Your Fertility, Your Environment: Is there a Link?
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Fertility, the ability of people to produce offspring, was a concept formerly applied only to the female. For example, demographers traditionally defined the fertility rate as the average number of live-born children per woman of reproductive age. However, fertility is one of the few measures that reflect the joint health of two individuals, and we have only recently begun to appreciate the extent to which fertility depends on the health and environment of both the male and female partner, as well as the interaction between partners. Males appear to be solely responsible for infertility in about 20% of infertile couples and contribute to infertility in another 30-40% (Thonneau 1991).

Using the demographic definition above, fertility declined 50% worldwide between 1950 and 2000 (Glebatis 1981). Between 1976 and 1998, the percent of women in the United States aged 35-39 who were childless increased from 10.5% to 19.8% (United Nations Populations Information Network 2002). Moreover, the number of annual office visits for infertility increased from 600,000 to 2 million between 1968 and 1990 (Seibel 1997). Recent data from Denmark show a significant decline in teen pregnancies (Jensen 2002) which, the authors argue, reflects a decrease in fecundity. While these data indicate that fertility, at least by the demographers' definition, has declined, they do not answer the following critical question; Are a woman and her partner who desire pregnancy less able to conceive today than a comparable couple of the same age 50 years ago? They also do not address causes of the decline and, in particular, the role of environmental factors which is the focus of this discussion.

These trends undoubtedly reflect, at least in part, changes in non-environmental factors that affect a couple's ability and/or desire to conceive. For example, women and their partners may choose to delay childbearing resulting in decreased fertility when their first pregnancy attempt occurs at an older age. Couples may also make life style choices to decrease family size, or not bear children at all. These non-environmental factors, some of which are listed in Table 1, are very difficult to quantify.

TABLE 1: NON-ENVIRONMENTAL FACTORS THAT MAY INFLUENCE TRENDS IN FERTILITY

- **Women's education and increasing role in the workforce**
- **Availability, affordability, attitudes towards and education concerning contraception**
- **Availability, affordability and attitudes towards assisted reproduction**
- **A woman or couple's decision to remain childless or to limit population size**
- **A woman or couple's decision to remain childless or to limit population size**
- **A woman or couple's decision to delay childbearing**
- **Sexually transmitted diseases**
- **Changing attitudes toward marriage, sexual behavior and family size**
- **Changing attitutes toward elective pregnancy termination**
- **Decreasing age at which premature infants can survive**

All of these factors may vary both geographically and temporally, as well as within ethnic/racial groups. Moreover, they are interrelated in complex ways. Several more useful measures of "fertility potential" are available. Fecundity (or fecundability) has been defined as, "the monthly probability of conception in the absence of contraception outside the gestation period and the temporary sterile period following the termination of a pregnancy" (United Nations Populations Information Network 2002). The National Center for Health Statistics uses a measure of decreased fecundity, "impaired fecundity", which they define as a woman's inability to conceive or bear a child to term. The number of cycles of unprotected intercourse without conception, or "time-to-pregnancy" (TTP) is another useful measure and infertility is often diagnosed when TTP exceed 12 months (or cycles).

Changes in fecundity and impaired fecundity in the US have been examined by comparing responses to the National Survey for Family Growth (NSFG) in 1982, 1988 and 1995 (Chandra 1998). This analysis found increases in impaired fecundity over that time period and the authors suggested that this change was due to more couples voluntarily delaying child-bearing. We questioned that interpretation, however, since the greatest increase in impaired fecundity was seen in women under 25, precisely the age group in which subfecundity, because of delayed childbearing, would be least likely (Swan 1999). These data suggest that, at least in the US, fecundity declined between 1982 and 1995. Limited data have recently become available from the sixth cycle of the NSFG (Ventura 2004). However, data on live birth rates between 1990 and 2000 suggest a reversal of the decline seen in previous reports. This reversal is seen across race/ethnic groups and for most age groups. Data on impaired fecundity, perhaps the most relevant statistics for assessing trends in involuntary subfertility, are not yet available but are expected later in 2004. On balance, the limited data available do not allow us to draw any conclusions about trends in fecundity.

Since it is so difficult to draw conclusions about trends in fecundity and environmental causes, researchers have examined trends in reproductive parameters which are easier to measure in the hope that these will shed light on the larger problem of fecundity. Trends in sperm counts have been the most widely studied to date. This brief discussion of sperm count decline provides a "case study" of how studies of temporal and geographical variation in a reproductive parameter may give us clues to causes of impaired fecundity.

Sperm count and fertility

Evaluation of a man's semen quality is an important component of an infertility workup. How strong is the connection between semen quality and fertility? There is no doubt that severely impaired semen quality impairs fecundity, and there is now new evidence that reduced sperm count, even in apparently healthy men, can affect fertility. For example, two studies (Bonde 1998, Zinaman 1996) found that couples stopping contraception in order to become pregnant had a reduced probability of conceiving in the first six months of trying when sperm concentration was low (less than 40×10^6/ml). However, since fecundity is a function of the fertility and sexual function of the couple, sperm concentration may well decline without an accompanying decrease in fertility on the population level if, for example, female fertility increased over the same period.

A great deal of research has been conducted on factors affecting semen quality in part because of its link to fecundity. Reduced sperm counts can be caused by a range of factors including genetics, infectious agents (e.g. mumps) and anatomic abnormalities. However, environmental causes have been of primary concern since 1992 when a group of Danish researchers concluded that over the average, sperm count in normal men had declined 1% per year during the past 50 years, and postulated that "environmental influences, particularly compounds with 'estrogen-like activity'" may be responsible (Carlsen 1992). This controversial study produced considerable debate and led us to conduct a reanalysis of the 61 studies (Swan 1997). We concluded that, at least statistically, trends differed geographically and while the average sperm count in the US and Europe had declined significantly, there were not sufficient data to draw any conclusions about other areas. This issue is still controversial and is likely to remain so since historical data are necessarily subject to uncertainty and potential bias.

Even if we assume that semen quality has declined, these trend studies do not address the question of whether environmental chemicals can (or have) reduced semen quality. This question was first examined in the workplace, where exposures are usually far higher than those encountered environmentally. There is a large body of literature demonstrating strong relationships between work place exposures and decreases in semen quality and other factors that can affect a couples' fertility. For example, widespread concern was generated in the late 1970's, following reports of sterility and decreased sperm counts in workers exposed to the agricultural nematocide DBCP(Thrupp 1991, Goldsmith 1997, Slutsky 1999). The chlorinated hydrocarbon pesticide chlordecone (kepone) was withdrawn because of its severe effects on semen quality (Faroon 1995). Ethylene dibromide (EDB) was an active component of approximately 100 pesticides. Its use was severely restricted in 1984 due to reduced sperm counts and semen quality (Whorton 1981, Schrader 1988). For a more complete treatment, see Schettler et al Generations at Risk (1999).

More recently, adult exposure to several pollutants at low environmental levels have been linked to reduced semen quality. If these exposures have increased over time, these could, in principal, contribute to the reported declines in sperm concentration. For example, after we saw significantly poorer semen quality in men living in agricultural mid-Missouri compared to men living in urban centers, (Swan 2003a) we examined metabolite levels in the men's urine. We found several (alachlor, atrazine and diazinon particularly) to be linked to poor semen quality (Swan 2003b). A range of other low-level environmental exposures have been linked to impaired semen quality including phthalates (Duty 2003), PCBs and DDT (Hauser 2003), maternal smoking (Jensen 2004), water chlorination by-products (Fenster 2003) and air pollution (Evenson 2004).

Does it follow that men (or couples) exposed to these environmental chemicals have impaired fecundity? Among Danish couples attempting to conceive for the first time, men whose initial sperm concentration was less than 40 x 10^6/ml had significantly reduced fecundability and took longer to conceive (Bonde 1998). In mid-Missouri, sperm concentration of 35% of fertile men fell below 40 x 10^6/ml, a point below which fecundity decreases significantly. Among men living in central Minneapolis, only 19% fell below this cut-off. Since poor semen quality in these men was linked to pesticide exposure, it is plausible -though far from proven- that these chemicals can impair human fecundity.

We cannot, however, conclude that a decrease in sperm count directly implies a decrease in fecundity on a population level. Even if semen quality is declining there may be no net decrease in couple fecundity. For example, if couples trying to conceive are better educated (such as through the use of home kits to detect ovulation) this will tend to increase conception success. Increased female fertility, for example, as a result of the declining incidence of sexually transmitted disease, which has occurred in the United States since 1980 (CDC 2000), will also increase couple fecundity.

Reproductive factors in the female

Measures of female fertility are more difficult to quantify. For example, a measure analogous to sperm count, ovarian follicular number, is extremely difficult to ascertain even with ultrasound. Thus, this endpoint has been rarely studied. However, failure to conceive may be the reflection of a hidden increase of early pregnancy loss. Several studies have examined early loss and it has been estimated to occur in 20% to 70% of pregnancies (Hakim 1995). Since a marker for early loss must be ascertained in urine samples collected soon after conception, this too is logistically difficult and few studies have related this endpoint to environmental exposures. Endometriosis is a fertility-related endpoint that has been examined with respect to some environmental exposures, notably dioxin. However, human data on this association are conflicting. Alterations in menstrual function, such as short follicular phase, may also contribute to impaired fecundity. These studies are also quite difficult since they require prospective collection of daily urine samples and extensive hormonal analysis. For these reasons, there are far fewer studies of environmental causes of impaired female factors than male. However, it should be noted that many environmental agents that have been shown to adversely effect male fertility have also been related to impaired female reproductive function when that has been examined. Notable examples include; cigarette smoke, radiation, lead, ethylene glycol ethers and water chlorination by-products (total trihalomethane).

Factors that may alter a couples' fertility

While we have focused here on environmental exposures, a wide range of environmental, infectious, endocrine, life style and genetic factors may play a role in infertility. These factors may result in a range of clinical endpoints including which can include fetal loss (both subclinical and clinical), menstrual dysfunction, endometriosis, uterine fibroids, and hormonal irregularities. Clearly, a full discussion of all factors and their influence on each of these endpoints is beyond the scope of this brief discussion. However, several general comments may be helpful.

Exposure to factors that can alter fertility may occur at any time from gestation to adulthood. While the fetal period has been shown to be the most sensitive for a range of exposures, an adult attempting conception has no control over these. Adults today carry an enormous body burden of chemicals of which we are likely unaware, since these exposures are "invisible" except by examining levels in human samples (such as blood and urine). In a study led by Mount Sinai School of Medicine in New York, in collaboration with the Environmental Working Group and Commonweal, researchers at two major laboratories found an average of 91 industrial compounds, pollutants, and other chemicals in the blood and urine of nine volunteers, with a total of 167 chemicals found in the group (http://www.ewg.org/reports/bodyburden/). Like most of us, the people tested do not work with chemicals on the job and do not live near an industrial facility.

While it is not possible to provide full toxicological profiles of the chemicals found to be prevalent today, an overview of the contaminants tested and found most frequently in the Mt. Sinai survey may be useful. PCBs, which were used as industrial insulators and lubricants prior to being banned in the US in 1976, persist for decades in the environment and accumulate up the food chain, to man. A recent study (Hauser 2003) found PCBs to be associated with reduced semen quality. There are 210 different dioxins and furans, which are by-products of PVC production, industrial bleaching, and incineration. These chemicals can also persist for decades in the environment and are found in air, water, soil and food. Dioxins are developmental toxicants affecting the developing endocrine (hormone) system. For example, a significant deficit of male babies was reported among couples exposed to high levels of dioxin (Mocarelli 1996). Organochlorine pesticides (such as DDT and chlordane) also accumulate up the food chain to man and have been shown to cause cancer and numerous reproductive effects. There are a range of organophosphate insecticide metabolites, such as breakdown products of chlorpyrifos and malathion which are potent nervous system toxicants found most commonly as residues in food. Metals, including lead, mercury, arsenic and cadmium have long been shown to cause lowered IQ, developmental delays, behavioral disorders and cancer at doses found in the environment. For lead, most exposures are from lead paint. For mercury, most exposures are from canned tuna. For arsenic, most exposures are from arsenic (CCA) treated lumber and contaminated drinking water. For cadmium, sources of exposure include pigments and bakeware. Phthalates, plasticizers found in a wide range of cosmetic and personal care products, have recently been shown to be associated with reduced semen quality (Duty 2003) and in animal models cause birth defects of male reproductive organs.

Unfortunately, we cannot reduce our body burden of past exposures, most of which persist in the body for decades. Work place exposures, which may be avoidable, can be far higher, and it is in those settings that we have learned much of what we know about human reproductive risks. Workers, particularly those attempting to conceive, should be provided with full information on the reproductive risks of the agents with which they are working. If economics permit, it would be prudent for those of reproductive age to avoid occupational exposure to reproductive toxins.

Setting aside fetal and childhood exposures and occupational setting exposures, we are left with exposure to currently used chemicals in the home, the workplace and the surrounding environments. The routes of these exposures (ie water, air, food, skin) are limited. There are steps that one can take to limit exposure via each of these routes. There are several non-governmental organizations that have produced excellent web-based facts sheets for consumers that provide practical information based on good science. These are provided in the Appendix.

What should a concerned couple do in the face of uncertain risks?

The Collaborative For Health and Environment has a check list which recommends limits on certain exposures in our food, air, water and homes. Few of the exposures have been definitively shown to impair fecundity in humans. Nonetheless, it would be prudent for a couple attempting pregnancy to limit their exposure to as many of these as possible. This precautionary action makes sense on several levels. First, while the evidence in humans is absent or weak for many exposures, the animal data is much stronger, and toxicology has traditionally been used as an early step in identifying human risk. Without animal testing we would, for example, have few of the drugs and vaccines we rely on. Second, reducing risk while attempting conception will also limit risk during early fetal development, the most sensitive period, if conception is achieved. Third, the recommendations for decreasing toxic exposures will, at worst, have little effect on health; they are not harmful. Finally, most of the steps to reduce risk are simple and relatively inexpensive.

Appendix

Web-based Resources

Food: Food News, an affiliate of the Environmental Working Group (EWG) has compiled a Shoppers Guide for Pesticide in Produce. The report suggests substituting organic for conventional produce that is consistently contaminated with pesticides and, when organic products are not a choice, to consume fruits and vegetables with consistently low pesticide loads (http://www.foodnews.org/walletguide.php).

Water: The EWG has conducted an extensive survey of drinking water sources by state and compiled the Clean Water Report Card (that will help consumers evaluate the quality of their own drinking water (http://www.ewg.org/reports/reportcard/home.html))

Personal care products: The EWG has conducted an extensive, chemical-by-chemical evaluation of personal care products called Skin Deep (http://www.ewg.org/reports/skindeep).

Fish consumption: A report with a pocket size shopping guide on contaminants in fish, Healthy Fish, Healthy Families has been compiled Physicians for Social Responsibility (http://www.mercuryaction.org/fish). A check list compiled by the Children's Environmental Health Coalition entitled "Protecting Your Baby from Environmental Toxins During Pregnancy" provides a useful summary of recommendations for living a healthy and toxin free life style (http://ecomall.com/greenshopping/checbaby.htm).

General information on fertility and the environment: An excellent overview, Infertility and Related Reproductive Disorders by Ted Schettler includes an excellent discussion of the role of the environment (http://www.protectingourhealth.org/newscience/infertility/2003-04peerreviewinfertility.htm).

The Collaborative for Health and the Environment (CHE) maintains a web page that provides accurate and timely information on infertility (http://www.protectingourhealth.org/newscience/infertility/infertilityknow.htmcurrent) and more general information on environment and health

www.protectingourhealth.org.

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