Aerosol penetration through surgical masks

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Background: Surgical masks are used in hospitals to reduce postoperative infection in patients. The presence of aerosols containing pathogens makes it desirable to protect the medical staff as well.

Methods: The collection efficiencies of surgical masks were measured with two aerosol-size spectrometers. The flow rates through the masks were varied from 5 to 100 L/min to study the flow dependency. For comparison, several industrial-type respirators were also tested.

Results: A surgical mask consisting of filter material performed better than did a surgical mask consisting only of a shell with a coarse pore structure. The latter passed 80% of submicrometer-sized aerosols with little flow dependency, whereas the penetration of submicrometer-sized aerosols through the mask made of filter material ranged from 25% at a flow rate of 5 L/min to 70% at 100 L/min.

Conclusions: The mask that has the highest collection efficiency is not necessarily the best mask from the perspective of the filter-quality factor, which considers not only the capture efficiency but also the air resistance. Although surgical mask media may be adequate to remove bacteria exhaled or expelled by health care workers, they may not be sufficient to remove the submicrometer-sized aerosols containing pathogens to which these health care workers are potentially exposed. (AJIC AM J INFECT CONTROL. 1992;20:177-84)

Surgical masks are worn to protect patients from infection with bacteria or viruses exhaled or expelled by health care workers. Activities such as sneezing, coughing, shouting, crying, and even normal breathing may release nasopharyngeal, oral, and dermal bacteria that can cause postoperative infections. 1.2 Detailed information on the aerosol-size distributions resulting from these activities is not available; however, the large

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aerosol particles generated by these activities are sometimes visible to the naked eye, which indicates that those particles are most likely 10 μm or larger in size. The term *aerosol* refers to liquid or solid particles, whether viable or nonviable, suspended in air.

Recently, there has been increased concern regarding respiratory protection for both patients and the operating team from pathogen-containing aerosols. This concern has been prompted by the use of innovative laser surgical methods and the discovery of new diseases such as AIDS. It has been shown that viable material and viral DNA are released during carbon dioxide laser surgery, especially when low radiant energy is applied.3-5 These new concerns are forcing reconsideration of the filtration efficiency of current surgical masks. For instance, a "laser plume" - the smoke and debris from cell vaporization-was found to contain particles with a mass median aerodynamic diameter of 0.31 µm,4 which is much smaller than the size of droplets expelled by the medical staff. The use of surgical power tools such as electrocautery generated aerosols with a mode

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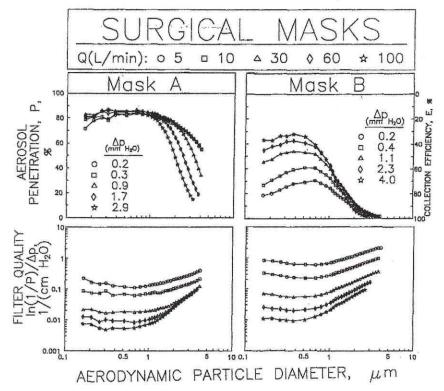


Fig. 1. Aerosol penetration and filter quality factor of two surgical masks.

aerodynamic diameter of 0.07 µm.6 The filtration performance of surgical masks must therefore be examined to ensure protection at a wide range of particle size, from less than 0.1 µm to several micrometers.

Several studies have shown that surgical masks filter microbial aerosols released from the natural flora of the human body1,7,8 or from nebulizers.9-13 Other studies, 14-16 however, have claimed that the use of surgical masks had little benefit for the health of the patients in the operating room and in the ward. It has even been recommended that the wearing of masks in hospitals, a standard practice for decades, be abandoned. Disagreements among the studies are probably due to variations in experimental design, test agents, and test methods. Nevertheless, there is general agreement that surgical masks with higher filtration efficiency performed better than did those with lower efficacy.

In 1962 Green and Vesley8 developed a method for measuring bacterial filtration efficiency (BFE).8 In their test, 92.8% of the bacteria are contained in droplets that are 4 µm or larger in aerodynamic diameter. A slightly modified version of this test is still in use. In the in vivo BFE test mask retention is measured while the wearer coughs several times and expels a natural test aerosol of water and bacteria. In the in vitro BFE test the challenge aerosol is generated by aerosolizing Staphylococcus aureus bacteria with 0.1% peptone in water with a standard nebulizer. In both BFE tests retention by the mask is not dependent on the size of the bacteria but on the size of the droplets in which they are suspended. The size of a droplet may change with time and distance from the source, depending on the temperature and relative humidity of the environment through which it moves.

Both BFE tests require at least 24 hours for microbiologic culturing, counting, and analyzing. In contrast, testing with inert aerosols can be performed in minutes.17 Polydisperse corn oil,11 monodisperse dioctylphthalate (1.8 µm physical diameter),12 and monodisperse polystyrene latex (0.8 µm physical diameter)13 aerosol particles have been used to measure the filtration efficiency of surgical masks. Masks that pass the physical

tests (with monodispersed PSL particles of bacterial size) normally perform well in the biologic tests. ^{13,17} Masks that perform well in the biologic tests with large particles, however, do not necessarily perform well in the physical tests with small particles, as we will show.

The protection provided by a surgical mask depends on the amount of aerosol that penetrates through the filter material and the degree of perimeter leakage, that is, the flow of aerosol through open spaces between the mask edge and the wearer's face. As we will show, the penetration of submicrometer-sized particles through the filter material of a mask can be high for available surgical masks, making most commercially available surgical masks ineffective for protection against submicrometer-sized aerosols. Face-seal leakage at the perimeter of a mask further increases the percentage of environmentally present aerosols that can penetrate to the breathing zone of the wearer.

The degree of face-seal leakage can be determined with masks made of high-efficiency particulate air (HEPA) filter material. In a fit test performed with a mask made of HEPA filter material, it is assumed that there is no aerosol penetration through the filter material. All aerosols measured inside the mask are therefore assumed to have penetrated through face-seal leaks along the perimeter of the mask. Several methods for testing fit have been developed and used by our laboratory18-20 and new methods are currently under development, but these will not be discussed in this article because almost all surgical masks in use today are made of less-efficient filter material, for which perimeter leakage cannot be differentiated from filter penetration by available test methods.

Industrial hygienists refer to masks as respirators and differentiate between disposable filtering face-piece respirators and elastomeric respirators with one or two air-purifying cartridges attached to the rigid body. The Occupational Safety and Health Administration requires the fit testing of elastomeric respirators for specific industrial uses to ensure that the respirator selected seals well and thus provides a minimum of protection to the wearer.21 Current fit-test methods use HEPA filter cartridges to eliminate aerosol penetration through the cartridges. For a filtering face piece with a rank below the HEPA filter, one cannot replace the filter material with a HEPA filter layer for testing without changing the physical characteristics of the face piece; perimeter leakage

therefore cannot be clearly separated from filter penetration. The fit of non-HEPA face masks cannot be quantitatively determined.

Surgical masks of the cone type are similar to industrial-type disposable respirators. No method yet exists by which perimeter leakage on surgical masks can be differentiated from aerosol penetration through the mask. In this article we therefore present only data on aerosol penetration through the filter material of surgical masks. In actual wear situations, aerosol penetration to the wearer's breathing zone may be higher than the penetration percentages presented here.

The principal objective of this study was to examine the filtration performance of two surgical masks at a wide particle size range at different constant flowrates through the mask. For comparison, we also examined the filtration efficiency of four different types of industrial-type respirator. Filter medium performance in the submicrometer-size range is not a predictor of filter media performance for larger particle sizes, and vice versa. This means that the BFE with large droplets may not adequately measure the efficacy of surgical mask materials in removing small pathogen-containing particles, for example aerosolized blood-borne pathogens. Conversely, filter testing with submicrometer-sized aerosols may not adequately measure the efficacy of surgical mask materials in removing large expelled droplets.

METHODS

Most surgical masks and most filtering face pieces used in industry are made of three layers: cover web, filter layer, and shell. The cover web protects and the shell supports the filter layer. The cover web and shell contribute only a small percentage to the overall collection efficiency and there is only a small pressure drop across these layers. The filter layer is responsible for most of the particle removal and airflow resistance. The thickness of the filter layer is increased when high filtration efficiency is needed, normally at the cost of air resistance. Most studies have evaluated the filtration efficiency of surgical masks without considering airflow resistance. Most surgical masks offer little airflow resistance compared with industrial-type high-efficiency masks. However, surgical operations are becoming more complicated and delicate, increasing the length of time a surgical mask may be worn. This may make small differences in air resistance an important issue in terms of comfort. The pressure drop Δp



across each mask is therefore also shown for each condition. In addition, the data are presented as a function of the filter quality factor, defined as $\ln(1/P)/\Delta p$ where P is the fractional aerosol penetration. The filter quality factor thus represents filtration efficiency per unit pressure drop.

To relate the performance levels of the surgical masks to those of industrially used masks, data will be shown for four categories of industrial-type respirators. In order from lowest to highest filtration efficiency, the types are nuisance dust (ND), dust-mist (DM), dust-mist-fume (DMF), and HEPA respirators. Dust is defined as a solid particle formed by crushing or other mechanical breakage of a parent material. Mist is a liquid particulate aerosol, typically formed by physical shearing of liquids such as nebulizing, spraying, or bubbling. Fume is a solid particulate aerosol produced by the condensation of vapors or gaseous combustion products. Nuisance dust refers to aerosols that "have a long history of little adverse effect on lungs and do not produce significant organic disease or toxic effect."22 ND respirators are single-strap, lightweight devices that normally have no filtration layer; they therefore induce little filter resistance. HEPA respirators are approved by the National Institute for Occupational Safety and Health (NIOSH) for respiratory protection against aerosols with a permissible exposure limit, measured as a time-weighted average (TWA), of less than 0.05 mg/m³. The permissible exposure limit may be considered the TWA concentration for an 8-hour workday to which nearly all workers may be exposed, day after day over a working lifetime, without adverse effect. A TWA is an arithmetic mean for some period; it is distinct from an exposure limit or guideline, although exposure limits and guidelines are almost always expressed in terms of TWAs. DM and DMF respirators are approved by NIOSH for aerosols with a permissible exposure limit of not less than 0.05 mg/m3. ND respirators, which are not approved by NIOSH, may not legally be used in the workplace if respiratory protection is required.21

NIOSH is responsible for certification of all industrial-type respirators, but it does not certify ND respirators or surgical masks. NIOSH-regulated filter tests specify a range of mean particulate sizes and measures of spread permissible for the test aerosols used to certify a specific category respirator. For example, DM respirators are required to collect 99% (based on mass) of silica aerosol, with a count median diameter of 0.4 to 0.6 µm and a geometric SD not greater than 2.

A flat surgical mask, a molded-cone surgical mask, and four industrial-type respirators were evaluated in a filter test chamber previously described^{24,25} that was modified for this study. A corn oil test aerosol was generated by a newly developed size-fractionating aerosol generator, which produces aerosols with a selected size distribution. The aerosols were neutralized by a 10 mCi krypton- 85 radioactive source to reduce the electrostatic aerosol charges. The neutralized aerosols were mixed into filtered air and introduced into the test chamber.

The data represent the average performance of at least five masks of the same brand. Most samples deviated less than 10% from the mean; this result indicated that the tested masks had been subjected to good quality control. The masks were sealed to a mannequin with petroleum jelly. The aerosol number concentrations inside and outside the mask were measured by an Aerodynamic Particle Sizer (model APS33B; TSI Inc., St. Paul, Minn.) and a Laser Aerosol Spectrometer (model LAS-X CRT; PMS Inc., Boulder, Colo.). The sampling flows of the Aerodynamic Particle Sizer and the Laser Aerosol Spectrometer were fixed at 5 L/min and 0.06 L/min, respectively. The flow rates through the masks ranged from a constant value of 5 to a constant value of 100 L/min, thus simulating the different physiologic workloads that result in a wide range of instantaneous flow rates during respiration. The pressure drop across the mask was monitored with an inclined manometer. The challenge aerosol concentration was about 600 particles/cm3 (measured by the Aerodynamic Particle Sizer), with a count median diameter of 2.3 µm and a geometric SD of 1.7.

The density and shape of an aerosol particle may affect the gravitational settling velocity and the impact characteristics of the particle in the human respiratory tract. The aerosol particle size is therefore presented in terms of the aerodynamic diameter, which is defined as the diameter of a unit-density sphere that has the same gravitational settling velocity as the particle in question. The filter performance data will be presented as a function of the individual particles' aerodynamic diameters. Such a presentation allows one to predict the performance of a tested mask in an aerosol cloud of a specific size distribution, given by its geometric SD and a mean or median size, such as the count, surface, or mass median aerodynamic diameter.

Two surgical masks, denoted A and B, were tested. Mask A is a thin molded-cone mask that

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lacks a filter layer; it is similar in appearance to the ND masks used in industrial environments. Mask B is a flat mask that contains a layer of filter material. Note that some brands of molded-cone mask include a filter layer.

RESULTS

The aerosol penetration characteristics of the two surgical masks were quite different, as seen in Fig. 1. Mask A without filter material passed about 80% of the aerosols and had low airflow dependence for filtration of particles in the submicrometer size range. The penetration of aerosols greater than 1 µm was more dependent on airflow. For 4 µm aerosol particles, the penetration percentages ranged from about 10% at an airflow of 100 L/min to about 55% at 5 L/min. This corresponds to collection efficiencies of 90% and 45%, respectively. For mask A airflow dependence increased with aerosol size, as can be seen from the wide spread of the penetration curves. Note that the aerosol penetration data were obtained by counting the particles in specific size ranges inside the mask and comparing the number inside with the corresponding number of particles outside the mask. If the mass of each particle size had been measured by a different technique, the same curves would have resulted. Thus the aerosol penetration data of Fig. 1 are given as a function of particle size, independent of the method of measuring particle size. When challenged by a particle cloud, the overall aerosol penetration (considering all particle sizes) depends on the median size and measurement method for that cloud. The penetration efficiency, P, which is 100% minus the collection efficiency, E, is shown on the right-side of Fig. 1.

Aerosol penetration through mask B, with a filter layer, was less than that through mask A, without a filter layer. The capture of submicrometer-sized aerosol particles by mask B was strongly dependent on airflow. The penetration percentages for the 0.3 μm particles (normally regarded as the most penetrating size in filter testing) ranged from about 25% at an airflow of 5 L/min to about 65% at 100 L/min.

Our work on industrial-type respirators has shown that removal by electrostatic attraction is the primary filtration mechanism for submicrometer-sized aerosols. At low flow rates, there is more time for aerosol particle removal by electrostatic forces and therefore less penetration for mask B. For aerosols greater than 1 μ m, removal by mechanical action such as intercep-

tion and impaction dominates; removal of these larger particles is therefore higher at high flow rates, as is clearly seen for mask A. More than 95% of the aerosols larger than 3 μm are captured by mask B at all flowrates.

Fig. 1 clearly shows that mask B removes aerosols more effectively than does mask A: however, the pressure drops across these masks, also shown in Fig. 1, are somewhat higher for mask B than for mask A. We have therefore also presented the filter quality factor for our data. This represents the filtration efficiency per unit pressure drop and is shown in Fig. 1 for both masks. Because mask B contains a filter layer, which removes particles effectively, its filter quality factor is considerably higher than that for mask A. which consists only of a barrier cone. For example, the filter quality factor is 0.78 for mask B and 0.15 for mask A on challenge with a 0.3 µm aerosol at 5 L/min. That is, mask B provides five times more filtration per unit pressure drop than does mask A. Because pressure drop is independent of particle size at a given flow rate, the filter quality factor increases with particle size, corresponding to the aerosol penetration decrease with particle

Fig. 2 compares the performance of the two surgical masks with three of the four industrial-type respirators at a constant flow rate of 30 L/min. Fig. 3 compares the performance of the two surgical masks with all four industrial-type respirators at a constant flow rate of 100 L/min. An instantaneous flow rate of 30 L/min during inhalation or exhalation corresponds to an average breathing rate of 15 L/min or less, a low to medium workload. An instantaneous flow rate of 100 L/min corresponds to an average breathing rate of 50 L/min or less, a heavy workload. The flow rate across a mask is not affected by building ventilation.

The penetration and filter quality data are shown on a linear scale in Fig. 2. To show the performance data for the HEPA mask as well, which was tested only at the high flow rate because of its low number of penetrated particles, the data in Fig. 3 are shown on a logarithmic scale.

The aerosol penetration characteristics of surgical mask A are similar to those of the ND mask. At a flow rate of 30 L/min (Fig. 2), both pass more than 80% of the submicrometer-sized particles and a significant percentage of the larger particles (more than 50% of 3 µm particles). At 30 L/min, aerosol penetration of surgical mask B is lower than that of the ND mask but higher than those of

Mask 6- Las filter, and shows 65%.

Senetration at = 3 microns during external contact experienced during normal EXHAZ

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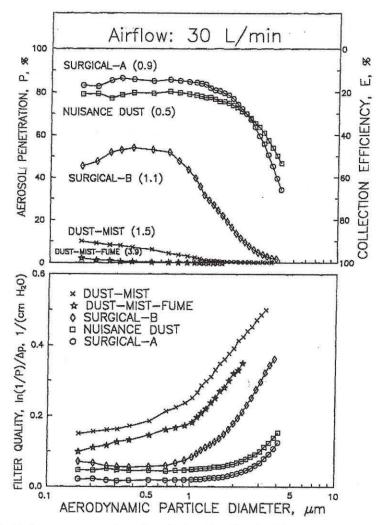


Fig. 2. Performance comparison of surgical masks with industrial-type respirators at a flow rate of 30 L/min. *Top*, The pressure drop across each mask (in mm H₂O) is given in parenthesis.

the DM and DMF respirators. Mask B passes about 50% of submicrometer-sized aerosol particles but passes a much lower percentage as the particle size increases. DM respirators are normally used to protect workers from inhaling aerosols greater than 1 μm . Fig. 2 shows that the DM respirator we tested effectively removed particles greater than 1 μm and passed about 10% or less of submicrometer-sized particles. DMF respirators are expected to remove most of the submicrometer-sized aerosol particles; Fig. 2 shows that 2% or less of the submicrometer-sized particles passed through the DMF respirator.

When rank ordered by collection efficiency (from high to low), mask DMF appears to perform best, followed by DM, and surgical mask B. Masks ND and surgical mask A perform worst in terms of aerosol penetration. The rank-order changes, however, when the filter quality factor is used as the indicator of performance. Fig. 2 shows that mask DM has the best filter quality, followed by DMF, surgical mask B, ND, and surgical mask A. This indicates that mask DM, is designed best for air to pass through and for particles to be retained. The pressure drop across the DM mask is higher than for the surgical masks, however, which is an

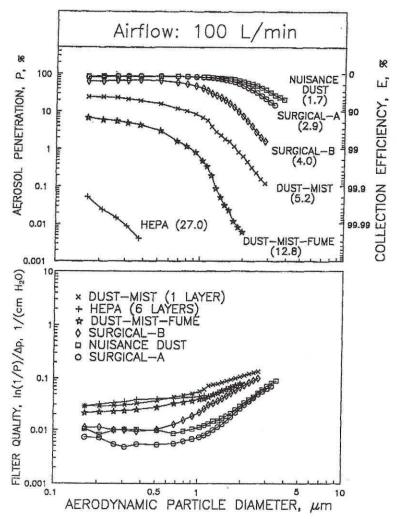


Fig. 3. Performance comparison of surgical masks with industrial-type respirators at a flow rate of 100 L/min. Top, The pressure drop across each mask (in mm H₂O) is given in parenthesis.

important consideration for health care workers.

At a flowrate of 100 L/min (Fig. 3) the HEPA mask is seen to have the least aerosol penetration, less than 0.03% at 0.3 µm. Its filter quality is about the same as that of the DM respirator, because the tested DM respirator consists of one filter layer and the tested HEPA respirator, which is made by the same manufacturer, consists of six of the same filter layers.

DISCUSSION

Surgical mask B, with a filter layer, effectively removed large aerosol particles at all air flow rates tested. As such it satisfies the intended purpose of

removing bacteria expelled by the wearer. Nevertheless, neither of the two surgical masks tested may be considered sufficiently effective in removing submicrometer-sized aerosol particles Such airborne pathogens as aerosolized blood-borne pathogens may be in this size range. Perimeter leakage further increases the percentage of externally present aerosols that penetrate to the wearer's breathing zone.

Industrial-type respirators with different filtration efficiencies are available. DM masks are more effective than are ND masks. DMF masks are even more effective, and HEPA masks retain nearly all aerosol particles. However, the pressure drop

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across the filter, and therefore breathing resistance, increases with the rank order of filtration efficiency. The latter two mask categories must therefore have exhalation valves built in to reduce the effort of exhaling. This design is unacceptable for use in surgical operations.

During mask use, perimeter leakage between the mask and the face may carry aerosol particles into the mask. The fit of a respiratory protection device to the wearer's face must therefore be qualitatively or quantitatively tested before use in an industrial setting. 18-21,26 The protection provided by a mask depends on the amount of aerosol penetration through the mask and the face-seal leakage.27 If a high degree of protection is needed in a hospital environment, more efficient masks ("respirators") can be used but must be tested for fit. Even if a person is successfully fit tested with a HEPA filter respirator, however, varying amounts of face-seal perimeter leakage may still occur from wearing to wearing.28,29 At this time, no quantitative method of testing fit has been accepted for filtering face pieces (including surgical masks) with a rank order below the HEPA filter.

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References

- Hogan B, Samaranayake LP. The surgical mask unmasked: a review. Oral Surg Oral Med Oral Pathol 1990;70:34-6.
- Schiff FS. The shouting surgeon as a possible source of endiphthalmitis. Ophthal Surg 1990;21:438-40.
- Walker NPJ, Matthews J, Newsom SWB. Possible hazards from irradiation with the carbon dioxide laser. Lasers Surg Med 1986;6:84-6.
- Nezhat C, Winer WK, Nezhat F, Nezhat C, Forrest D, Reeves WG. Smoke from laser surgery: is there a health hazard? Lasers Surg Med 1987;7:376-82.
- Sawchuk WS, Weber PJ, Lowy DR, Dzubow LM, Infectious papillomavirus in the vapor of warts treated with carbon dioxide laser or electrocoagulation: detection and protection. J Am Acad Dermatol 1989;21:41-9.
- Heinsohn P, Jewett DL, Balzer L, Bennett CH, Seipel P, Rosen A. Aerosol created by some surgical power tools: particle size distribution and qualitative hemoglobin content. Appl Occup Environ Hyg 1991;6:773-6.
- Quesnel LB. The efficiency of surgical masks of varying design and composition. Br J Surg 1975;62:936-40.
- Green VW, Vesley D. Method for evaluation effectiveness of surgical masks. J Bacteriol 1962;83:663-7.

- Dineen P. Microbial filtration by surgical masks. Surg Gynecol Obstct 1971;133:812-4.
- Rogers KB. An investigation into the efficiency of disposable face masks. J Clin Pathol 1980;33:1086-91.
- Tuomi T. Face seal leakage of half masks and surgical masks. Am Ind Hyg Assoc J 1985;46:308-12.
- Cooper D, Hinds WC, Price JM, Weker R, Yee HS. Common material for emergency respiratory protection: leakage tests with a manikin. Am Ind Hyg Assoc J 1983;44:720-6.
- Wadsworth LC, Davis WT. A rapid latex filtration efficiency test method for simulating bacterial filtration efficiency. Particulate Microb Control 1983;3:30-7.
- Orr NWM. Is a mask necessary in the operating theatre?
 Ann R Coll Surg Engl 1981;63:390-2.
- Rogers KB. Face masks: which, when, where, and why?
 J Hosp Infect 1981;2:1-4.
- Ransjö U. Masks: a ward investigation and review of the literature. J Hosp Infect 1986;7:289-94.
- Davis WT. Filtration efficiency of surgical face masks: the need for more meaningful standards. AM J INFECT CONTROL 1991;19:16-8.
- Willeke K, Ayer HE, Blanchard JD. New methods for quantitative respirator fit testing with aerosols. Am Ind Hyg Assoc J 1981;42:121-5.
- Carpenter D, Willeke K. Noninvasive, quantitative respirator fit testing through dynamic pressure measurement. Am Ind Hyg Assoc J 1988;49:485-91.
- Han D, Xu D, Foo S, Pilacinski W, Willeke K. Simplified pressure method for respirator fit testing. Am Ind Hyg Assoc J 1991;52:305-8.
- Labor. Code of federal regulation title 29, part 1910.134.
 Washington DC: Office of the Federal Register, National Archives and Records Administration 1988:726-34.
- The American Conference of Governmental Industrial Hygienists. 1990-1991 threshold limit values for chemical substances and physical agents and biological exposure indices. 2nd printing. Cincinnati: ACGIH, 1990.
- Mineral resources. Code of federal regulation title 30, part
 Washington DC: Office of the Federal Register, National Archives and Records Administration 1983;7-71.
- Chen CC, Ruuskanen J, Pilacinski W, Willeke K. Filter and leak penetration of a dust and mist filtering facepieces. Am Ind Hyg Assoc J 1990;51:632-9.
- Pilacinski W, Chen CC, Willeke K. Size-fractionating aerosol generator. Aerosol Sci Technol 1990;13:450-8.
- Willeke K, Krishnan U. Focus on present procedures in quantitative respirator fit testing: problems and potential solutions. Appl Occup Environ Hyg 1990;5:762-5.
- Xu M, Han D, Hangal S, Willeke K. Respirator fit and protection through determination of air and particle leakage. Ann Occup Hyg 1991;35:13-24.
- Lenhart SW, Campbell DL. Assigned protection factors for two respirator types based upon workplace performance testing. Ann Occup Hyg 1984;28:173-82.
- Galvin K, Selvin S, Spear RC. Variability in protection afforded by half-mask respirators against styrene exposure in the field. Am Ind Hyg Assoc J 1990;51:625-31.