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Medical and microbiological problems arising from airborne infection in hospitals

K. P. Schaal

Institute for Medical Microbiology and Immunology, University of Bonn, Sigmund-Freud-Straße 25, D-5300 Bonn 1, Germany

Summary: The practical importance and frequency of airborne nosocomial infections has been a matter of dispute for many years. This is because most of the pathogens acquired in hospitals are able to use various different routes of infecting the patient's body so that it may be difficult or even impossible to prove an individual infection to be airborne. Only microbes such as *Streptococcus pyogenes*, *Neisseria meningitidis*, *Corynebacterium diphtheriae*, *Mycobacterium tuberculosis*, or certain respiratory viruses that are known to be predominantly transmitted by droplet infection from infected persons or healthy carriers, have been accepted to be the cause of airborne nosocomial infections. Other pathogens such as legionellae, pseudomonads or clostridia may be distributed in the hospital environment via an insufficient or defective air-conditioning system, with or without humidification. The assessment of indirect airborne infections caused by infective particles derived from dust which has settled on furniture or the floor or which has been introduced to the hospital environment by shoes, open windows, building works or potted indoor plants is much more difficult. Many Gram-positive bacteria such as *Staphylococcus aureus*, mycobacteria, nocardiae, and endospores of clostridia and bacilli, as well as the reproductive elements of fungi do remain viable and infective in dry dust and may therefore infect patients when the dust is disturbed. In contrast to nosocomial infections due to Gram-negative bacteria, against which most preventive measures have been concentrated in the past and which are usually not airborne in origin, it appears that the possibility of direct or indirect transmission of hospital pathogens by air has been underestimated. When other routes of nosocomial infections are well controlled, airborne infections may gain more practical importance in hospitals.

Keywords: Airborne nosocomial infection; Gram-positive nosocomial pathogens; nocardiosis; tuberculosis; legionellosis; respiratory viruses.

Introduction

The practical importance and frequency of airborne nosocomial infections has been a matter of dispute for many years. Although the possibility of transmission of nosocomial pathogens by air has generally been accepted, the extent to which airborne infections contribute to nosocomial morbidity and mortality remains to be defined. The relative incidence of airborne infections in hospitals has been estimated to be about 10%¹ and airborne postoperative wound infections at about 8%.²
However, such estimates are probably of little general value because the incidence of airborne nosocomial infections is highly dependent upon factors such as local respiratory pathogens, susceptibility of patients, climatic conditions, construction work, ventilation equipment and organization of the individual hospital. Furthermore, the assumption of such a route of infection is usually an indirect one derived from the presence of a potentially airborne pathogen, the identification of a possible source for this pathogen, its presence in air samples, and the occurrence of infections by this pathogen only in patients who were exposed to the presumably contaminated air. These indications may be considered conclusive when the pathogen involved is highly virulent and when it is known to be transmitted predominantly or exclusively via air. In the case of pathogens which may also infect the patient’s body by other routes, none of these possible clues is a proof of the airborne nature of a microbial disease. Thus, the main medical and microbiological problem arising from airborne infection in hospitals still consists of proving this type of infection. When this has been done conclusively, measures can be taken to prevent the further spread of the pathogen.

### Possible sources of airborne nosocomial infections

The source of an airborne nosocomial infection may be primarily inside or outside the hospital (Table I). The most important source of airborne

| Inside the hospital                                      |
|----------------------------------------------------------|
| Infected or colonized patients/hospital personnel/visitors:|
| droplet infection                                        |
| infections by other airborne particles derived from the human body (e.g. dried skin or pustule content, skin scales, hair particles, textile fibres) |
| Infective dust or aerosols:                              |
| from floor, furniture                                    |
| from potted indoor plants or flower vases                |
| from washbasins, shower cabinets                         |
| from nebulizers, humidifiers, suction devices            |
| Contaminated (colonized) ventilation or air-conditioning systems: |
| infective aerosols                                       |
| infective dust                                           |
| colonized filters                                        |

| Outside the hospital                                    |
|----------------------------------------------------------|
| Soil:                                                    |
| as natural habitat of certain pathogens                  |
| contaminated by e.g. animal faeces                       |
| Water (e.g. cooling towers):                             |
| colonized by potential pathogens                         |
| Decaying organic materials:                              |
| colonized by potential pathogens                         |
| Dust from building works                                 |
pathogens inside the hospital is the infected or colonized patient. The predominant mechanism that makes the pathogens airborne is the production of droplets by sneezing or coughing and their subsequent loss of water which allows them to float in air over considerable distances and for a long time. Under special clinical circumstances, skin lesions may also be the source of airborne particles. Dust particles and aerosols loaded with pathogens are another potential source of airborne infection. The dust may originate from infected or colonized patients, but may also have been introduced into the hospital environment by shoes, through open windows, from building works nearby or from potted indoor plants. Infective aerosols may be derived from washbasins, shower facilities, nebulizers or humidifiers. In this case, the water necessary for the function of these facilities is the primary source of the pathogens. Contaminated or colonized ventilation or air-conditioning systems with absent or defective filters present another hazard. They may introduce environmental aerosols or dust with a high microbial load into the hospital. The pathogens may multiply in moist places inside the air-conditioning system but may also be introduced from outside the hospital building by the intake fan. Reservoirs of potential airborne nosocomial pathogens outside the hospital are soil, water, decaying organic materials or dust derived from building works, especially when old buildings are renovated or reconstructed. The number of pathogens that may originate from soil, decaying organic materials or building works dust is limited to a few bacterial and fungal species that are able to multiply in soil and to survive drying for longer periods. Water, combined with aerosol-forming equipment (e.g. cooling towers) may provide a broader spectrum of pathogenic microorganisms although most of them possess low virulence to humans and therefore only present a health hazard to the immunocompromised or when they are released into the air in very high concentrations.

**Causative agents of airborne nosocomial infections**

A number of pathogens have been known for decades to be predominantly or exclusively transmitted by droplet infection from man to man and such transmission may also occur in hospitals. These pathogens include various respiratory viruses (Table II) and bacteria such as *Streptococcus pyogenes*, *Neisseria meningitidis*, *Corynebacterium diphtheriae*, *Bordetella pertussis* or *Mycobacterium tuberculosis*. Additional pathogenic viruses and bacteria may use the air as an alternative medium for their spread or may, as in the case of *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Klebsiella pneumoniae* or *Staphylococcus aureus*, colonize the patient’s body via air, especially in the upper respiratory tract. The potential of *C. diphtheriae* to spread in hospitals was shown again during the 1976 outbreak of the disease in Cologne when an intensive care unit patient acquired wound diphtheria from a severely ill diphtheria patient brought to the unit
Table II. Potential airborne nosocomial pathogens* that may be transmitted directly from infected persons or healthy carriers

1. Viruses
   - Rhinoviruses
   - Influenza viruses
   - Respiratory syncytial virus
   - Parainfluenza viruses
   - Parvoviruses (Coxsackieviruses)
   - Varicella-zoster virus
   - Adenoviruses (Coronaviruses)

2. Bacteria
   - *Streptococcus pyogenes*
   - (Streptococcus pneumoniae)
   - *Neisseria meningitidis*
   - *Corynebacterium diphtheriae*
   - *Mycobacterium tuberculosis*
   - (Haemophilus influenzae)
   - (Mycoplasma pneumoniae)
   - (Klebsiella pneumoniae)
   - (Staphylococcus aureus)
   - *Bordetella pertussis*

* Organisms in brackets use the air only as an alternative medium for their spread; they primarily colonize rather than infect via air.

Table III. Potential airborne nosocomial pathogens* that may be acquired by inhalation of infective dust particles or aerosols generated inside the hospital

Bacteria
(a) via dust:
   - *Staphylococcus aureus*
   - *Corynebacterium diphtheriae*
   - *Mycobacterium tuberculosis*
   - Other mycobacteria
   - *Nocardia* spp.
(b) via aerosols:
   - Pseudomonads
   - *Enterobacteriaceae*
   - Legionellae
   - Other non-fermenters

Fungi
   - *Aspergillus* spp.
   - (Mucoraceae)

* Organisms in brackets use the air only as an alternative medium for their spread; they primarily colonize rather than infect via air.

to treat his life-threatening cardiac arrhythmia. Airborne transmission of pathogens from skin lesions is well documented by cases of chickenpox in children or non-immune adults acquired from zoster patients who only release the virus from their skin vesicles (personal observation of the author).
The risk of acquiring airborne nosocomial infections from infected dust particles that have been whirled up is usually considered to be low because it has been difficult to demonstrate a correlation between counts of airborne bacteria and clinical infection. However, wound contamination rates were found to be higher in operating theatres without laminar airflow facilities than in those equipped with a laminar airflow system. Furthermore, it has to be considered that this type of airborne infection is highly dependent on the concentration and virulence of the respective pathogen (Table III), on the status of the local or general defence mechanisms of the patient, and on the time of exposure. The medical and microbiological problems arising under these circumstances are best explained when considering *S. aureus* infections. This potential pathogen is widely distributed on the skin and the mucous membranes of infected patients as well as of healthy carriers. It is often distributed to surfaces in the surroundings where it remains viable for months when no or insufficient disinfection is performed. Table IV shows an example of the occurrence of *S. aureus* at various places on an intensive care unit. Interestingly, three different phage types were encountered which were all related to the occurrence of the respective type at three corresponding air inlets. It is not clear whether these inlets were the primary source of *S. aureus* contamination in the respective intensive care unit sections or if they were secondarily contaminated. More detailed information was derived from data collected during an outbreak of *S. aureus* infections on a ward for premature infants (Figure 1). During this outbreak which lasted about 5 months 34 babies were either colonized or infected by three closely related phage types of *S. aureus*. Fourteen of them showed symptoms of severe infection. The same phage types were isolated from the air and various objects inside six different rooms of the ward. In addition, a nurse suffering from chronic pyoderma was identified as a carrier of the same type of organism. Although this nurse did not have direct contact with all of the children affected, the series of infections came to an end after the nurse had been transferred to another ward and after thorough disinfection measures had been performed. It cannot be stated with any certainty the extent to which airborne transmission contributed to this outbreak although the causative agent was isolated from the air of all rooms involved. The risk of airborne infection due to aerosols generated by nebulizers, humidifiers, suction devices or similar equipment is well documented and will not be discussed in detail. It was only recently demonstrated that potted indoor plants may represent a health hazard to hospital patients, especially the immunocompromised. We related pulmonary aspergillosis in liver transplant patients to the occurrence of large amounts of (aspergillus) spores in the mould of indoor plants cultivated in the hall connected to the corridor of a liver transplant unit. An apparently airborne spread of spores from the flower pots had occurred in the corridor and, in smaller numbers, into the patients' rooms.

Airborne transmission was also assumed in an outbreak of nocardiosis in the surgical department of a University Hospital. In this outbreak pulmonary nocardiosis was surprisingly not a characteristic feature, but
Table IV. Prevalence and phage patterns of *Staphylococcus aureus* in an intensive care unit (all samples taken June 15, 1990)

| Source                  | I  | II | III | M  |
|-------------------------|----|----|-----|----|
| Sink unit               | 29 | 52 | 52A | 79 |
| Dressing trolley        | 3A | 3C | 55  | 71 |
| Air intake 1            | 6  | 42E| 47  | 53 |
| Bedside table           | 54 | 75 | 77  | 83A|
| Perfusor                | 84 | 85 | 91  | 94 |
| Sphygmomanometer cuff   | 95 | 96 |
| Laundry                 | ++ | +/-| +   | ++ |
| Telephone               | ++ | ++ | ++  | ++ |
| Address list            | ++ | ++ | ++  | ++ |
| Air intake 2            | ++ | ++ | ++  | ++ |
| Bedside table           | ++ | ++ | ++  | ++ |
| E.C.G. monitor          | ++ | ++ | ++  | ++ |
| Sink unit               | ++ | ++ | +/- | ++ |
| Air intake 3            | ++ | ++ | +/- | ++ |

Phage groups: I, II, III, M (Miscellaneous); ++, confluent lysis or more than 50 plaques; +, 20–50 plaques; +/-, 1–19 plaques.
Figure 1. Distribution of three closely related *Staphylococcus aureus* phage types on a ward for premature infants over a period of 5 months (abbreviations: Lu, air; Ge, inanimate objects inside the ward; Mu, mother’s milk; A, physician; Sr, nurse; +, patients with clinical symptoms of disease; PEr, penicillin resistant). 17 infants (●) II 3A/3C/55 (PEr); 10 infants (○) II 3A/3C/55/71 (PEr); 2 infants (▴) II 3A/3C (PEr). 152, phage group I, type 52; Δ, □, ○, V, ◊, other phage types not related to the main types.

Postoperative (nocardia) wound infections following blood vessel or cardiac surgery did predominate. The causative agent, *Nocardia farcinica*, had a characteristic antibiotic sensitivity pattern, and was isolated from all of the patients involved and sporadically and in low numbers, from the air of a storeroom of the operating theatre. The definite source of the organism remained obscure because soil in the surroundings of the hospital did not contain *N. farcinica*. However, in a similar hospital setting, it was possible to demonstrate high counts of *N. farcinica* in dust derived from reconstruction works on an old half-timber house. As could also be demonstrated in vitro,¹⁰ *N. farcinica* is apparently able to multiply in or on the materials used for this type of house construction and to survive in the dry state for years or even decades.

Potentially dangerous pathogens that are spread by ventilation or air-conditioning systems have been known for several years (Table V). Health hazards are usually related to the methods of humidification used and to the types and maintenance of the filter systems. The spread of *legionellosis* by contaminated ventilation systems is well recognized. In this case, the pathogens colonize the humidification unit of the system and are distributed to the whole building when inappropriate or defective terminal filters are present. However, under similar circumstances pathogens may
Table V. Potential airborne nosocomial pathogens* derived from contaminated (colonized) ventilation/air-conditioning systems

| Bacteria          |
|-------------------|
| Legionellae       |
| Pseudomonads      |
| Clostridia        |
| Nocardiae         |
| Chlamydia psittaci|
| Atypical mycobacteria |

Fungi

Aspergilli

(Cryptococcus neoformans)

(Histoplasma capsulatum)

(Coccidioides immitis)

*Organisms in brackets use the air only as an alternative medium for their spread; they primarily colonize rather than infect via air.

Table VI. Potential airborne nosocomial pathogens* derived from soil, water or decaying organic materials

| Bacteria          |
|-------------------|
| Nocardia asteroides |
| Nocardia farcinica |
| (Nocardia brasiliensis) |
| Legionellae       |
| Atypical mycobacteria |
| Clostridia        |

Fungi

Aspergilli

Mucoraceae

Cryptococcus neoformans

(Histoplasma capsulatum)

(Coccidioides immitis)

*Organisms in brackets use the air only as an alternative medium for their spread; they primarily colonize rather than infect via air.

also originate from the environment. This was demonstrated by an outbreak of gas gangrene infections following gynaecological operations and also by a case of ornithosis acquired in a modern hospital building near Bonn. In the latter case, a colony of pigeons had settled immediately in front of the air intake of the respective ventilation system. The carriage rate for Chlamydia psittaci in this pigeon population was estimated to be at least 30%. Similar problems could be caused by Cryptococcus neoformans which may also be present in pigeon faeces in high numbers.

Finally, airborne pathogens may be introduced into the hospital from the environment through open windows, by wind or by shoes of personnel and visitors that carry in dust from the street (Table VI). The number of pathogens that may use this route of access to patients is comparatively limited. Such bacteria include Nocardia asteroides, N. farcinica, Legionella
species, certain atypical mycobacteria and clostridial spores. Among fungi with similar properties, Aspergillus species appear to be most important in Europe.

Conclusions

In recent years, most preventative measures used in hospitals have concentrated upon nosocomially-acquired Gram-negative bacteria which, apart from certain exceptions (see above), are transmitted by direct contact and not via air. These measures have resulted in a decrease in Gram-negative nosocomial infections, but there has been an increase in other nosocomial infections, especially due to Gram-positive bacteria known to be comparatively resistant to desiccation and by conidia-forming fungi. Most of these pathogens possess a low virulence for healthy individuals, but are able to cause severe infections in immunocompromised patients. Thus, with a steady increase in this group of patients in hospitals, another change in the spectrum of agents responsible for nosocomial infections appears to be imminent. These 'new' pathogens may gain access to the human body via air indicating that the preventative measures should be altered or broadened accordingly.

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