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Risks to Assess When Selecting Clean Benches And Biosafety Cabinets For Animal Research

ABSTRACT

Many research animals require isolation. In the past, cage-transfer protective equipment was designed primarily to prevent contamination of such animals. While that concern has not diminished, recent events have focused attention on protecting lab workers as well. In some cases, contamination has spread from lab animals to attendants, and in many cases, occupationally-induced asthma has been linked to excessive exposure to animal residue. This paper surveys some of the literature describing passively-transmitted hazards which may be created when animals are manipulated, when they are transferred, or when their cages are cleaned.

CHANGING RISKS IN ANIMAL RESEARCH

Risks in animal research facilities are changing, so more attention is being given to equipment selection. In the past, the risks were primarily to animals. Contamination can result from exposure to other animals in the colony, or to organisms brought into the animal room by workers. However, as research changes, the risks to humans are increasing. For example, in the past, animal viruses were seldom a risk to people. But now human viruses are being studied by inoculating them into animals grown specifically for that purpose. Consequently, the new risks to workers must be considered, as in the following cases.

In February, 1993, biomedical research at Kyoto University in Japan was interrupted because of an outbreak of

Animals of Concern	Common Name *Organism*	Risk *Concern*	Symptoms of Infection
Dogs, Sheep, Cattle, Swine, Goats	Brucellosis *Brucella sp.*	Low *Moderate to high*	Gradual onset, undulating fever, chills, sweats, headache, myalgia, weight loss; extended convalescense, may be chronic, with stress-related relapses; complications may include emotional and cardiac symptoms.
Vertibrates	Colibarillosis *Eserichia coli*	Low *Moderate*	Pneumonia, urinary tract disease, diarrhea.
Rodents	Hemorragic fever *Hantanan virus*	Low *High*	Fever with renal shutdown, headache, tremors of tongue and extremeties, shock; 20% fatality rate.
Rodents	Lymphocytic choriomeningitis *LCM virus (adenavirus)*	Low *High*	Fever, myalgia, malaise, stiff neck, headache, sleepiness, unusual skin sensations, paralysis; usually self-limiting, although some fatalities occur.
Armadillo	Leprosy *Mycobacterium leprae*	Low *Low*	Range from single, localized lesion to diffuse, generalized infiltrations.
Wild rodents, ground squirrels	Bubonic & pneumonic plague *Yersinia pestis*	Low *High*	*Bubonic* - fever, chills, nausia, diarrhea, or constipation, headach, menigitis, tachycardia, coma, regional lymphadenopathy; 60% fatality rate if untreated. *Pneumonic* - cough and dyspnea with mucoid to bright red sputum, may progress to septicemic form, with vascular collapse, hemmoragic rash; 95% fatality rate in these two forms if untreated.
Rodents, guinea pigs, rabbits, dogs, cats, cattle, sheep, swine, monkeys	Pneumocyctis pneumonia *Pneumocystis carinii*	High for immunocompromised individuals *High*	Generally seen only in those with serious underlying disease or suppressed immune system; pneumonia, dyspnea, nonproductive cough, moderate fever, tachypnea, cyanosis.

Table 1a. *Organisms which can be transmitted through passive contact. Equipment and protective garments can reduce the risk of such transmission. (Reprinted by permission of The American Association for Laboratory Animal Science [1])*

Animals of Concern	Common Name *Organism*	Risk *Concern*	Symptoms of Infection
Sheep, cattle, goats	Q-fever *Coxiella burnetti*	Moderate *Moderate*	Sudden onset of fever, retrobular or frontal headache, chills, myalgia, sweating, weakness, malaise, pneumonia, endocarditis, hepatitis.
Cats, rabbits, dogs	Ringworm *Microsporium*	High *Low*	Generally: scaling, hair loss,or breakage, occasional ittching; less frequently: erythemia, induration, crusting, supporation.
All	Salmonellosis *Salmonella app.*	Low *Moderate*	Dirrahea, vomiting, low-grade fever, may progress to dehydration, prostration, death; septic syndrome has high-spiking fever, septicemia, splenomegaly, headache.
Non-human primates	Simian hemoragic fevers (Ebola, Marburg) *Rhabdovirus.*	Low *Very high*	Fever, malaise, headache, myalgia, vomiting, conjunctival infection, diarrhea, sore throat, hemorrages; high fatality rate.
Cats	Toxoplasmosis *Toxoplasmosa gundii*	Moderate *Moderate*	Usually: lymphadeopathy, fever, headache, myalgia, stiff neck, anexoria; occasional arthralgia, maculopapular rash, confusion.
Cattle, birds, non-human primates, humans	Tuberculosis *Mycobacterium app.*	Moderate to High *Moderate to High*	*Pulmonary* - productive cough, fever, weight loss, fatigue, night sweats, chest pain, hemoptysis. *Extrapulmonary* - cervical lymphadenitis, menigitis, osimyelitis, pericarditis, infections of most other organs.
Non-human primates	Yaba virus *Pox virus*	Moderate *Moderate*	Papulae develop to subcutaneous tumors on limbs, hands, face, feet, ears; regional lymphadenopathy.

Table 1b. *Additional organisms which are transmitted through passive contact. Equipment and protective garments can reduce the risk of such transmission. (Reprinted by permission of The American Association for Laboratory Animal Science[1])*

hemorrhagic fever with renal syndrome (HFRS) among the research animals. The infection also spread to a researcher. Consequently, research was halted, and 2,000 rats were destroyed before work could continue.[3]

In February, 1990, Lusso and Gallo reported their concern that although the use of SCID mice (severe combined immunodeficiency) could speed AIDS research, the technique may allow the generation of new viruses which could be transmitted by novel routes, such as through air.[4]

At a third institution, during a project which spanned the period from 1975 to 1989, the LCMV mouse virus infected seven researchers working with the nude mice which were used to produce the virus.[5]

These events and others like them have raised the issue of contamination control among those responsible for safety in laboratory operations. Responsible officials have logically suggested that precautions taken when working with animals infected with viruses should not be different, or certainly not less stringent, than the precautions taken when working with the virus itself.[6]

Finally, although occupationally-induced asthma may have been seen in the past as an acceptable risk of the research profession, managers today are increasingly concerned with worker safety from a natural humanitarian perspective. Managers also recognize that healthy workers enjoy higher job satisfaction, they have higher morale, they are more productive, and do not generate costly and distracting workers compensation claims.

POTENTIAL EXPOSURE RISKS

Risks of cross-contamination between animals or between animals and the surrounding environment are well understood. Each animal is housed in a cage, and every cage is equipped with an air filter. Risks of cross-contamination are reduced by maintaining a separate environment for each animal.

Potential risks increase when animals must be removed from their micro-environments for experimental manipulation or when they are transferred to clean cages. In typical animal research, prudent managers assess risks to:

1. Employees
2. Animals
3. Research results
4. Liability insurance costs

When decisions must be made about procedures and equipment put in place to reduce such risks, it is useful to understand the nature and extent of some of the more common hazards. Hazardous agents have been separated into four general categories by Dr. Jonathan Y. Richmond, Director of the Office of Health and Safety at the Centers for Disease Control.[2] These include:

- Allergens

  Such items as animal hair, skin flakes (dander), serum animal proteins, mite droppings and fungal spores are commonly found in large quantities in labs and cages.

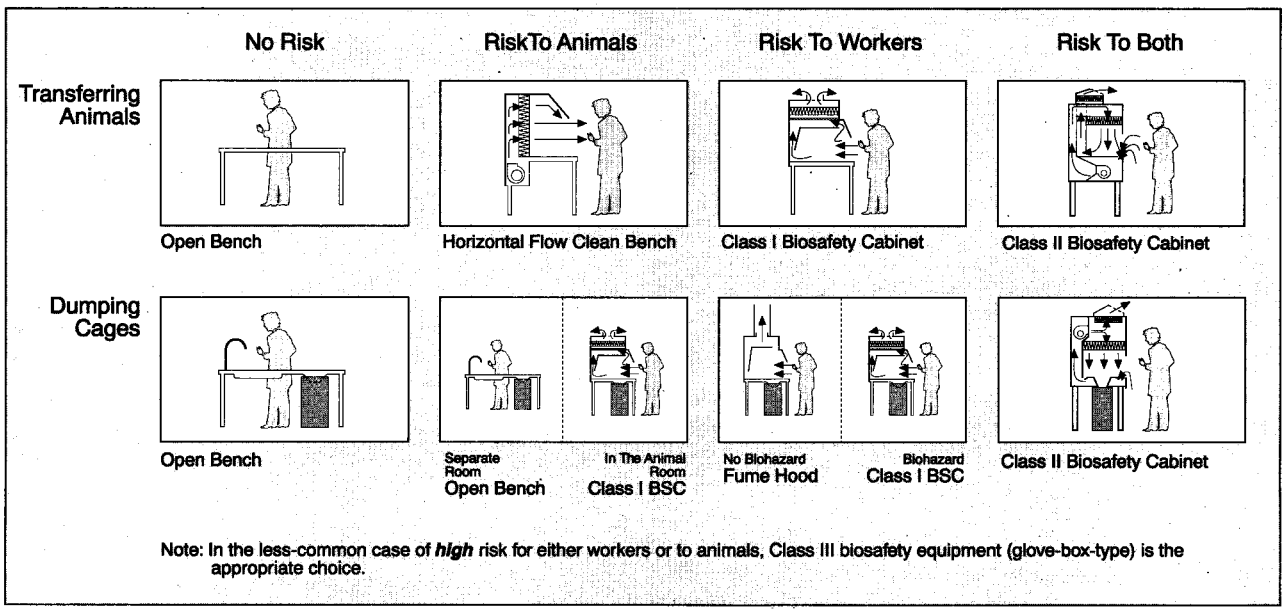

Figure 1. Suggestions for equipment selections based on the nature of the risks and the type of operation. (Reference 8)

- Biohazards
  Human pathogens and zoonotic agents, can be latent in the environment, or introduced from the exterior of the lab.
- Chemicals
  Hazardous materials on test, cleaning fluids or powders, decontamination solvents or acids for cage washes are commonly present.
- Radiation
  Research isotopes or X-ray equipment can contribute to hazardous exposure risks to the animals and the researchers.

As described by James Boardman in reference 1. Biological hazards can be divided into two broad categories: active hazards and passive hazards. Active hazards are those which are transferred by non-casual contact, such as a bite or scratch. Such hazards are difficult to control, and require skill and caution on the part of the people handling the animals.

Passive hazards, in contrast, are transmitted through casual contact such as touching, brushing or breathing. Risk from these types of hazards can be minimized through the use of protective equipment: clothing, gloves, respirators, clean benches and biosafety cabinets. However, before equipment selection can proceed, prudent research managers assess the nature and extent of risks from current and future research. To assist such risk assessments, tables 1a and 1b are reprinted from material published by the American Association for Laboratory Animal Science.[1]

DOCUMENTATION & RISK MANAGEMENT

Written documentation of worker education and documentation of the risk assessment factors which governed equipment selection serves as proof that the institution has made every effort to minimize hazards to personnel. Such documentation is not only evidence of concern and prudent management of hazards, it is useful to employees, equipment suppliers and insurance companies as all parties work together to minimize risk

When employees are informed in writing of the anticipated risk, it also informs the individual of the degree of emphasis that the institution places on safety in general and animal management practices in particular.

For equipment suppliers, understanding the risk assessment encourages the manufacturer to look broadly at the required equipment functions. This perspective can be valuable to the institution, as the supplier's expertise is added to the equipment selection process, reducing misunderstandings and resulting in safer environments.

For the insurance company, risk assessment documentation reduces the uncertainty faced by the actuaries in determining the cost of the coverage. In general, a greater degree of uncertainty is more costly to insure, so a realistic and well-documented assessment of risks of current research and future projects may help reduce the cost of insurance coverage.

CONCLUSIONS

This paper reviews the nature and extent of some of the passively-transmitted hazards in animal research. It concentrates on those hazards which can be transferred from animals to humans during necropsy, or when animals are transferred to fresh cages, or when cages are cleaned. Information describing different equipment alternatives for these functions is described by ACUMEN Volume 3, Number 2, entitled: "Selecting animal-transfer stations and cage-dumping units for research facilities."

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