

CORRESPONDENCE

What is the economic impact of preschool viral upper respiratory infection?

To the Editor:

In a previous issue of the *European Respiratory Journal* STEVENS *et al.* [1] suggested that preschool children with wheeze account for a significant proportion of the UK healthcare budget. Most preschool wheezing is caused by viral infection and, therefore, we wondered how much preschool children with upper respiratory tract infection (URTI) without wheeze would cost the National Health Service?

On average, a preschool child will catch 6–8 URTIs per year [2], and 11% of children <14 yrs will be taken to their family doctor when unwell. These figures may be higher in younger children [3]. If a child has six colds per year and is seen by a doctor for 11% of these infections, then, based on the 2.94 million UK preschool population estimate and a £16 consultation cost estimation [1], the primary care costs of viral URTI would be £31 million. This compares to the £34 million estimated by STEVENS *et al.* [1] as the cost of preschool wheezing. Therefore, the additional cost burden of wheeze seems small.

We believe the villains are not wheeze and asthma but the respiratory viruses!

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References

1. Stevens CA, Turner D, Kuehni CE, Couriel JM, Silverman M. The economic impact of preschool asthma and wheeze. *Eur Respir J* 2003; 21: 1000–1006.
2. Coughs and colds in children. www.prodigy.nhs.uk/clinicalguidance/releasedguidance/webBrowser/pils/PL43.htm
3. Bruijnzeels MA, Foets M, van der Wouden JC, van der Heuvel WJ, Prins A. Everyday symptoms in childhood: occurrence and general practitioner consultation rates. *Br J Gen Pract* 1998; 48: 880–884.

Exhaled breath condensate pH

To the Editor:

VAUGHAN *et al.* [1] are to be congratulated for the most extensive study of the pH of exhaled breath condensates (EBC) yet reported. However, there is reason to doubt that the pH of the condensate provides a reliable measure of the pH of fluid lining the airways. As noted in our recent study [2], the average concentration of NH_4^+ is 20 times greater than that of any other EBC cation in normal condensates, and NH_4^+ accounts for most of the ions and buffer in the condensate (as judged by total conductivity).

Several previous studies have shown that most of this NH_4^+ is derived from NH_3 generated in the mouth, in part from the bacterial degradation of urea [2–4]. In the study by VAUGHAN *et al.* [1], collection of condensates through endotracheal tubes did not seem to have an effect upon average pH. Since both intubation and tracheostomy significantly reduce NH_4^+ concentrations of the EBC [2, 4], they should be associated with more acidic condensates. This paradox could only be explained if intubation also reduced concentrations of some atmospheric or oral acid (*e.g.* residual CO_2 or acetic acid) in the EBC. It must be concluded that the pH of normal condensates reflects buffering by these volatile constituents from the mouth, rather than buffers in the airway fluid, and therefore EBC pH cannot provide reliable estimates of airway pH.

Although the normal condensate pH is set by oral and atmospheric buffers, HUNT and coworkers [5, 6] observed

"acidopnoea" in asthmatics, which they attributed to airway acidification. We have suggested that reductions in exchange of NH_3 in the mouth and condenser are responsible in part for the reduction in EBC NH_4^+ seen in asthmatics [7], and consequently contribute to acidification. It is also possible that reflux of gastric fluid, which is extraordinarily common in asthmatics [8], is responsible for EBC acidification. Aerosolisation of tiny quantities of gastric acid (pH often 1–2) from the stomach or pharynx would be difficult to avoid or detect in these patients but could have a profound effect on EBC pH.

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References

1. Vaughan J, Ngamtrakulpanit L, Pajewski TN, *et al.* Exhaled breath condensate pH is a robust and reproducible assay of airway acidity. *Eur Respir J* 2003; 22: 889–894.
2. Effros RM, Biller J, Foss B, *et al.* A simple method for estimating respiratory solute dilution in exhaled breath condensates. *Am J Respir Crit Care Med* 2003; 168: 1500–1505.
3. Norwood DM, Wainman T, Liou PJ, Waldman JM. Breath

- ammonia depletion and its relevance to acidic aerosol exposure studies. *Arch Environ Health* 1992; 47: 309–313.
4. Vass G, Huszar E, Barat E, *et al.* Comparison of nasal and oral inhalation during exhaled breath condensate collection. *Am J Respir Crit Care Med* 2003; 167: 850–855.
 5. Hunt J, Fang K, Malik R, *et al.* Endogenous airway acidification: implications for asthma pathophysiology. *Am J Respir Crit Care Med* 2000; 161: 694–699.
 6. Hunt JF, Erwin E, Palmer L, *et al.* Expression and activity of pH-regulatory glutaminase in the human airway epithelium. *Am J Respir Crit Care Med* 2002; 165: 101–107.
 7. Effros RM. Do low exhaled NH_4^+ concentrations in asthma reflect reduced pulmonary production? *Am J Respir Crit Care Med* 2003; 167: 91–92.
 8. Harding SM. Recent clinical investigations examining the association of asthma and gastroesophageal reflux. *Am J Med* 2003; 115: 137–143.

From the authors:

In R.M. Effros' frequent letters in response to data regarding exhaled breath condensate (EBC) pH, there is one constant: he states that his speculations must be correct, despite the accumulation of substantial data to the contrary. To his credit, R.M. Effros now accepts that indeed there are acids involved in the acidification of exhaled breath condensate. Additionally edifying is that, in this current letter, he has not repeated his previous strongly stated, yet incorrect, notions that: pH cannot be measured in EBC; that glass electrodes will provide irreproducible readings; that asthmatic hyperventilation causes EBC acidification; or that facilitated diffusion would cause increased ammonia to be exhaled when the airways are acidic [1]. Much data have emerged that have thoroughly negated these notions.

This time R.M. Effros has manufactured a false paradox compelling him to speculate an unnecessary solution. He makes the false assumption that removal of oral ammonia should be acidifying to a relevant degree. Indeed, R.M. Effros' "paradox" disappears when we discard his underlying false assumption. Because EBC pH and ammonia experiments indeed solidly dispel his assumption, we are easily left with no paradox, and an internally consistent set of findings regarding EBC pH.

Although R.M. Effros references his suggested mechanism for artifactual EBC pH decline in asthmatics, we respectfully remind him that the data in our paper specifically and directly disprove his suggestion. Scientists uniformly agree that it is more reasonable to discard hypotheses proven wrong, than to discard data inconsistent with hypotheses.

We have to agree with R.M. Effros that oral ammonia, as a base, should indeed have some alkalinising effect. However, the data show clearly that this effect in EBC is too tiny to be noted without a huge enrollment of subjects, and such a quest is pointless. Neither oral ammonia, nor the lack of it, is responsible for the profound EBC acidification seen in various diseases. Indeed, that EBC acidification is characteristic of intubated patients with lung disease, but not of intubated patients without lung disease [2–4], helps further to

dispel R.M. Effros' argument that the mouth is the controller of EBC pH. As part of the airway, the mouth assuredly contributes to EBC. But the mouth is a small part of the airway, and its contribution to EBC may be likewise.

Gastro-oesophageal reflux certainly affects tracheal pH [5], with tracheal pH probe readings falling to 4.0, and therefore we believe aspirated acid to be one mechanism that acidifies EBC. We are convinced that reflux contributes to lung disease, but if reflux is the sole reason why EBC pH falls, then reflux must be a factor in most every lung disease patient, even while intubated, which is more than even the most vocal advocates suggest.

Over the years, we have appreciated R.M. Effros' strongly and repeatedly asserted, albeit incorrect, speculations. Without these thoughtful speculations, we might not have so aggressively and rigorously tested every facet of the exhaled breath condensate pH assay. In the end, exhaled breath condensate pH has proven to be thoroughly robust and entirely useful. Patients with respiratory diseases, including asthma, chronic obstructive pulmonary disease, bronchiectasis [6], cystic fibrosis [7], acute lung injury and acute respiratory distress syndrome [2] exhale more acid. This is particularly true of patients who are undergoing disease exacerbations. To us, this is very interesting indeed both as a marker of disease activity, and as a clue to underlying pathologic mechanisms.

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References

1. Effros RM, Bosbous M, Foss B, Shaker R, Biller J. Exhaled breath condensates: a potential novel technique for detecting aspiration. *Am J Med* 2003; 115: Suppl. 3A, 137S–143S.
2. Gessner C, Hammerschmidt S, Kuhn H, *et al.* Exhaled breath condensate acidification in acute lung injury. *Respir Med* 2003; 97: 1188–1194.
3. Moloney ED, Mumby SE, Gajdosi R, *et al.* Exhaled breath condensate detects markers of pulmonary inflammation after cardiothoracic surgery. *Am J Respir Crit Care Med* 2004; 169: 64–69.
4. Vaughan J, Ngamtrakulpanit L, Pajewski TN, *et al.* Exhaled breath condensate pH is a robust and reproducible assay of airway acidity. *Eur Respir J* 2003; 22: 889–894.
5. Jack CI, Calverley PM, Donnelly RJ, *et al.* Simultaneous tracheal and oesophageal pH measurements in asthmatic patients with gastro-oesophageal reflux. *Thorax* 1995; 50: 201–204.
6. Kostikas K, Papatheodorou G, Ganas K, Psathakis K, Panagou P, Loukides S. pH in expired breath condensate of patients with inflammatory airway diseases. *Am J Respir Crit Care Med* 2002; 165: 1364–1370.
7. Tate S, MacGregor G, Davis M, Innes JA, Greening AP. Airways in cystic fibrosis are acidified: detection by exhaled breath condensate. *Thorax* 2002; 57: 926–929.