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POLICY DECISIONS BEFORE DESIGN OF A MICROBIOLOGICAL RESEARCH LABORATORY

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POLICY DECISIONS BEFORE DESIGN OF A MICROBIOLOGICAL RESEARCH LABORATORY

Arnold G. Wedum
G. Briggs Phillips

Safety Division
OFFICE OF THE SAFETY DIRECTOR

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ABSTRACT

In the design and equipment of a microbiological research laboratory for the study of diseases infectious for man and animals, it is necessary to provide for protection of the experimenter, the experiment, and the surrounding community. The U.S. Army Biological Laboratories often act as a consultant in such design. In our experience, the most conspicuous error in planning is failure to make all the necessary policy decisions before design is begun. This failure results in protective or precautionary features that are excessive, inadequate, incompatible, or inconsistent. This article is directed to the administrator, the microbiological technical consultant, the architect, and the engineer who need decisions on policy before they design and equip a unit for the study of agents infectious for man and animals.

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I. INTRODUCTION

A. BACKGROUND

Approximately 175 million dollars per year currently are being spent in this country for the construction and remodeling of biomedical research facilities.[1] A significant proportion of this money is for facilities in which infectious microorganisms are handled. The magnitude of this annual investment suggests the importance of assuring that microbiological safety measures consistent with the purpose of the laboratory are included in the design. Several recent architectural and planning guides are available[2,3] and a comprehensive bibliography on laboratory design has been prepared.[4] Beyond this, several articles have dealt with specific features and equipment for use in infectious disease laboratories.[5-9]

B. ENVIRONMENTAL CONTROL

The facilities provided in microbiological laboratories have an important relationship to the safe-being of personnel working therein and, in some circumstances, to the validity of the experiments. Good design and good equipment can be valuable in containing and controlling infectious materials; indifferent or inconsistent arrangements can complicate or limit efforts to minimize the risk of accidents and infections. Microbiological environmental control, the objective of good design, involves any technique, equipment, or building feature or combination of these that confines microorganisms within a specific environment. In the early stages of planning a new building, the specific problem is one of selecting those engineering features that, in relation to the research and the people doing the research, can best provide the desired control. Features commonly used for microbiological environmental control in infectious laboratories and animal rooms include (a) ventilated cabinets and cages (Figures 1 and 2) to contain microbes at their point of use; (b) differential, increasingly negative air pressures as one moves from clean areas to those of greater infectious risk; (c) appropriately effective filtration of air from rooms, cabinets, and ventilated cages;[10] (d) change rooms and showers for personnel; (e) ultraviolet air locks and door barriers to separate areas of unequal risk; (f) treatment of contaminated liquid effluents; (g) room arrangement or layout to achieve traffic control along a clean-contaminated axis; and (h) an effective intercommunication system. For those faced with initiating a design plan the problem is one of determining which, if any, of the above items are to be used and to what extent.

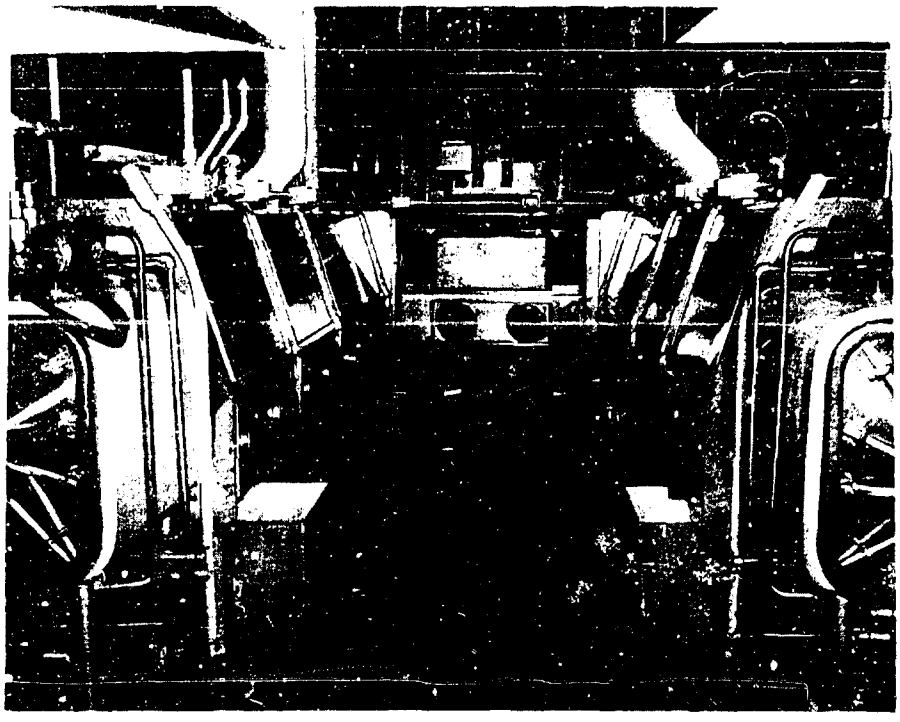

Figure 1. Gastight Cabinet System.
(FD Neg C-5720).

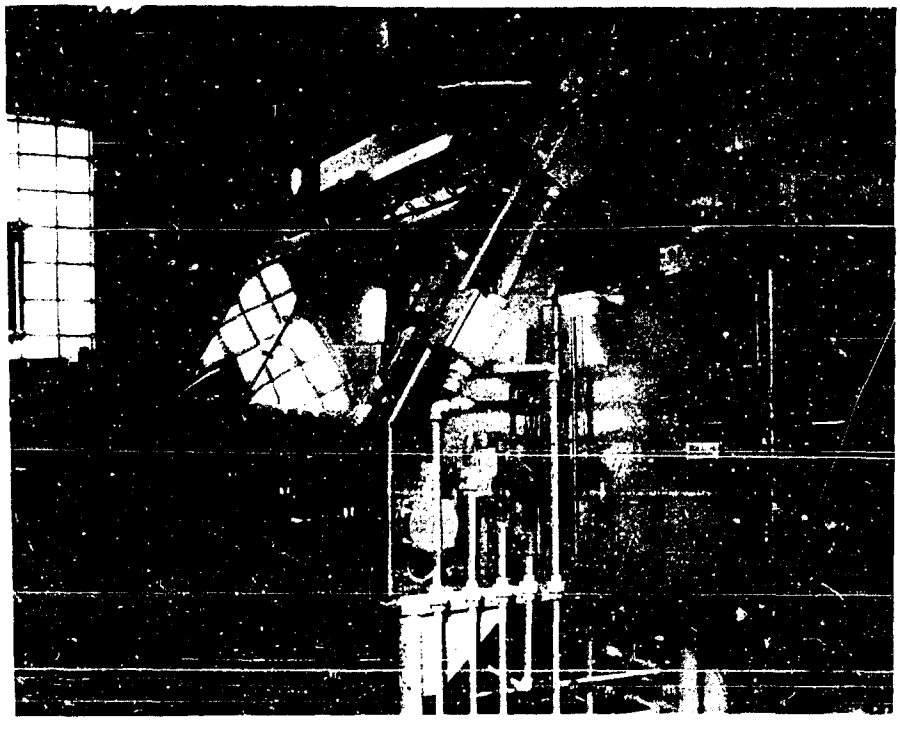

Figure 2. Single Microbiological Work Cabinet.
(FD Neg C-4172).

C. DESIGN PROBLEMS

Even though a substantial amount of information is available to those planning to construct or remodel infectious disease laboratories, we have been impressed with the difficulties often encountered in design. It is our impression that decisions made in the planning phase all too frequently result in an arrangement that:

1. Provides a degree of inflexible protection for personnel that is excessive in relation to the risk-level of the infectious operations actually to be done, or

2. Provides adequate protection for the experiment but little or none for the experimenter,

3. Provides excellent microbiological protection for the surrounding community but little for the building occupants, or

4. Provides a degree of protection for personnel below that found to be needed when the laboratory gets into full operation.

To avoid these situations, we believe that certain questions must be asked and answered before a design is started. In our experience in our own laboratories and during consultations and inspections we have been privileged to make at laboratories elsewhere, the most conspicuous error in planning a microbiological laboratory is the failure to make all the necessary policy decisions.

This article is directed to the administrator, the microbiological technical consultant, the architect, and the engineer who need these decisions on policy. To some extent, the criteria and ideas set forth may be applied to any laboratory handling hazardous chemicals or toxic substances. Our opinions and recommendations in the following pages are based upon visits to many laboratories in this country and abroad, upon thorough investigation of many laboratory-acquired infections, upon probing into the psychological, mechanical, and operational causes, and upon assessment under experimental and operational conditions of the value of various protective measures.[11-13] The following presentation is not intended to encompass all the engineering problems that arise, but to furnish some major examples.

II. QUESTIONS ON POLICY

Early in the process of designing the building, policy decisions are necessary beyond the usual ones concerning size, shape, building materials, location, personnel capacity, general purpose, etc. These additional decisions will determine construction details. Some of the questions to be considered and some of the reasons for these questions are:

1. Is this building for the use of one man or for a specific project, and will the building at the departure of the man or conclusion of the project be remodeled to suit the next occupant or next project?

2. To what extent do the views of the laboratory director or of whoever has the final authority to determine the level of precautionary design, equipment, and techniques, reflect the probable view of his eventual successor? This is a sobering thought that sometimes is not considered.

3. How many persons will be at work and what will be the conditions of supervision? The larger the number of nonprofessional personnel, the more desirable it is to provide building design and equipment engineered to insure use of the desired method, from which few deviations will occur because it is easier to do it the right (safe) way. Conversely, the smaller the number of persons, the better the judgment based on education and experience, and the closer the supervision of the group, the fewer will be the mechanical safeguards that will be necessary. However, there are some operations in which no amount of judgment and experience can substitute for special equipment.

4. What will be the ratio of men to women? The numbers usually are not the same. More flexibility in personnel policy may be facilitated by dividing the total change room space in a 40:60 or 30:70 ratio so that the predominant sex may use the larger room.

5. Does the stated justification and objective of the laboratory require the building to be suitable for study of any microorganism in any kind of experiment, with only the size of the equipment or animal as limitation? If so, a gastight cabinet system (Figure 1 or equivalent) will be mandatory for some operations.

6. Will infectious microbial aerosols be studied as aerosols, relative to (a) aerodynamic stability; (b) particle size; (c) natural means of accidental dissemination; (d) effect of ultraviolet irradiation, temperature, humidity, and aerial chemical disinfectants; and (e) other types of investigations? Special airtight chambers and an associated gastight cabinet system are required for many agents.

7. Will any limitations be placed upon the type of etiologic agent that may be studied? Categories of agents, and examples of associated recommended requirements for equipment, are outlined in Section III and in Table I.

8. What methods of animal inoculation will be permissible?

(a) Respiratory challenge: Whole-body exposure, head only, nose and mouth only? For these techniques, a protective cabinet and other housing (Figures 1, 2, and Table I) are essential for the aerosol apparatus and the animals. Each step in the handling of animals and cages must be thought out carefully. Pressure-tight ducts should conduct exhaust air from the site of aerosol liberation to a filter. If the volume of aerosol and concentration of agent is high, the filter should be followed by an air incinerator. Absence of pressure-tight exhaust lines is inconsistent with precautionary air filtration or air sterilization by incineration. With some organisms, use of masks on immunized personnel will permit certain types of work on an open laboratory bench, but we advise that this expedient be avoided.

(b) Intranasal, intratracheal, intraperitoneal, intravenous, subcutaneous, intramuscular, intracerebral, oral, etc? If personnel are vaccinated, it may be possible to perform injections on an open bench top, but the range of permissible operations and agents is extended by presence of a protective cabinet (Table I).

9. Which of the following animals will be used: mouse, rat, hamster, guinea pig, ferret, monkey, chimpanzee, fowl, cat, dog?

Animal caging arrangements must be examined for the possibility that cross-infection between animals may impair the integrity of the experiments. Whether this will happen depends upon the agent, the animal, and the method of inoculation.[14]

When infected animals the size of monkeys or smaller are to be housed, thought should be given as to how the animals are to be isolated. The best isolation is that obtained with individually ventilated, closed cages with small inlet and outlet air filters. Ventilated cage racks are suitable in many instances. The possibility of using open cages on ultraviolet-irradiated racks should not be overlooked.[15] Permanently mounted cages have the disadvantage that dependence must be put on chemical sterilization. When infectious organisms are combined with animal excreta, bedding, and other matter, chemicals are not reliable for all microorganisms. Usually, portable stainless steel cages that can be moved to an autoclave or other adequate sterilizing equipment are the most desirable, although disposable or autoclavable plastic cages are useful in some instances.

TABLE I. CORRELATION OF ESTIMATION OF RISK WITH RECOMMENDATIONS FOR PROTECTIVE CABINETS[a]

Disease or Agent	Cabinet System[c]	Single Cabinets[d]	
	Aerosol Studies	Aerosol Studies	Other Techniques
Brucellosis	+++		+++
Coccidioidomycosis	+++		+++
Russian s-s encephalitis	+++		+++
Tuberculosis	+++		+++
Monkey B Virus	+++		++
Glanders	++	+++	+++
Melioidosis	++	+++	+++
Rift Valley fever	++	+++	+++
Encephalitides, various		+++	++
Psittacosis	++	+++	++
Rocky Mt. spotted fever	++	+++	++
Q fever	++	+++	++
Typhus	++	+++	++
Tularemia	++	+++	++
Tularemia[b]		++	+
Venezuelan encephalitis[b]		+++	+
Anthrax	+++		±
Botulism[b]	++	+++	±
Histoplasmosis		+++	±
Leptospirosis		+++	±
Plague	+++		±
Poliomelitis	+++		±
Rabies	+++		±
Smallpox[b]	+++		±
Typhoid		+++	0
Adeno, entero, viruses		++	±
Diptheria[b]		++	0
Fungi, various		++	0
Influenza		+	±
Meningococcus		++	0
Pneumococcus		++	0
Streptococcus		++	0
Tetanus[b]		++	0
Vaccinia[b]		++	0
Yellow fever[b]		++	0
Salmonellosis		+	±
Shigellosis		+	±
Infectious hepatitis			±
Newcastle virus		+	0

a. +++ = mandatory; ++ = strongly advised; + = optional, but in absence of a cabinet a few infections will occur; ± = depending upon technique and supervision. 0 = not required.

b. For persons receiving live vaccine or toxoid.

c. Figure 1 or equivalent.

d. Figure 2 or equivalent.

If the larger animals have been exposed to infectious aerosols, obtaining temperatures, blood samples, etc. is difficult unless they are kept in the open room or in open-front cages, with or without ultraviolet irradiation, in a special room in which personnel are protected by ventilated suits, ventilated head hoods served by air lines, gas masks, or respirators. Gas masks and respirators are not advised for daily routine use as the primary barrier to human infection because of (a) difficulty in maintaining a good fit on the face, (b) respiratory difficulty experienced by some persons, (c) maintenance troubles, and (d) the practice of occasionally moving the mask or respirator "to get a good breath of air." Masks and respirators should be reserved for the purpose for which they were designed, namely, emergencies and short-term special occasions. In such a room all ceiling and wall openings for air ducts, electrical wall switches, lights, water, etc. should be sealed airtight to prevent air-borne organisms' entering the basement, attic, or adjoining rooms. Light fixtures inset flush with the ceiling are unsuitable if they permit air to pass into the attic. Placing light switches outside the room is a good idea. To maintain an infection-free attic, exhaust air ducts serving the animal room should be airtight, thereby minimizing the dependence on inward air leakage through duct joints. A disinfectant airlock entryway to the room may be warranted.

Hair and dander in animal rooms create problems with air ducts and bacterial filters. Prefilters are advised. Even with prefilters there may be filter-loading problems in a room housing chickens. Prefilters should be located in the animal room where they may be changed easily by laboratory personnel. This situation typifies a difficult engineering problem of how to maintain air balance when filters serving different building areas load at different rates.

Year-around climatic control in the animal-holding area is important. It is easier to achieve in the absence of windows.

Dead animals should be incinerated. It is safest and most convenient to do this in an incinerator constructed in the same building as the animal room. This incinerator also may handle other combustible trash. Otherwise, there is a safety and materials handling problem that requires packaging and preliminary autoclaving before transportation to an outside central incinerator, or transportation in a closed, disposable leakproof bag by a trained crew. A study of comparative costs is suggested. Size and design of the incinerator require very careful study, with special attention to the local building code, the largest expected cadaver, and the amount of plastics to be burned.

10. Will animals as large as swine, sheep, burros, or calves be used? Rooms for them require good drainage. Flushing-type drains are preferable because of the volume of excreta.

11. What will be the usual physical form of the infectious material - wet or dry? Dry infectious materials aerosolize more easily than wet and therefore are more dangerous. Maximum precautions are necessary.

12. Will infected arthropods be grown and studied in transmission experiments? Will any of these arthropods be exotic to the geographic area of the laboratory? If so, additional air locks with fine mesh screen are desirable. Walls should be smooth, with high-gloss white paint to facilitate detection of escaped insects. Incoming utility lines should be sealed around the point of entrance to the room. Exotic vectors require careful control even if uninfected because of their potential ability to set up a heretofore unknown cycle of transmission of disease.

13. Will there be work with several tissue culture cell lines, used to grow viruses? A special room or enclosure with filtered air may be necessary. Positive air pressure in a room may be requested for uninfected tissue cultures if no "clean" space is provided outside the infectious unit.

14. Will large numbers of eggs be used as culture material? Will egg contents be pooled, and into about what liquid volume? Egg trays are difficult to sterilize except by autoclaving. Eggs externally contaminated during inoculation require special precautions during handling, incubation, and subsequent processing. If infection of man has a serious outcome, it is best to have the egg incubator (as part of a gastight cabinet system) sealed to and part of the gastight cabinet where the eggs are inoculated.

15. Is it desirable to be able to change the size, shape, and purpose of the rooms and of their installed equipment from time to time as the years go by? A common finding is that the space needed for animals is underestimated, but the reverse also occurs. Planning for alternative use as laboratory or animal room is worthwhile. At Fort Detrick, our experience with laboratory-acquired illness has caused us to increase installation of gastight cabinet systems, replacing the single cabinets to some extent. Less dangerous agents are examined and less dangerous techniques are performed in the single cabinets, of which there is a considerable variety (Figure 2). Nonhazardous agents or easily controlled operations are done on the open laboratory bench top. A summary of minimum recommended requirements is shown in Table I.

The space allotted the engineers for mechanical equipment serving the building utilities often is grossly inadequate. Likewise, the attic and/or basement should be 7 to 10 feet high to permit access for workmen installing or changing air ducts, service lines, filters, and motors. Motors and blowers produce less objectionable noise if they are placed outside the laboratory. Nonengineering personnel unacquainted with a building of this kind find it difficult to understand the need for this amount of space. Sometimes it must be seen to be believed. The attic becomes very crowded and needs mechanical ventilation. It should be sealed airtight from the

potentially infectious areas below. Likewise, if potentially contaminated pipes or ducts run in the basement, there should be a concrete floor. Otherwise, the attic and basement become microbiological, chemical, mechanical, and fire traps. If ducts and utility lines are placed in wall chases or above corridor false ceilings, these spaces should be designed to permit changes in the ducts and lines. To reduce risk during maintenance, as much engineering service equipment as possible should be in the "clean" area.

16. Will the nature of the experiments, or the species of animals used, or significant change in type of agent and experiment, or resident microbial contamination in the room endangering validity of experiment and product, or nonspecific animal infection such as epidemic diarrhea of mice, or potential infection of personnel, or periodic repair or modification by engineering personnel, make it desirable that all, or some, rooms, air ducts, air filter plenums, and air filters be sterilized periodically by gas such as Betapropiolactone or steam-formaldehyde? If so, attention must be given to air-tightness of walls, ceilings, light fixture, air duct and utility insertions, windows, if any, and sometimes even the electrical conduit and electrical switches. These precautions also will assist in controlling condensation and vermin. False ceilings are undesirable in laboratories and animal rooms. If perforated false ceilings are used in the corridors, there may be large unsealed openings in the barrier wall above the false ceiling, between the "clean" and "contaminated" parts of the building. These openings should be made airtight. The air ducts are not suitable conveyors for decontaminating gases; condensation occurs at angles and bends, which causes maldistribution and rusting. Instead, a portable decontaminating apparatus is positioned in the open room, from which gas enters the air ducts if this is desired. All surface finishes must be evaluated for chemical resistance to decontaminating agents.

17. Will shaking machines holding microbial cultures be operated in walk-in incubators or refrigerators? In case of breakage of flasks on the shakers there is needed (a) a light switch, an ultraviolet light switch, and a power switch for the shaker, all located outside the incubator or refrigerator; (b) a view glass in the door for observation before entrance; (c) an ultraviolet fixture inside the incubator or refrigerator to reduce air-borne microbial contamination before entrance after an accident. (In a laboratory, the 10 to 12 air changes per hour will be an effective substitute.)

18. Will any of the experiments result in animal excreta, the uncontrolled disposal of which would endanger domestic, farm or feral animals? Examples: anthrax, glanders, equine encephalitides. In general, it must be presumed that all excreta from experimental animals is infective until proved otherwise. Are there any other reasons of law, public relations, volume of material, or microbial virulence that make disinfection or sterilization of sewage necessary?

It is well to check this matter in advance with the local civil officials. Infectious disease units handling only small animals, amounts of cultures in test tubes and flasks, and infectious agents characteristic of a hospital or diagnostic laboratory ordinarily do not need to decontaminate sewage. The autoclaving of infected cages and debris and the sterilization of cultures before discard assures that few if any infectious organisms are discharged in the liquid wastes.

However, if the sewage is to be decontaminated, this commonly is done by steam in a retention tank in the basement or outside the building. The tank should be in an enclosure (which could be in the open air without a roof) with concrete floor and walls high enough to hold all the contents in case of leakage. It is wise to have a removable port large enough to introduce sufficient hypochlorite or other disinfectant to achieve chemical sterilization in event of power failure. A recording thermometer and easily accessible control panel for convenient daily observation and adjustment is desirable. If spores are not a consideration, pasteurization may be sufficient (200°F for 30 seconds). Where sterility is needed, our tests show that 260°F for about ten minutes will be effective. Whether batch sterilization in a tank or continuous flow through heated pipes is used, depends upon an engineering economic evaluation. Water from showers, toilets, urinals, hand basins, drinking fountains, and cooling systems need not be sterilized or pasteurized; this greatly reduces the volume of waste.

19. What is the personnel policy regarding occupational health?

(a) As a condition of employment, must employees accept vaccination with commercial standard vaccines and with experimental vaccines when, in the opinion of the laboratory director, administration of these would decrease the chance of clinically apparent illness? A "yes" answer will reduce the need for mechanical protection, if only those agents are studied for which a vaccine is available.

(b) What level of occupational infection is acceptable to management? Subclinical infection detectable only serologically? Minor discomfort no more than from a reactive avirulent living vaccine, which causes only a minority to cease work for one to three days? A "no" answer to these questions may make the difference between installation of individual protective cabinets (Figure 2) and installation of much more expensive gastight systems (Figure 1), depending again upon the agent and the experiments.

20. For public relations, economic, legal or other reasons, to what extent is protection from infection of persons not working in this laboratory considered to be of comparatively great importance?

A common observation of the authors is that, in a building that amply protects the community with some or all of such arrangements as air locks, change rooms, filtration or incineration of exhaust air, special treatment of sewage, and ultraviolet barriers, the building occupants themselves do not have a corresponding degree of protection. For instance, (a) only chemical fume hoods are installed, or no protective ventilated microbiological work cabinets are provided, or those installed are only three feet wide. This size is recommended as suitable only for very limited and specialized operations on a small scale, typically in a general laboratory characterized by absence of air locks, change rooms, etc. Often these three-foot units become merely display items, not connected to the air exhaust system, rarely used for the good reason that they are too small for routine work. In a laboratory constructed primarily for work with highly infectious agents, cabinets need to be constructed, equipped, and placed so that they are the most convenient place to work. This assumes that work with truly hazardous agents is underway. When not so used, the glass door panel can be raised and the cabinet used as if it were a laboratory bench top. In the absence of such cabinets, conscious or unconscious choices are made to avoid hazardous agents. Sometimes use of a nonpathogenic simulant is rationalized as being adequate to study the "basic mechanisms of action" of the pathogen. It is the experience of our laboratories that this rationalization often is unwarranted. In any event, nonpathogens can, and should, be studied in less expensive surroundings. Another likely discrepancy is the absence of an autoclave or a satisfactory equivalent to sterilize animal cages before cage litter is removed, prior to cleaning, or, if present, the autoclave is not convenient to the animal rooms. Both of these conditions encourage human infection. Often, no provision is made to prevent animal-to-animal cross infection, and presumably, in such instances for some diseases, animal-to-man transmission.

The reason for disproportionate emphasis on microbiological safety often lies principally with the resident microbiologists who act as consultants during design. There is an understandable human tendency to approve or tolerate arrangements that require little change in working habits, such as passage through a clothing change room and shower, clean laboratory clothing, air handling, and sewage decontamination. Objection most likely arises when the working site at the laboratory bench is affected by proposals for protective cabinets and enclosures of various kinds. Unfortunately, operations at the laboratory bench or animal cage within a few inches of the worker's nose are the source of most human infections. All other protective features are secondary in importance as far as safety of the employee is concerned.

Of course, this disproportionate emphasis is completely justified if the diseases to be studied will be limited to those that are not dangerous for man but would be a serious threat to domestic animals if they escaped from the laboratory. A few examples are: African swine fever, African horse sickness, lumpy skin disease, and blue tongue of sheep and cattle.[16]

21. What are the local zoning laws and building codes relative to an infectious laboratory? What changes in these laws and codes can be foreseen? In what direction are they moving as concerns disposal of potentially infectious wastes and noncombustible trash?

22. Is study contemplated, now or in the future, of diseases for which permission, and in some cases inspection, may be required by the U.S. Department of Agriculture and/or the U.S. Public Health Service? Examples: Rift Valley fever and African swine fever. We are informed that increase in importation of infectious agents and their vectors, and the increased number of laboratories handling infectious agents, has caused USDA and USPHS to plan for closer examination of imports and laboratories handling them. Both government agencies will give great weight to the competence and integrity of the scientist as well as to the quantity of material being handled in determining whether or not a laboratory is suitable under their regulations. Since there are no clear-cut criteria, if there is any plan to handle highly infectious material it is very strongly suggested that the responsible government agencies be consulted regarding the plans before commitment for construction is made.

23. Will any equipment, significantly contaminated by an infectious microorganism or toxin, need to be sent periodically to the manufacturer for repair or adjustment, or need to be repaired or adjusted by his service men? If so, some arrangement for decontamination of this apparatus may be desirable. For delicate apparatus, ethylene oxide gas is very useful. For economy, it must be used in a leakproof space such as an autoclave.

24. In the geographical area concerned, are there sufficient dusts, bacterial spores, fungi, molds, or insects so that intake air should pass through a coarse filter? Our experience is that such filtration is highly desirable. The air supply fan should shut off automatically if the exhaust fan for a contaminated area accidentally stops, to prevent pushing contaminated air into clean areas. However, the exhaust fan should not cut off automatically when the intake fan stops. An alternative but less certain method of controlling nonspecific microbial contamination is to provide ultraviolet ceiling fixtures, to be turned on overnight.

25. Where will the experimental animals be obtained? Unless the effort is relatively small, it is better for animals to be produced and prepared apart from the area of research, to avoid complicating accidental infection. A "clean" area where animals can be quarantined for a suitable time before use is helpful.

26. As part of a periodic cleaning or disinfection process will it be necessary to flood the floors? If so, special attention must be given to prevent cracks, not only around floor or sink drains but also anywhere else. Apparently it is very difficult to make a concrete floor that will not crack enough to permit seepage of water into the room below.

27. How reliable is the source of power for the building? The major danger to employees is an air flow stoppage in a protective ventilated cabinet during a hazardous experiment with aerosolized microorganisms. Perishable refrigerated materials usually can be transferred to a cooler that uses solid carbon dioxide. Contaminated sewage is no problem if personnel leave the building and the retention sewage tank is large enough for batch chemical sterilization. Inasmuch as work stops, exhaust air is of no concern. However, animals in closed, mechanically ventilated cages will die in about an hour if there is no ventilation. For this reason, the extent of use of ventilated cages will be a factor in evaluating the need for standby auxiliary power.

28. Is the probable cost of this laboratory fully realized by management? Our engineers report that only about 43 per cent of the roofed floor space of this building will consist of "working space" for laboratories, incubators, refrigerators, animals, dish washing, and cage washing. The other 57 per cent will be used for offices, conference rooms, storage, corridors, change rooms, airlocks, machine rooms, pipe chases, stairwells, elevator, walls, basement, and attic. Attic space is defined as any part of the attic with at least five feet of headroom. On this basis, if the entire building cost is divided by the square feet of "working space" as defined above, the cost of working space will range from $76 to $147 per square foot without installed or portable equipment, and from $98 to $179 with all equipment. Pieces of equipment costing less than $200 and the cost of land are not included. Moreover, the cost of building maintenance is high. For example, at Fort Detrick, maintenance costs per square foot for laboratory buildings are almost twice that for family housing and more than four times that for warehouses. These costs are mentioned because, with the complex facilities of an adequate infectious disease building, it should be made clear at the outset that maintenance costs are of a different order of magnitude than those for some other types of construction. It is recommended that provision be made so that these costs are not charged to the budget for animals, scientific equipment, and laboratory supplies, lest it bear the burden of maintenance costs to the detriment of the research effort.

III. ESTIMATION OF RISK

To assist in answering some of the questions concerning policy and to provide a basis for making other decisions and accepting or rejecting some of the suggestions outlined above and in Table I, the following "Estimation of Risk" is offered for consideration:

As a guideline, the following orders of decreasing magnitude of risk and decreasing complexity of precautionary measures are proposed for diseases of man and animals as studied in the laboratory. The emphasis upon aerosol dissemination derives from the belief that future research will make increasing use of aerosol challenge in the study of respiratory diseases.

1. Suitable for any type of experiment with any microorganism and any animal up to the size of a chimpanzee.

2. Preparation of dry powders of infectious agents.

3. Dissemination of pathogenic microbial aerosols.

(a) Organisms highly infectious for man, producing a distressing disease for which there is an incompletely protective vaccine and only partially successful specific chemotherapy. The difficulty in treating such syndromes as pneumonic plague causes their aerosolized pathogenic agents to be included at this level of hazard, even though they are not as readily infective as some others.

(b) Organisms infectious for man, producing disease that is incapacitating but usually not serious when acquired in the laboratory, for which there is an incompletely protective vaccine and no specific chemotherapy. Although the glanders organism is less infective and the disease may be treated with sulfadiazine, it should be included here because of the dangerous clinical syndrome produced.

(c) Toxins or organisms highly infectious for man, producing disease for which there is either effective vaccination and/or effective specific chemotherapy.

4. Laboratory studies not involving planned dissemination of aerosols. The subclassification would be the same as in 3 above.

5. Dissemination of dry or fluid aerosols of organisms with comparatively low invasiveness, usually with no vaccine available, often subject to specific chemotherapeusis, but sometimes causing serious pneumonia, such as staphylococcus, streptococcus, and pneumococcus.

6. Laboratory studies not involving dry powders or planned dissemination of aerosols, with organisms of less serious risk because of various mitigating factors present to varying degrees, such as availability of vaccination, specific treatment, and low infectivity in the laboratory.

7. Minor infections.

(a) Nuisance diseases such as Newcastle virus conjunctivitis.

(b) Organisms seldom causing laboratory infection such as pneumococcus, streptococcus, staphylococcus, meningococcus, vaccinia virus, and diphtheria and tetanus bacilli.

8. Classroom demonstrations or student work with killed, stained preparations or with attenuated strains.

IV. COMMENT

The most common source of laboratory-acquired infection is the inhalation of accidentally or experimentally created microbial aerosol. Therefore, control of air is very important. Control should begin where the aerosol is formed. To the extent that this is achieved, other features such as differential air pressures in rooms, protective respiratory equipment, ultraviolet irradiation, and personnel showers become less important in protecting the employee.

When air is filtered or incinerated close to where microbial aerosol arises, then filtration of air from the open room and building becomes less critical. Incineration ordinarily is limited to air exhausted from aerosol vessels and from gastight cabinet systems.

Separate air-handling systems for the clean area, the contaminated area, and the animal room area are useful when the size of the building permits. These may facilitate the flow of air from the less hazardous areas to the more hazardous. The effectiveness of ultraviolet air locks between such areas has been tested.[17] To illustrate the efficiency of air pressure differentials, a difference of 0.1 of an inch of water pressure at 70°F will result in an air velocity flow of 1266 linear feet per minute. Even a pressure difference as low as 0.001 of an inch of water will result in a flow of 126 linear feet per minute.

One problem often encountered in control of the climatic environment is an oversized inflexible refrigeration component of the system. This makes it quite difficult to maintain satisfactory operation in seasons when there is a very small cooling load and when some areas require cooling and others require heating at the same time. It may be necessary to add heat in excess of actual requirements to maintain satisfactory operation of the refrigeration equipment.

V. CONCLUSIONS

Efficient programming for the construction of infectious disease laboratory facilities requires (a) that a number of policy decisions be made, (b) that the types of isolation and containment features and equipment to be utilized be decided before design work begins, and (c) that the magnitude of the probable construction and maintenance cost be realized from the beginning. Major decisions derive from the fact that most laboratory infections occur at the laboratory bench and consequently that is where microbiological safety provisions should begin. As far as the safety of the employee is concerned, all other features are secondary in importance.

LITERATURE CITED

1. Snow, D.L. "Principles of space planning for biomedical research laboratories," National Institutes of Health, Division of Research Services, Bethesda, Maryland. 1962.

2. "Medical school facilities, planning considerations and architectural guide," U.S. Government Printing Office, Washington 25, D.C. 1961. (U.S. Public Health Service Publication 875). ($1.00). p. 185.

3. "Planning and design of medical research facilities," National Institutes of Health, Division of Research Services, Bethesda, Maryland. 1962. p. 29.

4. Fox, G. "Design of laboratory facilities, a classified list of selected references 1947-1962," National Institutes of Health, Division of Research Services, Bethesda, Maryland. 1962. p. 13.

5. Wedum, A.G.; Hanel, E., Jr.; Phillips, G.B.; and Miller, O.T. "Laboratory design for study of infectious diseases," Am. J. Public Health 46:1102-1113, 1956.

6. Jemski, J.V., and Phillips, G.B. "Microbiological safety equipment," Lab. Animal Care 13:2-12, 1963.

7. "Guide for laboratory animal facilities and care," U.S. Government Printing Office, Washington 25, D.C., 1963. (U.S. Public Health Service Publication 1024). p. 35. (20¢)

8. Chatigny, M.A. "Protection against infection in the microbiological laboratory, devices and procedures," in "Advances in applied microbiology," New York, Academic Press, 1961, Vol. 3, pp. 131-192.

9. Hill, B.F., Ed. "Procedure of the symposium on research animal housing," Lab. Animal Care 13, Part 2 of 2:221-467, 1963.

10. "Air filtration of microbial particles," U.S. Government Printing Office, Washington 25, D.C. 1962. (U.S. Public Health Service Publication 953). (40¢)

11. Wedum, A.G. "Control of laboratory air-borne infection," Bacteriol. Rev. 25:210-216, 1961.

12. Wedum, A.G. "Laboratory safety in research with infectious aerosols," Safety Division, U.S. Army Biological Laboratories, Frederick, Maryland. 1963. (Technical Manuscript 84).

13. Phillips, G.B., and Jemski, J.V. "Biological safety in the animal laboratory," Lab. Animal Care 13:13-20, 1963.

14. Kirchheimer, W.F.; Jemski, J.V.; and Phillips, G.B. "Cross infection among experimental animals by organisms infectious for man," Proc. Animal Care Panel 11:83-92, 1961.

15. Phillips, G.B.; Reitman, M.; Mullican, C.L.; and Gardner, G.D. "Applications of germicidal ultraviolet in infectious disease laboratories. III. The use of ultraviolet barriers on animal cage racks," Proc. Animal Care Panel 7:235-244, 1957.

16. Mauer, F.D. "Emerging animal diseases," Military Medicine 128:327-333, 1963.

17. Wedum, A.G.; Hanel, E., Jr.; and Phillips, G.B. "Ultraviolet sterilization in microbiological laboratories," Public Health Rept. 71:331-336, 1956.