LABORATORY ANIMAL MEDICINE AND SCIENCE - SERIES II

NONHUMAN PRIMATES:

Biosafety

V-9018

J. Roger Broderson, DVM, PhD

Centers for Disease Control
Atlanta, Georgia

The Laboratory Animal Medicine and Science - Series ll - has been developed by the Autotutorial Committee of the American College of Laboratory Animal Medicine (ACLAM): C. W. McPherson, DVM, Chair; J. E. Harkness, DVM; J. F. Harwell, Jr., DVM; J. M. Linn, DVM; A. F. Moreland, DVM; G. L. Van Hoosier, Jr., DVM; L. Dahm, MS. Instructional development and production assistance provided by L. Dahm, MS, and B. J. McGough, BS Medical Comm. The development of these programs is supported by a grant from the US Department of Agriculture: National Agricultural Library grant 59-32U4-9-45

Laboratory Animal Medicine and Science - Series II
is produced by the
Health Sciences Center for Educational Resources
University of Washington.

AUDIENCE Laboratory animal veterinarians, animal technologists, animal facility managers, investigators using nonhuman primates, veterinary students, facility service and maintenance persons.

GOAL To provide an understanding of the most important health hazard considerations when using nonhuman primates and to relate standard practices for preventing disease or injury as result of contact with nonhuman primates.

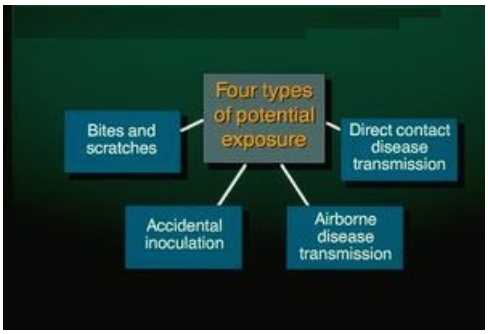
OBJECTIVES When you have completed this program, you will be able to state four major types of exposure to potential health hazards associated with use of nonhuman primates in research, testing and teaching. You will also be able to describe actions that facilities and individuals should take to prevent disease or injury and reduce associated morbidity.

1. Series Laboratory Animal Medicine and Science - Series II

2. Program title NONHUMAN PRIMATES: Biosafety

3. Objectives When you have completed this program, you will be able to state four major types of exposur to potential health hazards associated with use of nonhuman primates in research, testing ar teaching. You will also be able to describe actions that facilities and individuals should take t prevent disease or injury and reduce associated morbidity.

4. Four classifications



There are four major types of exposures to potential health hazards within nonhuman primate facility: exposure to bites or scratches; accidental inoculation, such as needle slicks; airborne disease transmission; and contact disease transmission (for example, direct contact with contaminants).

5. Section title **BITES AND SCRATCHES**

We will first address bites and scratches. All bites and scratches should be considered serious.

6. Teeth

Nonhuman primates, both wild caught and domestically bred, are wild animals and tend to react aggressively to restraint and handling. Most of them have large, sharp teeth and strong jaws, which they will use to inflict puncture wounds or lacerations as they attempt to either escape or resist handling.

7. Toenails

The animals also have sharp fingernails and toenails that can scratch and abrade the skin of handlers.

8. Infectious Agents In addition to the immediate injury, broken skin provides easy entry for infectious agents carried by the animal. Secondary infection may occur as a result of exposure to a variety of aerobic and anaerobic bacteria from the animal, including *Pasteurella multocida and Clostridium tetani. Clostridium tetani* causes tetanus, a painful disease that acts upon the central nervous system to cause sustained muscular contractions. Therefore, it is important that all persons working with nonhuman primates have current tetanus immunization status.

A more serious, but less frequent, sequel to bites and scratches is exposure to zoonotic viral infections carried by the nonhuman primates, such as *herpesvirus simiae* and rabies virus.

9. *Herpesvirus simiae* *Herpesvirus simiae* (herpes B virus) is the most serious of the zoonotic viruses. In monkeys, may be subclinical or cause mouth lesions resembling cold sores. But in humans it can result in fatal encephalitis. Over thirty cases have been reported in the last forty years in persons who have had contact with macaque monkeys, usually following an incident of a bite or scratch, as the virus is shed in saliva and lacrimal secretions. Cases have also been reported following exposure to monkey tissues. Each animal care facility should have on-call medical care personnel who are knowledgeable about the hazards of *Herpesvirus simiae,* as well as its symptoms and treatment.

10. Rabies virus Rabies infection is rare in nonhuman primates in laboratory settings, but several cases have been reported in newly captured New World primates. For this reason, rabies vaccinations should be considered for everyone who works with unconditioned monkeys and all bites should be evaluated for rabies potential.

11. Squeeze cage

To reduce the risk of bites and scratches, a squeeze-back cage apparatus is often used to restrain nonhuman primates for examination or for administration of injectable anesthetics.

Transfer boxes and other special restraint apparatus can be used to help hold nonhuman primates safely, while primary cages are being cleaned or to move the primate from one room to another.

12. Handling

When it is necessary to handle nonhuman primates without chemical restraint, gloves reinforced with leather or padding material must be used to reduce the probability and severity of injury from bites or scratches. Even with the precautions shown here, bite wounds remain a common - and often serious - injury, when working with only partially restrained or unanesthetized primates.

13. Care of wounds — Immediate care of bite wounds calls for thorough cleansing of the wound with soap and water. Incidents should be reported to institutional authorities and recorded in an occupational health surveillance logbook, and the health status of the animal should be evaluated. Medical care should be sought for deep or serious wounds, and the animal handler should be instructed to report any skin lesions, neurologic symptoms, or unusual illness following a bite.

14. Section title — **ACCIDENTAL INOCULATIONS**

15. Needlestick — Most accidental inoculations occur as the result of needle sticks when performing veterinary procedures such as chemical restraint, tuberculin testing, or collection of blood samples. Lacerations and scratches from equipment with sharp edges can also result in accidental inoculation.

16. Filoviruses — All of the zoonotic diseases carried by nonhuman primates can be transmitted by accidental inoculation; however, filoviruses deserve special consideration as a potential complication.

In 1967, 31 humans became ill and 7 died following exposure to the tissues of apparently healthy African Green Monkeys. The incident, which affected personnel in West Germany and Yugoslavia, became known as the Marburg incident, and the virus was named the Marburg virus. A related disease, Ebola fever, has been transmitted from human to human in Africa via needles. Viruses belonging to the Marburg-Ebola family (filoviruses) were implicated in the 1989-90 outbreaks of fatal febrile-hemorrhagic disease in cynomolgus monkeys that had been recently imported into the U.S. Although no human disease was documented, the incident was another reminder of the need for rigid safety practices when handling newly imported animals or animals in transit.

17. Retroviruses — Retroviruses, particularly those of type D morphology, have been implicated in causing neoplasia, immunosuppression, anemia, and other problems in nonhuman primates. Simian immunodeficiency virus is closely related to HIV virus, which causes human AIDS. There has been no evidence of humans contracting disease from these simian agents.

18. Precautions — However, when working with animals infected with a retrovirus, the same safety precautions are followed as when working with animals infected with hepatitis B: prevent exposing mucous membranes and unprotected skin to materials that may be contaminated with the virus, and particularly, prevent accidental inoculation.

19. Other diseases — Other diseases that could be sequelae to accidental inoculation are the pox viruses (monkey pox and yaba-like disease), and *Trypanosoma cruzi,* a blood-borne flagellated protozoan.

20. Yaba-like disease

This is a manifestation of yaba-like disease in a human.

21. Experimental agents Accidental inoculation is even more serious when the inoculum contains infectious agents or tissues from animals that have been experimentally infected with agents such as hepatitis B virus, hepatitis C virus, or malaria.

22. Needle disposal

Needles and other sharp objects must be carefully discarded, preferably into specially designed containers. Needles should never be placed directly into trash containers where other persons could unknowingly harm themselves. To avoid unintentional injury, needles should never be recapped by hand.

23. Follow-up care All needle stick or puncture wounds should be reported for follow-up medical care and monitored for disease sequelae.

24. Section title **AIRBORNE DISEASE TRANSMISSION**

There are several diseases that ran be transmitted between nonhuman primates and humans via the airborne route, including tuberculosis and measles. It is probable that other pathogens causing respiratory disease can also be transmitted by air.

25. Tuberculosis Tuberculosis is a disease that can progress very rapidly and is often fatal in Old World Primates. Transmission from nonhuman primates to humans has been documented in only a few cases; however, it is not uncommon for persons to convert from a negative to positive tuberculin test after working with nonhuman primates or following an outbreak of disease in a colony.

26. Human TB testing

The health screening program for all persons with access to nonhuman primates should include annual skin tests in previously negative persons and regular examinations of persons who test positive. Facility directors may consider denying entry to individuals who are skin-test positive, as they could become active spreaders of the disease to nonhuman primates.

NHP TB test

Nonhuman primates should also be skin tested regularly to enable early detection of tuberculosis.

27. Measles

Measles is the other major zoonotic disease transmitted by the airborne route.

Respiratory disease and skin rash seen in monkeys imported from both Asia and South America has been attributed to human measles virus. Therefore, it is important for persons working with nonhuman primates to have current immunization status.

29. Section title **CONTACT DISEASE TRANSMISSION**

Nonhuman primates and their environment are potentially contaminated with a host of bacterial and viral pathogens associated with saliva, hair coat, lacrimal secretions and excrement. In addition, humans and nonhuman primates also share common parasites.

30. Caretaker

Only minimal contact is required. Traces of biological materials are easily transferred from an animal, cage, or cage pan to the clothing or hands of an animal caretaker or investigator, and from there to the mouth. Animal tissues are also a source of contact disease transmission.

31. Diarrhea

Diarrheal disease caused by enteric bacteria or parasites is perhaps the most common ailment in captive nonhuman primates that can be transmitted to personnel.

32. Human hepatitis A

Human hepatitis A is transmitted mainly by the fecal to oral route. This may occur when an animal caretaker handles soiled materials and then touches the mouth directly or even indirectly - for example, later while eating. This disease has been seen in humans who have been in contact with newly imported nonhuman primates, including chimpanzees, the gorilla, siamang, celebes black ape, patas monkey and woolly monkey.

33. Ringworm

Ringworm is also spread by direct contact with infected nonhuman primates. Early signs of the disease are redness and flaking of the skin, with subsequent focal hair loss. Any such lesion should be examined by a medical clinician for possible treatment.

34. Section title

REDUCING RISKS

The risk of exposure to both airborne and contact pathogenic agents is reduced by correct use of protective clothing, adherence to hygiene practices and an effective animal health surveillance program.

35. Protective clothing

Everyone entering a nonhuman primate area for any reason should wear protective clothing.

36. Minimum protection

The minimum protection acceptable is a surgical mask, gown and gloves. Long sleeves should be worn by anyone handling animals.

The mask is often thought of as a method of protecting personnel from airborne pathogens; however, it also serves the purpose of keeping personnel from puffing their own fingers or other objects to their mouth after handling contaminated objects.

37. Full protective clothing

This image demonstrates protective clothing required for handling materials from a room containing quarantined nonhuman primates: disposable gown, cap, mask, gloves and shoe covers or water-repellent footwear. Potential exposure to splashing waste materials or close contact with the nonhuman primates would require the use of a face shield or goggles in addition to a mask.

38. Bag it

All protective clothing should be removed upon leaving the animal room or facility. Contaminated items should be bagged for incineration or autoclaving.

39. Laundry worker

An on-site laundry encourages the use of clean garments by animal care persons, and therefore, enhances the safety of the work environment. But remember that personnel handling potentially contaminated garments must themselves use increased safety practices.

40. Personal hygiene

The second important safeguard against potential exposure to pathogenic agents is adherence to hygiene practices.

41. Washing hands

Each nonhuman primate holding area should be equipped with a hand washing sink, soap and paper towels. Personnel should wash thoroughly each time they leave the holding area, even though they have been wearing protective gloves. Note that the trash container is lined with an autoclavable liner and is tightly covered.

42. Lounge area

No food or beverages should be taken into primate holding areas. A separate lounge area, as shown in this image, should be available where persons who work with nonhuman primates can retreat for breaks, lunch, and on-site staff meetings. And, of course, protective clothing that has been worn in animal holding areas should always be removed before entering this area.

43. Waste disposal

All waste in a nonhuman primate area must be considered contaminated and must be disposed of in accordance with the protocol developed for the area. Fecal waste may be disposed of through a property functioning sanitary sewer system. Depending on the required level of containment, other wastes from nonhuman primate areas may be double bagged and autoclaved before disposal, or double bagged and incinerated.

44. Freezer

Animal carcasses can be double bagged in leak-proof containers, then placed in a freezer such as this until scheduled transport or incineration.

45. Drums for shipment

If waste is transported to remote sites, it is recommended that the bags be inserted into metal cans or sealed metal drums for shipment.

46. Equipment on cart

It is advisable to remove all non-essential items from the primate holding area, as all surfaces should be considered potentially contaminated. Frequently needed supplies such as the needles, syringes, specimen containers, and notebooks shown here can be stored on carts and brought into the room when needed.

47. Hosing floor

Disinfectants can be dispensed when hosing down the area by using a hose-end spray attachment, as shown here, which automatically dispenses the appropriate amount. Notice that the protective clothing should include a face shield, as there is potential for splashing up contaminants while working.

48. Section title **ANIMAL HEALTH SURVEILLANCE**

Risk of exposure to pathogenic agents is also reduced by an adequate animal health surveillance program, with emphasis on identification and treatment of diseased animals.

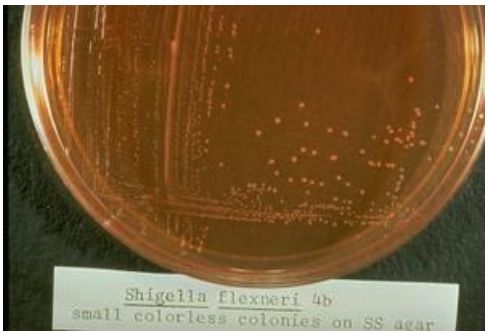
49. Observation

Animals should be observed frequently. Signs of disease, such as respiratory infection or diarrhea, should be reported and evaluated promptly.

50. Screening

Periodic surveillance for pathogens by laboratory methods will enable detection of potential zoonotic agents in the animal colony.

51. *Shigella flexneri*



In this case, the isolation of *Shigella flexneri* from an outbreak of diarrheal disease enabled appropriate therapy and use of methods to prevent further infection.

52. Necropsy

In some cases, a necropsy may be required to rule out or define conditions with zoonotic potential.

53. Biohazard area

Nonhuman primate facilities are a biohazard area. Hazards are *reduced by* compliance with a biosafety program - but not eliminated. Everyone entering the facility must be prepared to respond to potential injuries and illness.

54. Serum-banking

A serum-banking program is recommended for staff to provide baseline information. Protocols should be developed in collaboration with the institutional health service providers, so they are prepared to treat nonhuman primate bites and other exposures.

55. Emergency procedures

Staff should also be informed of any special risks associated with research activities. Clear procedures should be developed for anyone who may be confronted with a medical emergency and these instructions should be posted in an easily accessible location.

56. Section title **SUMMARY**

In summary, everyone entering nonhuman primate colonies should be educated regarding the four major types of exposure to potential health hazards associated with nonhuman primate colonies: bites and scratches; accidental inoculation; airborne disease transmission; and contact disease transmission.

57. Summary

They should be thoroughly trained regarding safe handling. Whenever possible, squeeze cages or transfer cages should be used to avoid handling unanesthetized animals. When handling animals that are not fully anesthetized, reinforced elbow-length gloves are essential to reduce the probability of bites or scratches.

All persons entering the facility should be required to wear protective clothing. Preferably, all surfaces of the body should be covered. Gloves should be worn at all times. Goggles and face shields are indicated whenever there is risk of splashing up contaminants.

Screening and inoculations must be carried out according to schedule. All entrants should have a record of recent tuberculosis testing. Those working in the facility should also have tetanus inoculations and, in some situations, rabies prevention.

Personal hygiene practices must be observed faithfully: hands must be washed thoroughly when leaving the primate area and hand-to-mouth contact should be avoided.

Protocols for containment of contaminated materials must be observed.

An animal health surveillance program should be practiced.

And, lastly, standard operating procedures for handling bites and scratches should be clearly posted; and a record should be kept of incidents and febrile illnesses among employees.

59. ACLAM credits

The Laboratory Animal Medicine and Science Series II has been developed under the guidance of the following committee for the American College of Laboratory Animal Medicine:

C. W. McPherson, DVM, Chair
J. E. Harkness, DVM
J. F. Harwell, Jr., DVM
J. M. Linn, DVM
A.F. Moreland, DVM
G.L. Van Hoosier, Jr., DVM
L. Dahm, MS

Instructional development, editing and production management provided

by
L.Dahm, MS, and Bob J. McGough, BS Medical Communication. Illustrations, graphics
and imagery produced by Dale Leuthold, BA, and Joseph Wilmhoff, BIS.
Guide produced by Pamela Young.

The development of these programs is supported by a grant from the US Department of Agriculture: National Agricultural Library grant 59-32U4-9-45

60. HSCER credits

Produced by the
Health Sciences Center for Educational Resources
University of Washington
Seattle WA 98195

2000

ACKNOWLEDGMENTS

The author would like to thank
Dr. John Richardson, Dr. Jonathan Richmond, and Dr. James Ebert, for advice in preparing the text;
Dr. Bobby Brown, Dr. Samuel Adams, and Dr. Daryl Rowe, for contributing images.