The study of Pesch and colleagues (1) investigated the impact of occupational exposure on bladder cancer risk and its modulation by the polymorphic N-acetyltransferase 2 (NAT2), based on a follow-up of the EPIC cohort, recruited within 1991-2000. With regard to interpretation of the results, we have the following comments.

The study investigated 52 at-risk occupations ever performed in 754 bladder cancer cases and 833 controls and did not reveal significantly elevated occupational bladder cancer risks stratified for gender. This may be due to dilution effects by low-level and/or short-term exposures and few observations. However, the results were adjusted for age and region as well as for multiple testing also for infrequent occupations. At present, the coherence of aromatic amine exposures and bladder cancer risk can be seen only in groups of persons or specific areas with higher present or past occupational exposures to aromatic amines. Such a
recently detected industrial hot spot is the use of carcinogenic azo dyes in sprays for metal crack testing (2).

The authors address the rapid \textit{NAT2} genotype as a bladder cancer risk factor in occupationally exposed persons. This assignment is based on two studies in Chinese benzidine production and use facilities. But it contrasts to results obtained in Caucasian populations, where slow acetylators, when exposed to aromatic amines, are at the higher risk(3).

Based on their study, the authors concluded that the \textit{NAT2} genotype had no impact on bladder cancer risk. In Europe, the production of most carcinogenic aromatic amines, such as benzidine, was stopped in the 1960s and early 1970s, mostly due to legal regulations. From 1991 to 1993, we conducted a hospital-based study in the county of Leverkusen, a hot spot area of human bladder cancer and of former manufacture of carcinogenic aromatic amines (4). 55\% of the 196 phenotyped bladder cancer patients comprised slow acetylators at a normal percentage (55 \%). However, the portion of slow acetylators was higher (62-71 \%) in subgroups with specific histories of occupational exposure.

It also appears that the “slow” \textit{NAT2} genotypes comprise combinations of different “slow” haplotypes with different resulting metabolising capacities. In this context, we could recently show that the frequent “ultra-slow” \textit{NAT2*6A} was associated with an elevated bladder cancer risk, based on 1,712 bladder cancer cases and 2,020 controls (5).

In essence, we regard the final statement of the authors (1) that “testing for \textit{NAT2} would be inappropriate in occupational settings” as an over-interpretation.

References


NAT2 and bladder cancer - Letter
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