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 dibromochloropropane (DBCP), which lowers sperm count and is associated with a highly significantly lowered offspring sex ratio.1

Zober et al. report that although the testosterone concentrations of exposed men were unchanged their follicle stimulating hormone (FSH) concentrations were significantly higher than those of controls (P = 0.004). Similarly, increased FSH and unchanged testosterone were found in men exposed to DBCP.1 Increased gonadotrophin, or lowered testosterone concentrations, or both are characteristic of many illnesses in men.2

The offspring of men exposed to vinclozolin numbered 44 sons and 51 daughters.1 Compared with an expected Caucasian live birth sex ratio (proportion male) of 0.515, these figures yield a chi2 of 1.05 (P = 0.15, one way). So although not formally significant, they may be thought to be suggestive. I suggest that further study of the possible effects of vinclozolin on the male reproductive system are merited. Its known similarities to an established hazard, DBCP, are disturbing. Especially interesting (and easy to gather) would be the sex ratios of offspring of men exposed to vinclozolin.

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 to vinclozolin and heightened, 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 v current intensity measure). Also, the man in the exposed group whose FSH level of 14.0 mIU/ml was at the upper limit of normal had unilateral atrophy only later 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 gonadotrophin suppression at effective dose levels 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 2 of our paper do 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 children, but no families with more female than male children. A further point is there were 11 families with more female than male children and two families with one male and one female child born after exposure. All families with more female 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 developmental events in male1

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.2 This mechanism of sex ratio imbalance is quite different from 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 prudent 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.

AZOBER M G OTT B VAN RAVENSWAY


Modifiers of non-specific symptoms in occupational and environmental syndromes

Editor—In a thorough review Spurgeon et al.1 concluded that various occupational or environmental factors may lead to an increase of non-specific symptoms such as headache, tiredness, and irritation, 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 anxiety and dissatisfaction with the perception of health and the tendency to report symptoms. Most probably some people are more sensitive to the psychosocial factors mentioned than others.2

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

(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
Correspondence

We thank the correspondents

workplace where the results of any such
reporting of symptoms and complaints, to
for the assessment of the psychosocial fac-
sational factors as well as physical character-

focus of any prevention and control strate-
gies. In many cases this focus may turn out
focus of any prevention and control strate-

tors which seem to affect the perception and
belief, etc.

This is particularly important in the
workplace is well taken and supported by
literature. It was our intention that these

The New England Epidemiology Institute

The theme of the conference is preparing for
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The 15th Asian conference on occupational
health 31 August–3 September 1997.
Kuala Lumpur, Malaysia

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

The Conference, organised by the
Japanese National Organising Committee for
the Ninth International Conference on
Occupational Respiratory Diseases, in col-
aboration 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 practition-
ers, hygienists, engineers, management,
workers, and legislators to share experiences
and ideas on the management and preven-
tion 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 lead-
ers in the several disciplines of occupational
health. We particularly encourage submis-
sions from junior scientists, as well as from
senior investigators.

Themes:

establishment in developing countries,
pharmacoepidemiology, meta-analysis, epi-
demiology in public health practice, clinical
trials, survival analysis in epidemiology,
decision and cost effectiveness analysis in
health care, the biology and epidemiology of
cancer, health care use and outcomes
research, regression modeling in epidemiolo-
gy, perinatal epidemiology, occupational and
environmental epidemiology, molecular epi-
demiology and the use of biomarkers, ethics
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tion in a scientific journal. Invited faculty
include excellent teachers and prominent
researchers from leading universities.
Registrants may receive graduate-degree
credit or continuing education credits from
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tion (AMA category 1) through Tufts
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maintenance from the American Industrial
Hygiene Association.

Further information from: The New
England Epidemiology Institute, Depart-
ment PA-ORI, One Newton Executive
Park, Newton Lower Falls, MA 02162-
1450, USA. Phone: (617) 244–1200;
Fax: (617) 244–9669; E-Mail: epidemiol@aol.com; World Wide Web
Home Page: http://www.epidemiology.com

The symposium is organised within the
framework of Asclepios (a european con-
certed action on occupational hazards to
male reproductive capacity).

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 recommenda-
tions for future research. There is a need to
identify environmental risk factors as well as
suspected factors with none or limited sig-
nificance for infertility and there is a need to
identify studies and methods to be recom-
mended and not recommended.

The symposium will include the following
stages of the conference:

• The use of time to pregnancy in a demo-
graphic and epidemiological perspective:
Alfred Spira

• Design and bias issues related to studies
of subfertility: Jens Olen

• 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
Roeleveld

• Occupational and environmental impact
on fertility: Stevo Schrader

The symposium is open for free communi-

Further information from: Asclepios, Pia
Poulsen Bolesen, Department of Occu-
pational Medicine, The Steno Center of Public
Health, Aarhus University Hospital,
Noerrebrogaade 37–39, DK-8000 Aarhus
C, Denmark. Phone: + 45 8949 4294;
Fax: +45 8949 4260; E-mail: akh gp22s.
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statistics for epidemiologists, clinical
research, theory and practice of epidemiolo-
gy, occupational epidemiology, meta-analysis, epi-
demiology in public health practice, clinical
trials, survival analysis in epidemiology,
decision and cost effectiveness analysis in
health care, the biology and epidemiology of
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• Health surveillance of workers exposed to
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• Aetiology, pathogenesis, diagnosis and
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• Health hazard assessment by environ-
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• Control measures against health hazards

• Occupational respiratory allergies

• Natural and synthetic fibres

• Relationship between occupational respi-


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