



Center for Occupational

and Environmental Health

COEH Faculty and Associates Assess Health Risks in Semiconductor Industry

The U.S. semiconductor industry prides itself on its attention to worker health and safety. Exposures to chemical and physical agents in plants manufacturing silicon chips for computers are recognized as low, by any standards. So, in the mid-1980s, when a small but striking study by researchers at the University of Massachusetts revealed that women working in the fabrication facilities of a chip-making plant were having a greater number of miscarriages than women in non-fabrication jobs, shock waves rolled through the industry.

The Semiconductor Industry Association (SIA) responded by underwriting an independent, four-year, \$3.5 million national Worker Health Study to learn if, indeed, chip fabrication work was associated with increased risk of miscarriage or spontaneous abortion (SAB). Marc Schenker, COEH program director at Davis, headed the pioneering project, which involved 14 companies in seven states and an original study pool of more than 50,000 workers.

The results of the study, announced last December, confirmed the earlier findings.

In this issue of the newsletter, we describe the study, hear from some of those involved and discuss the industry's follow-up efforts to date.

National Study Confirms Earlier Research

Women Who Make Computer Chips Face Greater Risk of Miscarriage



Employee at work in a semiconductor fabrication room. Source: Sematech.

A four-year study by COEH faculty and associates has confirmed that working in computer chip manufacturing facilities poses a real hazard to the reproductive health of women.

Previous research had pointed to a higher risk of miscarriage for women who manufacture chips than for their co-workers in non-manufacturing positions, but the original study was done in only one semiconductor facility and no one had studied this potential health hazard on a large-scale, national level.

With cooperation from 14 semiconductor companies and about 15,000 employees in seven states, COEH Program Director Marc Schenker and co-investigators at Davis, Berkeley, and the University of Massachusetts Medical Center set out in 1989 to learn if chip fabrication work is associated with increased risk of miscarriage or spontaneous abortion (SAB).

They also hoped to ascertain if risk of miscarriage is associated with specific jobs, exposures, work environments, or other factors. In addition, they surveyed

male and female "fab" and non-"fab" employees to learn how chip-making affects general health and male fertility.

Schenker is professor of medicine and chief of the Division of Occupational/Environmental Medicine and Epidemiology in the Department of Internal Medicine at Davis as well as COEH program director. His co-investigators included James Beaumont, Ellen Gold, William Lasley, Stephen McCurdy, and Steven Samuels of Davis; Brenda Eskenazi and Shanna Swan of Berkeley; and Katharine Hammond of the University of Massachusetts Medical Center. All investigators except Hammond are COEH faculty or affiliates.

Results

The study results, announced last December, showed that:

- Pregnant women working in fabrication facilities were 20 to 40 percent more likely to suffer a miscarriage than women working in non-fabrication jobs.
- Women in "fabs" who reported they were moderately to extremely stressed at work were twice as likely to miscarry

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than women in non-"fab" positions.

- Women involved in chip manufacturing were slightly less likely to become pregnant than their co-workers in non-manufacturing positions during the period of the study follow-up.

- Men and women in manufacturing positions had a slightly elevated reported incidence of respiratory symptoms (nose and throat irritation, wheezing), musculoskeletal problems (hand, wrist, elbow, and forearm pain), dermatitis, and hair loss.

- Male fabrication workers showed no statistically significant difference in fertility from males in non-"fab" positions.

Glycol Ethers Suspected

What did not emerge from the study was a "smoking gun." The researchers were unable to definitively pinpoint a specific cause for the higher incidence of miscarriages, reduced female fertility, and general health problems; however, they did find that women who worked with photoresist/developer solvents had higher rates of SAB that were not accounted for by other risk factors.

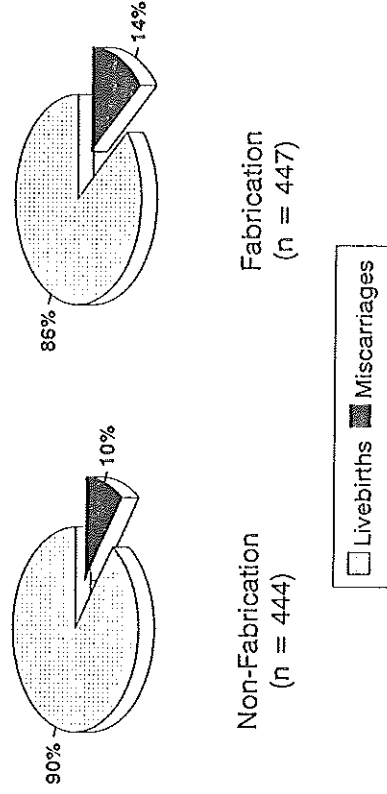
The team also observed a dose-response relationship between the use of photoresist/developer solvents and increased risk of miscarriage; that is, with increased levels of exposure, there was an increased risk of SAB. A dose-response relationship is generally thought to provide strong evidence that what one is seeing may be causal.

Analyses and comparisons with other epidemiologic studies and toxicologic data led the researchers to suggest in their final report to the industry that "the glycol ethers (a group of photolithography chemicals, and, specifically, the ethylene-based glycol ethers used in these processes) are likely causal agents of SAB among women in semiconductor manufacturing."

But the team stopped short of indicting the glycol ethers, because these chemicals were not used alone in semiconductor manufacturing.

"Because exposures were clustered together," the researchers cautioned, "we cannot exclude a possible contribution of other photoresist/developer chemicals or

Miscarriage Rates Among Women In Fabrication And Non-Fabrication Jobs (Historical Component)



solvents to the SAB risk." In addition, they said, a woman's actual risk of miscarriage would depend on her exposure dose and on individual risk factors, such as age and smoking.

While the researchers also observed fluoride exposure during etching to be associated with increased rates of SAB, the association was inconsistent for all fluoride exposures in the study. The researchers said further work is needed to learn more about modes, levels and toxicity of fluoride exposure.

Finally, the team did not find any independent association of miscarriages with exposure to cleaning solvents (acetone, isopropyl alcohol, methanol), dopants (arsenic, antimony, boron,

phosphorus), extremely low frequency magnetic fields, or radiofrequency radiation. However, when researchers looked at different aspects of fertility, they found statistically non-significant suggestions of relationships between work in dopant/thin film processes (where impurities are implanted in the chips to affect their conductive properties), increased menstrual cycle lengths, and reduced rates of conception, which all bear further investigation.

Four-Part Study Design

The study—the most comprehensive of its kind in terms of study population size,

geographic diversity and number of participating companies—was designed in four parts: an *historical* investigation of SABs among current and former women employees aged 18-44; a *prospective* investigation of conception, SABs, and menstrual cycles among current female employees aged 18-44; a *cross-sectional* investigation of the general health of male and female employees and of infertility among male employees, and an *industrial hygiene/exposure assessment* component to characterize exposures in the semiconductor industry and to classify the exposures of individuals participating in the other three parts of the study.

Historical

The historical component sampled 7,269 women, 84 percent of whom completed screening questionnaires on their work and reproductive histories. Of these, 953 women had eligible pregnancies, and 904 (95 percent) completed more detailed interviews. Based on these interviews, the researchers found that women who worked in fabrication facilities while pregnant were 1.45 times as likely to have a miscarriage as those who worked in non-fabrication positions (14 percent adjusted SAB rate for "fab" workers vs. 10 percent for non-"fab").

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SIA Study

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Women who appeared to be at greater risk were those who did photolithography and/or etching. In addition, women in the "fabs" who reported they were extremely stressed at work had a significantly increased risk of SAB (2.18 times as likely to have a miscarriage). The researchers could not identify specific, consistent risk factors that explained this association, saying only that "stress may reflect greater chemical exposure, ergonomic or psycho-social factors."

Prospective

The prospective component corroborated the findings of the historical component. Women aged 18-44 were screened for eligibility, recruited for the study, then followed for six months, during which time they kept daily diaries and collected daily urine

samples that were analyzed for human chorionic gonadotropin to determine conceptions and early fetal losses. This laboratory part of the SAB study, initially considered to be the researchers' most powerful tool, suffered from employee attrition in the course of the study, primarily due to a significant downturn in the industry, which led to lay-offs at some participating companies. The team had expected to enroll twice as many women as actually enrolled. Nonetheless, of the 3,915 women from seven sites in the original sample, 2,639 (76 percent) completed screening. 739 were found eligible, and 408 participated in the follow-up analysis for one month or more.

The researchers found that the adjusted relative risk of miscarriage for women making chips was 1.21, which, although not statistically significant, was similar to the risk found in the historical component. The apparent association with masking (photolithography and etching) held true in the prospective component, but risk was also similarly elevated for women working in the dopant/thin film

group.

The researchers observed fewer pregnancies than originally anticipated (they had calculated an expected pregnancy rate that turned out to be high for this population). Indeed, the prospective component suggested that women in fabrication work, including those who worked with ethylene-based glycol

male "fab" workers as compared to their colleagues in other parts of the plant.

Industrial hygiene/exposure

Investigators involved in this component of the study developed exposure assessment strategies: visited work sites to collect information; conferred with industrial hygienists at the participating companies to develop an overview of the industry, the processes, and the materials being used; and collaborated with the other component investigators by creating exposure categories (types of work, work groups, and workers), taking measurements (air sampling for fluorides), and analyzing data. The research team visited approximately 50 chip manufacturing facilities around the country.

"This was an extremely important investigation in many ways. It was the largest occupational reproductive study ever conducted, and addressed the research questions in a comprehensive, multidisciplinary way. There were many challenges in conducting this unique, nationwide investigation, including communication with a multicultural, multilingual workforce, development of state-of-the-art methods for handling large numbers of biological specimens in an epidemiologic investigation, and creation of a unique industrial hygiene approach to assessing exposures to various chemical, physical and ergonomic exposures in this complex, highly technical industry. I am very proud of the study co-investigators and staff who worked hard and diligently in this effort."

—Marc Schenker

Recommendations

The researchers concluded their report with several recommendations to the industry. They noted that more work is needed to confirm their findings and to evaluate the exposures and processes suggested as risk factors for SAB, with particular attention to women working in etching and photolithography and those handling glycol ethers or other photoresist/developer solvents.

However, they also noted that reasonable health policy would be to reduce exposures as much as possible, even though some areas of uncertainty persisted. In this context, however, Professor Ellen Gold points out that, "Federal worker safety standards are usually set based on acute toxicity, such as respiratory symptoms, rather than on reproductive hazards, which are not life-threatening. It may be that the reproductive system is compromised at much lower levels than are other systems. Looking at reproductive effects may give a more sensitive indication of toxicity at lower exposure levels."

ethers, may have a reduced conception rate compared to those in non-fabrication work.

Cross-sectional

This part of the study used a questionnaire-based survey to identify health problems and specific exposures requiring further investigation. The final sample consisted of 3,175 men and women (51 percent women and 53 percent "fab" employees) at eight sites. In addition to the survey, the team conducted a detailed analysis of the fertility history of male participants.

The researchers found that "fab" workers experienced slightly more upper respiratory and musculoskeletal problems than their non-"fab" counterparts. While this result was not surprising, given the nature of the work involved, the team was surprised—and could not explain—its finding of an increased association of self-reported hair loss. The fertility analysis found no statistically significant evidence of increased infertility among

How SIA Awarded Worker Health Study Grant

What do you do when you want to fund research affecting your own industry, and you need to structure it so that people will believe the results?

This is the question the semiconductor industry faced as it sought more information about possible hazards to pregnant employees working in chip-making facilities.

Federal funding was not a possibility. Compared to other developed countries, the United States devotes a tiny amount of money to studying health in the workplace. The cost of a comprehensive industry study would approach the entire annual extramural research budget of the federal government's National Institute for Occupational Safety and Health (NIOSH).

Would NIOSH conduct the study if the industry provided the funds?

"This is the most important epidemiological study COEH faculty members have ever done. We now know definitively that spontaneous abortions among female employees in clean rooms of one of this nation's largest, most important industries is a real problem for occupational health and safety."

- Robert C. Spear

Ironically, when asked, NIOSH declined, because the agency traditionally deals with management and workers, as represented by unions. The semiconductor industry is essentially non-organized. Instead, the agency provided a list of distinguished researchers who could serve on a Scientific Advisory Panel that would be an intermediary between the industry and a research team, to ensure the objectivity of the work to be done.

Using the NIOSH recommendations, the Semiconductor Industry Association (SIA) selected a five-member panel to solicit and evaluate proposals, monitor the research, and advise the SIA. Chaired

"The power of epidemiological research is in its statistical ability to detect the magnitude of the effect that you want to detect. Its limitation is that it plays out within the constraints of a real world setting, in which individual chemicals are often part of a mixture, and human populations must be protected from exposure to possible hazards. A well conducted study can give us the best evidence possible about the degree to which a population is at risk and how to address that risk...."

"I've found that, when you explain to the public what we can and can't do, people's expectations can be quite realistic. But there are always those who want to find the culprit. In the case of this study, some people want to pin everything on the glycol ethers. The downside to this is that the culprit may be another chemical—or a mixture, or another agent.

While we should reduce exposures to the glycol ethers, it's important to do follow-up studies in all the areas of concern. I would hate to think that a follow-up might be impeded by lack of interest, because of a premature conclusion about one aspect of the study. For example, the role of stress in the increased SAB rate needs to be pursued. Women in the clean rooms have to wear protective clothing, they stand for long hours, their movements and their verbal interaction is severely limited.

They are producing against the clock, and lack control over their activities. If they need to leave, they must completely unsuit and then resuit again. A higher proportion work evening and night shifts. Many are of different ethnic and cultural backgrounds. These factors deserve further consideration."

—Patricia A. Buffler

Defining a Role

As their first task, panel members defined and negotiated the role they would play vis-a-vis the industry and the investigators, drawing up a charter to ensure that the sponsors would not be in direct communication with the researchers and would therefore be unable to influence their work.

The panel designed a request for proposals, then reviewed proposals from investigators at 13 universities and recommended three to the SIA. In January, 1989, Marc Schenker, COEH program director at Davis, and his co-investigators won a \$3.5 million contract for the Worker Health Study.

A New Model

The Scientific Advisory Committee's charter has become a model for private sponsorship of public research. Buffler foresees a growing need for this kind of research: "If we don't find a way to assure that we have adequate (public) funding for large-scale investigations, we will have to find ways in which (privately funded) research can be conducted in a structured setting."

To this end, the dean and her colleagues on the panel have produced a paper, "Private Funding of Public Research, soon to be published in the *Journal of Occupational Medicine*, comparing their model to other approaches.

Industry Response

Within days of receiving the Worker Health Study results, the Semiconductor Industry Association (SIA) launched a worldwide information campaign using a letter from the researchers, video, and presentations to tell employees what was known, what the unanswered questions were, and how the industry was responding.

The SIA, which represents over 60 U.S.-based semiconductor manufacturers, also immediately announced an action plan to provide additional protection for semiconductor workers. The plan called for:

- Continuing to improve procedures and technology to minimize exposure to potentially hazardous chemicals.
- Accelerating efforts to eliminate the use of ethylene-based glycol ethers in manufacturing processes.
- Opening discussions to share information and technology among semiconductor companies to expedite the search for alternative safe chemicals and the elimination of ethylene-based glycol ethers.
- Forming a high level task force that would make specific recommendations to the industry. (The task force is completing its recommendations as we go to press.)

Semiconductor workers have been largely silent about the study results, according to SIA spokesperson Tom Beerman: "To the best of my knowledge, about half a dozen requests for transfer (out of fabrication facilities) have been received since the results were announced—that's out of about 40,000 employees who work in clean rooms."

For the past several months, SIA representatives have briefed a broad spectrum of interested parties about the study, addressing the chief executive officers of its member companies; professional associations; federal and state legislators; officials of the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the California Department of Health Services; chemical manufacturers; semiconductor companies that did not participate in the study; semiconductor companies that are not SIA members, and community groups. "Our member companies—particularly

Liu Heads Occupational Health Clinic



and is seeking to expand services to the business community.

The clinic is gearing up to provide health evaluations of prospective employees, on-site medical surveillance (monitoring the workplace for early signs of exposure to hazards such as lead or asbestos), and occupational health consultations. "We are able to go to the worksite to assist employers in improving their health and safety programs," Liu said.

In addition to such activities as medical surveillance examinations and environmental monitoring, the clinic can now test the fit of respirators quantitatively (comparing concentrations in the workplace air with concentrations in the mask) and conduct screening hearing tests. "We are hoping to expand our audiological services to include making custom-fitted earplugs for hearing protection," Liu said.

With a new director and expanded outreach activities, the clinic will provide new opportunities for research and expand the educational opportunities for students, according to John Balmes, director of the Occupational Medicine Residency Program at San Francisco.

"Diane brings a wealth of training and experience in occupational health to her new position, and she fills a leadership void by becoming the first full-time director the clinic has had in more than a year. I'm delighted with her appointment," Balmes said.

For her part, Liu is excited about her new responsibilities and enthusiastic about her colleagues, many of whom she has known for many years. "The primary focus of my work is clinical and administrative, but I very much enjoy its academic aspects as well," she says, citing the opportunity to teach and to do clinical research.

In her new position, Liu is drawing upon her recent experience as assistant medical director of the Center for Municipal Occupational Safety and Health (CMOSH), which administers occupational health services for the City and County of San Francisco and oversees the Employee Health Services program for San Francisco General. Liu completed a residency in internal

Diane Liu, MD, MPH, has been appointed medical director of COEH's Occupational Health Clinic at San Francisco General Hospital.

Liu is working as part of a team with Occupational Health Nurse Practitioner Mary Spangler, who joined the clinic in November and manages its daily activities, and with Industrial Hygienist Patricia Quinlan.

The multidisciplinary, fee-for-service clinic helps train occupational health residents, occupational health nurse practitioners, and industrial hygienists. Liu is responsible for clinical activities.

Industry Response, continued

those who are members of the SIA Task Force on Worker Health—are working with us to implement the four-part action plan," said Beerman.

Task force members include: Advanced Micro Devices, Allegro Microsystems, Allied Signal, Analog Devices-PMI, Apple Computer, AT&T, Cherry Semiconductor, Digital Equipment Corporation, General Electric, Harris Semiconductor, Hewlett-Packard, IBM, Intel, International Rectifier, LSI Logic, Micron Technology, Motorola, National Semiconductor, Northern Telecom, Philips Semiconductor, Texas Instruments, and VLSI Technology.