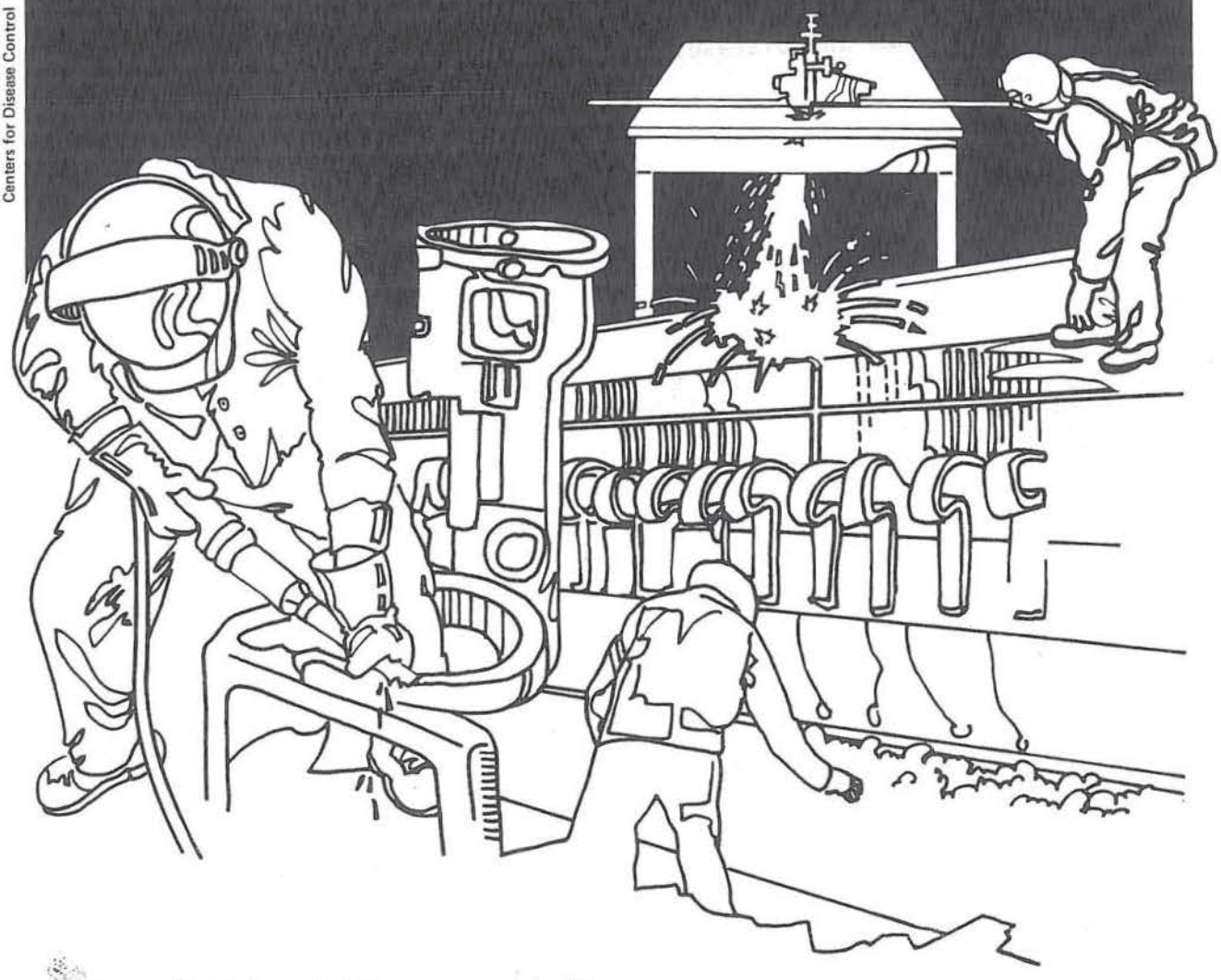
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES ■ Public Health Service
Centers for Disease Control ■ National Institute for Occupational Safety and Health

NIOSH



Health Hazard Evaluation Report

HETA 84-014-1507
DAVIS & GECK, INC.
DANBURY, CONNECTICUT

PREFACE

The Hazard Evaluations and Technical Assistance Branch of NIOSH conducts field investigations of possible health hazards in the workplace. These investigations are conducted under the authority of Section 20(a)(6) of the Occupational Safety and Health Act of 1970, 29 U.S.C. 669(a)(6) which authorizes the Secretary of Health and Human Services, following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found.

The Hazard Evaluations and Technical Assistance Branch also provides, upon request, medical, nursing, and industrial hygiene technical and consultative assistance (TA) to Federal, state, and local agencies; labor; industry and other groups or individuals to control occupational health hazards and to prevent related trauma and disease.

HETA 84-014-1507
SEPTEMBER 1984
DAVIS & GECK, INC.
DANBURY, CONNECTICUT

NIOSH INVESTIGATORS:
Kevin P. Mc Manus, IH
Matthew London, IH

I. SUMMARY

In October, 1983 the National Institute for Occupational Safety and Health (NIOSH) received a request from the International Chemical Workers Union to evaluate adverse reproductive effects related to employee exposure to ethylene oxide (EtO) and xylene in certain areas of Davis & Geck, Inc., Danbury, Connecticut. The request stated that employees in the Specialties Department, where xylene is used, seem to have an increased incidence of hysterectomies.

At the time of this investigation, NIOSH was concurrently conducting an Industry-Wide Study relating to ethylene oxide and this plant was included as part of that study. Evaluation of ethylene oxide levels in this facility was deferred to the Industry-Wide Studies Branch.

Environmental samples were collected indicative of employee exposure to xylene. The only three areas of the plant with xylene in use revealed 8-hour personal exposure levels of <0.1 ppm (Specialties), 2.97 ppm (Silastic Coating), and 4.43 ppm (Needle Wash). One sample collected during roller cleaning in the Silastic Coating area indicated 105.7 ppm for the duration of exposure (2-hours). The exposure criterion for xylene is 100 ppm as an 8-10 hour Time Weighted Average.

An epidemiologic investigation of reported gynecologic effects involved the administration and analysis of two questionnaires: one to establish the number of hysterectomy cases in the Specialties Department, and a second to further study those cases.

The occurrence of hysterectomies did not seem to relate temporally to having worked in the Specialties Department. Ten women employed in this area had ever had a hysterectomy. Using age specific rates obtained in 1982 to women residing in upstate N.Y., 9.98 hysterectomies would be expected. No excess is indicated.

Based on the results of this investigation, NIOSH investigators have determined that work in the Specialties Department is not associated with an increased prevalence of adverse reproductive or gynecologic effects. It must also be noted that chemicals used in the Specialties Department (xylene, and formerly trichloroethylene and 1,1,1-trichloroethane) have not been found by other researchers to cause gynecologic or reproductive effects in humans.

Keywords: SIC 3842, Xylene, Reproductive Effects, Hysterectomy

II. INTRODUCTION

In October, 1983 the National Institute for Occupational Safety and Health (NIOSH) received a request from the International Chemical Workers Union to conduct a Health Hazard Evaluation at Davis & Geck, Danbury, Connecticut. The request was concerned with possible adverse reproductive health effects as a result of exposure to ethylene oxide, xylene or trichloroet ene in specific areas of the plant. Of particular concern was the reportedly high incidence of hysterectomies in the Specialties Department, where xylene is the only solvent in use.

At the time of this request, the Industry-Wide Studies Branch of NIOSH was concurrently performing an ethylene oxide investigation at this plant. To avoid duplication of effort it was agreed that although environmental samples would be collected during this evaluation for EtO, interpretation of the results would be handled as part of the Industry-Wide Study. Therefore, this evaluation deals with the potential for reproductive hazards associated with employee exposure to xylene as used in this facility.

III. BACKGROUND

Davis & Geck, a subsidiary of American Cyanamid Company, is involved in the production of surgical sutures, scrub sponges, burn dressings, serum tubes and other miscellaneous medical products. This facility opened in 1953 utilizing heat sterilization and formaldehyde packaging for the suture operation. As technology advanced over the next few years, EtO sterilization was phased in until it became the predominant method used after 1959.

The Company has had an industrial hygiene program in place for the past 20 years. It began with annual IH surveys by American Cyanamid and in 1978 the program was developed full time on-site. EtO levels have been monitored since first used, employing direct reading instruments attached to an alarm system to warn of dangerous atmospheres. Presently, there is a 15 point, GC/FID system to monitor EtO areas. The Company has personal sampling results dating back to 1977. The alarm triggers at 1ppm.

Xylene is used in the plant as a solvent in the Specialties, Braid Wash, and Silastic Coating Departments. Xylene is used in the Specialties area to soften the plastic protective coating on the needles. In the other two areas it is used as a carrying solvent.

Prior to 1977, trichloroethylene and trichloroethane were used in the Specialties Department in place of xylene.

The Company operates two shifts between 7:00 am and 12:00 midnight. All employees receive pre-employment physical exams. A respirator program is in effect with routine training, cleaning, maintenance and qualitative fitting.

IV. EVALUATION DESIGN AND METHODS

A. Environmental

Three (3) full shift air samples were collected to determine employee exposure to xylene in the Specialties area, Needle wash area and Silastic Coating area. One additional charcoal tube air sample was collected during the cleaning of the rolls in the Silastic Department.

The xylene samples were analyzed according to NIOSH Method S318.(10).

B. Medical

The epidemiologic investigation of reported gynecologic effects involved the administration and analysis of two questionnaires.

The first questionnaire, one page long, inquired about the subjects' name, age, years worked in each department at Davis & Geck, whether a hysterectomy had been performed, and when it had been performed.

Those women who were currently employed in the Specialties Department, and on whom a hysterectomy had been performed subsequent to their initial employment in Specialties, were then selected for further study. In addition, a control population from the Specialties Department, matched on age, was also selected. This further study consisted of a more in-depth, orally administered questionnaire. This second questionnaire included a demographic section, a more complete work history, a smoking history, a reproductive history, and a gynecologic history.

Seventy-six of the short questionnaires were administered. They were given to all current employees of the Specialties Department, six people who had worked in Specialties at some point in the past, and four people who had never worked in Specialties. A total of eighteen women had ever had a hysterectomy. Eleven of those 18 women presently worked in Specialties, five formerly did, and two never had.

The list of individuals to whom the lengthy questionnaire would be administered was compiled, though modifications were made due to illness and the refusal of four people to participate.

Twenty-eight women were administered the full questionnaire. Eight of the women were not current employees of the Specialties Department, but were included because they or their union requested that they be interviewed. Thus, 20 of the women worked in Specialties at the time of the survey. Six of them had had hysterectomies since having begun work in the Specialties Department. The "controls" were selected in such a way that their age distribution would be similar to that of the group which had hysterectomies. The intended ratio of two controls for every hysterectomy was altered somewhat due to the refusal of a few individuals to participate.

V. EVALUATION CRITERIA

A. Environmental

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours er week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, and thus potentially increase the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent becomes available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH Criteria Documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV's), and 3) The U.S. Department of Labor (OSHA) occupational health standards. Often, the NIOSH recommendations and the ACGIH TLV's are lower than the corresponding OSHA standards because they are usually based on more recent information than the OSHA standards. The OSHA standards may also be required to take into account the feasibility of controlling exposures in various industries where the agents are used. The NIOSH recommended standards, by contrast, are based soley on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for reducing these levels found in this report, it should be noted that industry is legally required to meet only those levels specified in an OSHA standard.

A time-weighted average (TWA) exposure refers to the average airborne concentration of a substance during a normal 8 to 10-hour workday. Some substances have recommended short term exposure limits or ceiling values which are intended to supplement the TWA where there are recognized toxic effects from high short term exposures.

In the following tabulation of criteria, appropriate values are presented:

Substance	NIOSH	ACGIH TLV	OSHA standard
Xylene	100 ppm 200 ppm(C) (10 min)	100 ppm 150 ppm(STEL) (15 min)	100 ppm

B. Physiologic Effects/Toxicology

1. Xylene

Xylene (also called xylol or dimethylbenzene) is a colorless liquid that exists in three isomeric forms, differing in the distribution of the methyl groups. These isomers are often found as components of solvents used in paints, laquers, cleaning agents, and gasoline, and in laboratories in the preparation of histologic tissue specimens. Commercial xylene is produced both from petroleum and from coal tar. NIOSH estimates that approximately 140,000 workers are potentially exposed to xylene in the United States.

Xylene is metabolized in humans to methylhippuric acid, which unlike hippuric acid, is not a normal urinary constituent.

Like other solvents such as toluene, xylene has narcotic properties. Thus, exposure to high concentrations can cause incoordination, eventually leading to unconsciousness and death at very high concentrations. It is also an irritant of the eye, mucous membranes, and skin.

Baselt[3] claims that chronic organ toxicity has not been noted in man. Reports of hematopoietic (bone marrow) suppression associated with xylene exposure in the past, may have been due to the presence of benzene in the xylene.[5]

A search of the literature reveals no evidence of gynecologic effects or adverse reproductive outcomes in humans due to xylene exposure. Marks and Ledousl investigated the teratogenicity of a xylene mixture in mice. Feeding pregnant mice (by gavage) a xylene mixture, they observed reduced fetal weights and an increased number of malformations. These effects were observed with xylene dosages of 2.4 ml/kg-day and higher, doses which approach lethal levels. Other researchers report that embryotoxicity is not observed, except at doses where maternal toxicity results.[2,3]

2. 1,1,1-Trichloroethane4,5

1,1,1-Trichloroethane, also called methylchloroform, is a colorless liquid, generally utilized as a solvent or as a cleaning agent.

As with xylene and other solvents, 1,1,1-trichloroethane acts as a narcotic and depresses the central nervous system. Exposure to high concentration can produce dizziness, incoordination, drowsiness, increased reaction time, unconsciousness and death. The first effects usually noticed are irritation of the eyes, mucous membranes, and skin.

A search of the literature indicates that neither gynecologic nor adverse reproductive outcomes have been associated with exposure to 1,1,1-trichloroethane.

3. Trichloroethylene4,5

Trichloroethylene is a colorless liquid, primarily used as a solvent in vapor degreasing.

As with the previously mentioned solvents, trichloroethylene has narcotic properties, depressing the central nervous system at high concentrations. Trichloroethylene also causes irritation of the eyes, mucous membranes, skin, and the respiratory tract.

Additionally, injury to the cardiovascular system, gastrointestinal system, the liver and the kidneys has also been observed.

A search of the literature indicates that trichloroethylene has not been associated with adverse reproductive outcomes nor gynecologic effects.

C. Epidemiology

A number of researchers have calculated the prevalence and/or incidence of hysterectomies within various populations.6-9 Recently, Howe has published prevalence rates for women of all ages in upstate New York.9 Given the similar geographic location and the recent study period (1982), we have compared the prevalence of hysterectomy among our study population at Davis & Geck with that among Howe's population.

VI. RESULTS

A. Environmental

The results of the environmental sampling were sent out under separate cover on March 14, 1984. The following table lists both the NIOSH data and the results of the Company data (taken simultaneously) provided to the investigator.

Results of Sampling 1/12/84

Xylene

Location	Time	NIOSH Result (ppm)	Company Result (ppm)
Specialties	8:09-2:56	0.1	0.2
Silastic	8:25-3:30	2.97	0.65 (a) 3.80 (b)
Needle Wash	8:51-2:50	4.43	4.9 (a) 6.2 (b)
Silastic Cleaning*	4:20-6:20	105.7	99.7 (b)

* = exposure reported for 2 hour sample
(a) = charcoal tubes
(b) = 3M 3500 Organic Vapor Badge

B. Epidemiologic/Medical

The long questionnaires were reviewed for all people with hysterectomies, and for the 14 control people without hysterectomies currently in the Specialties Department.

The occurrence of the hysterectomies did not seem to relate temporally to having worked in the Specialties Department (Table I).

The possibility that one or two doctors had recommended the hysterectomies was considered. This was not found to have occurred, as eleven different doctors were mentioned, none by more than two people.

People were asked whether they had ever had a number of specific gynecologic symptoms or conditions (Tables II and III). The only condition which was reported by a significantly greater proportion of hysterectomy cases than controls within the Specialties Department, was the occurrence of abnormally heavy menstrual bleeding.

Reproductive histories were examined (Tables IV and V). No significant differences were found within the Specialties Department when comparing people with hysterectomies versus those without.

Other factors considered included age, tenure at Davis & Geck, tenure in the Specialties Department, and smoking history (Table VI). The only statistically significant difference found was that those women with hysterectomies had worked longer at Davis & Geck than those who hadn't had a hysterectomy. However, there was not a significant difference in the number of years worked in the Specialties Department.

Finally, the question of whether there was an excess of hysterectomies among women in the Specialties Department was addressed.

Hysterectomy is a fairly common medical procedure in the United States. Using age-specific rates obtained by Howe9 in 1982 for women residing in upstate New York, we compared the number of hysterectomies observed among current employees of the Specialties Department with the number we would expect using Howe's prevalence data.

Ten women employed in the Specialties Department at the time of the survey had ever had a hysterectomy. Compared to an expected 9.98 hysterectomies, this did not represent an excess (Table VII).

VII. CONCLUSION

Based on the results of this investigation, NIOSH has determined that work in the Specialties Department is not associated with an increased prevalence of adverse gynecologic or reproductive effects.

Finally, it must be noted that the chemicals used in the Specialties Department (xylene, trichloroethylene, and 1,1,1-trichloroethane) have not been found by other researchers to cause gynecologic or reproductive effects in humans.

IX. AUTHORSHIP AND ACKNOWLEDGMENTS

Report Prepared By:

Kevin P. Mc Manus
Regional Industrial Hygienist
NIOSH - Region 1
JFK Federal Building Rm 1401
Boston, Massachusetts

Matthew A. London
Medical Officer
Medical Section
Hazard Evaluations and
Technical Assistance Branch
Cincinnati, Ohio

Originating Office:

Hazard Evaluations and
Technical Assistance Branch
Division of Surveillance, Hazard
Evaluations and Field Studies
Cincinnati, Ohio

X. REFERENCES

1. Marks TA, Ledous TA. Teratogenicity of a Commercial Xylene Mixture in the Mouse. Journal of Toxicology and Environmental Health 1982; 9:97-105

2. Tatrai E et al. Embryotoxic Effect of m-xylene. Egeszsegtudomany 23, 147-151 (abstract)

3. Ungvary G et al. Studies on the Embryotoxic Effects of ortho-,meta-, and para-xylene. Toxicology 18, 61-74 (1980)

4. Proctor N, Hughes J. Chemical Hazards of the Workplace 1978.

5. DHEW, NIOSH Occupational Diseases, A Guide to their Recognition. 1977.

6. Centers for Disease Control. Hysterectomy among Women of Reproductive Age, United States, Update for 1979-1980. In: CDC Surveillance Summaries, August 1983; 32 (suppl. 3): pp 1SS-8SS.

7. Lyon JL and Gardner JW. The Rising Frequency of Hysterectomy: Its Effect on Uterine Cancer Rates. American Journal Of Epidemiology 1977; Vol. 105, No. 5; 439-443

8. Nolan TF, Ory HW, Layde PM, Hughes JM, and Greenspan JR. Cumulative Prevalence Rates and Corrected Incidence Rates of Surgical Sterilization Among Women in the United States, 1971-1978. American Journal of Epidemiology 1982; Vol 116, No. 5: 776-781

9. Howe HL. Age Specific Hysterectomy and Oopherectomy Prevalence Rates and the Risks for Cancer of the Reproductive System. American Journal Of Public Health, June 1984: Vol 74, No. 6, pp 560-563.

10.NIOSH Manual of Analytical Methods, Second Edition, Vol.3, DHEW/NIOSH #77-157C, April 1977.

11.NIOSH Current Intelligence Bulletin 35, "Ethylene Oxide", DHEW/NIOSH #81-130, May 22, 1981.

TABLE I

ID# Perf.	Years Worked At Davis & Geck	Years Worked in Specialties Dept.	Year in Which Hysterectomy
1	1965 -	1965 -	1978
3	1971 -	1972 -	1982
6	1957 -	1962 -	1970
8	1969-79 1983 -	1969-76 1978-79 1983 -	1971
11	1960-63 1973 -	1960-63 1973-79 1981 -	1960
18	1966 -	1966-1971	1970
10	1966-69 1970 1973 -	1966-69 1970 1973-79	1973
20	1968	NEVER	1983
21	1965 -	1965-1976	1982
22	1966 -	1968-1973	1972
23	1957 -	NEVER	1982
24	1961 -	1961-1976	1983
25	1970 -	NEVER	1974
29	1968 -	1968-73 1980 -	1974

TABLE II

Frequency Distribution of Gynecologic Symptoms & Conditions

Current Employees of the Specialties Department

	People w/Hysterectomies n=6	People w/out Hysterectomies n=14
Increasingly or Abnormally Painful Menstrual Periods	3	3
Abnormally Heavy Bleeding*	5	3
Abnormally Prolonged Bleeding	4	2
Abnormally Irregular Periods	1	2
Post-Menopause Bleeding	0	2
Anemia Caused by Menstruation	1	2
Cancer of the Cervix	0	0
Ovarian Cyst, Non-cancerous	1	3
Ovarian Cancer	0	0
Endometriosis	0	0
Endometrial Hyperplasia	0	0
Polyps of Endometrium or Uterus	0	0
Endometrial Cancer	0	0
Other Uterine Cancer	0	0
Tuberculosis of the Endometrium	0	0
Adenomyosis	0	0
Fibroids	3**	1
Enlarged, Tender Uterus	1	0
Tipped Uterus	0	2
Prolapsed Uterus	0	1
Incontinence	0	0
Serious Infection of Uterus Tubes, or Ovaries Requiring Surgery	1	0
Choriocarcinoma	0	0
Hydatidiform Mole	0	0
Ectopic Pregnancy	0	0
Gonorrhea, Syphilis, or Other Venereal Disease	0	0
Tubal Ligation	1	8
Removal of the Ovaries or Tubes	4	0

* A greater proportion of hysterectomy cases than controls reported this condition, p less than .05.

** One of the people was unsure of the diagnosis.

TABLE III

Frequency Distribution of Gynecologic Symptoms and Conditions
Former Employees of the Specialties Department

	People Formerly in Specialties, n=5
Increasingly or abnormally painful menstrual periods	3
Abnormally heavy bleeding	4
Abnormally prolonged bleeding	2
Abnormally irregular periods	1
Post-menopause bleeding	0
Anemia caused by menstruation	1
Cancer of the cervix	0
Ovarian cyst, non-cancerous	1
Ovarian cancer	0
Endometriosis	1
Endometrial hyperplasia	0
Polyps of the endometrium or uterus	0
Endometrial cancer	0
Other uterine cancer	0
Tuberculosis of the Endometrium	0
Adenomyosis	0
Fibroids	5
Enlarged, tender uterus	1
Tipped uterus	1
Prolapsed uterus	1
Incontinence	0
Serious infection of the uterus, tubes, or ovaries requiring surgery	0
Choriocarcinoma	0
Hydatidiform Mole	0
Ectpic pregnancy	0
Gonorrhea, syphilis, or other venereal disease	0
Tubal ligation	1
Removal of the ovaries or tubes	5
Hysterectomy	5

TABLE IV

Frequency Distribution of Adverse Reproductive Outcomes & Conditions

Current Employees of the Specialties Department

	People w/Hysterectomies, n=6	People w/out Hysterectomies, n=14
Total Pregnancies	17 (x^2=2.8)	49 (x^2=3.5)
Miscarriage	3**	6****
Stillbirth	0	0
Abortion	0	1
Live Births	14 (x^2=2.3)	42 (x^2=3.0)
Birth Defects	1***	1*****
Difficulty Conceiving*	0	0

*"Has there ever been a time when you tried for at least 1 year to have children and were unsuccessful?"

** One person had all 3 miscarriages

*** A "slow learner"

**** One person had 2 of the miscarriages

***** Died after 19 hours

No significant differences were found for any of these outcomes or conditions when comparing the two groups, p greater than .05.

TABLE V

Frequency Distribution of Adverse Reproductive Outcomes & Conditions

	Former Employees of the Specialties Department
	People Formerly in Specialties, n=5 (all with hysterectomies)
Pregnancies	12 (x^2=2.4)
Miscarriage	1
Stillbirth	0
Abortions	1
Live Births	10 (x^2=2.0)
Birth Defect	0
Difficulty Conceiving	1

* "Has there ever been a time when you tried for at least 1 year to have children and were unsuccessful?"

TABLE VI

SPECULATED RISK FACTORS FOR HYSTERECTOMY
Current Employees of the Specialties Department

	People w/Hysterectomy, n=6 (Mean Value + Standard Deviation)	People w/out Hysterectomy, n=14 (Mean Value & Standard Deviation)
Age	46.2 ± 7.4	45.1 ± 7.2
Years at Davis & Geck	16.5 ± 6.0	10.2 ± 6.8
Years in Specialty Dept.	14.0 ± 5.4	8.9 ± 6.8
Proportion of People Who Ever Smoked Regularly	3/6	7/14
Pack-Years for Smokers	26.3 ± 16.5	15.3 ± 13.2

* Those people with a hysterectomy worked more years at Davis & Geck than those without, p less than .05 (one-tailed t-test).

TABLE VII

HYSTERECTOMIES

All Women Employed in Specialties Department
at Time of Survey, n=66

AGE	PREVALENCE OF HYSTERECTOMY*	NO. OF WOMEN FROM SPECIALTIES DEPT.	EXPECTED HYSTERECTOMIES	OBSERVED HYSTERECTOMIES
less than 25	.000	6	0.00	0
25-29	.009	6	0.05	0
30-34	.013	4	0.05	0
35-39	.067	11	0.74	2
40-44	.151	10	1.51	2
45-49	.243	12	2.92	3
50-54	.259	3	0.78	1
55-59	.286	9	2.57	2
60-64	.351	3	1.05	0
Unknown	.151	2	0.30	0
Total		66	9.98	10***

* Using rates obtained from Howe (Reference 9)

** For the two women whose age was unknown, the mean age of the whole group, 42 years, was used.

*** Using the poisson statistic, the probability of finding at least 10 hyster ectomies when 9.98 are expected is equal to .54, or 54%. Thus, there is not a statistically significant excess of hysterectomies within the Specialties Department.