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Title: Modeling of exhaled nitric oxide in relation to smoking history – A population based study

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Body: Smokers produce less NO in central airways compared to nonsmokers whereas the effect of smoking on NO concentration in the peripheral alveolar regions remain unclear, particularly if axial diffusion of NO is considered. It is also unclear to what extent exhaled NO recover among ex-smokers. We have measured exhaled NO (FENO) at three flow rates in a population sample of 3968 subjects and the aim of the present analysis has been to try and clarify effects of current and previous smoking on exhaled NO and its central and alveolar origin and to provide reference equations for exhaled NO for healthy smokers. The essential findings are 1) FENO of ex-smokers and nonsmokers are indistinguishable, 2) the apparent association between FENO and time since smoking cessation in ex-smokers disappears when age is taken into account, 3) smokers have higher NO concentration in the alveolar region than nonsmokers as detected when axial diffusion is considered, 4) the higher limit normal of healthy smokers is considerably lower than the corresponding limit of normal healthy nonsmokers.