Reviewer's report

Title: Breath acidification in adolescent runners exposed to atmospheric pollution: a prospective, repeated measures observational study

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Reviewer: john hunt

Reviewer's report:

General
Interesting manuscript by leaders in the fields of EBC pH, lung assessment and ambient pollution effect on lung disease in children. Negative primary result (no association of EBC pH before or after running with ambient air pollution in relatively nearby testing sites). Interesting positive secondary or post hoc results relating to substantially augmented EBC pH variability in the group of exercising teenagers (runners) compared to sedentary controls.

Study design is generally good, although lack of personal monitoring of pollution exposure makes it likely that an explanation for the negative primary result could be that the study was underpowered. Lack of personal monitoring also no doubt substantially reduced the potential cost of the project and made it performable, so this is not a strong critique, just a comment.

There is an excellent up to date table summarizing EBC pH values from the published literature that can be quite helpful in this evolving field.

Minor Critiques:
Abstract
Fine.

Introduction
Page 3. Glutaminase likely represents 1 controller of airway pH, but there are others and it is unkown what is primary.

Methods
No personal monitoring of pollutants was presented. This was commented on somewhat in the MS, and is not overcomable in the current data set.

Results
Sedentary patient EBC pH values should be presented in the results section and not left for the supplment

Discussion
Non carbonated sports beverages consumed prior or duing exercise couild affect
the pH results if they had a low pH (citric acid containing fluids, for example may provide sufficient acid to the oropharynx to affect the EBC pH results. I don’t think this possibility should be minimized in this group if they were drinking at all during their exercise.

On page 12 is mentioned the post hoc analysis (convenience sample) of healthy sedentary adults. This is mentioned as somewhat of an afterthought and placed mostly in the supplement. (the post hoc nature is noted), but it is of primary concern for readers attempting to interpret this whole paper. I would think that this non-exercising control group data would be appropriate to mention in the introduction and results section, because the positive findings presented in this paper are primarily in comparison to these (alongside published) data. But these comparison data performed using the same methodology will carry more weight in this study than attempting to compare to published normal data. Supplemental Figure 1 should be the primary figure in the manuscript in my opinion.

1. It would be good to expand the normal nonexercising control comparison group.

2. Data analyses on this group, if comparable to the published data, would give more weight to the conclusion that running leads to more EBC pH variability than the sedentary lifestyle, and opens up the possibility that intermittent airways acidification may even be good (highly speculative—but an apple a day keeps the doctor away and exercise is supposed to be good for us!)

In regard to variations in pH of previous published norm data for healthy pH values: It is likely that there was some inclusion of subjects with unidentified respiratory disease or laryngopharyngeal acid reflux, and these factors may provide an explanation for why EBC pH is occasionally low in seemingly healthy subjects. Nothing was mentioned about GER as potential contributor to EBC acidification. Do runners at baseline tend to have silent reflux more than sedentary people? Does hurrying from class to the field for practice trigger reflux events? It seems likely that reflux is a major cause of intermittent EBC acidification in asymptomatic subjects. Maybe “endogenous” or intrinsic airway acidification. Maybe reflux/aspiration.

Figures
Table 1: nice and clear structured, did any participant take respiratory medications?
Table 2: nice and clear
Table 3/4: Didn’t understand these. I don’t know if the average reader will glean much meaning from them either. But of interest to statisticians certainly. I would recommend placing these two tables in the supplemental data section, but some readers of this journal may prefer them up front and visible as they are presented here.
Table 5: great reference with important detail regarding deaeration
Figure 1: clear and informative regarding the biomodal distribution.
Figure 2: Would appreciate indicators for (sprinter / long distance), smoke exposure, asthma or the 4 subjects with reported wheezing. Please explain what the boxes represent in terms of % range (or some other)

Supplemental figure 1 seems the most valuable of all (because it is a positive result—admitedly post hoc). Would consider expanding and presenting supplemental Figure 1 as the dominant figure in the primary publication (not supplement). (it is also the most appealing visually!)

Supplemental table—sulfate and predicted pH values. The explanation and table could be done more clearly I believe. I struggled to understand the process whereby the pH was estimated based on sulfate levels in EBC (although there was apparently modeling that involved SOME of the other relevant ions that would affect the pH//=I think it very hard to estimate pH effect of sulfate given the rest of the mix of compounds in EBC weren’t measured. Also, I could not understand sufficiently easily the “predicted vs measured” sulfate concentrations. IT may be understandable with more careful reading, but it isn’t easy to grasp in current format.

Conclusions
Appropriate to restress here for clarity, that in comparison to a group of sendentary subjects, much higher EBC pH variability was found in the exercising group

References
No concerns.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions