Animal Source

PSU Animal Resource Program

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Risky Business: Research using infectious agents

Infectious disease research, especially concerning potential bioterrorism agents, has increased dramatically in the last several years. People who work with infectious agents in research or diagnostic laboratories are at risk for laboratory-associated infections (LAI's) due to these agents. Although actual infection rates for LAI's are not known, historical data, epidemiological surveys and clinical reports provide evidence that laboratory workers are at higher risk for infection with certain agents than the general public.

The majority of reported LAI's are associated with zoonotic agents (i.e., infectious agents that may be transmitted between humans and other animals). The ten most commonly acquired LAI's between 1979 and 1999 (Fleming and Hunt 2000) were all zoonotic agents. These included *Mycobacterium tuberculosis*, Q fever (*Coxiella burnetii*), Hantavirus, *Salmonella* species and *Cryptosporidium* species.

One survey found that 18% of LAI's could be traced to known accidents caused by either human error or carelessness (Fleming and Hunt 2000). The most common routes of exposure for these LAI's involved hypodermic needles and syringes or other sharp objects, spills and sprays, mouth pipetting, and animal bites or scratches. The source of exposure for

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The effects of environmental enrichment on brain and behavior

In the 1940's Canadian psychologist Donald O. Hebb hypothesized that environmental enrichment could alter the anatomical and physiological characteristics of the brain. Hebb reported anecdotally that laboratory rats who spent time living in an enriched environment in his home performed better on behavioral tests than laboratory housed littermates (van-Praag, Kempermann et al. 2000). Hebb's hypothesis has since evolved into the concept of neuronal plasticity, which is a central theme of modern neurobiology (van-Praag, Kempermann et al. 2000).

Many experimental studies from the 1960's through the 1980's demonstrated that environmental stimulation could lead to anatomical, physiological and behavioral changes in the adult rodent brain. Similar effects resulting from environmental stimulation have been found in other species including cats, monkeys and birds (Rosenzweig and Bennett 1996).

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Enrichment induced anatomical changes are primarily seen in the cortical and hippocampal regions of the brain and include increases in gliogenesis, neurite branching and synapse formation (van-Praag, Kempermann et al. 2000). Changes in levels of various growth factors and neurotransmitters such as brain derived neurotrophic factor and acetylcholine have also been shown to occur after exposure to enriched environments (van-Praag, Kempermann et al. 2000; Gresack and Frick 2004).

Correlated with anatomical and physiological changes in experimental animals are improvements in learning and memory. Learning and memory are typically evaluated in nonhuman subjects with behavioral tests such as the Morris water maze, radial arm maze and object recognition tests (van-Praag, Kempermann et al. 2000; Gresack and Frick 2004; Schrijver, Pallier et al. 2004). Exposure to an enriched environment also improves motor and memory function and decreases neuropathological changes seen in rodent models of aging, stroke, Huntington's disease and others (van-Praag, Kempermann et al. 2000).

The remaining question in evaluating the effects of environmental enrichment seems to be in differentiating the effects of social stimulation versus inanimate stimulation versus voluntary exercise. Increased physical activity can induce many of the same effects on brain and behaviors as have been attributed to environmental enrichment. At present, the effects of environmental enrichment have not been dissociated from a concomitant increase in voluntary locomotor behavior (van-Praag, Kempermann et al. 2000).

In addition, many of the early studies combined social stimulation (group housing) with inanimate stimuli (toys, etc…) in their experimental enriched environments. More recent work has attempted to address this issue. Schrijver and Pallier (Schrijver, Pallier et al. 2004) found that social isolation impaired reversal learning regardless of the presence of inanimate stimulation. In the same study, inanimate stimulation, regardless of group or isolation housing, enhanced spatial memory and learning behavior compared to rats in nonenriched housing.

Overall, the effects of environmental enrichment in laboratory animals, whether social or inanimate, appear to be beneficial. Further work needs to be done to determine the extent of these effects and how long they last, particularly after enrichment stops. In addition, the question remains, are the effects of environmental enrichment a result of enhancement of normal living conditions or simply reversal of a state of impoverishment?

References:

Gresack, J. E. and K. M. Frick (2004). "Environmental enrichment reduces the mnemonic and neural benefits of estrogen." Neuroscience **128**(3): 459-471.

Rosenzweig, M. R. and E. L. Bennett (1996). "Psychobiology of plasticity: effects of training and experience on brain and behavior." Behavioural Brain Research **78**: 57-65.

Schrijver, N. C. A., P. N. Pallier, et al. (2004). "Double dissociation of social and environmental stimulation on spatial learning and reversal learning in rats." Behavioural Brain Research **152**: 307-314.

van-Praag, H., G. Kempermann, et al. (2000). "Neural consequences of environmental enrichment." Nature Reviews Neuroscience **1**: 191-198.

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http://www.research.psu.edu/arp
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Life Sciences Animal Facility to Open Fall 2005

The rodent barrier facility in the new Life Sciences Building is projected to open for animal housing in the fall of this year. Construction of the facility is complete, and cage-washing equipment, including tunnel, rack, and bottle washers will be installed over the summer. Ventilated cage racks are on order for use in this facility. Additional funding sources are being explored in order to hire personnel to staff the facility and to purchase other necessary equipment. Procedure rooms and biosafety cabinets will be available for investigator use.

A group of potential barrier facility users, in conjunction with ARP veterinarians, have developed specific entrance requirements for people using the Life Science Facility, and the animals to be housed there. These requirements are intended to help prevent the introduction and spread of infectious rodent diseases. Entrance into the facility will be limited to faculty, staff and students who have undergone proper training in barrier techniques. People entering the facility will be required to wear protective gear including gowns, face masks and booties. Personnel will also be expected to follow specific procedures for handling animals to minimize the potential for contamination or transmission of disease.

Copies of the entrance requirements will be sent to all animal users approximately two months prior to the scheduled opening of the facility. In addition, training sessions in barrier technique will be held, and potential facility users will be advised of the requirements for animal entrance. Regular disease surveillance testing will be conducted in all animal rooms and confirmation of a disease outbreak would require removal of exposed animals from the building.

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the remaining 82% of LAI's could be attributed only to the infected individual working with the agent, being in or around the laboratory or being exposed to infected animals.

Although all those who work with infectious agents are at risk, some individuals may be at greater risk due to underlying health conditions. For example, certain skin conditions may lead to wounds or lesions that disrupt the natural barrier that the skin provides. Antibiotic therapy may alter the normal microbial flora of the gastrointestinal tract allowing colonization of the gut with pathogenic organisms. Immunodeficiency caused by diabetes mellitus, cancer chemotherapy or HIV infection may also place a worker at higher risk of infection.

The behavior of the laboratory worker is also an important variable in defining risk factors for LAI's. Adequate education, training and experience to perform the tasks required are essential for worker safety. A study conducted at a large microbiological research laboratory found that younger workers (age 20-29 years) had a higher accident rate than other age groups (Fleming and Hunt 2000). Eighty percent of all accidents in this study could be attributed to human error or unsafe acts.

The risks associated with infectious agent research can be minimized if appropriate laboratory procedures and protocols, including work practices, protective clothing requirements and waste management practices are followed to prevent exposure. Specific recommendations describing safe practices when using animals in infectious disease research are available and designated by Animal Biosafety Levels (ABSL). ABSL's 1 through 4 provide increasing levels of personnel and environmental protection and are recommended as minimal standards for activities involving infected laboratory animals.

More information on infectious disease research may be found at:

Biosafety in Microbiological and Biomedical Laboratories, 4th ed. May 1999. U.S. Department of Health and Human Services.

Fleming, D. O. and D. L. Hunt, Eds. (2000). Biological Safety: Principles and Practices. Washington, D.C., ASM Press.

Proceedings on the Fourth National Symposium on Biosafety: Working Safely with Research Animals, 1996. Centers for Disease Control and Prevention.

Infectious Disease Research in the Age of Biodefense. Institute for Laboratory Animal Research, National Research Council 46(1), 2005.

Animal Resource Program

101 Centralized Biological Laboratory
Pennsylvania State University
University Park, PA 16802

(814) 865-1495
Fax: (814) 865-3685

Rodent Surgery Workshop
March 2, 2005
1-4 pm in CBL

Call the ARP office to register to attend.

The Animal Resource Program (ARP) is committed to providing PSU faculty, staff and students with high quality, cost-effective research animal resources. In addition to suitable housing facilities and animal husbandry services for animals used in biomedical research, ARP provides veterinary and diagnostic services, personnel training and expertise in laboratory animal technology and medicine. ARP veterinarians are also available to participate in collaborative research projects with PSU investigators. Areas of interest include animal behavior and welfare, infectious disease, and pathology.

Surgery in Research expands to a full semester course

Starting fall semester 2005 Surgery in Research (Vet Sci 497A) will be offered as a 2 credit, full semester course. The class will meet once a week on Thursdays from 2:30 to 4:25 pm and include a combination of lecture and laboratory work. Topics covered in the course will include surgical planning and preparation, anesthesia and analgesia, post-operative care, large animal surgery and others. We are planning to expand the laboratory sessions to include rat, mouse, fish and amphibian surgeries.

The Surgery in Research course is designed for graduate level students although junior/senior undergraduate students who have previously taken Vet Sci 405 (Laboratory Animal Science) will be considered for enrollment. The objective of the course is to provide students with the information necessary to plan and conduct basic surgical procedures in a research setting. Students will have ample opportunity for practicing patient preparation, suturing and knot tying, tissue handling and other basic surgical techniques.