● PESTICIDES AND MALE FERTILITY

MASCULINITY AT RISK

Sperm counts in healthy men around the world have fallen about 50 percent in the last 50 years. Detailed studies of how sperm counts have changed over time in a particular area show the same pattern, with a few exceptions. Researchers hypothesize that exposure to toxic chemicals may be an important cause of the decline.

In laboratory tests, researchers exposed pregnant or nursing mother rats to certain chemicals found in pesticide products. This exposure disrupted the hormonal balance in their male offspring and limited the development of their sperm-producing cells, resulting in permanently reduced sperm counts.

Over 50 pesticides are known to disrupt sperm production or male hormones. Some of these pesticides are among the most commonly-used pesticides in the U.S. in both agricultural and household situations. About 200 million pounds of sperm-damaging pesticides are used in agriculture every year, and over half a billion applications of these same pesticides are made in our homes and gardens.

Chemicals that can have so dramatic an effect on our physiology do not belong on our farms, in our communities, or in our homes.

BY CAROLINE COX

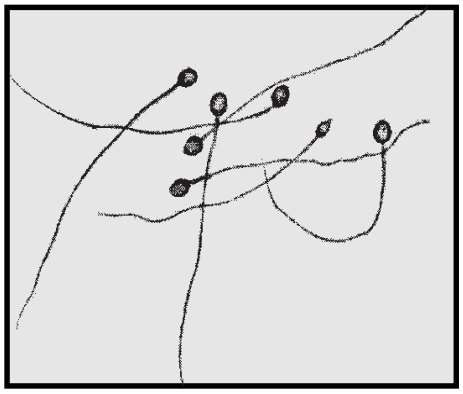
"No New Dads in the Plant,"[1] screams the headline. "The men noticed it first, swapping stories over lunch," continues the article. "None had fathered children lately." The year was 1977, and the men manufactured a pesticide commonly known as DBCP in the central California town of Lathrop. "I started looking around and there weren't any children being born," said a union steward. So begins one of the first chapters in the story of how pesticides impact male fertility.

Since 1977, the story has grown. Not only have scientists collected evidence that human sperm production has declined over the last half century, but the list of pesticides known to disrupt sperm production or male hormones continues to lengthen.

Falling Sperm Counts

In 1992, when four Danish scientists published a study suggesting that sperm counts in men worldwide had declined about 50 percent since 1940,[2] the story made headline news. Sperm are a man's immediate and personal connection to the future of our species, and the disappearance of half of this connection is hard to ignore. "Every man in this room," a wildlife biologist told a hearing before a subcommittee of the U.S. House of Representatives, "is half the man his grandfather was."[3] His audience listened.

This study, the first widely publicized study of trends in human sperm counts in the last half-century, was authored by research fellow Elisabeth Carlsen and a team of Danish scientists.[2] Carlsen and her colleagues analyzed the results of over 60 studies of sperm counts published between 1938 and 1991 with what they called a "meta-analysis," a statistical analysis that linked results of a large number of independent studies. Using a model which assumed that sperm counts changed over time in a linear way, the results of the meta-analysis indicated average sperm counts declined from 113 million per milliliter (ml) of semen to 66 million per ml during the half century for which they had data. (See Figure 1.) The studies came from around the world,



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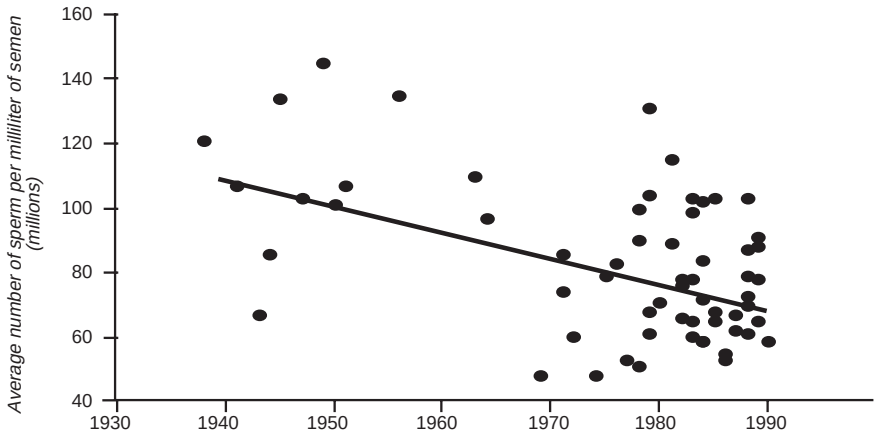
Caroline Cox is JPR's editor.

Figure 1
Decline in Average Sperm Counts Since 1938



Source: Carlsen, E., et al. 1992. Evidence for decreasing quality of semen during the past 50 years. *Brit. Med. J.* 305:609-613.

Danish researchers combined the results of 61 studies from around the world to show that average sperm counts had dropped about 50 percent in the last 50 years.

with about half from in the U.S. The results had truly profound implications: were such a decline to continue, the human race would be unable to reproduce beginning sometime in the next century.

Supporting Evidence

Since Carlsen's study was published, three other studies have found similar declines in sperm counts in smaller groups of men. Researchers at the University Hospital in Ghent, Belgium, found that counts among their sperm donors had declined about 10 million per ml between 1977 and 1994.[4] At Edinburgh, Scotland's Centre for Reproductive Biology, Stewart Irvine found that median sperm counts among its sperm donors had declined about 40 percent when he compared men born in the 1940s with men born in the late 1960s.[5] At a sperm bank in Paris, France, mean sperm counts among donors declined by about 2 percent per year from 1973 to 1992, for a total decline of 32 percent.[6]

Older studies show a similar pattern: sperm counts in Washington D.C. dropped about 25 percent during the 1980s[7] and sperm counts in Denmark dropped about 25 percent between 1952 and 1972.[8]

Perhaps of greater concern, these studies found that other measures of sperm quality also showed problems; both the amount of semen produced and the vigor of the sperm declined. Carlsen's study found that semen volume decreased about 20 percent. In addition, the proportion of men with sperm counts below 20 million per ml (sperm counts this low are referred to as "subfertile"[2]) tripled. (See Figure 2.) The Belgian study found that both the proportion of abnormal sperm and their mobility decreased during the last 20 years.[4] The French study had similar, and just as unsettling, results.[6]

Particularly telling were comments made by Dr. Pierre Jouannet, one of the scientists involved in the French study. "We always had the idea that there was no decline in sperm characteristics,"[9] he explained. In fact, he and his colleagues began the study because they believed it would overturn Carlsen's hypothesis of a "general decline in the quality and quantity of sperm,— at least, in Paris."[9] The results, showing just the opposite, astonished everyone involved.

Again, older studies show similar results. The Danish study mentioned above found that between 1952 and 1972 the proportion of abnormal sperm increased (from 26 percent to 45 percent) and sperm movement decreased.[8] In Oslo, Norway, the proportion of abnormal sperm rose from 40 percent to 59 percent between 1966 and 1986.[10]

Further evidence of a large-scale problem comes from studies of other male reproductive disorders. The incidence of testicular cancer has increased as much as 3 or 4 times since the 1940s. The incidence of undescended testes and other anatomical abnormalities of male genitals also seems to have increased.[11]

These results, not surprisingly, have not been accepted uncritically. Several researchers felt Carlsen's results could be a statistical artifact, or caused by changes in sperm counting equipment.[12-14] A team of researchers, most of whom were employed by Dow Chemical Company, pointed out that the data used by Carlsen and her coworkers could be analyzed with different statistical models.[15] The three models that seemed to fit the data best showed a 50 percent decline around 1965, but a constant or slightly increasing sperm count in the years since 1970.

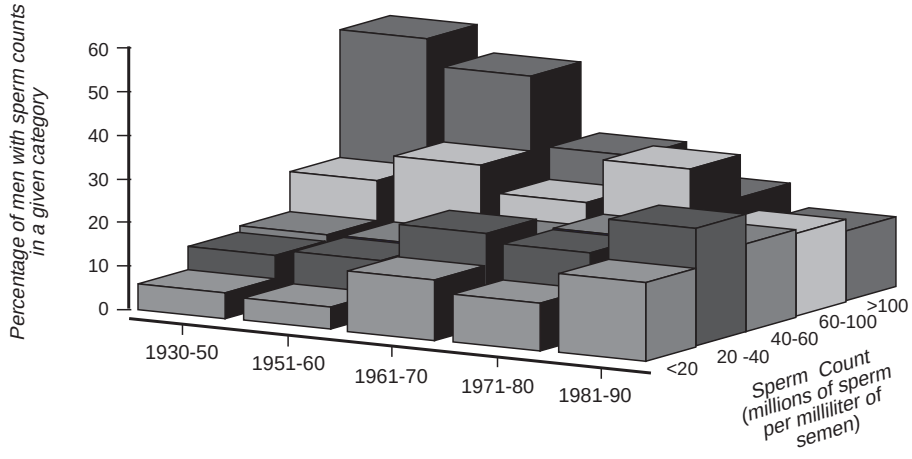
In addition, a recent analysis of sperm counts from three U.S. cities (New York, New York; Roseville, Minnesota; and Los Angeles, California) indicated that sperm counts in those cities had not declined in the last twenty-five years.[16] A study from southern France found no changes between 1977 and 1992.[17] A study of Seattle-area college students found similar results.[18]

Sperm counts vary enormously between countries or regions, between individual men, and even between counts on the same men. Therefore it is not surprising that not all analyses of sperm counts find the same patterns. Whether the decline in sperm counts observed by Carlsen and others is in fact world wide, or whether it includes only certain geographical areas, the overall conclusion is clear: we should act now to protect our reproductive health.

Searching for Causes

Studies of sperm counts over time leave a critical question unanswered. What could account for a precipitous decline in sperm production by otherwise healthy men? Carlsen suggested that environmental causes

Figure 2
Trends in the Distribution of Sperm Counts Since 1938



Source: Carlsen, E., et al. 1992. Evidence for decreasing quality of semen during the past 50 years. *Brit. Med. J.* 305:609-613.

In the last 50 years, the percentage of men with low sperm counts has tripled, while the percentage of men with high sperm counts has declined by a factor of three.

were likely, particularly those toxins that could affect human hormone systems.[2] Richard Sharpe, a research physiologist in Edinburgh, Scotland, developed a more specific hypothesis,[19] and suggested that the decline "is the result of endocrine changes in fetal/prepubertal life [prior to birth or during childhood]."[20]

This hypothesis paints a particularly chilling picture. The endocrine system is made up of the glands and hormones (chemical messengers) that regulate growth, development, behavior, and sexuality. Sharpe hypothesized that this complex system might be disrupted before birth or during childhood by substances acting like natural hormones. The result is a permanent impairment of the reproductive system.

In particular, he hypothesized that hormone disruption at a sensitive time in development could block the development of Sertoli cells, cells within the testes that "nurse" sperm cells as they develop. The number of Sertoli cells sets a cap on the number of sperm which a man is able to produce; therefore a chemical exposure that blocked hormones involved with Sertoli cell development would irreversibly limit sperm production.

The hormones Sharpe thought might be important in determining adult sperm production are follicle-stimulating hormone (FSH) and estrogens. Like most hormones, these have multiple functions in our bodies. Their relevance to sperm production is that FSH in juvenile mammals promotes multiplication of the Sertoli cells. Without enough FSH, fewer Sertoli cells are produced. Levels of FSH are regulated by estrogens; higher levels of estrogen result in lower levels of FSH. So Sharpe hypothesized that synthetic chemicals acting like estrogens might lower levels of FSH, resulting in fewer Sertoli cells and permanently decreased sperm production.

A laboratory test of this hypothesis has been completed. Sharpe and his colleagues studied mother rats who drank water contaminated with two synthetic chemicals, octyl phenol and butyl benzyl phthalate, that are known to act like estrogens.[21] The rats used in the study were pregnant and nursing; the study spanned the interval when their male offspring would be developing Sertoli cells. The results fit Sharpe's hypothesis perfectly: sperm production was reduced (10 to 20 percent) in the offspring of the rats drinking contaminated water and the number of Sertoli cells (as estimated by testes size) was reduced.

The development and growth of the male reproductive system is obviously a complex process. It is therefore not surprising that synthetic chemicals might effect male fertility in more than one way. Earl Gray, a toxicologist with the U.S. Environmental Protection Agency, studied how dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin) exposure of mothers affects sperm production in their male offspring.[22] In both rats and hamsters, a single small exposure (1-2 micrograms per kilogram of body weight) during a sensitive stage of pregnancy resulted in permanent decreases of up to 60 percent in the sperm count of male offspring. Dioxin likely causes this decrease in a completely different manner than the mechanism demonstrated by Sharpe; it appears to affect growth factors rather than involving estrogens.

The Link with Pesticides

All three of the chemicals discussed above are found in pesticide products. Octyl phenol and butyl benzyl phthalate are both used as "inert" ingredients, ingredients used in a pesticide product to make it more efficient or easier to use. Dioxin is a contaminant of at least one currently-used pesticide, the herbicide 2,4-D. This connection leads to several other questions. Are there other pesticides that adversely affect sperm? Has the use of pesticides contributed to the decline in sperm counts? Three different kinds of evidence point to pesticides as part of the problem facing men today:

• Several organochlorine pesticides have had dramatic impacts on male fertility. In 1975, a worker from a chemical factory in Hopewell, Virgina visited his family physician for help with persistent headaches, tremors and irritability. Further investigations showed that he, and his fellow workers, were contaminated with chlordecone, an insecticide made at the Hopewell factory, and that only one quarter of the workers at the plant had normal sperm counts. The sperm produced by these workers also did not swim as well as normal sperm. The workers' sperm counts increased over the next five years as medications removed chlordecone from their body tissues.[23]

Dibromochloropropane (DBCP), a soil fumigant, became notorious in the late 1970s because of its ability to reduce or

eliminate sperm production in exposed workers. A 17-year follow-up study of 15 exposed workers found that recovery had occurred in only 6 of them.[24] Workers who were able to father children had mostly girls; less than 20 percent of the children born to men with the lowest sperm counts were sons.[24] In laboratory tests, exposure of pregnant rats to DBCP caused small and abnormal testes in their male offspring.[25]

The story of how a pesticide as toxic as DBCP became widely used, both in the U.S. and abroad, is basically a story of corporate greed. The first toxicology tests on DBCP were done in 1954 and 1955. Even at the lowest doses tested, DBCP caused damage to testes. Shell and Dow Chemical Companies, manufacturers of DBCP, estimated a "safe" exposure level for workers exposed to DBCP, but it was not based on any actual data. When the researchers who had done the toxicology tests produced a product data summary to give customers, Shell advised them to understate hazards and exclude some toxic effects. The manufacturer convinced the U.S. Department of Agriculture to require only mild safety warnings on the labels of DBCP products.[26]

• Over 50 currently used pesticides have caused problems related to male fertility in laboratory or clinical tests. Some of these pesticides are among the most commonly used pesticides in the U.S. (See Table 1 for a complete list.) Eight out of the 25 pesticides most extensively used in U.S. agriculture[27] have adversely affected sperm production or the functioning of sex hormones in laboratory animals or humans. Estimated annual use of these chemicals totals nearly 200 million pounds, about 25 percent of total agricultural pesticide use. Seven out of the top ten pesticides used in commercial and industrial situations[27] have similar effects; their use accounts for almost 80 percent of this kind of pesticide use. Similar effects have also been shown by 8 out of the 25 pesticides most commonly used in American households.[28] We make an astonishing five hundred million applications of these chemicals in our homes every year.

• Pesticide exposure is associated with infertility. Large-scale studies assessing pesticide exposure and its relationship to infertility have not been done. However, several small studies have demonstrated this relationship. Patients treated at Vienna, Austria's Institute of Sterility Treatment, because they produced little sperm or sperm of low quality, were ten times as likely to work in agriculture as those referred to the clinic for other reasons.[29] In the Netherlands, wives of farmers who applied pesticides took longer to become pregnant, and became pregnant less often, than wives of farmers with less pesticide exposure.[30]

It's Time to Take a Stand

Precaution and prevention must be our watchwords as we respond to the new research regarding declines in sperm production. Sperm are "canaries in the coal mine" that help us begin to understand the many effects that pesticides can have on our health and the health of the wildlife around us. Take the information in this article to the people who make pesticide use decisions in your community, in your state, and in our country. Talk to your school board, your city councilors, your county commissioners, your state legislators, your representative, or your senator. Tell them that for your own health and the health of future generations of both people and wildlife we need to promote alternatives to sperm-damaging pesticides as aggressively as the chemicals themselves have been promoted. Tell them that chemicals having so dramatic an effect on our physiology do not belong in our communities. After all, it's our future.

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Table 1
Currently-used Pesticides Linked to Male Fertility Problems

Pesticide	Type of Hazard	Source
Organophosphate and carbamate Insecticides		
acephate	increased proportion of abnormal sperm in mice	1
azinphos-methyl	atrophied, small, or abnormally shaped testes in birds	2
carbaryl	increased proportion of abnormal sperm in exposed workers, reduced sperm motility (ability to move) in rats	3,4
carbofuran	decreased libido (sexual drive) and sperm number in rabbits, decreased number and motility of sperm in rats	5,6
chlorpyrifos	damage to semen-producing structures in testes in rats, undescended testicles in boys exposed prenatally	7,8
diazinon	atrophied testes, arrested sperm production in dogs	9
dimethoate	decreased sperm number and libido, increased proportion of dead or abnormal sperm in rabbits	10
disulfoton	decreased percentage of "sperm-positive" females in multi-generation rat study	11
fenitrothion	arrested or delayed sperm production in fish	12
malathion	decreased testes weight and activity of testicular enzymes in rats (not completely reversible)	13
methyl parathion	increased proportion of abnormal sperm in rats	14
methomyl	increased proportion of abnormal sperm in mice	15
parathion	inhibited binding of testosterone to its receptor proteins, reduced ability of sperm to fertilize eggs in mice	16,17
phorate	atrophied Leydig (testosterone-producing) cells in gerbils	18
phosphamidon	reduced testes weight in rats, increased proportion of abnormal sperm in mice	19,20
profenofos	decreased sperm number and motility	21
propetamphos	increased proportion of abnormal sperm in mice	22
Synthetic pyrethroid insecticides		
cypermethrin	increased proportion of abnormal sperm in mice	23
deltamethrin	decreased sperm number and libido in rabbits, increased proportion of dead or abnormal sperm in mice	10,24
fenvalerate	increased proportion of abnormal sperm in rats	25
fluvalinate	binds to sex hormone receptors in human genital skin and blood cells	26
d-phenothrin	binds to sex hormone receptors in human genital skin and blood cells	26
permethrin	binds to sex hormone receptors in human genital skin and blood cells	26
resmethrin	binds to sex hormone receptors in human genital skin and blood cells	26
tetramethrin	increased testicular tumors in rats	27
Organochlorine insecticides		
endosulfan	profound sex hormone imbalance in genital organs of male rats	28
	decreased sperm number, increased proportion of abnormal sperm in mice	29
lindane	atrophied testes, decreased sperm production, decreased testes weight	30,31
methoxychlor	decreased sperm number, delayed puberty, abnormal mating behavior in rats	32,33
Other insecticides		
abamectin	increased proportion of abnormal sperm in mice	34
boric acid	increased proportion of abnormal sperm, decreased sperm number and motility in mice	35
Fungicides		
benomyl	decreased testes weight, decreased sperm number, and degeneration of testes in rats	36,37
carbendazim	increased proportion of abnormal sperm, decreased sperm number, some irreversible infertility in rats	38,39
copper oxychloride	atrophied testes, arrested sperm production in chickens	40
copper sulfate	atrophied testes, arrested sperm production in chickens	40
ferbam	increased proportion of abnormal sperm in mice	41
hexaconazole	increased tumors in Leydig (testosterone-producing) cells in rats	27
iprodione	increased testicular tumors in rats	27
mancozeb	increased proportion of abnormal sperm in mice	42
thiram	increased proportion of abnormal sperm in mice	42
vinclozolin	prenatal exposure caused abnormal penis anatomy and abnormal ejaculations in rats	43
ziram	increased proportion of abnormal sperm in mice	42
Herbicides		
asulam	reduced testes weight in dogs	44
atrazine	interferes with testosterone (sex hormone) metabolism and binding in rats	45
benefin	decreased fertility of male rats	46
2,4-D	decreased sperm number and motility, increased proportion of abnormal sperm in exposed farmers	47
	inhibited DNA (genetic material) synthesis in testes of rats	48
	contaminated with 2,3,7,8-TCDD which reduces sperm number in prenatally exposed rats	49,50
glyphosate	decreased sperm number in rats	51
	decreased sperm number and libido, increased proportions of dead and abnormal sperm in rabbits	5
linuron	atrophied testes, decreased sperm number in rats	52
MCPP	decreased synthesis of DNA (genetic material) in testes of mice	48
paraquat	increased proportion of abnormal sperm	53
prometryn	interferes with testosterone (sex hormone) metabolism in rats	45
pronamide	increased testicular tumors in rats, with some effects on the concentration of sex hormones	54
simazine	atrophied testes in sheep	55
sulfometuron methyl	atrophied and degenerated testes in dogs	56,57
Other pesticides		
chromium	decreased sperm number, increased proportion of abnormal sperm in mice	58
methyl bromide	degeneration of testes in rats and mice	59
paclobutrazol	increased tumors in Leydig (testosterone-producing) cells in rats	27

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