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Lowbury lecture

# Airborne transmission and precautions: facts and myths

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## SUMMARY

Airborne transmission occurs only when infectious particles of  $<5\ \mu\text{m}$ , known as aerosols, are propelled into the air. The prevention of such transmission is expensive, requiring N95 respirators and negative pressure isolation rooms. This lecture first discussed whether respiratory viral infections are airborne with reference to published reviews of studies before 2008, comparative trials of surgical masks and N95 respirators, and relevant new experimental studies. However, the most recent experimental study, using naturally infected influenza volunteers as the source, showed negative results from all the manikins that were exposed. Modelling studies by ventilation engineers were then summarized to explain why these results were not unexpected. Second, the systematic review commissioned by the World Health Organization on what constituted aerosol-generating procedures was summarized. From the available evidence, endotracheal intubation either by itself or combined with other procedures (e.g. cardiopulmonary resuscitation or bronchoscopy) was consistently associated with increased risk of transmission by the generation of aerosols.

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## Introduction

In the past, there has been a tendency to consider all infections of the lungs as a possible source of airborne transmission. This seems logical because such infections often present with cough and this will propel secretions into the air. However, it is apparent now that only small particles of  $<5\ \mu\text{m}$ , known as aerosols, will result in airborne transmission potentially over longer distances because these particles can remain suspended in the air for prolonged periods. Most lung infections result in droplet transmission whereby the larger particles from

the cough are transmitted for  $<1\ \text{m}$  and do not remain suspended in the air.

Airborne transmission can be classified into three categories, namely obligate, preferential, and opportunistic.<sup>1</sup> Obligate airborne infections are initiated solely through aerosols and the classic example is tuberculosis. Preferential airborne infections such as chicken pox and measles can be initiated through multiple routes, but predominately by aerosols. These three infections are the only ones classified as airborne in international guidelines including those of the US Centers for Disease Control and the World Health Organization (WHO).<sup>2,3</sup> Finally, opportunistic airborne infections typically transmit through other routes but under favourable conditions, especially when aerosol-generating procedures such as intubation are undertaken, transmission can occur; examples include influenza and severe acute respiratory syndrome

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(SARS). This last category is generally not taken as airborne, since, in the routine care of the patients, only droplet and contact precautions are required.

In terms of infection control precautions, it is now accepted in these infection control guidelines that 'airborne transmission precautions' must be adopted. This will require isolating the patient in a negative-pressure airborne infection isolation room (AII), and to use an N95 respirator rather than a surgical mask.<sup>2,3</sup>

Recent research has confirmed that the N95 respirator is able to block 95% of aerosols and indeed it is the preferred form of facial protection for airborne infections.<sup>4</sup> It should, however, be appreciated that implementing airborne precautions is relatively expensive because the availability of AII is often limited and the use of the N95 respirator is definitely more costly than the surgical mask. Still, there is a tendency to play safe and to consider all viral chest infections as possible airborne infections, and to include a wide range of procedures as aerosol-generating procedures. It is thus important to separate the facts from the myths, and this brief presentation deals with two key issues. The first is to establish whether viral infections such as SARS and influenza are airborne, and the second is to come up with a definitive list of aerosol-generating procedures. The evidence from systematic reviews on these issues is summarized by WHO.<sup>3</sup>

## Are most respiratory viral infections airborne?

Perhaps the two most intensively researched respiratory viral infections are influenza and SARS. There is now general consensus that SARS is not airborne. Seven case–control studies were identified by WHO showing that hand hygiene could make a difference to the outcome.<sup>3</sup> There have also been well-designed case–control studies published showing that droplets and contact precautions can control SARS, and that an AII is not needed.<sup>5</sup> If SARS were indeed airborne, these measures would not be as effective as reported.

## Reviews on transmission of influenza

A vast number of studies for influenza have been conducted; these will now be summarized briefly. Two reviews are concerned with the research conducted before 2008.<sup>6,7</sup> Many experimental studies have been reported, but as Brankston *et al.* rightly pointed out, these were done with artificial aerosols where <10% of the particles were larger than 8 µm whereas in natural coughing >99% are larger than 8 µm. Therefore they questioned whether these studies are relevant to the natural route of human transmission.<sup>6</sup> There were outbreaks reported which Tellier considered as strong evidence for airborne transmission, but Brankston *et al.* argued that, in these reports, many confounders were not addressed and in none of these studies were the air exchange rates reported.<sup>5,6</sup> The most well-known evidence for airborne transmission was the outbreak in a stationary airplane with a non-functional ventilation system; however, an outbreak of similar size was reported in another stationary plane, but with a functional ventilation system.<sup>8,9</sup> The outbreaks in these planes could also have been related to the free movement of passengers when the planes were parked for several hours, and are not convincing evidence for or against airborne transmission.

## Clinical trials comparing N95 and medical/surgical masks

Several controlled trials comparing N95 respirators with surgical masks have been reported. The first was reported in Canada by Loeb *et al.* showing no significant difference.<sup>10</sup> In 2009, MacIntyre *et al.* published a study carried out in China, which originally reported a significant difference between the two; however, it was later retracted at the annual meeting of the Infectious Diseases Society of America and then published in another journal as showing no significant difference when surgical masks are compared with all N95 used.<sup>11,12</sup> The statistical powers for both studies were low and cannot be conclusive. MacIntyre *et al.* then reported another study by the same centre in China that showed a significant difference ( $P = 0.024$ ).<sup>13</sup> However, this was for subjects presenting with clinical respiratory infections. When only those with positive viral culture results were compared, there was no significant difference ( $P = 0.4$ ). On the other hand, there was a significant difference in rates of positive bacterial cultures ( $P = 0.02$ ). As these bacteria are not known to be airborne, the interpretation of the results was rather complicated. This, together with the previous retraction of their first paper, suggests that further confirmation from other researchers is needed to resolve the issue.

The Respiratory Protection Effectiveness Clinical Trial (ResPECT) currently underway in the USA is due to finish in 2015 and hopefully it will bring closure to this important question.<sup>14</sup> During the 2009 H1N1 pandemic, the author reported the use of medical/surgical masks, not of N95 respirators, for all public hospitals in Hong Kong and found no significant difference between the infection rate among the clinical staff and their non-clinical colleagues who had no contact with patients ( $P = 0.82$ ), suggesting that the medical/surgical mask was sufficiently protective.<sup>15</sup>

## New experimental studies

Experimental studies in which only polymerase chain reaction was used for a diagnostic test cannot be considered conclusive because it would not be possible to ascertain whether such particles contained viable virus that could result in transmission.

However, there are now at least two studies showing the presence of viable viral aerosols in exhaled breath.<sup>16,17</sup> Nevertheless this is not sufficient to confirm airborne transmission unless there is also evidence to indicate inoculation of these viable viral particles into a susceptible patient. Milton *et al.* found that most of these particles did not possess viable viruses in large numbers and commented on the possibility that the 'vast majority of the virus exhaled by influenza A patients is actually non-infectious' to others.<sup>16</sup> At least two studies have shown that viable virus may be transmitted to the host but these were by artificial aerosols generated by simulators and it was difficult to assess whether the situation was similar to real life.<sup>4,18</sup> The study by Noti *et al.* used both a coughing and breathing simulator.<sup>4</sup>

Finally, a study has now been reported in which the sources were naturally infected influenza volunteers.<sup>19</sup> This was claimed to be the first 'end-point host-exposure and sampling study' in which special manikins were exposed to these volunteers. None of the specimens taken from the manikins was found to be positive after the exposures, and the authors suggested that influenza might not be readily transmitted from a naturally

infected human source. However, only 15 patients were recruited and larger studies are needed to confirm the results.

## Studies by ventilation engineers

These studies fall into another category of research but it is always worthwhile to link expertise in different fields together. There is evidence that most of the droplets produced by a patient will evaporate totally. Xie *et al.* reviewed the literature and estimated that ~1% of particles from the mouth were larger than 100 µm.<sup>20</sup> They plotted an evaporation curve and showed that a particle of such a size would be fully evaporated in 1.5 s.<sup>21</sup> Thus, unless the host was intimately close, cross-infections might not be that easy by air, suggesting again that airborne transmission may not be a frequent occurrence.

## What is an aerosol-generating procedure?

A systematic review of aerosol-generating procedures with respect to SARS was summarized in the 2014 WHO guideline.<sup>3</sup> From the available evidence, endotracheal intubation either by itself or combined with other procedures (e.g. cardiopulmonary resuscitation or bronchoscopy) is consistently associated with increased risk of transmission by the generation of aerosols. Eight studies were quoted in support of this in a review published by Tran *et al.*<sup>22</sup> Recently, a study on influenza further confirmed that only bronchoscopy and intubation are actually aerosol-generating procedures.<sup>23</sup>

Studies implicating other procedures have been reported, albeit with flaws, such as one study reporting that non-invasive ventilation was significant, but also admitting that infection control practices were inadequate.<sup>24</sup> In fact, nearly 90% of subjects in this paper reported inappropriate hand hygiene practices. There were also studies refuting widely held erroneous concepts – for example, that nebulizers are aerosol-generating – and one such study showed that efficient transmission of SARS had already occurred before the machine was turned on.<sup>25</sup>

## Conclusion

The current evidence for viral respiratory airborne infections is not strong. Infective aerosols seem to be present in the mouth but there is no firm evidence that they will survive the journey to a susceptible host to cause an infection. The only aerosol-generating procedures for which there is clear evidence for aerosol production is endotracheal intubation. Infection control guidelines should take all this information into consideration and ensure that current practices are in line with scientific evidence rather than with unsubstantiated myth.

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