Reply

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The letter of Samuelsson and Palmblad has been helpful in prompting further discussion of our findings, which nonetheless do not appear to contradict their own. The respiratory burst oxidase (NADPH oxidase complex) catalyzes the production of O_2^- by activated phagocytes. This activation depends on multiple signal transduction pathways. Failure to produce O_2^- is characteristic of chronic granulomatous disease, an inherited phagocyte function disorder and of other diseases, some hematologic malignancies in particular. When we assessed NADPH oxidase activity by the photometric method, no significant differences were found between findings in polycythemia vera (PV) patients and those in control subjects, whether the polymorphonuclear leukocytes (PMN) were stimulated or not (resting PMN).

The only stimulus employed in our published study was phorbol myristate acetate (PMA). The activation of the respiratory burst oxidase by PMA is thought to be mediated through the protein-kinase-C-catalyzed phosphorylation of p47phox and possibly other oxidase subunits [1], whereas N-formyl-methionyl-leucyl-phenylalanine (fMLP) showed protein-kinase-C-independent pathways and receptor-mediated activation. In our paper, the first study by Samuelsson et al. [2] was quoted as showing normal burst oxidase activity in PV PMN, assessed by chemiluminescence and in response to PMA stimulation: this finding was in agreement with ours obtained with the photometric method. Moreover, in the same study, those authors found that the oxidative metabolism in PV patients was subnormal only after fMLP stimulation, suggesting the presence of a stimulus-response coupling defect and in a more recent detailed studies on the different biochemical steps performed they demonstrated phospholipase-D-mediated activation impairment [3]. In our paper, we found that patients with myelodysplastic syndromes (MDS) and those with chronic myeloproliferative disorders (cMPD) had similarly reduced scores when evaluated by microscopic NBT reduction, whereas the photometric method showed a cMPD reduction only in patients susceptible to infection. The photometric method was therefore more specific than the microscopic one, this explaining some apparently contradictory findings. Furthermore, since microscopic NBT reduction was performed in whole blood, the interaction between PMN, platelets, monocytes, lymphocytes and their environment should be further investigated.

References

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