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## Asthma deaths: we need to identify risk factors early and construct at-risk asthma registers

See linked article by Anagnostou *et al.* on pg 71

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Studies into asthma deaths began in the 1960s in response to increasing mortality rates.<sup>1</sup> Since then, various Confidential Enquiries and related reports from around the world<sup>2-7</sup> have highlighted many factors – both medical management- and patient-related – which increase the risk of death in patients with asthma. Many of these are now well recognised, and have been incorporated into national<sup>8</sup> and international<sup>9</sup> guidelines. The longest running Confidential Enquiry is based in the eastern region of the UK,<sup>6,7</sup> and in this issue of the *PCRJ* Anagnostou *et al.* report on 20 deaths in children aged 17 or under (median age 11.5 years) which occurred between 2001 and 2006.<sup>10</sup> The authors have done a great service in reminding us that people still die from asthma, and that some of these deaths – albeit rarely – occur in children. The paper is also timely, since the 12-month UK Royal College of Physicians National Review of Asthma Deaths led by Mark Levy started on 1st February 2012.

Paediatric asthma deaths in the UK peaked in the mid-1960s with a mortality rate of 10 per million/year in the under-5s and 14 per million/year in children aged 5-14; rates then dropped to 2 per million/year in both age groups between 1990-2000.<sup>11</sup> The eastern region of the UK has a population of approximately 5.25 million. Of the 20 childhood asthma deaths between 2001 and 2006,<sup>10</sup> none of these were in children aged under 5; there were 13 deaths in the 5-14 age group, and seven in children aged 15-17. The absence of any deaths in the under-5s may simply be due to chance and the

relatively small numbers involved, but our improved understanding (over the last 15 years) of the different diagnostic categories and more selective use of the term ‘asthma’ in this age group<sup>12,13</sup> may also be a contributory factor.

Confidential enquiries have inherent methodological limitations; they are uncontrolled, retrospective and observational, and are more akin to audit or significant event analysis. Therefore the data need to be interpreted with caution. Nevertheless, the authors highlight a number of important points for clinicians and policy makers.<sup>10</sup> Nine of the 20 children who died had mild to moderate asthma, 10 had severe asthma, and one had no previous diagnosis. This is a salutary reminder that death can occur in patients with mild or moderate disease (albeit that the risk of death in children with severe asthma is higher since the proportion with severe disease is much smaller<sup>14</sup>); seven out of the nine suffered sudden death, one was unwell for three days after a thunderstorm, and one suffered possible anaphylaxis after exposure to guinea pig.<sup>10</sup> Two-thirds had documented poor adherence, and denial (either on the part of the patient or the parents) was a factor in two. The challenges of managing this patient group will be hard to address; most children who died did not have a written asthma action plan, and perhaps more attention should be given to this aspect of education – with more focus on acute crisis management – when dealing with someone with ‘less troublesome’ asthma.

A strength of this Enquiry is the emphasis on elucidating allergic factors involved in the patient's death; 13 of the 20 children had a clinical picture consistent with atopy, but only three had had formal allergy testing in an allergy clinic. 50% died between June and August, and three deaths occurred during a thunderstorm. Furry pet animal dander was thought to be the trigger for four children. Together, these data highlight the need for clinicians to take a detailed allergy history (focussing on a range of external triggers) followed by appropriate testing when indicated. Unfortunately, we cannot tell whether prior allergy testing and knowledge about these allergies could have modified behaviour and prevented the deaths. The fact that half the deaths occurred in June to August suggests that clinicians should optimise therapy when the danger season approaches and ensure adherence with inhaled corticosteroid (ICS) treatment at appropriate doses. September and early October were not associated with high deaths, but there is an annual peak in asthma hospitalisation for younger children at this time<sup>15</sup> which is

probably related to viral respiratory infections<sup>16</sup> and parents failing to restart ICS after the summer holidays.

Many of the other risk factors have been highlighted previously.<sup>2-7</sup> Five of the 10 children with severe asthma were being managed solely in primary care and none of them had a written asthma management plan. In 40% of cases, asthma follow-up was considered inadequate. Nine children were poorly compliant with medication, and six (30%) had poorly controlled asthma despite good compliance – i.e. they were being undertreated. 60% had psychosocial or behavioural factors which contributed to their death; half of these came from dysfunctional families with domestic problems. In six cases, children were on long-acting  $\beta_2$ -agonist (LABA) inhalers but not on ICS – two had no ICS prescribed and four were not taking their separate ICS inhaler. The Food and Drug Administration (FDA) in the USA now recommends that only combination ICS/LABA inhalers should be prescribed in paediatric and adolescent patients who require LABA to be added to ICS treatment.<sup>17</sup>

We have known for a number of years what the clinical management failings are which contribute to asthma death,<sup>2-7</sup> that most fatal attacks are *not* of severe sudden onset (therefore the opportunity for intervention exists), and we know what factors put an asthma patient 'at-risk'.<sup>7,8</sup> A systematic review on promoting the use of asthma management plans highlighted several ways in which their use could be encouraged.<sup>18</sup> A retrospective pilot study in primary care showed reductions in hospital admissions, out-of-hours attendances, courses of oral steroids and healthcare costs in patients on at-risk asthma registers compared to controls.<sup>19</sup> A randomised controlled trial to be published soon will show that patients on at-risk asthma registers have more courses of oral steroids and less hospitalisations than matched controls (Prof D Price, personal communication).

Children placed on the at-risk asthma register would include those with known severity-based risk factors:

- A previous severe exacerbation (admission in last year, admission to the intensive care unit)
- Previous brittle / anaphylactic reactions especially if associated with food allergy
- Those already known to have difficult-to-treat asthma (BTS/SIGN steps 4 and 5<sup>a</sup>)

Until more is understood about the reasons why asthma death is more common in children with psychosocial problems (including those who fail to attend for appointments) such children should also be placed on at-risk registers even if they only have mild disease.

Children on the at-risk asthma register could have targeted management that promotes the use of asthma action plans<sup>18</sup> which include the best course of action to treat an attack, with more focussed attention on non-adherence, allergy assessment and trigger avoidance. LABAs should only be prescribed in a combination ICS/LABA inhaler to prevent poor ICS adherence. Undertreatment with ICS and oral steroids, which also puts patients at risk, could be identified and avoided.

We believe that at-risk asthma registers will make a difference, and that they should be constructed in every primary care practice worldwide. Now is the time for action.

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