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Built Environment Today

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**Final Report**

**Investigate and Identify Means of Controlling Virus in Indoor Air by  
Ventilation, Filtration or Source Removal**

**776-RP**

**American Society of Heating, Refrigerating, and Air-Conditioning  
Engineers, Inc.**

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## **Glossary of Terms and Abbreviations**

**Aerobiologists** - a term used to describe those biologists who study viable aerosols.

**Aerosol and viable aerosol** - an aerosol is a dried residue formed by the evaporation of droplets suspended in air. Viable aerosols are those aerosols that contain living microorganisms such as bacteria, fungi and viruses.

**Animal viruses** - those referred to in this paper include foot-and-mouth disease, lymphomatosis (avian leukosis virus), Rauscher murine leukemia virus, and Yaba virus.

**Bacteriophage** - a virus that infects bacteria; often used as a safe virus for testing virus control systems since they cannot infect humans.

**Cell cultures** - see tissue cultures.

**Collison nebulizer** - a device used to aerosolize viruses into an air supply and deliver a dose of virus to the intended experimental host.

**CPE** - cytopathic (or cytopathogenic) effects. Cytopathic means damaged, diseased, or dead cells. Various types of injuries occur, depending on the virus and cell type involved. Examination of tissue culture for the specific CPE is used to identify viruses.

**CPU** - cytopathic effect units

**Disease** - infection with an agent that results in actual disease symptoms being present (see infection).

**DNA probes** - consist of a small piece of DNA which will interact with a specific target molecule in the unknown virus. Used in the identification of specific DNA sequences and thus specific viruses.

**Droplet nuclei** - term originally coined by Wells in 1934 to refer to droplets so small, from 0.5-3  $\mu\text{m}$ , that they evaporate before settling and remain suspended in air as tiny particles. Viruses and other viable microorganisms may persist in the airborne state on the droplet nuclei and become dispersed via room air currents and ventilation systems.

**ELISA** - enzyme-linked immunosorbent assay. Labeled antibody is used along with specific anti-viral antibody to identify specific viruses.

**Enteric virus** - those viruses that invade and infect cells within the digestive system, commonly the intestines. Their usual spread is by the fecal-oral

route. However, once excreted they may become airborne from waste water or other sources and be inhaled. Examples are Coxsackie virus, polio, and enteroviruses.

**Epidemic** - refers to an outbreak of disease at a rate much higher than the usual rate.

**FAT** - fluorescent antibody test. A method to detect specific viruses by reacting the unknown with specific antibodies labeled with a fluorescent dye.

**HI** - hemagglutination inhibition. A virus detection method for those viruses that agglutinate red blood cells i.e. cause them to clump together. (Called hemagglutination to indicate blood cells are agglutinating.) When the virus is combined with antibody, this agglutination reaction is inhibited if the antibody is specific for the virus, and the virus is identified.

**Human infectious dose 50 - (HCID)50**. The dose of an infectious agent that infects 50 % of the humans exposed to it. The dose is often expressed in terms of tissue culture dose, or other indirect measure for viruses since counting viral units is difficult.

**IgG** - Immunoglobulin G. The main type of antibody found in the blood, it is produced in response to infection by most microorganisms. Specific antiviral IgG may be produced and used to identify the specific virus.

**Index case** - refers to the first case of a particular disease at a particular place and time. This person is considered the source of viruses that cause infection in the subsequent cases.

**Infection** - Colonization of the host with a virus which may live and multiply in the host's cells. Does not necessarily cause disease, but the host often acts as a reservoir for spread of the virus.

**LVAS** - Large-volume air samplers.

**Minimum infective dose** - the smallest amount of virus that will infect a host. Can be as low as one virus particle.

**MPN** - most probable number. A method for quantification of microorganisms using serial dilutions and probability tables. These relate the number of dilutions positive for the organism to the estimated number of infectious particles in the original sample.

**Odds ratio** - the ratio of the odds of exposure to a risk factor among the diseased group to the odds of exposure among those not ill.

**Papilloma virus - causative agents of warts in humans and animals. Numerous types exist.**

**PCR - Polymerase chain reaction. A method of identifying viruses by amplifying specific DNA sequences to enable easier detection. See DNA probes.**

**PFU - plaque forming unit (see plaque).**

**Phage - see bacteriophage**

**Plaque - a "hole" seen a monolayer of cells in tissue culture caused by one virion infecting cells and causing their death. The number of plaques is a rough estimate of the number of viable viruses that are in the particular sample and culture media.**

**Respiratory virus - refers to those viruses that are usually spread by the respiratory route and cause infection of some portion of the respiratory system, either upper airways or the lungs themselves. Examples are adenoviruses, rhinoviruses, parainfluenza viruses, and reoviruses.**

**Tissue culture - the medium in which viruses are grown. These consist of monolayers of living cells which provide the necessary environment for the growth of viruses. Different viruses need different types of cells to grow in and survive.**

**Tissue Culture infectious dose (TCID)<sub>50</sub> - the amount of virus that will infect 50% of tissue cultures that are exposed to that dilution.**

**Virion - one virus particle, or infectious unit.**

**Virus - an organism smaller than bacteria that cannot multiply outside a living host. Common cause of various diseases of humans and animals; usually species specific, each virus prefers a particular species.**

**VN - virus neutralization. A method of identification for those viruses that produce CPE in tissue culture. They are mixed with specifically known antibodies. If they react, the virus is unable to infect the tissue culture, and is neutralized and identified.**

## **A. Introduction**

### **1. Summary of problem**

Control of indoor air quality has become an issue of increasing concern in recent years. It is generally accepted that aerosols represent an important mode of transmission for many respiratory and non-respiratory viral diseases (104), although this view has not always been as widely accepted as it is today. Virus aerosols can be generated and spread to environments external to the host either directly through coughing or sneezing, or indirectly by aerosolization of previously excreted or secreted body fluids. Droplets generated via the respiratory tract evaporate and become "droplet nuclei" with sizes ranging from 0.5 to 20  $\mu\text{m}$ , the latter occurring when viruses are attached to larger non-viable particles (118). These droplet nuclei aerosols then become dispersed throughout enclosed spaces by room air current movements or by building ventilation systems.

In hospitals, prevention of airborne viral particle spread from human reservoirs to susceptible patients is accomplished through the application of high efficiency filtration, ultraviolet disinfection of viral sources, individual room ventilation, and isolation. In at least one hospital, it has been demonstrated that airborne particle control can be achieved in patient rooms through the use of HEPA filtration at room intakes and higher than normal room air exchange rates (106).

The transmission of viral illnesses has also been known to occur in places other than hospitals, e.g., offices, homes, public buildings, and schools. In these environments, the ventilation system can play a significant role in the dissemination of viral aerosols throughout the building from a variety of sources. Because the source of such aerosols, while similar to that in hospitals, is more mobile and is difficult to isolate, control of virus transmission is much more difficult in these types of buildings.

Modification of filtration, ventilation, disinfection, and source removal techniques used successfully in hospitals for offices and other public environments could produce significant benefits in improved occupant health. There is a significant need for the development of a comprehensive source of information which will aid professionals whose duties include the recognition, evaluation, and control of exposure to virus aerosols in indoor environments.

This report reflects the results of a three-month project addressing the problem of airborne spread of viruses in indoor environments and possible means for reducing or eliminating this problem. The project consisted of a literature search in which articles, books, and reports were assembled, reviewed, and evaluated with respect to their relevance to four topics: 1)



epidemiologic evidence of airborne spread of viruses in indoor environments; 2) sampling methods relevant to evaluating viral aerosol concentrations in indoor air; 3) assay and characterization methods for determining the presence of specific viruses in indoor air samples; and 4) control techniques and their efficacy for eliminating or reducing airborne viral particle spread. Further details on the literature search, including a list of all articles used in this report, are included in Appendix I.

In addition, a telephone survey of researchers and consultants presently working in relevant areas was carried out. An example of the survey and copies of completed surveys with curriculum vitae are included in Appendix II.

This report will first address the four topics mentioned above with respect to epidemiologic studies, sampling and assay, and control of airborne viruses in indoor environments. A summary of the investigator surveys then follows, including a discussion of the more important issues raised by the interviewees with respect to the four general topic areas. A concluding discussion of our findings follows, which includes suggestions for future areas of research to address the shortcomings we have noted from our literature search and interviews.

## **2. Work statement**

This proposal will involve the following tasks.

2.1 We will conduct an extensive literature search, utilizing a variety of computer-based electronic databases, including medline, Engineering Index, Compendex, DOE Energy, Pollution Abstracts, the Commonwealth Agricultural Bureau Index, and Excerpta Medica. These are all available through the University of Minnesota libraries. The search will address the points indicated in 2.4 below.

2.2 We will discuss our findings with researchers located at a minimum of five institutions. These researchers will be asked to give input with respect to the topics listed in 2.4 below.

2.3 Most of the current knowledge of and research on viral aerosols presently lies within research institutions. We will attempt to identify consultants with expertise in this area; if this is not possible we will increase the number of researchers interviewed to a minimum of ten.

2.4.a We will develop tables indicating viruses by type, particle size, typical and infective airborne concentrations, and health effects.

2.4.b We will review and critique existing virus aerosol sampling and measurement methods. We will summarize methods by the type of equipment used and types of results possible. We will also suggest possible modifications for particular virus aerosols based on information about particle size, health effects, and other virus properties.

2.5 We will prepare comparison charts and tables displaying the results of this project.

2.6 We will critically evaluate all filtration, ventilation and source removal data applicable to virus aerosols. Much of the general information on the effectiveness of currently employed filtration techniques has been previously discussed by T.H. Kuehn (a Co-Principal Investigator) et al. as a part of ASHRAE-funded project RP-625 Phase 1 "Matching Filtration to Health Requirements." We will extend this research to the specific area of viral aerosols.

2.7 Based on the literature search and interviews, we will develop recommendations for viral control techniques which may be evaluated in the Phase II project.

2.8 We will submit one quarterly report during the project period; a final report summarizing the findings of the project; and a final technical report indicating in detail all literature used, the results of interviews, tables of virus information, identification and measurement techniques, discussion of information in these tables, a description of the recommended Phase II project, and a summary of all significant findings and suggested needs for the future.

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## **B. Background**

### **1. Significance of viral aerosols**

Aerosols are dried residues formed by the instantaneous evaporation of droplets suspended in air and may, on occasion, contain living microorganisms e.g., bacteria, viruses, and fungi. These are called viable aerosols in contrast to the non-viable aerosols that contain industrial residues, photooxidants, and petrochemical compounds, etc. (104). Numerous epidemics of infectious diseases have been known to be transmitted by viable aerosols containing human pathogenic microorganisms. In addition, bacteria, higher plants, insects, and animals are susceptible to airborne infection.

Viruses of foot and mouth disease, Newcastle disease, and swine vesicular disease can be transmitted by the airborne route to cattle, poultry, and pigs, respectively, and cause significant economic losses (36,57). Aerosol hazards for humans may be present in hospitals, day care centers, office buildings, abattoirs, animal processing facilities, scientific laboratories, and waste water treatment facilities. Spray irrigation of waste water (103) and wind-borne sprays from ocean surf have been shown to create virus-laden aerosols (115).

The infection of humans and/or animals by the airborne route can occur either by inhalation or by subsequent ingestion, although the former is more significant. Viruses can not multiply outside a living host. The source of viruses in aerosols is, therefore, aerosolized excretions and secretions of man or animals with active or inapparent viral infections. Sneezing and coughing are two activities that produce the most aerosols; a single sneeze may produce up to  $10^6$  droplets (97). Talking, singing, and toilet flushing in the household are also considered to be potential sources of disease-causing aerosols (85,115). The nose, eyes, and mouth are important portals of entry for viral aerosols. The droplet nuclei in the range of 0.5 - 3  $\mu\text{m}$  are too small to settle quickly but are small enough to be inhaled and deposited in the lung tissue (81). In addition, they can remain suspended in air for extended periods of time and may infect many susceptible individuals. Even if they are capable of settling, droplet nuclei may still be hazardous if they can survive on surfaces for extended periods of time.

Certain orthopedic and surgical procedures on bones, soft tissues, and body fluids may expose surgeons and other health care workers to infectious aerosols. For example, papilloma virus DNA has been recovered from laser plumes of wart lesions and nasal papilloma has been seen to develop in physicians and operating room staff exposed to laser papilloma plumes (42).

The viruses in aerosols can survive for varying periods of time depending upon various factors e.g., virus type, humidity, temperature, and exposure to ultraviolet light. Viable aerosols have been found to travel long distances. Whether a person coming in contact with viral aerosols will become infected or not depends on many factors e.g., host susceptibility, viral virulence, virus concentration, aerosol particle size, minimum infective dose of virus, and the size and density of an exposed population (Table I)(104). It is believed that even one infectious unit of coxsackievirus A21 and adenovirus

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**Table 1: Parameters that Influence Virus Perpetuation**

- |   |
|---|
| <ol style="list-style-type: none"><li>1. Size of population.</li><li>2. Rate of population turnover: Losses are partially immune and are replaced by susceptibles.</li><li>3. Density of population: Contacts per unit time may increase with density.</li><li>4. Immunity of population: Primary infection confers long-lasting immunity.</li><li>5. Transmissibility or infectiousness: The probability per unit time that an infected individual will transmit to a contact.</li><li>6. Duration of infectiousness.</li><li>7. Generation period: The average interval between acquisition and transmission of an infection.</li></ol> |
|---|

( From 104: Spendlove, J.C. and Fannin, K.F., 1982. Chapter 12 Methods of characterization of virus aerosols. Methods in environmental virology. Gerba, C.P. and Goyal, S.M. eds. Marcel Dekker Inc. New York)

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can cause infection in a susceptible host although it may not be able to produce overt disease (2). Epidemiologically, the transmission of viruses by aerosols is difficult to prove because the virus infection by aerosols may not result in overt disease but may produce subclinical infection, especially if the virus concentration in aerosols is too low. However, these subclinically infected individuals may, in turn, become sources of infection to others.

Aerosols containing enteric viruses can be produced by flushing toilets, changing of babies' diapers, and spray irrigation of waste water. Although enteric viruses are transmitted mainly by the fecal-oral route, some of them have been suspected to be transmitted by the airborne route (79). For example, poliovirus and coxsackievirus type A21 have been shown to be transmitted by 'droplet' infection (111). Even if enteric virus aerosols, when inhaled, do not infect the respiratory tract, it is possible that they may be trapped in respiratory secretions and be eventually swallowed to produce intestinal infection (79). Also, aerosolized viruses, upon settling, can

contaminate surfaces. Contact with contaminated surfaces can result in self-inoculation by touching of the nose or mouth (54).

Both respiratory and non respiratory viruses can spread via the airborne route. Examples are: influenza virus, rhinoviruses, measles, mumps, rubella, coronavirus, rabies virus (124), smallpox virus (6), and enteric viruses e.g., enteroviruses, adenoviruses, reoviruses, and hepatovirus (104). Rhino- and coronaviruses are adapted to grow in respiratory epithelium and cause colds (110). Viruses acquired from contaminated laboratory air include smallpox virus, hepatitis virus type A, Venezuelan equine encephalitis, and Epstein-Barr virus (EBV). Viruses that have been transmitted in infected animal holding facilities include Rift Valley fever, yellow fever, rabies, and polyoma viruses. The latter is excreted in the urine of mice and can become airborne in animal housing facilities (74).

Table II indicates the more important airborne viruses considered during this study for spread among humans in indoor environments. While this report focuses primarily on public buildings (containing offices), there are other important environments where airborne spread of some viruses becomes particularly important. These include day care centers, medical offices, animal care facilities, and sewage treatment plants, to name just a few. However, the focus of this report has been on viruses which may undergo significant airborne spread in general office buildings; these include rhinoviruses, influenza viruses, adenoviruses, and sometimes enteroviruses. Since day care facilities are being located in office or other public buildings with increasing frequency, we also considered chicken pox and measles viruses, as these are extremely infectious viruses which may be spread through common ventilation systems. Discussion of the other environments mentioned above has been included where the literature illuminates or is relevant to our primary focus of public office buildings.

**Table II**  
**Important Human Viruses for Indoor Environments**

Disease	Virus	Virus Family	Virus Size (nm)	Envelope	Nucleic Acid Type
Common cold	Rhinovirus	Picornaviridae	22-30	-	RNA
Common cold	Coronavirus	Coronaviridae	80-160	+	RNA
Smallpox	Variola	Poxviridae	200x300	+	DNA
Influenza	Influenza virus	Orthomyxoviridae	20-120	+	RNA
Measles	Measles virus	Paramyxoviridae	150	+	RNA
Chickenpox	Varicella virus	Herpesviridae	120-200	+	DNA
LCM	Lymphocytic choriomeningitis virus	Arenaviridae	110-130	+	RNA
EBV	Epstein-Barr virus	Herpesviridae	120-200	+	DNA
Rabies	Rabies virus	Rhabdoviridae	180x75	+	RNA
Gastroenteritis	Rotavirus	Reoviridae	60-80	-	RNA
Korean hemorrhagic fever	Hantaan virus	Bunyaviridae	80-100	+	RNA
Gastroenteritis	Enteric viruses	Picornaviridae	22-30	-	RNA
Gastroenteritis	Adenovirus	Adenoviridae	70-90	-	DNA
Respiratory infection	Respiratory syncytial virus	Paramyxoviridae	150	+	RNA
Warts	Papillomavirus	Papovaviridae	40-55	-	DNA
German Measles	Rubella	Togaviridae	60-70	+	RNA

- = non-enveloped virus; + = virus with an envelope

## **2. Estimated costs to society from airborne viral infections**

"As human populations increase in size and density, there is a greater probability that infection with aerosolized agents will also increase. This has been well documented in indoor environments with viruses such as measles (88) and adenovirus (11). In the latter case, the 'tightness' of the building was implicated." (1)

Estimates from the 1981 National Health Interview Survey (113) indicate that over 200 million episodes of respiratory infection occur each year. Thus, each adult in the United States experiences 2 to 4 respiratory infections annually. The morbidity of these infections is estimated to result in 75 million physician visits per year, 150 million days lost from work, and more than \$10 billion in cost for medical care (43). Another estimate of these costs (35) concludes that these infections result in about \$15 billion in direct treatment costs with 1.25 million persons hospitalized each year. Of this dollar amount, one-third is for hospital care and two-third is for home care costs. In addition, the loss in income of those too ill to work is estimated to be in the range of \$9 billion per year.

To update these estimates, we looked at data in the most recent National Health Interview Survey (112). The reported number of episodes of respiratory infection was about 250 million in 1991. Approximate 130 million of these infections occur in those aged 18 to 64, 104 million in those under 18, and about 15 million in those over the age of 65. The rate was about 106 per 100 persons in the 18-24 year old range, 88 per 100 in 25-44 year olds, and 62 per 100 in those over the age of 45.

For all ages, 47% of all respiratory conditions were medically attended. For those over 18 who are currently employed it is estimated that 149 million days of work were lost in 1991. About 106 million lost days occurred for those between 18 and 44, with the remaining 43 million days for those over 45 years of age. The data show nearly twice the rate of illness caused by influenza virus as by the common cold virus. This probably is due to under-reporting of colds, and therefore under-reporting of the total incidence of respiratory disease.

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## **C. Disease Transmission and Epidemiology**

### **1. Introduction**

Although there is a large body of evidence which implies that indoor air is the vehicle for transmission of a number of childhood and adult respiratory diseases, many questions remain relative to the mechanisms and extent of this involvement. In 1983, Spendlove and Fannin (104) stated "It is evident that in spite of the considerable body of data available on indoor microbial aerosols, little is known of their true significance to human health except in terms of overt epidemic disease. Continued research is needed in this area, particularly in respect to situations of high risk in such locations as hospitals and schools for young children...."

Review of the literature relative to evidence of viral disease transmission via the aerosol route can be organized into four different categories. In this section we will consider the evidence for airborne spread which has emerged from animal studies, anecdotal reports, epidemiological investigations and human volunteer or other experimental approaches. It is noteworthy that a significant majority of the studies referred to in this section date from the 1960s and 1970s with surprisingly few from the 1980s and 1990s. The interest in airborne infections appears to wax and wane and may parallel the fluctuating predominance of opinion relative to the role played by true airborne transmission in the epidemiology of respiratory infections.

### **2. Animal models**

Considerable work on viral disease transmission has been carried out using animal models. These studies have the obvious advantage of challenging subjects directly via the airborne route while allowing exclusion of other possible routes of transmission. In addition, they allow the use of relatively high challenge doses for a range of viruses of varying disease severity. The only disadvantage, albeit a major one, is the difficulty in extrapolating animal data to human effects. Nonetheless, these studies do provide unequivocal evidence that viruses can be transmitted via the aerosol route.

A wide variety of viruses can be transmitted to different animal hosts. For example, Jericho et al. (62) directly infected calves with bovine herpesvirus-1 using a Collison nebulizer attached directly to a face mask (droplets were less than 3  $\mu\text{m}$  in size). Schulman and Kilbourne (98) provided evidence of influenza virus transmission to mice via airborne droplet nuclei. They further demonstrated that the infection rate could be decreased by increasing the ventilation rate in a closed chamber system and showed that the rate of infection via the airborne route was as high as the rate for mice directly exposed to other infected mice. Sellers et al. (99) studied the airborne dispersal of foot-and-mouth disease (FMD) virus into the air of housing pens



relative to vaccination status of cattle, sheep and pigs. Their results suggest that movement of animals should be restricted for two weeks following exposure to this virus. Suptel (108) demonstrated airborne transmission of coxsackie virus to newborn mice, showing 100% fatality with a dose of 13,000 LD<sub>50</sub>/0.03 mL. They showed the minimal infective dose to be less than 1.3 LD<sub>50</sub>/0.03 mL.

There has been considerable interest in airborne transmission of animal oncogenic viruses because of the concern for possible laboratory safety implications for research workers studying those viruses. For example, Sevoain et al. (100) demonstrated the airborne transmission of lymphomatosis virus (causing avian leukosis) from infected to non-infected chicks via an interconnected ventilation system. Similarly, McKissick et al. (75) experimentally transmitted Rauscher murine leukemia virus to mice, further demonstrating horizontal transmission from the aerosol exposed mice to unexposed cage mates. In a particularly pertinent study, Wolfe et al. (126) demonstrated the aerosol transmission of Yaba virus, causing pulmonary tumors in 5 of 12 rhesus monkeys and 1 of 3 cytologus monkeys. The monkeys were kept in cages inside of rigid or flexible plastic isolators to prevent accidental cross-contamination. In this study, horizontal transmission to cage mates was not demonstrated. This virus is considered to be important because of its potential pathogenicity to humans.

In still another approach, Hugh-Jones et al (56) performed both laboratory experiments and field measurements to conclude that Newcastle disease virus of poultry was spread via the airborne route.

### **3. Anecdotal or case studies**

A number of unusual incidents or occurrences have resulted in investigations which have suggested, with varying degrees of certainty, that building ventilation systems can play a role in viral disease transmission.

Several of these incidents involved airborne transmission of the now extinct smallpox virus. The British Medical Journal (6) reported on an incident which occurred at a smallpox hospital in Merschede, Germany in 1970. Twenty cases of smallpox resulted from an index case who was confined to his cubicle for his entire six day stay in the hospital and had no contact with the other victims. The distribution of cases within the hospital together with smoke tests to trace air movement were strongly indicative of airborne transmission. Similarly, a well publicized incident at the University of Birmingham in England (50,53) clearly implicated a faulty service duct as the likely means of spread of a smallpox virus aerosol generated during research procedures. Another incident in which air tracer studies were utilized to demonstrate the likely mechanism of transmission involved a chickenpox epidemic in a pediatric hospital (69). Thirteen cases were

reported to result from an index case. Again no direct contact between the index case and secondary cases could be identified and airborne spread was considered the most likely means of transmission.

An outbreak of influenza aboard a commercial airliner was reported by Moser et al (82). The airplane had been delayed for three hours on the runway because of a mechanical problem. Most of the passengers remained on the plane during that time with the ventilation system inoperative. Serological evidence linked some 20 cases to the apparent index case, a passenger who was ill at the time of the incident. In another incident, an unusual outbreak of measles in 1982 was reported among children visiting a pediatrician's office in Muskegon, Michigan (86,18). Measles was also the virus which reportedly spread via a ventilation system with a high percentage of recirculation in an upstate New York elementary school in 1982 (88). This incident was notable because some 97% of the children had been vaccinated, presumably with an ineffective vaccine given to children less than one year of age.

#### **4. Human epidemiological studies**

Epidemiological investigation of populations in various settings has yielded evidence of airborne spread for a number of common viral illnesses. Included among these are the common cold, influenza, measles, chickenpox and a variety of other respiratory viruses.

There have been a number of noteworthy general reviews of the epidemiology of respiratory viral infections which have addressed, to some extent, the potential role of intramural airborne spread. As early as 1960, Williams (122) pointed out how opinion as to relative importance of airborne transmission had fluctuated over the years. He also identified the difficulties of resolving the issue by epidemiological or experimental means. His views appear to be just as relevant today as they were more than 30 years ago. Twenty years later in 1980 Langmuir (68) reviewed the evidence for airborne transmission of three specific viral diseases. He concluded that airborne spread of smallpox was rare, although it had been conclusively shown to be possible. He decided that air was a common vehicle for spread of measles and was probably a major vehicle for rubella as well. In the same year Gwaltney (49) reviewed the epidemiology of the common cold and played down the role of airborne transmission. The role of air as a vehicle for the common cold has been particularly contentious over the years and has been subject to frequent fluctuation. In 1964, Andrewes (5) reviewed the epidemiology of colds and influenza concluding that control would always be difficult due to the close proximity of individuals in indoor environments. Riley (89), in a 1974 review, expressed the most vociferous opinion citing the importance of air as a vehicle of viral infections, particularly noting measles, influenza and smallpox. He also advocated a mathematical model for predicting the spread of droplet

nuclei and he remains a strong advocate for ultraviolet light (UV) as a preventive measure.

Numerous investigators have studied defined populations relative to the potential for respiratory viral infections with conclusions pertinent to the question of airborne transmission. Summaries of selected articles from this group follow in chronological order:

Willmon et al. (123) studied respiratory diseases in Navy recruits during World War II. The investigators admitted that they were unable to distinguish the relative importance of airborne vs. contact transmission, but felt that ultraviolet air disinfection was a promising control approach.

Dick et al. (33) studied rhinovirus infections in University of Wisconsin student families in the 1960s. They reported relatively high transmission rates within families with much lower transmission between families.

Sims (102) conducted a two year prospective study of hospital-acquired respiratory viruses in pediatric wards in an English hospital. Without direct evidence, he implied that transmission was more likely to occur in open wards than in areas with cubicle confinement, again hinting that the airborne route was important.

Brundage et al (11) reported specifically on building ventilation effects in a study of acute respiratory disease among army recruits. They compared buildings which had been updated for energy conservation with those which predated such improvements. They concluded that respiratory disease rates were significantly higher (adjusted relative risk estimate of 1.51 with a 95% confidence interval of 1.46-1.56) in the energy efficient buildings, citing this as direct evidence of the importance of dilution via ventilation in preventing respiratory infections.

In the 1970s several investigations were carried out on the transmission of respiratory viruses within the population of an isolated Antarctic research station (101,116). The study population included longer term residents mingling with newly arrived individuals. The study implied that transmission among this healthy but susceptible population was relatively slow and difficult.

Jaakkola et al. (60) carried out an investigation of common cold transmission among 893 office workers in a modern mechanically ventilated building in Helsinki, Finland. A self administered questionnaire was utilized to provide data. They identified several significant risk factors including: One or more roommates (Odds Ratio (OR) =1.35), having young children at home (O.R. = 1.46), and a history of hay fever (O.R. = 2.07). Being female and under 40 years old also implied slightly increased risk although these factors were not

statistically significant. The authors suggested that the presence of other individuals increased the risk of common cold due to indoor air transmission.

Recently, Monto and Sullivan (80) described an eleven year study of respiratory illness among residents of Tecumseh, Michigan. Although this study did not directly address the potential role of air as a vehicle, one of the observations was that these illnesses were less common among working women than among those not working outside the home. On the surface, this might imply an unimportant role for building ventilation systems. However, it is more likely that the greater contact time of non-working women with young children was responsible for this finding.

Several investigators have attempted to include direct air sampling for virus recovery relative to investigations of respiratory illness. Artenstein and Cadigan (7) studied patients at two army hospitals and attempted to recover respiratory viruses from the air near patients hospitalized with acute respiratory infections. They succeeded in recovering parainfluenza virus from one patient and suggested the need for more such sampling. McLean et al. (76) also used air sampling in the same manner in a study of 300 children under three years of age who had been hospitalized within the last 48 hours with acute laryngotracheobronchitis. They also succeeded in recovering parainfluenza virus from one of thirty children who were found to be harboring that specific virus. They cited this as evidence that the virus is disseminated into the air.

## **5. Human volunteer and other experimental approaches**

A surprising number of investigations into airborne spread of respiratory viruses have been carried out using human volunteers. These studies are based on the premise that common colds and other minor respiratory infections are relatively innocuous, and thus such infections can be transmitted with minimal risk to human subjects. Other approaches included tracer type experiments using surrogate organisms or environmental sampling to detect airborne organisms.

In the 1960s an extensive series of human volunteer experiments were carried out at the U.S. Army Biological Laboratory at Fort Detrick, in Frederick, Maryland (17, 21, 22, 23, 64, 65, 24, 25). These investigators experimentally infected human volunteers with aerosolized rhinovirus, coxsackie virus and adenovirus. They determined the human infectious dose (HID)<sub>50</sub> in terms of tissue culture infectious dose (TCID)<sub>50</sub> for these viruses and also compared infectivity via the aerosol route with infectivity induced by direct nasopharyngeal inoculation. They concluded that infection was more readily induced by the small particle aerosols (1.5  $\mu\text{m}$ ) reaching the lower respiratory tract, citing this as evidence of the importance of true airborne spread of these viruses.

Dick et al. (34) at the University of Wisconsin later used human volunteers in a different type of experiment to determine the mechanism of transmission of rhinovirus colds. Laboratory-infected adults played cards for 12 hours with susceptible volunteers. Eighteen susceptibles were restrained to eliminate all but the aerosol route while 18 others were unrestrained so that infection could be transmitted by aerosol, direct or indirect contact. The infection rates (56% in restrained subjects vs. 67% in unrestrained subjects) were not statistically different leading to the conclusion that airborne spread was the most significant means of transmission. These investigators also utilized married couples as volunteers to determine rates of spread and factors influencing spread of rhinovirus colds (29). The most important factors leading to transmission included: 1) A TCID<sub>50</sub> of at least 1000, 2) having detectable virus on the hands and nares, 3) being at least moderately symptomatic and 4) spending many hours with the spouse. This investigation did not address the relative importance of airborne vs. contact spread.

A different approach was used by Buckland and Tyrrell in England (12). They inoculated human volunteers with a tracer organism (*Bacillus mycoides*) and then measured the effects of expulsion via coughing, sneezing and talking. They concluded that sneezing produced the largest number of particles, including many in the respirable size range, indicative of possible airborne spread.

Still another approach was attempted by Petersen (84). Using extensive air sampling in dialysis centers, laboratories and dental operatories to assess the potential for hepatitis B (HBV) transmission via aerosols, he concluded that the airborne route is not a major factor in HBV transmission.

## 6. Summary

In total, the reports summarized in this section do not definitively identify the role of airborne transmission in human respiratory viral disease. It is obvious that there is no simple yes or no answer to that question. However, the literature reviewed herein provides convincing evidence that airborne transmission of these viruses can and does occur. When the critical combination of source presence, viral concentration in the air, ventilation parameters (insufficient dilution, filtration, etc.), and availability of susceptible hosts all coincide the potential for airborne transmission of these viruses is clearly present. Hopefully, this report will point toward future investigations which may shed further light on how those control factors can be manipulated to minimize the potential for respiratory viruses to spread through public buildings.

## **D. Sampling for Airborne Viruses**

### **1. Background**

Laboratory studies of airborne viruses have centered on either 1) determinations of aerosol stability for a specific virus under different environmental conditions (e.g., relative humidity or temperature) or 2) assessment of infectivity as it relates to type and strain of virus and aerosol particle size. These studies have utilized a variety of sampling procedures and assay methods for determination of airborne concentrations of virus aerosols. While it is possible to derive general conclusions about viral aerosol sampling from laboratory studies, it is important to keep in mind that airborne concentrations of viruses in a field setting will be significantly less than found in any laboratory experiment. Thus, studies utilizing laboratory-derived samplers have been unable to demonstrate, in most cases, the presence of airborne virus in indoor environments. Only in studies employing so-called "large volume" samplers have investigators been able to demonstrate the presence of airborne virus particles. There have been no or few attempts to correlate these findings with laboratory measurements of infectivity, largely because it is not possible to establish a quantitative relationship of sampling efficiency (both as it concerns collection and particle viability) between samplers used in experimental setups with those employed in field settings.

The aerobiological sampling techniques presently used for detecting viable virus aerosols have been adapted from those used for measurement of airborne bacteria, pollen, and fungal spores. The most significant difference between these microorganisms and viruses is that the latter require a living host for assaying their presence. (This is discussed in more detail in the next section on Assay and Characterization.) In general, viruses are more susceptible to desiccation than other microorganisms, and thus require the use of sampling methods which minimize drying during the sampling period. The use of either liquid or agar collection media will ensure the best retention of aerosol viability. In some cases, viruses can be broken apart by the high shear forces exerted during sampling (27); thus, a sampler which minimizes such forces also allows greater viability retention.

It is important also to consider the possible particle size distribution with which viral particles will be associated. While viruses are generally very small (Table II), it is unlikely they will be found as single airborne virions. Rather, it is more likely that they will be attached to larger particles composed of material dependent on the method of generation. In the case of human-generated respiratory viruses, the associated material will most likely consist of mucus, saliva, and other respiratory system-derived substances. The size of such particles will depend on the initial size, the evaporative quality of the aerosol material, and the length of time particles are airborne.

In general, it is assumed that virus particles can be associated with particles ranging from 0.5 to 20  $\mu\text{m}$  (19).

The type of sampling employed depends on the virus, the likely airborne concentration, the method of assay, and whether one wishes to know the number of viable particles or the number of virus particles (the latter usually being larger than the former). The latter measurement is the more useful in determining infectious dose, but relies on using a sampling and/or assay method which causes the breakup of aerosol particles into single virions. In general, the infectious dose for specific viruses is not known for humans, due to the problems associated with sampling mentioned above.

The most useful application of laboratory studies for viral aerosol stability concerns the effect of humidity on viability when sampling in field settings. It has been found that humidification immediately prior to sampling can significantly improve the recovery of some airborne viruses (19,27,78). For other viruses, however, such humidification can cause significant loss in viability (19,27,30); thus, it is important to know or evaluate the effect of pre-humidification on the virus of interest before sampling. For example, De Jong (30) found that measles virus survived well at very low and very high relative humidities (less than 50% and greater than 70%). Miller and Artenstein (78) found that adenovirus aerosols (unlike those of influenza and parainfluenza) decayed more rapidly at low than at high relative humidity. According to Cox (27), phages and viruses with no structural lipids will survive best at high relative humidity and benefit the most from rehumidification, while viruses with structural lipids are the least stable at high relative humidity and are inactivated by rehumidification.

Each virus sampling device has unique characteristics that can result in differences in collection efficiencies for aerosols in certain size ranges, sampling capacities, and operational capability (104); thus it is difficult to draw comparisons from data collected with different samplers under different conditions (19).

## **2. Samplers**

The principal aerosol collection mechanisms that have been employed in sampling for microorganisms are impingement, inertial impaction, sedimentation, filtration, cyclone scrubbing, and electrostatic precipitation. Although an attempt was made to recognize certain low-volume samplers (Andersen cascade impactors and all-glass impingers) as standards for studies in aerobiology, the need for greater sampler sensitivity in field studies of virus aerosols has resulted in the development of nonstandard large-volume air samplers. Examples of the application of each concept for viable microbial aerosol collection are discussed below and presented in

Table III. Figures for a number of these samplers are included at the end of this section, as well.

#### Sedimentation:

*Concept and Operation:* Virus aerosols settle onto exposed open surfaces depending on air flow velocity and angle as well as particle size and density (38). Larger particles with greater density have a higher settling velocity and are collected more efficiently. Mechanical means are not required to bring the aerosol in contact with the collecting medium using this method. Sedimentation studies use either nutritional agar-based petri dishes (Figure 1) or adhesive-coated surfaces (e.g. slides). Under certain conditions, settled microorganisms may be assayed directly on the collecting surfaces. Direct virus assays are not possible when collected in an environment contaminated with other microorganisms; virus recoveries in these situations may require cumbersome and inefficient washing or elution procedures. For example, virus aerosols have been recovered on prewetted gauze pads by assaying eluate (44).

*Advantages:* simplest, least expensive method.

*Disadvantages:* This method is not quantitative because there is considerable bias toward the collection of larger particles. Since smaller particles are more likely to penetrate into the lung, assessment of the risk of respiratory infection by using the method of sedimentation is extremely limited. In general, this method is not recommended for the collection of indoor viral aerosols.

#### Filtration:

*Concepts and Operation:* Virus-containing aerosol particles, depending on their size and electrical charge, can be captured on filters. Aerosol filtration devices such as cotton, soluble gelatin, or membrane filters have been used for bacterial aerosol studies (104). Membrane filters (Figure 2) are the most useful when it is necessary to evaluate particle size analyses by microscope. However, air sampling studies concerned with microbial survival and infectivity have indicated that filtration is a very unsatisfactory technique. Difficulties result from non-consistent recovery of microorganisms from the filter, effects of airflow on viability, and release of growth inhibitors from filter materials (26). Use of filters for virus aerosol detection may be impractical for long-term or large-volume sampling application since viability losses can be substantial due to desiccation of fragile viruses (1, 38)

*Advantages:* Simple, relatively inexpensive method.

*Disadvantages:* The most significant problem concerns that of desiccation of viruses during long-term and large-volume sampling applications.



Table III: Virus Aerosol Sampling Concepts and Instruments

Principle / Sampling device	Collection medium	Sampling rate (LPM)	Sampling time	Sampling capacity	Comments
<b>Sedimentation</b>					
Open Petri dish	Agar;	—	0-4 hr	Low	Simple, inexpensive, nonquantitative, collection biased towards large particles
Adhesive-coated surface	Surface, e.g. slides	—	unlimited	Low	
<b>Filtration</b>					
Filter	Membrane, gelatin	5--50	1--20 min	Low	Simple, inexpensive, some viable loss due to dessication of fragile virus
High-volume filter		140-1400	5--60 min	High	
<b>Electrostatic precipitation</b>					
Litton LVAS	Compatible fluid	500--10000	Unlimited	High	High sensitivity due to collecting large volume of aerosols; allow longer sampling time. Complex, expensive, bulky, limited availability, subject to mechanical failure, difficult to sterilize, collection effi. is 45-90% that of the AGI-30. High collection effi, but low recovery effi.
LEPA					
<b>Centrifugal separation / impaction</b>					
Cyclone scrubber	Compatible fluid	50--950	Unlimited	High	Simple, relatively inexpensive, autoclavable. Operation subject to relative humidity variation
Biotest Reuter Centrifugal	Agar in plastic strips	40			Low collection effi. for particle with dia. $\leq 4 \mu\text{m}$
<b>Impingement</b>					
AGI-30 (Proton )	Compatible fluid	12.5	15--30 min	Low	Simple, inexpensive, dependable, high efficiency, preserves viability, suitable for different assay methods, autoclavable,
AGI-4	Compatible fluid	12.5			

Shipe impinger	Compatible fluid	10				Sampling rate low, requires high vacuum pump and temperature control, violent agitation kill virus
Midget impinger	Compatible fluid	2.5-5				
Multistaged impinger	Compatible fluid	55, 20, 10		High		Simple, size classification with cut points of $\geq 7$ , $\geq 3$ and $\geq 1$ $\mu\text{m}$ . Limited availability.
Multislit impinger	Compatible Fluid	1000		High		
Impaction						
Slit sampler	Rotating agar	28.3-1 short slit	1--60 min	Low		Simple, provides aerosol concentration/time data, available with a single or with multiple slits and variable rotation speeds, good viable recovery, high efficiency. Bulky, noisy.
Casella slit sampler	Rotating agar	750-4 slits	1--60 min			
Andersen multistage	Agar	28.3	1--30 min	Low		Simple, dependable, provides particle size data, good viable recovery. Expensive.
Surface air sampler (SAS)	Agar	180	20sec--6 min	High		Inefficient for particles $\leq 5\mu\text{m}$ , portable.
Cascade impactor (Sierra)	Filters or Media	2000				Microscopic determination of no. and size of the particles
Direct flask	Cell culture	1				Effi is closer to AGI.

### Impingement:

**Concepts and Operation:** Impingement refers to striking "into" a liquid collection medium. Impingers trap particles by means of high speed impaction with the jet submerged in or located immediately above a collecting fluid. In some cases the jet is operated as a critical orifice so that particles impinge near sonic velocity. Liquid impingers are used to determine the number of viable microorganisms in aerosols, rather than the number of viable aerosol particles, because sonic velocity impingers cause the breakup of large particles. Some impingers (also called bubblers) collect aerosols at less than sonic velocity. These cause less damage to particles and viruses, but generally exhibit lower particle collection efficiency than sonic velocity impingers.

The all-glass impinger (AGI-4) (Figure 3) was initially designed for sampling laboratory-generated aerosols at 12.5 L/min by high-speed impingement into a collecting medium. The AGI-30 (with an increased jet-to-liquid distance of 30 mm)(Figure 3) was developed to reduce physical trauma and splashing, and later was recommended as a standard sampler by a committee of aerobiologists (1). In addition, to minimize microorganism reatomization and vegetative cell destruction during the high-speed impingement process, low-speed bubbling and washing samplers such as the midget impinger, fritted bubbler, and tangential jet impingers (e.g. Shipe impinger) (Figure 3) were developed (104). A preimpinger for use with the AGI, and a multistaged liquid impinger (discussed later) have been used for aerosol size discrimination. The pre-impinger divides the total sample into two size fractions ( $>5 \mu\text{m}$  and  $1-5 \mu\text{m}$ ).

Impinger sampling fluid is under low pressure and tends to evaporate quickly and freeze in cool dry air; changes in fluid pH, volume, and osmotic pressure can also occur, necessitating sampling time restrictions. Relatively low air sampling rates and short sampling durations limit the sensitivity of impinger samplers. Therefore, some sampling designs have employed multiple impingers in parallel, multiple jet impingers, a continuous impinger, and a large-volume multi-stage impinger (MSI) to increase impinger sampling capacity and sensitivity. The MSI is a three-stage impinger (Figure 4) with relatively gentle impingement to minimize impact trauma and viability loss by impaction into a liquid film-coated rotating disk. The sampler is available in three sizes with corresponding flow rates of 55, 20, and 10 L/min. MSIs have been used in field studies of waste water-generated microbial aerosols (127). As for a multislit impinger, aerosols are impacted into a liquid film-coated rotating disc at a flow rate up to  $1 \text{ m}^3/\text{min}$  (38,104). The multislit impinger had collection efficiency of 82% and 78% for *S. marcescens* and *B. subtilis* var *niger* spores, respectively, when compared to the efficiency of an AGI-30 (38).

*Advantages:*

**AGI-30:** simple, inexpensive, high efficiency, suitable for different assay methods, dependable, easily sterilized.

**MSI:** More portable, less spillage than the combination AGI-30 and pre-impinger, lower evaporation rate and less freezing, efficient for large particles with 82% collection efficiency of one cascade impactor (19), particle size classification, suitable for different assay methods, more sensitive than the AGI-30 due to higher air flow rates.

*Disadvantages:*

**AGI-30:** Low sampling rate, noisy, violent agitation during impingement may lower virus viability, requires high vacuum pump and temperature control.

**MSI:** Difficult to maintain, expensive, less reliable and field dependable, difficult to sterilize, limited availability.

Electrostatic Precipitation:

*Concept and Operation:* Microbial aerosols carrying a charge can be collected with relatively high efficiency by drawing them over an oppositely charged agar surface (38). The concept of aerosol collection by electrostatic precipitation onto a wetted surface has been employed in the development of large-volume air samplers, with air sampling rates ranging from 1 m<sup>3</sup>/min to 10 m<sup>3</sup>/min with a disc rotating at 200 or 300 rev/min which is covered by a thin flowing film of metered collecting fluid (28). The Litton Model M (Figure 5) and the Environmental Research Corporation LEAP electrostatic precipitator large-volume air samplers (LVAS) have been used for detecting low-concentration virus aerosols. Indoor sampling with the Model M demonstrated recovery of adenovirus aerosols from a military recruit camp during an acute respiratory disease epidemic (104). Field recoveries of rabies, foot-and-mouth disease and Newcastle disease viruses have been demonstrated with LVAS samplers (104,109). In addition, large-volume electrostatic precipitator have been used in field studies in detecting sewage-borne bacteriophages and enteroviruses (38). Other studies have shown electrostatic precipitation to be less effective than liquid impingement for detecting viable airborne viruses. Such observations have been attributed to electrostatic precipitator-generated ozone, or rapid evaporation of polar liquids, enhanced by electric current, or by a critical concentration of unipolar air ions (38).

*Advantages:* Effective in recovering very dilute concentrations of microbial aerosols. Most effective in still air. Low pressure drop.

*Disadvantages:* Expensive and complex. Requires a trained technician for continuous monitoring of electrical current fluctuations. Difficult to sterilize and subject to electrical arcing. Corona discharge produces oxides of nitrogen and ozone; ozone and its reaction products can be highly toxic for airborne microorganisms (28).

### Centrifugal Separation (Cyclone Scrubbing):

**Concept and Operation:** Microbial aerosol cyclone scrubbers collect airborne particles by tangential impingement into a continuous fine fluid film created as a mist impacted onto the sampler wall. Centrifugal samplers are suitable for sampling respirable size aerosols and can be applied to provide particle size distributions by simultaneously operating in parallel or by controlling the physical dimensions and flow rates (39, 28). There are three main types of cyclones: axial flow, returned flow tangential inlet and returned flow axial flow. The most common type used for sampling microbial aerosols is the returned flow tangential inlet cyclone (Figure 6); its sampling efficiency can reach 75% (28). It operates by applying suction at the exhaust pipe when a controlled flow of air enters the inlet, strikes the body of the cyclone and acquires a tangential velocity component. The largest particles tend to be deposited first and at the top of the cyclone. The fluid film removes deposited particles and travels spirally to a reservoir. Such a device, constructed in either stainless steel or glass, has air sampling rates of up to 0.95 m<sup>3</sup>/min and scrubbing fluid flow rates of 1 to 4 ml/min (104). Scrubbing liquid lost due to evaporation must be replaced. This device has been used in field studies to recover low concentration waste water-generated viral aerosols. During sampling, the scrubbing fluid was recirculated to concentrate the collected particles during sampling for enteric virus, and evaporation losses were replaced with sterile distilled water (40). The collection efficiency of a cyclone scrubber depends on sampler configuration, aerosol particle size, specific test organism, and composition of collection fluid (39).

**Advantages:** Relatively easy to operate, simple, inexpensive, autoclavable, particle size selective.

**Disadvantages:** Operation subject to relative humidity variations; evaporative loss of fluid must be adjusted for.

### Impaction:

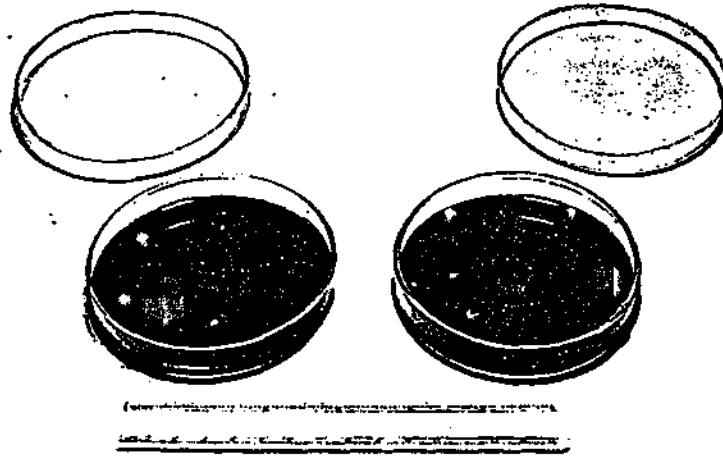
**Concept and Operation:** Aerosol particles are accelerated to gain sufficient inertia to leave an airstream and impact onto a collecting medium. In a cascade impactor, each subsequent stage collects smaller particles, allowing size discrimination of the aerosol. The device consists of a series of progressively smaller jets below which are located impaction surfaces (plates, slides, petri dishes, etc.). The Andersen cascade impactor (also referred to as the multi-stage impactor) (Figure 7) has been proposed as a "standard" microbial aerosol sampler, and has been widely employed in laboratory and field settings. There are a variety of cascade impactors with a range of stages and sampling flows.

A slit sampler accelerates air through a slit of critical size and distance from an agar collection surface. Airborne particles are collected onto the agar surface, which rotates slowly to allow for time discrimination of microbial

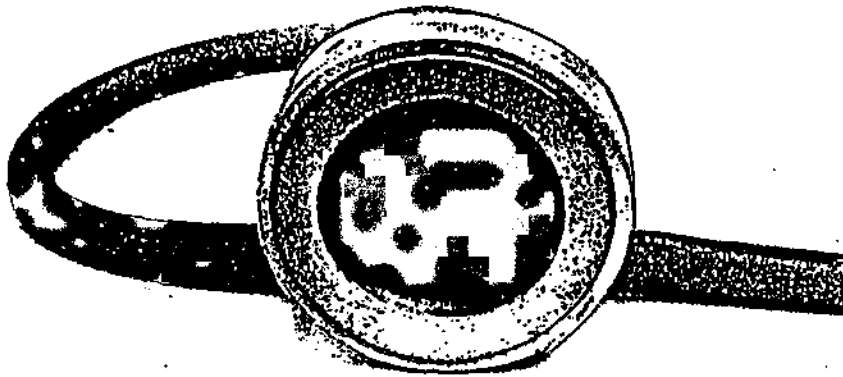
aerosol concentrations. The most common sampling flow rate is 28 L /min; a Casella multislit sampler (Figure 8) has been designed to sample up to 750 L /min.

**Advantages:** Suitable for enumeration of virus-containing particles rather than for total number of virus particles. Viruses can be washed from the collecting surface for assay or assayed directly with a cell overlay.

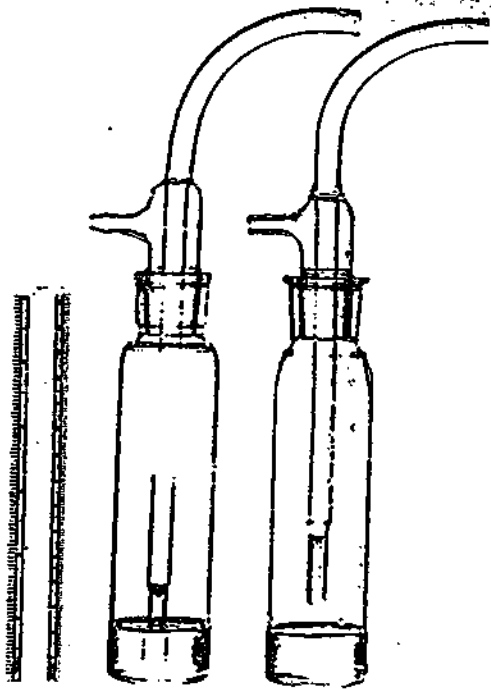
**Disadvantages:** Limited sampling capacity due to low air sampling rates and possible drying of agar surfaces. Application of an evaporation retardant to the agar surface has been found to help in some instances (38).



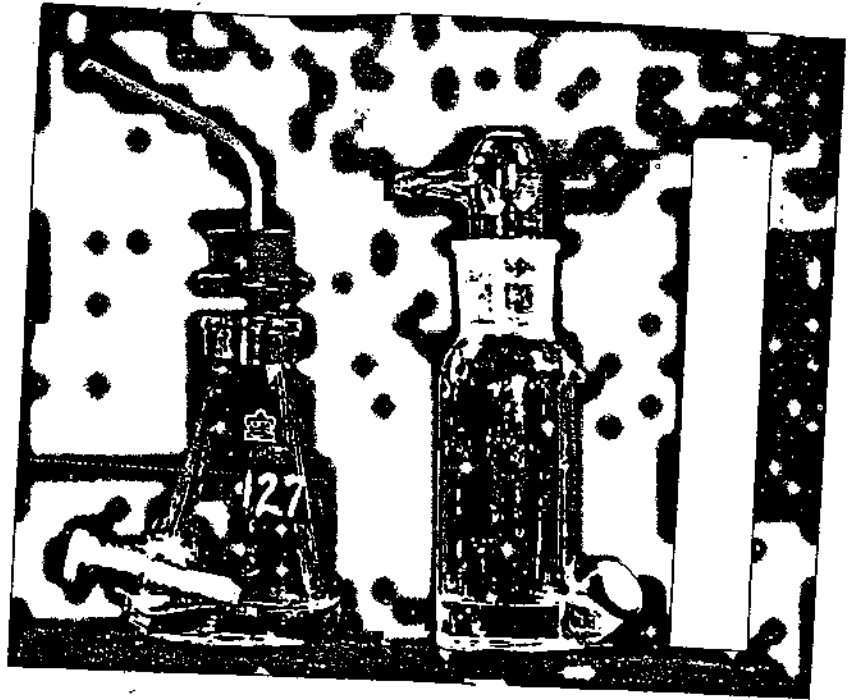
**Figure 1: Agar-based Settling Plate ( From 125: Wolf, H.W., Skaliy, P. , Hall, L.B. and Harris, M.M., 1964. Sampling microbiological aerosols. Public Health Monograph 60, US Government Printing Office. Washington, DC#683.)**



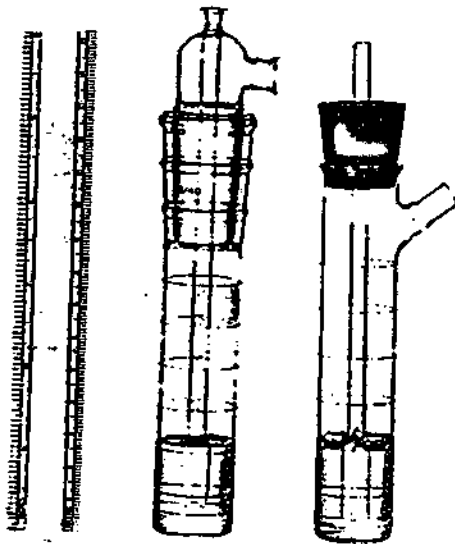
**Figure 2: Membrane Filter Aerosol Sampler ( From 38: Fannin, K.F. , 1980. Method for detecting viable microbial aerosols. Wastewater aerosols and disease. Health Effects Lab. 600/9-80-028. US-EPA.)**



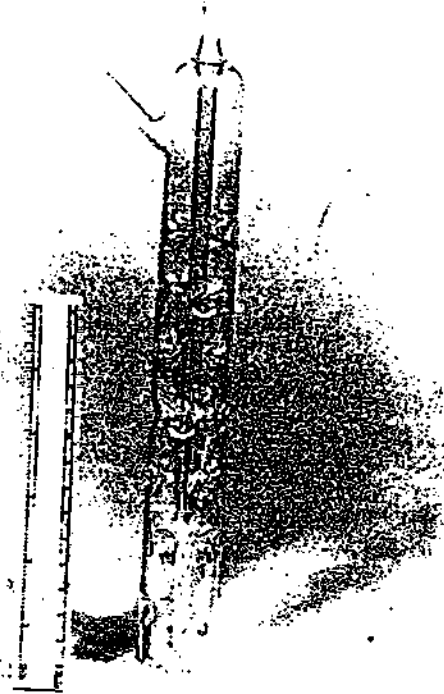
(a)



(b)



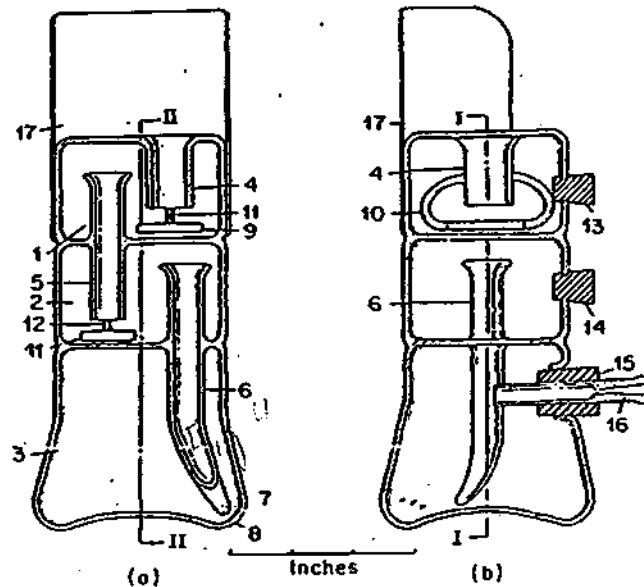
(c)



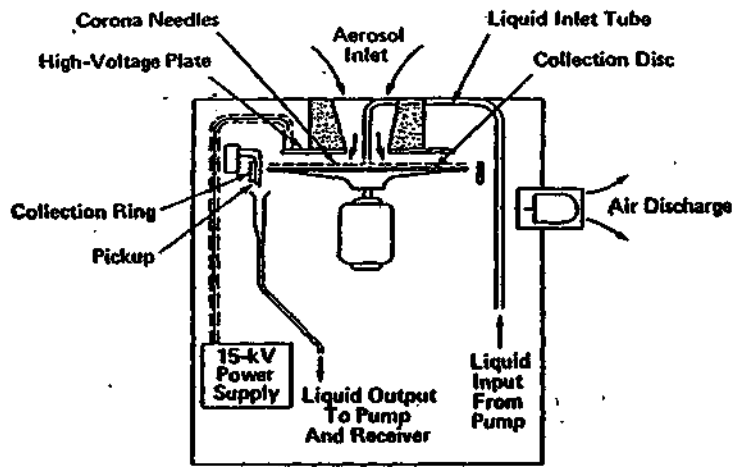
(d)

**Figure 3: All-glass Impingers: (a) AGI-4, AGI-30, (b) tangential jet impinger, (c) midget impinger, (d) fritted bubbler. ( From 125: Wolf, H.W., Skaliy, P., Hall, L.B. and Harris, M.M.,1964. Sampling microbiological aerosols. Public Health Monograph 60 US Government Printing Office, Washington, DC. )**

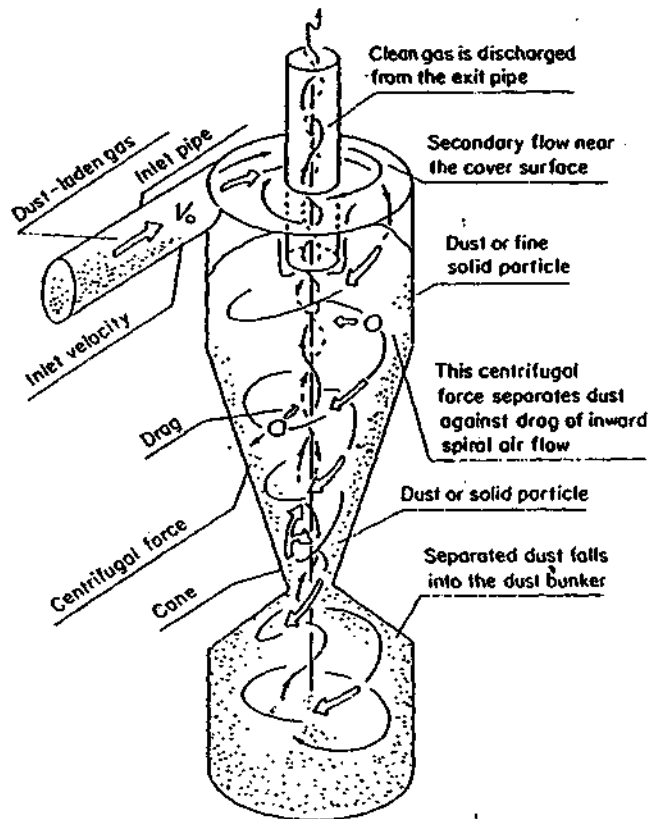




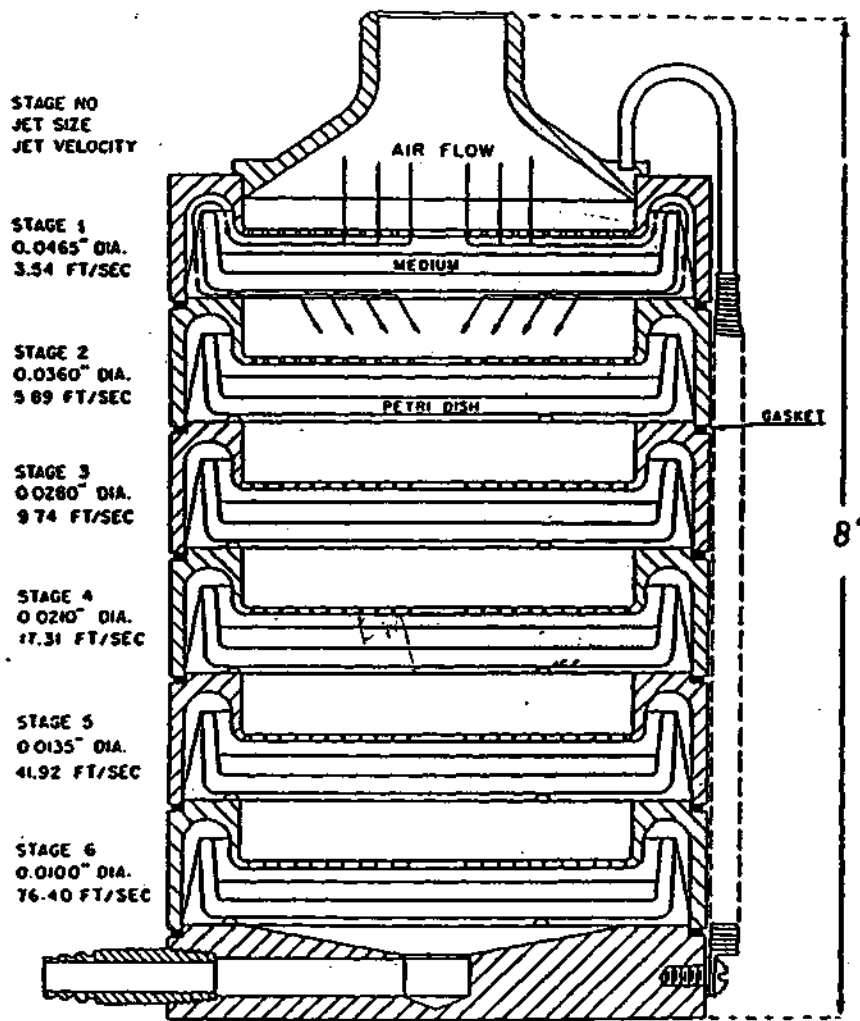
**Figure 4: Sectional Drawing of a 50 L/min May Multistage Liquid Impinger (MSI).** A and B are sectional side elevations at right angles to each other in the directions I-II and II-II, respectively. The air inlet tube 4 is smoothly curved to promote laminar flow and has a flat ground lower end. The straight tube 5, also with a smoothly curved bell-mouth, a flat ground lower end and a bore of 10 mm, is sealed into the flat floor of stage 1. Tube 6 with a smooth bell-mouth is sealed into the floor of stage 2. At its lower end it bends and tapers smoothly and continuously to the nozzle 7. Two circular discs, 9 and 11, of coarse sintered glass 3 mm thick are held 1mm above the floor of their respective chambers. The discs 9 and 11 are twice the diameter of the bores of respective tubes 4 and 5 and are separated from the flat ends of these tubes by a distance equal to three-eighths of the bore. Access holes to each chamber are sealed by rubber bungs 13, 14 and 15. The lowest bung 15 is fitted with a tube 16 for connection to a suitable pump. (From 28: Cox, C.S., 1987. Chapter 3 Aerosol samplers. The aerobiological pathway of microorganisms, John Wiley & Sons, New York.)



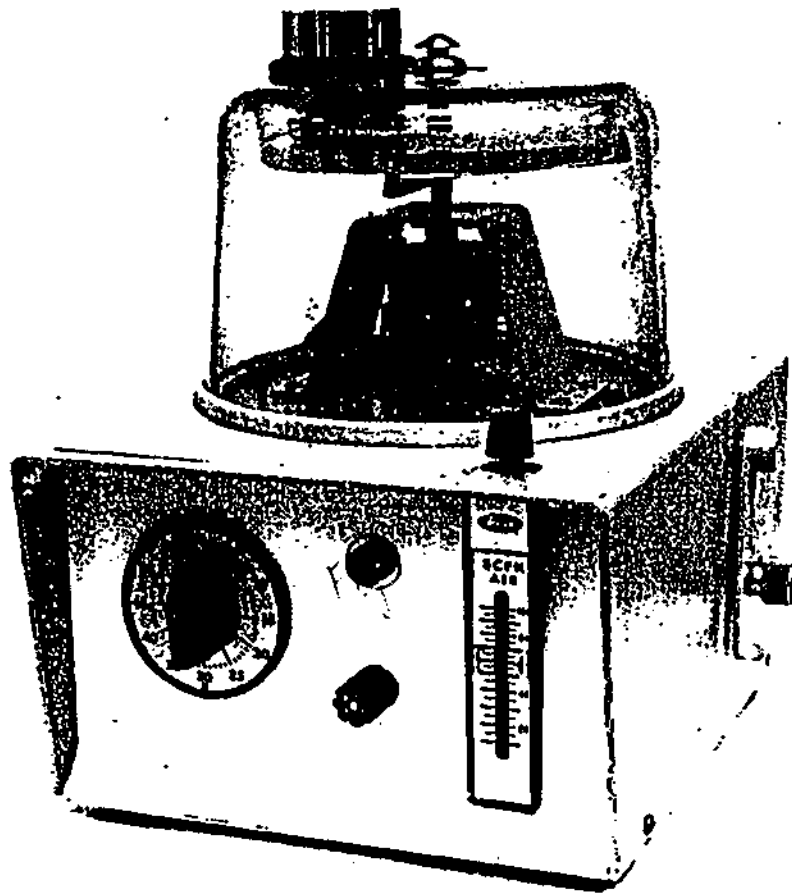
**Figure 5: Litton Large-volume Air Sampler. Diagram of operation.** (From 104: Spendlove, J.C. and Fannin, K.F., 1982. Chapter 12 Methods of characterization of virus aerosols. Methods in environmental virology. Gerba, C.P. and Goyal, S.M. eds. Marcel Dekker Inc., New York.)



**Figure 6: Cyclone Scrubber** (From 28: Cox, C.S., 1987. Chapter 3 Aerosol samplers. The aerobiological pathway of microorganisms, John Wiley & Sons, New York.)



**Figure 7: Andersen 6-stage Impactor ( From 38: Fannin, K.F., 1980. Method for detecting viable microbial aerosols, Wastewater aerosols and disease. Health Effects Lab. 600/9-80-028. USEPA.)**



**Figure 8: Casella Multislit Sampler ( From 104: Spendlove, J.C. and Fannin, K.F.,1982. Chapter 12 Methods of characterization of virus aerosols. Methods in environmental virology. Gerba, C.P. and Goyal, S.M. eds. Marcel Dekker Inc., New York.)**

### Personal samplers

Personal samplers measure a true breathing zone exposure, which is different from the aforementioned area samplers. At present, no personal microbial aerosol sampler has been used or designed for virus aerosols, although some personal biological samplers have been used to sample bacteria and have shown good results for spore-forming bacteria. They have not been successful in sampling vegetative bacteria, however, due to rapid dehydration. Examples of personal bioaerosol samplers are presented in Table IV (1,19,104,114,125). Among them, the IOM-Personal Inspirable Dust Spectrometer (IOM-PIDS) and the IOM-Personal Inspirable Aerosol Sampler (IOM-PIAS) have never been used for sampling bioaerosols. However, their inlet design provides data which are the most representative of human exposures. To obtain truly representative samples of personal exposures to viruses, high collection efficiencies and low sampling flow rates will be the most important factors to consider when designing such samplers.

Table IV: Personal Bioaerosol Samplers

Principle /Sampling device	Collection medium	Sampling rate (LPM)	Sampling time	Sampling Capacity	Comments
<b>Impaction</b>					
Spiral sampler	Agar	0.6--25		Low	Size discriminating sampler. Collection efficiency is very low for particle $\leq 1\mu\text{m}$ .
Personal cascade impactor	Membrane filter; Gelatin-filled tray	2		Low	Particle size classification. Viable recovery is very low.
<b>Impinger</b>					
Modified personal impinger	Compatible fluid	up to 1.42			The jet tip is 0.5 cm above the liquid: help recovery
Spill-proof personal impinger	Compatible fluid	1			Collection efficiency $\geq$ AGI
Plastic Midget impinger	Compatible fluid	1			
<b>Filtration</b>					
Cassette Filters	Membrane; Gelatin filter	7.5 for 47 mm open filter 15 for 32 mm open filter	5--60 min		Simple, inexpensive, easily portable, dissolve in liquid. Desiccation of fragile organisms.
<b>Modification &amp; Development</b>					
IOM-PIDS* (cascade impactor)		2			Representative Inlet; not designed and used for sampling microorganism
IOM-PIAS** (filter)		2			

PIDS\*: Personal Inspirable Dust Spectrometer

PIAS\*\*: Personal Inspirable Aerosol Sampler

### 3. Sampling media

The selection of an appropriate sampling medium for virus aerosols has not been standardized. Knowledge of the physical and chemical characteristics of the virus will determine the correct sampling medium. The medium must be compatible with the sampling method, must not inhibit virus viability, and should lend itself to the assay method selected. The sampling medium chosen should help increase the probability of virus survival during the sampling process by reducing the likelihood of desiccation or by minimizing rapid shifts in relative humidity and other environmental stresses. Rehumidification before sampling can help maintain viability for some viruses. Sampling media for virus aerosols can be divided into liquid, semi-solid and solid media. Various types of sampling media for virus aerosols and examples of those used for common airborne transmitted viruses are presented in Table V.

#### Liquid collection media

Virus aerosols sampled into a liquid medium must be transferred into a susceptible host or cell culture, a more laborious method than direct collection onto agar. However, a method which uses liquid collection media allows more flexibility in length of sampling and thus collection of a wider range of viable aerosol concentrations. The liquid allows, if necessary, for subsequent concentration or dilution depending on the assay method; samples can be plated out on numerous types of culture media. This method provides information about the number of virions rather than the number of virus-containing particles. Eagle's minimum essential medium is most widely used for collection of virus aerosols. Adenovirus, parainfluenza, rhinovirus, rotavirus, coxsackievirus and poliovirus have been successfully recovered using this medium (19,45,58,63,70). Impingers, electrostatic precipitators and cyclone scrubbers all utilize liquid collection media.

**Table V: Sampling Media for Virus Aerosols**

Sampling Media	Examples of Virus Type	Reference Numbers	Comments
Liquid			ADV: Allows for concentration or dilution;
Sterile distilled water		19	can be plated on numerous types of culture agar;
Hanks balanced salt solution	Polyoma virus; Enteric virus	19,40, 74	can be used for other assay methods;
Phosphate buffered saline (PBS)	FMDV	19,104,109	provides information about number of viable cells;
Nutrient broth		19	more flexible sampling duration.
Tryptose phosphate broth (TPB)	Rhinovirus type 14; Poliovirus type 1; Rotavirus; Coronavirus	58,59	DISADV: Must be transferred to nutrient media; more laborious than other methods
Eagle's minimum essential medium (MEM)	Adenovirus types 4 & 7; Parainfluenza; Poliovirus type 1; Rotavirus; Rhinovirus type 14; Coxsackievirus A type 21	19,45, 58,63,70	
Brain/heart infusion broth		19	
Agar & appropriate cell culture			
Agar-covered cell monolayer	poliovirus	104	More convenient; requires cell culture in a susceptible growth stage. The range of species is limited by sampling time & number of samplers.
Agar with overlaying gelatin	Bacteriophage; coxsackievirus A type 21	45,104,117	Liquefy the gelatin overlay; virus is assayed from suspension.
Skim milk film on agar base	Adenovirus; Coxsackie B-1; Influenza A	61,104	
Gelatin in tissue culture media	Influenzavirus	104	
Cell monolayer overlaid with MEM on agar	VEE virus; T5 coliphage	9, 51	
Filter			
Glycine buffer-moistened filter	Poliovirus	115	increased survival
Slides			
Slides coated with 5% gelatin in 10% glycerol	Newcastle disease virus	104	The coat can be dissolved for subsequent virus assay, allows for microscopic examination



### Semi-solid and solid collection media

Semi-solid sampling media refer to agar or its combination with appropriate cell cultures. Solid sampling media such as filters and slides are the least used. If the goal is to determine the number of virus-containing particles, devices such as the Andersen and slit samplers with a semi-solid collecting medium should be considered. A special adhesive surface has been suggested, employing equal parts of saturated sucrose solution and glycerol with 0.1% to 10% bovine serum albumin. Following sample collection this medium can be assayed either by direct cell overlay or, following a rinse and solubilization procedure, by conventional virus assay procedures (104). Other semi-solid virus aerosol sampling media include an agar-covered cell monolayer, gelatin and skim milk on an agar base, and gelatin in tissue culture media. When using semi-solid sampling media, a variety of procedures for subsequent viral analysis are possible: (a) directly observe PFU on agar-covered cell monolayer; (b) melt gelatin and plate the suspension onto a cell monolayer; (c) wash the agar surface with skim milk; or (d) invert the agar medium on a monolayer of susceptible cells. Guerin and Mitchell (48) impacted a poliovirus-containing aerosol onto agar-covered cell monolayer in Andersen sampling plates. Initiation of infection required that infectious virus diffuse through the agar depth to the cell monolayer. This method was successfully applied to some viruses, but it had several disadvantages: cell cultures had to be in a susceptible growth phase, some viruses could not be propagated in tissue culture, and sampling in contaminated environments was difficult. Jensen (61) washed the surface of Andersen sampler plates, containing 2% nutritionally based agar, with 20% skim milk suspension and Hanks balanced salt solution, followed by virus assay. Thornley (19) inverted the medium of each sampled plate on a monolayer of susceptible cells and observed plaque-forming units in each aerosol size range. Bolton et al. (10) directly overlaid plates with a suspension of susceptible *E. coli* cells, sampled T5 coliphage aerosols and observed plaque formation in the *E. coli*.

Virus desiccation occurs in both filtration and impaction devices. Viruses collected on low-moisture filter media will decay very rapidly. Lengthy sampling times or high air flow rates dehydrate solid and semi-solid media, such as the agar surfaces in the upper stages of the Andersen sampler. In some cases, an evaporation retardant, e.g. oxyethylene docosanol, is used with agar-type samplers to reduce medium dehydration and thus to extend sampling time. In one study, a cascade impactor contained slides coated with 5% gelatin in 10% glycerol; the gelatin-glycerol coat was subsequently dissolved at 37° C in phosphate buffer and the suspension was assayed for virus. Couch et. al (21) collected particles by sedimentation on glass slides coated with Permout and measured particles under light microscopy.

Most sampling procedures are aimed at culturable contaminants. However, there is no relationship between culturability of organisms and their significance as indoor air pollutants. Viruses fail to be detected when they are dead, dormant, inhibited, or if they are not provided with adequate conditions. These characteristics do not necessarily reflect the capacity of virus aerosols to cause adverse health effects when inhaled (41).

### Function and effects of additives

#### Antifoam

Sampling by impingement involves violent agitation which may result in excessive foaming of sampling fluid. This can cause fluid losses during sampling; antifoaming agents are added to reduce foaming. The effects of antifoam emulsion were studied by Gerard et al. (74). When sampling airborne polynoma virus; they found that antifoam alone without Tween 80 in the sampling fluid of a Litton LVAS did not reduce virus titer. However, some antifoaming agents have been reported to have an adverse effect on the survival of collected microorganisms, which may depend on the concentration of the agent used (104).

#### Antibiotics

When sampling in a contaminated environment, it is sometimes difficult to recover virus particles due to an overabundance of other microorganisms. Selected antibiotics can be used to reduce the growth of bacteria on the sample. It has been reported by some researchers that an overlay of a 5 ml suspension of 3% gelatin containing antibiotics will suppress bacterial contamination (19,104).

#### Evaporation retardant

The probability of virus desiccation is greatest for filtration or impaction samplers. Lengthy sampling times or high air flow rates will dehydrate solid media unless evaporation retardants are used. It has been found that a monomolecular film of oxyethylene docosanol on agar can significantly extend sampling time (104).

#### Wetting agents

A wetting agent is used to prevent clumping of collected particles. The effects of wetting agents on the viability of viruses have not been well studied.

#### Other Additives

The survival of collected viruses can be enhanced by addition of proteinaceous substances in the sampling medium. Sugars such as sucrose and melezitose can improve survival and may be used to prevent freezing when sampling at low temperatures. The effects of these additives depend on the sampling conditions. Virus death during collection may result from

osmotic shock which is caused by the transient rise in internal osmotic pressure when organisms rehydrate on collection media. In this case, collection into sampling fluids with high osmotic pressure has been used to reduce the degree of osmotic shock. Salts contained in Hanks balanced salt solution or phosphate-buffered saline have been used to minimize osmotic shock (3,19). However, evaporation will concentrate the salts so that addition of sampling fluid may also be required.

#### **4. Particle size selective sampling**

Depending on experimental objectives, aerosol particle size measurement can be determined by microscope, by the use of direct reading instruments (usually a light-scattering device), gravimetrically, or by using methods which exploit the aerodynamic behavior of particles. The measurement of aerodynamic particle size is most desirable in deposition studies because it allows evaluation of respiratory system deposition. For some diseases caused by viruses, deposition in the lower lung may be of greatest importance. Thus a method which allows quantitation of the smaller particles gives a better picture of the likelihood of disease than one which simply samples the total number of particles.

##### Air samplers allowing size discrimination

Virus aerosol sizing studies have most commonly employed either a multistage impactor (e.g. the Andersen 6-stage cascade impactor), or a multistage impinger such as the one developed by May (73). In addition, a cyclone scrubber has been suggested to be a promising size selective sampler for microbial aerosols (28, 39).

##### Andersen impactor (6-stage)

The lower limit of the particle diameter range collected by each of the Andersen cascade impactor stages is, respectively:  $\geq 7$ , 4.7, 3.3, 2.2, 1.1, and 0.65  $\mu\text{m}$ . Gerone et al. (45) determined the number of virions within a particle size range by pouring 21 ml hard agar base and a 6 ml overlay of 12 % gelatin in suspension. The results from the experiment using coxsackievirus found that the virus concentration appeared to be more closely related to particle volume distribution than to particle number distribution of the aerosol.

##### Liquid impinger (3-stage)

The virus aerosol is collected in liquid sampling fluid in each of three chambers, which roughly corresponds to the three principal deposition sites in the human respiratory system: the upper respiratory tract, the bronchioles and the alveoli. The rate of evaporation of sampling fluid is less than for other impingers and fewer organisms are killed during prolonged sampling periods due to the design of a gentle tapered jet at stage 3. This sampler

enumerates the number of virus cells rather than the number of virus-containing particles (73).

#### May cascade impactor

For a May cascade impactor, sampled aerosol passes through a succession of impactor stages. Each stage takes the form of an air jet directed onto a solid surface (114). The narrower the jet and the higher the air velocity, the finer particles to be collected. The impactor has been used to contain slides with 5% (wt/vol) gelatin in 10% glycerol for sampling virus aerosols. Following sample collection, the gelatin-glycerol coat is dissolved at 37°C in phosphate buffer and the suspension is assayed for virus. Particle diameter ranges are as follows: >6.0, 3.0-6.0, 1.0-3.0, and 0.5-1.5  $\mu\text{m}$  (72).

#### Cyclone Scrubber

In order to properly design cyclone scrubbers the distribution of the air velocity which in turn depends on the physical dimensions and flow rate, have to be considered. Ogawa (28) provides a thorough account of theories for deriving these variables together with theories predicting the efficiency-particle size relationship; specific cyclone designed by Ogawa gives a superior collection efficiency of 99.7% for particle sizes less than 1  $\mu\text{m}$ . Lippmann and Kydonies operated six 10 mm nylon cyclones simultaneously in parallel; each had a different flow rate (0.9 to 5 L/min) and its own backing filter (28). This experiment successfully provided particle size distributions ranging from 1 to 10  $\mu\text{m}$ , which is comparable to the multistage impactor. The other centrifuge-type aerosol spectrometer called a "Conifuge" is capable of classifying particles within the range of 0.5 to 30  $\mu\text{m}$  at a sampling flowrate of 25 ml/min, and can be used for particles as small as 0.01 (114); its application to virus aerosols, however, has not been confirmed. A cyclone scrubber has been suggested by Fannin and Vana (39) to be used for microbial aerosol studies where low concentrations are expected until the collection substrate is optimized and the sampler design concept is developed. It is because a cyclone scrubber classifies sizes of aerosol particles and has continuously wetting collecting surface. However, varied operating conditions such as sampling medium, air sampling flow rates, sampling fluid flow rates and duration of sampling should be further evaluated to optimize collection efficiencies of cyclone scrubber.

#### Light microscope

A direct method of aerosol particle diameter measurement was reported by Couch et al. (21). In their studies, a virus aerosol sample was drawn into an evacuated 64 oz mason jar and allowed to settle on glass slides coated with Permunt. Particles were then measured by light microscopy using a calibrated graticule. This method gives only the physical measurement of particle diameter.

## 5. Sampling for viral aerosols in indoor environments

Hierholzer (55) suggests that air sampling for human viruses "is practical when people are apparently getting sick in a building, and when there is epidemiologic evidence to confirm this." Burge (14) agrees:

"If factors promoting microbial contamination are clearly present, it is usually more cost-effective to assume that a bioaerosol problem exists and recommend well-proven remedial measures than first to attempt confirmation by air sampling. Air sampling is expensive, time consuming, and all too often, does not provide the precise answers desired."

For general air sampling in buildings, the advice extended above appears applicable. Only a few studies have shown the presence of airborne virus in locations where many such particles would be expected, and the sampling methods used (usually the LVAS) generally required considerable expertise. However, several samplers hold promise for measurement of low airborne concentrations when conducting research in indoor environments. In particular, the cyclone scrubber appears to have the greatest potential for use as a high volume sampler, although its use is not simple. In addition, agar-based samplers, such as the Andersen cascade impactor, may be employed if dehydration problems can be minimized (as discussed above). At this time, however, none of the samplers discussed can be considered adequate for routine sampling of virus aerosol in low concentration, indoor environments.

## E. Virus Detection Methods

For the analysis of bacteria and bacteriophages, aerosol samples can be collected in either solid or liquid media. For the detection of human or animal viruses, however, liquid media are more suitable. The samples should be shipped to the laboratory on ice. If immediate testing is not possible, the samples should be frozen at  $-70^{\circ}\text{C}$  until assay. When processing for virus isolation, the samples should be treated with antibiotic and then centrifuged at  $1000 \times g$  for 10 min to remove debris and bacteria. They can then be examined for the presence of viruses by (i) the isolation/propagation of viruses in a susceptible host system e.g., laboratory animals, embryonating chicken eggs, or cell cultures or (ii) by direct detection of virus (without virus propagation) in samples by detection of viral antigens and/or its nucleic acid. An indirect measure of detecting viruses in aerosols, which may be useful for epidemiological purposes, is to test the exposed population for the presence of virus and/or antibodies.

### 1. Virus isolation and identification

This is theoretically the most sensitive system because it is capable of detecting even one infectious unit of virus. The virus present in the sample is grown/propagated to larger amounts in a susceptible host system before its identification by various methods. As opposed to bacteria, viruses cannot replicate on non-living artificial media; living cells are needed for their growth. Three different host systems that are routinely used for virus isolation are laboratory animals, embryonating chicken eggs, or cell cultures. One of these is chosen for virus isolation depending upon the virus type suspected to be present in the sample.

(a) Laboratory animals: This is an expensive and time consuming procedure and is not widely used. However, certain viruses are capable of growth only *in vivo* in live animals and not in *in vitro* systems. For example, some of the group A coxsackie viruses grow poorly in cell cultures but grow easily in suckling mice.

(b) Embryonating chicken eggs: Some viruses grow better in embryonating chicken eggs (e.g. pox and influenza viruses). For initial isolation of these viruses, cell cultures are not suitable because either these viruses do not grow in cell cultures or grow poorly. Once the viruses have been grown in eggs, they can be adapted to grow in cell cultures. Egg inoculation can proceed by the amniotic, allantoic, yolk sac, intravenous, or chorioallantoic membrane routes. The age of the embryo and the route of inoculation are selected based on the properties of the suspected virus. Following growth in chick embryos, the virus can be identified by the methods given below for cell culture-grown viruses.

(c) Cell cultures: Many types of cell cultures are available; some of them are single use primary cell cultures whereas others are established cell lines that can be passaged and used numerous times. Depending upon the virus to be isolated, a particular cell type is chosen; unfortunately not all viruses grow on all types of cell cultures. For example, Buffalo Green monkey kidney cells are suitable for the isolation of many viruses of the enterovirus group, but are not suitable for all viruses of that group. Similarly, influenza viruses grow better in vero cells (African green monkey kidney cells) or in embryonating chicken eggs. Other cells that are suitable for the isolation of human viruses include human laryngeal carcinoma cells, diploid human embryonic lung cells, and human embryonic kidney cells. In fact, it is often better to utilize more than one cell type to increase the chance of virus isolation.

Usually a single sheet of cells, called a monolayer, is produced in sterile vessels, e.g., tissue culture flasks using growth media consisting of balanced salt solutions, fetal bovine serum, other growth factors such as non-essential amino acids, and antibiotics to control bacterial contamination. Before use, the growth medium is decanted and the sample is inoculated in cell cultures. Following adsorption at 37° C for one hour, the cells are fed with maintenance medium and the flask incubated at 37° C for a number of days. If a virus is present and if the cells are susceptible to that virus, the monolayers of cells will show cytopathic effects (cpe) after 2-21 days of inoculation, depending upon the virus type. A blind passage of the material in fresh cell cultures will usually increase the chances of virus recovery. The identity of the virus can be confirmed by various procedures such as electron microscopy, fluorescent antibody test (FAT), hemagglutination inhibition (HI), virus neutralization (VN), and enzyme-linked immunosorbent assay (ELISA).

(d) FAT: Once the virus has grown in cell cultures, it can be confirmed/identified by FAT. Infected cells are placed on a glass slide and fixed with acetone. They are then flooded with a fluorescein-conjugated antiviral IgG; the antiviral IgG used will, of course, depend on the type of virus suspected to be present in the sample. After incubation for 30 min in a humid chamber, the slides are washed, counterstained, mounted in buffered glycerol, and examined under a fluorescent microscope for specific, greenish-yellow fluorescence.

(e) VN: A fixed amount of the isolated virus is incubated with serial dilutions of a specific serum against the suspected virus for 1 to 2 hr. This mixture is then inoculated in cell cultures. Another set of cell cultures is inoculated with the virus alone (without antiserum). If a virus specific to the antiserum is present in the sample, the first set of cell cultures will not show any cytopathic effect because the virus would have been neutralized by

antiserum. However, cells inoculated with virus alone will show cpe. This test is commonly used for the identification of enteroviruses (46).

(f) HI: Some viruses are capable of causing hemagglutination of erythrocytes from various animal species. If the isolated virus causes hemagglutination, it can be identified by the HI test. This test is similar to the VN test in that the virus is treated with antiserum followed by the addition of indicator erythrocytes. A set of virus dilutions without antiserum is also included. If the virus is specific for the antibody used, hemagglutination will be inhibited in the first set but will be present in the second set (virus alone). This test is used for identification of influenzaviruses (94).

## **2. Virus quantitation**

Enumeration of viruses in aerosols can be accomplished by the plaque forming unit (pfu) method or by the multiple tube dilution method (most probable number procedure, MPN). The latter is expressed as MPN cytopathic effect units (CPU) per sample volume (104) and has been shown to be more sensitive than direct enumeration procedures.

The viruses present in a sample can be quantitated if serial dilutions of the sample are inoculated in multiple cell cultures. The highest sample dilution that produces cpe is considered to be the end point and the dilution that causes cpe in 50% of the inoculated cell cultures is termed the TCID<sub>50</sub>. Virus can also be quantitated by inoculating in cell cultures followed by overlaying with a semisolid maintenance medium. Each infectious unit of the virus will produce changes at a single spot because viruses are not able to diffuse very far in the semisolid medium. After staining with a vital dye, these changes appear as clear areas in an otherwise stained monolayer of cells and are called plaques. Counting of these plaques yields a direct count of the number of infectious units of the virus present initially in the sample and is expressed as the plaque forming units (pfu). The aerosol concentration can then be expressed as pfu/m<sup>3</sup> of air.

## **3. Direct detection of virus or its antigens**

(a) Electron microscopy: The viruses can be detected by negative contrast electron microscopy of the aerosol sample. However, in order for this technique to be successful, a minimum of 10<sup>6</sup> virus particle/ml of sample are needed. The number of viruses present in aerosol samples are usually much lower than this. It is appropriate, therefore, to propagate these small numbers of viruses in an appropriate host system before their identification. Following their growth in cell cultures or embryonating chicken eggs, the viruses can be easily visualized under an electron microscope (47).



(b) ELISA: In this technique, the sample (before or after growth in cell cultures) is incubated with a solid support (plastic beads or wells of a microtiter plate) coated with an antibody against the suspected virus. After appropriate incubation, the wells are washed followed by the addition of a second enzyme-labelled antiviral antibody. If the virus is present in the sample, it will attach to the first antibody coated on the wells and will stay attached even after washing. The second antibody can subsequently combine with viral antigen forming a sandwich. The second antibody can then be detected by the addition of a substrate for the enzyme which will cause a change in the color of the complex. This technique has been used in many formats and with the advent of monoclonal antibodies, it has been used with increasing frequency in various tests.

#### 4. Detection of viral nucleic acid

(a) DNA probes: Molecular hybridization involves the interaction between a molecule of labeled DNA probe and a molecule of the intended target to form a molecular hybrid. A probe consists of a short sequence of nucleotides that will bind to specific regions of a target sequence of nucleotides. The method for preparing a DNA probe involves the identification and isolation of a sequence of specific nucleotides, its reproduction by cloning or synthesis, and its labeling with an enzyme, biotin, or radioisotope. This probe can then be used in dot blot, slot blot, or *in situ* hybridization formats to detect a specific sequence of nucleic acid in a given sample. Briefly, the DNA from the sample is extracted and fixed to a nitrocellulose filter. It is then treated to denature the DNA molecules, separating the two strands. The labeled, single-stranded probe is then added which binds to the complementary sequences on the sample DNA molecule. The matrix is washed to remove unbound probe and the presence of the probe can then be determined by color change or autoradiography depending on whether the probe was labeled with enzyme or with radioisotopes.

(b) Polymerase chain reaction (PCR): The PCR is an *in vitro* method of amplifying specific DNA sequences up to  $10^6$ -fold using a pair of oligonucleotide primers for a target gene and a thermostable DNA polymerase (95). Briefly, the DNA present in the sample is denatured by heating at  $94^{\circ}\text{C}$ . Oligonucleotide primers (20-25 base pairs long) are then annealed to these single strands of DNA at  $50^{\circ}\text{C}$ . Heat stable DNA polymerase (Taq polymerase) and nucleotides are then added for primer extension at  $70-72^{\circ}\text{C}$ . Thus, a copy of the target DNA is synthesized. The progeny DNA is then denatured, primers are annealed, and DNA is allowed to be synthesized. Approximately 30 cycles of denaturation, primer annealing, and DNA synthesis can amplify DNA initially present in the sample to one million fold. This DNA can then be detected by gel electrophoresis and/or DNA probe. The advantage of this method is that

even inactivated viruses can be detected by this method. However, one must know what virus to look for because a different set of primer pairs and a separate PCR reaction is needed for each different virus. The procedure for the detection of RNA viruses is the same except that the RNA is first converted to DNA by reverse transcriptase (RT); this reaction is termed as RT-PCR.

## 5. Summary

Virus survival in aerosols is influenced by virus type, humidity, temperature, and ultraviolet light. Viable aerosols have been found to travel long distances through ventilation and/or dispersion. Whether a person coming in contact with viral aerosols will become infected or not depends on factors such as host susceptibility, viral virulence, virus concentration, aerosol particle size, minimum infective dose of virus, and size and density of exposed population. Both respiratory and nonrespiratory viruses can spread via the airborne route. Examples are: influenza virus, rhinoviruses, measles, mumps, rubella, coronavirus, rabies virus (217), smallpox virus (8), and enteric viruses e.g., enteroviruses, adenoviruses, reoviruses, and hepatovirus (191).

For viral analysis, the aerosols are collected in liquid media and are shipped to the laboratory on ice. They can then be examined for the presence of viruses by the isolation/propagation of viruses in a susceptible host system followed by their identification by immunofluorescence, electron microscopy, virus neutralization, and hemagglutination inhibition etc.. Another method consists of direct viral detection (without virus propagation) in aerosols by the detection of viral antigens and/or its nucleic acid. Virus or viral antigens can be detected by electron microscopy, enzyme-linked immunosorbent assay, or hemagglutination whereas viral nucleic acids can be detected by DNA probes and polymerase chain reaction.

## **F. Control of Viruses in Buildings**

### **1. General review articles**

Control of viruses in indoor environments has been the subject of several review publications. Wells (118) summarized much of his work in the area of airborne droplet infections from bacteria and other aeroallergens, including viruses. Kundsinn (66), noting that no threshold limit values have been established for airborne microorganisms as for chemicals and particulates, stated: "Airborne transmission is the most important mode of transmission of respirable infections from person to person indoors....there is, however, no standard for viable particles that would determine how much outdoor air intake, how much recirculation is essential for the safety of aggregations of people in the indoor environment." Couch (20) discusses three methods that could be used to control airborne viral disease: 1) the reduction of air contamination by infected persons; 2) the inactivation or removal of airborne virus; and 3) providing susceptible individuals with resistance to airborne viruses. Quarantine has been the only widespread method used to control the source and this has been largely ineffective. Inactivation by ultraviolet light has met with mixed success for measles and other viral diseases. Ventilation can dilute the airborne concentration and can be used to prevent transmission; however, Couch indicates that this may be too costly. The most effective approach so far has been the control of viral disease by vaccinating susceptible individuals for viral resistance. This approach eradicated smallpox and relegated measles and mumps to a minor problem.

Infection in modern buildings has been discussed by LaForce (67) although virus control was not specifically addressed. Satar and Ijaz (96) prepared an excellent review article that discusses the effects of temperature and humidity on the survival of airborne virus particles, experimental challenge of animals and human volunteers to virus aerosols, and the spread of naturally occurring viral infections by the airborne route (this article contains 285 references). Burge and Feeley (15) discuss the general issue of indoor airborne infectious diseases, although they also did not specifically address viruses.

### **2. Case studies that give proof of airborne transmission of viruses**

A good summary of airborne transmission of viral diseases was given by Couch (20). A discussion of some specific publications follows. McLean et al. (76) conducted a study of young children in Toronto in which they confirmed previous observations that parainfluenza I virus is disseminated in the air. Langmuir (68) describes the change in attitude toward the importance of contact and airborne routes of infection from 1930 to the 1960s, which was largely the result of work by Wells. During this period,

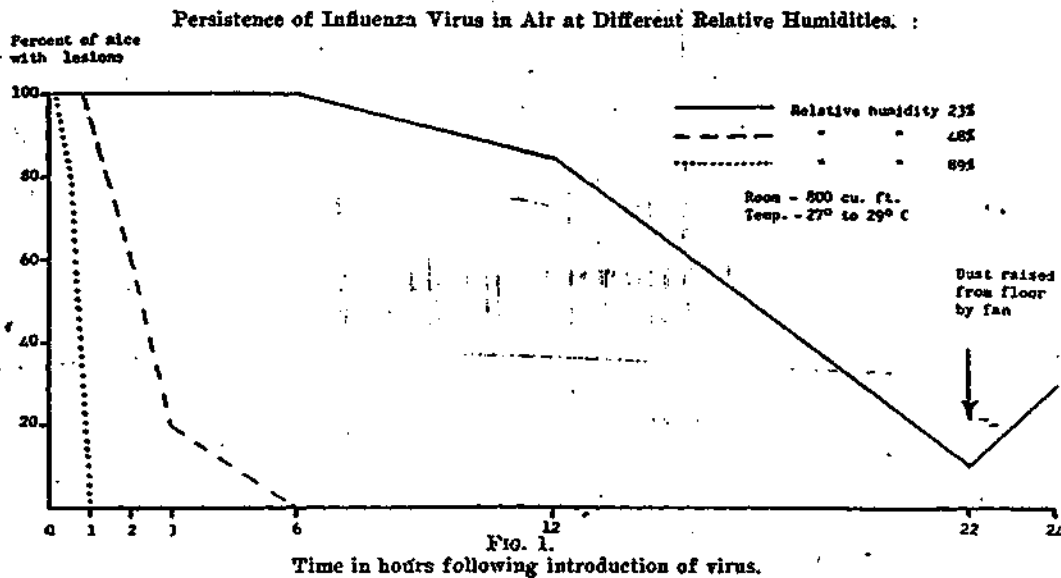
airborne transmission was gradually accepted as an important means of viral disease transmission. Leclair et al. (69) and Remington et al. (86) documented the airborne transmission of chickenpox and measles in a hospital and a physician's office, respectively. Jaakkola et al. (60) conducted a study of roommates and transmission of the common cold. However, it is not clear in this study whether fomite and/or airborne transmission was involved or whether other environmental factors could be implicated.

### **3. Effect of relative humidity and temperature on aerosol virus survival**

One of the earliest studies of temperature and relative humidity effects on the survival of virus aerosol was conducted in 1943 by Loosli et al.(71). They used mice to determine the decay rate of influenza virus as a function of relative humidity near room temperature. Results of their tests are shown in Figure 9 . They showed a strong dependence of influenza virus survival on the air relative humidity. Sattar and Ijaz (96) provide a comprehensive review of studies conducted between 1943 and 1986 on the survivability of viruses with respect to temperature and relative humidity. They state that these two factors are perhaps the most important in determining how well viruses survive in the airborne state, while also indicate that the mechanisms involved are not clearly understood. Some viruses survive best at either low or high relative humidity whereas others survive best when the relative humidity is near 50%. Some survive better at higher relative humidities and others at lower values. Temperature has a strong effect on some viruses and a negligible effect on others. They conclude that in general, lipid-containing viruses survive better at low levels of relative humidity and that high levels are more conducive to the survival of lipid-free viruses, although exceptions exist. Table VI lists several viruses that had been studied previously. The range of temperature, relative humidity, age of the aerosol, and comments regarding the survivability are given for each virus listed (96). DeJong et al.(31,32) discuss several factors that could cause virus aerosol inactivation. Ijaz et al.(58) have been developing methods to study airborne virus survival that are much more rigorous than methods used previously, including the effects of tracer dye, nebulization and virus mixtures.

### **4. Control by ultraviolet light**

Ultraviolet (UV) light has been known since the mid 1930s to render airborne virus particles non-infective when tests were conducted by Wells and Brown on ferrets and mice (120). Other controlled laboratory tests include the work by Edward et al. (C-4a) who studied the effect of UV light on influenza A, vaccinia and herpes simplex particles. Jensen (61) found between 91 and 100% inactivation of five different airborne virus particles (adenovirus, coxsackie B-1, influenza A, sindbis and vaccinia) when passing between 100 and 200 ft<sup>3</sup>/min of air through an irradiated helical baffled cell. The aerosol concentration ranged from 690 to 29,000 plaque-forming units



**Figure 9: Persistence of Influenza virus in air at different relative humidities.** (From 71: Loosli, C.G., Lemon, H.M., Robertson, O.H. and Appel, E., 1943. Experimental air-borne Influenza infection. I: Influence of humidity on survival of virus in air. *Proc. Soc. Exp. Biol. Med* 523: 205-206)

**Table VI: Effect of Temperature and Relative Humidity on the Survival of Aerosolized Viruses. (From 96: Sattar, S.A. and Ijaz, M.K., 1987. Spread of viral infections by aerosols. *CRC Critical Reviews on Environmental Control*. 17 (2): 89-131)**

Virus(es)	Temperature (°C)	Relative humidity (%)	Period of aerosol aging	Remarks
Influenza A	27—29	23, 48, 89	24 hr	Experiments were performed in a room of 800 ft <sup>3</sup> capacity; low RH experiments were performed in winter, and high RH was generated by vaporizing steam into the room; the virus survived best at 23% RH
Influenza (PR8), polio virus type 1 (CSL)	?	0-100	2 min	For influenza virus, inactivation rate was high at 50—90% RH and low at 15—40% RH; for polio virus, the reverse was true; they emphasized the role of RH indoors as an important factor in the seasonal fluctuation of outbreaks due to these viruses
Vaccinia, influenza (PR8), Venezuelan equine encephalitis (VEE), and polio type 1 (Brunhilde)	7—11.5, 20—24, 30—33.5	17—36, 48—65, 80—86	up to 23 hr	For all the virus types studied, survival at all RH ranges tested was better at the lower than at the higher temperature; polio virus survived best at high RH levels, whereas the other 3 viruses tested survived best at low RH levels
Measles (Edmonston strain)	20—21	10—100	?	The virus was sprayed in a temperature- and RH-conditioned room; best survival was observed below 40% RH; indoor RH was thought to be an important factor in the seasonal variations of outbreaks due to the virus
Encephalomyocarditis (Mengo, Maus Elberfeld, and Columbia SK)	16, 26	5—95	6 hr	At 16°C, virus inactivation during the first 5 min after spraying was maximal at high (>80%) and low (<5%) RH; at 26°C, mid-range RH (40—60%) was the most deleterious to virus survival; inactivation patterns of the virus during aerosol storage were found to be similar to other small RNA viruses such as polio
Semliki Forest	22	20—90	24 hr	Inactivation of the airborne virus was found to be maximal at high RH (84—90%) and decreased gradually as RH decreased; removal of salts from the spray fluid resulted in improved survival over the whole range of RH tested; extraneous protein was essential for survival at high RH and polyhydroxy compounds protected the virus well at low RH
Adenovirus types 4 and 7 and parainfluenza type 3	23.7	20, 50, 80	6 hr	Both types of adenovirus were most stable at 80% RH, whereas parainfluenza was most stable at 20% RH
Polio virus type 1 (strain LSc2ab)	20	0—100	1 hr	Virus survival was high below 35% and above 70% RH, but low in the range 40—60% RH; they believed that denaturation of viral RNA caused the inactivation of airborne polio virus

Variola (Yamada) and yellow fever (Asibi)	26.7	30, 50, 80	1 hr	Variola virus survived better than yellow fever virus at all RH levels tested; biological decay rates not affected by RH
Adenovirus type 12	28—29.5	32, 51, 89	20 min	The virus was found to survive best at the highest level of RH tested (89%)
Simian virus 40 (SV-40)	21 or 32	15—100	1 hr	The virus was found to be stable at 21°C at all RH levels tested, but aerosols maintained at 32°C were inactivated within 60 min at mid-range RH (50—60%)
Japanese B encephalitis virus	24	30—80	1 hr	The half-life of aerosolized virus was 28, 38, and 62 min at RH levels of 80, 55, and 30%, respectively
Influenza (WSNH strain)	21	20—80	1 hr	Minimum virus survival was observed at RH 50—70% with higher recoveries at RH >80% and maximum stability at RH <30%; airborne stability of the virus was found to vary from one preparation of virus to the next for virus propagated in both cell culture and embryonated eggs; polyhydroxy compounds were found to have a protective effect on the airborne stability of the virus
Reovirus type 1 (Lang strain)	21—24	25—95	3 hr	Aerosol stability of infectious and potentially infectious virus particles was maximal at 85—95% RH; an increase in recovery of the aerosolized virus was observed upon prehumidification
Lassa virus (Josiah strain)	24, 32, 38	30, 55, 80	4—60 min	Biological half-lives of aerosolized virus ranged from 10—55 min; virus survived best at low humidity and low temperature
Human rotavirus	6, 20	30, 50, 80	24—75 hr	At 20°C, the virus aerosolized from TPB survived best at 50% RH with a half-life of 44 hr; at 30 and 80% RH, its half-life was 24.5 and 3.8 hr, respectively; virus survival was further enhanced at 6°C and mid and low RH. When aerosolized from feces, and held at 20°C and 50% RH, nearly 80% of the virus remained infectious at 24 hr
Human coronavirus (229E)	6, 20	30, 50, 80	75 hr	At 20°C, virus half-lives were 67 hr (50% RH), 27 hr (30% RH), and 3 hr (80% RH) when aerosolized from TPB; the lower temperature (6°C) generally enhanced virus survival, but the most dramatic effect was seen at high RH (80%), a 30-fold increase in half-life
Human rhinovirus	20	30	24 hr	Infectivity of the virus was rapidly lost at low and medium RH levels; less than 0.25% could be detected in the first air sample; at the high RH level (80%), however, airborne virus had a half-life of 13.7 hr and nearly 30% of infectious virus could be detected even after 24 hr

per cubic foot of air. The inactivation was more effective at the lower air flow rate.

Various field measurements have also been made beginning with the work by Wells et al. (121) who studied the spread of measles in public schools. Numerous other studies followed, including reports by the Subcommittee for the Evaluation of Methods to Control Air-borne Infections (107), Perkins et al. (83) and a report by the British Air Hygiene Committee (77). More recently, Riley (92) expressed his opinion that it may be possible to interrupt the airborne transmission of influenza by UV air disinfection. However, in most of these studies, the occupant activities were not controlled so that exposure could occur at locations other than those that were irradiated. In addition, the harmful effects of UV radiation issues such as maintenance and cost have not been addressed. In a recent American Conference of Governmental Industrial Hygienist publication (1) it is stated that "Areas where UV light could be used include ductwork in HVAC systems, airlocks, operating rooms and pipe chases in schools, laboratories, and crowded offices." However, there does not appear to be conclusive evidence of a safe, economically feasible, low maintenance UV system that will provide a significant reduction in the transmission of airborne viral disease in buildings. A study which evaluates different types of UV radiation equipment at different locations within a building for a variety of building types with a range of HVAC systems is needed before UV light can be said to be an appropriate method of control for airborne viruses.

## 5. Control by filtration

Penetration of virus particles through air filters has been studied since the 1950s. Thorne and Burrows (109) found a filter efficiency of 99.998% at an airflow of 0.1 m/sec using a challenge of foot-and-mouth disease virus. Washam et al. (117) measured the filter efficiency of four types of filter media for aerosolized bacterial viruses under two airflow conditions. Harstad and Filler (52) found that air velocity, particle size, aerosol charge, and high humidity affected the aerosol penetration of T1 bacteriophage through filter paper and HEPA filter media. They found that neutralizing the aerosol with bipolar ions increased the penetration 2- to 5-fold and that relative humidity levels above 95% resulted in a roughly 3-fold increase in penetration through the HEPA filters. Commercial air filters were tested by Roelants et al. (93) who found that HEPA filters under clean room operating conditions could remove 99.996% of airborne actinophage. Burmester and Witter (16) used live chickens as indicators of the presence of virus in air and found that filters with a dust spot rating of over 93% will effectively remove Marek's disease virus from the air. A recent study by Rapp et al. (85) developed a more sophisticated filter test procedure using bacteriophage  $\Phi$ X174. They claim that their procedure is sensitive enough to measure a  $10^8$ -fold reduction in aerosol concentration; they consider bacteriophage to



be the best aerosol challenge to use as more reproducible assays have been developed than for animal or human viruses. From the literature reviewed here, it would appear that filtration of virus aerosols is governed by the same factors that affect particle filtration, namely particle size, particle charge, air velocity and type of filter media. The small size of virus particles (20 to 300 nm) suggests that most airborne virus is attached to large particles and that the filter efficiency at these larger particle sizes is a more realistic estimate than the filter efficiency for particles at the size of the actual virion itself.

## 6. Control by ventilation

Dilution by ventilation has long been recognized as a method for controlling indoor disease transmission. Wells (119) used the term "sanitary ventilation" to describe the effect of ventilation on the rate of disease transmission and developed empirical equations to demonstrate how ventilation can be used effectively. However, in a paper by Buckner et al. (13) studying bone marrow transplant recipients, patients in laminar flow isolation areas were compared to those in normal hospital rooms. They found that "the overall rates of virus isolation and clinical syndromes attributed to viral infection were high in both groups with no significant difference between laminar airflow and control groups."

Recent publications have appeared which are more anecdotal in nature. Morris (81) indicates that if virus particles survive for two and one-half hours once airborne, and if 80 to 90 percent of the air in a building is recirculated with no filtration of the particles, then the virus droplets can be returned to the space more than 10 times an hour. This is probably an overestimate as many virus particles lose their infectivity sooner than two hours and a significant reduction in virus droplet particles should occur through normal HVAC system filters and other loss mechanisms such as impaction and settling. Morris proposes an air handling system which incorporates a "virucide/biocide distribution system". However, this may not be feasible considering the large number of viruses present, their mutable nature, and the possible hazards associated with spraying a disinfecting agent into the supply air stream.

Streifel (194) addressed the issue of ventilation for the immune-compromised patient. He states that laminar airflow rooms with high room air changes and high efficiency filtration seem to be the best technology for providing the cleanest environment. Hierholzer (90) speculates that "a practical solution to indoor airborne contamination is the redesign of air flow in enclosed spaces...For example, conditioned air could be routed to be circulated upwards and then passed through filters or ultraviolet light before being cooled and recirculated."

On the other hand, some studies have suggested that the ventilation system has been responsible for the spread of viral disease. Riley (B-30) described an outbreak of measles in an elementary school and estimated the number of infectious particles emitted per minute per infectious person. He estimates that the dissemination rate per infected person lies between 1.5 and 70 Quanta per minute with a 95% confidence interval. "The single index case, a second grader in classroom 16 who walked to school, infected 28 other susceptible children during the three days she attended class during the infectious period. Two cases resulted from home room contacts but 26 secondaries occurred in 13 different classrooms served by the large general ventilating system for the main school building." Brundage et al. (26) studied army trainees over a 47-month period and concluded that the results "support the hypothesis that tight buildings with closed ventilation systems significantly increase the risks of respiratory-transmitted infection among congregated, immunologically susceptible occupants."

## 7. Summary of control techniques

Human viral disease transmission involves an infected person, a route of transmission, and a susceptible individual. Assuming that there is no source control of the infected person (i.e. the individual does not stay home and does not wear a mask) or the susceptible person (i.e. no immunization), the only viable control measures are those which deal with the route of transmission. If we only consider airborne viral particle control and not fomite transmission, there are several options available. Those reviewed here include: 1) viral particle removal from the air, 2) viral particle loss of infectivity and 3) viral particle dilution. Removal occurs by a variety of mechanisms which also affect non-viable particles.

Control by filtration can be effective when high efficiency filters are employed if particles are collected and passed through the filter before they can infect the susceptible individual. Filters located in the air handling system (as is currently done) would allow the supply of large amounts of cleaned air to an occupied zone. Small, individual filtration units could also be used if airflow through the unit and capture of aerosol from various locations in a room are adequate.

Control of airborne viruses can also be accomplished by bringing about a loss of viability. While temperature and relative humidity appear to have strong effects on virus viability, no single set of values appears likely to provide control for the wide variety of viruses present in the indoor environment. Thus, manipulation of these variables is probably not an adequate control technique. On the other hand, the use of UV radiation could be effective in some cases. Duct-mounted UV sources and/or units located in occupied rooms could be used; other types of radiation or chemical treatment may also be effective. However, the same problem

exists as with filtration in that the particles must be collected and inactivated prior to contact with a susceptible individual.

The use of outdoor air for dilution appears to be a good control technique as very few human viral particles should be present in the outdoor air. In a book by the American Conference of Governmental Industrial Hygienists (1) it is stated that "the least expensive and least complicated control measure is probably good ventilation by dilution with outdoor air." In some cases, one virus particle may be sufficient to cause disease, thus dilution reduces the probability of becoming infected. However, this technique does not necessarily prevent disease transmission.

Most of the techniques outlined above have been applied at one time or another for control of airborne viruses. However, there are very few data to quantify their effectiveness or demonstrate their long term performance. Issues such as cost, maintenance, and occupant acceptance have not been addressed. Carefully designed and controlled research is needed to provide information concerning the best control technique(s) to use for airborne viruses in indoor environments.

## **G. Interviews with Researchers and Consultants**

A brief summary of the more important points obtained from the surveys with researchers and consultants is given below. The surveys themselves, along with a sample survey, a list of interviewees, and accompanying curricula vitae are included in Appendix II.

Almost all the interviewees mentioned the following as the most problematic viruses in commercial indoor settings: Parainfluenza, influenza, enteroviruses, rhinoviruses, and measles. The most common sources mentioned included humans, children, surfaces (things people handle), and toilet flushing (for enteric viruses).

The sampling methods mentioned (and their advantages and disadvantages) included the following:

- Andersen cascade impactors. Simple design, 1-5 min samples for viruses, difficult to get virus off plate, use Hank's and gelatin in petri plates and melt gelatin into liquid for virus isolation.
- All glass impinger with pre-impinger for smaller particles. Collect in protein solution for 1-5 min. Has low sensitivity, however.
- High volume electrostatic precipitators. Difficult to maintain aseptic conditions.
- Cyclone scrubbers (high volume). Used sampling rate of 900 L/min for 30 min. Can use either 100 ml liquid once through or as recirculating fluid. Must correct for evaporation and slippage.
- Cox addressed a variety of samplers in his book: The Aerobiological Pathway of Microorganisms. He is also editing a new book: Bioaerosols: Samplers and Sampling.

Methods of analysis which have been employed included tissue culture and infection of animals (mice).

When asked about the use of ventilation as a control method, responses included that they have recommended its use, or have employed ventilation in laboratory settings, where it can be very expensive when no recirculation is used.

When asked about source removal the responses were as follows. Dick's work demonstrated that isolation of donors from recipients with continued hand and fomite contact can prevent spread of rhinoviruses demonstrating that rhinoviruses spread primarily by the airborne route. Morey suggested that the best source control in commercial buildings is that "sick people should stay home until they are better." Fannin suggests decreasing either the number of people or the number of people with viruses; he also notes

that bacterial viruses are found in air ducts and can be eliminated by cleaning with vacuums and brushes.

With respect to the use of filtration as a control technique, they responded as follows. Fannin recommends the use of HEPA filters in combination with UV or ozone. Dick has not used ventilation as a control technique to date in his research, but believes it would be effective (he plans future research to evaluate its use in indoor environments with rhinoviruses).

When asked about other methods of control several of them responded. Cox recommended surface cleanliness. Dick found that the diligent use of virucidal tissues by infected individuals could prevent transmission of rhinoviruses. Fannin suggested the use of air movement past UV lights. In industry, he suggested the use of incineration.

Finally, when asked to discuss possible future directions of virus research in measurement, analysis or control the responses were as follows. Sattar noted the need for a method that can sample larger air volumes, which is simple, inexpensive and has high virus recovery. He also noted an urgent need for air decontamination methods, especially in commercial buildings where air is recycled. Fannin also noted the need for better collection and detection methods. He described a possible control technique which would interrupt transmission and recommended the concept of "clean zones" separated from non-clean areas. The former could be used by sensitive individuals. Hierholzer also mentioned the limitation of virus spread by use of better air circulation techniques; he noted the need for better epidemiologic studies, as well. Morey stated that we need better measures of airborne virus concentrations both as background and when "sick people" are present. Dick mentioned both UV and ventilation as needing more research as control methods. Cox mentioned the use of cyclone scrubbers as samplers in low concentration environments, in combination with vapor phase rehydration if the virus of interest would benefit from that technique. He also mentioned that PCR may be a method requiring further research for virus identification efforts.

## H. Discussion and Conclusions

Viruses appear to be important airborne contaminants in some indoor settings, accounting for significant costs in medical care and loss of work time. A variety of viruses present hazards to health in these environments, most of which are generated by infected humans (and animals, in some cases). For many of the more important viruses, the airborne route appears to be the main exposure pathway. However, due to a variety of problems, sampling for airborne viruses in these environments can be quite difficult. To date, no information exists on "typical" airborne virus concentrations, and few data have been gathered concerning "infective" concentrations. Even less is known about viral particle size distributions and no data on personal exposures have been collected.

The assay and measurement of viral aerosol particles is also difficult, requiring growth in a living organism for enumeration. New techniques, however, may allow the presence and type of virus to be determined with much greater ease; these techniques are yet in the development stage.

This report discusses the application of a variety of control techniques for reduction of airborne viral hazards. The singular difficulty with most feasible control techniques is that their application occurs at some distance from the source of virus particles (i.e. building occupants) and thus may not be able to prevent transmission to nearby non-infected individuals. Three primary techniques, i.e. ventilation, ultraviolet light, and filtration, each have some application to control of viral aerosols in buildings. It would appear that some combination of these three is probably the best control method. However, no studies presently exist that adequately quantify the effect of each of these techniques in reducing and controlling airborne virus particles and preventing the spread of infection in buildings. In the next section we have proposed several studies aimed at evaluating each of these control methods.

## **I. Recommendations for Future Work**

The results of this literature search suggest that there remain several important areas of uncertainty with respect to measuring and controlling airborne viruses in public indoor environments. In most cases it has been extremely difficult, if not impossible, to obtain samples of viruses from the environment; most sampling has been carried out in high concentration experimental settings. The samplers developed for such situations are generally not applicable to the much lower concentrations found in the general environment, with some exceptions.

It would appear that the cyclone scrubber, described in the Sampling section, may be adequate for sampling in such settings. This instrument can sample large volumes of air for relatively long periods; it has the added advantage of providing information on particle size distribution when employed in parallel or series. Also, it does not subject virus particles to high shear forces, nor does it cause any significant dehydration.

It would appear, also, that there are new analytical techniques which will further enhance our ability to sample for airborne viral particles. In particular, PCR (described in the section on analytical techniques) holds significant advantages over other techniques as it does not require inoculation of the virus in living animals or cells and has greater sensitivity for detecting a particular virus.

The control of viral infections has been difficult in the past because, for many viruses, their route of transmission has been so uncertain. It is clear from our work that any of the important human viruses found in indoor environments are transmitted primarily by the airborne route, either by so-called "direct contact" with droplets or by circulation of droplet nuclei through the environment. Our review suggests that UV light, filtration and ventilation can all be effective control methods. Thus we propose that future study of viral aerosols should explore the above mentioned sampling, analysis and control techniques in both laboratory and field settings.

The experimental work we propose would occur in three different settings. In a controlled laboratory experiment, we would evaluate the use of the cyclone scrubber sampler and PCR analytical techniques for measuring airborne viruses. We suggest the use of bacteriophages or relatively benign animal viruses for this work.

In the second set of experiments, work with human volunteers in relatively small spaces, similar to the model employed by Dr. Elliot Dick with rhinoviruses, would explore the effects of ventilation, air filtration and UV light on the prevention of virus transmission.

Finally, we propose a third set of experiments to be carried out in an appropriate field setting. In order to study disease transmission it is necessary to find a setting in which a large number of viral infections occur--we believe day care centers present such a situation. Again, a comparison of ventilation, air filtration and UV light control techniques could be pursued by studying the number of viral diseases (influenza, rhinovirus, measles, etc.) reported. This third experiment would require careful epidemiologic design in order to evaluate the effect of each control method on reducing viral disease incidence. This experimental setting could also be used to evaluate the effects of air recirculation, the alteration of the number of air changes per hour in a room, and low versus high activity levels.

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## **Appendix I Bibliography**

## BIBLIOGRAPHY

### 1 ACGIH 1989

#### Viruses

#### Guidelines for the Assessment of Bioaerosols in the Indoor Environment pp.1-9

Characteristics of viruses, routes of entry, collection, preservation and analysis. Good references included. Recommends that aerosol sampling for viruses not be done routinely, but be reserved for incidents where verification of spread of viral disease among workers is needed. Three basic remedial measures are useful: 1) proper ventilation, 2) filtration, and 3) ultraviolet light.

#### KEY WORDS

aerosol  
sampling

### 2 Adams, DJ Spendlove, JC et al. 1982

#### Aerosol Stability of Infectious and Potentially infectious Reovirus Particles.

*Appl. and Envir Microbiol* 44(4): 903-908.

The aerosol stability of two particle forms, infectious and potentially infectious, of reovirus were examined under static conditions for a range of relative humidities at 21 and 24 °C. At 90 to 100 % relative humidity, both reovirus particle forms showed less than 10-fold loss of infectivity after 12 hours of aging. At lower relative humidities the aerosol decay curve showed rapid initial decay followed by a markedly slower decay rate. The authors state: these findings reveal that reovirus particles are relatively stable in the airborne state.

#### KEY WORDS

aerosol  
survival

### 3 Akers, TG 1969

#### Chap 12 Survival of Airborne Virus, Phage and Other Minute Microbes

*Introduction to Experimental Aerobiology* 1969. ed. Dimmick and Akers pp.296-339.

Studies of virus in the airborne state have lagged behind studies of airborne bacteria, but technology in place for bacteria can be adapted for the viruses. This article goes on to discuss the survival of representative viruses, as well as some rickettsia, psittacosis, phage, and mycoplasma as reported in the literature. Tables of aerosol stability and airborne transmission are included along with the appropriate references. Mention is made of humidity, temperature, and other environmental conditions as well as immunization studies. Includes approximately 90 references.

#### KEY WORDS

survival  
virus

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#### New Sampler for the Collection, Sizing, and Enumeration of Viable Airborne Particles.

*J Bacteriol* 76: 471-484

This report describes an instrument with which viable airborne particles are sized and counted, sets forth proper operational procedures, and presents some of the results of the experimental studies conducted. The sampler is generally termed the "Andersen sampler" and consists of six stages through which the air sample is consecutively drawn until it lands on culture plates of agar. Experimental studies with the instrument on bacterial aerosols showed that the instrument is extremely sensitive and useful to calculate the particle size spectrum of the aerosol. It is suggested that the sampler could be used to assess the health hazard in particulate air pollution.

#### KEY WORDS

sampling  
aerosol  
airborne

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#### The complex epidemiology of respiratory virus infections.

*Science* 146:1274-1277.

Respiratory viruses can undoubtedly spread from one person to another, though the spread of manifest disease is not shown so readily. One explanation may be that all sorts of respiratory viruses are constantly passing back and forth in a population. Normally they would multiply and be shed only at a minimum level. When something interferes with the balance, there is unhindered multiplication and spread of the virus leading to overt symptoms. Meanwhile, the virus is shed more freely into the environment. Some form of "stress" is theorized to occur to which the body can not adjust quickly enough to avoid disease.

#### KEY WORDS

respiratory

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Brief summary of the airborne transmission of smallpox. This is a summary that describes a case in a German hospital where the index case was an engineer recently returned from Karachi. The patient was rigorously isolated, yet 20 additional cases with 4 deaths occurred. The index patient was in a cubicle entire time, and had no contact with others who became ill.

**KEY WORDS**  
transmission  
airborne

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Air Sampling In Respiratory Disease.  
*Arch Env Health.* 9:58-60.

Respiratory viruses are acquired by direct contact with large particles of infective secretions, or by inhalation of true aerosols consisting of droplet nuclei. Infective aerosols produced by ill people were sampled directly in front of patient with impingers, (AGI), 5-20 minute duration. The authors note Riley's observation that one human infectious dose was contained in 3,000 cubic feet of sampled air for measles. The recovery of virus aerosols was lower than in the laboratory where artificial virus aerosols were produced. This represents the result of physical and biological processes as well as an inefficiency of the sampling apparatus. Research done at the Dept. of Virus Disease, Walter Reed.

**KEY WORDS**  
sampling  
airborne

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Virus transfer from surf to wind.  
*Science.* 198 : 575-580.

Bubbles in the sea surf adsorb and carry viruses to the surface where they are propelled in to the air on tiny jets of seawater when the bubble bursts. These jets become tiny drops of aerosol. Bubble levitation of viruses infected into the surf produced 200 times more virus per milliliter in the aerosol than were present in samples from the water itself. Some of the aerosol drops are carried by the wind and fall out on the beach. The frequency of virus laden drops decreased exponentially with the distance downwind of the site.

**KEY WORDS**

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A method for biological testing of containment systems for viral agents.  
*Am Ind Hyg Assoc. J* 37: 427-431.

This article details methods to verify the integrity of containment systems. A technique utilizing coliphage as the test material has been developed and employed to evaluate the effectiveness of a containment system for zonal centrifugation of hepatitis viruses. An Anderson Sampler is used, and is loaded with plates containing a base layer of agar with E. coli. The containment system, including a HEPA filter, was then challenged with an aerosol of coliphage (which is detected by its infection of the E. coli layer).

**KEY WORDS**  
sampling  
aerosol

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Air Sampling for Evaluation Of Viral Excretion Level By Vaccinated Pigs Infected With Aujeszky's Disease (pseudorabies).  
*Res Vet Sci.* Mar;52(2):182-6

Five groups of eight pigs were vaccinated and then infected with Aujeszky's disease virus. Virus excretion was measured by deep nasal swab and air sampling. It appeared that infectious airborne virus could be recovered from day 1 to day 6 after infection in the isolated units where control animals were raised. Results with nasal swabs and with air samples were closely related. Air sampling has low sensitivity, but could be an efficient tool for reflecting infectious viral pressure in a confined atmosphere

**KEY WORDS**  
sampling  
airborne

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Building-Associated Risk of Febrile Acute Respiratory Diseases in Army Trainees  
*JAMA* 259:2108-2112.

States that respiratory tract infections are the most common infectious illnesses among adults. The authors hypothesize that energy conservation measures that tighten buildings also increase risks of respiratory infection. At four Army training centers during a 47-month period, incidence rates of febrile acute respiratory disease were compared between modern and old barracks. Rates of diseases were significantly higher among trainees in modern barracks. The authors state that this supports the hypothesis that tight buildings with closed ventilation systems significantly increase risks of respiratory transmitted infection among congregated susceptible occupants.

**KEY WORDS**  
airborne  
transmission

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*J. Hyg (Camb.)* 62:365-377.

Colds are due to infections with a number of different viruses and it is unwise to generalize about the epidemiology of the disease. The authors have attempted to measure some of the processes which may operate when infected nasal secretion leaves the upper respiratory tract of a model "patient" and reaches that of another subject. There is a description of work using biological tracers to measure the clearance of foreign material from the nose, mouth and conjunctiva and the dispersal of material from the mucous surfaces of normal subjects while sneezing or coughing.

**KEY WORDS**  
transmission  
airborne

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Protective Environment for Marrow Transplant Recipients  
*Ann of Int Med.* 89(6): 893-901.

Laminar air flow isolation accompanied by skin cleansing, gastrointestinal decontamination with oral nonabsorbable antibiotics, and sterile or low bacteria-content food has been shown to decrease infection acquisition in patients with severe granulocytopenia and undergoing remission-induction therapy for acute leukemia. This report presents results of a prospective study of these methods on bone marrow transplant recipients. Laminar flow protected patients from septicemia and major local infections. A Seattle Marrow Transplant Team collaborative effort.

**KEY WORDS**  
airborne

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Bioaerosols: Prevalence and Health Effects in the Indoor Environment.  
*J of Allergy and Clin Immunol* 86(5):687-701.

States that indoor air concentrates pollutants, and discusses microbial ecology and health effects, as well as sick building syndrome. Measles, influenza and tuberculosis are some upper respiratory infection viruses that commonly spread through the air. Included is a discussion of on-site inspection which is often needed to determine a source of biological contamination. Assessment of the role of bioaerosols in residence related symptoms involves determining that symptoms are related to the residence, connecting the symptoms with known effects of airborne viruses, examining the building, and finally air sampling if needed using a reliable volumetric method.

**KEY WORDS**  
aerosol  
ventilation

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Indoor Air Pollution: A Health Perspective. Samet, JM and Spengler, JD Eds. Johns Hopkins Press.

Includes information on viruses, reservoirs, amplifiers, disseminators, aerosol characteristics, disease agent, host factors and prevention of airborne infection. Lower ventilation rates to save energy are causing increased problems in the authors' opinion. In summary, airborne disease transmission involves a complex sequence of events involving a reservoir, amplifier, and disseminator. The mere presence of a pathogen in the environment does not necessarily lead to human illness. For infection to occur the pathogen must be amplified and disseminated. Prevention of airborne infection can be effected by removal of the source or reservoir, or by interruption of the reservoir/amplifier/disseminator sequence.

**KEY WORDS**  
respiratory  
airborne

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*Appl. Microbiol* 23(3):505-508.

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**KEY WORDS**  
airborne  
filtration

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Production of Tracheobronchitis in Volunteers with Rhinovirus in a Small-Particle Aerosol

*Am J of Epid* 81(1):95-105

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**KEY WORDS**  
aerosol

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*MMWR* 32:401-403.

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**KEY WORDS**

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Air Sampling Instruments for Evaluation of Atmospheric contaminants 7th ed. American Conference Of Government Industrial Hygienists. Cincinnati.

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**KEY WORDS**  
sampling

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Viruses and Indoor Air Pollution

*Bull N.Y. Acad Med.* 57(10):907-921

A number of viruses may contaminate the air of rooms and be capable of initiating disease in those who inhale them. All these viruses are transmitted from person to person, but limited quantitative information about infectious dose is available. This report summarizes data that suggest that under certain circumstances and with certain viruses, airborne transmission occurs. Includes tables of human viral diseases spread by airborne route, recovery of virus in cough and sneeze particles, and relation of virus quantity in secretions to virus in room air samples. Concludes that airborne transmission of viral diseases is an indoor phenomenon only.

**KEY WORDS**  
airborne

## BIBLIOGRAPHY

21 Couch, RB Cate, TR *et al.* 1966

Effect of route of inoculation on Experimental Respiratory Viral Disease in Volunteers and Evidence for Airborne Transmission  
*Bact. Rev.* 30(3):517-529.

State that airborne transmission is intended to mean transfer of infection by means of small-particle aerosols. These particles less than 5 microns in size enter and deposit in the lower respiratory tract. Larger particles such as those of coughing and sneezing do not form stable aerosols, and thus result in contact transmission. Conclusion of this study is that both contact and airborne transmission of the respiratory viruses probably occur in natural circumstances, and that the predominant method of transmission may vary with the virus and with the particular environmental situation.

**KEY WORDS**  
aerosol  
transmission  
respiratory

22 Couch, RB Cate, TR *et al.* 1966

Aerosol-induced Adenoviral Illness Resembling The Naturally Occurring Illness In Military Recruits  
*Amer. Rev Resp Dis* 93: 529-534

There is a major disease problem due to febrile respiratory disease in military recruits caused by adenovirus types 4 and 7. This study developed methods to create an aerosol of adenovirus and use it to induce disease in human volunteers. Fifteen volunteers were inoculated with aerosols, nine received 5 to 11 TCID<sub>50</sub> and six received 1,000 units in a larger-particle aerosol. Disease produced resembled the natural disease in symptoms and distribution within the lungs.

**KEY WORDS**  
aerosol

23 Couch, RB Cate, TR *et al.* 1965

Production of Illness with a Small-Particle Aerosol of Coxsackie A21  
*J of Clin Invest* 44(4):535-545

Determined a 50% human infectious dose of two strains of Coxsackie virus as 30 TCID<sub>50</sub> of virus. Syndromes of disease varied depending on the type of tissue culture used to passage the viral strain. Virus was recovered frequently from the nose and throat of infected subjects.

**KEY WORDS**  
aerosol

24 Couch, RB Douglas, RB *et al.* 1970

Airborne Transmission Of Respiratory Infection With Coxsackie Virus A Type 21.  
*Am J Epidemiol.* 91: 78 - 86.

This study made use of a barracks divided by a double wire barrier. On one side, 10 volunteers were inoculated, while 10 controls on that side and 19 on the other received sham inoculations. Air was then sampled with a LVA sampler. Airborne transmission of coxsackie virus was documented.

**KEY WORDS**  
transmission  
airborne

25 Couch, RB Knight, V *et al.* 1968

The Minimal Infectious Dose Of Adenovirus Type 4; The Case For Natural Transmission By Viral Aerosol  
*Trans. Am Clin Clim Assoc.* 80:205- 211.

Acute respiratory disease of military recruits (ARD), is most commonly caused by adenovirus type 4. The test involved an aerosol of size 1.5 micron, which is small enough to deposit in the lower respiratory tract. (or be exhaled). The study found that the aerosol infectious dose was much lower than that of nasal exposure. In nature, infected persons must produce sufficient amount of small particle aerosols to produce infection. To control spread of disease, the authors suggest purification of air in barracks rooms and other places with close contact to diminish the spread of infection.

**KEY WORDS**  
respiratory  
transmission

## BIBLIOGRAPHY

### 26 Cox, CS 1987

Section 4.3 Microbiological Methods.

The Aerobiological Pathway of Microorganisms. John Wiley and Sons pp. 85-87.

Potential biohazards associated with hospital, industrial and laboratory procedures involving infectious materials need to be ascertained, monitored and controlled. Required processes include sampling and assay of actual pathogens or tracers that may be non-living materials or non-pathogenic microorganisms. Depending on the nature of the aerosol, its monitoring can be achieved through different physical or microbiological assays. The most pertinent of them will depend on particular applications and facilities, with the most sensitive one likely to be microbiological.

#### KEY WORDS

sampling

### 27 Cox, CS 1989

Airborne Bacteria and Viruses.

*Sci. Prog. Oxf.* 1989. 73:469-500.

Coughing, sneezing, talking, bed-making, turning pages of books, etc. all generate microbial aerosols which are carried and dispersed by air movements. Inhalation of these particles may cause allergic responses, but whether or not infectious disease ensues depends in part on the viability and infectivity of the inhaled microbes and their landing sites. Desiccation is experienced by all airborne microbes; for lipid-free viruses these reactions occur most rapidly at low RH. Radiation, oxygen, ozone and various pollutants also decrease viability and infectivity. At least indoors where desiccation is the predominant stress, airborne transmission is virtually assured.

#### KEY WORDS

airborne  
transmission

### 28 Cox, CS 1987

Chapter 3 Aerosol Samplers

The Aerobiological Pathway of Microorganisms. John Wiley and Sons pp. 50-77.

Artificial aerosol sampling is fundamental to experimental aerobiology. Determining the airborne state requires that accurate samples be taken. The sampling process can modify the survival and infectivity of the collected samples. This chapter is a review of numerous varieties of samplers and a discussion of their efficiencies

#### KEY WORDS

sampling

### 29 D'Alessio, DJ Peterson, JA et al. 1976

Transmission of experimental rhinovirus colds in volunteer married couples.

*J Infect Dis.* 133: 28.

Communicability of rhinovirus was studied in 24 childless couples lacking specific antibody to either of two adenovirus types. One partner was infected with the virus. Rates of transmission were 41% and 33% for the two virus types used. Transmission rarely occurred unless at least 1,000 TCID<sub>50</sub> was recovered from the donor's nasal washing, the donor had virus on his hands and anterior nares, he was at least moderately symptomatic, and he spent many hours with his spouse. Since person-to-person transfer was so dependent on shedding large amounts of virus and on time spent together, it seems possible that the chain of infection could be interrupted by environmental manipulation.

#### KEY WORDS

### 30 De Jong, JC and Winkler, KC 1964

Virology: Survival of Measles Virus in Air.

*Nature* 201:1054-1055.

Examines survival of measles virus in air at various humidities and temperatures. The authors used a 5 micron size droplet nuclei produced by an atomizer, then took frequent air samples with capillary impingers. Measles virus survives better than influenza at all humidities, this corresponds to the clinical observation that measles is more infectious than influenza. Measles is also more stable at low humidity.

#### KEY WORDS

airborne

## BIBLIOGRAPHY

### 31 DeJong, JC Harmase, M *et al.* 1975

Factors in the inactivation of encephalomyocarditis virus in aerosols.  
*Infect Immun* 12: 29.

Studies on the survival of the encephalomyocarditis virus in aerosols under various conditions of temperature and relative humidity. **KEY WORDS**  
survival

### 32 DeJong, JC Trouburst, T *et al.*

Mechanisms of inactivation of viruses and macromolecules in air. 31. The mechanism of virus decay in aerosols.  
*Airborne transmission and airborne infection*, pp. 124-130. Hers and Winkler eds.

Another study relating environmental conditions of temperature and humidity to viral survival in aerosols. **KEY WORDS**  
survival

### 33 Dick, EC Blumer, CR *et al.* 1967

Epidemiology of infections with rhinovirus types 43 and 55 in a group of Wisconsin student families.  
*Am J Epidemiol* 86: 386-400.

Study of the spread of disease within student families. An outbreak of disease occurred in the spring of 1964. This article discusses the epidemiology and clinical aspects within this study group including spread within families, and within the student neighborhood. Notes that there are 55 strains of rhinovirus currently (1967) recognized as distinct antigenic types. **KEY WORDS**  
transmission

### 34 Dick, EC Jennings, LC *et al.* 1987

Aerosol Transmission of Rhinovirus Colds  
*J of Inf Dis* 156(3). 442-448.

Rhinovirus infections may be spread by aerosol, direct contact, or indirect contact involving environmental objects. These authors examined aerosol and indirect contact in transmission of rhinovirus type 16 colds between laboratory-infected men and susceptible men. In three experiments; the infection rate of restrained recipients who could not touch their faces and that of unrestrained recipients was not significantly different. In a fourth experiment, transmission via fomites heavily used for 12 hours by eight donors was the only possible route of spread; no transmissions occurred among 12 recipients. These results suggest that rhinovirus transmission, at least in adults, occurs chiefly by the aerosol route. **KEY WORDS**  
aerosol  
respiratory

### 35 Dixon, RE 1985

Economic Costs of Respiratory Tract Infections in the United States  
*The American Journal of Medicine* 78: (suppl. 6B) : 45-51.

Overall, upper and lower respiratory tract infections are estimated to be responsible for approximately \$15 billion in direct treatment costs. Physician charges account for about one half and hospital care accounts for approximately one quarter of these costs. An estimated 1.25 million patients are hospitalized yearly for community-acquired respiratory tract infection, and charges for their care are projected to exceed \$4 billion. Although not possible to calculate the full magnitude of the indirect cost, losses in income of employed person missing work due to respiratory infection are calculated to be more than \$9 billion per year. **KEY WORDS**  
respiratory



## BIBLIOGRAPHY

### 36 Donaldson, MA 1978

Factors Influencing The Dispersal, Survival And Deposition Of Airborne Pathogens Of Farm Animals.  
*Vet Bull* 48(2):83-94.

Considerable evidence suggests that many animal pathogens can be spread by the airborne route. The assumption is that they travel on droplet nuclei; actual isolation has occurred for only a few organisms. Temperature exerts a minor effect on survival, humidity is more important. Lipoprotein enveloped viruses survive best at low RH while non-enveloped viruses are unstable in dry conditions but survive well at high RH. Non-ionizing radiation has a variety of effects, gaseous pollutants also affect survival. Suggestions for control and prevention include filtered-air systems and closed flocks.

#### KEY WORDS

survival  
airborne

### 37 Edward, DG Lush, D et al. 1943

Studies on Airborne Virus Infections. II. The Killing of Virus Aerosols by Ultra-Violet Radiation  
*J Hyg* 43:11-15.

The use of UV radiation for disinfecting air appears likely to become of considerable practical importance. Under laboratory conditions, UV radiation has been shown to be effective against sprays of bacterial cultures. The purpose of this paper is to describe quantitative studies carried out early in 1940 regarding the killing effect of ultra-violet radiation upon aerosols of three viruses: influenza A, vaccinia and herpes simplex.

#### KEY WORDS

survival  
aerosol

### 38 Fannin, KF 1980

Methods for Detecting Viable Microbial Aerosols

Wastewater aerosols and disease. Health Effects Lab. 600/9-80-028, US EPA pp. 1-22.

Aerosols formed during processes of waste water treatment can contain viable microorganisms that survive transport to distant locations from the site of origin. Detection of such aerosols under field conditions requires the application of reliable methodologies, determined before sampling. Aerosol collection can include sedimentation, filtration, impingement, precipitation, centrifugal separation, or inertial impaction. Large volume samplers have been developed to handle situations with low concentrations requiring greater sensitivity. Vigorous quality control is necessary in both the field and analytical laboratory.

#### KEY WORDS

aerosol  
sampling

### 39 Fannin, KF and Vana, SC 1982

Development and Evaluation of an Ambient Viable Microbial Air Sampler.

US EPA -600/S1-81-069. pp. 1-3

Brief overview and project summary paper. This article makes three conclusions: 1) methods used for detecting low-level ambient microbial aerosols should be standardized. These methods should employ a sampler that is specifically designed for this application, and that is reliable, robust, and effectively sterilized. Currently, the cyclone scrubber should be used. 2) The standard sampler should be evaluated under varied and controlled conditions to optimize collection efficiency by selecting appropriate media and controlling factors such as fluid flow and air sampling rates. 3) These evaluations should employ a viable microbial aerosol reference sampler that operates at an air sampling rate is similar to that of the device under evaluation.

#### KEY WORDS

sampling  
airborne

### 40 Fannin, KF Vana, SC et al. 1985

Effect of an Activated Sludge Wastewater Treatment Plant on Ambient Air Densities of Aerosols Containing Bacteria and Viruses.  
*App. and Environ Microbiol* 49(5):1191-1196

Bacteria and virus-containing aerosols were sampled with multistage impactors and large-volume scrubbers near an activated sludge waste water treatment plant, located in a midwestern suburb. Sampling was done in late summer and fall. There is discussion of field sampling approach, air sampling methods, and assays and enumeration were mentioned. Enteric viruses were the only virus studied. The article also talked about human exposure to infectious bioaerosols and related health risks. The authors feel that the techniques used in this study may be employed to establish microorganism containing aerosol exposure during epidemiological investigations.

#### KEY WORDS

aerosol  
virus  
sampling

## BIBLIOGRAPHY

### 41 Fradkin, A 1985

"Sampling of Microbiological Contaminants in Indoor Air"

*Sanitation and Calibration for Atmospheric Measurements* ed. John K. Taylor ASTM STP 957, American Society for Testing and Material, Philadelphia pp. 66-77.

Strategies for sampling airborne biogenic contaminants should include specific considerations for each group of microorganisms. The determination of target pollutants and sampling strategy is based on preliminary investigation of the indoor environment by a walk-through inspection and clinical, epidemiological, and immunological features of health effects. Two samplers, the six-stage Andersen and the all-glass impinger Model AGI-30 are suggested as standards. Attention should be given to sampling location, number of samples per interiors, reference data, and methods to confirm the findings of air sampling.

#### KEY WORDS

airborne  
sampling

### 42 Garden, JM O'Banlon, K et al. 1988

Papillomavirus in the vapor of carbon-dioxide laser treated verrucae.  
*JAMA* 259:1199-1202.

Vapor produced by the carbon dioxide laser during the vaporization of papillomavirus-infected verrucae was analyzed for viral DNA content. Two models were used for evaluation. These studies indicate that intact viral DNA is liberated into the air with the vapor of laser-treated verrucae. It would be prudent for all practitioners who use the laser in treating patients with viral infections of conditions associated with viruses to practice extreme care and safety throughout the laser procedure.

#### KEY WORDS

airborne  
transmission

### 43 Garibaldi, RA 1985

Epidemiology of Community-Acquired Respiratory Tract Infections in Adults: Incidence, Etiology, and Impact.  
*The American Journal of Medicine* 78(suppl. 6B):32-37.

Upper respiratory tract infections are the most common types of infectious diseases among adults. It is estimated that each adult in the United States experiences two to four respiratory infections annually. This totals to an estimated 75 million physician visits per year, almost 150 million days lost from work, and more than \$10 billion in costs for medical care. Rhinoviruses account for 20 to 30 % of episodes of the common cold. The article also discusses pneumonia rates among the elderly, and other bacterial complications or viral respiratory disease.

#### KEY WORDS

### 44 Gerba, C.P. Wallis, C. et al. 1975

Microbiological Hazards of Household Toilets: Droplet Production and the Fate of Residual Organisms.  
*Applied Microbiology* 30(2): 229-237.

Large numbers of bacteria and viruses when seeded into household toilets were shown to remain in the bowl after flushing, and even continual flushing could not remove a persistent fraction. This is due to adsorption of the organisms to the porcelain surfaces of the bowl. Both bacteria and viruses may remain in the droplets produced. The detection of bacteria and viruses falling out onto surfaces in bathrooms after flushing indicated that they remain airborne long enough to settle on surfaces throughout the bathroom. Thus, a person may acquire infectious organisms from aerosols produced by toilets.

#### KEY WORDS

airborne  
survival

### 45 Gerone, PJ Couch, RB et al. 1966

Assessment of Experimental and Natural Viral Aerosols  
*Bact Reviews* 30: 576-587

The authors performed studies on artificially prepared aerosols (using the Collison atomizer) containing Coxsackievirus, and natural aerosols produced by infected subjects. The main purpose was to explore the properties of the small particle viral aerosol. Virus was recovered by having the subject sneeze or cough into a weather balloon. A newly developed large volume sampler (LVS) made by Litton Systems of Minneapolis MN, which samples up to 10,000 liters per minute, was found to be an efficient sampler but had two limitations: evaporation of collecting fluids and no size information. Diagram of the sampler, and virus recovery by different samplers were shown.

#### KEY WORDS

aerosol

## BIBLIOGRAPHY

### 46 Goyal, SM, Gerba, CP et al. 1979

Human Enteroviruses in Oysters and Their Overlying Waters  
*Appl. Environ. Microbiol.* 37: 572-581.

Viruses in the waters of the Texas Gulf coast were monitored over 10 months. Viruses were detected periodically in waters that met current bacteriological standards for shellfish harvesting. Viruses were moderately correlated with total coliforms. Bacteriological standards for determining the safety of shellfish and shellfish-growing waters do not reflect the occurrence of enteroviruses. Viruses were detected after concentration from seawater samples, by filtering through a 0.45 micron filter. They were isolated by the PFU method or by observing CPE in monkey cell lines.

**KEY WORDS**

### 47 Goyal, SM Rademacher, RA et al. 1987

Comparison of electron microscopy with three commercial tests for the detection of rotavirus in animal feces.  
*Diagn Microbiol infect Dis.* 6: 249-254.

Three commercial test kits were evaluated to detect the presence of rotavirus antigens in bovine, porcine, and turkey feces by comparing their results to those obtained via electron microscopy. The enzyme immunoassay was the best method. Considering only the two latex agglutination tests, the Virogen was found to be a little more sensitive and specific.

**KEY WORDS**

virus type

### 48 Guerin, JF and Mitchell, CA 1964

A Method For Determining The Concentration Of Airborne Virus And Sizing Droplet Nuclei Containing The Agent.  
*Can J Comp Med. Vet Sci.* 28: 283-287.

A poliovirus containing aerosol was impacted onto agar-covered cell monolayers in sampling plates through use of an Anderson sampler. In order to initiate infection, the viruses had to diffuse through the agar layer to the susceptible cells in the monolayer. This was successful with some viruses, but had some disadvantages: Cells had to be in a susceptible growth phase, viruses had to be viable in cell culture, and it was difficult to sample in contaminated environments. Addition of an overlay of a 5 ml. suspension of 3% gelatin containing antibiotics to suppress bacterial contamination helped. The sampler plates were placed in an incubator to liquefy the gelatin before viral assay.

**KEY WORDS**

airborne

### 49 Gwaltney, JM 1980

Epidemiology of the Common Cold  
*Ann NY Acad Sci.* Vol. 353. Airborne Contagion. ed. Kundsins, R B. pp. 54-60.

Studies of the common cold are complicated by the many viruses involved, many of which behave quite differently from the others. This review considers the rhinoviruses which cause about 30 % of colds, and have received the most study. Includes studies in volunteers, both successful and non-successful, and examines the reasons for failures. Airborne transfer requires sufficient quantities of virus from the donor, survival in the aerosol, and ability of the aerosol to reach the susceptible host. Also included is a table on estimated frequency of rhinovirus shedding on the third day of infection. The author concludes that the natural route of spread is not totally known.

**KEY WORDS**

airborne  
respiratory

### 50 Halvett, M 1979

Smallpox: Ignorance Is Never Bliss  
*Nature.* 277:75-81.

Discussion of the release of smallpox virus in a Birmingham, England laboratory in Aug. 1978 that resulted in the last case of smallpox in the world. Discusses the need for knowledge of the potential for airborne transmission of any virus, and states that ignorance of these matters is intolerable. Both the biology of infection and the physics of spread of an infectious agent being handled in a laboratory should be studied and known.

**KEY WORDS**

airborne  
transmission

## BIBLIOGRAPHY

### 51 Hankins, WA Hearn, HJ 1970

Direct Assessment of Viral Aerosols on Cell Cultures.  
*Appl. Microbiol.* 1970. 20(2): 284-285.

A technique is described for the direct exposure of cell cultures to airborne virus enabling quantitation of the virus in concentrations as low as one plaque-forming unit per liter of air. Known volumes of viral aerosols were drawn directly into flasks containing cell culture monolayers that were then used to quantitate the virus by allowing plaques to develop. Results of these tests indicate that the direct exposure of cell culture monolayers to viral aerosols provides a simple and sensitive technique for the assessment of infectious airborne viral particles. This technique permitted the recovery of virus in very low aerosol concentrations that could not be detected by conventional impinger techniques.

#### KEY WORDS

sampling  
airborne

### 52 Harstad, JB and Filler, ME 1969

Evaluation of air filters with submicron viral aerosols and bacterial aerosols  
*Am Ind Hyg Assoc. J.* 30: 280-290.

Velocity, aerosol particle size, aerosol charge, and exposure to high humidity were found to affect the performance of air filters. Filter papers and the DOP scan tested filter units (HEPA) filters fabricated from these papers were evaluated with submicron T1 bacteriophage aerosols having a number median diameter (NMD) of 0.12 micron. High humidity increased penetration. HEPA filters will protect people from spread of agents in aerosols, but installation must be properly done to ensure full efficiency.

#### KEY WORDS

filtration  
sampling

### 53 Hawkes, N 1979

Smallpox Death in Britain Challenges Presumption of Laboratory Safety  
*Science* 203 855-856.

Last known case of smallpox, laboratory acquired in 1978. Janet Parker, a medical photographer in a room one floor below the smallpox laboratory, was fatally infected by the smallpox virus which traveled in the air through loose panels in a serviced duct. As smallpox was being eradicated, labs were closing, this lab was due to close by the end of the year. Safety procedures were apparently allowed to be lax due to the imminent closing even though the researcher had helped outline proper procedures. The researcher committed suicide 5 days before Janet Parker died of smallpox.

#### KEY WORDS

airborne  
transmission

### 54 Hendley, JO Wenzel, RP et al. 1973

Transmission Of Rhinovirus Colds By Self-inoculation.  
*New Eng. J Med.* 288: 1361-1364.

The authors investigated transmission of rhinovirus colds by examining shedding by infected patients, survival of virus outside the host, and inoculation of susceptible person. Two of 25 infected persons expelled virus in a cough or sneeze; four of 10 had virus on their hands. Dried rhinovirus could be picked up by the fingers from skin or environmental surfaces. Four of 11 volunteers became infected after touching their nasal or conjunctival mucosa with fingers previously contaminated by rubbing a dried drop of rhinovirus. Adults expose the nasal or conjunctival mucosa to the fingers frequently under natural conditions.

#### KEY WORDS

transmission

### 55 Hierholzer, JC 1990

Viruses, Mycoplasmas as Pathogenic contaminants in Indoor Environments.  
*Biological Contaminants in Indoor Environments.* ASTM STP 1071

A review article that covers all areas regarding spread of viruses by the respiratory tract via droplets and fomites. Viruses are diverse in their biological properties and are commonplace in all populations. Viruses are found in 11 different families including 270 serotypes which affect mainly the respiratory, and/or gastrointestinal systems or involve the conjunctiva of the eye. Viruses with lipoprotein envelopes are labile and die quickly upon drying; unenveloped survive longer. All can be sampled by impelling onto agar surfaces and eluting into cell culture medium for growth. Good personal hygiene, hand washing, and low humidity will decrease virus contamination.

#### KEY WORDS

airborne  
sampling  
survival

## BIBLIOGRAPHY

56 Hugh-Jones, M Allan, WH *et al.* 1973

The Evidence for the Airborne Spread of Newcastle Disease  
*J Hyg Camb* 71:325-339.

Newcastle disease is a highly infective and contagious disease of poultry. Newcastle disease virus has been shown to survive when airborne in small particles both in the lab and in open air. Field outbreaks have been studied and viable virus has been recovered from the open air short distances downwind of infected premises.

**KEY WORDS**  
airborne  
transmission

57 Hugh-Jones, ME

The epidemiology of airborne animal diseases.

*Airborne Transmission and Airborne Infection* With International Symposium on Aerobiology pp. 399-404

"... if a bacterium, fungus, mycoplasma or virus can be grown, someone has purposefully made an aerosol of it and measured its viability. Any that have been missed have been tested accidentally in the laboratory..." Diseases with an airborne component in their normal epidemiology are fewer. Lists those diseases of animals where this is a concern.

**KEY WORDS**  
airborne

58 Ijaz, M.K. Karim, Y.G. *et al.* 1987

Development of methods to study the survival of airborne viruses  
*J of Virol Methods* 18:87-106.

A number of viruses have been shown to be transmitted by the airborne route. It is the ability of these viruses to retain their infectivity for living hosts which plays a key role in their aerial dissemination. Data generated by a number of workers on the airborne survival of viruses varies considerably because laboratory techniques have not been standardized. This paper describes the methodology developed to study the aerobiology of human and animal airborne viruses. Includes consideration of virus suspending medium, aerosol generation, storage, and collection (AGI), and effects of RH, temperature, and suspending medium on viral survival. This study is a follow-up to studies on airborne survival.

**KEY WORDS**  
aerosol

59 Ijaz, M.K. Sattar, S.A. 1985

Effect Of Relative Humidity, Atmospheric Temperature, And Suspending Medium On The Airborne Survival Of Human Rotavirus.  
*Can J Microbiol* 31: 681-685

The Wa strain of rotavirus was suspended in either a broth or in feces from a case. It was then aerosolized in a rotating drum. The drum air was sampled using an all-glass impinger containing broth as collecting fluid. Survival was measured at various temperatures and humidity levels. When suspended in broth at 20° C the virus survived best at 50% RH, at higher temperatures, and higher humidity, survival was less. At low temperature airborne survival of the virus at mid and low RH was enhanced, at high RH survival was similar to 20° survival. Aerosols of suspended rotavirus from fecal sources survived and remained infectious at 24 hours.

**KEY WORDS**  
aerosol

60 Jaakkola, JJK Heinonen, OP *et al.* 1990

The Occurrence of Common Cold and the Number of Persons in the Office Room.  
*Proceedings Indoor Air Conference.* vol. 1 pp. 155-160.

This study was done in a modern mechanically ventilated eight story office building with 2150 workers located in Helsinki. The study evaluated the effect of various numbers of office mates on cold occurrence. The authors controlled for other variables such as number of children at home, allergies, smoking and age. They found an increase in the number of colds which was correlated with an increase in the number of office mates; indoor air transmission is suggested as the cause.

**KEY WORDS**  
airborne  
respiratory

## BIBLIOGRAPHY

61 Jensen, MM 1964

Inactivation Of Airborne Viruses By Ultraviolet Irradiation.  
*Appl. Microbiol* 12:418-420.

Aerosolized viruses were passed through a high-intensity UV cell which consisted of a long cylindrical aluminum tube with a highly reflective inner surface and a longitudinally extending helical baffle system which directed airborne particles in close proximity to a centrally located UV lamp. Inactivation rates of greater than 99.9% were obtained for Cocksackie, influenza, Sindbis, and vaccinia viruses and 96.8% for adenoviruses. at 100 cubic feet per minute airflow. Slightly less inactivation occurred with 200 cubic feet per minute air flow.

### KEY WORDS

airborne

62 Jericho, KWF Lejeune, A. et al. 1986

Bovine herpesvirus-1 and Pasturella Haemolytica Aerobiology in Experimentally Infected Calves.  
*Am J Vet Res* 47(2):205-209.

In animal studies it was learned that the cranial part of the respiratory tract serves as an efficient filter on inhalation and exhalation, but this filter is deficient in the animal when coughing occurs. Experimental methods for the production of bovine herpesvirus - 1 (BHV-1) aerosols, air sampling, assay and isolations are included. The production of bovine herpesvirus - 1 (BHV-1) aerosols from diseased calves was demonstrated, but the infective nature of such aerosols was not. The viability of these infective agents in aerosols determines their disease transmission potential via air. The purpose of this study was to provide a better definition of the transmission of respiratory tract pathogens by cattle.

### KEY WORDS

aerosol

63 Karim, YG Ijaz, MK et al. 1985

Effect of Relative Humidity on the Airborne Survival of Rhinovirus-14.  
*Can J Microbiol* 131:1058-1061.

Rhinovirus - 14 in tryptose phosphate broth supplemented with uranine as a tracer and an antifoam, were aerosolized by use of a Collison nebulizer. An all-glass impinger was used to recover virus from air in the drum, several samples were taken at various times for the next 24 hours. At low and medium relative humidity (RH), the infectivity was rapidly lost and less than 0.25% could be detected at 15 minutes. At high RH, the airborne virus had a half-life of 13.7 hours and nearly 30% was still present after 24 hours of aerosolization. These findings suggest that under high RH air may act as a vehicle for the spread of rhinovirus infections.

### KEY WORDS

aerosol  
sampling  
survival

64 Knight, V 1966

1. Discussion of relationship infective agents and host cells

Transmission of Viruses by the Water Route ed. Gerald Berg

Discussion of the recent work to define minimal infectious doses for several respiratory viral agents by inoculation of volunteers. Includes a table defining the infectious dose in terms of human infectious dose 50% (HID<sub>50</sub>) for several agents. Lower doses are needed to produce infection with aerosols than with nasal drops.

### KEY WORDS

aerosol

65 Knight, V Gerone, PJ et al. 1963

Studies in Volunteers with Respiratory Viral Agents  
*Amer., Rev Resp Dis* 88:135-147

This report describes four investigation of viral infection in volunteers and discussed the various approaches used in volunteer studies. Almost 400 volunteers have been used in the study of about 20 different viral infections. Preparation and titration of aerosols, using the Ft. Detrick Collison atomizer is discussed. Includes diagrams of the apparatus, tables of various virus preparations and their titers, isolation of viruses from subjects, and various treatment attempts.

### KEY WORDS

aerosol

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### 66 Kundsln, RB 1980

Opening Remarks (on airborne contagion.)

*Ann NY Acad Sci.* Vol., 353. Airborne Contagion. ed. Kundsln, R B pp. 1-2.

The editor discusses reasons to hold a conference on airborne contagion: 1) threshold limit values (TLV) are not established for viruses, 2) energy conservation will cause the increased problems of less ventilation and less make up of outdoor air and 3) as a tribute to William Firth Wells who first called attention to airborne contagion in the nineteen thirties. "Airborne transmission is the most important mode of transmission of respiratory infections from person to person indoor. It may well be the most important mode of transmission for other human infections not considered as primarily respiratory. There is published evidence of droplet nuclei transmission of hepatitis B virus, smallpox, rabies, chicken pox, mumps, and measles; as well as tuberculosis."

#### KEY WORDS

airborne  
transmission

### 67 LaForce, FM 1986

Airborne Infections and Modern Building Technology

*Environ International.* 12:137-146.

Discusses various organisms, water cooling systems, and patient isolation. New technology tries to guarantee a controlled internal environment. Airborne agents may be efficiently spread by ventilation systems. Includes a diagram of a typical ventilation unit. Viruses spread mostly from person-to person rather than from contaminated cooling towers, air ducts, outside air brought in, or internal construction. Control of airborne infections is largely an effort at identifying and controlling reservoirs of infection. This includes regular biocidal treatment of cooling towers and evaporative condensers and identification and isolation of patients with disease that may be spread via the airborne route.

#### KEY WORDS

airborne

### 68 Langmuir, A D 1980

Changing Concepts of Airborne Infection of Acute Contagious Diseases: A Reconsideration of Classic Epidemiologic Theories.

*Ann NY Acad Sci.* Vol. 353. Airborne Contagion. ed. Kundsln, R B pp. 35-44

During the preceding 15 years, major programs were launched against smallpox, measles, and rubella. In this paper the author endeavors 1) to recall the prevailing attitudes among epidemiologists at the time these programs were started; 2) to reexamine the scientific validity of some of the theories that we so blithely accepted at the time; and 3) to appraise what we think we have learned from our experiences over these 15 years.

#### KEY WORDS

transmission

### 69 LeClair, JM Zala, JA et al. 1980

Airborne transmission of chicken pox in a hospital.

*N Eng. J of Med.* 302: 450-453.

This article describes "an epidemic of chicken pox which occurred in a pediatric hospital in which airflow and epidemiologic studies document transmission by an airborne route." One three year old girl developed chicken pox while in the hospital and receiving immunosuppressive drugs. Ten days after her death, another case and then several more occurred. Blueprints of the ventilation system were examined, velocity of air, cross ventilation and the room HVAC systems were evaluated. Tracer studies using sulfuric acid smoke puffs, oil of wintergreen, and sulfur hexafluoride were done. Airborne spread of the virus by droplet nuclei is strongly implicated by the results. Details of the buildings air flow are included.

#### KEY WORDS

airborne  
transmission

### 70 Linnemann, CC Jaffa, R et al. 1984

Risk of Infection Associated with a Wastewater Spray Irrigation System Used for Farming.

*J of Occ Med.* 26(1):41-4

Workers at a land application system involving low-pressure spray irrigation of corn field with waste water were followed through a growing season to determine if they had an increased risk of infection as compared with a control population who had no direct exposure. No increase in clinical illness among workers was found, and there was no evidence of increased risk of infection. Spray nozzle cleaners had higher antibody levels against Coxsackie virus, but symptomatic infections with viral excretions were not documented. This study indicates that there is very limited risk of infection among workers using partially treated waste water for agriculture purposes.

#### KEY WORDS

aerosol

## BIBLIOGRAPHY

71 Loosli, CG *et al.* 1943

Experimental Airborne Influenza Infection. I: Influence of Humidity on Survival of Virus in Air.  
*Proc. Soc. Exp Biol Med.* 523: 205-206.

Detailed analysis of the ability of airborne influenza virus to survive and subsequently cause infection depending on the relative humidity. Includes a graph of survival at various humidities, and tables of studies done on this subject.

**KEY WORDS**  
survival

72 May, KR 1945

The Cascade Impactor: An Instrument For Sampling Coarse Aerosols.  
*J Sci. Instruments (London)* 22: 187-195.

This is a description of a new instrument, the May cascade impactor. By means of four progressively finer jets impinging on glass slides in series, the air sample is split up into size-graded fractions in a form suitable for microscopic analysis. The greatest efficiency of sampling is achieved for particles in the range 1.5-50 microns. The size grading greatly facilitates the detailed microscopic examination of heterogeneous samples and in some cases enables approximate size-distributions to be obtained by bulk estimations of the samples without the need for microscopic sizing. Descriptions are given of new methods of dealing with volatile droplets and of analyzing the samples.

**KEY WORDS**

73 May, KR 1966

Multistage Liquid Impinger  
*Bact. Rev.* 30(3): 559-570.

Two types of instruments collect viable airborne particles - Type I project the particles straight onto the surface of a nutrient agar gel; Type II project the particles into liquid where they are broken up into their individual component cells. The liquid is then diluted, plated out, and incubated to give a colony count. This paper describes a new cascade impinger of Type II. The advantages of type II instruments are 1) their ability to cope with high concentrations, 2) they permit counts of several types of organisms, 3) convenient to add nondecaying tracers to, 4) that virus aerosols can be estimated, and 5) that they are more accurate with varying sizes of particles in the stream.

**KEY WORDS**  
aerosol

74 McGarrity, G.J. and Dion A. S. 1978

Detecting of Airborne Polyoma Virus  
*J Hyg Camb* 81: 9-13

Airborne Polyoma virus (PV) was sampled by a high volume air sampler and further concentrated by high speed centrifugation. Assay for PV was by mouse antibody production tests. Assay and air sampling were mentioned and well described. PV can remain viable in bedding for prolonged time and can become airborne when disturbed. The combined use of high volume air sampling and biophysical concentration could and should be used for other viruses of interest.

**KEY WORDS**  
airborne  
sampling

75 McKissick, GE Griesemer, RA *et al.* 1970

Aerosol Transmission of Rauscher Murine Leukemia Virus  
*J Nat Cancer Inst.* 45:625-634

Aerosols of this leukemogenic virus are infectious which emphasizes the potential hazards of lab infections to animals and humans. The virus was experimentally transmitted to BALB/b mice by exposure to an aerosol of Rauscher Murine Leukemia Virus (RMLV). Cagemates also readily developed the disease.

**KEY WORDS**  
aerosol  
transmission



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76 McLean, DM Bannatyne, RM et al. 1967

Myxovirus dissemination by air.  
*Can Med. Assoc. J.* 96:1449-1453.

Myxoviruses including 150 strains of parainfluenza were isolated from nasopharyngeal secretions obtained from young children who were acutely ill. Parainfluenza 1 virus was isolated from air obtained in the vicinity of one of 30 children whose nasopharyngeal secretions yielded this agent. Samples of 150 liters of air were collected by placing an Andersen sampler about 60 cm. from the child's face inside an oxygen tent which surrounded the patient. The findings show that the virus is disseminated in the air.

**KEY WORDS**  
transmission

77 Medical Research Council 1954

Air disinfection with ultraviolet irradiation; its effect on illness among school children.  
Special Report Series no. 283. London England 1954.

**KEY WORDS**

78 Miller, WS and Artenstein, MS 1967

Aerosol Stability of Three Acute Respiratory Disease Viruses.  
*Proc. Soc. Exptl Biol Med.* 125:222-227.

Viruses vary in stability in different humidity conditions, polio is more stable at high relative humidity (RH), influenza and measles at lower RH. Aerosols were produced in a 500 liter rotating drum with a Collison disseminator. Single-stage impactor samplers with particle diameter cut-offs of 1, 3, and 5 microns were employed along with a liquid impinger of the Greenburg-Smith type without size selection for estimation of total aerosol concentration. Includes tables of decay rates in aerosols, and average concentrations of viruses in the aerosols.

**KEY WORDS**  
aerosol  
survival

79 Moe, K. and Harper, GJ 1983

The Effect of Relative Humidity and Temperature on the Survival of Bovine Rotavirus in Aerosol  
*Arch of Virol* 76:211-216.

Bovine rotavirus is stable both at low and high relative humidity. Infectivity is lost more rapidly at high temperature than at lower temperatures.

**KEY WORDS**  
aerosol

80 Monto, AS and Sullivan, KM 1993

Acute Respiratory Illness in the Community. Frequency of Illness and the Agents Involved.  
*Epidemiol Infect.* 110 : 145-160.

This study was of Tecumseh, Mich. over a period of 11 years. Several papers were produced over the course of the study. Adult females had more frequent illnesses than adult males, illness was less common in working women than homemakers. The likely reason for the difference is exposure to school children. Although most infectious diseases are being controlled, acute respiratory disease control has been slower. The authors discuss the seasonality of disease occurrence, the relation of age to frequency of infection, and the various agents involved.

**KEY WORDS**  
respiratory

## BIBLIOGRAPHY

### 81 Morris, Robert, H 1986

Indoor Air Pollution: Airborne Viruses And Bacteria Steps To Protect The Work Force From Infection Due To Airborne Viruses And Bacteria From "indoor Air Pollution"  
*Heating, Piping, Air Conditioning* 58(1): 59-67

This article has lists of various indoor pollutants, for viruses the list includes Coxsackie, influenza, "respiratory virus," and smallpox. There are now over 33 million office workers in US (1986), who are therefore potentially exposed. Included is a discussion of particle size, indoor phenomenon for virus aerosol, and droplet nuclei. Then discusses air handling, has charts of constant volume vs. variable volume and several particulate sizes. Mentions that ventilation rates over the last several decades have been slowly reduced because of energy costs. Also included is information allergic and bacterial cooling tower problems.

#### KEY WORDS

airborne  
virus

### 82 Moser, MR Bender, TR et al. 1979

An Outbreak of Influenza Aboard a Commercial Airliner  
*Am J of Epidemiol* 110(1): 1-6

A jet was delayed on the ground for three hours, no ventilation system was operating. A large outbreak of influenza occurred among the passengers and the crew; those who stayed on the plane the longest had the highest attack rates.

#### KEY WORDS

ventilation  
airborne

### 83 Perkins, JE Bahlke, AM et al. 1947

Effect of ultraviolet irradiation of classrooms on the spread of measles in large rural central schools.  
*Am J Pub Health* 37:529-537.

This study was done in rural central schools to obtain a study population in which the primary contact among children was in the school environment. These analyses of the occurrence of measles in the three centralized rural schools seem to indicate that ultra-violet lights in the classrooms did modify the spread of measles in those classrooms. It is not necessarily recommended however, that ultra-violet lights be routinely installed in classrooms. Further investigation is needed, including observing the effects on other communicable diseases, and in other controlled situations.

#### KEY WORDS

transmission  
airborne

### 84 Petersen, NJ 1980

An Assessment of the Airborne Route in Hepatitis B Transmission  
*Ann NY Acad Sci. Vol. 353* Airborne Contagion Ed. Kundsin, R.B pp. 157-166

Hepatitis B can be transmitted by means another than the traditional blood-borne route. The virus appears to be able to go through mucous membranes; or transmission can be indirect via inanimate surfaces. Since this occurs, airborne transmission of hepatitis B is theoretically possible. Epidemiologic evidence is inconclusive. In the areas investigated in this study, other major routes of transmission that can explain the spread of the disease are invariably present. The authors conclude that airborne virus does not play a major role, and that true airborne transmission is rare. There is a fine line dividing true airborne from contact transmission via droplets; the need for precautions against this spread in laboratories is emphasized.

#### KEY WORDS

airborne  
transmission

### 85 Rapp, ML Thiel, T et al. 1992

Model system Using Coliphage X174 for Testing Virus Removal by Air Filters.  
*Appl. and environ Microbiol.* 58(3):900-904.

Short term (15 minute) and long term (5-6 day) duration tests for determining the efficiency of the removal of phage by air sterilizing filters have been developed. These procedures were sensitive enough to measure a  $10^8$  fold reduction in the number of bacteriophage. A filter commonly used in industrial air sterilizations (Domnick-Hunter Bio-X borosilicate glass) effected a  $10^8$  fold removal of viable phage in both short-term and long-term tests. A prototype low-flux hollow-fiber membrane gave similar results; however a prototype high-flux, hollow-fiber membrane removed only about 99.999% of the bacteriophage in short-term tests.

#### KEY WORDS

filtration

## BIBLIOGRAPHY

86 Remington, PL Hall, WN et al. 1985

Airborne Transmission of Measles in a Physicians's Office  
*JAMA* 253(11):1574-1577.

Three children who arrived 60-75 minutes after a child with measles had departed, developed measles. The index patient was estimated to be producing 144 units of infection per minute while in the office. Discusses coughing, increased warm air recirculation, and low RH that may have increased the likelihood of transmission.

**KEY WORDS**  
airborne  
respiratory  
transmission

87 Riley, E C 1980

The Role Of Ventilation In The Spread Of Measles In An Elementary School  
*Ann NY Acad Sci.* Vol. 353, Airborne Contagion. ed. Kumsin, R B pp. 25-34.

Includes mathematical model of disease spread, as well as figures of 1) pattern of epidemic spread throughout the school, 2) general plan of the school building, 3) variation in amount of make-up air with the outside temperature. Three important exposure sites were characterized quantitatively: the classrooms with infected kids, other classrooms on the same ventilating system, and the school buses. Attempts to establish the actual infective dose are not complete; it may be as small as one or several airborne infectious particles.

**KEY WORDS**

88 Riley, EC Murphy, G et al. 1978

Airborne spread of measles in a suburban elementary school.  
*Am J Epidemiol* 107:421-432.

Epidemic occurred in a school with 97% vaccinated kids, although some were less than 1 year old when originally vaccinated and had not received a booster. Recirculation of the organism by the ventilating system was strongly implicated. The authors calculated that the index case produced approximately 93 units of airborne infection per minute and that the secondaries were less infectious by an order of magnitude. The exceptional infectiousness of the index case, inadequate immunization of many of the children, and the high percentage of air recirculated throughout the school, are believed to account for the extent and sharpness of the outbreak.

**KEY WORDS**

89 Riley, RL 1974

Airborne Infection  
*Am J of Medicine* 57:468-475.

A review article discussing that 1) respiratory secretions from infected patients will contaminate surrounding surfaces and become suspended in the air as tiny droplet nuclei. 2) ultraviolet disinfection is a means of reducing the concentration of viable airborne droplet nuclei without affecting other mechanisms of transmission making this useful in identifying airborne infection. (Mention is made of the school in Pennsylvania protected from measles by UV as discussed by Wells; and a 1957-58 VA hospital with an influenza outbreak showing similar difference in infection rates.) 3) the effect of relative humidity and 4) the author's formula of a mathematical model for a measles epidemic.

**KEY WORDS**  
airborne

90 Riley, RL 1982

Indoor Airborne Infection  
*Environ International* 8:317-320.

Respiratory conditions account for more than 1/2 of all acute conditions. Airborne infection from person to person is an indoor phenomenon. The infectious organisms are dispersed, surviving in the air on the smallest droplets. Droplet nuclei have negligible settling velocity and travel wherever the air goes. Outdoor, dilution is so rapid that the chance of inhaling a particle is minimal. Estimates of the rate of production of infectious droplet nuclei range between 8 and 93 per minute, and the concentration in the air by a measles index case was about 1 quantum per 5 m<sup>3</sup> of air. Control of indoor airborne infection can be approached through immunization, therapeutic medication, and air disinfection with ultraviolet radiation.

**KEY WORDS**  
airborne

## BIBLIOGRAPHY

### 91 Riley, RL 1979

Indoor Spread Of Respiratory Infection By Recirculation Of Air.  
*Bull European de Physiopathol Resp.* 15: 699-705.

This article looks into the possibility of preventing spread of airborne disease in air conditioned buildings. The amount of air recirculated by air conditioning systems increases as the temperature difference between indoor and outdoor air increases and often exceeds 70 percent. Germicidal ultraviolet radiation in central supply ducts seems almost ideally suited for disinfecting recirculated air since it is effective, safe, and cheap. The effectiveness can be predicted to be great at the beginning or a potential outbreak and negligible during an established epidemic. Infection introduced by the air conditioning process might be prevented. Air disinfection could supplement immunization and be cost effective.

**KEY WORDS**  
respiratory  
airborne  
transmission

### 92 Riley RL 1977

Ultraviolet Air Disinfection for Protection Against Influenza.  
*Johns Hopkins Med. J* 140: 25-27

Three converging lines of evidence support the belief that it may be possible, under appropriate circumstances, to interrupt the airborne transmission of influenza by ultraviolet (UV) air disinfection. The lines of evidence are: 1) that influenza is airborne; 2) that UV irradiation of the upper air of a room can provide safe and effective disinfection of air in the lower part of the room; and 3) that epidemic spread of airborne viral infections of humans can be prevented if the population under consideration remains in the UV-protected environment.

**KEY WORDS**

### 93 Roelants, P Boon, B et al. 1968

Evaluation of a Commercial Air Filter for Removal of Viruses from the Air.  
*Appl. Microbiol* 6:1465-1467.

The effectiveness of a commercial absolute air filter for removal of viruses from air was tested with an actinophage, under the usual condition of a laminar airflow clean room. A new method of dry phage dispersion is described. The filter showed an average reduction of 99.996% of airborne actinophage.

**KEY WORDS**  
sampling  
airborne

### 94 Roepke, DC Halvorson, DA et al. 1989

An Adsorption-Elution Technique for the Recovery of Influenza Virus From Water.  
*Avian Dis.* 33: 649-653.

A virus adsorption elution (viradel) procedure was modified and evaluated for the concentration of influenza virus from water in which water fowl reside. Influent pH, flow rate, eluent pH and composition, and a second-step concentration method were evaluated. The viradel procedure in combination with a chicken erythrocyte (red blood cell) adsorption technique resulted in up to 3200 fold concentration of influenza virus from 100 liters of tap water.

**KEY WORDS**  
water  
sampling

### 95 Saiki, RK Gelfand, DH et al. 1988

Primer-directed Enzymatic Amplification of DNA with a Thermostable DNA Polymerase.  
*Science* 239:(4839) :487-491.

A thermostable DNA polymerase was used in an *in vitro* DNA amplification procedure, the polymerase chain reaction. The enzyme simplifies the procedure and enables the amplification reaction to be performed at higher temperatures, significantly improves the specificity, yield, sensitivity, and length of products that can be amplified. Single-copy genome sequences were amplified by a factor of more than 10 million with very high specificity, and DNA segments up to 2000 base pairs were readily amplified. In addition, the method was used to amplify and detect a target DNA molecule present only once in a sample of  $10^5$  cells.

**KEY WORDS**  
virus type

## BIBLIOGRAPHY

96 Sattar, S.A. and Ijaz, MK 1987

Spread of Viral Infections by Aerosols  
*CRC Critical Reviews on Environmental Control*. 17(2):89-131.

Review article including temperature and humidity effects on viral survival, size of aerosols, and generation of aerosols. Concludes that air can be an important vehicle in the spread of many viral infections although it is often difficult to obtain definite evidence of this. Many technical limitations exist in the quantitative recovery of infectious viruses from large volumes of air which has restricted attempts to assess the true role of air in the spread of viral infections. Also, virtually nothing is known about the response of the host to simultaneous exposure to infectious viruses and other airborne contaminants. Continuing pursuit of this field is necessary to develop good air monitoring instruments, and to further study indoor pathogen survival and spread.

### KEY WORDS

survival  
aerosol

97 Schneider, T 1991

Indoor Aerosols: Measurement and Analysis  
*J Aerosol Sci.* 22 ( Suppl 1): S817-S822

Rates of airborne particle removal by surface deposition can be as large or larger than common room ventilation rates making the cleaning of surfaces very important in controlling particle contamination in the indoor air. Airborne particles are removed from the room air by air infiltration, mechanical ventilation and by deposition. This article states that a comprehensive strategy and surface dust monitoring system has been developed. This provides, for the first time, a quantitative method for assessment of the quality of cleaning.

### KEY WORDS

aerosol  
sampling

98 Schulman, JL and Kilbourne, ED 1963

Airborne Transmission of Influenza Virus Infection in Mice  
*Nature* 195: 1129-1132.

Describes a model for the study of transmission of influenza virus infection in mice. This study covered variations in air flow rates, and relative humidity. The authors found that the chance of acquiring airborne infection is inversely related to the rate of ventilation. Higher relative humidities are associated with a lower rate of transmission. Included is a chart of relative humidity versus the product of effective transmission rate times air-flow.

### KEY WORDS

airborne  
transmission

99 Sellers, R.F. Herniman, KAJ *et al.* 1977

The Airborne Dispersal of Foot-and-Mouth Disease Virus from Vaccinated and Recovered Pigs, Cattle and Sheep After Exposure to Infection.  
*Res. in Vet Sci.* 23:70-75.

Virus of foot-and-mouth disease (FMD) was detected in the air on the first day after the animals were exposed; probably due to surface virus on the animals. It was subsequently detected in the air on days 2-7. This is thought to be due to limited multiplication in the respiratory tract and subsequent dispersal in exhaled air. Vaccination of animals before exposure resulted in less or no virus being detected. Control of movement for two weeks after contact with infections is suggested as a means of preventing spread of foot-and-mouth disease in areas that contain vaccinated animals.

### KEY WORDS

airborne

100 Sevolan, M Chamberlain, DM *et al.* 1963

Avian Lymphomatosis. V. Air-borne Transmission.  
*Avian Diseases.* 7: 102-105.

Clinical research was done to test whether air is a carrier of the virus of avian lymphomatosis. Chicks were placed across the room as "samplers" to detect spread of the disease without direct contact. These chicks became infected within 3 weeks of exposure. In contrast controls held in modified Horsfall units showed no sign of disease. This part of the study was a series of 5 trials to investigate whether air was a carrier for the virus of lymphomatosis. Air was circulated from the infected chicks through the Horsfall units before being exhausted. The rate of demonstrable transmission was 24 of 30 chicks after 24 and 40 days of exposure. The disease produced was indistinguishable from the natural infection.

### KEY WORDS

airborne

## BIBLIOGRAPHY

### 101 Shult, PA Polyak, F. et al. 1991

Adenovirus 21 Infection in an Isolated Antarctic Station: Transmission of the Virus and Susceptibility of the population. *Am J Of Epidemiol* 133(6): 599-607.

This study was of the summer personnel's arrivals at an isolated antarctic station with subsequent introduction and spread of adenoviruses. Natural dissemination of viral respiratory illness was shown to occur with surprising difficulty, even with this virus of known epidemic potential in a harsh environment with prolonged gatherings of susceptible personnel.

#### KEY WORDS

aerosol

### 102 Sims, DG 1981

A Two Year Prospective Study of Hospital-Acquired Respiratory Virus Infection on Paediatric Wards *J Hyg. Camb.* 86:335.

In this hospital study 169 cases of respiratory infection occurred over 24 months. Isolation of a virus from the patient occurred in 82 of the cases. Commonest isolations were respiratory syncytial virus (RSV), influenza, parainfluenza, adeno and rhinoviruses. Most acquired infections in toddlers were in those hospitalized in cots, in open wards. Duration of hospital stay had little effect on incidence of disease. Suggestions were made for testing and isolation of, then limiting contact with infected workers. However, it is noted that parents and friends also visit and are sources of many viruses.

#### KEY WORDS

respiratory  
transmission

### 103 Sorber, CA Bausum, HT et al. 1974.

An Assessment Of A Potential Virus Hazard Associated With Spray Irrigation Of Domestic Waste Water. in *Virus Survival in Water and Wastewater Systems* ed. JF Malina Jr. & BP Sagik.

Spray irrigation with incompletely treated sewage has been associated with a number of disease outbreaks.

#### KEY WORDS

transmission  
airborne  
water

### 104 Spendlove, JC and Fannin, KF 1982

Chapter 12 *Methods of Characterization of Virus Aerosols*  
*Methods in Environmental Virology.* Gerba CP, and Goyal, SM eds. New York, Dekker Inc.

The authors state the basic theory that droplets are naturally aerosolized, then evaporate to a dried residue which is termed a droplet nucleus. Methods of study of sizes of particles, sampling techniques and apparatus are discussed. Includes figures, pictures and diagrams of samplers. Numerous references are included.

#### KEY WORDS

aerosol  
sampling

### 105 Spendlove, JC and Fannin, KF 1983

Source, Significance, and Control of Indoor Microbial Aerosols: Human Health Aspects  
*Public Health Reports.* 98(3):229-244.

Indoor aerosols place human occupants at greater risk because an enclosed space confines and protects the aerosol and can give extended doses. This review article gives characteristics of various indoor microbial aerosol sources, significance of these aerosols to the health of the human occupants of these indoor areas, and state-of-the-art methodology for their control.

#### KEY WORDS

aerosol

## BIBLIOGRAPHY

### 106 Strelfel, AJ 1991

Ventilation for the Immune Compromised Patient  
ASHRAE Hospital Design Conference

Discusses the prevention of spread of airborne viral particles. Includes a list of infectious diseases requiring special ventilation. Air filtration is effective in preventing large numbers of airborne particles from entering the susceptible patient environment. Optimal air changes per hour require a balance between control of potential infection and patient comfort.

#### KEY WORDS

ventilation

### 107 Subcommittee for the evaluation of 1947

Present Status Of The Control Of Airborne Infections.  
*Am J Public Health* 37: 13-22.

The authors make five points to summarize their evaluation of methods to control airborne transmission of disease: 1. Oiling floors, blankets and bedding helps. 2. Air disinfection ventilation, ultra-violet (UV), and glycol vapors are useful, 3. One can't compare glycol and UV, 4. General use of UV and vapors not justified at present - (1947). 5. NO justification for use of UV etc., in homes, offices or public areas.

#### KEY WORDS

survival  
airborne

### 108 Suptel, EA 1963

Pathogenesis of Experimental Coxsackie Virus Infection: Distribution of Coxsackie Virus in Mice After Air-borne Infection  
*Acta Virol* 7:61-66

This article is part of a study to reproduce the natural disease in a laboratory setting. Air borne infection was performed in a hermetically closed plexiglass chamber with a 40 liter working capacity at 20-22° C temperature and 68-73% RH. Newborn mice were exposed by being placed in cages that were hung in this chamber. The dose inhaled was 13,000 intraperitoneal LD<sub>50</sub>. The mice were examined, and virus then titrated and injected into more one day old mice. Typical clinical signs resulted from the airborne infection, the lungs were the initial site of multiplication.

#### KEY WORDS

aerosol

### 109 Thorne, HV and Burrows, TM 1960

Aerosol Sampling Methods For The Virus Of Foot-and-Mouth Disease And The Measurement Of Virus Penetration Through Aerosol Filters.

*J Hyg Camb.* 58: 409-417.

Efficient sampling of FMD virus can be accomplished by slight modification of standard aerosol methods. The apparatus for producing and sampling aerosols by impingers is shown in Fig. 2. The virus penetration through filter materials was then determined. Single and multi-jet liquid impingers and membrane filters were found to be efficient sampling devices. Attaclay, an adsorbent, improved the detection of virus by concentration.

#### KEY WORDS

aerosol  
sampling  
filtration

### 110 Tyrrell, DAJ 1983

Rhinoviruses and Coronaviruses - Virological Aspects of their Role in Causing Colds in Man.  
*Eur. J Respir Dis* 64(Suppl. 128): 332-335.

Rhinoviruses are picomaviruses (very small viruses) that cause colds. They are temperature sensitive, very small at 27 nm, and highly adapted to grow in respiratory epithelium. Coronaviruses are structurally quite different, being enveloped viruses, but are also adapted to grow in respiratory epithelium and also cause colds. They are larger viruses with a size range of 80-160 nm. Estimates are that 20 to 35% of common colds may be due to rhinoviruses and 10% may be due to coronaviruses. It was found that the real proportions may be higher than these since it is not always possible to isolate the virus from truly infected patients.

#### KEY WORDS

respiratory  
virus

## BIBLIOGRAPHY

### 111 Tyrrell, DAJ 1967

The Spread of Viruses of the Respiratory Tract by the Airborne Route  
*Airborne Microbes* 17th symposium of the society for general microbiology Cambridge

Types of viruses involved in respiratory disease are covered. People average 2 to 10 respiratory illnesses per year. Bacteria are unimportant in initiation, but may be in sequelae. Respiratory disease may be transmitted by direct prolonged contact, and often by those who seem well. The article goes on to cover sites of recovery, dispersal of viruses and particles, and loss of infectivity in air over time.

**KEY WORDS**  
aerosol

### 112 U.S. Dept. HEW 1992

Current Estimates from the National Health Interview Survey, 1991  
*Vital and Health Statistics* Series 10 No. 184

Includes estimates on incidence of numerous acute conditions, episodes of persons injured, disability days, physician contacts, prevalence of chronic conditions, limitation of activity, hospitalizations, and assessed health status.

**KEY WORDS**  
respiratory

### 113 U.S. Dept. HEW 1982

Current Estimates from the National Health Interview Survey, 1981  
*Vital and Health Statistics*

Includes estimates on incidence of numerous acute conditions, episodes of persons injured, disability days, physician contacts, prevalence of chronic conditions, limitation of activity, hospitalizations, and assessed health status.

**KEY WORDS**  
respiratory

### 114 Vincent, J.H. 1989

*Aerosol Spectrometers*

In: *Aerosol Sampling: Science and Practice*. John Wiley & Sons, New York.

Sampling instruments (called aerosol spectrometers) that are capable of classifying particles into narrow ranges of diameter are described and discussed. These include centrifuge-type aerosol spectrometers, cascade impactors and personal inspirable dust spectrometers, etc.

**KEY WORDS**  
sampling  
aerosol

### 115 Wallis, C. Melnick, J. L. et al. 1985

Method for Detecting Viruses in Aerosols

*Applied and Environ Microbiol* 50(5): 1181-1186

Describes the development of a simple method using poliovirus as a model for recovering human enteric viruses from aerosols. Filterite filters moistened with glycine buffer were used to adsorb aerosolized poliovirus. The construction and operation of a filtration device for measuring the amount of virus aerosolized during toilet flushing was described (Fig 1). Virus was detected regularly in aerosols produced by flushing when  $3 \times 10^8$  PFU of poliovirus were present in the toilet bowl. This is an amount that could be excreted by infected persons.

**KEY WORDS**  
aerosol



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116 Warshauer, DM Dick, EC *et al.* 1989

Rhinovirus Infections In An Isolated Antarctic Station: Transmission Of The Viruses And Susceptibility Of The Population. *Am J Epidemiol* 129(2):319-340.

Rhinoviruses were the cold viruses found in this particular year. The research showed that only a small percent of personnel become ill with the introduced viruses. In brief, this isolated polar group was not especially susceptible to respiratory illness, and virus movement through the group was deliberate. Includes a description of the housing and buildings where higher or lower rates of transmission occurred, graphs of infection rates among incoming personnel, and of the spread of colds throughout the station.

### KEY WORDS

airborne  
transmission

117 Washam, CJ Black, CH *et al.* 1966

Evaluation Of Filters For Removal Of Bacteriophages From Air. *Appl. Microbiol* 14: 497-505.

Glass wool, nonabsorbent cotton, fiberglass filter medium and a commercial absolute filter were tested for effectiveness in removing aerosolized bacterial viruses under low flow rate and high flow rate conditions. The authors suggest use of a stainless-steel filter of simple design, fitted with three layers of fiberglass mediums which was found to be greater than 99.999% efficient in removing high concentrations of aerosolized bacteriophages from air moving at a low flow rate (1 ft<sup>3</sup>/min.), on pressure-vacuum tanks in the fermentation industry. Other uses in hospitals, culture labs, and within the food service industry are suggested.

### KEY WORDS

airborne

118 Wells, WF 1955

Airborne contagion and air hygiene. Cambridge, Harvard

The entire book is concerned with droplet nuclei theory. Part One deals with physics, atomization, evaporation, condensation, aerodynamics, biology, viability of parasites, biochemistry, physiology, and response to inhalation of these nuclei. Part Two covers air hygiene in such areas as sanitary ventilation, examples of air hygiene, an essay on dust borne infection, and the ecology of droplet infections.

### KEY WORDS

airborne

119 Wells, WF 1948

Sanitary ventilation.

*Am J Public Health* 38: 775-780.

A discussion of the control initially of bacterial contamination in air, to control the spread of disease, now extended to viruses as well. Previous control was only through quarantine, now ventilation can be considered as a control measure also. A diagram of "threshold sanitary ventilation" is included showing the links of the chain of infection both with and without irradiation in the room and different amounts of ventilation. Suggests that a survey of the atmospheres being breathed by various groups is necessary to evaluate methods of control.

### KEY WORDS

airborne  
transmission

120 Wells, WF and Brown, HW 1936

Recovery of influenza virus suspended in air and its destruction by ultraviolet radiation.

*Am J Hyg.* 24(2):407-413.

An attempt to confirm by means of animal inoculation the recovery of the influenza virus from air, after suspending microorganisms in a steel chamber holding 200 cubic feet of air. Potency of the virus preparation was determined by ferret inoculation. The influenza virus was recovered from the air by drawing samples through sizzized tubes into two Wells air centrifuges 1) directly and 2) through a chamber where the air was irradiated with UV. Final results included that influenza was recovered after air suspension of at least 30 minutes, and UV destroyed the infectivity.

### KEY WORDS

survival  
sampling  
airborne

## BIBLIOGRAPHY

### 121 Wells, WF Wells, MW *et al.* 1942

The Environmental Control Of Epidemic Contagion . An Epidemiologic Study Of Radiant Disinfection Of Air In Day Schools. *Am J Hyg* 35:97-121.

These experiments were undertaken to test the hypothesis that the confined atmospheres of our buildings constitute the vehicle for the epidemic spread of contagion. Two schools were used to compare the effects of UV irradiation on spread of disease. The conclusions: epidemic contagion is spread through the medium of confined atmospheres, and it can be prevented by radiant disinfection of air. The suggestion is made to use ultraviolet irradiation in army barracks, schools, and other areas of overcrowding. Includes details of epidemics of various diseases and their spread over 1937-1941 in two schools systems and discussion of the installation of the UV lights. Also notes that irradiation improves the 10 air exchanges per hour of winter to the equivalent of 100 per hour in bacterial elimination.

**KEY WORDS**  
transmission

### 122 Williams, REO 1960

Intramural Spread of Bacteria and Viruses in Human Populations.

*Ann Rev Microbiol.* 14: 43-64.

This is a review article on the spread of microbes by the airborne and contact routes. Most studies of airborne spread are unsatisfactory because there is a lack of applicability to the general population. Includes discussion of articles on: various samplers available in 1960, survival of microbes in the environment, laboratory studies of air disinfectants, experiments on dispersal of microbes from people, introduction to the new host, and epidemiological investigations.

**KEY WORDS**  
transmission

### 123 Willmon, TL Hollaender, A *et al.* 1948

Studies Of The Control Of Acute Respiratory Diseases Among Naval Recruits: A Review Of A Four-year Experience With Ultraviolet Irradiation And Dust Suppressive Measures. 1943-1947

*Am J Hyg* 48: 227-232.

Irradiation was done in half the barracks, the others being left as controls, in several regiments of 1000 to 5000 men. Measurements were made to keep the UV levels below the toxic level. Respiratory admission rates from the irradiated groups were lower than from the control groups. In some cases this reduction was very minor, in others 20-25% reductions in disease rates occurred. Oiling of the floor was done in some areas to see if this had an effect on disease transmission; results were inconclusive. Irradiation in combination with oiling gave the best results, but not much different than UV irradiation alone.

**KEY WORDS**  
survival

### 124 Winkler, WG 1968

Airborne Rabies Virus Isolation.

*Bull of Wildlife Disease Assoc.* 4:37-40.

This article reports the results of a study using mechanical air samplers [AGI-4 and LYAS] to sample airborne rabies virus, present in the cave air. Only an electrostatic precipitation sampler [LYAS-L] worked; probably because of its greater capacity to process large amounts of air in a given period of time. The author felt this was a better method than using susceptible animals as samplers.

**KEY WORDS**  
airborne

### 125 Wolf, HW Skally, P *et al.* 1967

Sampling microbiological aerosols.

Public Health Monograph 60 US government Printing Office, Washington, DC #683.

53 page monograph on sampling, concentrates on bacteria, but also mentions viral aerosol sampling. Pictures of lots of kinds of samplers, discussion of basic methods of sampling, operation methods, selection of samplers, and descriptions. Produced by the Technical Development Laboratories, and US Army Chemical Corps.

**KEY WORDS**  
aerosol  
sampling

## BIBLIOGRAPHY

126 Wolfe, LG Griesemaer, RA *et al.* 1968

Experimental Aerosol Transmission of Yaba Virus in Monkeys  
*J Nat Cancer Inst.* 41:1175-1195

Yaba virus infection led to tumor formation after aerosol transmission. One monkey was clinically ill, several others had lesions visible only on pathological examination. Horizontal transmission to cage mates was NOT observed. The dose of Yaba virus was not correlated with the susceptibility of individual monkeys to aerosol transmission. There is an obvious concern with the possible hazard to humans working with this or other tumorigenic viruses that may become aerosolized.

**KEY WORDS**

aerosol

127 Zimmerman, N.J. Reist, P. C. *et al.* 1987

Comparison of Two Biological Aerosol Sampling Methods  
*Applied and Environ Microbiol* 53(1): 99-104.

Two biological aerosol samplers the May three stage glass impinger (new) and the Andersen two-stage microbial impactor were compared. Samples were collected during a simulated waste water spray irrigation dispersion. Although the May sampler reports 82% of the Andersen values, the correlation between the two samplers is good with an  $r^2 = 0.84$ . This comparison indicates that although there are differences between the two samplers, they do give comparable results. Also, when both are used in a sampling program they tend to complement each other.

**KEY WORDS**

aerosol

## Appendix II Surveys

INTERVIEWER NAME: \_\_\_\_\_

DATE: \_\_\_\_\_

**1. Project Description**

This research project is funded by the American Society of Heating, Refrigerating, and Air-Conditioning Engineers, Inc. (ASHRAE) and is entitled "Investigate and Identify Means of Controlling Virus in Indoor Air by Ventilation, Filtration or Source Removal." The project involves an extensive literature search for information on exposure to virus aerosols in commercial buildings, including a review of health effects, aerosol sources, means of transmission, methods of aerosol measurement and characterization, and techniques for controlling individual exposure. It is recognized that much of the current knowledge of and research on airborne viral aerosols presently lies within research institutions. Thus, we have identified a number of investigators and consultants who we hope will provide additional insight in the subject areas mentioned above. We thank you in advance for your interest and cooperation with this survey.

**2. Basic Information about Interviewee:**

Title: \_\_\_\_\_

Affiliation &amp; Address: \_\_\_\_\_

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Phone #: \_\_\_\_\_

Fax #: \_\_\_\_\_

e-mail address: \_\_\_\_\_

In order to help us with the documentation of this survey, we would appreciate a copy of your CV or resume. Please send (or fax) to: Lisa Brosseau, Sc.D., University of Minnesota, Division of Environmental and Occupational Health, School of Public Health, Box 807 Mayo, 420 Delaware Street SE, Minneapolis, MN 55455. FAX: 612-626-0650. Thank you.

**3. Area(s) of Expertise:**

Please check all areas which you feel are applicable to your specific interests and expertise:

Area of Interest or Expertise	Specific Information and Comments
<input type="checkbox"/> Viral Aerosol Sampling	
<input type="checkbox"/> Viral Aerosol Characterization	
<input type="checkbox"/> Viral Aerosol Sources	
<input type="checkbox"/> Viral Aerosol Transmission	
<input type="checkbox"/> Viral Aerosol Health Effects	
<input type="checkbox"/> Viral Aerosol Control	

**4. Type(s) of Work**

Please check those descriptions which best identify the type(s) of work you do in this field:

Type of Work	Specific Comments and Information
<input type="checkbox"/> Basic Research	
<input type="checkbox"/> Applied Research	
<input type="checkbox"/> Private Consulting	
<input type="checkbox"/> Professional Consulting	

**5. Specific Questions**

Please indicate your response to any of the questions which are applicable to your area(s) of expertise:

**A. Do you perceive viral health threats from aerosols in:**

- |                                  |                              |                             |
|----------------------------------|------------------------------|-----------------------------|
| Hospitals                        | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| Surgery Suites                   | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| Office Buildings                 | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| Public Buildings (schools, etc.) | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| Other (please list)              | _____                        |                             |
|                                  | _____                        |                             |
|                                  | _____                        |                             |

**B. What, in your opinion, are the most problematic airborne viruses found in commercial indoor settings?**

**C. What are the principal sources of the airborne viruses described in (B) above?**



D. What methods have you used to sampling airborne viruses? Describe the advantages and disadvantages of each method.

E. What have you found concerning "typical" airborne concentrations of viral aerosols?

F. What methods of analysis and characterization have you used (or are you investigating) for airborne viruses?

G. Have you ever used ventilation to control the spread of airborne viruses?

Yes

No

If yes, please describe:

H. Have you ever used the technique of source removal to control the spread of airborne virus?

Yes

No

If yes, please describe:

H. Have you ever applied filtration as a means of controlling airborne viruses?

Yes

No

If yes, please describe:

I. Are there any other methods of airborne virus control you have tried?

Yes

No

If yes, please describe:

**J. What do you see as future directions for viral measurement and/or control in commercial buildings? (Or more generally, what, in your opinion, needs to be done to advance the field of viral aerobiology?)**

**K. Are there other investigators or consultants you would recommend we contact with respect to any of the topics mentioned above?**

**List of Interviewees:**

1. **Dr. Kerby F. Fannin**  
**Life's Resources, Inc.**  
**Addison, MI 49220**
  
2. **Dr. Syed A. Sattar**  
**Microbiology and Immunology**  
**University of Ottawa**  
**School of Medicine**  
**Ottawa, ON, K1H 8M5**  
**Canada**
  
3. **Dr. Christopher Cox**  
**Ministry of Defense**  
**Chemical Defense Establishment**  
**Porton Down**  
**Salisbury Wiltshire SP4 0JQ**
  
4. **Dr. Elliot C. Dick**  
**Department of Preventive Medicine**  
**University of Wisconsin**  
**517 Stovall Building**  
**465 Henry Mall**  
**Madison, WI 53706**
  
5. **Dr. Philip Morey**  
**Clayton Environmental Consultants**  
**1729 Christopher Lane**  
**Norristown, PA 19403**
  
6. **Dr. John Hierholzer**  
**Respiratory and Enteric Viruses Branch**  
**Division of Viral and Rickettsial Diseases**  
**Center for Infectious Diseases**  
**Centers for Disease Control**  
**1600 Clifton Road NE**  
**Atlanta GA 30333**

**Dr. Philip Morey  
Clayton Environmental Consultants  
1729 Christopher Lane  
Norrstown PA 19403  
215-630-4657  
215-630-4684 (FAX)**

### **3. Areas of Expertise**

**Viral Aerosol Sampling--one or twice has performed field measurements using a method designed by Hierholzer at CDC. Used impaction onto a culture plate, stripped off 1 mm culture and sent to Hierholzer for analysis.**

### **4. Types of Work**

**Professional Consulting**

### **5. Specific Questions**

**A. Perceives viral health threats in hospitals, office buildings and public buildings. In the latter two the problem is primarily with the common cold, due to ventilation efficiency problems (see 1989 Janssen article in the ASHRAE Journal).**

**B. The common cold is the most problematic airborne virus in commercial indoor settings.**

**C. Humans are the principal source of the common cold.**

**D. Not answered.**

**E. Cannot say what are "typical" airborne concentrations; work needs to be done to establish "baseline" data.**

**F. Used the CDC Hierholzer method (see ASTM reference).**

**G. No.**

**H. Yes, "sick people should stay home until they are better."**

**H. No.**

**I. No.**

**J. Recommends something like Dr. Dick's work: measure airborne virus levels, background levels, and levels when "sick people" are present. Use**

detection methods other than culture (perhaps membrane filter with radioassay or gene probes?). Human productivity is the biggest issue, believes EPA should fund academic research in these areas.

**Dr. John Hierholzer**  
**Centers for Disease Control and Prevention**  
**Retired as of 6/30/93**

**3. Areas of Expertise**

Viral Aerosol Sources  
Viral Aerosol Transmission  
Viral Aerosol Health Effects

**4. Types of Work**

Basic Research  
Applied Research

**5. Specific Questions**

A. Perceives viral health threats from aerosols in office and other public buildings. Also mentioned airplanes.

B. The most problematic airborne viruses in commercial indoor settings are parainfluenza, influenza, enteroviruses, and rhinoviruses.

C. Principal sources of these viruses are people (coughing and sneezing).

D. Not answered.

E. Not answered.

F. Has used tissue culture as method of analysis and characterization of viruses.

G. Has employed ventilation to control spread (opening windows).

H. No.

H. Has not used filtration as control technique, but favors its use over UV lights.

I. No.

J. Future directions include: limitation of spread by using better air circulation. Need better, more specific epidemiologic studies.

K. Not answered.

**Dr. Syed A. Sattar**  
Department of Microbiology and Immunology  
University of Ottawa, School of Medicine  
Ottawa, Ontario, K1H 8M5, CANADA  
613-787-6615 (Fax=613-738-5379)

**3. Area of Expertise:**

1. **Viral aerosol sampling-available technology for large volume sampling (thousands of liters of air) needs further improvement. It is crucial handicap. Virus recovery efficiency should be high.**
2. **Viral aerosol characterization: For aerosol size, 6-stage Anderson sampler is one of the standards and does a good job of separating aerosols according to size especially those that belong in the inhalation range.**
3. **Viral aerosol sources: none**
4. **Viral aerosol transmission: none**
5. **Viral aerosol health effects: none**
6. **Viral aerosol control: Hope to get into it. Physical (filtration) and chemical methods can be tried. UV was used in 1930's for disinfection of air in school bldgs. UV technology has improved over the years but has not been investigated for air disinfection.**

**4. Type of Work:**

1. **Basic research: Effect of relative humidity, temperature, and suspending media on virus survival in aerosols. This has been done by aerosolizing mixtures of viruses using poliovirus as a reference.**
2. **Applied Research: Interested in using this information to determine the mechanism of virus survival in aerosols and eventually to inactivate them.**
3. **Private consulting: Provincial Government of Alberta wanted to set up a lab on aerobiology.**
4. **Professional consulting: Educating people about viral aerobiology.**



**5. Specific questions:**

**A. Hospitals:** Long list of viruses including measles, flu, rota, entero, Norwalk, rubella.

Surgery suites: Papilloma virus (cauterization of warts) inhalation by surgery team; HIV in blood has been suspected (researcher at Stanford U) but is difficult to prove.

Office Bldg: Respiratory and enteric viruses.

Elem. school: Rotavirus

Middle school: Any virus

College dorm: Measles

Day care: Norwalk, respiratory

Research lab: Whatever they are working on.

Animal Housing: Hemorrhagic viruses are asymptomatic in rats but can be passed in feces which can be aerosolized after drying.

**B. Problematic viruses:** rubella, flu, Norwalk, rhino, possibly rota in younger population.

**C. Sources:** Nasal secretions  
Toilet flushing (enteric viruses)  
Changing of diapers in day care, hospitals, nurseries, invalids.

**D. Methods used by you:**

1. Anderson sampler: Simple in design. Very good for sizing but not too good for aerosol. For virus collection, use Hank's and gelatin in Petri plates. Melt gelatin at low temp and use liquid for virus isolation. Run for 1-5 minutes.
2. All glass impinger: Simple to use and is efficient for collecting inhalation sized aerosols. Aerosols of  $\leq 0.1 \mu\text{m}$  may not be captured well (they usually bounce back). To avoid this problem, you can use pre-impinger. Collecting fluid is a protein solution e.g., tryptose phosphate broth, BSA, MEM with FBS. Can not run for more than 1-5 min because the fluid will evaporate and the viruses already collected may get inactivated. The distance between the tip of the orifice and the surface of the media is critical.

**E. Typical virus concentration:** no idea.

**F. Methods of analysis and characterization:**

1. To differentiate between biological decay and physical settling of large sized particles, they have aerosolized radiolabelled virus plus a fluorescein dye (sodium fl or rhodamine) and then have measured virus, dye, and radioisotope concentrations.
2. Virus detection is by cell cultures.
3. Henderson apparatus allows you to do studies in small lab animals. This is basically a tube with ports on sides; the noses of mouse are fastened in these ports; the aerosols are generated that pass thru this corridor where mice can inhale them.

**G. Used ventilation control? No**

**H. Used source removal? No**

**H. Filtration? Indirectly used HEPA filter in biosafety cabinets. Also use HEPA filters in the room in which they do their aerosolization experiments.**

**I. Any other method? No**

**J. Future:**

1. Methodology for sampling large air volumes. It should be simple, inexpensive, with a decent virus recovery efficiency (30-40% OR more). These days, sensors for gas, humidity, and temp control are available. It may be appropriate to devise an equipment that can collect aerosols as well as characterize the air simultaneously (physical and chemical).
2. Urgent need for air decontamination methods especially in commercial bldgs where air is recycled.

**K. Other investigators? None**

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**Note 1: International Society of Aerobiology studies pollen and fungal spores but not infectious aerosols. They also have a journal.**

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**Note 2: Lisa: Everybody I talked to, wants a copy of the report after we generate it. Please keep in mind so that we can send it to them when it is ready and appropriate.**

**Sagar**

Dr. Kerby F. Fannin  
Life's Resources Inc.  
Addison, MI 49220 (50 miles SW of Ann Arbor)  
517-547-7494 (Fax=517-547-5444)

**3. Area of Expertise:**

1. Viral aerosol sampling-Methods for detecting viruses in aerosols.
2. Viral aerosol characterization: yes
3. Viral aerosol sources: Human and environmental sources (sewage and sludge).
4. Viral aerosol transmission: How aerosols reach from source to target.
5. Viral aerosol health effects: Effect of contaminanats on exposed parsons in work place and hospital settings.
6. Viral aerosol control: Develop methods for control. Equipment to capture virus and then destroy. Needed a method to remove virus from air stream and then to increase its exposure to UV light for inactivation. Hepa filters are good because they can trap viruses on account of their particle-association.

**4. Type of Work:**

1. Basic research: No
2. Applied Research: Industrial applications. Removal of phages from pharmaceutical (fermentation) industries.
3. Private consulting: Hospitals and bldg owners (Health Department bldgs where they were owned by somebody else). Routine virus monitoring is expensive. Frequently you get negative results. Monitor CO<sub>2</sub>, bacteria, and particles to establish conditions that may be conducive to high virus density (sentinel monitoring). Underlying problem is low ventilation rate and high population of occupants/visitors. Low conc.-of viruses is also important because of low MID<sub>50</sub>. We use cyclone scrubbers with recirculation of collecting fluid for a day. Electrostatic methods are now being tried.
4. Professional consulting: No

**5. Specific questions:**

A. Hospitals: Flu, Norwalk, RSV, CMV, rhino, other resp viruses

Surgery suites: Not clear. HIV is controversial. Opening of chest cavity may create large droplets that may contain organisms. Emergency surgery and attending surgery may be important.

Office Bldg: Respiratory viruses.

Public Bldg: Yes

B. **Problematic viruses:** respiratory viruses (flu, rhino, RSV)  
enteric viruses in nurseries, day care

C. **Sources:** Humans, children. Mode of transmission is respiratory.

D. **Methods used by you:**

1. Anderson Impactor: Very simple but requires some effort in getting the virus off the plate. Sensitivity is low. 28.3 l/min is not a very large sample.
2. All glass impinger: Low sensitivity.
3. High volume electrostatic precipitation: maintaining aseptic conditions is difficult.
4. Cyclone scrubbers-high volume. Sampling rate of 900 l/min for 30 min. Collection fluid is aerosolized in the throat of the scrubber. This causes the particles to grow in size. Either use 100ml once through or use 100ml as recirculating fluid. Correct for evaporation and slippage (fluid loss). Fluid should be of good wetting capacity.
5. Other plating methods are needed that can maintain aseptic conditions and high volumes.

E. **Typical virus concentration:** Mainly isolated enteric viruses from outdoor situations. Fairly low amount. Hard to say what is typical.

F. **Methods of analysis and characterization:**

1. MPN for enrichment and then either MPN or plaquing.
2. Virus detection is by cell cultures (BGM). Plaquing is not efficient.
3. Contaminants is a problem.

G. Used ventilation control? Recommended to many. Other indicators can be used e.g., ventilate to  $\leq 1000$  ppm of CO<sub>2</sub> (Use heat recovery ventilator that is controlled by certain parameters).

H. Used source removal? Decrease number of people or people with problems. Bacterial viruses are usually in air ducts. Clean by vacuum and brushes.

H. Filtration?

HEPA filters and UV or ozone.

Filters with lower pressure drop (polarized fiber filter) and ozone

Experimental-tungsten filament captures viruses and then inactivates; not very efficient; abandoned.

I. Any other method?

1. Air moving thru UV

2. Incineration in industry. Pass air thru a small orifice and then heat it. Limited by air flow across the heater.

J. Future:

1. Not everybody wants to measure viruses. Important for research.

2. Better methods of collection and detection. Sensitive instrumentation.

3. Control: interrupt transmission and decrease exposure by reducing levels of contaminants; involves reduction and not elimination. Concept of plumes of clean zones e.g., separation of clean and non-clean areas. Clean areas to be used by susceptible people. Involves virus elimination.

K. Other investigators? None

**Dr. John Hierholzer**  
**Centers for Disease Control and Prevention**  
**Retired as of 6/30/93**

**3. Areas of Expertise**

Viral Aerosol Sources  
Viral Aerosol Transmission  
Viral Aerosol Health Effects

**4. Types of Work**

Basic Research  
Applied Research

**5. Specific Questions**

A. Perceives viral health threats from aerosols in office and other public buildings. Also mentioned airplanes.

B. The most problematic airborne viruses in commercial indoor settings are parainfluenza, influenza, enteroviruses, and rhinoviruses.

C. Principal sources of these viruses are people (coughing and sneezing).

D. Not answered.

E. Not answered.

F. Has used tissue culture as method of analysis and characterization of viruses.

G. Has employed ventilation to control spread (opening windows).

H. No.

H. Has not used filtration as control technique, but favors its use over UV lights.

I. No.

J. Future directions include: limitation of spread by using better air circulation. Need better, more specific epidemiologic studies.

K. Not answered.

**Dr. Elliot C. Dick**  
**Department of Preventive Medicine**  
**University of Wisconsin**  
**517 Stovall Building**  
**465 Henry Mall**  
**Madison, WI 53706**  
**608-262-2638**  
**608-262-3257 (FAX)**

### **3. Area(s) of Expertise**

**Viral Aerosol Sources**  
**Viral Aerosol Transmission**  
**Viral Aerosol Health Effect**  
**Viral Aerosol Control**

### **4. Type(s) of Work**

**Basic Research**  
**Applied Research**  
**Private Consulting**  
**Professional Consulting**

### **5. Specific Questions**

**A. Most of his work has been with rhinoviruses, some influenza virus. He perceives threats from these viruses particularly in offices and public buildings.**

**B. The most problematic airborne viruses are probably influenza and measles.**

**C. Sources are humans.**

**D. No sampling for airborne viruses.**

**E. Not applicable.**

**F. Not applicable.**

**G. Has not used ventilation to control virus spread, but has demonstrated that rhinovirus transmission occurs primarily by the airborne route.**

**H. Has demonstrated that isolation of donors (infected individuals) from recipients (uninfected individuals) but continued contact by hands and**

fomites will prevent spread of rhinoviruses. Thus, concludes that rhinovirus transmission occurs primarily by airborne route.

H. Has not used filtration as control method.

I. Yes, has demonstrated that the diligent use of virucidal tissues (containing citric acid and sodium laurel sulfate) by donors will prevent the transmission of rhinoviruses.

J. Future directions for control probably should include ventilation and ultraviolet light.

K. Recommends Drs. Richard Riley (retired) and Chris Cox.



## **Additional Information**

Dr. Dick has conducted research over the past twenty years with human volunteers to investigate how rhinoviruses are spread. Beginning with families on the University of Wisconsin campus, he found that viruses do not spread easily from person to person, even in groups with much close contact. He concluded from this early work that it would be difficult "to protect against respiratory infections using a multivalent vaccine or all-purpose antiviral drugs. For really broad protection, some type of environmental control would seem almost necessary."

Dr. Dick's group also traced the spread of a number of respiratory viruses in the same population, and found only 3 of 14 different rhinovirus (RV) serotypes spread beyond a single family. Thus, it appears that the RV must be a good "spreader" for dissemination. However, Dr. Dick also notes that later research suggests that "actual RV type has (nothing) to do with dissemination, but that severity of illness does."

Dr. Dick's research then focussed on studying human volunteers in controlled environments. Several different experiments were performed using donors (infected individuals) and recipients (uninfected individuals) in small rooms for varying periods of time and performing various activities. Very little infection took place in most of these experiments. Only with married couples where one of the spouses (donor) was shedding lots of virus and the couple spent lots of time together did significant virus transmission take place.

These experiments led to the development of an even more controlled experimental situation, using a 12 x 6 x 3 meter room with donors and recipients monitored continuously for 50- to 700-hr exposures. Individuals generally spent the entire exposure period in the room. The investigators were able to establish a linear correlation between transmission and exposure duration (Figure 10). Further refinements to this model, using a smaller room with all individuals playing poker continuously allowed the investigators to obtain significant transmission in a 12-hr period.

With this final model, Dick et al. then began to investigate methods of preventing transmission. They demonstrated that the use of virucidal tissues could prevent transmission, if used diligently. However, the application of this control technique to the general population does not appear feasible, because most individuals will not be as diligent in their use of such tissues as will experimental subjects. More importantly, however, was the demonstration that it was possible to prevent RV transmission.

Dick's group then used the same poker playing model to investigate the route(s) of transmission of RV. When recipients were prevented from direct

physical hand-to-face contact (by the use of collars or arm braces) no change in transmission rate was seen between restrained and unrestrained groups. This suggested that RV transmission occurred primarily by the airborne route. A further experiment was then designed in which aerosol transmission was blocked by walls and cards, etc. were passed from a donor room to a separate recipient room every hour for 12 hr. No transmission occurred in these latter experiments, confirming the theory that RV transmission is essentially an airborne phenomenon.

Additionally, measurements of RV transmission in an isolated Antarctic station showed that crowding and severe colds were necessary for high transmission rates. When buildings were well-ventilated, however, the incidence of respiratory infection was much lower than in poorly-ventilated buildings. Conversely, however, when well-ventilated buildings experienced crowded conditions, the attack rate increased considerably. Dick hypothesized this was due to rapid dissemination of viral particles throughout the building by the ventilation system.

Dr. Dick concludes from his work to date that it may very well be possible to use air filtration as a means of controlling the spread of rhinoviruses in public buildings. Since airborne transmission appears to be such an important route by which at least some rhinoviruses are passed from one individual to another, he believes that either "careful nasal sanitation with virucidal tissues and/or...purposeful air handling and filtration" may control respiratory virus transmission.\*\*

Dr. Dick is planning to continue his research. In particular, he would like to demonstrate that ventilation can be used to control the spread of rhinoviruses. In addition, he also believes that ultraviolet light may be a useful method of control for the spread of viruses throughout buildings.

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\* Jennings, LC and Dick, EC: Transmission and Control of Rhinovirus Colds. Eur. J. Epidemiol. 3(4) 327-335 (1987).

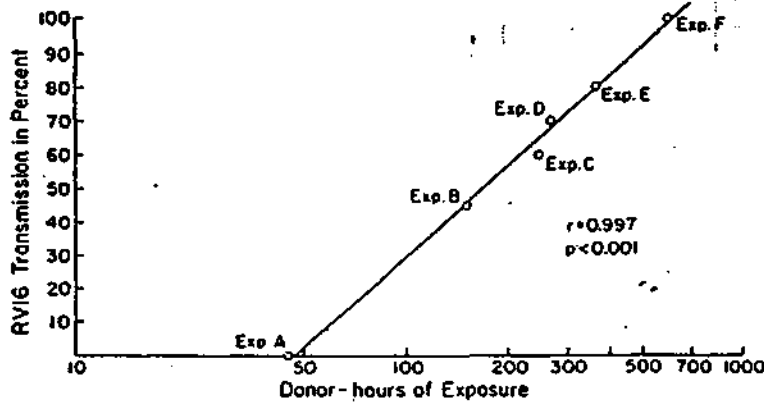


Figure 3. Semi-logarithmic plot of donor-hours of exposure vs. transmission of RY16 between artificially infected donors and susceptible recipients.

From: CK Meschievitz, SB Schultz, and EC Dick: A model for obtaining predictable natural transmission of rhinoviruses in human volunteers. *The Journal of Infectious Diseases*. 150(2):195-201 (1984).

## Summary of Curricula Vitae

Information on professional background was received from four of the six interviewees. These are summarized below:

### 1. Dr. Sattar

Dr. Sattar is a Professor in the Department of Microbiology and Immunology at the University of Ottawa in Ottawa, Canada. He received a masters in microbiology in 1960 from the University of Karachi in Pakistan and a masters and Ph.D. in virology in 1964 and 1967, respectively, from the University of Ottawa. He became a Registered Member of the Canadian College of Microbiologists in 1979. Dr. Sattar has received over 2.2 million dollars in research funds in the past 10 years; he specializes in evaluation of water-borne microorganisms. He has written a book entitled Viruses, Water and Health published in 1978 by the University of Ottawa Press. He has over 80 peer-reviewed publications and abstracts and has delivered 70 invited lectures and papers around the world.

### 2. Dr. Fannin

Dr. Fannin has been the president of Life's Resources, Inc. in Michigan since 1983, where he specializes in the development and implementation of methods to identify and control sources of environmental contaminants. He publishes a newsletter: Residential and Institutional Hygiene. His work has included evaluating methods for detecting and controlling sources of biological and chemical contamination in buildings, environmental emissions of thermal gasification systems, virus contamination of pharmaceutical processes employing generally engineered bacteria, virus aerosol emissions from cooling towers of coal-fired power plants, and enteric bacteria and viruses during the anaerobic digestion of biomass and wastes. Dr. Fannin was responsible for a research program on biotechnology and environmental research as an assistant director at the Institute of Gas Technology in Chicago from 1985 to 1987. From 1979 to 1983, he was Manager of Microbiological and Environmental Research at that organization. While there, he directed multidisciplinary research programs in environmental health and microbiology in indoor environments, waste degradation, and energy bioconversion. He was also in charge of research investigations for developing and evaluating environmental microorganisms and the occurrence of microorganism-containing aerosols. From 1976 to 1979 Dr Fannin worked as a research scientist at the IIT Research Institute, where he directed research on the survival and transmission of microbial aerosols, epidemiology of enteric and respiratory infections, aquatic virology and bacteriology, and the development and evaluation of instrumentation and procedures for studying microbial aerosols. Dr. Fannin received his

masters and doctoral degrees in environmental health from the University of Michigan.

### 3. Dr. Cox

Dr. Cox works as a researcher at the Ministry of Defence, Chemical and Biological Defence, in Porton Down, England. He received a bachelors degree in biochemistry and a Ph.D. in biophysical chemistry (1961) from the University of Bristol. Since 1961 he has worked primarily at Porton Down; from 1968 to 1970 he was at the Department of Defense in Fort Detrick, Maryland and from 1970-1971 he was at the Naval Biological Laboratories in Oakland, California. Dr.Cox has 56 refereed papers and has written 3 books; he has been an invited speaker to a variety of conferences and is world-renowned expert on bioaerosols.

### 4. Dr. Dick

Dr. Elliot Dick is presently a Professor of Preventive Medicine at the University of Wisconsin at Madison, where he teaches graduate and medical courses in preventive medicine and medical virology as well as conducting research in the epidemiology, pathogenesis, diagnosis, and prevention of respiratory infections, particularly those caused by rhinoviruses. Dr. Dick received his bachelor, masters, and doctoral degrees (1950, 1953, 1955, respectively) in bacteriology from the University of Minnesota. Dr. Dick's work has focussed on the study of rhinovirus transmission; he has over 90 peer-reviewed publications.