Outdoor air pollution and sperm quality

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Exposure to air pollution has been clearly associated with a range of adverse health effects, including reproductive toxicity, but its effects on male semen quality are still unclear. We performed a systematic review (up to June 2016) to assess the impact of air pollutants on sperm quality. We included 17 semi-ecological, panel, and cohort studies, assessing outdoor air pollutants, such as $PM_{2.5}$, PM_{10}, NOx, SO_2, and O_3, and their effects on DNA fragmentation, sperm count, sperm motility, and sperm morphology. Thirteen studies assessed air pollution exposure measured environmentally, and six used biomarkers of air pollution exposure (two did both). We rated the studies using the Newcastle-Ottawa Scale and assessed with the exposure method. Taking into account these factors and the number of studies finding significant results (positive or negative), the evidence supporting an effect of air pollution on DNA fragmentation is weak but suggestive, on sperm motility is limited and probably inexistent, on lower sperm count is inconclusive, and on sperm morphology is very suggestive. Because of the diversity of air pollutants and sperm parameters, and the studies' designs, we were unable to perform a meta-analysis. In summary, most studies concluded that outdoor air pollution affects at least one of the four semen quality parameters included in the review. However, results lack consistency, and furthermore, studies were not comparable. Studies using standardized air pollution and semen measures are required to obtain more reliable conclusions.
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The prevalence of infertility has increased notably in recent decades. Male factors contribute strongly to infertility, accounting for approximately 40% of all cases (1). A decline in semen quality has been observed generally over the past 70 years, including a decline in sperm count and ejaculate volume (2), as well as alterations in sperm concentration and morphology, even in fertile men, and regardless of age (3). Over time the World Health Organization (WHO) (4) has lowered the accepted values for classic normal sperm parameters, including count, motility, and morphology, because in the last decades those parameters have consistently decreased even in healthy men. Some authors have suggested that this decrease in sperm quality is associated with the observed decrease in fertility (5).

It is essential to understand the causes of this decrease in sperm quality (6). In addition to several specific chronic diseases (7–11), various lifestyle and environmental factors have been associated with decreased sperm quality (12, 13), such as smoking (14), drinking (15), obesity (16), social stress (17), exposure to polycyclic aromatic hydrocarbons (PAHs) or heavy metals, and air pollution (18), the latter of which is the focus of this review.

Air pollution is widely known to have adverse effects on human health (19), including cardiovascular (20) and respiratory diseases (21), adverse

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perinatal outcomes, and even impaired neurodevelopment (22). It has also been classified as carcinogenic to humans (23) by the International Agency for Research on Cancer (the cancer investigation division of the WHO). Although many animal studies have shown a link between air pollution and fertility, particularly semen quality (24–27), the relationship in humans remains unclear. The aim of this review was to assess current evidence regarding the impact of air pollution on sperm quality in humans.

MATERIALS AND METHODS

This study did not require approval by the institutional review board because it is a systematic review. We adhered to the preferred reporting items recommended by the PRISMA statement (28) on reporting the results of systematic reviews. The details of our protocol for this systematic review have been registered on PROSPERO and can be accessed at CRD42015007175.

Search Strategy

We performed an exhaustive search of the three following electronic databases: PubMed, ISI Web of Knowledge, and Cochrane Library, updated to March 31, 2016, without restriction on the starting date. The search combined terms referring to outdoor air pollution and semen quality. We used the following key words, combining them with Boolean hints in the three databases queried: (air pollution OR particulate matter OR diesel OR soot OR carbon OR black smoke OR smog OR traffic OR motor vehicles OR carbon dioxide/monoxide OR nitrogen dioxide/oxide OR ozone OR CFCs OR VOCs OR industrial activity OR ammonia OR sulfur oxide/dioxide OR power plants OR landfills OR methane) AND (sperm function OR sperm count OR sperm motility OR sperm morphology OR semen volume OR liquefaction OR sperm DNA fragmentation). These terms were used as shown in the three databases queried and the search restricted to "males" using the database filter option.

After revision of the manuscript we updated the search on June 30, 2016 in PubMed, using the same terms and restricting the start date to March 1, 2016. We also hand-searched the reference list of all the included articles and reviews identified during the search to ensure we did not miss any further studies.

Eligibility Criteria

We included cohort and case–control studies that analyzed the impact of outdoor air pollutants on sperm quality in humans (Table 1). We excluded studies that analyzed the effects of air pollution on perinatal outcomes, as well as those assessing the effects of tobacco exposure or other nonenvironmental toxics (alcohols, drugs of abuse), in vitro studies, studies in animal models, and occupational exposure studies (except those in which the occupation implied exposure to the environmental toxins covered by our review). We also identified and included several studies that used measured biomarkers of air pollution exposure in blood and urine. We only included studies published in English.

TABLE 1

Study eligibility criteria.

Target population	**Males of fertile age**
Intervention	Environmental air pollution PMx Gases (NOx, CO, SO_2, O_3) General traffic air pollution Biological markers of air pollution (blood, urine and seminal plasma) PAH NO_2 Pb, Cd
Outcome measures	Sperm quality parameters DNA fragmentation Sperm count Sperm motility Sperm morphology
Design	Cohort, cross-sectional, semi-individual studies, case–control studies

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Outcomes

The outcomes of interest were DNA fragmentation and sperm count, motility, and morphology.

Exposure

We also obtained information about air pollution exposure, type of pollutant (e.g., PM_{10}, $PM_{2.5}$, NO_2), and the method used to measure exposure.

Data Extraction

The title and abstract of the articles identified by the search were reviewed by two independent authors, who determined their eligibility. Discrepancies were resolved by the intervention of a third independent author. In a following step, full text of the eligible articles was then reviewed by two independent authors to determine their inclusion. Data were extracted from the final selected articles. Data extracted were type of study, population characteristics, detailed outcomes and exposures, and main effects: β estimates or percent change from linear regression (from adjusted models when available). All this information was compiled in Excel tables (Microsoft, Redmond, WA) that included the following: authors, year of publication, type of study, characteristics of participants, number of cases, pollutants, outcomes included, and main effects, which we adapted for the present review (as merging author and year, or type study and characteristics of participants), and we also decided to add a comments column to state important information to better understand the study.

Assessment of Risk of Bias

We used the Newcastle-Ottawa Scale to assess the risk of biases of the studies included in the review (29). We only considered the scale applicable to cohort studies because no case–control studies met our inclusion criteria. This scale considers various items ranking the possibility of bias for three categories: Selection, Comparability, and Outcome. To