Indoor pollutants and asthma in children

The great indoors

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Further evidence for the role of indoor pollutants in the development of childhood asthma

The prevalence of asthma (especially childhood asthma) is high, and children in particular spend a lot of time in their homes. In addition, our homes contain many pollutants so, understandably, we'd like to know to what extent pollutants in the home environment cause and/or worsen asthma in our children.

WHAT DO WE KNOW?

In many children asthma is closely associated with allergy, and many asthmatic children are allergic to dust mite and pet allergens. For them, reduction of exposure is likely to be beneficial. But does this mean that mite and pet exposure causes asthma? This issue is surprisingly complex. Whereas studies suggest that exposure to specific allergens increases sensitisation to those allergens, this does not necessarily mean that such exposures also increase the incidence of asthma.[1 2] Some studies even suggest that early life exposure to pets (and other animals) may reduce the incidence of asthma.[3–7]

Compared with the already complex role of exposure to allergens and other biological contaminants, the evidence with respect to chemicals such as nitrogen oxides, sulfur oxides, and particles produced by combustion appliances, environmental tobacco smoke, and volatile organic compounds (VOCs) is even less clear.

In this issue of *Thorax* two new studies from Australia attempt to provide further evidence for the role of unvented heating appliances and of VOCs, respectively. Phoa *et al*[8] retrospectively collected data on unvented heater exposure in a sample of children aged 8–11 years. Early—but not current—exposure to unvented space heaters was found to be associated with airway hyperresponsiveness and wheeze. Rumchev *et al*[9] conducted a case-control study in young children and found that children aged 6–36 months, discharged from a hospital emergency department with a diagnosis of asthma, had higher concentrations of VOCs in their homes than control children living in the same community.

WHAT EVIDENCE CAN WE GLEAN FROM THESE NEW STUDIES?

Effect of gas heaters on development of childhood asthma

The study by Phoa *et al* was questionnaire based and grouped all sorts of ''fume emitting'' space heaters into one category—including gas heaters, kerosene heaters, open fireplaces, and wood stoves, each of which have distinctly different patterns of emissions of noxious substances. No measurements of pollutants were performed in the homes. Flued gas heaters, open fires, and wood stoves were all included in the fume emitting category, whereas it is likely that these are connected to chimneys and flues which would prevent most of the emissions from entering the indoor space. Adjustment for socioeconomic status (a likely covariate of flueless heater use) was not attempted, so some uncertainty remains about the extent to which the findings could be attributed in part to differences in socioeconomic status. The authors reported no association between asthma and *current* use of flueless heaters, but the analysis presented adjusted for the use of flueless heaters *early* in life. If there was a substantial correlation between early and current use of flueless heaters, this may mean that the lack of association with current heater use is to some extent due to overadjustment.

Unvented space heaters, fireplaces, and wood stoves have been studied before by several investigators. In a small study Cooper and Alberti[10] found no effect on the lung function of healthy residents of homes with kerosene heaters. In a study in small children Triche *et al*[11] found a slight increase in cough with the use of kerosene heaters and wood stoves and slightly more wheeze with the use of unvented gas heaters in the home. In a study from Seattle neither asthma nor wheeze in 5–9 year old children was found to be related to the use of either gas heaters, wood stoves or kerosene heaters.[12] A prospective study from Tasmania did find a relationship between gas heater usage in the first year of life and asthma at the age of 7 years.[13] A large study from Finland found a *negative* association between the use of wood stoves and asthma outcomes, but argued that this was because wood stoves were used more on traditional farms. The association disappeared after adjustment for living on a farm.[14] Wood smoke is a well known respiratory irritant, and the use of wood stoves was found to be related to lower respiratory tract illness in a case-control study in small children.[15] A study conducted among a panel of asthmatics found that subjects had more symptoms of cough and shortness of breath on days with reported use of gas stoves, fireplaces or wood stoves.[16] Although the evidence is not entirely consistent, it is clear that unvented combustion appliances increase the exposure of inhabitants to combustion products to a sufficient extent to cause exacerbations and, perhaps, induction of respiratory diseases and symptoms. The study by Phoa *et al* adds to this evidence, albeit with less specificity than previous studies.

Effect of VOCs on development of childhood asthma

Rumchev *et al* found differences in indoor VOC concentrations between children with asthma and controls. This was a study in very young children at an age when the diagnosis of asthma is notoriously difficult. Measurements of VOCs were of short duration only (8 hours), but this is likely to lead to random misclassification primarily which would reduce differences between cases and controls. More ''asthma'' cases than controls reported recent indoor painting which probably shifted the VOC concentrations upwards, and no attempt was made to investigate differences between cases and controls after exclusion of subjects reporting recent indoor painting.

Few studies have addressed the effects of indoor exposure to VOCs on respiratory health. The focus in experimental studies has mostly been on sensory and neurological effects, observed at rather higher concentrations than those measured by Rumchev *et al* (median 36 μg/m^3, maximum 600 μg/m^3). In the experimental studies by Molhave and others, the concentrations tested have typically been in the range 3–25 mg/m^3 and, more often than not, no effects were seen at the lower end of this range.[17 18] Occupational studies among painters other than spray painters (who may be exposed to isocyanates) have provided evidence of increased asthma rates.[19] However, a study comparing painters using water based paints with VOC exposures in the 1–3 mg/m^3 range with painters using solvent based paints with VOC exposures in the 100–380 mg/m^3 range

found evidence of increased airway symptoms in the latter group only.[20] A recent large study from the UK[21] failed to document any effects of VOCs on persistent wheezing illness in school children at total VOC concentrations that were higher than in the study by Rumchev *et al*, but a study from Leipzig found that early life exposure to low concentrations of 25 selected VOCs related to house painting was associated with increased respiratory infections in infants.[22] Other studies have suggested that VOC emissions from recent house redecorations and floorings might be related to asthma-like symptoms.[23 24] Whether such associations reflect direct effects of indoor VOCs at low concentrations or, for example, confounding by traffic related pollutants covarying with indoor VOCs[25] remains to be seen.

The issue of whether indoor VOCs are a risk factor for asthma in children therefore seems still to be largely undecided. In view of the methodological difficulties outlined above, prospective studies are more likely to produce progress in deciding whether we need to worry about indoor VOCs as determinants of asthma at the relatively low concentrations typically encountered in the home environment.

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TRPV1 and cough

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Iodo-resiniferatoxin, a new TRPV1 inhibitor, shows promising antitussive activity in an animal model

Cough is one of the most common respiratory complaints and intractable cough remains one of the most distressing and difficult to treat conditions of the lung. It is ironical that the billions of dollars spent worldwide on proprietary over the counter remedies of questionable efficacy[1] for cough exceeds, by orders of magnitude, the money spent on basic cough research. It is therefore not surprising that the cough pharmacopoeia has altered little in the last 50 years, with no important advances over opiate based compounds and cromones. However, basic researchers have not been idle. In this issue of *Thorax* Trevisani and colleagues[2] present new information pointing to a causative role for an ion channel called transient receptor potential vanilloid-1 (TRPV1) in cough. They show that the highly selective and potent TRPV1 inhibitor iodo-resiniferatoxin, derived from a plant toxin found in *Euphorbia* species, strongly suppresses cough induced by inhaled capsaicin or citric acid in conscious guinea pigs, a widely used animal cough model.

The basis of this work is careful molecular dissection of precisely why coughing occurs when irritants are inhaled. It has been known for years that irritants such as citric acid and capsaicin (the pungent tongue burning constituent of hot chilli peppers) trigger coughing. It has also been known for decades from electrophysiological studies that such irritants activate respiratory tract sensory fibres—especially unmyelinated C fibres—to discharge information via the vagus to the medullary cough centre.[3] From this early work it was inferred that the cough receptor on sensory fibres might be an ion channel able to rapidly depolarise afferent nerve membranes and hence trigger cough inducing impulses. This view was reinforced by the inhibitory activity of crude agents such as the dye ruthenium red. The discovery that capsazepine, a capsaicin derivative and a known ion channel blocker, had antitussive activity in animal models[4] focused attention on the vanilloid receptor family as candidate ion channels.