CORRESPONDENCE

Lymphocyte subsets in subjects exposed to asbestos: changes in circulating natural killer cells

Sir,—After reading the paper by Jarad *et al* (1992;**49**:811-14) on the changes in circulating natural killer cells in subjects exposed to asbestos, and in particular the last inevitable sentence, "This reduction may be at least partially responsible for the increased susceptibility to development of malignancies in asbestos workers," we have an urge to comment.

Firstly, definite proof for such a conclusion can only originate from a prospective study of asbestos workers. With regard to asbestosis or development of malignancy, only post hoc analysis of the number and proportion of CD 16 positive cells will show the predictive value (sensitivity) and specificity of this biological indicator.

Secondly, this study was done on workers with asbestosis and workers without asbestosis and as such can only report differences in a biomarker either caused by asbestosis or susceptibility. Clearly the authors report no difference in CD 16 number or proportion between the two groups of exposed workers. On the other hand in the total asbestos group (with and without asbestosis) a decrease in CD 16 positive cells was found with increasing duration of exposure. We are interested to know what differences existed in duration of exposure between both asbestos exposed groups, as generally workers without asbestosis are less exposed to asbestos compared with subjects with asbestosis. Also, fibre-years rather than duration of exposure should be applied as a measure of asbestos dose. As such we claim that the concluding suggestions of Jarad and colleagues should be considered with reservation: number of CD positive cells could also prove to be an exposure index of asbestos dose or asbestosis instead of an indicator of susceptibility. In that context, we also do not understand why subjects with asbestosis were studied when asbestos related malignancies were of greatest interest.

Cross sectional studies often report the expression of biomolecular mechanisms in occupational settings, and it seems a trend to end such papers with concluding remarks on variations in susceptibility or on predictive power of such indicators. Unfortunately however, a thorough follow up design, the only empirical method to prove such hypotheses, is mostly lacking.

Currently our group is evaluating several cross sectional studies that were performed in 1987 in coal miners with regard to development and progression of coal workers' pneumoconiosis.[1] This follow up will probably enable us to show whether or not and to what degree tumour necrosis factor α and type III procollagen peptide can be used as predictive biological markers for pulmonary fibrosis in coal miners.[2]

As such, our awareness of the importance and relevance of this field of biological research, which we usually refer to as molecular epidemiology,[1] has increased. Also, of course, we have become familiar with major methodology, the statistical limitations, and the pitfalls in such studies, and as such, we stress that a statistical approach, epidemiological methodology, and terminology in general discussion should be used unambiguously. We believe that much more attention should be paid to the actual follow up of subjects involved in studies that generate hypotheses regarding the predictive power of biological markers. Only in this way can markers of susceptibility be used in occupational or environmental settings as a powerful tool better to understand, and maybe even to control, the interindividual variation in health prognosis in populations at risk.

P J A BORM
P F R SCHINS
Department of Health Risk Analysis and Toxicology, University of Limburg, PO Box 616, 6200 MD Maastricht, The Netherlands

1 Borm PJA, Meijers JMM, Swaen GMH. Molecular epidemiology of coal workers' pneumoconiosis: application to risk assessment of oxidant and monokine generation by mineral dusts. *Exp Lung Res* 1990; **16**:57–71.
2 Borm PJA, Schins R, Janssen YMW, Lenaerts L. Molecular basis for differences in susceptibility to coal workers' pneumoconiosis. *Toxicol Lett* 1992;**64/5**:767–72.

Authors' reply

Sir,—There was no significant difference in duration of exposure to asbestos between asbestos workers with asbestosis and those without (mean 15·9 (SD 2·8) and 13·0 (1·9) years respectively).

The concentration of fibres encountered by workers in diverse occupations in which exposure was not monitored systematically cannot be determined retrospectively. Duration of exposure is the most robust measure of exposure in such circumstances because it can be determined with reasonable accuracy.

Asbestos workers without malignant diseases were studied because the presence of clinically overt malignancy such as lung cancer is itself associated with changes in natural killer cell activity.[1] Changes in asbestos workers with malignant disease might be a consequence of the malignant disease or of exposure to asbestos. Changes in workers who do not yet have overt malignant disease are more likely to be a result of exposure to asbestos.

We did not claim to have provided "definite proof" of anything. We reported the results of a cross sectional study and quite properly hypothesised as to the possible relevance of our findings. The need for longitudinal studies does not imply that results of cross sectional studies should not be reported or that the significance of their findings should not be speculated on; a useful function of such studies is the generation of hypotheses to be tested.

1 Al Jarad N, Poulakis N, Macey M, Uthayakumar S, Newland AC, Rudd RM. Lymphocyte subsets in peripheral blood and bronchoalveolar lavage in patients with lung cancer. *Am Rev Respir Dis* 1990;**141**: A57.

Smoking adjusted mortality due to asthma in a population of Swedish working women

Sir,—In an earlier register based cohort study we reported that men with occupational exposure to organic dusts, such as farmers and woodworkers, had an increased mortality from asthma.[1]

We have now carried out a similar study on women aged 20–64 in 1960 who reported an occupation in the 1960 National Census. For each occupation the observed number of deaths from asthma was obtained from a linkage between the Register of Causes of Death 1961–86 and the occupational information in the 1960 National Census. When calculating the expected number of deaths all

Occupation	No of cases	Crude SMR	Smoking (95% CI) adjusted SMR
Caretakers	90	963	988 (788–1187)
Other sheet metal workers	16	585	531 (245–818)
Maids	69	317	331 (256–406)
Waitresses	38	337	289 (181–396)
Dressmakers	18	240	248 (137–359)
Housekeepers	24	192	190 (114–267)
Textile fabric workers	26	174	173 (106–239)
Farm workers	22	144	165 (105–225)
Working proprietors	27	151	150 (93–207)
Stock clerks	37	153	146 (96–104)
Sewers	43	151	143 (97–188)
Primary education teachers	53	105	109 (70–147)
Cooks	23	111	105 (59–150)
Shop assistants	110	110	102 (82–122)
Auxillary nurses	43	105	97 (65–128)
Book keepers	25	86	78 (44–111)
Office clerks	23	71	62 (33–91)
Other clerks	27	61	54 (31–77)
Housemaids	17	20	18 (9–28)

Swedish women with an occupation in the 1960 Census were used. The expected numbers of deaths were standardised for age based on comparisons in five year birth cohorts and standardised mortality ratios (SMRs) were calculated for each occupation. As in our earlier study we calculated smoking adjusted SMRs,[2] based on data from a survey in 1963 of smoking habits in different occupations. We assumed that smokers had a twofold increased risk for asthma compared with non-smokers. Confidence intervals (95% CIs) were calculated based on a Poisson distribution. The analyses were only carried out on occupations with more than 15 observed cases (n = 19). The table shows the results.

An increased mortality due to asthma was found in eight occupations. In three, textile fabric workers, dressmakers, and farm workers, occupational exposures such as cotton dust and microorganisms could be risk factors. Textile fabric workers are probably exposed to dust from crude cotton. Hence some misclassification between asthma and byssinosis may exist in that occupation.

With a reservation for waitresses, the increased risks in the other occupations, caretakers, maids, housekeepers, and other sheet metal workers, may be explained by selection factors—that is, subjects with asthma or respiratory symptoms seek physically light occupations.

LARS-GUNNAR HÖRTE
Department of Forensic Medicine, University of Uppsala, Uppsala, Sweden
KJELL TORÉN
Department of Occupational Medicine, St Sigfridsgatan 85b, S-412 66 Göteborg, Sweden

1 Torén K, Hörte LG, Järvholm B. Occupation and smoking adjusted mortality due to asthma among Swedish men. *Br J Ind Med* 1991; **48**:323–6.
2 Axelson O. Aspects on confounding in occupational health epidemiology. *Scand J Work Environ Health* 1978; 4:85–9.

NOTICES

The Centers for Disease Control, National Institute for Occupational Safety and Health have released the Work-Related Lung Disease (WoRLD) Surveillance Report, Supplement 1992. The original report, released in 1991, summarises surveillance data for occupational respiratory diseases. The 1992 supplement includes data not previously presented. The report contains information of use to public health officials, researchers, management and labour officials, and others working in occupational health disciplines.

Copies of the original WoRLD report and the 1992 WoRLD supplement may be obtained by calling 1–800–35NIOSH or by writing to: Epidemiological Investigations Branch, Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, 944 Chestnut Ridge Road, Morgantown, West Virginia 26505, USA.

Nato advanced study institute on modulation of cellular responses in toxicity, Ponte di Legno, Brescia, Italy, 24 January—3 February 1994

Composed of an integrated series of invited lectures, the Institute will focus on current concepts and strategies in research on cellular responses in toxicity. Topics for discussion will include: modern methods in toxicology; milestones in cell toxicology; target organ toxicity; strategic applications. Panel discussions and round tables will be organised to encourage exchange of ideas among participants and faculty. Directors of the course are: professor Corrado Lodovico Galli of the University of Milan and professor Alan Marvin Goldberg of the Johns Hopkins University of Baltimore.

Attendance is restricted to a maximum of 60 participants. A limited number of grants will be available to defray part of the expenses of pre and postdoctoral trainees. Persons wishing to attend the Institute should send a curriculum vitae and a list of publications to the organising secretariat. Deadline: 10 November 1993. The deadline for application for grants is 10 October 1993. For more information contact the organising secretariat: Mrs Daniela Galli, Nutrition Foundation of Italy, Via G. Balzaretti 9-20133 Milano, Italy. Telephone (+39/2) 29404672-20488320; fax (+39/2) 29404961.

International section of the ISSA for the Prevention of Occupational Risks in the Chemical Industry

15th International Symposium, safety pays! Safety in interaction with quality, productivity, and economy, 30 August—1 September 1993 in Lugano, Switzerland.

Simultaneous translation: German, English, French, and Italian. For further information contact: AISS–Chemistry Section c/o Berufsgenossenschaft der chemischen Industrie, Kurfürsten-Anlage 62, D-6900 Heidelberg, Germany. Fax 06221—523323.

16th International Symposium, machinery in the chemical, plastics and rubber industries—safe design and safe use, 6 to 8 June 1994 at the ACHEMA 94 in Frankfurt am Main

Simultaneous translation: German, English, and French. Deadline for papers 10 August 1993. For further information contact: AISS Chemistry Section c/o Berufsgeossenschaft der chemischen Industrie, Kurfürsten-Anlage 62, D-6900 Heidelberg, Germany. Fax 06221—523323.