

Comment on Den Hond E., Roels H.A., Hoppenbrouwers K., Nawrot T., Thijs L., Vandermeulen C. et al. Sexual Maturation in Relation to Polychlorinated Aromatic Hydrocarbons: Sharpe and Skakkebaek's Hypothesis Revisited. *Environ. Health Perspect.* (2002), 110(8), p. 771-776.

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Dear Editor,

The paper of Den Hond *et al*(1) is very interesting. The main reason is that the reported work demonstrates the potential of biomarkers in environmental health programmes. However, we argue with the conclusion of the authors that “our findings suggest that, in line with the concept of endocrine disruption and Sharpe and Skakkebaek’s hypothesis (...), environmental exposure to PCAHs may adversely interfere with the sexual maturation during the foetal and pubertal stages of development.”

The description of the project suggests that the study was designed to investigate the effects of incinerator emissions in Wilrijk, Antwerp on the local population. However, the study was part of a larger research project commissioned by the Flemish government to determine the feasibility and issues to be considered in developing environmental health monitoring. More particular, the study of Den Hond *et al* was designed to determine whether evaluation of biomarkers measured at the regular medical examination of adolescents at the end of their secondary education period would be feasible. We were asked by the Flemish government to review the results of this project.(2;3) We feel that the objectives and hypotheses underlying a feasibility study should not be convoluted with those relative to the hypotheses arising from specific concerns in certain a priori defined regions.

A major shortcoming of the design (if the paper is to be considered as a report of a local environmental health issue) is the lack of randomness regarding both the study areas and the recruitment of the participants. The study areas were well known polluted regions within the conurbation of Antwerp. This knowledge may have influenced the choice of tests to be performed. Researchers should be cautious regarding a priori choices of study areas, whether or not the sponsor influences the choice.

The use of volunteers instead of randomly selected participants is another flaw, introducing an extra risk of confounding. As a consequence, e.g., the proportion of boys to girls in the three study areas differed considerably: from 0.7 to 3.0. In this case there may have been a selection bias of adolescents in lesser physical condition volunteering for examination.

Reported results were the outcome of analysing a multitude of associations among the empirical data. They did not emerge after a rigorous test of an *a priori* formulated hypothesis, at least not to our knowledge. Such findings are valuable as they may generate hypotheses for further research. In this respect we agree with the authors’ closing sentence: “(...) further studies should be undertaken to confirm or to refute our interpretation of the present findings.”(1)

The sexual development of the study subjects was judged by the examining physicians. The correspondence in ratings varied between fair and good (as validated by *kappa* coefficients).(4) It is then important to exclude a

systematic over- or underestimation by one of the examining physicians. This test has not been reported in the study.

A final remark relates to the reference the authors make to an earlier report on pregnancy outcome in Flanders (... in 1997 the Flemish government reported a higher percentage of medically assisted conceptions in the district around the waste incinerators compared with the rest of Flanders...).(1;5) We feel that this report is incorrectly and selectively referenced, suggesting that the findings are in line with earlier results. Taking into account the mother's age no significant differences in way of delivery were found in the earlier study. Furthermore, the report does not contain statements about the necessity of medical assistance at delivery.

Part of the above criticism was outlined in the review reports(2), but unfortunately not addressed in the paper in your journal.

To conclude, we would like to reiterate the statement in our review reports that we commend the authors with their highly relevant and extensive research work. However, they should have placed their study more clearly in the perspective of the Flemish environmental health project. Their conclusions generate interesting hypotheses for further work, but should not be viewed as the results of a cause and effect study.

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References

1. Den Hond E, Roels HA, Hoppenbrouwers K, Nawrot T, Thijs L, Vandermeulen C, Winneke G, Vanderschueren D, Staessen JA. Sexual Maturation in Relation to Polychlorinated Aromatic Hydrocarbons: Sharpe and Skakkebaek's Hypothesis Revisited . Environ Health Perspect 110:771-776 (2002).
2. Cuijpers C, Molenberghs G, Passchier WF, Pieters JLL. De vinger aan de pols van een gezond Vlaams milieu (2). Rapportage van een review-commissie van het Project 'Milieu en Gezondheid' [Taking the temperature of environmental health in Flanders (2). Findings of a review committee of the Project 'Environment and health' - in Dutch']. Brussel:Ministerie van de Vlaamse Leefgemeenschap,2000.

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3. Ghoetghebeur EJT, Passchier WF, Pieters JIL. De vinger aan de pols van een gezond Vlaams milieu. Rapportage van een review-commissie van het Project 'Milieu en Gezondheid' [Taking the temperature of environmental health in Flanders. Findings of a review committee of the Project 'Enviornment and health' - in Dutch']. Brussel:Ministerie van de Vlaamse Leefgemeenschap,2000.
4. Fleiss JL. Statistical Methods for Rates and Proportions. New York:John Wiley & Sons,1981.
5. Aelvoet W, Bekaert Y, Dejonghe M. In: Gezondheidsindicatoren 1997 (Aelvoet W, Fortuin M, Hooft P, Vanoverloop J, eds). Brussels:Ministerie van de Vlaamse Gemeenschap,1999;130-141.