Is vinclozolin a reproductive hazard to men?

Zober et al. examined fertility, hormones, and offspring sex ratio of men exposed to the fungicide vinclozolin. These authors were inclined to dismiss the possibility that it has any deleterious effect on the male reproductive system. I should like to suggest in contrast, that its effects in two respects resemble those of the nematocide dibronochloropropene (DBCP), which lowers sperm count and is associated with a highly significant lowered offspring sex ratio. Vinclozolin is not genotoxic and does not affect testicular tissue or fertility. It resembles those of the nematocide dibronochloropropene (DBCP), which lowers sperm count and is associated with a highly significant lowered offspring sex ratio.3

As was pointed out by James, the mean value of the serum FSH measurements was significantly higher in the exposed than in the control group (P = 0.004 both before and after exclusions based on known pre-exposure health conditions) and this would suggest a possible causal relation between exposure and increased LH. Furthermore, for both luteinising hormone (LH) and FSH, non-significant but negative dose-response trends were found relative to current intensity as well as estimates of cumulative dose of vinclozolin exposure (see fig 4 of original paper for scatter plot of FSH vs current intensity measure). Also, the man in the exposed group whose FSH level of 14.0 mU/ml was at the upper limit of normal had unilateral atrophy only found to have been present since childhood. All other readings among exposed men were within the reference range. From toxicological studies on vinclozolin and studies on other agents that block the testosterone receptor such as flutamide, the pattern of gonadotrophins at effective dose rates typically consists of increased testosterone, greatly increased LH, and marginally increased FSH concentrations.1 In the absence of dose-response and any abnormal FSH findings within the restricted exposed group and the lack of similarity between observed gonadotrophin patterns and what would be expected for an antiandrogenic agent, it is difficult to conclude that our findings are indicative of an effect related to vinclozolin.

Because the medical histories reported in table 3 of our paper did not distinguish between births occurring before and after first exposure, we reviewed the medical and work history data of all study group participants to find the number and sex of children born nine or more months after the date of the first exposure. Within this restricted observation period, there were 31 births, 13 male and 18 female, reported by 21 members of the study group. The number of births per family unit ranged from one to three. There were eight families with more male than female births. In 10 families, the testicular function was normal in both sons and in another 11 families with more female than male children and two families with one male and one female child born after exposure, 11 families with more females than male children and two families with one male and one female child born after exposure. These more detailed data are consistent with the trend noted by James, but are also consistent with a chance distribution of children by sex. Again available toxicological data for vinclozolin indicate that at toxicologically effective doses, it is not the sex ratio of offspring that is affected, but rather development in males.

A further issue raised by James was the resemblance between the effects of vinclozolin and those of DBCP on the basis of our FSH and sex ratio findings. From a toxicological viewpoint, there are few similarities between the two substances. DBCP has been shown to affect testicular tissue through direct genotoxic effects.1 Vinclozolin is not genotoxic and does not affect Sertoli cells directly, but rather acts by blocking the testosterone receptors.7 This mechanism of action must be different than that of DBCP and the anticipated pattern of gonadotrophin findings and their implications would be expected to be different as well.

In conclusion, we do concur with the suggestion that further systematic observation of people likely to have contact with vinclozolin is important and would be of scientific merit. However, we do not agree with the analogy drawn between vinclozolin and DBCP, which is not, in our opinion, supported by existing toxicological and epidemiological data.

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Modifiers of non-specific symptoms in occupational and environmental syndromes

Editor—In a thorough review Spurgeon et al. concluded that various occupational or environmental factors may lead to an increase of non-specific symptoms such as headache, tiredness, suggestive, and backache, when they are (rightly or wrongly) perceived as health hazards. Dissatisfaction with specific aspects of work may stimulate the occurrence of a similar pattern of health complaints. The authors discussed the role of individual and social factors in the perception of health and the tendency to report symptoms. Most probably some people are more sensitive to the psychosocial factors mentioned than others.1

Spurgeon et al did not pay attention to one point. If anxiety and dissatisfaction affect the perception of health, there might be a comparable effect on the perception of environmental factors. If so, negative or anxious feelings may also intensify the reporting of complaints about aspects of work in a non-specific way.

Many studies in the field of occupational epidemiology are at least partly based on self reported health or work related exposures. It is obvious that the tendencies mentioned may lead to biased results. Any particular problem that crops up in a work situation may generate anxiety or dissatisfaction, which in turn stimulates the tendency to report non-specific symptoms and complaints. Assuming that this tendency is stronger in some people than others, spurious associations between exposure and effect can be expected. This is an additional reason to explore how psychosocial factors may colour the reporting of complaints.2 Two topics should therefore be added to the recommendations for further research as formulated by Spurgeon et al.

(1) Empirical evidence should be searched for our hypothesis that feelings of anxiety or dissatisfaction may lead to increased complaints about (probably non-specific) aspects of work. Research done on

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Authors reply—In his letter, James raises questions about two specific health outcome measures reported in our paper, namely, serum follicle stimulating hormone (FSH) and sex of children born to fathers in the study group, and suggests that our findings for vinclozolin are similar to those reported by others for dibronochloropropene (DBCP), a known reproductive toxin in men.
 Correspondence

Author’s reply—We thank the correspondents

(2) A valid method should be developed for the assessment of the psychosocial factors which seem to affect the perception and reporting of symptoms and complaints, to evaluate their influence in a particular study, and—if possible—to correct for their effects.

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Author’s reply—We thank the correspondents for their comments on our paper, and fully agree. The point that psychosocial factors may also affect awareness, and thus reporting of possible hazards in the workplace is well taken and supported by the literature. It was our intention that these aspects should be identified and addressed within the psychosocial pathway, particularly in relation to contextual factors, attitudes, beliefs, etc.

We also endorse the view that there is a need for a valid method to assess the influence of psychosocial factors on symptom reporting in relation to any particular hazard. This is particularly important in the workplace where the results of any such assessment should help to determine the focus of any prevention and control strategies. In many cases this focus may turn out to be psychosocial rather than, for example ergonomic, physical, or chemical.

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9th International conference on occupational respiratory diseases.
13–16 October 1997. Kyoto International Conference Hall, Japan

The Conference is organised by the Japanese National Organising Committee for the Ninth International Conference on Occupational Respiratory Diseases, in collaboration with the Ministry of Labour of Japan, the International Labour Office and the Japan Industrial Safety and Health Association.

This Conference provides an excellent opportunity for scientists, health practitioners, hygienists, engineers, management, workers, and legislators to share experiences and ideas on the management and prevention of occupational respiratory diseases and to set priorities for the next century. The success of the meeting will depend upon contributions of papers and exhibits by leaders in the several disciplines of occupational health. We particularly encourage submissions from junior scientists, as well as from senior investigators.

Themes:
• Epidemiology of occupational respiratory diseases
• Health surveillance of workers exposed to respiratory hazards
• Aetiology, pathogenesis, diagnosis and treatment of occupational respiratory diseases
• Health hazard assessment by environmental and exposure monitoring
• Control measures against health hazards at the workplace
• Respiratory protective equipment
• Information, education and training on occupational respiratory diseases
• Working Groups
• ILO international classification of radiographs of pneumoconioses
• Global action on elimination of silicosis
• Occupational respiratory allergies
• Natural and synthetic fibres
• Relationship between occupational respiratory diseases and lung cancer.

Further information from: International Communications Specialists, Kashi Building, 2-14-9 Nihombashi, Chuoku, Tokyo 103, Japan.

The symposium is organised within the framework of Asclepios (a European concerted action on occupational hazards to male reproductive capability).

Two European concerted actions have been launched with the objective of mapping the European occurrence of infertility and identifying occupational hazards to male reproductive function. Dozens of national studies in Europe, the United States, and throughout the world within reproductive epidemiology have provided additional knowledge to add to agreed recommendations for future research. There is a need to identify environmental risk factors as well as suspected factors with none or limited significance for infertility and there is a need to identify studies and methods to be recommended and not recommended.

The symposium will include the following topics:
• The use of time to pregnancy in a demographic and epidemiological perspective: Alfred Spira
• Design and bias issues related to studies of subfertility: Jem Olsen
• Validity of time to pregnancy data in men and women: Michael Jaffe
• Semen quality as marker of fecundity in epidemiological studies: Jens Peter Bonde
• Endocrine markers of male fecundity: Richard Sharpe
• Impact of life style and social factors: Nel Roosveld
• Occupational and environmental impact on fertility: Steve Schrader

The symposium is open for free communication papers, however, the oral and poster session with plenary review will also be organised. The symposium language is English. Deadline for registration and submission of papers is 1 September 1997.

Further information from: Asclepios, Pia Pontt/Jane Bolten, Department of Occupational Medicine, The Steno Center of Public Health, Aarhus University Hospital, Noerrebrogade 37–39, DK-8000 Aarhus C, Denmark. Phone: +45 8949 4294; Fax: +45 8949 4260; E-mail: skmplp1@aaa.dk