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Occupation and semen parameters in a cohort of fertile men

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Abstract

Objective: We examined associations between occupation and semen parameters in demonstrably fertile men in the Study for Future Families (SFF).

Methods: Associations of occupation and workplace exposures with semen volume, sperm concentration, motility, and morphology were assessed using generalized linear modeling.

Results: Lower sperm concentration and motility were seen in installation, maintenance, and repair occupations. Higher exposure to lead, and to other toxicants, was seen in occupations with lower mean sperm concentrations (for lead, prevalence ratio 4.1; pesticides/insecticides 1.6; solvents 1.4). Working with lead for >3 months was associated with lower sperm concentration, as was lead exposure outside of work.

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Ethics Approval: The present study was considered as exempt from human subjects protection approval by the Icahn School of Medicine at Mount Sinai as it used only extant de-identified data obtained in the original study. Institutional Review Board (IRB) approval from all SFF-participating centers was previously obtained for data collection for the original SFF study and all participants signed informed consent.

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Conclusions: We found evidence in demonstrably fertile men for reduced sperm quality with lead, pesticide/herbicide and solvent exposure. These results may identify occupations where protective measures against male reproductive toxicity might be warranted.

Keywords

infertility; occupational exposures; occupational reproductive hazards

INTRODUCTION

Male reproductive dysfunction remains an important health problem with limited understanding of its etiology. Half of the cases occurring within the 10 to 15% of couples affected by infertility in the US are estimated to arise from an identifiable male factor, while as many as a quarter of unexplained cases may arise through an unidentified or occult male exposure or characteristic [1]. Although a number of specific workplace exposures increase male reproductive dysfunction, investigations of occupational etiologies have usually taken place in response to clear cases of infertility arising from exposure to a single defined reproductive toxicant, such as lead or dibromochloropropane (DBCP), or in worker cohorts with high, distinct exposures, such as pesticide applicators. Assessment of demonstrably infertile male workers with a broader range of exposures has proven less successful in delineating other possible exposures that may contribute to male reproductive dysfunction [2, 3]. A large case-control study drawn from men in infertility clinics found no association of male infertility with exposure to shift work, metal fumes, electromagnetic fields, solvents, lead, paint, pesticides, work-related stress, or vibration, and indicated protective associations with workplace radiation and video display unit exposures. [3] This latter report appears problematic, since some of these exposures, including lead and radiation, are known male fertility hazards. Manual work was identified as a risk factor for poor semen quality, independent of other lifestyle factors. [4]. Methodologic considerations highlight the difficulty of examining work-related contributors to male infertility and subfertility, including accurate exposure assessment and the difficulty of determining contributory factors specific to the male partner. Importantly, male outcomes have been most often dichotomized as ‘infertile’ versus not, which may reduce the ability to observe more subtle consequences of male occupation on reproductive capacity. Occupational exposures may affect male fertility through several distinct mechanisms (e.g., impaired Sertoli cell function, decreased androgenic stimulation); when these toxicity pathways are aggregated into a single construct of ‘infertility,’ associations linked to a particular pathway may be missed in that broad definition of outcome. Although the association of reduced fertility with male factors such as sperm count and concentration can be quite variable [3, 5, 6], it may be useful to evaluate the role of occupation and its association with male semen parameters. Increases in recent decades in symptomatic and asymptomatic low testosterone and androgen insufficiency, as well as in testicular cancer, suggest additionally that broader environmental exposures (which can include occupation) may be implicated, since genetic or heritable patterns would be unlikely to arise as abruptly as has been recorded. [7]

We report here on analyses of male reproductive parameters, occupational data, and relevant covariates collected by the multi-center US Study for Future Families (SFF) in 2000–

2002. Our principal objective was to examine the associations between semen quality and occupation, extending any findings to the potential for exposure to male reproductive toxicants within those occupations. SFF data provide a novel approach to questions of male semen quality, and offer several opportunities to study these associations. Semen parameters were obtained from a sample of men who had recently conceived a child, which eliminates broad female and male ‘infertility’ diagnoses as a biasing factor in study participants.

METHODS

The SFF is an NIEHS-funded prospective study designed to examine semen quality in five US cities in 2000–2002. Women and their partners were recruited from prenatal clinics affiliated with university hospitals in Los Angeles (Harbor-UCLA and Cedars-Sinai Medical Centers); Minneapolis (University of Minnesota Health Center); Columbia, MO (University Physicians Medical Group); Iowa City (University of Iowa Hospitals and Clinics) and New York (Icahn School of Medicine at Mount Sinai). Detailed study methods have been published [8, 9]. Couples were eligible unless: the woman or her partner was < 18 years of age; the pregnancy was medically assisted; either partner did not read or speak Spanish or English; the father was unavailable or unknown; the couple did not plan to stay in the area; the pregnancy was medically threatened; or either partner was incompetent or a prisoner. Of those who volunteered for the study, 945 couples were initially enrolled in the study and provided questionnaire data for both partners. Of these, 148 (16%) men who were enrolled declined to give a semen sample. Another 34 men (4%) who had very short or very long abstinence times were also excluded. As a result, there were 763 couples, or 81% of the initial enrollees, in the final study cohort. Institutional Review Board (IRB) approval from all centers was obtained for data collection for the original SFF study and all participants signed informed consent. The present study was considered as exempt from human subjects protection approval by the IRB of the Icahn School of Medicine at Mount Sinai, as it used only extant de-identified data obtained in the original study.

Questionnaires administered to the pregnant woman and her partner on admission into the study included data on occupation, work and home exposures, race/ethnicity, personal habits, and reproductive and other medical history. Occupational data collected included both partners’ occupation and industry held at the time of conception, a series of questions on current and past exposures to lead, other metals, pesticides/herbicides/fungicides, solvents and degreasers, photographic chemicals, radioactive materials, and X-rays, and on work environment, including long hours, shiftwork, and heat exposure. Hobbies and other outside activities involving the above materials were also sought. SFF participants’ job and industry were mapped to Standard Occupational Classification (SOC-O*NET) codes [10] by the project’s data analyst at the time of data coding.

Semen samples were obtained from all male participants. Men were requested to observe a 2–5 day abstinence period and then provide semen samples by masturbation at the study clinics. Almost all samples (95%) were analyzed within 45 min of collection. Most men (approximately 85%) provided two samples, an average of 24 days apart. Semen volume was measured by both weighing and pipetted volume, and sperm concentration was determined using a haemocytometer (first semen sample only) and μ-cell disposable counting chamber (for both samples if two were provided). For purposes of this analysis, we report semen parameters for men measured by the first semen specimen, using volume determined by weight, sperm concentration determined by haemocytometer, and sperm motility and morphology by using WHO 1999 criteria [11]. To assure consistency in semen analysis methods across sites, the study's central andrology laboratory at the University of California, Davis trained all lab technicians and instrumentation was standardized [12]. Proficiency testing and quarterly quality control testing was performed throughout the study period [13].

For occupational analyses, participant data were aggregated by 3-digit SOC occupational group. To create a referent group that was considered *a priori* unexposed to known male reproductive toxicants, participants who were in office-based jobs were aggregated into a single occupational group titled 'office workers'. This category comprised participants with SOC codes classifying them in executive and managerial, financial, legal, secretarial, and office administrative occupations.

Participants in SFF were asked to report their occupational exposures to specific materials as *current* (within the past three months) and also whether they occurred in the past (earlier than three months before the survey). These responses, encompassing exposures to: a) lead; b) solvents and degreasers; c) pesticides, herbicides, or fungicides; and d) radioactive materials or X-rays, were aggregated for analyses in two ways. Those reporting that exposures occurred *either* currently or in the past were classified as 'ever-exposed' while those with neither were considered 'never-exposed.' In additional analyses to evaluate the effect at the time of conception of more prolonged exposures, participants who endorse *both* current and past exposures were coded as having 'ongoing' exposure, while those with exposures for only the past three months were coded as 'current-only' exposed. The referent groups for both of these exposure classifications were those who reported neither current nor past exposure to the specific toxicant ('never-exposed' as outlined above).

To examine occupational physical activity levels, matrices derived from the Occupational Information Resource Center (O*NET) were used to categorize subjects' exposures. The O*NET publishes measures of occupational descriptors based upon survey data from workers on skills, generalized work activities, work context, and knowledge [O*NET Resource14, 15]. Using a modification of the scoring method of Mamelle and Munoz [16] an aggregate score was compiled by assigning one point for each of the following factors scoring above the median on the O*NET 5-point scale: frequent walking or running at work, handling and moving objects, bending and twisting the body, climbing (ladders/scaffolds), exposure to hazardous conditions, and exposure to very hot or cold environments. Participants with scores of 0 or 1 were considered as having low work physical activity and used as referents; those scoring 2–3 were classified as medium, and 4 and above as high.

Data on experiences or exposures with other known or potential effects on semen parameters were obtained from the SFF dataset. Covariates included in final models included men's age, body-mass index (BMI), and duration of abstinence time before the sample was provided, all continuous variables. Dichotomous variables included in analyses were current tobacco smoking, recent drug use, a history of sexually-transmitted disease, and whether the participant had a recent fever (within the past 3 months).

Initial analyses examined frequencies of semen parameters, demographic variables, occupation, and exposures. For outcomes with continuous variables (concentration, motility, morphology), associations with occupation and with workplace exposures were modeled using generalized linear models assuming a gamma distribution to account for the right-skewed non-negative parameters of the semen data [17]. The aggregate category of "office workers" was used as a reference group. Occupations with fewer than 5 participants in the SFF dataset were excluded from these analyses. To reduce the number of potential false-positive results arising from multiple-comparison testing, a Benjamini-Hochberg procedure using a false-discovery rate reduction of 50% was applied to the results for individual occupations [18]. Estimated marginal mean values for semen parameters in participants exposed to the four main categories of reproductive toxicants outlined above, and to high levels of physical activity, adjusted for the covariates above, were also obtained through generalized linear modeling. Prevalence ratios for exposure to the four main toxicant categories for occupational groups with significantly lower semen parameters were calculated using a Poisson loglinear model, using the overall group of employed participants as a referent.

RESULTS:

A total of 763 men provided at least one semen sample in SFF. The analyses we present includes 680 men who provided a semen sample with an abstinence time between 2 and 240 hours and who indicated that they were working at the time of conception and into the first trimester. Demographic data, semen parameters, broad occupational classes, and self-reported exposures at work are shown in Table 1. Mean semen parameters in SFF male participants who reported an occupation did not differ significantly from those who did not report working. A total of 80 occupations (by SOC-O*NET classification) were held by men in the SFF; five or more men were working in 57 of these SOC-coded occupations. SFF male participants worked in a wide variety of occupations, with approximately two-thirds found in "white-collar" work, including business, computer work, and education. Estimates of occupational physical activity, using O*NET job descriptors, paralleled this distribution, with 58.8% of participants in a low-physical-activity job, and 17.3% in high-physical-activity work. Exposures to known and potential reproductive toxicants were not widespread in the sample, again reflecting the extent of professional, white-collar, and other non-manual occupations; 5.5% reported current or past exposure to lead, 6.2% to radiation (both ionizing and non-ionizing), 14.2% to pesticides or herbicides, and 30.5% to solvents. Although the Missouri site reported slightly more lead-exposed participants, differences in exposure proportions did not differ significantly between sites (p=0.18 by Fisher's exact test).

Specific occupations with adjusted mean sperm concentration, motility, and morphology values which were significantly lower than the mean parameters for office workers are shown in Tables 2, 3, and 4 respectively. Only one lead exposed worker had a sperm concentration below 15×10^6/mL and total count below 40×10^6. Additionally, prevalence ratios (PR) as estimates of exposure to lead, solvents, pesticides/herbicides, and radiation for those occupations with low mean semen parameters were calculated against the total employed SFF study base, with PRs for office workers also shown for comparison. Increased exposure to lead was associated with the highest PRs in occupations with low mean semen parameters, particularly for those with lower sperm concentration (aggregate PR 4.10; 95% confidence interval (CI) 2.13–7.88). Exposure to pesticides and herbicides was also seen in several occupations with low sperm concentration, which was consistent with performance of outdoor work in these jobs. A significantly increased prevalence of exposure to all four toxicant groups was also noted when all occupations with statistically low sperm concentration were aggregated. Physical scientists had an increased probability of exposure to all four sets of toxicants, and had the lowest values for sperm morphology, although their sperm concentration and motility were not significantly reduced compared to office workers. As expected, prevalence estimates for these exposures in office workers were uniformly lower than that of the overall working study base (Table 2).

Of the four exposure groups noted above, only lead was consistently significantly associated with reduction in sperm motility and concentration (adjusted mean concentration reduction -21×10^6 per mL for any lead exposure; $p<0.006$ versus non-lead-exposed workers) in the overall dataset. Table 5 presents additional detail on lead exposure. Decrements in sperm concentration was seen in workers who noted work with lead for longer than three months, with a mean reduction of -17.4×10^6 sperm/mL, whereas reported work with lead for less than three months (ie current, but not past, work) showed no decrease. Participants who reported lead exposure outside of work were found to have still lower sperm concentration (a reduction of -31.5×10^6/mL versus those not exposed), although the questionnaire did not query the duration of non-occupational exposure as was done for work exposure. Exposure to lead from both work and non-occupational sources appears to compound the drop in sperm concentration from either one alone, as a reduction was seen in every category of workplace lead exposure in those additionally reporting lead use outside of work. The lowest sperm concentration was seen in those with longer-term (current plus past) lead exposure at work who also had outside lead exposures (adjusted mean concentration 28.6 $\times 10^6$/mL; $p<0.001$ versus the non-lead-exposed). Similar decrements in semen parameters were not seen for reported exposures outside of work to solvents, pesticides and herbicides. Table 6 shows mean sperm concentrations in participants having combined exposures to two toxicants at work (lead, solvents, or pesticides/herbicides) contrasted with a referent group who were unexposed to all three sets of toxicants. Reduced sperm concentration was seen with lead exposure alone and in combination with solvent exposure, an effect not seen with combined exposures to solvents and pesticides/herbicides. (No working men had combined exposure to lead and pesticides/herbicides together, so that the combined effect of these could not be tested). Physical activity, as assessed by O*NET variables appeared not to affect sperm concentration, as also shown in Table 6; these values did not change significantly when stratified by season of sample collection, a possible proxy for heat exposure.

DISCUSSION:

In this group of fertile men, we found evidence for associations of reduced sperm quality with several occupational factors, principally lead, and to a lesser extent, pesticides/herbicides and solvents. Lead exposed occupations demonstrated the most consistent findings, particularly in reduction of sperm concentration, although the number of SFF participants exposed to lead was low. Additionally these findings were not apparent in those with recent exposure, but instead in those for whom exposure had continued for over three months (Table 5), which is consistent with a toxic effect that may not be clinically apparent until the 2–3 month course of spermatogenesis has proceeded. Reduced semen parameters associated with lead were seen both in the overall sample and in specific occupations where higher exposures might be expected: in law enforcement officers and in vehicle mechanics and repairers. Officers, particular police, are exposed to lead at firing ranges [19], while exposures to lead and solvents are known hazards of work in auto repair and related jobs [20–23]. Exposures to lead in these two occupations may be more extensive, or less controlled, than seen in larger industries because of smaller numbers of workers in any one place and hence lower uptake of control measures such as ventilation, respirator use, and personal hygiene measures such as handwashing. Consistent with the known effects of exposure to lead were findings of lower sperm concentration in those who noted exposure outside of work in avocations or hobbies, and a combined reduction seen in those who both worked with lead and were exposed outside of the job.

Strenuous occupational physical activity did not appear to be associated with reduced sperm quality in this sample of fertile men. An effect had been previously described in association with manual work [4] where physical effort was self-reported. The imputed nature of occupational activity via the O*NET used here may perhaps be leading to non-differential misclassification of exposure and biasing results of individual physical effort to the null. However, other results we present suggest that workplace physical activity should not be discounted as a possible explanation for reduced sperm quality. Of the occupations with significantly reduced sperm concentrations (Table 2) only material moving workers showed no association with any of the four main reproductive toxicants in these analyses, which is consistent with the general lack of toxicant exposures encountered in this work. Material moving workers do however demonstrate very high physical demand levels, in most cases placing them at the 90–95th percentile of physical demands among the occupations in which physical stressors are quantified [15]. While other, possibly unmeasured, factors may be operating, uniformly high occupational physical activity could be one explanation for the low sperm concentration seen in material handling workers.

Higher-level and long-term lead exposure has been demonstrably associated with reduced sperm concentration and motility [24–26]. Reduced sperm counts and motility were noted in painters having mean blood lead levels in the 15–20 μg/dL range [26], although its effect at lower levels more characteristic of current workplace exposure levels in high-income countries is less certain [27, 28]. Our results are consistent with known effects of workplace lead exposure, although the exposure assessment in the SFF is qualitative and we did not have individual blood lead measurements to correlate with semen parameters. Additionally, (as noted above) evidence for reduced sperm concentration and motility is only evident in those with current lead exposure lasting over three months, which is consistent with exposure effects across the cycle of spermatogenesis. Associations of other toxicants with poorer semen quality across occupations in the SFF were less strong. These findings may be the consequence of the diversity of exposures, or of lack of specificity encompassed by broader terms such as ‘solvents’ or ‘pesticides/herbicides’ which may subsume known male reproductive toxins (use of glycol ethers, or organochlorine pesticides for example) with materials of lesser toxicity. Any potential effect of the use of specific male reprotoxins may therefore be diluted by the inclusion and reporting of other exposures.

Identification of specific occupations associated with adverse male reproductive effects has been inconsistent outside of demonstrably high single-agent exposures. Gracia and colleagues [3], in a large case-control study drawn from men in infertility clinics found no association with exposure to shift work, metal fumes, electromagnetic fields, solvents, lead, paint, pesticides, work-related stress, or vibration, although exposures were reported as those which occurred within the month prior to interview. The difference in findings between this study and ours may arise from differences in exposure assessment. While their estimates of exposure prevalence to various toxicants were very close to those we report, Gracia et al considered any exposure occurring within the month prior to assessment as a positive exposure whereas our results, particularly for lead, show differences in semen parameters between longer- and shorter-term exposures. Other subsequent studies have noted increased probability of infertility in workers exposed to lead and other heavy metals, solvents, heat, and non-ionizing radiation [26, 29–31], findings more consistent with those we report here. Inconsistencies between studies highlight the difficulty of examining work-related contributors to male infertility and subfertility, including accurate exposure assessment and the difficulty of determining factors specific to the male partner when infertility is used as an endpoint.

The results we present here are novel in their use of semen quality data from a sample of fertile donors (whose partners were also demonstrably fertile), which enables us to examine occupational exposures in men with semen parameters predominately within ‘normal’ ranges. Advantages to this approach include the reduction in other confounding conditions or exposures that may be causing infertility when study subjects are drawn from infertility clinics or chosen on that basis, along with confidence that female infertility is not operating as a confounder. Additionally this approach has the potential to reduce response or information bias since the male subjects’ responses are not conditioned on a diagnosis of infertility. By the same logic, the main disadvantage to the use of the SFF dataset is the possibility that the effect of a strong reproductive toxicant may be missed, since men with sperm parameters sufficiently abnormal to reduce fertility will not be represented. Finally, subfertility has long been described as a continuum with no clear or defining bright-line between the fertile and infertile [5]. On balance, the results we present provide an innovative look at depression of semen indices within still-normal ranges and identify occupations where protective measures against excessive exposures might be warranted.

A few additional limitations to the study should be mentioned. Use of specific occupational codes (3-digit SOC code) may result in small numbers of participants in some jobs and thereby some difficulty in drawing clear associations with work. The results we present were limited to occupations with 5 or more SFF participants in order to limit this problem. As well, we used a larger group (office workers) for contrast, and Benjamini-Hochberg procedures to reduce possible false-positive results. Nonetheless, with smaller numbers within some occupations, and the variability of the measured outcomes, particularly sperm concentration, some figures could represent both false-positive and false-negative results. Moreover, the overall number of participants who reported exposure to lead and other toxicants is also small, limiting the robustness of results. Additionally, participants' reports of work with materials such as metals and solvents were essentially dichotomous (endorsing only work with the material, or not) without details on the extent and frequency of exposure, which may misclassify exposure or reduce useful information that could be obtained by finer gradations of exposure classification. This may be particularly true for reporting use of lead outside of work. Lastly, a methodological concern is the use of exposure metrics derived from a JEM; the critique being that these represent proxy and 'average' measures of attributes and exposures, and not individual work circumstances. However, these are widely used when individual exposure measurements and data are unavailable and demonstrate several strengths [32] including reduction of differential recall, common-instrument biases, and confounding by personal factors and attributes.

In conclusion, using a sample of demonstrably fertile men, we found several occupations in which workplace exposures may have early or subclinical effects on semen parameters, which may potentially lead to later problems with fertility if continued. In particular, lead, a well-described reproductive toxicant, is correlated with reduced sperm concentration even in these fertile subjects, while exposures to solvents and pesticides/herbicides appear more variable in their association. The results are consistent with prior studies in workers with known risk, such as lead exposure in motor vehicle repairers, but also highlight other occupational groups, including those in the physical sciences and law enforcement, where risks to male reproduction have been less well described, and suggest the need for attention to these occupations as sources of male infertility, as well as consideration of exposure reduction in these fields.

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TABLE 1.

Demographics, semen parameters, and job characteristics of working men in the SFF study sample (N = 680)

	Mean	**Std Dev**	**N**	**%**
Age (years)	31.7	6.1		
Body Mass Index (kg/m^2)	28.4	5.2		
Duration of abstinence (hours)	77.8	31.2		
Race/Ethnicity				
White			509	74.9
Hispanic			97	14.3
Black			43	6.3
Asian/Other			31	4.6
Education				
High school or less			258	38.0
Beyond high school			419	61.6
Missing			3	0.4
Tobacco smoking				
No			548	81.1
Yes			128	18.9
Missing				
Alcohol use				
No			279	41.0
Yes			400	58.9
Missing			1	0.1
Recent fever				
No			658	96.8
Yes			22	3.2
Missing			0	0
History of STD				
No			598	87.9
Yes			82	12.1
Missing			0	0
Recreational drug use				
No			618	90.9
Yes			60	8.8
Missing			2	0.3
Total Sperm Count (10^6) (IQR)	260.4	111.8 – 349.1		
Sperm Concentration (10^6/mL) (IQR)	79.6	38.7 – 104.1		
Motility (%)	51.0	11.5		

	Mean	Std Dev	N	%
Morphology (WHO 1999 criteria) % normal	10.8	5.1		
Major occupational category (Major SOC code)				
Management, Business, and Financial (11–13)			113	16.6
Computer, Engineering, and Science (15–19)			103	15.2
Education, Legal, Community Service (21–25)			78	11.5
Healthcare Practitioners, Technical & Support Occupations (29–31)			51	7.5
Transportation & Material Moving (53)			50	7.4
Office and Administrative Support (43)			43	6.3
Production (51)			38	5.6
Sales and Related (41)			37	5.4
Installation, Maintenance, and Repair (49)			36	5.3
Construction and Extraction (47)			33	4.9
Food Preparation and Serving-related (35)			32	4.7
Arts, Design, Entertainment, Sports, and Media (27)			32	4.7
Protective Services (33)			15	2.2
Building and Grounds Cleaning and Maintenance (37)			13	1.9
Personal Care and Service (39)			3	0.4
Farming, Fishing, and Forestry (45)			1	0.1
Military-specific (55)			1	0.1
Self-reported exposures at work				
Exposed to lead at work:				
Current (in past 3 months)			7	1.1
Current and Past (ongoing > 3 months)			15	2.4
Past only (>3 months ago)			12	1.9
Unexposed			586	94.5
Exposed to solvents at work:				
Current (in past 3 months)			30	4.5
Current and Past (ongoing > 3 months)			86	12.8
Past only (>3 months ago)			89	13.2
Unexposed			467	69.5
Exposed to pesticides/herbicides at work:				
Current (in past 3 months)			9	1.3
Current and Past (ongoing > 3 months)			22	3.3
Past only (>3 months ago)			65	9.6
Unexposed			578	85.8
Exposed to radiation at work:				
Current (in past 3 months)			6	0.9

	Mean	Std Dev	N	%
Current and Past (ongoing > 3 months)			14	2.1
Past only (>3 months ago)			22	3.3
Unexposed			632	93.8
Physical Activity Level (by O*NET scoring)				
Low			391	58.8
Medium			156	23.5
High			118	17.3

Table 2.

Male occupations with the lowest mean sperm concentration; unadjusted and adjusted means, and contrast estimates versus office workers. Odds of exposure of workers within those occupations to lead, solvents, pesticides/herbicides, and radiation contrasted with all working men in SFF dataset. Occupations with n ≥5 participants

SOC Occupation	**N**	**Mean (10 ^{6}/mL)**	**Adjusted Mean (10^6/mL)**	**Std. Error**	**Contrast Estimate vs Office Workers**	**Std. Error**	**Sig. vs Office Workers**	**Prevalence ratios (95% CI) versus full dataset, for exposure to:**			
								Lead	**Solvents**	**Pesticides/ Herbicides**	**Radiation**
333 Law Enforcement Workers	10	56.5	48.9	11.7	−37.1	12.1	0.002	**4.17 (1.16–15.1)**	1.32 (0.61–2.84)	**2.88 (1.32–6.31)**	3.32 (0.93–11.8)
492 Electrical and Electronic Equipment Mechanics, Installers, and Repairers	5	41.9	45.6	15.9	−40.4	16.1	0.012	4.08 (0.68–24.3)	0.65 (0.11–3.79)	-	-
537 Material Moving Workers	22	56.8	65.3	8.6	−20.8	8.6	0.016	1.78 (0.45–6.98)	0.81 (0.40–1.64)	0.60 (0.16–2.29)	0.69 (0.10–4.80)
499 Other Installation, Maintenance, and Repair Occupations	13	54.5	61.0	9.8	−25.1	10.7	0.02	1.34 (0.20–9.16)	**1.78 (1.09–2.90)**	**2.41 (1.15–5.06)**	1.07 (0.16–7.28)
194 Life, Physical, and Social Science Technicians	22	60.8	65.9	9.3	−20.1	9.5	0.034	2.76 (0.91–8.36)	0.96 (0.51–1.80)	**2.13 (1.11–4.09)**	**5.41 (2.68–10.9)**
274 Media and Communication Equipment Workers	5	51.3	53.9	15.2	−32.1	15.8	0.042	-	0.65 (0.10–4.67)	-	-
493 Vehicle and Mobile Equipment Mechanics, Installers, and Repairers	12	57.9	62.9	11.6	−23.1	11.9	0.05	**6.82 (2.81–16.6)**	**2.87 (2.22–3.73)**	0.54 (0.08–3.55)	-
All above occupations (n= 84)	**84**	**64.1**	**51.1**	**6.8**	−34.9	6.4	<0.001	**4.10 (2.13–7.88)**	**1.41 (1.06–1.86)**	**1.60 (1.02–2.51)**	**2.30 (1.20–4.41)**
OFFICE WORKERS	**139**	**82.6**	**86.0**	**5.8**	REF	-	-	0.35 (0.11–1.12)	***0.66 (0.47–0.92)***	0.82 (0.51–1.32)	***0.27 (0.09–0.87)***

Sperm concentrations as measured by haemocytometer. Mean values and prevalence ratios adjusted for age, duration of abstinence, BMI, tobacco smoking, drug use, history of STD, and recent fever.

Prevalence ratios not calculated where exposed numbers were insufficient to yield stable estimates

Table 3.

Male occupations with the lowest mean sperm motility; unadjusted and adjusted means, and contrast estimates versus office workers. Odds of exposure of workers within those occupations to lead, solvents, pesticides/herbicides, and radiation contrasted with all working men in SFF dataset. Occupations with n ≥5 participants

SOC Occupation	**N**	**Mean % motile sperm**	**Adj Mean % motile sperm**	**Std. Error**	**Contrast Estimate vs Office Workers**	**Std. Error**	**Sig. vs Office Workers**	**Prevalence ratios, versus full dataset, for exposure to:**			
								Lead	**Solvents**	**Pesticides/ Herbicides**	**Radiation**
519 Other Production Occupations	5	43.6	36.4	5.1	−13.5	5.0	0.014	**8.41 (2.73–25.9)**	0.65 (0.11–3.79)	1.41 (0.24–8.21)	-
492 Electrical and Electronic Equipment Mechanics, Installers, and Repairers	5	42.9	39.9	5.0	−10.1	4.8	0.042	4.08 (0.68–24.3)	0.65 (0.11–3.79)	-	-
499 Other Installation, Maintenance, and Repair Occupations	13	45.8	42.4	3.2	−7.6	3.1	0.028	1.34 (0.20–9.16)	**1.78 (1.09–2.90)**	**2.41 (1.15–5.06)**	1.07 (0.16–7.28)
All above occupations (n= 23)	23	44.7	40.8	3.7	−8.3	2.6	0.001	**3.48 (1.33–9.13)**	1.33 (0.81–2.18)	1.73 (0.84–3.57)	0.63 (0.09–4.42)
OFFICE WORKERS	139	52.5	49.2	3.0	REF	-	-	0.35 (0.11–1.12)	***0.66 (0.47–0.92)***	0.82 (0.51–1.32)	***0.27 (0.09–0.87***)

Motility assessed according to WHO 1999 criteria. Figures adjusted as noted in Table 2.

Table 4.

Male occupations with the lowest mean sperm morphology by strict criteria ([11]: unadjusted and adjusted means, and contrast estimates versus office workers. Odds of exposure of workers within those occupations to lead, solvents, pesticides/herbicides, and radiation against all working men in SFF dataset. Occupations with n ≥5 participants versus Office workers

SOC Occupation	N	Mean % normal morphol	Adj Mean % normal morphol	Std. Error	Contrast Estimate vs Office Workers	Std. Error	Sig. vs Office Workers	Prevalence ratios, versus full dataset, for exposure to:			
								Lead	**Solvents**	**Pesticides/ Herbicides**	**Radiation**
192 Physical Scientists	5	6.6	5.7	1.5	−3.2	1.4	0.028	**8.41 (2.73–25.9)**	**3.32 (2.96–3.73)**	**4.36 (2.06–9.05)**	**18.1 (13.2–24.7)**
274 Media and Communication Workers	12	7.2	5.8	1.8	−3.1	1.7	0.042	-	0.65 (0.11–3.79)	-	-
All above occupations (n= 17)	17	7.0	5.8	1.2	−3.1	1.2	0.03	**4.17 (1.15–15.1)**	**1.84 (1.01–3.34)**	2.14 (0.82–5.62)	**8.97 (4.48–17.9)**
OFFICE WORKERS	139	10.4	8.9	0.6	REF	-	-	0.35 (0.11–1.12)	***0.66 (0.47–0.92)***	0.82 (0.51–1.32)	***0.27 (0.09–0.87)***

Morphology assessed by WHO 1999 criteria, strict method. Figures adjusted as noted in Table 2.

Table 5.

Associations of lead exposure at work and outside of work on sperm concentration. Significance values calculated versus workers-unexposed-to-lead referent group

Lead Exposure at Work		**Mean (10^6/mL)**	**Std. Error**	**95% CI**		**Sig.**
				Lower	**Upper**	
Present+Past (ongoing > 3 months) n= 15		**45.3**	**4.8**	**35.9**	**54.6**	**0.03**
Present Only (most recent 3 mos only) n= 7		66.6	18.4	30.5	102.8	NS
Unexposed (REF) n= 583		62.7	6.6	49.7	75.7	REF
Lead Exposure Outside of Work		**Mean (10^6/mL)**	**Std. Error**	**95% CI**		**Sig.**
				Lower	**Upper**	
Yes n= 10		**42.4**	**4.5**	**33.7**	**51.1**	**0.02**
No n= 595		73.9	12.7	49.1	98.8	REF
INTERACTION		**Mean (10^6/mL)**	**Std. Error**	**95% CI**		**Sig**
Lead Exposure at Work	**Lead Exposure Outside Work**			**Lower**	**Upper**	
Present+Past	Yes	**28.6**	**1.2**	**26.3**	**30.9**	**<0.001**
	No	61.9	9.5	43.3	80.5	0.05
Present Only	Yes	**54.0**	**2.6**	**48.9**	**59.2**	**0.01**
	No	79.2	36.8	7.1	151.3	NS
Unexposed (Referent)	Yes	**44.6**	**13.0**	**19.0**	**70.1**	**0.006**
	No	80.8	2.4	76.1	85.6	***REF***

Table 6.

Associations of work exposure to combinations of two toxicants (lead, solvents, and pesticides/herbicides) and for physical activity (O*NET measure) on estimated marginal means for sperm concentration. Significance values versus an unexposed referent group for toxicant exposures.

Exposure at Work (n)	**Mean (x 10^6)**	**Std. Error**	**95% CI**		**Sig.**
			Lower	**Upper**	
Lead and Solvent exposure (12)	**52.0**	**6.22**	**39.8**	**64.2**	**0.001**
Lead exposure only (6)	58.2	26.6	6.0	110.4	NS
Solvent exposure only (88)	76.8	5.4	66.1	87.4	NS
Unexposed (referent) (534)	80.6	2.6	75.5	85.7	REF
Lead and Pesticide/Herbicide exposure (0)	-	-	-	-	-
Lead exposure only (6)	58.2	26.6	6.0	110.4	NS
Pesticide/Herbicide exposure only (15)	74.1	10.7	53.1	95.2	NS
Unexposed (referent) (534)	80.6	2.6	75.5	85.7	REF
Solvent and Pesticide/Herbicide exposure (12)	74.7	12.4	50.3	99.0	NS
Solvent exposure only (88)	76.8	5.4	66.1	87.4	NS
Pesticide/Herbicide exposure only (15)	74.1	10.7	53.1	95.2	NS
Unexposed (referent) (534)	80.6	2.6	75.5	85.7	REF
Physical activity (by O*NET)	**Mean (x 10^6)**	**Std. Error**	**95% CI**		**Sig.**
			Lower	**Upper**	
High n= 118	77.7	4.6	68.6	86.8	NS
Medium n= 156	75.0	4.8	65.7	84.4	NS
Low n= 391	82.8	3.1	76.6	88.9	REF