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.

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- 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