




Are aerosols generated during lung function testing in patients and healthy volunteers? Results from the AERATOR study

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ABSTRACT

Pulmonary function tests are fundamental to the diagnosis and monitoring of respiratory diseases. There is uncertainty around whether potentially infectious aerosols are produced during testing and there are limited data on mitigation strategies to reduce risk to staff. Healthy volunteers and patients with lung disease underwent standardised spirometry, peak flow and FE_{NO} assessments. Aerosol number concentration was sampled using an aerodynamic particle sizer and an optical particle sizer. Measured aerosol concentrations were compared with breathing, speaking and voluntary coughing. Mitigation strategies included a standard viral filter and a full-face mask normally used for exercise testing (to mitigate induced coughing). 147 measures were collected from 33 healthy volunteers and 10 patients with lung disease. The aerosol number concentration was highest in coughs (1.45–1.61 particles/cm³), followed by unfiltered peak flow (0.37–0.76 particles/cm³). Addition of a viral filter to peak flow reduced aerosol emission by a factor of 10 without affecting the results. On average, coughs produced 22 times more aerosols than standard spirometry (with filter) in patients and 56 times more aerosols in healthy volunteers. FE_{NO} measurement produced negligible aerosols. Cardiopulmonary exercise test (CPET) masks reduced aerosol emission when breathing, speaking and coughing significantly. Lung function testing produces less aerosols than voluntary coughing. CPET masks may be used to reduce aerosol emission from induced coughing. Standard viral filters are sufficiently effective to allow guidelines to remove lung function testing from the list of aerosol-generating procedures.

INTRODUCTION

Due to the pandemic, concerns about viral transmission by aerosols and droplets mean that many respiratory diagnostic services are being cancelled or delayed.¹ There is an urgent need to restart these vital diagnostic services and mitigate risks to patients and staff from viral transmission. However, there remains uncertainty around the role of lung function testing in the generation of aerosols and onward transmission risk.

A rapid systematic review identified seven sources that classified the aerosol-generating procedure (AGP) status of lung function tests.² Four of these defined lung function tests as an AGP, two defined them as a possible AGP and one source

stated that these were not an AGP. All cited sources were guidelines, none of which referred to primary experimental data that could support these recommendations. Current advice from expert groups and guidance bodies is contradictory, leading to variation in clinical practice.^{3–5} Previous experimental work has been performed outside an ultra-clean environment, which does not allow accurate attribution of aerosol and can potentially misclassify it, does not conform to clinical standards, and does not include patients with lung disease.

In this study, we aimed to generate primary data on aerosol generation during lung function tests and assess mitigation strategies using highly sensitive technology in an ultra-clean, laminar flow theatre.

METHODS

This study was performed as part of the AERo-solisation And Transmission Of SARS-CoV-2 in Healthcare Settings (AERATOR) study to assess the risk of aerosolised transmission of SARS-CoV-2 in healthcare settings.

Environmental set-up, recruitment and procedures

Full technical methods and images of the set-up are found in online supplemental appendix S1 and have been reported elsewhere.⁶ In brief, healthy volunteers and patients with lung disease were recruited to allow collection of aerosol emission in ultra-clean, laminar flow operating theatres. Participants underwent protocolised testing (breathing, speaking and coughing) followed by lung function tests designed to represent standard clinical practice. Time stamps were used to indicate timing and duration of tidal breathing and forced manoeuvres, including formal spirometry (as per American Thoracic Society/European Respiratory Society (ATS/ERS) guideline⁵), peak flow measurement and FE_{NO} measurement.

All testing was performed by an accredited lung function technician using a Vyntus spirometer (Vyaire), with FE_{NO} testing using a NIOX device (Aerocrine). The spirometer systems used single-use bacterial viral filters (BVF); peak flow meters were tested both with and without BVF (see online supplemental appendix S1 for images).

A proof-of-concept test of mitigation to reduce the risk of procedure-induced cough aerosolisation was undertaken using a reusable full-face



Table 1 Aerosol emission detected from respiratory activities (only APS results reported)

	Geometric mean number concentration/cm ³ (SD, n)	
	Volunteers (n=33)	Patients (n=10)
Background	<0.001 (n/a)	<0.001 (n/a)
Breathing	0.04 (3.37)	0.29 (2.50)
Speaking	0.10 (1.89)	0.22 (2.69)
Voluntary cough	1.61 (43.6)	1.45 (2.39)
Peak flow (without filter)	0.76 (3.21)	0.37 (1.89, n=9)
Peak flow (with filter)	0.09 (1.59)	0.01 (n/a, n=8)
FEV ₁	0.11 (2.10)	0.10 (3.22)
FE _{NO}	<0.001 (n/a)	0.005 (n/a)
CPET (breathing)	0.003 (n/a)	Not performed
CPET (speaking)	<0.001 (n/a)	Not performed
CPET (cough)	0.16 (8.65)	Not performed

We report peak concentrations for all instantaneous activities and average concentration for all continuous activities, as per the methods and previous literature.

APS, aerodynamic particle sizer; CPET, cardiopulmonary exercise test; n/a, not available.

cardiopulmonary exercise test (CPET) face mask with BVF in five subjects. The sampling funnel was positioned over the point of greatest exhalation flow.

Measurements of aerosol were taken simultaneously by two separate devices, an aerodynamic particle sizer (APS; measured size range 0.5–20 µm) and an optical particle sizer (OPS; measured size range 0.3–10 µm); details are found in online supplemental methods. We report geometric mean and SD, with comparisons made by unpaired t-tests on the log-transformed data from the APS, unless stated. Both devices rely on fundamentally different technologies (aerodynamic size vs optical size) and therefore both were included to provide robustness in all reported measurements and reduce the chance of technical bias affecting the results.

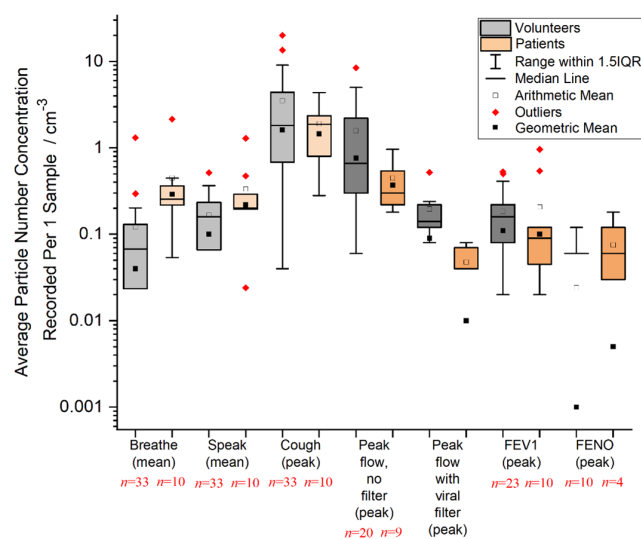
RESULTS

Full results and patient demographics are found in online supplemental appendix S2. Correlation between the APS and OPS was extremely high ($r>0.95$), and therefore only APS results are reported in the text. In brief, the highest aerosol emission was generated during a voluntary cough, with the next highest in unfiltered peak flow (table 1 and figure 1). Patients with lung disease generated higher aerosol concentrations than volunteers when breathing (0.29 vs 0.04 particles/cm³, $p<0.01$) and speaking (0.20 vs 0.10 particles/cm³, $p=0.04$), but not when coughing (1.45 vs 1.61 particles/cm³, $p>0.2$).

Unfiltered peak flow produced approximately half the aerosol of voluntary coughing, but the addition of a filter reduced this by an order of magnitude in volunteers (0.76 vs 0.9 particles/cm³, $p<0.01$) and patients (0.37 vs 0.01 particles/cm³, $p<0.01$), with no clinically significant change in measured peak flow value (online supplemental figure S3).

Filtered spirometry also produced little aerosol (0.11 particles/cm³ in volunteers and 0.10 particles/cm³ in patients), with voluntary cough producing on average 56 times more aerosol in volunteers (and 22 times more aerosol in patients). We could not elicit any aerosol emission from the FE_{NO} device.

A potential mitigation strategy for induced coughing, the CPET mask, was tested in five volunteers, with formal results reported in online supplemental appendix S2. Briefly, large reductions in aerosol emission during breathing (0.02 vs <0.0001

**Figure 1** Aerosol number concentrations measured during spirometric activities.

particles/cm³, $p=0.08$, paired t-test on log-transformed data for all comparisons), speaking (0.1 vs <0.001 particles/cm³, $p=0.06$) and coughing (1.12 vs 0.06 particles/cm³, $p<0.01$) were observed, although this did not meet a significance threshold due to the low number of participants.

Finally, we tested whether receiving nebulised salbutamol altered subsequent aerosol emission in patients and we identified no significant change (online supplemental results and figures S4–S6).

DISCUSSION

This study provides much-needed high-quality experimental data characterising aerosols generated during standard clinical lung function tests in volunteers and patients. The finding that spirometry, peak expiratory flow (with standard BVF) and exhaled nitric oxide testing do not generate significant aerosols (in comparison with cough) suggests there is likely limited additional risk associated with lung function testing outside of the potential to generate aerosols via coughing.

Peak flow testing without a filter does produce aerosols (although less than coughing). However, the addition of a filter reduces this aerosol concentration to negligible levels and renders the procedure non-aerosol-generating. Together this points to the effectiveness of standard CE-marked viral filters in reducing aerosol emission.

The study also identifies a potential effective mitigation measure (reusable filtered CPET mask) for aerosols generated by subjects who cough as a result of the procedure, with promising data showing large reductions in aerosol emission, although we caveat this is due to the small number of participants. Finally we provide reassurance that salbutamol nebulisation used as part of bronchodilator reversibility testing does not induce higher aerosol emission during subsequent testing. Taken together, we believe that this may allow for a significant increased diagnostic capacity through reduced need for air room changes between subjects.

This study has a number of strengths. First, we performed spirometry as following standard UK practice in an ultra-clean, laminar flow theatre with extremely low background aerosol concentration. This allows us to make confident conclusions

about the source and level of aerosols produced. Second, we measured aerosol production from healthy volunteers and patients with a mixture of chronic lung conditions that were suspected to affect aerosol emissions.

There are some limitations to our study. We included patients with a mixture of small airways and suppurative lung conditions in our study, but the patient group was too small and heterogeneous to draw any definitive conclusions about the comparison between individual lung diseases. Common to all prior studies and for safety reasons, none of the subjects was known to be suffering from viral infections which have been shown to increase aerosol production.⁷ Finally, the link between recorded aerosol concentration and risk of onward infection remains unknown, with the capture and quantification of infectious SARS-CoV-2 or other pathogens in exhaled aerosol remaining a considerable technical challenge at present.

There are three comparable studies that have examined this question.^{8–10} First, Helgeson *et al*'s⁸ small-scale study identified aerosol generation during spirometry performed by five healthy volunteers. It detected aerosol production despite inclusion of viral filters, but excluded participants who coughed and only measured aerosols at a distance from the source, being unable to definitively identify the source. Greening *et al*⁹ included 33 healthy volunteers who performed different respiratory manoeuvres outside of an ultra-clean environment using particles in exhaled air methodology. They identified cough as the major source of aerosols and found varied results with other lung function testing. However, the authors acknowledge that their pulmonary function tests (PFTs) did not meet the ERS/ATS spirometry criteria and 22 of the volunteers performed only tidal breathing. Finally, Li *et al*¹⁰ performed lung function testing on 28 patients. Only one measure of aerosol (OPS) was performed during PFTs and for 30–60 min following the procedure after the patients and researchers had left the room. The paper concludes that PFTs should be considered an AGP; however, on examination of the presented data, measured aerosol levels remained steady or fell during the procedures. The peak aerosol production occurs when the patients moved away from the apparatus and breathed, spoke and coughed without a mask on. In our view, these data more likely reflect aerosol emission from normal respiratory activity such as coughing, rather than relating to the lung function testing, and highlight the need for measurement at the source of aerosol emission and an ultra-clean background.

Bringing all the data together, including our and others' evidence that aerosol is generated from normal respiratory activity, this paper suggests that the major risk in lung function testing remains the potential for infectious aerosols to be generated by coughing rather than in performing spirometry. Risk assessments should focus on the risk of infection to the patient, ventilation of the room and whether induced coughing can be mitigated, rather than on the type of lung function testing performed.

CONCLUSIONS

Spirometry (performed with a standard filter) and FE_{NO} do not generate significant aerosol concentrations compared with

coughs in healthy volunteers and patients with lung disease. Peak flow does generate aerosols, although a viral filter reduces this >10-fold. Reusable CPET masks with filters applied to subjects prior to testing may be a potential solution to mitigate aerosol emission from induced coughing before and after the procedure.

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Collaborators The AERATOR group consists of (in alphabetical order) Arnold D, Brown J, Bzdek BR, Cook T, Davidson A, Dodd JW, Gormley M, Gregson F, Hamilton F, Maskell N, Morley A, Murray J, Keller J, Pickering AE, Reid J, Sheikh S, Shrimpton A and White C.

Contributors JWD, NAM, FWH, SS, FKAG, DTA, GWN and JB designed the experiments. CR performed the lung physiology testing. SS and FKAG analysed the data, with BRB and JPR providing supervisory support and analysis. GWN performed supplementary experiments.

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