with the work history in each woman's questionnaire to determine if and where the mother was working at the estimated time of conception. Both the possibilities that (1) exposure to the mother anytime before or during pregnancy or (2) exposure to the mother at the time of conception could be associated with adverse reproductive outcome were tested. The term "subcohort" will be used to designate those pregnancies with an estimated date of conception while the mother was working. For the purpose of the study, any work in the laboratory area at this facility is defined as exposure. Only pregnancies which occurred during the mother's period of eligibility were used in analysis.

In an effort to control for possible confounding variables, stratification was used. The covariates of age, parity, and alcohol and tobacco consumption of the mother were examined individually by work area with contingency tables. If all possible combinations of the various covariates had been considered at one time, the sample sizes would have been too small for meaningful analysis. However, if any of the covariates was distributed equally over both laboratory and administrative work areas, then its contribution as a confounder could be discounted in future analyses. Stratified analyses were used for covariables found to be distributed differently in laboratory and administrative work areas. The Mantel-Haenszel chi was used as an overall test of differences in pregnancy outcomes between laboratory and administrative areas. Separate contingency tables were generated for each age stratum and then pooled. Parity strata were handled in the same way.

Because of increased risk of low birth weight and perinatal illness inherent to multiple births, sets of twins were excluded. Where sufficient information was obtained to characterize an abortion as spontaneous, the pregnancy was classed as a "miscarriage"; otherwise, the pregnancy was excluded from analysis. Terms such as "missed abortion" or "incomplete abortion" were taken to indicate spontaneous abortions.

Analyses by pregnancy are somewhat compromised by the lack of independence of pregnancies within each woman. In an effort to alleviate this problem, an analysis was performed using women as the units of study instead of

pregnancies. A woman was categorized as having an adverse outcome if any of her pregnancies after she began work at the plant resulted in a miscarriage or stillbirth. If any eligible pregnancy was aborted, and if she had no other miscarriages or stillbirths among eligible pregnancies, she was put in the abortion category. Lastly, a woman was put into the live births category only if all of her eligible pregnancies resulted in live births.

C. Confirmation/Categorization of Malformation by Physician Panel

For each pregnancy, mothers were asked "Was [the child] born with any birth malformations or health condition? ... What type of birth malformation or condition?" The questions elicited many responses which required clarification. Independent confirmation that the reported malformation or health condition was a bona fide anomaly was sought from a panel of five physicians. Each physician was asked to classify the verbatim questionnaire response into one of the following five categories: a congenital malformation, the result of birth trauma or perinatal illness, a normal physiologic variant, an essentially normal occurrence and other or unknown. For the analysis by workplace at the time of conception, the panel also made recommendations for obtaining more information as necessary in order to classify the response properly.

Additional information was obtained from two sources: the mother of each case was re-contacted by telephone to answer questions suggested by the panel to clarify or to elaborate upon the questionnaire response. Of 14 women (15 affected children), one (with one affected child) refused to participate further and three (with one affected child each) could no longer be contacted. When the mother could be contacted, the current status of the child's health was also determined and the mother was asked if she would authorize NIOSH to request medical records pertinent to her child's condition. The physician panel re-evaluated all information obtained and, on the basis of their classifications, the proportion of malformations was reanalyzed. Those cases classified as "unknown" were considered non-malformations for the purposes of analysis.

III. RESULTS

A. Follow-up Results, Response Rate, and Temporal Trends:

Figure 1 shows the study participation data. Unlisted phone numbers and unanswered letters account for the three percent of women who could not be contacted. 223 (44%) of the 509 women interviewed had been pregnant between 1/1/68 and 8/15/79, with 9 still pregnant at the end of the study period. Table 2 shows that 321 live births occurred in women who made up the study population. Table 3 shows that a total of 113 of these live births occurred among the subcohort of women who were working at the estimated date of conception.

Table 4 compares the work history of interviewed and non-interviewed subjects. (The work history data in Table 4 are derived from company records, for consistency, and differ from those in the lower half of Figure 1, which shows work history as reported by the interviewed women.) Laboratory personnel had a higher participation rate than administrative personnel, but the difference in participation rates was not significant.

Although 60 of the 578 women contacted (10%) refused to participate, there was no significant bias in participation rates. Of the women contacted, a higher proportion of exposed workers were interviewed (Table 4) but the proportions of exposed and non-exposed women among those who refused to participate did not differ significantly from the proportions among those those interviewed. (Chi-square = 2.69 (4 d.f.); p greater than 0.50)

Many of the confounding factors thought to influence pregnancy outcome were found to be distributed evenly in both the exposed laboratory and unexposed administrative groups. Alcohol consumption of the mother, as measured by beer, wine, and mixed drink consumption was not significantly different between groups. The pattern of cigarette smoking was also similar among laboratory and administrative workers. There appeared to be no relationship between exposure of the husband to toxic agents and adverse pregnancy outcomes. There was no significant difference between laboratory and administrative groups in number of abortions excluded because of insufficient information.

Parity and maternal age at conception differed significantly between the laboratory and administrative workers; laboratory workers tended to be slightly older at the estimated time of conception than administrative workers (28.4 vs. 27.1 years, p = .002) and had slightly greater parity (1.94 pregnancies vs. 1.73, p less than .05). Age and parity groups were therefore used as strata when making comparisons on reproductive outcome between laboratory and administrative workers. Laboratory workers had a mean of 15.1 years of education while administrative workers had a mean of 14.0 years. The difference is significant (p = .0001).

Outcomes were also examined by calendar year of pregnancy to see if there were any secular trends. (See Figures 2 and 3) The women who had previously worked in the laboratory reported significantly greater proportions of malformations during the early 1970's than did the administrative workers (p = 0.003 for 1972-73).

Table 5 shows the number of women in each group who had ever been pregnant and the number of those pregnancies eligible for inclusion in this study. There are no significant differences among groups.

B. Adverse reproductive outcomes of women who worked before or during pregnancy.

This comparison examined the potential long-term effects of working in the laboratory before or during gestation. The proportion of miscarriages or still births was 0.118 for those who had worked in the laboratory prior to or during pregnancy and 0.149 for those who had never worked in the laboratory. The difference was not significant.

The proportion of infants found to have congenital malformations or perinatal illness was elevated but not significantly higher in women who had worked in the laboratory at any time prior to giving birth. The Mantel Haenszel test stratified by parity showed a pooled odds ratio of 1.94 with $X_1^2 = 3.09$, $p = 0.08$. Stratifying by 5-year age group yielded a pooled odds-ratio of 1.95 with $X^2 = 3.24$, $p = 0.07$ for congenital defects and perinatal illnesses combined (see Figure 2). Stratification by race yielded a similar outcome, with a pooled odds ratio of 1.76, $X_1^2 = 2.40$, and $p = 0.12$.

Birth weight did not differ significantly between groups, with 6.30% of births less than 2500 grams in exposed workers versus 2.58% in unexposed workers ($X^2 = 2.74$, $p = 0.10$). The sex ratio was higher for infants of exposed women (1.15) than for those of unexposed women (0.99); as before, this difference was not statistically significant ($X^2 = 0.44$, $p = 0.51$).

When analyzed by woman, rather than by pregnancy, no significant difference was found between the proportion of laboratory workers or administrative workers with adverse pregnancy outcomes ($X^2 = 0.98$, $p = 0.91$).

C. Adverse reproductive outcomes of women working at the estimated date of conception:

The proportion of infants born with malformations to mothers who worked in the laboratory at the estimated date of conception was significantly different from the proportion for controls (Table 7, $p = 0.01$). The proportion of infants with perinatal illness was not significantly different. Considering white women only, the proportion of malformed infants in the subcohort was still statistically significant ($p = 0.04$). Figure 2 shows the temporal distribution of malformations and perinatal illnesses among the subcohort.

Among women working at the estimated date of conception, the proportion of miscarriages and still births combined was 0.182 in the laboratory and 0.192 in the comparison group (Table 3); this difference was not statistically significant. The sex ratio was 1.25 (or 25% more males) for infants born to exposed women and 0.79 for the infants born to the unexposed women; this difference was not statistically significant ($X^2 = 1.49$, $p = 0.22$). The proportion of newborn infants whose weight was less than 2500 grams was not statistically different between the exposed and unexposed groups.

Table 6 summarizes the mother's initial response, the additional information obtained in the telephone interview, and the final classification of the case into the five categories of malformation/health conditions at time of birth by the reviewing physicians. In 13 of the 15 cases, sufficient information was available originally or was collected from the telephone interviews for categorization of the condition. Further information for documentation of two cases, classified as "unknown," remains incomplete because these mothers could not be contacted.

IV. DISCUSSION AND CONCLUSIONS

The data show that there was a significantly higher proportion of congenital malformations among children born to women employed in the laboratory area of a pharmaceutical research plant. The cluster was limited in time (with a peak in the early 70's). Sufficient industrial hygiene data were not available to permit investigation of specific agents. Organic solvents might have been involved, judging from other reports and the nature of this workplace, but the support for that hypothesis provided by these data is weak.

The significant difference in mean years of education suggests differences in social and economic traits which might extend to dietary practices, desired family size, and other factors with potential to affect this study.

Age at conception and parity were both significantly different between the laboratory and administrative groups. They were associated with each other and with the combined outcomes, congenital malformations plus perinatal illnesses, to the extent that controlling for either resulted in loss of statistical significance (p greater than 0.05). Since p levels were 0.07 and 0.08 even after controlling for age or parity, it is still possible that some other factor was also affecting pregnancy outcome.

The most serious limitation of this study stems from its origin as an investigation of a problem. The population studied was not randomly selected from a pool of populations with known exposure, it was a self-reported cluster of miscarriages and stillbirths. The effect found, an increase in malformations and perinatal illnesses, was related to the reported problem. Although we confirmed the existence of a cluster, extrapolation from this observation should be made very cautiously.

Most of the statistical analyses used in this study further assumed that each pregnancy, the unit of observation, was an independent event. The outcome of one pregnancy can, however, affect subsequent pregnancies. Using women as the unit of observation partially controlled for non-independence but reduced the number of observations. More elaborate analytical techniques are available, but were considered inappropriate, given the other limitations on the study.

Bias could originate in subject selection, ascertainment, willingness to participate, recall, or differences in interviewers. Ascertainment bias is possible, since 28% of the population at risk was not interviewed due to refusal, death or loss to follow-up. The possible biases of interviewers were examined by examining the responses obtained by each with regard to pregnancy outcome. There were no statistically significant differences among the 12 interviewers in the rates of "malformation(s) or birth conditions" reported to them, nor in rates of congenital malformation or birth injury/perinatal illness (as determined by the physician panel) among pregnancies of the women each interviewed.

Since the laboratory and administrative buildings are physically separated, and each woman was asked both in what building and in what department she had worked, classification into exposed and non-exposed categories is probably accurate.

Recall bias would have been more likely to occur for the outcome of spontaneous abortion than for term pregnancies. There is no reason to think that administrative workers may be more subject to recall bias than laboratory workers. However, the high level of public interest, manifest in newspaper and magazine articles at the time of the original request, may have prompted the exposed women to think more about their past pregnancies, particularly about any adverse events.

It is difficult to assess the magnitude of any of these biases. One would expect other adverse reproductive outcomes as well as congenital malformations to have been reported by laboratory workers if they, as a group, encompassed bias significant enough to influence the study results.

An association would be more convincing if there were a common pattern of defects among affected children. The small size of the study group, combined with the rarity of congenital malformations, makes it impossible to do meaningful analyses by specific defect. We may draw no conclusions from the absence of a clear pattern among the malformations and illnesses observed, but must note that grouping diverse conditions together, while necessary in this study, is less than ideal.

VI. REFERENCES

1. Stephenson, FW: Hazard Evaluation Report HE 76-44. April 21,1976. NIOSH, Division of Surveillance, Hazard Evaluations and Field Studies, Cincinnati, Ohio 45226

2. Suspected Carcinogens: A subfile of the NIOSH Registry of Toxic Effects of Chemical Substances.

3. Kucera J: Exposure to fat solvents: A possible cause of sacral agenesis in man. Journal of Pediatrics 1968;72(6):857-859.

4. Meirik O, Kallen B, Gauffin U, Ericson A: Major malformations in infants born of women who worked in laboratories while pregnant. Lancet ii July 14, 1979: 91.

5. Holmberg PC: Central nervous - system defects in children born to mothers exposed to organic solvents during pregnancy. Lancet July 28, 1979:177-179.

6. Hansson E, Jansa S, Wande H, Kallen B, Ostlund E: Pregnancy outcome for women working in laboratories in some of the pharmaceutical industries in Sweden. Scand J Work Environ Health 1980;6:131-134.

7. Hemminki K, Fransilla E and Vainio H: Spontaneous abortions among female chemical workers in Finland. Int Arch Occup Environmental Health. 1980;45:123-126.

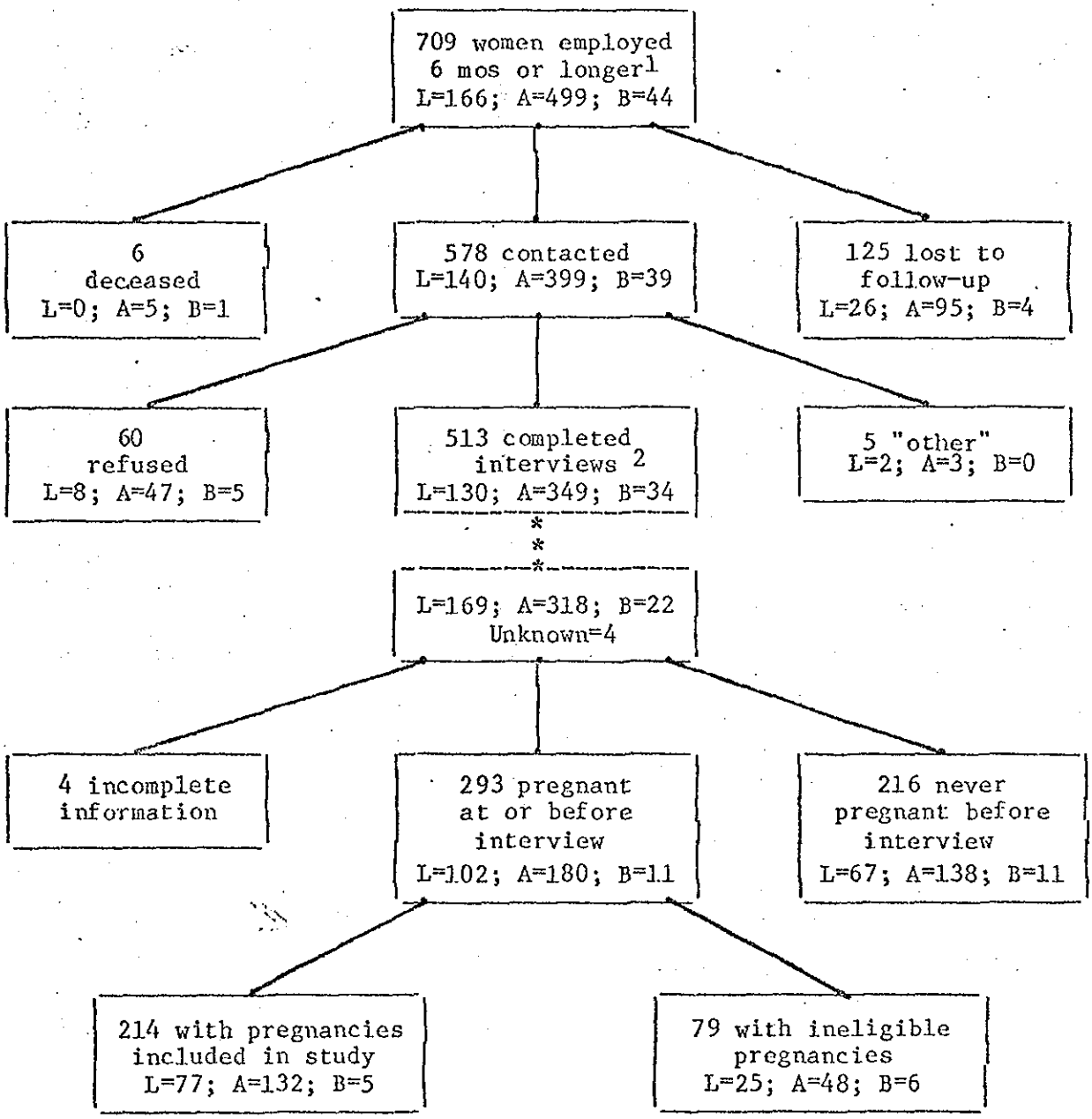
8. Funes-Cravioto F, Zapata-Guyon C, Kolmodin-Hedman B, Lambert B, Lindsten J, Norberg E, Nordenskjold M, Olin R, and Swensson A: Chromosome aberrations and sister-chromatid exchange in workers in chemical laboratories and a rotoprinting factory and in children of women laboratory workers. Lancet August 13, 1977:322-25.

9. Bridges BA: An approach to the assessment of the risk to man for DNA damaging agents. Arch Toxicol, Suppl. 3, 1980:271-281.

10. Ibsen GA and Ballweg JA: Telephone interviews in social research: Some methodological considerations. Quality and Quantity 1974;7:181-192.

11. Siemiatycki J: A comparison of mail, telephone, and home interview strategies for household health surveys. Am J Public Health 1979;69(3):238-245.

Figure 1: TRACING RESULTS FOR WOMEN PHARMACEUTICAL WORKERS



L = Laboratory only; A = Administrative only; B = Both; Unknown = Work area could not be ascertained.

[1] All work area classification in this Figure is by woman, not by pregnancy.

[2] Classification of work area below this cell is from questionnaire; for this cell and above, classification is derived from the employer's records (see text).

Table 1: Known or Suspect Carcinogens
Used in the Research and Development Unit

acetamide	chromium trioxide	o-dichlorobenzene
aniline	dicyclohexamine	o-tolidine
arsenic trioxide	hydrazine	p-chlorobiphenyl
benzene	hydroquinone	tannic acid
carbon tetrachloride	lead acetate	toluene
chloroform	mercury	

Table 2: Pregnancy Outcomes of Women Who had Worked During or Before Gestation, by Work Area

Work Area	Miscarriages + Stillbirths	Live Births	Total Pregnancies
Laboratory Area	17 (11.8%)	127	144
Administrative Area	34 (14.9%)	194	228
Total	51 (13.7%)	321	372

Relative risk = 0.76; X^2 = 0.72.

Table 3: Pregnancy Outcomes of Women Working at the Estimated Date of Conception, by Work Area

Work Area	Miscarriages + Stillbirths	Live Births	Total Pregnancies
Laboratory Area	12 (18.2%)	54	66
Administrative Area	14 (19.2%)	59	73
Total	26 (18.7%)	113	139

Relative risk = 0.95; X^2 = 0.02.

Table 4: Number and Percent of Women
With Laboratory, Administrative, or Combined Work History
By Contact and Interview Completion Status
(As ascertained from company records)

	Lab	Adm	Lab + Adm	Total
Not Contacted	26	100	5	131
(% of total)	16	20	11	18
Contacted				
Completed N	130	349	34	513
(% of contacted)	93	87	87	89
Refused N	8	47	5	60
(% of contacted)	5.7	12	13	10
Other N	2	3	0	5
(% of contacted)	1.4	0.8	0.0	0.9
Total contacted	140	399	39	578
(% of total)	84	80	89	82
Grand Total	166	499	44	709

Table 5: Number of Women Reporting Pregnancies by Work Area
(As ascertained from interview)

	Women Reporting:			
Area	Eligible Pregnancies	Ineligible Pregnancies	Without Pregnancies	Total Women
Laboratory Only	77	25	67	169
Administrative Only	132	48	138	318
Both	5	6	11	22
Total	214	79	216	509

$X^2_4 = 5.200$; $p = 0.15$

Table 6: Classifications of Infants Reported to Have Malformations/Health Conditions at Birth and Born to Mothers Reported Working at Estimated Date of Conception

Case #	Work Area**	Verbatim Questionnaire Response	Additional Information	Final Classification
1	L	entire body premature; went into intensive care; respiratory not developed; has cerebral palsy	wears braces due to spine - motor impairment; attends special school	perinatal illness
2	L	shallow breathing; very premature; intestinal wall not developed; ruptured (Note: child expired at 3 months old)	no further information	probably congenital malformation
3	L	prematurity, causing lungs to collapse	no further problems with lungs	perinatal illness
4	L	allergy to all milk	no further information necessary	normal physiologic variant
5	L	hematoma on the head	also described as birth mark, lump on head, "port wine stain"	normal physiologic variant
6	L	two fingers attached together on both hands	little finger and adjoining finger on both hands were surgically corrected	congenital malformation
7	L	feet turned in	feet were "casted" at age of 2 months	congenital malformation
8	L	pyloric stenosis	surgery performed	congenital malformation
9	L	pyloric stenosis; intestinal blockages; hyperactive; minimal brain dysfunction	corrective surgery performed for pyloric stenosis at 6 months old; intestinal blockages noticed during surgery	congenital malformation

Table 6 (Cont.)

10	L	eye problem (very poor vision in one eye)	pending response from mother	unknown*
11	L	heart murmur found at 3 months old	cardiologist consulted; drs. feel that source is "closing up"	congenital malformation
12	L	lungs: hyaline membrane disorder (Note: child expired at 2 days old)	no further information necessary	perinatal illness
13	A	heart murmur	pending response from mother	unknown*
14	A	egg-shaped head	no present problem with head shape; unusual shape influenced by mother's anatomical configuration during birth; no surgery necessary	normal physiologic variant
15	A	heart murmur	present at 1 mo. old; disappeared after that time	normal physiologic variant

* Unknown cases could not be classified by review panel due to insufficient information. Mothers had not responded to telephone calls and/or letters at the time of this writing. Further follow-up is pending.

Note: One set of twins were also reported in this group. However, they were excluded from analyses since the birth of twins is an unusual pregnancy outcome (i.e. birth of each child does not qualify as an independent event)

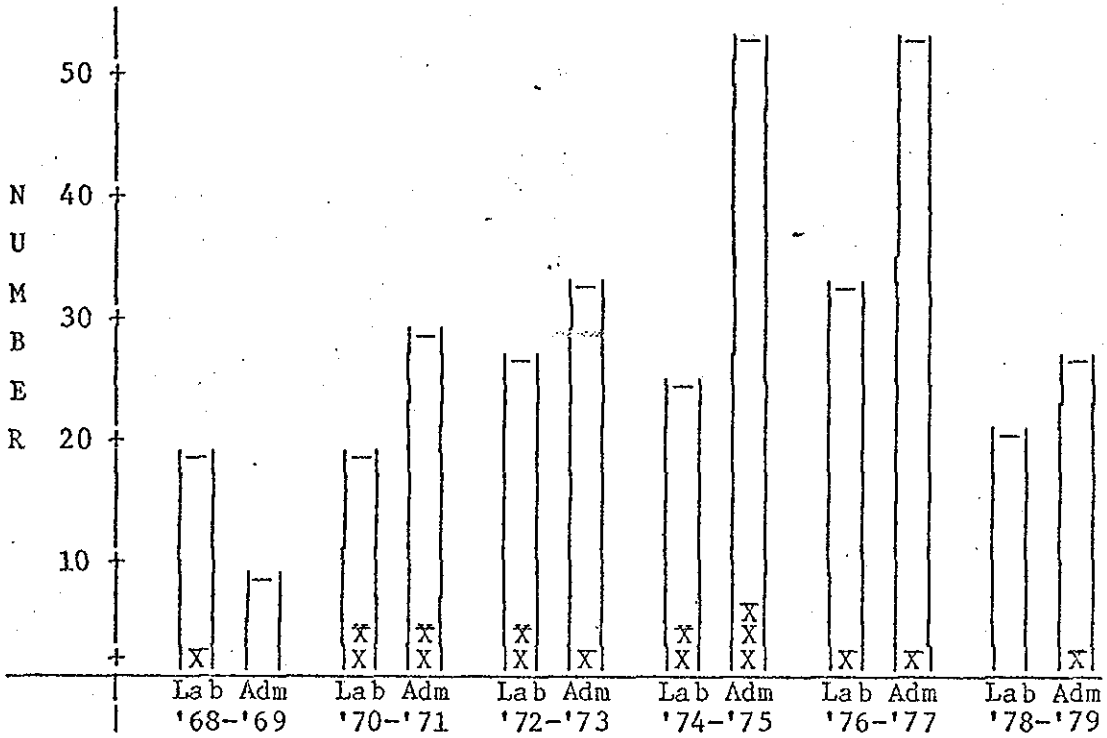
** "Work Area" refers to the area in which the woman was working when her child was conceived. The laboratory area and the administrative area are designated as "L" and "A" respectively.

Table 7: Congenital Malformations and Perinatal Illnesses By Work Area of Mother at Estimated Time of Conception

	Lab. Workers	Admin. Workers	Total	p*
1. Malformations				
Malformations	6	0	6	
Other Births	48	59	107	
Total Live Births	54	59	113	0.01
2. Perinatal Illnesses				
Perinatal Illnesses	3	0	3	
Other Births	51	59	110	
Total Live Births	54	59	113	0.11
3. Malformations plus Perinatal Illnesses				
Malformations plus Perinatal Illnesses	9	0	9	
Other Births	45	59	104	
Total Live Births	54	59	113	0.001
4. Race = White, Only				
Malformations	4	0	4	
Other Births	43	57	100	
Total Live Births	47	57	104	0.04

*P value, Fisher's Exact Test, one tailed

Figure 2
Numbers of Live Births and
Combined Malformations and Perinatal Illnesses
Among Women Who Worked Before or During Pregnancy
By Year of Conception and Work Area



| | = Live birth without congenital malformation or perinatal illness
|X| = Congenital malformation or perinatal illness (combined totals)