

CORRESPONDENCE

Exposure–response relationships for airborne allergens

In their recent review, Baur *et al.* [1], stipulate that only a few tentative exposure standards exist for airborne allergens, although exposure–response relationships are available for several allergens, which would allow standard setting for more allergens. They refer to some basic toxicological principles like evaluation of No Observed (Adverse) Effect Levels (NO[A]EL) for asthma as the basis for exposure standards.

Although we agree with Baur *et al.* in general terms, we would like to comment that standard setting for allergens present in the (work) environment is less straightforward as one might hope for. Baur *et al.* suggest that Threshold Limit Values (TLVs) for allergen levels in air should protect workers from developing work-related asthma. TLVs have in the past been proposed by the American Conference of Governmental Industrial Hygienists and have repeatedly been heavily criticized for their limited toxicological underpinning and corporate influence on the standard setting process [2,3]. The more generic term ‘Health-Based Recommended Exposure Level (HBROEL)’ is to be preferred instead since it refers to purely health-based exposure limits as developed by several European countries. Usually, a HBROEL is expected to protect a worker, and according to some definitions even his offspring, against adverse health effects after lifelong exposure for 8 hours a day and 40 hours a week.

The first question in this context is what should be regarded as an adverse effect? Baur *et al.* make an implicit choice for occupational asthma as the relevant adverse effect in their argumentation. Given the definition of a standard one might wonder if other endpoints should be considered instead. Asthma is one of the most serious and disabling diseases that might develop after exposure to allergens. However, less serious health effects or effects that precede allergic occupational asthma may be considered as well. A candidate could be allergic rhinitis, which occurs more frequently than asthma as a consequence of occupational allergen exposure [4–7]. Some also regard rhinitis as one of the first stages of an allergic airway inflammation [7]. However, for both asthma and rhinitis it is difficult to distinguish between new onset work-related disease and aggravation of pre-existing disease. An alternative could be the choice for sensitization as adverse effect since it is the first measurable manifestation of the allergic process. Moreover a clearer distinction can be made between work-related sensitization and pre-existing sensitization to common allergens. Although it is well known that not all sensitized workers appear to be symptomatic [5,6],

some longitudinal studies indicate that nonsymptomatic, sensitized workers have a high risk of developing symptoms after a short period of subsequent exposure [8].

Next to the choice of the relevant endpoint several technical issues need to be considered. Baur *et al.* refer to toxicological principles usually applied in risk analyses and establishing N(A)OELs or L(A)OELs. However, these values are usually derived from well-defined experimental animal studies. For sensitization a generally accepted animal model is presently not available and human data, e.g. epidaemiological studies, have to be used. In general, epidaemiological studies are to be preferred, since they provide data for the species for which the standard has to be developed, but the recently conducted epidaemiological studies cited by Baur *et al.* have some disadvantages. A major problem is the absence of information on baseline sensitization rates to occupational allergens in nonexposed populations. If baseline sensitization rates are not available extrapolation to lower exposure levels is further complicated and margins of error in the evaluation process cannot be assessed or have to be compensated by the use of safety factors.

Other problems relate to the proper extrapolation technique. The evidence for the presence of exposure sensitization relationships in human populations hardly allows analysis of the shape of the dose–response relationships. Different curves might have to be used to describe exposure–response relationships for different allergens and to evaluate the existence of threshold exposure levels. *A priori* choices for a model are often not possible because animal models are not available. Although these observations should not be used to decide not to develop exposure standards it tells us that some complex and unfortunately also arbitrary choices have to be made in the standard setting process. In addition, practical problems such as incomparability of exposure measurements using different immunoassays have to be accounted for [9,10]. This all makes the standard setting process less straightforward than one might hope and might lead to potentially lengthy procedures and discussions between stakeholders and scientists.

These arguments are not meant to discourage the concept of standard setting for aeroallergen exposures, but illustrate that more research is needed and more focused analyses are necessary of the material available and new studies to come.

References

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