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# Environmental Agents and Erectile Dysfunction: A Study in a Consulting Population

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**ABSTRACT:** We evaluated chemical and physical environmental agents as risk factors for erectile dysfunction among a consulting population. We studied 199 men who sought medical help for erectile disorders between 1996 and 1998 in 3 andrology units in the Litoral Sur region of Argentina. Patients were evaluated by monitoring nocturnal penile tumescence and rigidity, and were classified as having normal (n = 26), irregular (dissociation, short episode or low amplitude, n = 146), or flat erectile pattern (n = 26). Exposure to environmental agents was assessed by a detailed interview, and 4 groups were constituted: nonexposed, pesticide-exposed, solvent-exposed, and heat-exposed. A multivariate polytomous logistic regression model was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for association between quality of nocturnal erections and exposure groups adjusted for confounding factors. Exposure to environmental agents was a risk factor for a flat erectile pattern (OR 7.1, 95% CI 1.5–33.0 for pesticides; OR 12.2, 95% CI 1.2–124.8 for solvents; and OR 1.7, 95% CI 0.3–9.4 for heat). Associations were much weaker for an irregular erectile pattern (OR 1.8, 95% CI 0.5–6.7 for pesticides; OR 2.1, 95% CI 0.3–17.9 for solvents; and OR 1.2, 95% CI 0.4–4.0 for heat). Our results suggest that environmental agents constitute a risk factor for erectile dysfunction by interfering with erectile ability.

Key words: Argentina, environment, pesticides, solvents.
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In the last few decades, concern has been growing about the threat posed to male reproductive health by chemical and physical agents being released into the environment (Toppari et al, 1996). However, less attention has been paid to the effect of these agents on male sexual function than to their effect on male fertility.

Erectile dysfunction is the persistent inability to achieve or to maintain an adequate erection for satisfactory sexual performance (NIH Consensus Conference, 1993). It is one of the most frequent male sexual dysfunctions and has a profound effect on the quality of life of millions of men (Feldman et al, 1994; Laumann et al, 1999; Lewis, 2001). Medical disorders that impair blood flow, neuronal pathways, or endocrine regulation; and psychological factors and relationship problems may cause erectile dysfunction (Melman and Gingell, 1999; Morgentaler, 1999). Life style factors such as smoking (Feldman et al, 1994) and alcohol consumption (Lemere and Smith, 1973), and the side effects of therapeutic drugs (Keene and Davies, 1999) are considered to be additional risk factors. However, little is known about the effects that chemical and physical agents present in the environment have on sexual function. Previous observations showed that workers who are occupationally exposed to various environmental chemicals are more likely to complain of impotence (Espir et al, 1970; Sabroe and Olsen, 1979; Vanhoorne et al, 1994; Amr et al, 1997).

We screened subjects who consulted for erectile disorders in the Litoral Sur area of Argentina between 1996 and 1998, and investigated the relationship between environmental exposures and the quality of nocturnal erection. We estimated the risk of an association between environmental exposures and erectile ability by evaluating patient history, carrying out a physical examination and laboratory tests, and by monitoring nocturnal penile tumescence and rigidity.

## Materials and Methods

The study sample consisted of 199 who consulted the Andrology Unit of 1 of 3 private institutions (Hospital Italiano Garibaldi, Rosario; Centro de Urologia, Santa Fe; and Sanatorio Adventista del Plata, Libertador General San Martin, Entre Rios) for erectile dysfunction between January 1996 and December 1998. This study was approved by the institutional review board and took place in the Santa Fe and Entre Rios provinces of Argentina, which constitute the Litoral Sur region. The region has a predominantly agricultural economy; it also contains an industrial corridor that is centered around the 3 largest towns: the capital, Santa Fe (449 000 inhabitants); Rosario (1 200 000 inhabitants); and Paraná (320 000 inhabitants).

Information was collected at several stages. A structured interview was conducted during the first visit to obtain information

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on patients' basic demographic, medical, surgical, and reproductive history; recent illnesses and treatments; sexual activity; occupational history; and life style. Patients underwent laboratory exploration, and their nocturnal erections were monitored for 2 consecutive nights. An ambulatory RigiScan device (Dacomed Corp, Minneapolis, Minn) was used to monitor nocturnal penile tumescence and rigidity simultaneously and continuously. This device provides an objective measure of the ability to achieve and maintain an erection (Levine and Lenting, 1995). We measured the number and duration of erectile episodes, base and tip radial rigidity, and tumescence at the penile base and tip. RigiScan data were analyzed according to the criteria of Kaneko and Bradley (1986). During the second visit, which took place 2 to 4 weeks later, a complete physical and andrological examination was carried out.

Following the RigiScan evaluation, patients were classified as having nonorganic erectile dysfunction (normal erectile pattern, n = 26), organic erectile dysfunction (irregular erectile pattern, n = 147), or flat erectile pattern (n = 26). The nonorganic erectile dysfunction group consisted of men in which 2 consecutive normal nocturnal erection patterns were recorded, as defined by more than 1 consecutive 10-minute erectile episode with a base and tip radial rigidity greater than 70%, and a base and tip tumescence circumference of at least 6 cm. The organic erectile dysfunction group consisted of men with abnormal nocturnal erection patterns who were classified as having an irregular (presence of dissociation, short episode, or low amplitude) or flat erectile pattern (unmodified basal recording pattern; Kaneko and Bradley, 1986; Kaneko et al, 1990).

Exposure to environmental agents was assessed by studying the detailed history of past and present jobs and life style habits. Men were asked about their contact with chemical substances or physical agents. An industrial hygienist verified the correlation between jobs and the declared exposures. Patients were classified as nonexposed (men who did not report any exposure and whose occupation did not expose them to any of the agents, n = 112), exposed to pesticides (herbicides, fungicides, insecticides, fumigants, and rodenticides, n = 40), exposed to solvents (paints, varnish, lacquers, thinners, degreasers, and inks, n = 16), or exposed to heat (prolonged sitting position or radiant heat, n = 31).

We used polytomous multiple logistic regression analysis to produce odds ratio (ORs) and 95% confidence intervals (CIs) for an association between dependent variables (nocturnal erectile patterns) and independent variables (exposure groups) adjusted for confounding factors. Patients with normal erectile patterns constituted the reference group in all analyses. The significance of ratios of ORs between irregular and flat erectile pattern groups vs. normal erectile pattern group was assessed by the logistic likelihood ratio test with 2 degrees of freedom (Greenland, 1998). The covariates considered to be potential confounders were age, body mass index (kg/m$^2$), annual income (<$12 000, $12 000 to $36 000, or >$36 000), smoking habits (nonsmoker vs. current smokers), alcohol consumption (≤20 g/alcohol per day vs. >20 g/alcohol per day), diabetes, hypertension, cardiovascular disease (coronary and cerebrovascular), previous trauma (pelvic, perineal, or penile), and past or present use of therapeutic drugs that may affect sexual function. Factors were considered to be confounding if their inclusion in the model modified the estimate of the OR by more than 10% (Greenland and Rothman, 1998). Age was always included as a confounding factor in the final multivariate model. The Statview software package was used for all analyses (SAS Institute Inc., Cary, NC). All *P* values were two-sided, and were considered to be significant if $P < .05$.

Table 1. *Occupational circumstances of exposure*

| Exposure Groups | Occupation | Number |
|---|---|---|
| Nonexposed | Professional | 31 |
| | Sales worker | 25 |
| | Technician | 23 |
| | Administrative | 21 |
| | Other | 12 |
| Pesticides | Farming | 29 |
| | Animal husbandry | 7 |
| | Fumigation | 4 |
| Solvents | Mechanics | 11 |
| | Painting | 3 |
| | Woodworking | 2 |
| Heat | Driving | 14 |
| | Welding | 10 |
| | Baking | 5 |
| | Cooking | 2 |

## Results

The mean age of the overall study population was 48.7 years, and mean body mass index was 29.1. Thirty-one percent of men were current smokers and 33% drank more than the equivalent of 20 g alcohol per day. The prevalence of medical risk factors for erectile dysfunction was 11% for diabetes, 34% for hypertension, 16% for cardiovascular diseases, and 22% for use of therapeutic drugs. Subjects were assigned to 1 of 4 environmental exposure groups, and the occupational circumstances of exposure of the 199 men are shown in Table 1. Median exposure times were 12, 14, and 7 years for the pesticide, solvent, and heat-exposure groups, respectively.

Table 2 shows some of the characteristics of the patients according to the quality of nocturnal erection. Patients with organic erectile dysfunction tended to be older, had a higher prevalence of medical risk factors, and were more likely to be exposed to pesticides or solvents than patients in the nonorganic erectile dysfunction group.

We used polytomized dependent variables to assess the association between the exposure groups and erectile dysfunction groups by logistic regression. Table 3 shows the adjusted OR. The adjustment did not modify significantly the strength of associations. Exposure to pesticides slightly increased the risk of having an irregular erectile pattern (OR = 1.8), although not significantly. In contrast, exposure to pesticides significantly increased the risk of

Table 2. *General characteristics of nocturnal erectile activity*

| | Nonorganic Erectile Dysfunction | Organic Erectile Dysfunction | |
|---|---|---|---|
| | Normal Erectile Pattern | Irregular Erectile Pattern | Flat Erectile Pattern |
| Number* | 26 (13.1) | 147 (73.8) | 26 (13.1) |
| Age† (years) | 46.2 (11.1) | 48.4 (14.4) | 52.6 (12.8) |
| Body mass index† | 28.5 (4.2) | 29.2 (4.7) | 29.5 (3.2) |
| Tobacco* | | | |
| Nonsmokers | 18 (69.2) | 103 (70.1) | 16 (61.5) |
| Current smokers | 8 (30.8) | 44 (29.9) | 10 (38.4) |
| Alcohol* | | | |
| ≤20 g/day | 15 (57.7) | 105 (71.4) | 14 (53.8) |
| >20 g/day | 11 (42.3) | 42 (28.6) | 12 (46.2) |
| Diabetes* | 2 (7.7) | 16 (10.9) | 4 (15.4) |
| Hypertension* | 8 (30.8) | 47 (32.0) | 13 (50.0) |
| Cardiovascular* | 3 (11.5) | 24 (16.3) | 4 (15.4) |
| Therapeutic drugs* | 4 (15.4) | 30 (20.4) | 10 (38.5) |
| Exposure* | | | |
| Pesticides | 3 (11.5) | 27 (18.4) | 10 (38.4) |
| Solvents | 1 (3.9) | 10 (6.8) | 5 (19.2) |
| Heat | 4 (15.4) | 24 (16.3) | 3 (11.4) |

* n (%).
† Mean (SD).

having a flat erectile pattern (OR = 7.1). This effect was more pronounced in men who were frequently exposed to pesticides (OR = 8.4) than that in those who were exposed only occasionally (OR = 4.4). Exposure to solvents increased slightly, but not significantly, the risk of having an irregular erectile pattern (OR = 2.1) and significantly increased the risk of having a flat erectile pattern (OR = 12.2). Because only a small number of patients were exposed to solvents we were unable to classify this group according to frequency of exposure. We did not find a significant association between any of the abnormal erectile patterns and exposure to heat, although the risk was slightly elevated (OR = 1.7) for the flat erectile pattern. Odds ratios between irregular erectile pattern and flat erectile vs. normal erectile pattern suggested that the risk of flat erectile pattern was about fourfold higher than that of the irregular erectile pattern in the group exposed to pesticides ($P = .015$) and sixfold higher in the group exposed to solvents ($P = .024$).

## Discussion

We studied a population of men who sought medical help for perceived erectile disorders. This enabled us to investigate the association between highly prevalent risk factors and the pattern of nocturnal penile tumescence and rigidity. However, these men constitute a selected population, and any conclusions derived from such studies should be interpreted with caution.

Monitoring of nocturnal penile tumescence and rigidity is considered to be an objective diagnostic procedure that can verify patients' declarations and is a good means of differentiating between nonorganic and organic forms of erectile dysfunction (Davis-Joseph et al, 1995; Karadeniz et al, 1997). Although the nonorganic forms of erectile dysfunction are also considered to be psychogenic, the presence of psychological factors in patients with organic forms of erectile dysfunction cannot be excluded because all patients suffering from impotence also have a psychological component, regardless of the causes of the impotence. Most patients were referred to our andrology unit by general practitioners. Patients with clear psychological problems tended to be referred to a psychotherapist, and those whose problems had a suspected medical origin were preferentially referred to our services. This may ex-

Table 3. *Association between nocturnal erectile activity and exposure*

| | Nonorganic Erectile Dysfunction | Organic Erectile Dysfunction | | | | | |
|---|---|---|---|---|---|---|---|
| | | Irregular Erectile Pattern | | | Flat Erectile Pattern | | |
| | Normal Erectile Pattern (No.) | No. | OR (95% CI)* | *P* value† | No. | OR (95% CI) | *P* value† |
| No exposure | 18 | 86 | 1.0 | | 8 | 1.0 | |
| Pesticide exposure‡ | 3 | 27 | 1.8 (0.5–6.7) | .366 | 10 | 7.1 (1.5–33.0) | .013 |
| Occasional | 1 | 8 | 1.7 (0.2–14.1) | .643 | 2 | 4.4 (0.3–56.0) | .254 |
| Frequent | 2 | 19 | 1.9 (0.4–9.0) | .414 | 8 | 8.4 (1.4–49.1) | .018 |
| Solvent exposure§ | 1 | 10 | 2.1 (0.3–17.9) | .481 | 5 | 12.2 (1.2–124.8) | .034 |
| Heat-exposed‡ | 4 | 24 | 1.2 (0.4–4.0) | .735 | 3 | 1.7 (0.3–9.4) | .546 |

* OR indicates odds ratio; CI, confidence interval.
† Wald Test.
‡ Adjusted for age, therapeutic drugs and hypertension.
§ Adjusted for age, therapeutic drugs, hypertension and tobacco.

plain the low proportion (13%) of patients with nonorganic erectile dysfunction in our consulting population compared with other studies in which the percentage of psychogenic or nonorganic erectile dysfunction varied between 15% (Kaneko and Bradley, 1986) and 33% (Lee et al, 1994).

More than 40% of men included in this study were exposed to either chemical or physical environmental agents. This suggests a relationship between these factors and erectile dysfunction, but it may also represent a selection bias. Exposure prevalence may have been increased by the geographic region in which these men live, which is a major industrial and agricultural area. If this is the case, the bias should not be differential within erectile dysfunction groups. Another source of bias is the misclassification of the type of exposure. We evaluated the type of exposure based on detailed questionnaires, mostly consisting of questions about patients' occupations in order to obtain a qualitative assessment. However, many active compounds are combined in each of the exposure groups, and exposure conditions differ between individuals (ie, intensity and frequency). We could not divide patients into further subgroups or carry out a quantitative evaluation due to the limited size of our sample. Biological assessment of exposure would have provided more precise indicators, but this was not possible because of the cost and the large number of suspected chemicals to which individuals were exposed. Despite these limitations, it has been demonstrated that questionnaires provide good estimates of exposure (Tielemans et al, 1999).

We showed that among men who consulted for erectile disorders, exposure to pesticides or solvents is associated with an increased risk of having an abnormal nocturnal erectile pattern. Although the small study size limited the precision of the effect estimates, our results are consistent with previous observations. In 1970, a British study found that a team of 4 farm workers who had been using various pesticides for intensive agriculture became impotent (Espir et al, 1970). No other medical or psychological causes were apparent and they recovered their erectile function after discontinuing use, which suggests there was a relationship between exposure to pesticides and the occurrence of impotence. A more recent study found that nearly 27% of Egyptian pesticide formulators are impotent, compared with 4% in a control group matched for age (Amr et al, 1997). Erectile problems have also been reported among viscose-rayon production workers, who are exposed to the solvent carbon disulfide (Vanhoorne et al, 1994). Finally, the intensive use of solvents is suspected to be the cause of the increasing number of complaints of impotence among lacquer users in the Danish furniture industry (Sabroe and Olsen, 1979).

Male erection is basically a vascular event, controlled by a complex interplay between neural and endocrine factors. Some organochlorine pesticides and various industrial chemicals have estrogenic or antiandrogenic endocrine properties and interfere directly or indirectly with fertility and reproduction (Toppari et al, 1996; Cheek and McLachlan, 1998). In the past, male manufacturing workers who came into contact with the potent synthetic estrogen, diethylstilbestrol, and its industrial derivative, diaminostilbene, reported impotence and a decrease in libido (Shmunes and Burton, 1981; Quinn et al, 1990). It was recently shown that the endocrine disrupter, *p,p′*-DDE, a persistent antiandrogenic metabolite of the insecticide DDT, interferes with erectile function in rats (Brien et al, 2000). This supports the hypothesis that active environmental hormonal substances may cause erectile dysfunction. Other pesticides (eg, organophosphorus and carbamates) are recognized neurotoxicants, and cause a variety of problems in the human central nervous system. In the same way, exposure to solvents induces disturbances in the central nervous system and a number of claims have been made that common solvents may cause behavioral toxicity (White and Proctor, 1997). In addition, exposure to carbon disulfide has been shown to change serum levels of gonadotropins, suggesting that it acts on the hypothalamic-pituitary-gonadal axis (Lancranjan et al, 1969). Whether these properties are involved in the mechanisms by which these substances act on human erectile function remains to be determined.

Scrotal hyperthermia, for example, in individuals who submitted to thermal irradiation or who remain seated for prolonged periods of time, is recognized as a possible infertility risk factor (Thonneau et al, 1998). However, heat exposure was not found to be associated with the occurrence of abnormal nocturnal erectile patterns in our study, even though a slight increased risk was observed in patients with a flat erectile pattern.

The environmental agents we studied are more strongly associated with the forms characterized by a flat erectile pattern than with those characterized by an irregular erectile pattern. Whether this corresponds to a different pathogenic mechanism remains to be elucidated.

Considerable attention has been focused on the potential effects of a large variety of environmental contaminants of industrial origin on male reproductive function with particular attention to testicular cancer, genital malformations, and sperm quality. We believe that sexual dysfunction deserves further studies because it results from the deleterious effects of environmental chemicals.

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