

EQUAL PROTECTION FOR SPERM

Men, as well as women, are considered in new approaches to detecting occupational hazards that lead to infertility and birth defects

BY JULIE ANN MILLER

Concern focused on sperm, or rather on their absence, last July when the labor union at a chemical plant investigated a rumor that men in one area of the plant couldn't father children (SN: 9/3/77, p. 151). Traditionally, occupational hazards involving reproduction were thought to be a danger mainly to women. Men, it was believed, should be more worried about developing cancer. Fittingly, in this time of greater sexual equality, studies also have demonstrated an increased risk of cancer in certain women workers and interference with normal reproduction among men (SN: 4/8/78, p. 214).

"Workers have the right to procreate healthy offspring," Eula Bingham, Assistant Secretary of Labor and director of the Occupational Safety and Health Administration, told a recent workshop of the Society of Occupational and Environmental Health. But how can threats to that right be identified? At the four-day meeting in Bethesda, Md., a group of physicians, epidemiologists, biologists, labor union officials and governmental regulators discussed methods for examining reproductive hazards. "The effects on reproduction of chemicals in the environment need to be assessed from the standpoint of both female and male exposure," said Peter F. Infante of the National Institute for Occupational Safety and Health (NIOSH) in his opening remarks.

Among the promising methods for identifying chemicals that interfere with successful reproduction are analyses of sperm, monitoring of spontaneous abortions and questioning of specific populations. In some cases, as with DBCP (dibromochloropropane), chemical workers had such low sperm counts that they were infertile. Donald Whorton of the University of California at Berkeley calls that effect "chemical vasectomy." He told the conference that biopsies of the affected men showed a loss of the testicular cells that produce sperm. The chemical's effect was reversed in some, but not all, of the workers who had been away from DBCP for several years.

Such infertility is not likely to be re-

stricted to that one chemical. Whorton said that researchers are now on the alert for other cases and that NIOSH has preliminary evidence of a high probability of infertility among male workers at an elemental mercury plant.

More frightening to most than the threat of infertility is the possibility of an increased number of birth defects. Because birth defects are relatively rare and the number of exposed workers small, it is difficult to clearly relate abnormalities to occupations.

One approach to detecting chemical harm is to look directly at a sample of sperm. Some change in the sperm might lead to a deformed fetus. Whorton points out that convincing workers to provide a specimen of semen can be difficult and time consuming; still, analyzing sperm is a non-invasive medical procedure.

Researchers are most concerned about changes in the sperm chromosomes, which carry the paternal share of genetic material. Robert Kapp of Hazleton Laboratories in Vienna, Va., a doctoral candidate at George Washington University, uses a fluorescent stain to microscopically identify one chromosome, the tiny Y, in sperm cells. He finds that a few normal-looking sperm have two fluorescent spots, F bodies, which he interprets as two Y chromosomes. Two Y chromosomes could arise in a sperm cell through failure of a replicated Y to separate during cell division.

Kapp believes that a chemical that interferes with the separation of the Y chromosomes may also interfere with separation of the other chromosomes carrying more genetic information. Having an extra Y chromosome does not produce severe abnormalities in a man, but duplicates of other chromosomes cause fetal death or

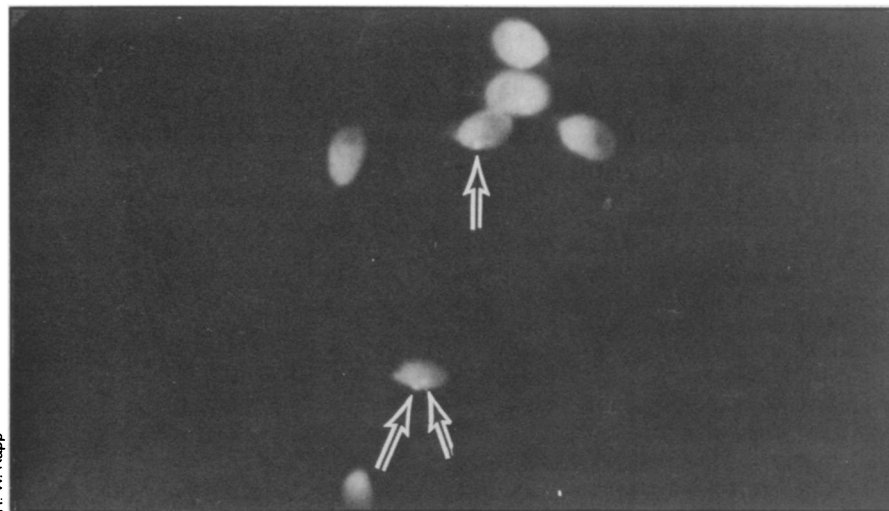
congenital abnormalities, such as Down's syndrome. So far Kapp has found increased levels of sperm with two F bodies in men occupationally exposed to DBCP (but who produce some sperm), patients receiving certain cancer and antibiotic therapies and in physicians performing fluoroscopy therapy.

The exact shape of sperm can signal the state of the genes within it, according to Andrew J. Wyrobek of the Lawrence Livermore Laboratory in Livermore, Calif. Wyrobek works with both human and mouse sperm. He believes that testing chemicals on mice can identify populations of men that should be screened. Wyrobek and colleagues are currently working on an automated technique for counting abnormally shaped sperm.

The shape of the heads of sperm vary little among untreated mice of a single strain. Wyrobek so far has tested the effect of 60 different chemicals. He finds no abnormalities associated with aspirin, vitamin C or glucose. "Those substances will kill the animal before they will produce abnormal sperm," Wyrobek says. However, he does find increased numbers of abnormally shaped sperm among mice treated with benzpyrene, lead acetate, methyl methane sulfate and gamma radiation.

Besides looking directly at the sperm, Wyrobek can mate mice and examine the sperm of their offspring to determine whether the abnormalities are passed on to the progeny. Wyrobek has detected abnormal sperm in a small fraction of the male offspring of mice exposed to X-rays, methyl methane sulfate and lead acetate.

Human sperm have been used to monitor chemicals in two ways. Repeated samples from a single man can provide a "biological dosimeter," measuring changes with exposure, for example in pa-



Human sperm displaying two fluorescent bodies are suspected of genetic abnormality.

tients receiving certain drugs as cancer therapy. The test can also be used on single samples from numerous donors. According to one report, the proportion of abnormally shaped sperm increased in proportion to the amount of lead detected in the blood of 150 workers at a storage battery plant. Another study, not yet repeated, correlates the number of cigarettes smoked daily with the proportion of abnormal sperm in 170 men.

Three lines of evidence convince Wyrobek that the shape of the sperm reflects their genetic content. Among the 60 chemicals tested so far, there is a strong correlation between those that cause abnormal sperm shape and those known to cause mutations in genes. In addition, the tendency to produce abnormal genes is transmitted to offspring.

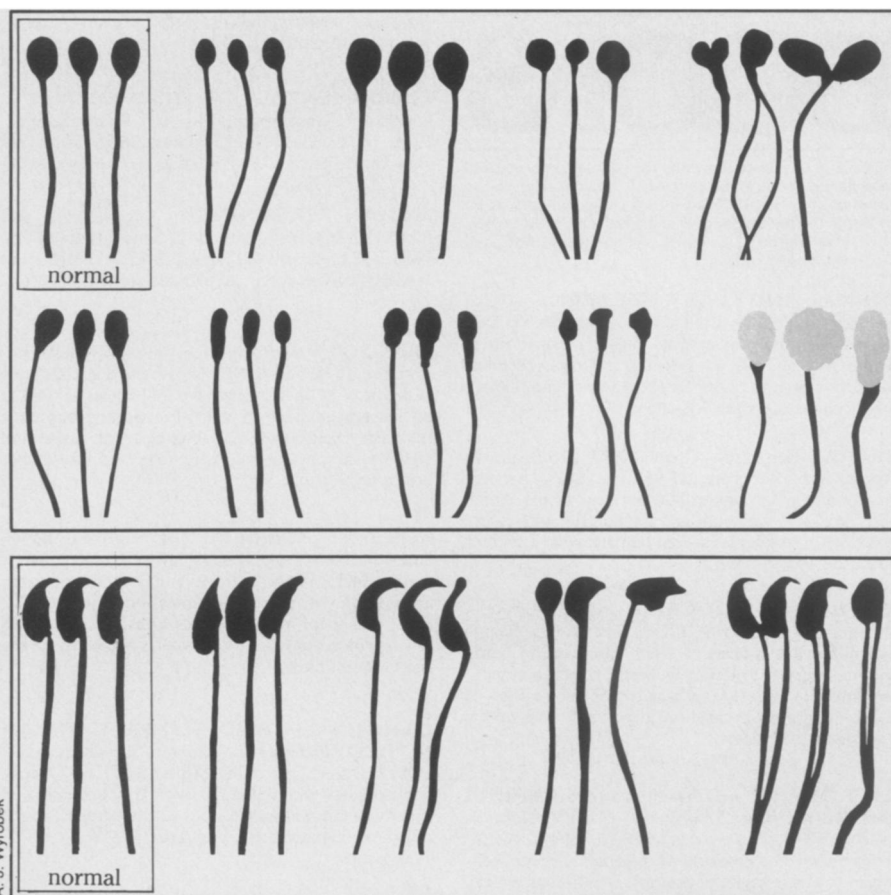
Finally, the shape of the sperm and the proportion of abnormal sperm are constant within a strain of mice, but differ between strains. These characteristics seem to be molded by a variety of dominant and recessive genes, including those that cause other abnormalities such as "quaking" behavior and hydrocephalic polydactyly.

Among men, identical twins have strikingly similar sperm, Wyrobek says. And in one case brothers, who were both infertile, were found to have only abnormal round-headed sperm. Abnormal sperm in men have also been associated with genetic disease, such as cystic fibrosis. "It is likely that many genes control the level of abnormal sperm," Wyrobek says.

Detecting birth defects before they happen is also the goal of Zena Stein of the Columbia University School of Public Health. For three years she has been studying spontaneous abortions (miscarriages) at three New York City hospitals. "Not everyone thinks spontaneous abortions are real reproductive hazards," Stein says. However, she argues that the same factors that favor anomalies in spontaneous abortions favor congenital deformations in live births.

Many birth defects are related to abnormal number or structure of the chromosomes. Chromosome anomalies are 100 times as common in spontaneous abortions as in full-term live births. Therefore, a smaller number of abortions than of births could clearly show an increased rate of abnormalities. Stein says also that it is often possible to examine the aborted fetus more effectively than it is to examine an affected child. Finally, the abortion occurs earlier than the birth, giving a five- to seven-month lead time.

The results so far give a "glimmer" of support for a link between spontaneous abortions and birth defects. Stein detected in November and December 1976 what she calls a "private epidemic" of chromosomal abnormalities. At the three hospitals under observation, the number of spontaneous abortions with one type of abnormality increased noticeably. The ab-



Silhouettes of sperm hold a clue to the state of the genes within. A variety of abnormal shapes have been observed in human sperm (top) and in mice sperm (bottom).

normality, called trisomy, results from fetus cells containing two, instead of one, copy of a maternal or paternal chromosome. When women who had conceived at the same time, but did not abort, reached the time for amniocentesis, there was a slight increase in the number of chromosome abnormalities. Finally, when women of that group reached term there was an unusually high number of trisomy cases. Although no cause appeared for the brief increase in abnormality, Stein believes the correlation supports the possibility of developing studies of spontaneous abortion, amniocentesis and live births for a new strength in monitoring the workplace and the environment.

Questionnaires asking workers about their reproductive histories are also used for identifying occupational hazards. The workshop discussed a 34-page draft of a questionnaire designed by Charlotte Cottrill of NIOSH in Cincinnati intended for use in a number of plants. The questions deal with exposure to potentially toxic conditions, personal habits such as drinking and smoking and the outcomes of pregnancies. In order to spot such chemical infertility agents as DBCP, the questionnaire also asks whether the respondent and spouse ever had trouble conceiving a child.

A mammoth survey performed in the 1950s may give valuable information on the effects of work experience on repro-

duction. Vilma Hunt of the Environmental Protection Agency described her exploratory analyses on data from the Collaborative Perinatal Program. The study included more than 50,000 pregnancies and followed the resultant children with physical, neurological and psychological examinations until their seventh birthdays. "The original records are admirably complete," Hunt says.

Hunt became interested in the study when she discovered that the socioeconomic part of the mothers' questionnaire asked about occupational hazards. It covered exposure to X-rays, radioactive elements, chemicals, heat and animals. The form asked for length of exposure, but not dates. Therefore, from the data there is no way to link the time of the exposure to the time of pregnancy. But Hunt believes it is reasonable to assume that at least part of the exposure included the period before conception. "I am surprised that the questions were asked," she says.

The 1950s study reflects the bias that work experience may impair women's, but not men's, reproductive ability. The data on the fathers' occupations are unreliable, and there was no question asked about the fathers' exposures. "The working women who bear children are only a third of the men who have children," Hunt says. Thus, she agrees with the others that future reproductive studies must give equal concern to the men. □