Congenital anomalies in the offspring of military personnel?

S-E Chia

Commentary on the paper by Mageroy *et al* (see page 92)

Human reproduction is a complex process and can be affected in many phases by both host and environmental factors. Many studies have found it difficult to distinguish the occupational causes of congenital malformations from other factors related to parents' characteristics and their living environment. The extrapolation of results of animal studies to humans is also complicated because there are structural and functional differences between the species, and the mechanisms of harmful effects are seldom known. At present, knowledge on the potential reproductive toxicity of even rather common occupational exposures is limited and only suggestive in many cases.¹ The conception of an embryo involves the fertilisation of the ovum by a spermatozoon. If the ovum and/or spermatozoon is defective, the resulting embryo may die early or late in gestation (resulting in spontaneous abortion or miscarriage). If the defective embryo develops to term, the infant could present with stillbirth or congenital anomalies may be detected at birth or later in life. Another scenario is that the embryo is conceived by a normal ovum and spermatozoon, but in the process of development in the uterus, it is exposed to agents that may be harmful to the different organ systems. Depending on the type of agents and at which stage of the developmental process of the organs' formation the exposure occurs, different congenital anomalies may result. Exposure to potential teratogens could come from the maternal or paternal side.

The fetus could be exposed to agents that cross the placenta or as a direct exposure (for example, when a pregnant woman is exposed to ionising radiation). Possible exposure from the father could come in the form of toxins in seminal fluids resulting in maternal contamination after sexual intercourse, and home contamination (working clothes, equipment), leading to exposure of the woman during pregnancy.¹

Many of the associations described between occupational exposures and adverse reproductive outcomes in epidemiological studies are equivocal and

often controversial. Common weaknesses in most of these studies included inaccurate assessment of exposures, different classification systems, different inclusion criteria for birth defects, potential bias and confounders, and low statistical power.²

The report by Mageroy *et al*³ on the risk of congenital anomalies in the offspring of personnel who served aboard a Norwegian missile torpedo boat is an interesting study which warrants discussion. This cross-sectional study included 2265 employees of the Norwegian Navy who responded to a questionnaire sent by mail at the end of 2002. The aims of the study were to estimate the risk of having children with congenital anomalies or having stillborn children among the offspring of workers who had served aboard a Norwegian missile torpedo boat compared with other subjects who work in the Navy, and to investigate possible differences in exposure and other risk factors between these groups.

The study response rate of 58% is lower than what is desirable, especially in birth defect studies where selection bias is of concern. Respondents could have been informed of the earlier concerns regarding possible adverse reproductive outcomes among personnel who had served aboard a Royal Norwegian Navy missile torpedo boat in the 1990s, in 1998, and again in 2001. It would be interesting to examine the percentages of respondents in the three categories—those who served aboard a ship, those who served aboard a missile torpedo boat, and those who served aboard the *KNM Kvikk* (the patrol boat)—and compare them to the non-respondents in each category. This step would determine whether any of the categories is overrepresented, which could confound the study's findings.

The job descriptions on board *KNM Kvikk* are very specific compared to those in the other sectors of the Navy. It could be expected to find, by chance, higher risks and even significant *p* values for some of these "possible risk factors" compared with "all other respondents". Furthermore, a statistically significant difference in risk

between Group A and Group B for exposure X does not imply that X is the causative factor. There may be other exposures that could have confounded the association. While the authors did compare smoking and alcohol consumption as possible confounders, other important confounders (for example, drug histories and abuses, medical conditions, and socioeconomic status) were not included. Finally, the interpretation of an association between an exposure and disease as being causal is strengthened when a plausible biological mechanism can be demonstrated. The findings reported by Mageroy *et al*³ have to be evaluated bearing in mind all of the above considerations.

One of the questions that need to be asked is whether electromagnetic fields could have been a contributory factor for congenital anomalies. To date, there are no persuasive data suggesting a health risk, but this research field is still immature with regard to the quantity and quality of available data. As technology is constantly changing, there is a need for continued research on this issue.

It would be premature to state that "service aboard a naval ship was associated with increased prevalence of congenital anomalies and stillbirth" given some of the methodological issues that have been discussed. However, it would seem a reasonable and possible proposition to conduct a prospective study on naval service and reproductive outcomes. It is well within the means of the naval service to do this as most of the staff would be on full time service over a long enough period of time to accrue the necessary number to achieve sufficient statistical power. Military services (understandably in some situations) are known for their secrecy because of the sensitive nature of some information. However, withholding this information may impede a better appreciation of the actual health risk, if any, that may be related to the service men in the course of their work. I look forward to the day when there will be more reports in the scientific literature regarding the health of workers in the military services.

Occup Environ Med 2006;**63**:82–83.
doi: 10.1136/oem.2005.023994

Correspondence to: Prof. Sin-Eng Chia, Department of Community, Occupational & Family Medicine (MD3), Yong Loo Lin School of Medicine, National University of Singapore, 16 Medical Drive, Singapore 117597, Republic of Singapore; cofcse@nus.edu.sg

Competing interests: none declared

REFERENCES

- 1 Shi L, Chia SE. A review of studies on maternal occupational exposures and birth defects, and the

limitations associated with these studies. *Occup Med (Lond)* 2001;**51**:230–44.

2 Chia SE, Shi LM. Review of recent epidemiological studies on paternal occupations

and birth defects. *Occup Environ Med* 2002;**59**:149–55.

3 Mageroy N, Møllerlokken OJ, Riise T, et al. A higher risk of congenital

anomalies in the offspring of personnel who served aboard a Norwegian missile torpedo boat. *Occup Environ Med* 2006;**63**:92–7.

Epidemiology

Micro-epidemiology of the healthy worker effect?

D Heederik

Commentary on the paper by Bakirci *et al* (see page 126)

Bakirci and colleagues¹ describe a high turnover of the workforce in cotton spinning mills and try to analyse if the high turnover is health driven. These observations actually relate to one of the driving forces underlying the so called “healthy worker effect”. The healthy worker effect was probably first described by William Ogle in an appendix of the Registrar General’s report on mortality in England and Wales.² It refers to the observation that the working population is healthier than the general population. Ogle identified two kinds of selection responsible: one working at the time of hire, and the other working at the time of employment. The first selectively attracts or rejects new workers depending on physical demands of the job and health selection, by for instance occupational physicians. The second forces people to leave industry because their health is too much impaired for the job they are in. Several respiratory morbidity studies have focused on selection out of the workforce. This Turkish study is relevant because workers were followed intensively: after 1, 3, 6, and 12 months of employment, and after they had left the industry. At first sight the results seem straightforward. A regression model indicated that those who left the industry had work related lower respiratory symptoms before they left, suggesting that they left because of their symptoms. However, only a few left because of health problems according to

the post-leaving survey, and baseline data indicate complete absence of respiratory disease. Surprisingly, cross-shift decliners in FEV₁ had a lower likelihood of leaving than non-decliners, since there was a negative borderline statistically significant association with leaving the industry.

Other determinants of leaving the industry could not be identified. Average endotoxin exposure levels were low in this population—around a few hundred EU/m³—but for some job titles the levels are around a few thousand EU/m³ (personal communication). The latter are exposure levels at which we expect to see relationships with acute lung function change and respiratory symptoms. The statistical modelling seems problematic because the model contains several correlating (proxy) exposure variables (job title, dust and endotoxin level) and intermediary variables (symptoms, and cross-shift and cross-week lung function change). Therefore collinearity and over-correction may have occurred, leading to biased or uninterpretable regression coefficients.

Somewhat puzzling are the observations on atopy. Atopy did not seem a predictor of leaving the industry. Earlier studies have shown that cotton dust exposure and atopy interact with acute lung function changes,³ suggesting that exposed atopics are more at risk for developing respiratory effects. The question remains what more detailed

explanatory models with interactions between exposure and atopy might have yielded. The atopy prevalence among these cotton workers is untypically low for most western countries, and this either reflects a rural background of this population, or the other force underlying the healthy workers effect: self-selection. We know that the atopic status may change over time, possibly also under influence of environmental factors such as a high endotoxin exposure.^{4,5} It would have been interesting to have information about the atopic status among leavers at the time they left the industry, to see whether there was any exposure related reversal.

Most striking is the high labour turnover in this study. Although this study did not convincingly show that there is health driven selection in or out of the workforce, this high turnover rate is a relevant observation in itself. We need to know to what extent workers who leave rapidly differ from those who remain in industry to be able to interpret study findings correctly.

Occup Environ Med 2006;**63**:83.
doi: 10.1136/oem.2005.024307

Correspondence to: Prof. Dr D Heederik, Division Environmental and Occupational Health, IRAS, Utrecht University, PO Box 80178, 3508 TD Utrecht, Netherlands; d.heederik@iras.uu.nl

Competing interests: none declared

REFERENCES

- 1 Bakirci N, Kalaca S, Fletcher AM, et al. The predictors of early leaving from the cotton spinning mill environment in newly hired workers. *Occup Environ Med* 2006;**63**:126–30.
- 2 Ogle W. Supplement to the 45th Annual Report of the Registrar General of Births, Deaths, and Marriages, in England, 1885.
- 3 Jones RN, Butcher BT, Hammad YY, et al. Interaction of atopy and exposure to cotton dust in the bronchoconstrictor response. *Br J Ind Med* 1980;**37**:141–6.
- 4 Horak F Jr, Studnicka M, Gartner C, et al. Parental farming protects children against atopy: longitudinal evidence involving skin prick tests. *Clin Exp Allergy* 2002;**32**:1155–9.
- 5 Portengen L, Preller L, Tielen M, et al. Endotoxin exposure and atopic sensitization in adult pig farmers. *J Allergy Clin Immunol* 2005;**115**:797–802.