



## Can Hyperventilation Lead to EBC pH Changes in Deaerated Samples?

The answer to this is an unequivocal and firm NO.

This speculation has been repeatedly raised by one investigator<sup>1-3</sup>, and it has become tiresome. Unfortunately, this investigator uses no data to support his speculations, yet forwards them repeatedly and with strongly worded assertions, primarily in the form of letters to the editor and in review articles. It is a frequent cause for communications from investigators regarding EBC pH assays.

The **false** argument that has been presented goes like this:

1. Asthmatics hyperventilate and have lower end tidal CO<sub>2</sub> levels.
2. The lower end tidal CO<sub>2</sub> levels then cause the EBC pH (before deaeration) to be more alkaline than it would be had the patient not been hyperventilating. This is "because" there would be less CO<sub>2</sub> to go into solution in the EBC.
3. Since the EBC pH would be higher, it would trap less oral ammonia
4. With less oral ammonia, the EBC, once deaerated, would be more acidic than if the patient had not been hyperventilating.

So, where does this argument fail? At every step of the argument after step 1.

1. Although asthmatics indeed hyperventilate, the effect is often mild (to an end tidal CO<sub>2</sub> of low 30s perhaps).
2. However, in the process of hyperventilating, asthmatics increase their metabolism and create *more* CO<sub>2</sub>. They also therefore exhale *more* CO<sub>2</sub>, not less. There is thus *more* CO<sub>2</sub> in the exhaled air during hyperventilation (which is how end-tidal CO<sub>2</sub> becomes low—reflecting blood CO<sub>2</sub> levels).
3. The higher amount of CO<sub>2</sub> in the exhaled breath, if anything, would serve to lower EBC pH, and trap more ammonia (if the rest of the false argument were to hold any water)
4. With more oral ammonia trapped, *if oral ammonia had anything to do with EBC pH*, the EBC pH would be higher in hyperventilating asthmatics (if we attempted to be consistent with the false argument). (see: "What About Ammonia Affecting EBC pH Assays")
5. However, EBC pH is clearly lower than normal in asthmatics.
6. Therefore, the false argument fails on theoretical grounds.

How about on empiric grounds? There is power in data collection, something which we have done extensively, and which our "pH critic" has not done at all. Indeed, we performed the simple experiment of having 10 subjects hyperventilate. They dropped their end-tidal CO<sub>2</sub> to 23 torr (far below what asthmatics can achieve) and supplied a 3 minute EBC collection while hyperventilating. There was no change in the EBC pH from their baseline. Likewise hypoventilation while breathing 5% CO<sub>2</sub> and increasing end-tidal CO<sub>2</sub> to 46 caused no change in the EBC pH<sup>4</sup>. These experiments further dispel the false arguments. We consider the case to be closed.

Why did our overly vocal "pH critic" never perform such a simple experiment in an attempt to support what turned out to be a false argument? We simply don't know. He should never have published, nor aggressively promoted his argument without any supporting data.

We are fortunate to have the RTube™, because with the RTube, the experiments readily were performed that dispel the concern of oral ammonia<sup>5</sup>. Only the RTube allows for collection of sample in as little as 90 seconds of breathing. No other equipment available or home-made would have allowed sufficient sample to be collected during the brief time one can maintain voluntary hyper- or hypo-ventilation.

We would like to discuss one more issue. Our pH critic and we agree that gastric acid in the airway can lead to EBC acidification<sup>6</sup>. Any cause of airway acidification readily can be identified by means of EBC pH assays, including gastro-esophageal reflux with aspiration, or reflux to the level of the larynx and pharynx. We consider this to be a potentially very important finding.

## References

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- 6 Ricciardolo, F. L., B. Gaston, and J. Hunt. 2004. Acid stress in the pathology of asthma. J Allergy Clin Immunol 113(4):610-9.