Men at Risk: Occupation and Male Infertility

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There is accumulating evidence that workplace exposure to toxic substances contributes to male infertility. Men suffering from infertility problems may do well to look at their occupations, where exposure to certain substances may be a contributory factor, if not a direct cause, of infertility.

Most of the studies to date are either case reports or epidemiological studies (population-based, case-control, or cohort studies). Additional, controlled studies need to be done to ascertain the effects of occupational toxins on male infertility. Until then, men and their employers should work together to minimize exposure to these substances.

- Growing evidence links job hazards to male fertility problems
- Men's exposure may lead to reduced sperm counts, and increased risk of miscarriage and birth defects

The study of workplace hazards and their effects on male reproductive function is arguably not new. The first reports were published in the late 1970s. The very first study, published in 1975, suggested that reproductive function might be impaired in workers exposed to lead (1). Two years later, another study observed that male workers exposed to the pesticide dibromochloropropane (DBCP) had a high incidence of infertility associated with markedly reduced sperm count (2). Interest in environmental toxins and male reproduction has also been piqued by recent data demonstrating significant declines in average sperm densities over the past century in men from Western industrialized nations. This is not seen in men from non-Western countries (3).

Since these first reports, interest in the subject has accelerated. To date, however, it has been difficult to single out the role of any one workplace hazard, as occupational exposure conditions tend to be complex, with multiple confounding variables such as smoking, alcohol consumption, diet, and socioeconomic status. Any of these might have adverse effects on male reproductive function (4). This field of study consists mostly of epidemiological data. Although epidemiological study by its nature is unable to prove harm, it does provide compelling data to

employers to minimize exposure to workers and to the individual suffering from infertility to consider lifestyle changes to avoid these toxins.

How the Male Reproductive System Functions

Male reproductive performance is dependent on a number of physiologic functions, all of which need to work interactively for normal reproduction to occur (Fig. 1). The medial basal hypothalamus is responsible for the release of the decapeptide gonadotropin-releasing hormone (GnRH) into the pituitary portal circulation. GnRH stimulates the pituitary synthesis and release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These pituitary glycoproteins in turn regulate testicular function. In response to the pituitary hormones, the testicle produces both sperm and steroid hormones (mainly testosterone). Testosterone is needed for both normal libido and normal sperm production.

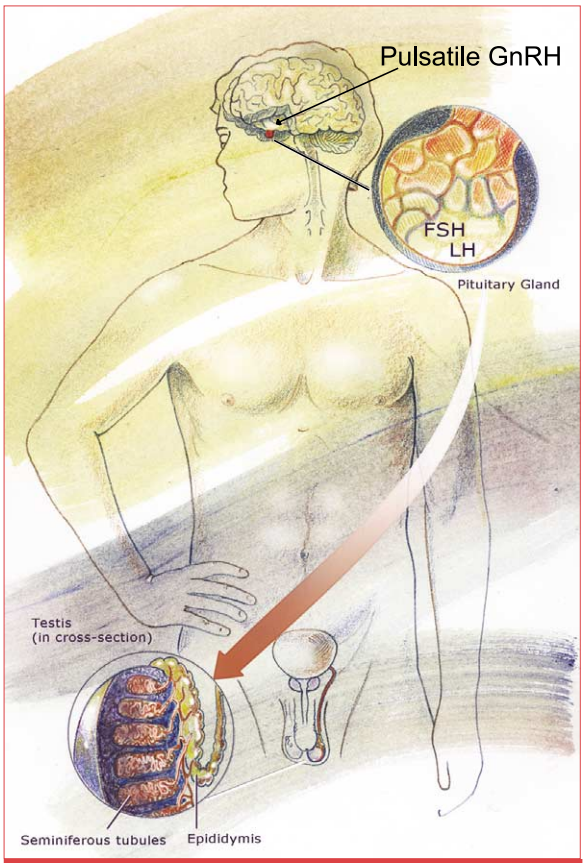

Fig. 1: The male reproductive system.

Sperm production takes about 72 days, during which primordial spermatogonia mature to spermatozoa in the seminiferous tubules of the testicle. Mature spermatozoa are then stored in a long curled tubular system next to the testicle, known as the epididymis, for 2–4 weeks. With ejaculation, spermatazoa move through the vas deferens, which joins up with the urethra at the base of the bladder. There the prostate gland contributes a buffered transport fluid that is responsible for almost all of the fluid volume found in the ejaculate. The seminal vesicles along the vas deferens supply fructose, which is the primary energy source to meet the demands of the actively motile sperm. Finally, an intact central nervous system is also needed for normal erectile and ejaculatory function.

Workplace hazards may adversely affect male reproduction by upsetting the function of any of the above interrelated physiologic functions needed for normal male reproduction.

Types of Studies

The studies done to date have been either case reports or epidemiological studies (population-based, case-control, or cohort studies). Each of these types of studies has both advantages and drawbacks:

Population-based studies are epidemiological studies linking paternal job description or title with reproductive outcomes. These studies can, of course, be performed only in those countries where birth records record parental occupation. It is difficult to reach any clear conclusions on the basis of this sort of study, as they do not have a comparison or control group and have potential confounding variables such as drug abuse, smoking, or alcohol consumption. It is also difficult to pinpoint specific toxin exposures.

Men in different job descriptions may be exposed to similar toxins. For example, fishery workers and crop farmers will both be exposed to pesticides. Furthermore, a job description may describe many different types of activity with different exposure implications. For

Table 1: Summary of Current Scientific Literature on Types of Employment and Their Effects on Male Reproductive Function

Type of employment	Lower sperm parameters	Lower pregnancy rates	Perinatal mortality/morbidity or miscarriage
Agriculture & herbicides	•	•	•
Construction			•
Machinists			•
Military (Vietnam)	•		
Plastic production (styrene and acetone)	•		
Printing industry			•
Service station Mechanics	•		•
Smiths			•
Taxi drivers	•		
Tobacco Processing			•
Welding	•	•	

example, "refuse removal workers" may be used as a job description for cleaning company workers, garbage dump workers, and incinerator employees. However, although all these jobs may be classified as "refuse removal," only incinerator workers are likely to be exposed to ash and smoke products. This confusion resulting from nonspecific job classification often makes it difficult to correctly isolate toxin effects on reproductive outcome using population-based studies. Despite this limitation, population-based studies can offer important clues regarding potential toxins and their effects on reproduction (5).

Case-control studies involve comparing the frequency of toxin exposure in men who have had reproductive problems (cases) to men who have not had reproductive problems (controls). Case-control studies have an advantage in that they can make statistical inferences with relatively small numbers of cases, which is of particular importance when trying to study an uncommon event. However, reporting or recall bias is a particular problem in case-control studies. A man who is suffering from infertility with poor sperm counts will be more apt to recall a work-related toxin exposure than a man who has not suffered any adverse consequences of his occupation. There may also be a higher tendency for men with a reproductive problem to complete and return questionnaires than unaffected men. Despite these limitations, case-control studies offer important information to suggest likely adverse effects that toxins may have on male reproduction.

Cohort studies compare the frequency of reproductive problems in a group of men exposed to workplace toxins versus problems in an unexposed group of men. Cohort studies may be historic (e.g., a questionnaire sent to a group of men who had been exposed as well as to a control population of unexposed men) to determine whether the exposed group might have had fertility problems more often than the unexposed group. A cohort study might also be done prospectively (i.e., a longitudinal study), where a group of men about to start a job involving toxin exposure are compared to a group of men who are about to start a job where they will be unexposed to toxins. Semen analysis could be done for both groups before and some time after the start of employment.

Cohort studies, like case-control and population-based studies, can provide preliminary evidence regarding the effects of toxins but they are unable to provide absolute proof of adverse effects or their absence. Cohort studies can be fraught with difficulties also found in other population comparison studies, such as the many uncontrollable variables between groups. Furthermore, studies requiring the production of a sperm specimen or even the returning of a questionnaire may be subject to participation bias. A population of men exposed to a toxin may

Table 2a: Summary of Current Scientific Literature on Types of Workplace Toxin Exposure and Their Effects on Male Reproductive Function

Type of exposure	Lower sperm parameters	Lower pregnancy rates	Perinatal mortality/morbidity or miscarriage
Aromatic Hydrocarbons	•		•
Carbaryl (sevin)	•		
DBCP	•	•	
Ethylene Dibromide	•	•	
Ethylene glycol Ether	•	•	
Ethylene oxide			•
Impregnants of Wood			•
Lead	•	•	•
Manganese		•	
Metals	•		•
Organic solvents			•
Paint			•
Pesticides	•		
Petrochemicals	•		•
Radiation			•
Rubber Chemicals			•
Solvents	•	•	•
TDA and DNT	•		

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be more likely than unexposed men to submit to tests or to spend the time completing a questionnaire.

Case reports or *case studies* are reports of a single individual or group of workers exposed to a toxic substance who experienced an adverse outcome. Case reports can, on occasion, provide very valuable evidence for a toxic effect. An example is that of a case report of a firearms instructor whose fertility and sperm parameters changed in association with work exposure and serum lead levels (6).

What Should Be Done?

Thus far, it has been difficult to obtain clear evidence on the adverse effects of workplace toxins compared to, for example, a prospective placebo control study of a new medication for the treatment of a disease. However, the available studies provide compelling data showing that many workplace toxins likely have profound adverse effects on human reproduction. Exposure may reduce sperm counts, affect egg quality, increase miscarriage risk, and increase the risk of birth defects. The adverse effects toxins have in animal studies also lend biological plausibility to the argument that they may lead to reproductive problems in people.

As such, it is incumbent on employers and regulators to minimize exposure to the population from those toxins where there is any evidence that they might lower fertility potential.

- Automobile fumes should be properly vented and mechanics mandated to wear protective gloves when handling degreasing agents such as trichloroethylene (7).

- Workers exposed to solvent fumes should be fitted with activated charcoal filtered masks, which reduce the concentration of toxins inhaled by these workers.

Table 2b: Summary of Current Scientific Literature on Types of Workplace Toxin Exposure and Their Effects on Male Reproductive Function

Type of exposure	Lower sperm parameters	Lower pregnancy rates	Perinatal mortality/morbidity or miscarriage
Benzene	•		
Bromine vapor	•	•	
Cadmium	•		
Carbon Disulfide	•		
Chromium	•		
Dibenzofurans	•		
Diesel exhaust	•		
Heat	•	•	
High voltage			•
Hydrocarbons	•		
Kepone	•		
Methylene Chloride	•		
Paint Shop Solvents	•	•	
PCB	•	•	
Perchloroethelyne (dry cleaning)	•	•	
Phthalate esters	•	•	
Radar	•		
Smoking	•	•	
Spray paint			•
Toluene	•		
Vibrations	•		
Xylene	•		

- Pesticides should not be used for cosmetic lawn care.
- Agricultural workers need to be warned with simple clear labeling to minimize exposure to toxins by use of protective clothing, gloves. and careful application techniques—including the routine use of enclosed tractor-covered cabs—during pesticide/herbicide application.
- Environments exposing workers to very high levels of ambient heat need to be properly ventilated or air conditioned (8).
- Government leadership needs to be stringent in its interpretation of the evidence extant in favor of protecting employees from occupational toxins where evidence suggests that workers' ability to have healthy children may be jeopardized.
- Further research is urgently needed to help obtain better evidence-based data on the effects toxins may have on human reproduction and health (9).

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