LAB SAFETY SEMINAR
- ANIMAL HEALTH

CONFERENCES OF
JONATHAN RICHMOND

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by

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INTRODUCTION

Dr. J. Y. Richmond prepared and gave four lectures to a group of some 70 Jamaican personnel drawn from interested groups from the public and private sector, in a seminar on Techniques for Achieving Laboratory Safety Measures in May, 1981. This is one of the activities executed in Jamaica by the Animal Health Division of IICA under the direction of Dr. Franz Alexander.

IICA is pleased to present the proceedings in the series Agriculture in Jamaica, the lectures given during the seminar, and wishes to state that it was a pleasure to have participated in the organization and the execution of this activity. It was well received by the participants and raised interests for future seminars of this nature.

Percy Aitken-Soux
Director
June 1st, 1982

FOREWORD

At the Second Hemispheric Reunion of Directors of Animal Health, REDISA II, held at IICA's Headquarters in San Jose, Costa Rica during September, 1980, the need for improved laboratory equipment maintenance was identified for many countries throughout the hemisphere.

In particular, the representatives of the Antilles Zone proposed that IICA should sponsor a training course in the proper use and maintenance of Veterinary laboratory equipment.

It was emphasized that although there was a need to keep laboratory equipment working properly in the region, maintenance services were not readily available, nor were laboratory workers trained in maintenance of these expensive instruments.

The Government of Jamaica agreed to host the seminar which was held at the Veterinary Division, Ministry of Agriculture, Hope, from May 18 - 22, 1981. The seminar was organized and co-ordinated by IICA/ Jamaica and the Veterinary Division of the Ministry of Agriculture.

Nine (9) Regional participants, Veterinarians and Laboratory Technologists from IICA member countries attended, together with twenty-three (23) Jamaicans including Ministry of Agriculture personnel, Medical Technologists from the Ministry of Health, Technicians from the Bureau of Standards and the University of the West Indies.

The agenda covered a wide range of instruments which emphasized mainly the principles of function and procedural application. Laboratory Safety was a subject that was highly recommended for inclusion by the Directors of Animal Health. It proved to be one of the topics found most useful by the participants.

The Plum Island Animal Disease Centre, United States Department of Agriculture, had kindly consented to the participation of Jonathan Y. Richmond, Ph.D., who presented a series of lectures on Laboratory Safety Procedures, Monitoring Safety in the Laboratory Environment and Containment of Infectious Micro-organisms. The opportunity was also taken

to introduce to the participants, the mission, goals and operations of the Plum Island Animal Disease Centre.

The lectures, which were highlighted by slides, are hereby presented in the collection of papers of IICA/Jamaica "Agriculture in Jamaica".

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THE PLUM ISLAND ANIMAL DISEASE CENTER:
Its Mission, Goals and Operation

SUMMARY

The United States Department of Agriculture operates the Plum Island Animal Disease Center on behalf of the U.S. taxpayer (1). The primary missions of this Center are to provide diagnostic capabilities, research facilities and training opportunities for evaluating economically important diseases of livestock animals. This Center is unique because it studies animal diseases that do not exist in the United States.

INTRODUCTION

Since long before recorded history, man has domesticated animals both for food and transportation purposes. Most domesticated animals in the third world countries today are used for draft purposes. The United States is free of many livestock diseases found elsewhere in the world. The benefit of this to the American people is measured both in having healthier animals and in the economics associated with participating in free world trade. Our animals and animal products can generally be shipped to other countries; the reverse is not always true.

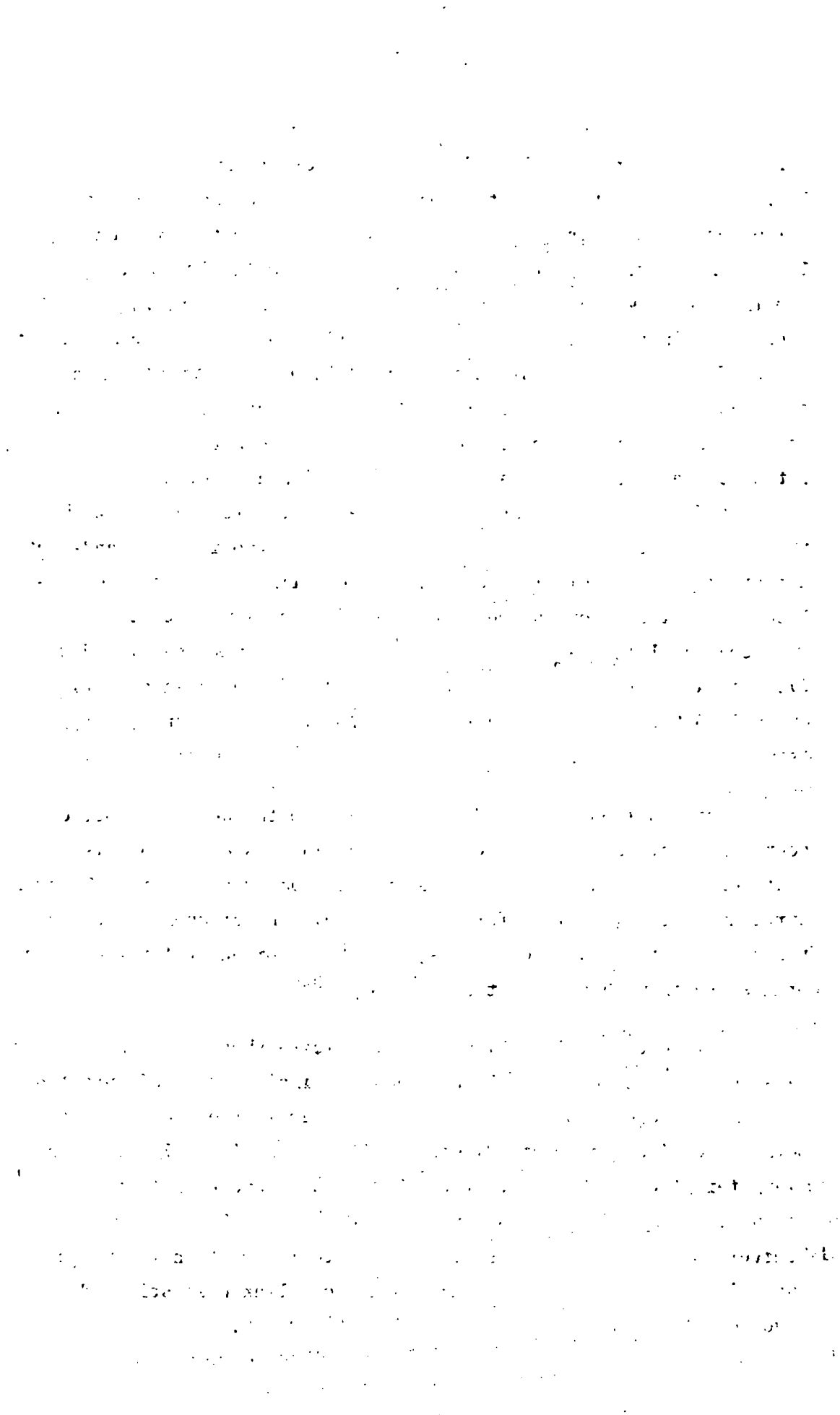
There are approximately 200 million domesticated farm animals (cattle, swine, goats, etc.) and nearly one billion poultry in the United States today. There is an increasing need throughout this country and the rest of the world to provide healthy animals. Today's animal producers rely heavily upon various branches of the United States Government to help protect their industries from devastation by foreign animal diseases entering into the United States. When a disease outbreak occurs, animals must be destroyed, premises quarantined and disinfected, and interstate and international commerce halted. The direct and indirect costs of such activities are tremendous and are often measured in billions of dollars.

HISTORY

Foot-and-mouth disease is one of the most economically and politically important animal diseases that exists in the world today. It is also one of the oldest known diseases to be recognized as being caused by a virus, having been described first in the early 1500's in Italy. The disease has been reported in virtually every country of the world since then. Foot-and-mouth disease was reported nine times in the United States between 1870 and 1929. A massive outbreak of foot-and-mouth disease occurred in Mexico in 1946. Nearly seven years was required to eradicate this disease from Mexico; the United States worked very closely with the Mexican veterinary authorities to carry out the slaughter, vaccination and surveillance programs (2). The Congress of the United States recognized at that time the need to establish a laboratory for diagnosing foot-and-mouth and other foreign animal diseases. The enabling legislation establishing the laboratory stipulated that the facility must be built on a coastal Island surrounded by deep navigable waters (3). However, it was not until 1952 when FMD was diagnosed in Canada, that the United States Congress actually appropriated the funds to establish this Center.

Animals imported from Europe years ago to the North American continent traveled by relatively slow sailing vessels. Animals that became sick and died aboard ship were dumped overboard. Today's air transportation allows for the rapid movement of animals and animal products between countries, and the opportunity for the spread of disease is much greater than it was years ago.

Our government's policy is to eradicate these foreign diseases by slaughter, followed either by burial or incineration of infected carcases. The cost of an eradication program is tremendous. The outbreak of foot-and-mouth disease in England in 1966-67 led to the slaughter of over 500,000 cattle. The 1952 outbreak of foot-and-mouth disease in Canada cost approximately $1,000,000 to eradicate; however, because the borders were closed to international commerce, the spinoff from this particular disease outbreak was estimated to have cost the Canadian people over $1,000,000,000.



Plum Island is a small 800 acre island, approximately 1½ miles east of Orient Point, Long Island, New York, and, is located 13 miles south of New London, Connecticut. The island was originally inhabited by local Indian tribes and did not come under the influence of the new settlers until 1638, when the island was purchased by a Mr. Wyllis of Hartford, Connecticut.

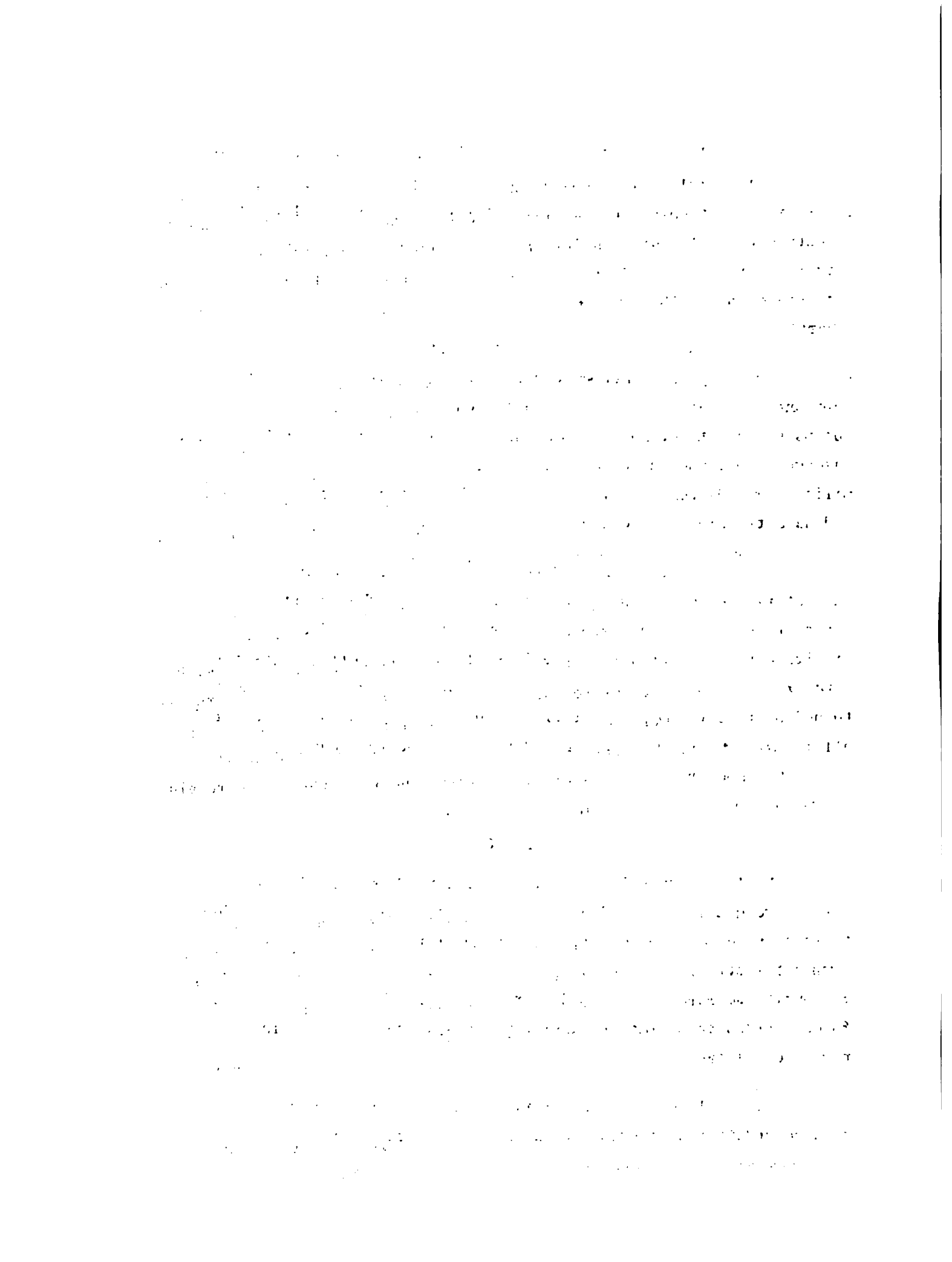
The island's location made it important in the early defense of New York City and New London harbors. Along with several other surrounding islands, Plum Island has been used for coastal watch purposes since the time of the Spanish-American War. By 1900, a large part of the island had been purchased for the establishment of a military base. Fort Terry was operated both as a coastal defense station and as a training camp during World Wars I and II.

It was proposed in 1947 that the new foreign animal disease laboratory should be built as a joint project by the Department of Agriculture and the United States Army. The military decided to withdraw from the project before the first laboratory building was actually, however, and the entire operation of the laboratory was subsequently turned over to the Department of Agriculture. The USDA had acquired all but a few acres of Plum Island by 1954, the remainder being retained by the Coast Guard to operate a lighthouse.

THE PIADC

Employees travel from Orient Point to Plum Island on one of three government owned and operated vessels. A large passenger ferry transports the day personnel, while a smaller passenger ferry operates during the evenings. A third boat transports both passengers and freight. The island is closed to the general public and a security force patrols the Island to assist persons whose boats may inadvertantly come ashore.

Plum Island is administratively divided into several areas to accommodate its diverse operations. Dock areas have been



established for easy movement of materials and supplies from the mainland to the island. This dock area includes a barn for storing animal feed, a warehouse for the receipt and storage of necessary supplies and equipment, and a dock guardhouse. The guardhouse contains transfer platforms, decontamination terminals, sterilizers, showers and other facilities necessary for maintaining biological safety operations.

Several animal quarantine facilities are maintained on the island. These facilities are considered to be "cleaner" than any other part of the island, and personnel must shower before going into the animal quarantine areas. Persons who have entered the laboratories are prohibited from going to any animal quarantine area, contacting certain species of animals, or from visiting any animal holding areas for a period of seven days after leaving the laboratory.

The two high containment laboratories operated on Plum Island are currently staffed by forty scientists. One laboratory is dedicated to diagnostic activities, training and other service-related functions. The second laboratory contains research diciplines in pathobiology, cytological investigations, biochemistry, immunology, vaccine development, and various support services. The remainder of the island helps provide a suitable buffer area between animal quarantine, the laboratories and the mainland.

Offices now occupy buildings which had been built at the time Fort Terry was established, but, with the exception of the cafeteria, no building is used for the same purpose for which it was originally built. For example, the mouse colony occupies the old jail house, the original chapel is now an assembly hall, and the former post infirmary houses the administrative offices. The diagnostic laboratory occupies a building that had originally been used during World War II to store anti-ship mines; the walls of the building are three feet thick. The main research laboratory was constructed in the mid 1950's to contain a series of laboratories, service areas, animal wings, and incinerators.

Animals to be delivered to Plum Island are transferred from livestock carriers to Center vehicles at a designated point on Long Island; the livestock carriers are suitably cleaned and disinfected before returning to farms. The Center's vehicles are transported via ferry boat to Plum Island. Animals are transferred through the dock terminal to waiting animal delivery trucks and are taken to animal supply facilities for general quarantine and holding. Animals needed in the laboratories are transferred back to the dock area. Additional personnel then transfer the animals to different trucks and move the animals to the laboratory. There is no direct contact between the animal quarantine personnel or equipment and the laboratories, maintaining the "break in the link" between animal quarantine and infected animal areas. Laboratory-based animal handlers assist in the delivery of the animals through the decontaminated airlocks into the laboratory buildings.

Visitors who come to Plum Island must read and sign an affidavit indicating that they will abide by the Center's biological safety rules and regulations, and to stay away from susceptible animals and/or certain specified animal holding facilities. Center employees are given color coded identification passes which indicate those areas of the Island to which they have access. Security personnel monitor access to Plum Island, to the animal supply areas, and to the laboratories.

CENTER OPERATIONS

Many procedures have been developed to provide maximum containment for the disease organism studies in the Center's laboratories. Persons who must enter the laboratory facilities proceed to clean change rooms where they remove all clothing, jewellery, eyeglasses, and other personal effects. They proceed into the interior change rooms to put on laboratory clothing. Personnel must disrobe and take thorough decontaminating showers before leaving the laboratories. It may be necessary to shower and change clothes while moving between certain contaminated areas within the laboratory

buildings. Laboratory personnel conduct all work with infectious micro-organisms within Class II laminar flow biological safety cabinets. These cabinets provide the primary containment barriers which are the foremost mechanisms for confining these disease organisms within the laboratory. All air is filtered before it is discharged from the laboratory buildings, so that airborne virus particles are trapped in the filters. All liquid sewage is collected and heat-decontaminated before it is piped to the Center's secondary/tertiary sewage treatment facilities. Animal carcasses and all other burnable trash are burned in pathological incinerators. Non-burnable material can be removed from the building only after appropriate chemical decontamination or sterilization procedures.

Diagnostic and other service-related activities are conducted in one high-containment building, while most research activities are located in a second high-containment laboratory building. Sometimes it is difficult to draw a clear line between service-related activities and research, as many of these activities are quite inter-related. Research done at this Center is closely tied to specific practical goals: developing new or better diagnostic tests or reagents (4-41), producing and testing new vaccines (42-73), establishing fundamental information about disease transmission or development (74-94), or determining suitable means of decontamination (95-108). Determining how viruses can survive in products prepared from infected animals has been another important area of research. Examples include hides, wool, silk, cheese, semen, pharmaceutical products and fresh, dried or smoked meats (109-126). Results of these studies can have tremendous economic impact if the importation of such products into the United States must be restricted or prohibited.

Livestock animals are prohibited from being imported into the United States from countries where certain animal diseases are present. Considerable interest has been expressed by livestock breeders to introduce new genetic stock into our herds, and several avenues are available to accomplish this. One has been to import

desired animals from other countries which have "clean" animals - i.e., animals free of these diseases. Procedures also have been developed for importing cattle semen, even from countries where these diseases are present (127-128). But, semen can act as a carrier for many different micro-organisms, and we have to assure that semen collected for importation is not contaminated (129-134).

Many of these tests were developed at the PIADC, and the final testing for these micro-organisms was done at this Center. An animal importation station was recently established in Fleming Key, Florida. The purpose of this station was to provide a facility to hold livestock in quarantine while certain diagnostic tests were conducted (again at the PIADC), to ensure the animals did not harbor undesirable micro-organisms.

This Center has been actively engaged in screening procedures which are required for animals being imported into the nation's zoos. Even after these animals have been "cleared" for entry into the United States, they must remain in designated zoological gardens and cannot be released into wildlife parks; only healthy offspring born in the zoological gardens may be transferred to these "safari" parks.

Some wildlife species - particularly the ruminants - are highly susceptible to many of these foreign animal diseases. Scientists at the PIADC have studied a number of these species to determine the possible fate of some of these organisms should they ever get into the wildlife reservoir (135-150).

By definition, the diseases studied at the PIADC are foreign to the United States. Consequently, American veterinarians have had little or no opportunity to observe these diseases in livestock animals. The PIADC has conducted a number of courses in the recognition and diagnosis of these foreign animal diseases. Indeed, training is an integral part of the Center's mission. Scientists from around the world come here for postgraduate educational and research opportunities. Close relationships are maintained with

other laboratories throughout the world to keep open the formal and informal exchange of information regarding matters of interest to international veterinary medicine.

The PIADC has been able to fulfill its primary missions for more than a quarter of a century. The Center faces a continuing challenge to meet the needs of a hungry worldwide population by producing better and healthier livestock.

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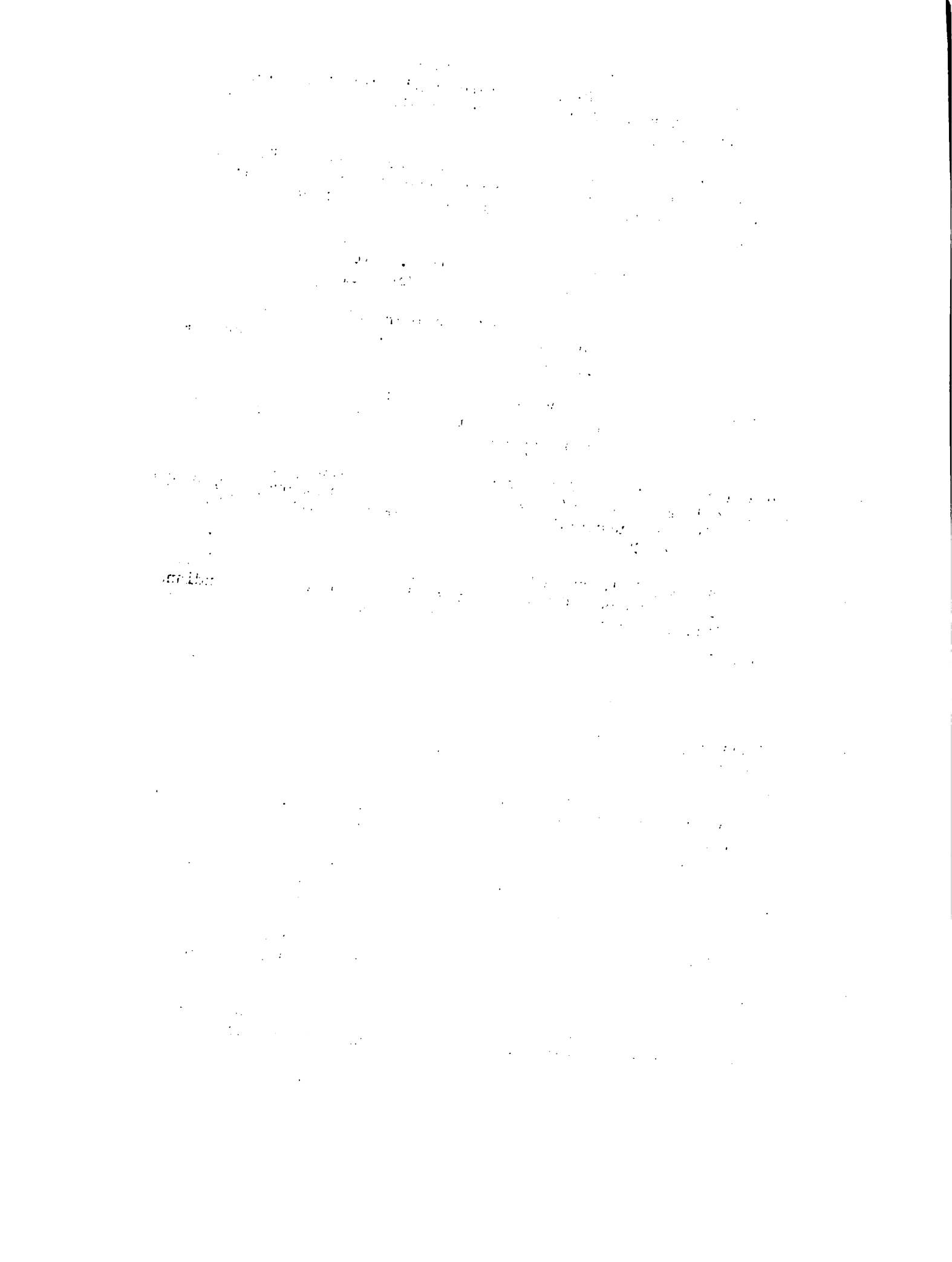

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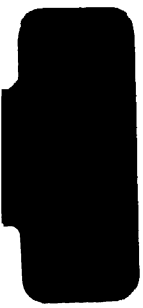
CONTAINMENT OF INFECTIOUS MICRO-ORGANISMS



SUMMARY

Laboratory environments can be dangerous places in which to work because of the materials and equipment that are used. Laboratories can also be very safe places to work when a positive attitude and suitable training are matched with adequate engineering systems and managerial support.

INTRODUCTION

Much information has been developed to determine the type of laboratory containment necessary to perform particular tasks safely. Etiological agents have been classified on the basis of hazard (1), and proposed guidelines have been developed for working with infectious organisms(2). These concepts can generally be extrapolated to laboratory working with toxic chemicals (3-5).

When the history of biological containment is written, one of the major highlights will clearly be the role that recombinant DNA (r-DNA) experimentation played in raising the consciousness of both the scientific community and of the general public to the dangers associated with certain laboratory activities. In the early 1970's, when it became apparent that the r-DNA techniques would allow transferring genetic information from one species to another species, a loud outcry went up which eventually led to a moratorium on conducting such research. The scientific community began an extensive analysis of the levels of containment desirable to allow such experimentations to be done safely. For r-DNA research, recommendations were developed for both biological and physical barriers (6,7). The biological Barriers were self-destructing vectors, organisms which were unable to survive outside the very restricted laboratory environment. The perceived potential hazards of the biological systems were matched to physical barriers designed to provide varying degrees of containment. Although acceptable self-destructing vectors were eventually developed for these studies (8), the principles for establishing and maintaining physical containment had been known for many years (9,10,11). Biological

containment systems are all the physical and administrative barriers which ensure that infectious micro-organisms remain within the laboratory. The extent of this containment is mandated by both the type of organism and the type of activity involved (12-16).

Tertiary barriers are those systems designed to minimize or control access to restricted areas. Physical barriers include compound fencing, guard houses, remote control and monitoring devices, and so forth. Administrative barriers include security, controlled access of unauthorized personnel, and controlled visitor or employee movement within the restricted areas.

Secondary containment barriers are those facility designs and layouts that prevent the escape of infectious micro-organisms from one interior area to another, or from the interior of the laboratory building to the outside environment. Such barriers may include appropriately filtered ventilation systems, zones of differential air pressure, sewage decontamination, double door autoclaves and airlocks, clothing changes and other restrictions on personnel activity. All personnel practices involved with maintaining the systems and minimizing personnel contamination in the spread on infectious micro-organisms must be considered as integral parts of the secondary containment system. The activities associated with good laboratory practices and good laboratory housekeeping are also parts of the secondary systems.

Primary containment barriers are the principle systems which isolate the investigator from the biohazard. These primary systems are generally designed to prevent or minimize exposure of the worker to the organisms and/or to provide some level of protection from cross-contamination with other organisms.

CABINETS

Several types of primary containment systems have been developed. Class III systems are gas-tight, absolute barriers used for the contain-

ment of very high risk organisms. These systems use cabinets equipped with glove or remote handling devices. Two or more cabinets are often connected together to provide a larger containment area; laboratory equipment may have to be modified to fit into the cabinet line. Materials are introduced into or removed from these lines via chemical dunk tanks filled with a suitable chemical disinfectant, through pass boxes or through double-door autoclaves. Class III systems provide maximum personnel protection. An alternative to the Class III cabinet system is the ventilated suit, which isolates the worker from the contaminated environment. Suits equipped with filtered and conditioned air offer the worker an opportunity to move and operate freely within a normal laboratory environment. Suits offer a way of protecting the worker where the biohazard source (e.g., an infected steer) cannot be placed in a Class III cabinet line.

Class II systems are vertical laminar flow biological safety cabinets which offer high levels of both personnel safety and product protection, without the restraints imposed by a Class III cabinet. Personnel must be properly trained in the appropriate use of these cabinets; maximum protection is obtained only when these Class II systems are properly maintained.

Class I cabinets are essentially similar to chemical fume hoods. They generally have a fixed opening, but may be equipped with glove ports. These cabinets rely on an inward flow of air to provide personnel protection; the air is filtered as it is withdrawn from the cabinet.

Horizontal laminar flow benches blow HEPA-filtered air across the work surface, offering product protection but no personal protection. Infectious micro-organisms, toxic chemicals and ratio-biologicals must never be handled on these benches; the risk of worker contamination is too high. Vertical laminar flow areas (benches, rooms, etc.) are low to moderate level containment systems designed to reduce the level of airborne containments on workers and

equipment by "washing" them with HEPA-filtered air. These systems are maximally effective when combined with floor level exhaust vents.

PROCEDURES TO MINIMIZE RISK

Essentially, all laboratory procedures have been analyzed for their hazard potential, often as a consequence of investigating the source of a laboratory-acquired infection. Experiments have shown that the major cause for dissemination is aerosols created by: pipetting, blending, using a needle and syringe, centrifuging, inoculating with a loop, opening screwcapped containers, spilling or splattering infectious materials, withdrawing materials from a vacuum bottle, etc. (17-29). Recognizing that such procedures have a high potential for release of organisms into the working environment should lead to curtailing these activities or for finding safe ways to perform these necessary tasks. Other infections have been traced to animal bites or scratches, cuts from broken glass, self-inoculation, and similar traumatic events (30-59). These hazards can be minimized by using appropriate protective devices and work practices.

General laboratory practices have been developed to lower the potential escape of organisms and their dissemination in laboratory environments. The combination of practices, potential human infection, and the consequences of risk assessment can be used to define minimal risk, moderate risk and high risk activities.

At the minimal risk level, acceptable practices are (2):

1. Keep laboratory doors closed.
2. Do not eat, smoke, drink or store food in the laboratory.
3. Wear laboratory gowns, coats or uniforms when appropriate.
4. Do not mouth pipette. Use mechanical pipetting devices.
5. Use procedures that minimize aerosol formation.
6. Avoid using hypodermic needles.
7. Wash hands after completing experimental procedures and before leaving the laboratory.

8. Disinfect work surfaces daily and immediately after a spill.
9. Decontaminate all biological waste materials before disposal. Decontaminate other contaminated materials before washing, re-use or disposal.
10. For off-site decontamination, package contaminated materials in closed, durable, leak-proof containers.
11. Control insect and rodent infestation.
12. Keep laboratory areas neat and clean.

In laboratories where moderate risk experiments are done, these are additional acceptable practices (2):

13. Post universal biohazard signs on all laboratory access doors and equipment storing the hazardous materials.
14. Only persons knowledgeable of the risks should be allowed to enter the laboratory.
15. Keep animals not exposed to the moderate risk agent out of the laboratory.
16. Wear gowns, coats or uniforms inside but not outside the laboratory.
17. Use biological safety cabinets to contain aerosol-producing equipment. Use centrifuges with sealed luads or safety cups.
18. Autoclave all laboratory wastes before disposal.

Guidelines for working with high-risk organisms have been prepared, but the details are beyond the scope of this report (1-4, 6, 11, 12, 60, 61).

GENERAL CONSIDERATIONS

When work is begun with new infectious organisms, a first requirement must be to determine what decontamination procedures are effective. Supplies of working solutions of the disinfectant must then be made available for all workers. Most disinfectants contain toxic chemicals which are potential hazards for man and suitable personal protective devices (gloves, goggles, respirators, gowns, etc.) must be worn by personnel handling these toxic substances.

The location of a laboratory can be important in meeting the concepts of containment; the higher the level of containment required, the more desirable it is to have well isolated facilities. "Isolation" is a relative term that will vary with organisms or chemicals being worked with, the presence or absence of susceptible animals in the immediate environment, their disease or immune status, as well as the other factors developed in the risk assessment. Administrative decisions to restrict access to the laboratory can be accomplished by sophisticated electronic security systems, personnel monitoring, or simple signing. Signs are important and should be uniform to adequately reflect the true activities in the laboratory. Placing a "biohazard" or "radioactive" sign on a door simply to prevent people from entering - when no biohazard or radioactive hazard is truly present - is not good practice.

Good housekeeping is dependent on the design of the laboratory: walls, floors and ceilings must be cleanable, impermeable to liquids and able to be sealed. Cleaning becomes a serious problem when extraneous pictures or other items are hung on the walls, when plants abound in the laboratory, when Venetian blinds are placed in windows, and when tiles or carpets are placed on the floors. Surfaces made of wood or other permeable materials absorb chemical spills, odors, and infectious materials with equal ease; appropriate disinfection is difficult. Chemicals such as formaldehyde must be used when it is necessary to completely decontaminate a laboratory building; the building must be sealed so that the critical concentration of the gas can be maintained for the specified period of time to ensure microbial killing.

Suspended acoustical ceilings look pretty, but are excellent dust catchers, almost as good as suspended light fixtures. Housekeeping personnel cannot adequately clean such laboratory areas without causing considerable contamination problems.

All housekeeping personnel should be properly trained in handling laboratory waste materials. Broken glass, chemicals, hypodermic needles, infectious materials, animal carcasses and all

other waste materials must be properly sterilized, processed and packaged so that they can be disposed of without chance of harming other laboratory workers. All personnel must know the meaning of posted signs and should be updated occasionally in current laboratory procedures. The housekeeping staff often works during evenings or other times when laboratory personnel are not present to assist in answering questions or pointing out changes in procedures. The laboratory supervisor or principal investigator has a responsibility in keeping these workers aware of proper procedures.

Vaccination programs may be initiated in some laboratories working with certain infectious diseases. Careful consideration must be given to the advantages of including support personnel in such programs, particularly since they are involved with handling potentially contaminated waste materials.

A variety of engineering features can be built into laboratories to reduce hazards to personnel. Laboratory ventilation should be sufficient both to provide nominal comfort and to dilute chemical fumes. Directional air movement should be established so that air changes occur not only in the immediate work area, but also in all parts of the room. Air put in at the ceiling can be withdrawn at floor level, thereby "washing" work surfaces and personnel; when inflow air is properly filtered, drastic reductions in microbial contamination can be realized.

In high risk laboratories, differential air pressure can be established and maintained to provide desired air flow. Negative air pressure can be maintained in rooms contaminated with hazardous chemicals or micro-organisms; as doors are opened, air flow will be from areas of lesser contamination to greater contamination. Rooms maintained at positive pressure (relative to adjacent areas) will be less subject to potential cross-contamination, as all air flow is outward.

Air from areas containing biohazards should be filtered before

it is discharged into the general environment. Laboratory air can be recirculated in some cases, but such recirculation must be through HEPA-filters. These filters do not remove toxic chemical fumes, however. Filtering air through charcoal filters will dramatically reduce such fumes, but generally not enough for the air to be recirculated. Air from chemical fume hoods should be discharged from the building after suitable filtration. Buildings which are maintained under controlled air pressure conditions should be equipped with interlocking electrical controls that will maintain the proper relative air inflow and exhaust with appropriate monitoring and alarm devices to provide indications of malfunctions and with back-up or redundant systems. Necessary routine maintenance and certification can be accomplished with minimal disruption to normal operations when redundant air handling systems are provided.

Appropriate procedures or devices must be operational for handling the liquid effluent and trash from containment facilities. Sewage may have to be collected and sterilized before discharge into municipal systems. Trash should be incinerated or sterilized in a steam autoclave before removal from the containment laboratory.

All maintenance personnel must be trained in the particular needs of containment laboratory operations; they must be aware of the hazards or potential hazards associated with working on contaminated sewer lines, air filtration systems, etc. Maintenance personnel provide the expertise for operating the delicate balance required for containment laboratories. They should be well staffed, funded, and recognized for the important role they play in laboratory management. A well-supported maintenance staff will support biocontainment with pride and dedication.

****

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BIOHAZARD AWARENESS AND RISK CONTROL IN LABORATORY ANIMAL FACILITIES

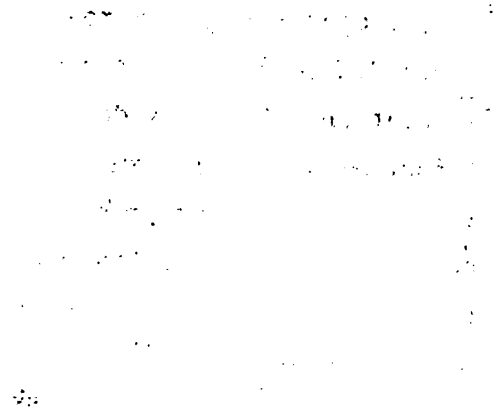
SUMMARY

The principles of risk assessment developed for the microbiology laboratory can, in general, be extended to the operations of a facility for laboratory animal experimentation. Facility design, operation and maintenance are principal factors in determining the level of biocontainment that is possible. The management practices, the extent of training given to personnel, and the suitability and availability of equipment will impact both animal and human safety. Knowledge of the intended experiment-gathered through organism registration programs and protocol reviews is important in the risk assessment process. A suitably-run health maintenance program will benefit the individual worker as well as the overall program and should be an integral part of any laboratory animal experimentation operation.

INTRODUCTION

From a biosafety point of view, the basic objectives for operating an animal facility are to protect the people who have to work in this environment from traumatic toxic chemicals or hazardous infectious micro-organisms, to protect the outside environment from exposure to these chemical hazards or infectious micro-organisms, and to protect experimental animals from cross-infection by providing the maximum level of containment required for a particular study. This is, of course, in addition to providing healthy animals for research while insuring their humane handling and treatment. In meeting these objectives, three broad categories must be considered: the design, operation and maintenance of the facilities; the handling of laboratory animals; and the people-related aspects of this work (1-12).

The type of facility required for animal studies will vary, depending upon the type of agent under study and the animal species involved. Different experimental designs will often have unique requirements. The alert laboratory manager will adjust and balance priorities as a consequence of the risk assessment to provide the desired level of containment and protection. Facilities which handle



small to medium-sized laboratory animals generally have individual cages and a series of rooms in which the caged animals may be held. Animals not exposed to the infectious micro-organisms or substances under study are housed in rooms or buildings separate from those containing treated animals (13-30). Large animals cannot easily be caged. Non-experimental large animals are generally maintained under standard farm conditions. Animals which are to be used in biohazardous experiments require suitable containment quarters. The biocontainment requirements for large and small animals are similar though differences exist.

CAGING REQUIREMENTS

Suitable caging is available to prevent cross-contamination between experimental animals and to protect the laboratory worker from accidental infection (31-45). The type of caging required varies with the size of the animal, the scope of the research and the risk assessment. "Germ-free" animals are often caged in flexible plastic units. Such units are routinely operated under positive pressure, creating an additional barrier which will help protect the animal from exposure to organisms found in the normal environment. Since the potential flow of air is from the interior of the cage outward, flexible cages used while working with infectious micro-organisms must not be under positive pressure. Negative air pressure (inward air flow potential) must be maintained and suitable support systems developed to prevent cage collapse.

Various types of cages are available to provide necessary biocontainment for the experimental animals. These range from simple non-ventilation, providing both inside sterile air and protection for the laboratory environment. Isolators with fixed glove ports, gas tight Class III type cabinets or laminar flow caging devices are examples of caging equipment offering levels of protection which can be matched to the experimental design to provide suitable biocontainment.

Rooms used to house either small or large animals under containment conditions should be equipped with operating air supply and air exhaust systems. Environmental controls are generally built into small animal facilities even at the minimum containment level. Small laboratory animals require rather narrow ranges of temperature and humidity for optimum health. Large animals generally do not require stringent regulation of temperature, although humidity control is important because of their high respiratory rates. Exhaust room air is passed first through a rather coarse filter to trap animal hair, dander, etc. A microbiological filter of suitable retention level is placed next in line to remove aerosolized contaminants. Infected animals often produce large quantities of aerosolized and high-infectious microbial droplets and filtration of exhaust air is therefore most critical.

Directional air flow is another way to reduce and minimize the levels of aerosol contamination within an animal room. Conditioned air introduced at the top of the room and exhaust air removed at the bottom will provide a vertical sweep of air. Directional air flow in rooms housing large animals will also help to control ammonia build-up. Horizontal air sweeps are also possible and may have application in certain facilities.

Rooms housing small animals on racks of cages generally do not require floor drains. Not having floor drains provides an additional safety feature: the chance that racks will topple over on an uneven floor can be minimized. Wet mopping the floors is required on a routine and recurring basis to meet the standards for good housekeeping. However, rooms designed for large animal studies need suitable floor drains so that animal waste materials can be properly washed off the floor. High pressure water is a suitable means for the initial removal of caked or dried animal wastes. When rooms are washed, suitable personal protective devices may have to be worn if the aerosolized animal waste is considered biohazardous. Decontamination of the cleaned room with a suitable disinfectant may be required before additional animals can be moved in. Most disinfectants are

toxic, and personnel must be provided suitable training and protection duress to prevent exposure to hazardous chemicals.

The disposal of both animal waste material and animal carcasses present different problems. Dumping animal cages creates major areosol problems (46-48). Laminar flow dumping stations have been developed to help minimize the release of organisms into the room environment. All animal waste and infected carcasses should be collected and either autoclaved, incinerated, or both. Containers of waste material must be suitably identified so that other workers will know what is contained inside and whether or not special precaution must be taken in handling the waste material. Most animal necropsy operations are potentially hazardous because of the potential exposure to highly contaminated tissue and fluids and the need for using sharp instruments. Personnel should receive special training in the proper precautions and procedures to be followed.

DISEASE TRANSMISSION

Only healthy animals should be purchased for experimental purposes. Animals received at a laboratory should be placed in a quarantine facility for a suitable period of pre-experimental observation, often several weeks. Close contact between newly arrived animals and other animals or people may be unwise, for animals and people often carry inapparent transmissible diseases (49-86). A proper animal facility will have a veterinarian overseeing the animal health care program for both normal and experimental animals.

Personnel who work with animals must be trained to provide care for the particular species under study. Training in proper handling and restraint techniques will help to prevent animal bites, scratches or injuries to both the personnel and animals. Animal caretakers should also be trained to identify clinical signs in sick animals, and to report their observations to the veterinarian in charge. Personnel who routinely care for only normal animals may not have experience in recognizing the signs of clinical illness; these persons should receive suitable training so that colonies of breeder animals or animals being held in pre-experimental quarantine

are maintained in good health.

Personnel working with laboratory animals should participate in a medical health maintenance program. This will help ensure the health of laboratory workers by reducing the risk of disease and by identifying allergic conditions which may affect their work performance. Animal caretakers must report accidents such as cuts, falls, bites, scratches or incidences of self-inoculation. Personnel should know that their health and well-being is jepordized by failure to promptly report accidents.

Health maintenance programs will vary depending on the scope of the laboratory/animal facility operation. Typical programs provide for the collection, storage and testing of serum, screening for specific animal-related allergies, and a variety of specific medical laboratory blood chemistry tests as indicated by the research efforts. Persons working with large animals should be periodically tested for T.B. exposure. Where applicable, personnel should be provided with suitable immunizations. Depending on the potential exposure risk and the nature of the infectious organisms under study, vaccination programs may be voluntary or required. The risk assessment process should indicate the need for and availability of needed vaccines. Part of establishing proper medical programs includes making suitable contacts with local health authorities to alert them to potential problems from accidents or infections.

SAFETY PRACTICES

Procedures should be established to minimize the health hazard to personnel (87-97). At the minimum hazard level, animal caretakers should at least wear laboratory coats. As the biohazard level increases the wearing of rubber boots which can be disinfected by immersion in a suitable foot bath, the changing of clothes between contact with infected animals and non-infected animals, and showering between procedures are practices that reduce the cross-contamination

potential. Additional personnel protective devices such as suitable rubber gloves, head protection, respirators, or even ventilated suits should be worn by persons working in environments with high biohazard potential.

All facilities designed for holding large animals must be equipped with chutes, restraints, floor/wall rings and other devices which will allow for the safe handling of each species. Hoists, carts, fork-lifts, etc., must be available for moving animal carcasses in confined containment spaces from the animal room to the pathological incinerators.

The liquid effluent of high-containment facilities must be collected in a suitable holding tank, and the material decontaminated before discharge into a local sewage system. It may be possible to collect and decontaminate small amounts of liquid wastes by autoclaving. The amount of material is often much greater, however, requiring the construction and operation of a decontamination plant large enough to handle bulk waste. Steam heat is the usual means of decontamination. This can be expensive, particularly as the cost of fossil fuel continues to increase, and recent attention has been given to using Cobolt^{60} sources to sterilize waste materials with gamma radiation (98-100).

Facilities for maintaining normal and experimental laboratory animals can be operated safely. The needs of the animals, animal caretakers, and the environment are interrelated and a suitable balance must be maintained to meet the needs of each. Such facilities require sufficient suitable staff to care for the animals and maintain the physical facilities. Funding must be adequate to provide necessary personnel, supplies and maintenance. The overall level of support required must coincide with increases in the desired level of biocontainment.

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A REVIEW OF LABORATORY SAFETY PROCEDURES

SUMMARY

How safe is safe? In the laboratory environment, a rational answer can be determined by conducting a risk assessment whereby suitable data is collected so that the facilities, support systems, personnel, training, and laboratory practices are matched and balanced to provide maximum protection to the workers, the products and the environment. Safety can only be assured by following these procedures.

INTRODUCTION

Concern for human illness or injury is paramount in most modern societies and forms the basis for a rational evaluation to determine the potential for laboratory-associated hazards (1-11). The laboratory workers are of primary concern, but we must also be concerned with possibility of spreading disease to the surrounding human, animal or plant communities.

All human experiences involve risk. The statement "There is a chance that something will happen" very often is extended to "It will happen". The risk of working in a microbiological laboratory can be minimized by recognizing that the laboratory environment has a fairly high potential for accidents, by appropriate safety training, and by adhering to a variety of good laboratory practices.

A first step to minimize this accident potential is to evaluate the various laboratory operations to determine what might happen, a process known as "risk assessment" (12-33). There are within the laboratory environment, a large number of isolated activities, each having its own potential for spreading infectious organisms. Many activities have been studied in great detail to provide the investigator with a background upon which to judge risk potential. The type of research being done is often an initial clue to the level of hazard involved.

The real or perceived benefits of the activity must be weighed against the real or potential effect of problems that might develop. In other words, does this work really have to be done in the first place, and what are the short and long term consequences of either having done the work riskily, or not having done the work at all? When a decision is made to begin that particular work, the next decision should be to minimize the risk, while remaining within the cost effectiveness of the laboratory's budget. Since no activity has zero risk, the basic questions are: "How much risk is tolerable?" and "Can I afford to reduce the risk?" The laboratory must be designed, maintained, equipped and operated in a manner suitable to provide appropriate containment (36 - 47).

RISK ASSESSMENT

An increase in the risk potential for human disease (34, 35) must be paralleled with an increase in the level of containment for the particular laboratory.

The level of biocontainment required for a particular laboratory must take into account its location, the isolation of the facility, the presence of disease agents in the local environment and the immune status of both the human and the animal population. What would be the effects of a particular disease agent being "free" within the laboratory environment, or escaping into the external environment (48 - 54)?

All living organisms are susceptible to the effect of chemicals or other toxic substances, but when dealing with infectious organisms, the concern is focused on the effect of the organism on a specific host. Natural hosts are those animals ordinarily susceptible to the particular disease agent in question; artificial hosts are animals which must be manipulated in some way before they can be infected with the specific organism. Occasionally, disease-causing organisms will cross species barriers; of particular concern are those zoonotic organisms infectious for animals which may also infect humans and vice versa.

Certain "high risk" populations of people should not be permitted in laboratory environments (55 - 57). Children, immunologically compromised individuals, pregnant women, (and in some instances, any women of child bearing age) should not be allowed access to laboratories, particularly when the potential for human disease or death is high. These restraints apply both to microbiological laboratories and to laboratories using chemical carcinogens, teratogens and other toxic chemicals, and perhaps, highly radio-active chemicals. The risk of accidental exposure increases tremendously when these substances are used in animal studies. Animal behavior, the dissemination of the disease through aerosols, biting or scratching, and hazards associated with handling tissues from treated animals all increase the risk to the laboratory worker.

One of the most helpful tools available for assessing risk is an "organism" registration program, which should be paralleled by a "hazardous substance" registration (14). An initial survey can be made to determine what materials are stored in each laboratory. The initial survey can be developed along the lines of an all-inclusive check-list of microbial, tissue culture and chemical materials in use or in storage. Or, an appropriate list of specific potentially hazardous materials can be developed, with further inquiry on the intended or actual use of such items. The specific needs and objectives for the particular survey must be established before developing such a program. It is easier to get the support and co-operation of the investigators in helping to gather the information and keep it updated when the reasons are spelled out before the program is begun. An initial indication of the biocontainment level necessary can be obtained with this information.

An investigator wishing to introduce a new organism or hazardous substance should complete a supplemental registration form. Such a form should include the proposed use and an indication of the health-hazards and methods for decontamination. The laboratory manager is then able to evaluate the impact of using the new material on other

laboratory activities. It also allows for interaction with other investigators to communicate possible changes in their operations. Maintaining such a registration program can also be helpful in complying with the reporting of possession, use and disposal of environmentally hazardous chemicals, controlled substances or organisms of public health significance.

The responsibility for operating and maintaining laboratories in a safe manner obviously rests with administrators and supervisory personnel; however, the individual laboratory worker is clearly responsible for his/her own activities. The effectiveness of any safety program depends completely on the training, the background and the willingness of the individual to accept the responsibility for the assumption of risk (4, 12, 13, 17, 22, 46). In recent years, the classic microbiologist's training and orientation has been lost to persons who have moved from other backgrounds into this sort of research. For example, in the area of molecular biology, certain genetic recombination research, cancer studies, toxic chemical evaluations, and perhaps even certain clinical laboratory operations have attracted people not attuned to the techniques of safely handling potentially biohazardous materials.

The modern researcher needs to be aware of the infection potential of micro-organisms and to realize that new infectious organisms may be isolated or developed through their research. Transformed tissue culture cells may contain potential oncogenic viruses; natural or laboratory produced genetic recombinants of various micro-organisms have been developed; pseudotypes (infectious viruses coated with the protein coats of less infectious viruses) have been isolated, greatly increasing the potential for infection across different species barriers.

There is an enormous variability among individuals in terms of their immunological response capabilities and their natural genetic susceptibility to infectious micro-organisms. Vaccination programs may be advisable for at-risk laboratory personnel dealing with infectious

micro-organisms. And serological studies may help evaluate worker exposure or illness.

The Laboratory environment very often represents an unnatural situation. It is only in a laboratory that one finds very large volumes or high concentrations of micro-organisms. Manipulations done with these materials very often create aerosols, while offering the possibility for ingestion or accidental injection.

SAFETY GUIDELINES

Guidelines that have been developed for operating safely within infectious disease laboratories include (adapted from 13):

A. General

1. Only authorized employees, students, and visitors should be allowed to enter infectious disease laboratories or utility rooms and attics serving these laboratories.

2. Food, candy, gum, or beverages for human consumption should not be taken into infectious disease laboratories.

3. Smoking should not be permitted in any area in which work on infectious or toxic substances is in progress. Employees who have been working with infectious materials should thoroughly wash and disinfect their hands before smoking.

4. Library books and journals should not be taken into rooms where work with infectious agents is in progress.

5. An effort should be made to keep surplus materials and equipment out of laboratory rooms.

6. Foot operated drinking fountains should be the sole source of water for human occupants.

7. Laboratory or protective clothing may be required for persons entering infectious disease laboratories, according to the level of risk. Showering with a germicidal soap may be required before exit.

8. Contaminated laboratory clothing should not be worn in clean areas or outside the building.

B. Disinfection and Sterilization

1. All infectious or toxic materials, equipment, or apparatus should be autoclaved or otherwise sterilized before being washed or discarded. Each person working with infectious material should be responsible for its sterilization before disposal.

2. Infectious and/or toxic materials should not be placed in autoclaves overnight in anticipation of autoclaving the next day.

3. At the close of each workday, all infectious or toxic material should be: (1) Placed in a refrigerator, (2) placed in an incubator, or (3) autoclaved or otherwise sterilized before the building is closed, to minimize hazard to firemen or disaster crews.

4. Autoclaves should be checked for operating efficiency by using appropriate controls (e.g., bacterial spore strips).

5. All laboratory rooms containing infectious or toxic substances should designate separate areas or containers labelled: INFECTIOUS - TO BE AUTOCLAVED or NOT INFECTIOUS - TO BE CLEANED. All infectious disease work areas, including cabinetry, should be prominently marked with the Biohazards Warning Symbol.

6. Floors, laboratory benches, and other surfaces in buildings in which infectious substances are handled should be disinfected with a suitable germicide as often as deemed necessary by the supervisor. When operations involving plating, pipetting, centrifuging, and similar procedures with infectious agents have been completed, the surroundings should be disinfected.

7. Building floor drains should be flooded with water or disinfectant at least once each week to fill traps and prevent sewer gases from backing up. (New construction plans should omit floor drains wherever possible).

8. Floors should be swept with push brooms only. Floor-sweeping compound is recommended for use because of its effectiveness in lowering the number of airborne organisms. Water used to mop floors should contain a disinfectant. (Elimination of sweeping through use of vacuum cleaners or wet mopping only is highly desirable, if the exhaust of the machine is vented through absolute filters).

9. Stock solutions of suitable disinfectants should be maintained in each laboratory.

10. Laboratories, change rooms, and airlocks should be sprayed with insecticides as often as necessary to control flies and other insects.

11. Vermin proofing all exterior building openings is desirable. Infectious substances should not be allowed to enter the building drainage system without prior sterilization.

12. Mechanical garbage disposal units should not be installed for use in disposing of contaminating wastes. These units release considerable amounts of aerosol.

C. Safety Cabinets and Similar Devices

1. A ventilated safety cabinet should be used for all procedures with infectious substances such as opening of test tubes, flasks, and bottles; using pipettes; making dilutions; inoculating; necropsying animals; grinding; blending; opening lyophile tubes; operating a sonic vibrator; operating a standard table model centrifuge, etc.

2. Safety boxes or safety shaker trays should be used to house or safeguard all containers of infectious substances on shaking machines.

3. A safety centrifuge cabinet or safety trunnion centrifuge cup should be used to house or safeguard all centrifuge tubes containing infectious substances. When centrifuging is done in a ventilated cabinet, the glove panel should be in place with the glove ports covered. A centrifuge in operation creates reverse air currents that may cause escape of an agent from an open cabinet.

4. A suitable respirator or gas mask should be worn when changing a glove or gloves attached to a cabinet if an infectious aerosol may possibly be present in the cabinet.

D. Pipettes

1. Infectious or toxic materials should never be pipetted by mouth.

2. No infectious mixtures should be prepared by bubbling expiratory air through a liquid with a pipette.

3. Infectious material should not be blown out of pipettes.

4. Pipettes used for pipetting infectious or toxic materials should be plugged with cotton.

5. Contaminated pipettes should be placed horizontally in a pan containing enough suitable disinfectant to allow complete immersion. They should not be placed vertically in a cylinder. The pan and pipettes should be autoclaved as a unit and replaced by a clean pan with fresh disinfectant.

E. Syringes

1. Only syringes of the Luer-Lok type should be used with infectious materials.

2. An alcohol-soaked pledget should be used around the stopper and needle when removing a syringe and needle from a rubber-stoppered vaccine bottle.

3. Excess fluid and bubbles should be expelled from a syringe vertically into a cotton pledget soaked with disinfectant, or into a small bottle of cotton.

4. Before and after injection of an animal, swab the site of injection with a disinfectant.

F. General Precautions and Recommendations

1. Before centrifuging, inspect tubes for cracks, inspect the inside of the trunnion cup for rough walls caused by erosion or adhering matter, and carefully remove bits of glass from the rubber cushion. A germicidal solution added between the tube and trunnion cup not only disinfects the outer surface of both of these, but also provides an excellent cushion against shocks that might otherwise break the tube.

2. Avoid decanting centrifuge tubes. If you must do so, afterwards wipe off the outer rim with a disinfectant; otherwise, the infectious fluid will spin off as an aerosol. Avoid filling the tube to the point that the rim becomes wet with culture.

3. Water baths and Warburg baths used to inactivate, incubate, or test infectious substances should contain a disinfectant. For cold water baths, 70 percent propylene glycol is recommended.

4. Suitable traps or filters should be interposed in front of the vacuum system.

5. Deep freeze, dry ice chests and refrigerators should be checked and cleaned out periodically to remove any broken ampules, tubes, etc., containing infectious material.

Rubber gloves and respiratory protection may be worn during this cleaning. All infectious or toxic material stored in refrigerators or deep freezes should be properly labelled.

6. Insure that all virulent fluid cultures or viable powdered infectious materials in glass vessels are transported, incubated, and stored in easily handled, nonbreakable, leakproof containers that are large enough to contain all the fluid or powder in case of leakage or breakage of the glass vessel.

7. All inoculated Petri plates or other inoculated solid media should be transported and incubated in leakproof pans or other leakproof containers.

8. Care must be exercised in the use of membrane filters to obtain sterile filtrates of infectious materials. Because of the fragility of the membrane and other factors, such filtrates cannot be handled as noninfectious until culture or other tests have proved their sterility.

9. Develop the habit of keeping your hands away from your mouth, nose, eyes and face. This habit may prevent self-inoculation.

10. No person should work alone on an extremely hazardous operation.

11. Broth cultures should be shaken in a manner that avoids wetting the plug or cap.

12. Diagnostic serum specimens carrying a risk of serum hepatitis or other human pathogen should be handled with rubber gloves.

F. Animal Cages

1. All animal cages should be marked to indicate the following information:

   a. Uninoculated animals.
   b. Animals inoculated with noninfectious material.

c. Animals inoculated with infectious substances.

2. Cages used for infected animals should be cared for in the following manner:

a. Careful handling procedures should be employed to minimize the dissemination of dust from cage refuse and animals.

b. Cages should be sterilized by autoclaving. Refuse, bowls, and watering devices should remain in the cage during sterilization.

c. All watering devices should be of the nondrip type.

d. Each cage should be examined each morning and at each feeding time so that dead animals can be removed.

G. Handling Infected Animals

1. Special attention should be given to the humane treatment of all laboratory animals in accordance with accepted principles of laboratory animal care.

2. Monkeys should be tuberculin-tested and examined for herpetic lesions.

3. Persons regularly handling monkeys should receive periodic chest X-ray examination and other appropriate tuberculosis detection procedures.

4. The animal caretaker should wear protective gloves and the laboratory workers should wear surgeon's gloves, when animals are to be injected with pathogenic material. Every effort should be made to restrain the animal to avoid accidents that may result in disseminating infectious material.

5. Heavy gloves should be worn when feeding, watering, or removing infected animals. Under no circumstances should the bare hands be placed in the cage to move any object.

6. Animals in cages with shavings should be transferred to clean cages once each week unless otherwise directed by the supervisor. If cages have false screen platforms, the catch pan should be replaced before it becomes full.

7. Infected animals to be transferred between buildings should be placed in aerosol-proof containers.

H. Animal Rooms

1. Doors to animal rooms should be kept closed at all times except for necessary entrance and exit.

2. Unauthorized persons should not be permitted entry to animal rooms.

3. A container of disinfectant should be kept in each animal room for disinfecting gloves, boots, and general decontamination. Floors, walls, and cage racks should be washed with disinfectant frequently.

4. Floor drains in animal rooms should be flooded with water or disinfectant periodically to prevent backing up of sewer gases. (Drains should be avoided where possible).

5. Shavings or other refuse on floors should not be washed down the floor drain.

6. An effective poison should be maintained in animal rooms to kill escaped rodents.

7. Special care should be taken to prevent live animals, especially mice, from finding their way into disposable trash.

I. Necropsy of Infected animals

1. Necropsy of infected small animals should be carried out in ventilated safety cabinets, whenever possible.

2. Rubber gloves should be worn when performing necropsies.

3. Surgeon's gowns should be worn over laboratory clothing during necropsies.

4. Fur of the animal should be wet with a suitable disinfectant.

5. Small animals should be pinned down or fastened on wood or metal in a metal tray.

6. Upon completion of necropsy, all potentially contaminated material should be placed in suitable disinfectant or left in the necropsy tray. The entire tray should be autoclaved at the conclusion of the operation.

7. The inside of the ventilated cabinet and other potentially contaminated surfaces should be disinfected with a suitable germicide.

8. Grossly contaminated rubber gloves should be cleaned in disinfectant before removal from the hands, preparatory to sterilization.

9. Dead small animals should be placed in proper leakproof containers and thoroughly autoclaved before being placed outside for removal and incineration.

The following information is included to assist in understanding some of the concepts discussed for handling and containing hazardous materials.

GLOSSARY OF TERMS

AEROSOL - a colloid of liquid or solid particules suspended in a gas, usually air

AIRLOCK - an unventilated space isolated by doors used to separate areas with different levels of contamination and at different air pressures, which permit passage of personnel and/or equipment without air flow.

ANIMAL CAGE RACK - a set of shelves, generally movable, used to hold animal cages; the rack is sometimes equipped for UV irradiation and sometimes provided with an exhaust manifold to accommodate ventilated cages.

ANIMAL HOLDING ROOM - a room, either in a contaminated or non-contaminated area, meeting standard suitable isolation criteria and used to house animals before or during experimental use.

ANTISEPTIC - a compound that prevents the multiplication of micro-organisms; it may be bacteriostatic in action but not necessarily bacteriocidal. The term refers to a germicidal agent which is applied to a living tissue rather than an inanimate object.

ASEPTIC TECHNIQUE - the performance of a procedure or operation in a manner that prevents the introduction of septic (contaminated) material.

BACKFLOW PREVENTER - a device that has two spring-loaded vertical check valves and one spring-loaded diaphragm-activated differential pressure release valve. It is installed in a water supply line to prevent reversal of water flow in case the supply pressure falls below the downstream pressure.

BACTERIOSTAT - an agent that stops the growth and multiplication of bacteria but does not necessarily kill them. Bacterial growth usually resumes when the bacteriostat is removed.

BACTERIOCIDAL - having the ability to kill bacteria.

BIOHAZARD - a contraction of the words "biological hazard"; infectious agents presenting a risk or potential risk to the well-being of man or other animals, either directly through infection or indirectly through disruption of the environment.

BIOLOGICAL CONTAINMENT LEVEL - the probability of escape(and survival) that is considered permissible for a given biological agent.

CHANGE ROOM(S) - a grouping of dressing rooms, locker rooms, laboratories, air locks and showers to provide personnel access to and egress from contaminated areas; clothing changes and showers will minimize the chance of machinically transferring infectious micro-organisms.

CLASS I SAFETY CABINET - a fume hood with open face and fixed opening. Air is drawn in from the room and exhausted through a filter in the hood. This cabinet is good for personnel protection but not product protection; it is suitable for low or moderate risk biological agents.

CLASS II BIOLOGICAL SAFETY CABINET - an open front cabinet which provides personnel and product protection, with HEPA-filtered exhaust of HEPA-filtered recirculated air for working with low to moderate risk agents.

TYPE A - has 30% make-up air and 70% recirculation, with 75 feet-per-minute (fpm) face velocity and 75 fpm down flow velocity. A positive pressure air curtain helps to contain the contaminated air. This cabinet is not suitable for working with flammable, toxic or explosive substances.

TYPE B - has 70% make-up air and 30% recirculated air, with 100 fpm face velocity and 50 fpm down flow velocity. This cabinet is suitable for use with some volatile solvents, particularly when equipped with a charcoal filter.

CLASS III SAFETY CABINET - a gas-tight cabinet providing total isolation from personnel and offers product protection; these cabinets are generally equipped with a HEPA-filtered air supply and a HEPA-filtered exhaust. The cabinet is fitted with gloves and is maintained under continuous negative air pressure. This cabinet provides the highest containment reliability and should be utilized for all activities involving high hazard risk agents.

CLEAN CHANGE ROOM - a dressing room for removal of street clothes before entering a contaminated change room through an air lock where laboratory clothing can be donned.

CONTAMINATION - the presence of hazardous or unwanted materials in an area, air space, fluid, etc.

CONTAMINATED AREA - a building area with definite boundaries where hazardous biological work is being carried out, while it is separated from non-contaminated and other contaminated areas by suitable barriers.

CONTAMINATED CHANGE ROOM - a dressing room for the removal of laboratory clothing before entering the clean change room (after a mandatory shower) to don street clothing.

DECONTAMINATION - the destruction or removal of living organisms to some lower level, but not necessarily to zero. This term applies also to the removal or neutralization of toxic agents and generally refers to making a contaminated item safe for handling without special precautions.

DISINFECTANT - a chemical agent that specifically or selectively kills certain vegetative bacteria, fungi and viruses, but not necessarily spores.

DRY HEAT STERILIZATION - thermal sterilization carried out in the absence of added moisture. Dry heat usually requires a higher temperature than moist heat to achieve the same degree of sterilization within the same time.

ETIOLOGICAL - pertaining to the cause of a disease or other abnormal condition.

FILTER - a device used for removing undesirable particles (particularly micro-organisms) from air, other gases or from liquids. Filters can be made of many different materials to provide a variety of matricies for trapping particles of different sizes.

FOMITES - inanimate objects or materials that act as intermediate carriers of microbial contamination. Examples of fomites are people, clothing, tools, research notes, or any other item carried from a contaminated to a non-contaminated area.

GAS STERILIZER - autoclave designed for or modified to permit operational use with a gaseous decontaminant instead of steam for sterilizing material. Ethylene oxide is one commonly used gas, and must be handled with extreme caution because of its toxic properties.

GERM FREE - the state of being free of all detectable microbial life.

HEPA (HIGH-EFFICIENCY PARTICULATE AIR) FILTER - a filter which has a nominal efficiency of 99.97% for the removal of 0.3 micron sized particles from the air.

HIGH-RISK AGENT - a micro-organism with the dangerous combination of the following characteristics (also includes any viruses proven to be oncogenic to man):

1. Low infective dose,
2. High mortality,
3. High potential for spread outside of lab,
4. High concentration,
5. Genetic alteration or recombination which increases pathogenicity.

INFECTIOUS - capable of invading a susceptible host, replicating, and causing an altered host reaction commonly referred to as a disease.

LAMINAR AIR FLOW - air flow in which the entire body of air within a designated space moves with uniform velocity in a single direction along parallel flow lines.

LOW-RISK AGENT - a micro-organism having minimal effect on personnel, other animals or plants under ordinary use conditions.

MODERATE-RISK AGENT - a micro-organism having known pathogenicity, high concentration, genetic alteration or synergistic effect with other materials which cause moderate disease hazard. They include some oncogenic viruses by virtue of the following criteria:

1. Suspected oncogenic virus isolated from man.

2. Viruses that produce cancer in subhuman primates at any age without the aid of experimental host modification.

3. Viruses that may cross species barriers to produce progressive tumors in juvenile or adult non-primate mammals without the aid of immunosuppression.

4. Viruses that transform human cells in vitro as evidenced by a morphological functional alteration and that can be transferred genetically.

5. A genetic recombinant between animal oncogenic viruses and a micro-organism infectious to man. This would be considered to be a moderate risk agent until its oncogenic infection for man is determined.

6. All concentrated oncogenic virus or infectious viral nucleic acids.

PHYSICAL CONTAINMENT LEVEL - the combination of special procedures, equipment and laboratory design required for experimentation with a given risk.

PLENUM - refers to the filter chamber upstream of the exhaust fan in the building ventilation system, when not otherwise specified. The terms "plenum" may also be used to refer to a specifically defined air-space or duct.

SANITIZATION - the reduction of the microbial contamination to a "safe" level; generally, at least a 5 log reduction in micro-biological "load".

STERILITY - the state of being free from all living micro-organisms.

TOXIC - having an adverse physiological effect on biological systems.

ULTRA VIOLET (UV) RADIATION - denoting the chemical rays beyond the violet end of the light spectrum. Specifically refers to the germocidal line at 2537 A (254 nanometers) produced by

mercury arc lamps used for decontamination purposes.

VECTOR - living organisms (often an arthropod) which have the ability to transmit infectious organisms from one area to another. In the recombinant DNA terminology, vector refers to the plasmid or phage which carries the donor DNA recombinant molecule into a new host organism.

VIRUCIDE - A chemical substance that kills viruses.

VIRULENCE - degree of pathogenicity or disease producing capacity of an organism.

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