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Air Movement in Laboratory Infections [and Discussion]

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Air movement in laboratory infections

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Microbiological safety cabinets are designed to contain aerosols generated during work with pathological material. The three currently available types are described, and the use of an operator protection factor to characterize containment by open-fronted class I and II types is discussed.

Methods for measuring operator protection are outlined and current cabinet containment performance is reviewed. Illustrations are given of the extension of safety-cabinet test methods to special facilities for handling carcinogenic or radiopharmaceutical material and to the evaluation of complete rooms housing specific containment facilities.

The safety-cabinet operator protection factor is proposed as a suitable index for assessing containment by laboratory fume cupboards.

Introduction

The risk of laboratory-acquired infection has been recognized as a hazard for some years, particularly among workers in microbiological laboratories in hospital pathology departments (Pike 1976). Apart from clearly identifiable incidents such as spillages, breakages, direct ingestion, self inoculation and wounding, the major risk of infection is from aerosols of infective particles or droplets generated in routine laboratory activities such as pipetting, plating, flaming and unscrewing bottles.

The prevention of such aerial infection has been one of the major laboratory safety problems tackled in recent years. Considerable impetus has been given to the implementation of effective precautions designed to reduce the risk of such infections by the legal requirement embodied in the Safety and Health at Work Act (1974) and by the aftermath of the 1978 outbreak of smallpox in Birmingham where the potential for aerial transmission of infective material was clearly demonstrated.

Microbiological safety cabinets

It is now customary to handle pathogenic material in so-called microbiological 'safety' cabinets. Recent improvements in the performance of these devices have provided a framework whereby quantifiable containment can now ensure a specified reduction in operator exposure (and therefore risk) to aerosols produced during laboratory procedures.

Several safety cabinet designs have evolved since the 1960s and the principles of three distinct classes are now embodied in a number of national Standards, notably in the U.K., U.S.A. and Australia (BS 5726 (1979), National Sanitation Foundation Standard no. 49 (1976), Australian Standard 2252, part 1 (1981) and part 2 (1980)). The three types of safety cabinet designated classes I, II and III and the essential design features are shown in figure 1.

Class III cabinets offer the highest protection, with the work and worker segregated by a physical barrier; pathogenic material is handled through gloves attached mechanically to the front of the cabinet. The working area is maintained at negative pressure with regard to the laboratory and has an inflow of filtered air to give a sterile environment. Exhaust air from the cabinet passes through high-efficiency filters before being discharged to the atmosphere. With care in design, construction and maintenance these cabinets can produce consistently high levels of worker protection. There are, however, a number of difficulties in using such cabinets

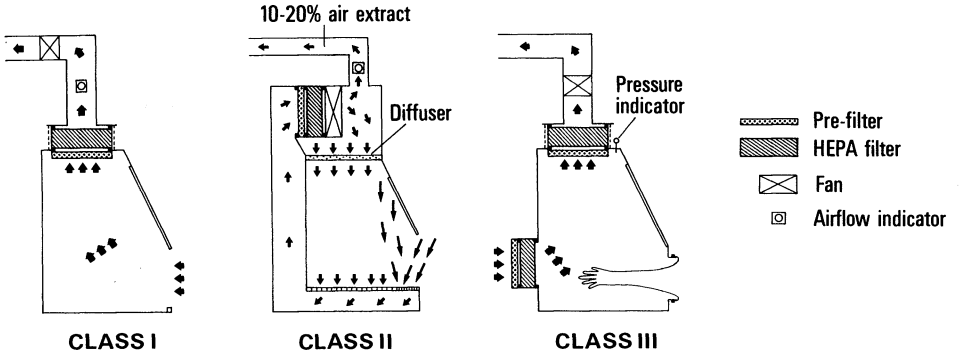

FIGURE 1. The basic airflow configurations in class I, II and III microbiological safety cabinets. These are not definitive in any constructional aspects but show the principles of the three types.

routinely, particularly when handling small equipment and making delicate manipulations through the gloves. In addition, the loading and removal of material from the working section is often time-consuming. Class III cabinets are generally used only for the most hazardous work, often in special accommodation.

For more general laboratory work, open-fronted class I and II types are normally used.

The class I cabinet has an inflow of air drawn from the laboratory and passing across the work surface before being exhausted to atmosphere through pre-filters and main filters.

The class II type is a more complex cabinet and has a downflow of sterile air in the working area bathing the material being handled. In addition an inflow at the front aperture ensures that aerosols generated in the working space do not escape back into the laboratory. Both airstreams join together in the base of the cabinet and pass through ducts to a system of fans and filters where most of the air is recirculated through the working area and the rest is exhausted to the atmosphere.

The class II type cabinet is designed to provide a high level of operator and product protection, whereas the class I type is designed exclusively for operator protection.

PERFORMANCE CRITERIA

Open-fronted safety cabinets have two main functions. One is to provide efficient filtration of the exhaust air to ensure that infectious aerosols are not discharged into the atmosphere (or recirculated to the laboratory); the second is for effective containment by the air curtain at the front aperture so that any aerosols produced in the working area do not spill out into the laboratory.

High-efficiency filters, tested in accordance with a relevant Standard (e.g. BS 3928), are required to be used in safety cabinets. Several methods are available for filter testing. They

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assess the penetration of the filter by a given aerosol challenge. The challenge may be microbiological (an aerosol of spores or bacteria) or chemical in the form of smoke or salt particles. Filter construction and testing techniques are well established, and standard requirements are routinely met in practice. As a consequence filters and their efficiency will not be considered further here.

Containment at the front aperture has, on the other hand, received less investigation and it has often been generally assumed that if there is an adequate inflow of air through the front, containment follows as a consequence. This is no longer regarded as a satisfactory criterion and a containment test with a challenge aerosol to determine 'leakage' from the aperture is now generally accepted. Such tests require the generation of a specific aerosol challenge within the cabinet and the detection and assessment of any leakage into the laboratory.

An important step forward was taken in 1979 in BS 5726 with the definition of an operator protection factor and the detailed description of a test method. The protection factor is defined as 'the ratio of the exposure to airborne contamination generated on the open bench to the exposure resulting from the same dispersal within the cabinet'. The requirement is that the protection factor exceeds 10^5, that is leakage from the cabinet aperture should not exceed one particle for every 10^5 present in the working area.

The protection factor derives from the concept of a transfer index (Lidwell 1960) that relates the exposure to an aerosol challenge experienced at a specific point (in an enclosed area) when a given number of challenge particles is liberated, and a known number is recovered at a known sampling rate. A transfer index can be defined between the inside of a safety cabinet (with a challenge liberated in the working space) and that area just outside the cabinet in the laboratory where an operator would be seated. A reference transfer index making the protection factor non-dimensional comes from the definition of a standard room with turbulent ventilation (at a rate of 10 m^3 min^{-1}) giving completely uniform mixing throughout the space. In this situation, the transfer index is equal to $1/V$, where V is the effective volumetric ventilation rate. The protection factor for the cabinet is then expressed by the relation $Ns/10^4n$, where N is the number of particles liberated in the challenge, n the number recovered at a sampling rate of s (litres per minute).

The concept of a protection factor does not rely on any specific species of aerosol or any particular method of generating the challenge, and it is necessary to adopt a semi-empirical approach to the evaluation of practical and reliable test methods to establish operator protection factors for open-fronted safety cabinets.

Practical test methods

A microbiological test has often been used to assess operator protection factors at the open fronts of class I and II type cabinets (Newsom 1974). An aerosol suspension of bacteria or spores produced by an air-driven nebulizer constitutes the challenge; any escape of this challenge into the laboratory is sampled with bacterial air samplers.

Titrations of the bacteriological suspension to determine the concentration of organisms in the aerosolized solution, together with a knowledge of the volume aerosolized, give estimates of the number of organisms constituting the total challenge.

In a microbiological test the organism acts as a convenient marker which, when incubated, produces an easily identifiable and countable bacterial colony. If this test is to be successful

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it must be carried out with scrupulous attention to technique to ensure that the challenge and background contamination levels within the laboratory are accurately known.

When containment tests are carried out at commissioning, or routinely during maintenance periods, it is unusual for a microbiological test method to be allowable or appropriate. In many laboratories it is impracticable to use such a test because contamination of the cabinet, and often of the laboratory, is unacceptable in 'clean' areas. Additionally, the time required for the incubation of a sampled organism (a minimum of 24 h) creates problems with on-site tests particulary if a result is unsatisfactory and the cabinet requires subsequent adjustment.

Because of these disadvantages, a test method has been developed that does not produce microbial contamination nor require the services of a trained microbiologist and where the results are immediately available (Clark & Goff 1981). This test employs an aerosol challenge of potassium iodide droplets produced from a spinning-disc generator. Special size-selective centripetal air samplers, placed outside the cabinet within the laboratory, sample any challenge escaping from the front aperture on to filter membranes. After a test these membranes are treated with palladium chloride and produce clearly identifiable grey-brown spots where any potassium iodide droplets were sampled. The droplets from the spinning-disc aerosol generator evaporate to leave a solid particle with a mean equivalent diameter of some 7 μm and an air settling rate of 0.3 m min^{-1}. The relatively narrow size range of particles generated in this way is in contrast to the wider spectrum produced by air-driven nebulizers, which have a range of droplets (before evaporation) between 0.5 and 30 μm, with the great majority being below 2 μm.

In ideal conditions, the transfer index takes account of loss of challenge by sedimentation and also assumes that, for the reference room, mixing of the challenge is uniform and consistent. In practice, the size of safety cabinets and the distances between aerosol generation and sampling (only some 200 mm) modify this situation. This produces some difficulties in specifying the particle size for the aerosol challenge, particularly as in a microbiological aerosol the test organism is in an aqueous suspension whereas for the potassium iodide method the solute is alcohol. There are different evaporation rates for the generated droplets in the two methods, and investigations have shown that it is unlikely in either system for the droplets to be fully evaporated while constituting the challenge at the front opening of a safety cabinet. A series of tests was conducted in a number of class I and II type cabinets and produced a correlation between the microbiological and potassium iodide test methods. The broad conclusions were that there was little significant difference in the operator protection factors evaluated by the two methods as long as care was taken to ensure that a specified nebulizer was used for the microbiological test. A number of air-driven nebulizers are available with nominal specifications meeting the requirements of BS 5726. However, the momentum of the droplets produced by different models varies sufficiently to produce inconsistent test results. The more violently generated droplets give rise to greater leakage from the working area and therefore lower protection factors.

For practical purposes, as long as aerosol challenge particles or droplets are below 10 μm effective diameter, the resulting operator protection factors are not substantially different. One of the reasons for this is the dominant effect on the containment performance of features such as turbulence at the front opening, which can cause leakage of challenge particles in a wider size range.

Figure 2 shows an example of the correlation between the microbiological and potassium iodide test systems for both class I and II cabinets.

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Safety-cabinet performance

Class I

The potassium iodide test system has enabled safety-cabinet containment performance to be comprehensively evaluated and for the operator protection factor to be directly related to design features such as inflow air velocity and internal geometry. For example, figure 3 shows the operator protection factor for two class I type safety cabinets plotted against inflow air velocity.

The lower curve is for a class I cabinet built before the introduction of BS 5726 with a stepped or bluff inlet, which produces some air turbulence at the front opening. The operator protection factor falls to a value of 10^5 at an inflow air velocity of around 0.5 m s^{-1}. The upper curve is for a 'streamlined' cabinet with a 'faired' or smoothed front entry with less turbulence at the aperture. The nominal performance of this cabinet exceeds 10^5 even at inflow air velocities

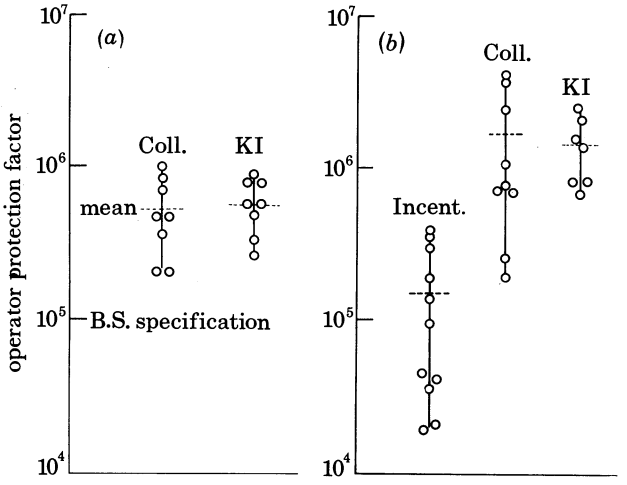

Figure 2. Comparisons of results of operator protection factor from (*a*) a class I cabinet and (*b*) a class II cabinet. KI represents results from the potassium iodide test system, Coll. are results from a microbiological suspension of spores generated by a Collison nebulizer. Incent. are results obtained from a plastic inhalation therapy nebulizer. The discrepancy between results from the Incent. nebulizer and the other two tests is clearly seen in (*b*) (see text).

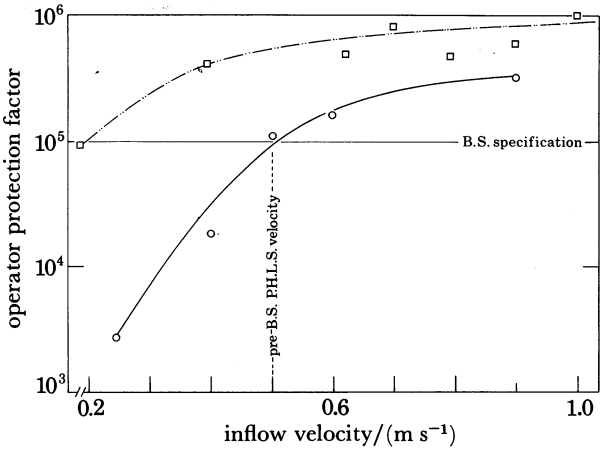

Figure 3. Variation of operator protection factor with inflow air velocity for a class I cabinet, antedating BS 5726, with a stepped inlet (lower curve) and a BS 5726 class I cabinet with a faired or streamlined inlet (upper curve).

as low as 0.2 m s^{-1}. Curves such as these characterize the overall performance of class I cabinets and serve as useful criteria during the development of new designs. They can also indicate at what stage in filter blockage the containment will fall below the minimum requirement.

As a general rule, the inflow air velocity at a class I cabinet should lie between 0.5 and 1.0 m s^{-1}. At higher air velocities there is increased turbulence at the front and 'bounce' from the rear wall, which can adversely affect the containment at the aperture. This is illustrated in figure 4, which demonstrates the fall in operator protection as the inflow velocity exceeds 1.0 m s^{-1}.

Class II

The performance of class II type cabinets has caused some concern in recent years, with many early models having operator protection factors of 10^2 or below. The introduction of BS 5726 has stimulated manufacturers to produce models with more satisfactory performances. Figure 5 shows the variation in operator protection for a number of cabinets at about the time that the Standard was published. The latest class II type cabinets, when tested in accordance with BS 5726, often produce protection factors greater that 10^6, and a number of class II models have a higher nominal performance than some class I types.

The complex air interactions between inflow and downflow in the working area of a class II

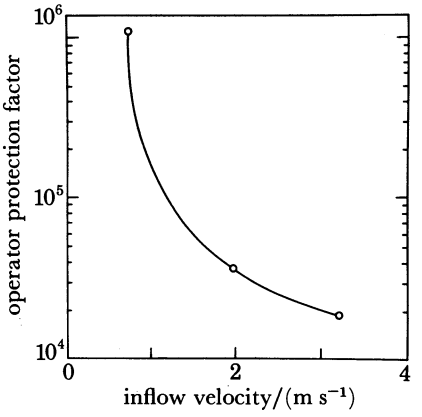

FIGURE 4. Variation of operator protection factor with increasing inflow air velocity above 1 m s^{-1} for a class I cabinet.

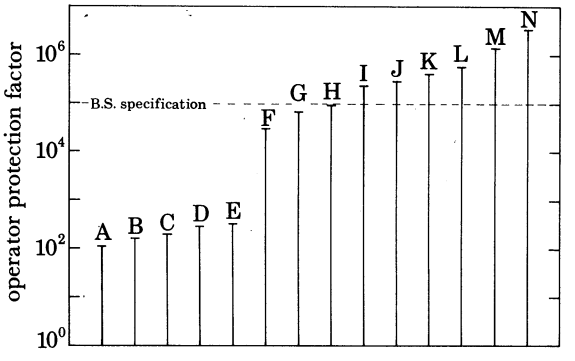

FIGURE 5. Operator protection factors for 14 class II type cabinets. Cabinets A, B, C, D and E were built before the introduction of BS 5726 and produced operator protection factors some 10^2–10^3 lower than the requirements of the Standard.

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cabinet require comprehensive evaluation if optimum performance is to be achieved. Figure 6 illustrates a performance diagram for these cabinets. For a specified downflow the protection factor can be plotted for a series of inflow velocities. The resulting 'envelope' of best and worst performance figures characterizes the containment efficiency. A family of such curves results when similar plots are made for different values of downflow. Such tests enable a designer to select downflow and inflow air velocities to give optimal performance.

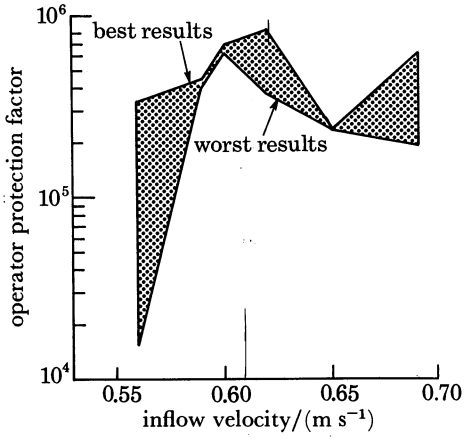

FIGURE 6. Diagram showing the operator protection 'performance envelope' for a class II cabinet plotted for a series of inflow air velocities at a constant downflow of 0.4 m s^{-1}.

Disturbances at the front opening

Many laboratories have less than ideal environmental conditions and limitations as to the siting of safety cabinets. Door movements and people walking near to a cabinet can produce turbulence and air disturbance within the laboratory. In these circumstances, the operator protection factor for both class I and II types may be reduced by 1 or 2 orders of magnitude, with class II models being rather more susceptible to such disturbances. However, when cabinets are correctly sited and are used with good technique and laboratory discipline such disturbances do not occur and the containment of both types can now comfortably exceed the requirements of BS 5726.

CONTAINMENT OF CARCINOGENIC AND RADIOPHARMACEUTICAL MATERIAL

The established methods for measuring operator protection factor in biological safety cabinets can be applied to containment facilities for other aerosol species. For example, special consideration must be given to the problems of handling carcinogenic or radiopharmaceutical materials where both particulates and vapours are produced. Hybrid facilities embodying the containment and filtration principles of safety cabinets and the dilution and dispersal features of fume cupboards are often appropriate for this work. Such a facility should have high-efficiency filters for the removal of the particulate phase of the contamination, with hazardous vapours reduced to concentrations below the 'threshold limit value' (Health and Safety Executive 1980) by dilution with large air volumes and exhausted at high velocity and level.

An important difference between microbiological aerosols and carcinogenic particulates is

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that the former may be rendered safe by fumigation whereas for the latter no such decontamination procedure exists. This problem can be tackled by the use of bagable filters to enable a contaminated filter to be removed with the minimum of contact by service personnel. Once safely bagged the filters are generally incinerated.

In many laboratories, sterile conditions for handling the work are necessary in addition to high levels of operator protection. In these special facilities it is often appropriate to use a modification to a class II type safety cabinet with bagable filters in the exhaust situated remotely from the laboratory. In this type of cabinet the air is not recirculated to the laboratory but is 'totally dumped' to the atmosphere, as illustrated in figure 7. In all such special installations the filtration and operator protection factor requirements of BS 5726 should be met.

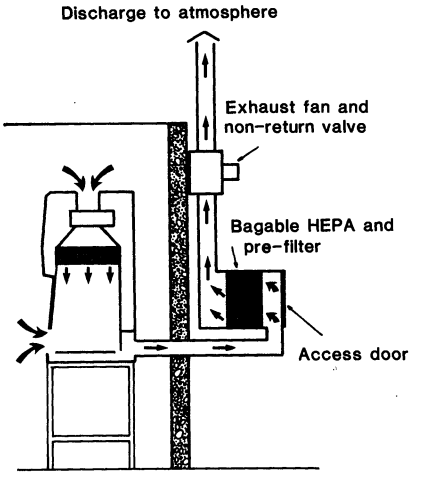

FIGURE 7. Diagram to illustrate a modified class II type of cabinet to produce 'total dump' of the air passing through the working section. There is no recirculation; all of the air is exhausted through a bagable filter before being discharged to the atmosphere where toxic vapours can be diluted. Such a system is suitable for handling carcinogenic vapours and particulates or radiopharmaceuticals.

ROOM CONTAINMENT

Many organizations are constructing special laboratories or suites of rooms to handle high-risk pathogenic, carcinogenic or other toxic material. These facilities are often built within existing buildings and there is an increasing need for these rooms, which often house safety cabinets or fume cupboards, to have a specified level of containment with regard to surrounding areas. Isolation of such rooms is generally achieved by maintaining the room at negative pressure in relation to the surroundings and by having an inflow of air to the room. In situations where 'clean' conditions are required these rooms may require more elaborate ventilation and the provision of airlocks supplied with filtered air is often appropriate. Figure 8 illustrates typical methods of achieving room isolation where negative pressure is maintained by a fume cupboard or a safely cabinet exhausting to the outside. The maintenance of the correct level of negative pressure for effective isolation of such rooms is critical if they are to perform satisfactorily. The principle of fume cupboard and safety cabinet containment can be extended to determine a 'protection factor' for the complete room. This is achieved by liberating an aerosol challenge within the room and sampling in the corridor or adjacent area just beyond the door of the containment facility.

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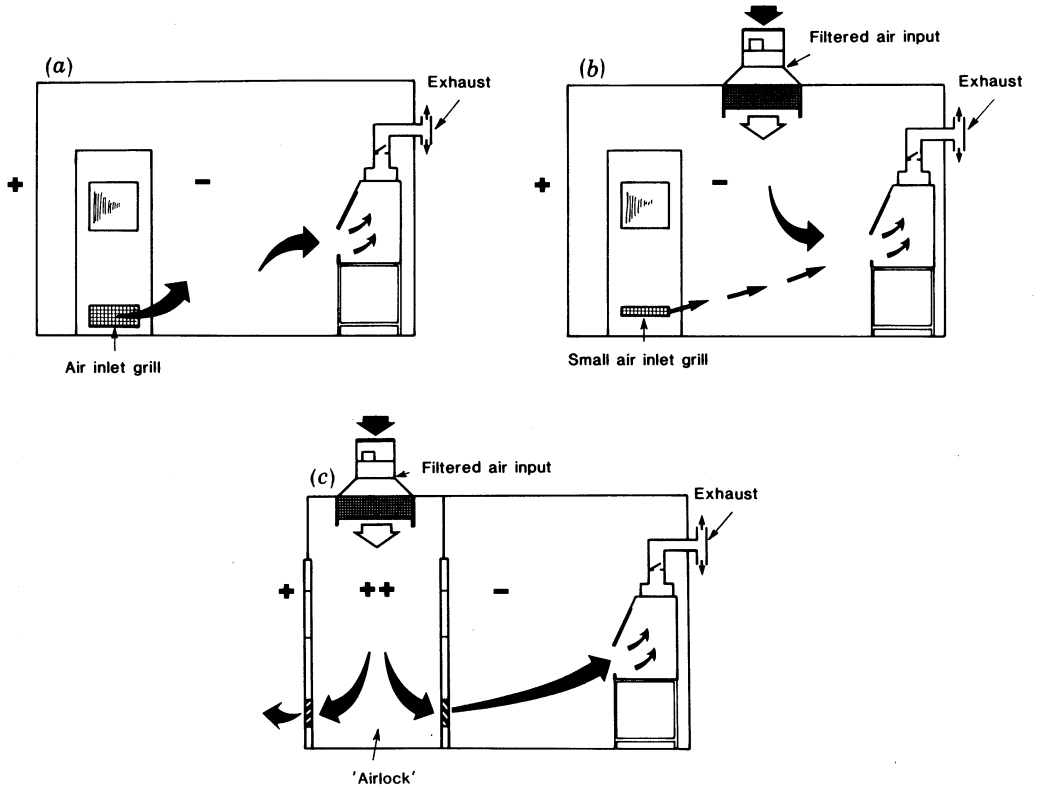

FIGURE 8. (*a*) Negative pressure maintained in a laboratory by a class I safety cabinet ducted to the outside. (*b*) Negative pressure maintained in a room by an exhaust of air at a slightly greater rate than a filtered air input. The remaining air is derived from a small inlet grill in the laboratory door. (*c*) Laboratory maintained at negative pressure by exhaust from a safety cabinet and incorporating an airlock supplied with positive-pressure clean air to segregate the laboratory from the surrounding areas.

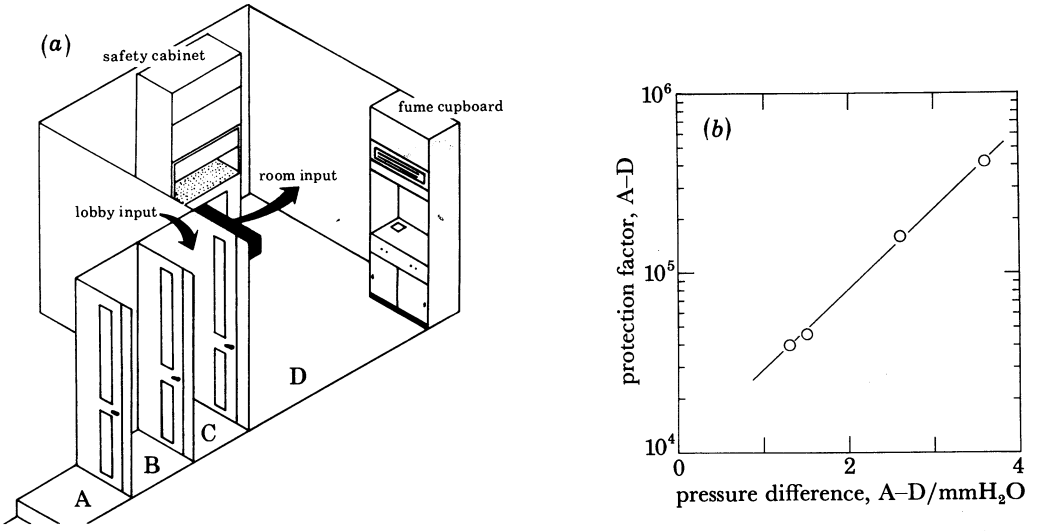

FIGURE 9. (*a*) Diagram of a room for handling carcinogenic material and containing a class II safety cabinet and a fume cupboard. An external door and an airlock separated the room from the rest of the building. The room D was maintained at negative pressure with respect to the outer area A. (*b*) Protection factor for the carcinogen room measured at different negative pressures in the room.

Figure 9*a* shows a diagram of a carcinogen-handling facility housing a safety cabinet and a fume cupboard. The cupboard provided constant exhaust to atmosphere and maintained the room D at negative pressure with respect to the lobbies B and C and the corridor A. By adjustment of the input air volume to C and D it was possible to vary the pressure difference between A and D. Containment tests were performed for the room, and figure 9*b* shows the relation between negative pressure and protection factor measured between the room D and the corridor when potassium iodide challenge aerosol was liberated within the room and sampled in the corridor area. A negative pressure difference of between 2 and 3 mmH_2O (between about 20 and 30 Pa) gave a protection factor of 10^5. By producing such diagrams for specific installations, designers and users can decide on the level of containment required for the room and then specify the pressure difference to produce the containment. Routine maintenance tests to determine operator protection factors for safety cabinets and fume cupboards can then be extended to include measurements of the room containment.

Conclusions

There now exist satisfactory methods to determine the containment performance of microbiological safety cabinets, fume cupboards and special facilities for handling carcinogenic or radiopharmaceutical material. These tests can be extended to quantify the containment of complete rooms housing such containment facilities.

Containment tests can be performed on cabinet 'types' to validate new designs. These tests can be repeated at commissioning and during routine maintenance periods to ensure that the design performance is maintained. Manufacturers are now producing containment facilities meeting the operator protection requirements of BS 5726 and other relevant Standards. In many cases this represents an improvement of several orders of magnitude compared with cabinets produced some 5 years ago.

The concept of quantifiable containment in facilities used for handling dangerous materials will help in the overall risk assessment of different procedures and in defining the facilities appropriate for such work.

With high standards of containment for protection against the transmission of aerial contamination within laboratories, the contact route assumes more relative importance. Contact transmission often has an airborne element, for example aerosols that sediment to surfaces may subsequently present a hazard with further transmission by direct contact. By reducing the aerosol component by the use of fume cupboards or safety cabinets it is possible to reduce the potential hazard in much contact transmission.

Current research is aimed at quantifying the relation between 'overall containment' by contact and airborne routes within laboratories and assessing the attenuation of contamination by laboratory disciplines and techniques such as the wearing of gloves, gowns and masks. The application of the results of this work is expected to be in the specification of complete laboratory facilities, including ventilation systems, and in determining methods of working to enable limits of total 'walked-out' contamination by all routes to be specified.

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Additional material

Two films illustrating air movements around microbiological procedures are available from the author: (1) *Laminar downflow cabinets: some unseen hazards*, and (2) *The open bench environment.* These are available as 16 mm colour optical sound prints or on VHS format videotapes.

Discussion

F. H. Howorth (*Ollerton Research Laboratories, near Chorley, U.K.*). Following the doubts expressed about the protection afforded by HEPA filters, owing to irregularities in manufacture or subsequent damage during handling and use, it should be realized that for class II and class I microbiological safety cabinets the protection factor afforded by the airflow pattern at the work entry aperture must be 10^5 in order to comply with BS 5726, whereas the penetration of an HEPA filter in good order is only 0.003%.

R. P. Clark. When containment performance is reviewed, the operator protection factor requirement of 10^5 (i.e. a leakage of 1 particle for every 10^5 present in the cabinet) should be compared with filter penetration (an efficiency of 99.997%), which allows 3 particles per 10^5 to pass through. Looked at in this way the operator protection requirement of 10^5 is stringent but can now be reliably achieved.

A. W. Frankland (*Harley Street, London, U.K.*). I should like to ask Dr Clark two questions. He talked almost entirely about aerosols and testing microbiological safety cabinets. He showed very well that a Collison nebulizer produces a very fine mist of uniform particles whereas another machine produced obviously quite different sized particles. Has he looked at the particle size of aerosols? My other question arises from this and concerns airborne particles of different sizes. My own interest happens to be laboratory workers (in a larger environment than a cabinet) who are becoming sensitized and developing rhinitis and asthma from rodent urine. The urine is a wet allergen but is not an aerosol. Can he relate his experimental data to airborne particles that are not aerosols? Man, if he becomes allergic to laboratory animals, may have problems that are very individual but these may be solved by wearing Racal helmets.

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R. P. Clark. We have investigated the range of protection factors produced when different-sized particles constitute the aerosol challenge to a safety cabinet. The detailed results are given in the references, but as a general rule it seems that protection factors are relatively independent of particle size (at least up to 10 μm) for open-fronted class I and II safety cabinets. The leakage at the front aperture is mainly determined by eddies and turbulence, which affect a wide range of particles. In addition the momentum imparted to the particles by their method of generation is also significant. These factors emphasize the importance of empirical correlations between practical test methods.

The second question raises the whole problem of overall containment which includes the contact as well as airborne routes. The Advisory Committee on Dangerous Pathogens recognizes that these interactions are complex and has made proposals whereby laboratory equipment and layout is designed to improve overall containment. There will be several classes of laboratory with the levels of precaution related to the hazard of the organisms being handled.

We are currently assessing the effectiveness of these proposals in terms of quantifying the containment by both airborne and contact routes. The potential for contact transmission is modified by airborne contamination. For example, when aerosols are removed from the vicinity of a worker by the use of a safety cabinet the chances of hand contamination from sedimentation droplets is reduced, therefore lowering the potential for further contact transmission.

A. I. Donaldson (*Animal Virus Research Institute, Pirbright, U.K.*). Has Dr Clark considered the use of ultrasonic nebulizers for the safety testing of cabinets? These instruments produce concentrated clouds of heterogeneously sized particles without the disadvantages of a strong driving air flow.

R. P. Clark. I should like to thank Dr Donaldson for this suggestion. We plan to assess ultrasonic nebulizers during the next phase of this work.

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