Exhaled breath condensates and COPD

To the Editors:

BORRILL *et al.* [1] have recently provided a timely review of exhaled breath condensates (EBC) in chronic obstructive pulmonary disease. However, there are several issues that deserve comment. BORRILL *et al.* [1] argue that although it would be useful to use dilutional indicators for estimating the dilution of respiratory droplets from the airway lining fluid (ALF) by water vapour, none of these have been ''validated.'' Dilution is both extreme (~1:20,000) and variable and represents a significant challenge for the application of the EBC procedure. Contrary to their assertion, there is no need to show that dilutional indicators ''diffuse through cell membranes at a constant rate'' [1]. It is only necessary to show that concentrations of dilutional indicators in the ALF remain equal to those in the plasma and that they are neither produced nor destroyed in the lungs. There is good reason to believe that urea meets these criteria as it readily diffuses passively between the blood and airspaces [2], and it is neither produced in nor lost from the lungs. Similarly, the selection of total nonvolatile cation concentrations or conductivity of lyophilised samples is based on the assumptions that, because of rapid movement of water across the pulmonary capillaries and epithelium, the osmolality of the plasma and ALF are normally similar under resting conditions [3–5]. Reasonable agreement between the dilution estimated from these three indicators has been published, providing strong evidence that they can be used to estimate dilution of ALF in EBC [6]. It should be emphasised that without a measure of dilution, neither the concentrations nor changes concentrations of EBC constituents can provide reliable information about ALF. Furthermore, salivary contamination of the EBC should routinely be evaluated: sensitive and inexpensive amylase procedures that can detect 1:200,000 dilution of salivary amylase are available.

Dilutional indicators are useful for calculating ALF concentrations of nonvolatile constituents in EBC but cannot be used for volatile substances (*e.g.* H_2O_2 and NH_3). In general, the EBC approach should not be used to evaluate either ALF concentrations or excretion rates of volatile substances because recovery of these markers can be unpredictably altered by numerous factors in the lungs and collecting device, including air-to-water distribution coefficients at different temperatures, pH, air flow, *etc.*

There are persuasive grounds for doubting that EBC pH can ever yield reliable values for ALF pH. It has been shown definitively that NH_4^+ represents ~90% of all cations in most samples of EBC, as judged from conductivity and ion chromatography [7]. Since there is much less NH_4^+ in EBC when collected from endotracheal or tracheostomy tubes, most of the NH_4^+ must be derived from extrapulmonary structures, particularly the mouth, much of it from bacterial degradation of urea to NH_3 [8]. The assertion that EBC pH is not influenced by oral NH_3 violates basic chemical principles, since NH_3 has a pK_b of ~5 and NH_4^+ derived from the mouth with similar concentrations of respiratory HCO_3^- represent the most abundant acids and bases in most EBC samples. Generally, lower concentrations of acetate and other volatile anions are sometimes observed in EBC, but these may also be derived from oral bacteria.

Much of the confusion regarding EBC pH is related to attempts to remove CO_2 by briefly purging samples with inert gases. Even if successful, this would yield pH values that differ from those in the lungs, where CO_2 is always present. Furthermore, purging with inert gases is not selective since it only removes a fraction of the CO_2 and can also remove some NH_3, volatile anions and water, thereby altering pH. Subtle differences in purging procedures can have important effects on the EBC pH and probably contribute to major differences reported for EBC pH by different laboratories. Nor has sufficient thought been given to the buffering capacity of the EBC. The overwhelming concentrations of NH_4^+ and HCO_3^- in EBC, which are added outside the lungs, tend to obscure any pH signal derived from the lungs.

The principal advantage of exhaled breath condensate approach is that samples can be collected from the mouth rather than the airways of the lungs. Unfortunately this also represents one of its chief weaknesses, because of the abundance of volatile substances that are generated in the saliva and mouth which contaminate the exhaled air.

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STATEMENT OF INTEREST

None declared.

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DOI: 10.1183/09031936.00191608