Author’s response to reviews

Title: Recognition of aerosol transmission of infectious agents: a commentary

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Author’s response to reviews:

We thank the reviewers for their insightful comments and suggestions, and we have accordingly made many changes to the manuscript.

In response to specific comments:

Reviewer 1

We must agree with the reviewer that unfortunately our original title seemed to promise more that we can deliver. We are reminded of an anecdote reported by Theodore Dalrymple about how the late Professor Shepherd was asked to review a book titled “Recent Progress in Psychiatry” and observed that perhaps a more accurate title would be “Recent activity in Psychiatry”. We think that we have achieved more than just “activity” and that our article will provide a welcome impetus toward the resolution of this important issue, but we have changed the tile, hopefully more appropriately, to “Obstacles to the recognition of aerosol transmission of infectious agents: a commentary. “

We share the reviewer's reliance on mechanistic and virological arguments, such as for MERS, and have been quite perplexed by the reluctance of some organisations such as the WHO to be swayed by these arguments. We note that there are discrepancies among Public Health organizations; for example the CDC does recommend N95 as part of the PPE for MERS whereas in Canada different provinces have different recommendations. Various Public Health authorities are indeed very reluctant to accept that an infectious agent can be transmitted by aerosols, probably in part because of the costly and extensive nature of the preventive measures required. Some Public Health institutions have had what could be deemed a disingenuous approach to the problem, for example when in 2014 the Ministry of Health of Saudi Arabia promulgated new infection control guidelines for MERS in which they stipulated that MERS –CoV is not airborne transmitted, unless “aerosol generating procedures “ such as a bronchoalveolar lavage or intubation are conducted; accordingly N95s were mandatory for such
procedures, but also when in the room of an hospitalized MERS patient just in case an aerosolizing procedure would need to be performed urgently.

One of the strongest statement made by Judge Campbell, Commissioner of the SAARS Commission in Ontario, Canada 2006 was that “We should be driven by the precautionary principle that reasonable steps to reduce risks should not await scientific certainty” But it is also clear that decision making by Public Health organizations also involve a great deal of politics, and in our commentary we aim to remain at the level of a purely scientific and medical discussion.

We agree with the reviewer that a historical approach to the issues might provide great additional insight and indeed we have offered some historical perspective. But it is worth noting that a comprehensive historical perspective would have to go all the way back to the work of Chapin in 1910, which denied the existence of airborne transmission “with the possible exception of tuberculosis; for every pathogen now accepted as being transmitted by aerosols, a long and often intense scientific debate had to ensue (even for tuberculosis) and a proper, comprehensive historical review is quite beyond the intended scope of this commentary.

Reviewer 2
1.1 As we pointed out in response to reviewer 1, the title was changed in order not to create unrealistic expectations; we do not think that we can convince just yet all the parties in the different controversies for different agents. We think and have highlighted in the manuscript that microbiological and mechanistic data are essential. Valuable contributions can also be gained from epidemiological and clinical studies but there have been historically confusion as to the expected behavior of aerosolized agents. Although we have not discussed this in our commentary, as it is somewhat out of scope, clearly, in the absence of evidence considered definitive the precautionary principle ought to be applied and especially when dealing with highly lethal agents such as MERS-CoV: this is in fact basic risk analysis: not only what is the probability of an event, but also what is the cost if it occurs.

1.2 We have added a short section on Ebola

1.3 We agree with the reviewer that elucidation of the mode(s) of transmission for a pathogenic agent ought to inform the choice of infection control procedures, including PPE, and consequently should ultimately lead to adequate recommendations. But as we pointed out earlier, we think that the scope of this commentary should focus on the scientific evidence and its discussion – even though we hope that the proper precautions that logically follow should be recommended.

2.1 The definitions of the Institute of Medicine are essentially similar to ours in that particles of 10 µm or less (“respirable particles “) are equivalent to what we call “aerosols”; and inspirable particles correspond “large droplets”. (The intermediate particles of 10-20 µm probably do not play a large role: they don’t stay in suspension very long nor do they penetrate significantly below the glottis; and their small size compared to the rest of the large droplets imply they can only deliver a small infectious dose in the upper airways). The CDC definition you refer to was presented at a Workshop attended by one of us (RT) and certainly there was no unanimity for many of the ideas presented. In the definitions proposed, “aerosol transmission” refer to both aerosol-size droplets and large droplets, which is a convention adapted by a few other authors (e.g. Herfst et al Science 2012; 336: 1534-1541). We think that this obfuscates the debate as aerosol-size droplets differ qualitatively in their behavior in terms of i) they can access the lower respiratory tract with obvious implications for pathogenesis ; ii) they will
remain in suspension for long periods of time; and iii) from a PPE point of view they will not be stopped by surgical masks. We think that conflating these concepts does not promote clarity of thought. “Droplet-spray transmission” as proposed in the CDC slide is but the upper end of large droplet size and “deposition by impaction on exposed mucous membranes” is an idea arguably unfortunate in the case of influenza since the “exposed” buccal and ocular mucosa are not permissive for influenza virus replication, the virus must reach the respiratory epithelium in the nasal and soft throat areas. We have added a brief comment about these alternate schemes.

2.2 We are grateful for the correction.

2.3 We have modified the text and removed Fig 2.

2.4 We have now removed Fig 3.

2.5 The point about the dangers posed by aerosolization of fluids containing pathogens has been made also in the section on Ebola, and we think that space consideration preclude a proper discussion of the epidemiology of noroviruses.

2.6 We have modified the “Method” section, now titled “Outline” and pointed out better how different strength of evidence have been accepted for different pathogens. We think the situation is especially perplexing for influenza where the controversy persist in spite of a very large volume of published supporting evidence, and we are reminded of Borges’ lines: “Hume noted for all time that Berkeley’s arguments did not admit the slightest refutation nor did they cause the slightest conviction”.

2.7 Fig. 3 has now been removed.

2.8 We think that influenza is an especially important virus in this context because i) ongoing controversies allow for an in depth discussion of several key concepts in aerosol transmission and ii) influenza is currently still the pathogen deemed most likely to trigger a massive pandemic and is thus especially important from a Public Health point of view.

2.9 We agree with the reviewer that the term “droplet transmission” can be confusing and in trying to achieve clarity we have now removed this term from the text.

2.10 We are grateful for the correction.

2.11 The choices of the pathogens discussed is somewhat difficult as aerosol transmission is a very broad topic; other pathogens of interest would certainly include M. chimaera in open heart surgery, dimorphic fungi, primary respiratory plague, etc. In the interest of space we have restricted the discussion mostly to viruses replicating in the respiratory tract, many of them emerging, with Ebola as an example of potential transmission though aerosolizing of high titer bodily fluids rather than strict production of aerosols in the airways, and tuberculosis as the first recognized pathogen transmitted by aerosols.