CARE, MANAGEMENT AND USE OF LABORATORY/ RESEARCH ANIMALS

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INTRODUCTION

- Why do we use animals?
  - Teaching
  - Initial phase of research
  - Non-animal vs Animal models

- THE THREE Rs IN RESEARCH
  - **REPLACEMENT** – the use of non-sentient material to replace methods which use conscious living vertebrates
  - **REDUCTION** – minimizing the number of animals used to obtain information
  - **REFINEMENT** – decrease incidence or severity of inhumane procedures applied to the animals

INTRODUCTION

- ANIMAL WELFARE VS ANIMAL RIGHTS
- Animal welfare
  - Human responsibility that encompasses all aspects of animal well being, including proper housing, management, nutrition, disease prevention and treatment, humane handling, and when necessary, humane euthanasia.
  - Well-being, characterized as the fulfillment of needs
- Animal rights
  - Animals have the same moral rights as human beings or in part because they have many of the same mental capabilities and activities as people.

INTRODUCTION

- The World Veterinary Association (WVA) has adopted an animal welfare policy, which includes the following statement:
  - "We do not accept the view that animals have specialized rights as an entity on their own. We believe that animals can benefit more from the point of view that man is responsible for the provision of animal welfare, rather than from the view which promotes animal rights alone."
- Anticruelty position – freedom from pain or suffering
- The only very strong interest that nonhuman animals possess is an interest in not experiencing pain or suffering - or, if they must undergo some pain or suffering in their use by people, in not experiencing unnecessary pain or suffering.

GOVERNMENT OFFICES

- **Bureau of Animal Industry (BAI)**
- **Philippine Association for Laboratory Animal Science (PALAS)**
- Committee on Laboratory Animal Resources Development and Standardization (LARDS)
- Protected Areas and Wildlife Bureau (PAWB)
- Philippine Council for Health Research and Development (PCHRD)

LAWS

- R.A. 8485 – Animal Welfare Act
- D.A. A.O. No. 40 – Rules and Regulations on the Conduct of Scientific Procedures Using Animals

PRINCIPLES & PROTOCOLS IN ANIMAL CARE AND USE

- Rationale
  - Relevance to human or animal health
  - Good of society
  - Unnecessary duplication of research
- Species used in research:
  - Rodents - mouse, rat, gerbil, hamster, guinea pig
  - Lagomorphs – rabbit
  - Carnivores – ferret, dog, cat
  - Ungulates – pig, cattle, sheep, goat, horse
  - Non-human primates – monkeys, apes
- Appropriate species, quality, number or animals
  - Justified statistically
  - Alternatives (less invasive procedures, other species, isolated organ preparation, tissue culture, computer models)

PRINCIPLES & PROTOCOLS IN ANIMAL CARE AND USE

- Appropriate sedation, analgesia or anesthesia
- Minimal discomfort, pain and stress
  - Best welfare = best science
  - What is meaningful to the animal
  - Aim at well-being (not mere absence of distress)
- Appropriate animal husbandry
- Conduct of experimentation by or under the close supervision of qualified and experienced persons
- Conduct of multiple major operative procedures
- Intervention, removal or euthanasia if stressful outcomes are anticipated

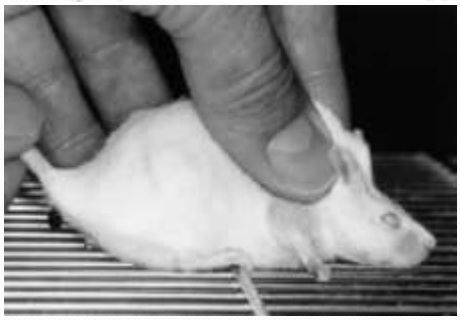
PRINCIPLES & PROTOCOLS IN ANIMAL CARE AND USE

- Postprocedure care
- Method of disposal or euthanasia
- Safety of working environment
- Know and anticipate what you are going to do before the start of the research.

PHYSICAL RESTRAINT

- Restraint devices are not normal methods of housing
- Not to be used simply as a convenience in handling
- Period of restraint should be minimum
- Train animals to adapt to restraint devices
- Observe animals at appropriate intervals
- Provide veterinary care in case of injury or illness due to restraint

Figure 21.15 Lifting a mouse from the cage. (Photo: T.P. Rooymans.)



.17 Restraint of a mouse. (Photo: T.P. Rooymans.)

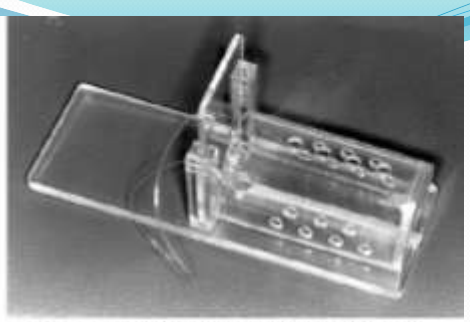
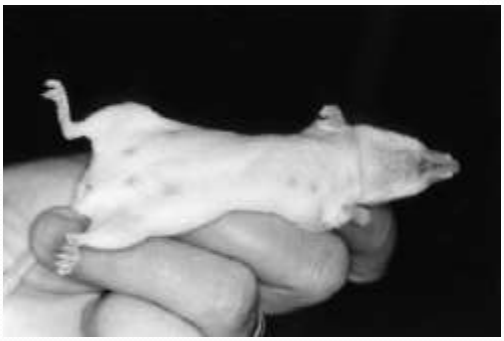


Figure 21.18 Plastic device for restraining mice. (Photo: T.P. Rooymans.)



RESTRAINT OF RATS

(a) (b)

Figure 27.4 Sexing a guinea pig. (a) In the female the vaginal membrane will be exposed. (b) In the male the penis is easily extruded from the genital opening using gentle pressure.

Figure 28.3 A rabbit, its movement restrained (a), taken by the scruff with one hand and carefully moved through the air (b), and held towards the body resting on the other arm with the face tucked under the arm (c). When the rabbit is lifted back to the cage again the other hand supports the body of the rabbit (d). (Photos: Ann-Christine Nordström.)

SURGICAL PROCEDURES

- Multiple major surgeries on an animal are discouraged
  - Permitted if scientifically justified
  - Cost savings alone is not an adequate reason
- Pay attention to animal well-being through continuing evaluation of outcomes

FOOD OR FLUID RESTRICTION

- Should be scientifically justified
- Monitor physiologic or behavioral indexes
- Use least restriction to achieve scientific objective
- Use highly preferred food instead of restriction for positive reinforcement

OTHER CONSIDERATIONS

- Veterinary care
- Personnel qualifications and training
- Personal hygiene
- Occupational health and safety of personnel
- Hazard Identification and Risk Assessment
- Facilities, Procedures and Monitoring
- Personal protection
- Medical evaluation and preventive medicine for personnel

ANIMAL ENVIRONMENT, HOUSING AND MANAGEMENT

- Species, strain and breed of animals
- Sex, age, size
- Maintained singly or in groups
  - Ability to form social groups through sight, smell, contact
- Design and construct of housing
- Availability and suitability of enrichments
- Project goals and experimental design
- Intensity of animal manipulation and invasiveness
- Presence of hazardous materials
- Duration of holding period

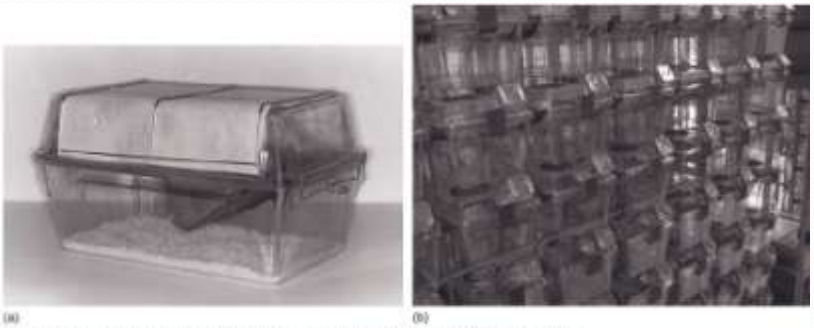
PHYSICAL ENVIRONMENT

- Microenvironment – primary enclosure
  - Immediate surroundings, temperature, humidity, air composition
  - Can induce changes in metabolic and physiologic processes
- Macroenvironment – secondary enclosure
  - Room, barn, outdoor habitat

HOUSING

- Naturalistic environments
- Sheltered or outdoor housing
- Primary enclosures
  - Allow normal behavior and physiologic needs
  - Allow social interaction, development of hierarchies
  - Adequate ventilation
  - Allow easy access to food and water and servicing
  - Provide a secure environment (no escape and no injury)
  - Allow observation with minimal disturbance

Figure 21.4 Polycarbonate cages for mice with sawdust-covered solid floors. (Photo: T.P. Rooymans.)



(a) (b)

Figure 21.10 (a) Filter-top cage. (b) Individually ventilated cage (IVC) rack. (Photos: T.P. Rooymans.)

SPACE RECOMMENDATIONS

TABLE 2.1 Recommended Space for Commonly Used Group-Housed Laboratory Rodents

Animals	Weight, g	Floor Area/Animal, in²[a]	Height,[b] in[c]
Mice	<10	6	5
	Up to 15	8	5
	Up to 25	12	5
	>25[d]	>15	5
Rats	<100	17	7
	Up to 200	23	7
	Up to 300	29	7
	Up to 400	40	7
	Up to 500	60	7
	>500[f]	>70	7
Hamsters	<60	10	6
	Up to 80	13	6
	Up to 100	16	6
	>100[g]	>19	6
Guinea pigs	<350	60	7
	>350[g]	>101	7

SPACE RECOMMENDATIONS

TABLE 2.2 Recommended Space for Rabbits, Cats, Dogs, Nonhuman Primates, and Birds

Animals	Weight, kg[a]	Floor Area/Animal, ft²[b]	Height[c] in[d]
Rabbits	<2	1.5	14
	Up to 4	3.0	14
	Up to 5.4	4.0	14
	>5.4[e]	>5.0	14
Cats	<4	3.0	24
	>4[e]	>4.0	24
Dogs[f]	<15	8.0	-
	Up to 30	12.0	-
	>30[e]	>24.0	-

TEMPERATURE, HUMIDITY AND VENTILATION

TABLE 2.4 Recommended Dry-Bulb Temperatures for Common Laboratory Animals

	Dry-Bulb Temperature	
Animal	°C	°F
Mouse, rat, hamster, gerbil, guinea pig	18-26	64-79
Rabbit	16-22	61-72
Cat, dog, nonhuman primate	18-29	64-84
Farm animals and poultry	16-27	61-81

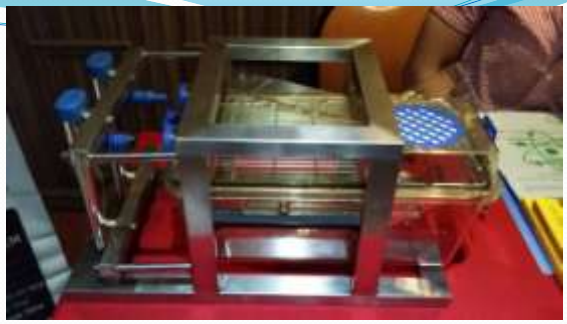
- Exposure to temperatures above or below the optimum ranges without shelter or protective mechanisms might produce clinical effects
- Ventilation should supply adequate oxygen, dilute gaseous contaminants, remove thermal loads
- Can differ considerably between primary and secondary enclosures

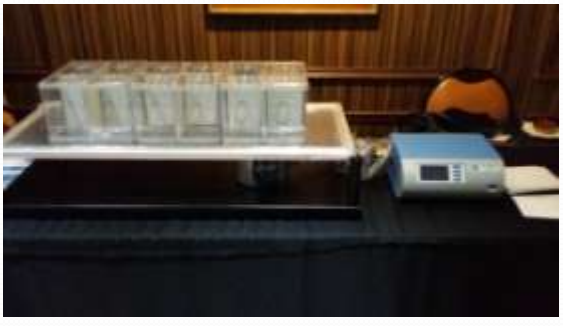
ILLUMINATION

- Light can affect physiology, morphology, behavior
- Sufficient lighting for animal well-being and good housekeeping practices
- Provide adequate vision and neuroendocrine regulation of diurnal and circadian cycles
- Management practices to provide animals with ways to modify their own light exposure by behavioral means

NOISE

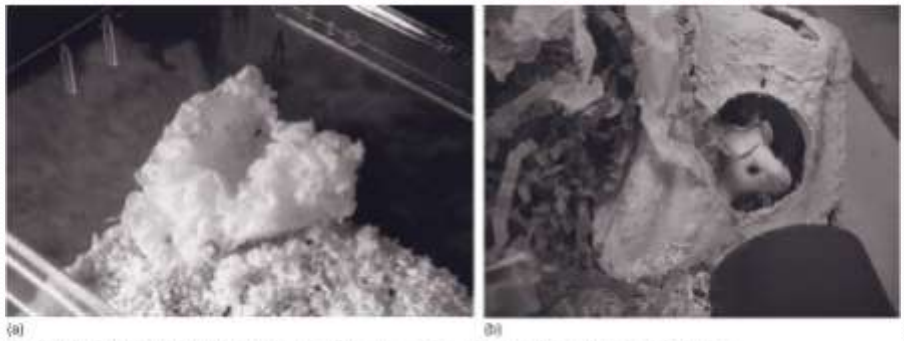
- Separation of human and animal areas to minimize disturbances
- Noisy animals should be separate from quieter animals
- Some effects of loud noise
  - Eosinopenia, increased adrenal weights, infertility, high blood pressure
- Some species are sensitive to frequencies of sound inaudible to humans
  - Example: video display terminals





BEHAVIORAL MANAGEMENT

- STRUCTURAL ENVIRONMENT
  - Cage furniture, enrichments, complexities
  - Depending on the animal species
- SOCIAL ENVIRONMENT
  - Physical contact and communication
  - Non-contact communication through visual, auditory and olfactory signals
  - Naturally territorial vs communal animals
  - Not all social species can or should be maintained socially
- ANIMAL ACTIVITY
  - Vertical dimension should be considered
  - Forced activity should be avoided



(a) (b)

Figure 21.5 (a) Bowl-shaped nest of BALB/c mice. (b) Environmental enrichment for mice. (Photos: T.P. Rooymans.)

(a) (b)

Figure 28.2 Group housing of does in a research laboratory in Sweden (a) and in a pharmaceutical company in Denmark (b) (Photos: a) Lena Lidfors; b) with kind permission of Novo Nordisk A/S.)

HUSBANDRY

- FOOD
  - Palatable, clean, nutritionally adequate
  - Animals with easy access to feeders and minimize contamination with urine and feces
  - Adequate access to all animals housed in groups
  - Provide wood chips, treats, etc (depending on species)
  - Clean and enclosed storage (off the floor)
  - Check shelf-life of food

HUSBANDRY

- WATER
  - Ad libitum
  - Consider any possible water treatments and effects
  - Daily inspection for cleanliness, maintenance and proper operation
- After refilling feeders and waterers, they should be **returned to the same cages** they were taken from!
- BEDDING
  - Appropriate material, sufficient to keep animals dry, should not come into contact with water tube and feeders

SANITATION

- BEDDING CHANGE
  - Daily, weekly, reproductive considerations
- CLEANING AND DISINFECTION OF PRIMARY ENCLOSURES
  - Chemicals, hot water or both
  - Frequency depends on type of cages
- CLEANING AND DISINFECTION OF SECONDARY ENCLOSURES
- WASTE DISPOSAL
- PEST CONTROL
  - Preferably via non-toxic means
- EMERGENCY, WEEKEND AND HOLIDAY CARE

OTHER CONSIDERATIONS

- ANIMAL PROCUREMENT AND TRANSPORTATION
  - Important to procure animals from reputable sources, accredited laboratories (NOT FROM PET SHOPS!)
  - Minimize transit time and risk of zoonoses, avoid overcrowding and environmental extremes
  - Provide adequate protection, food and water
- QUARANTINE, STABILIZATION, SEPARATION
  - Length of time of stabilization depends on species, type and duration of transport, intended use
- SURVEILLANCE, DIAGNOSIS AND TREATMENT OF DISEASE
  - Appropriate veterinary care when needed

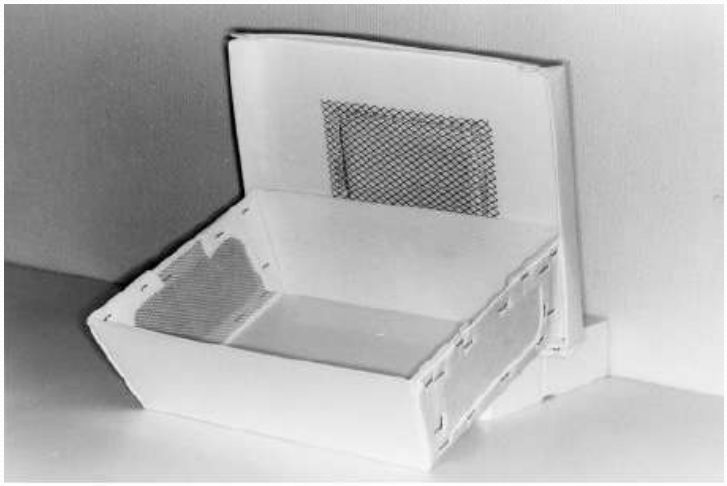
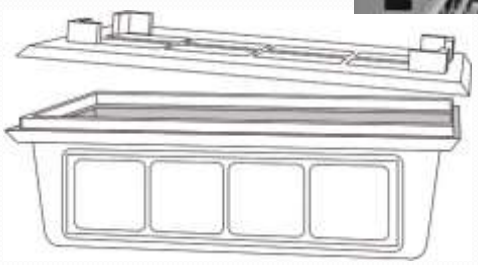


Figure 21.11 Disposable transport cage of cardboard, the inside covered with plastic, provided with wire mesh and filters. (Photo: T.P. Rooymans.)

SHIPPING CONTAINERS

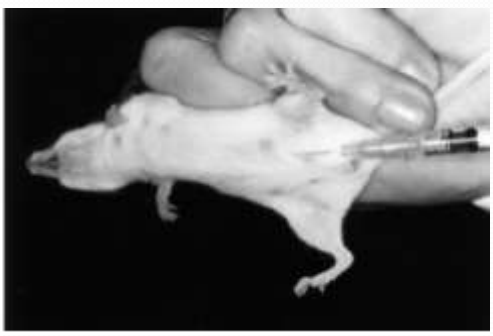


TRANSPORTATION

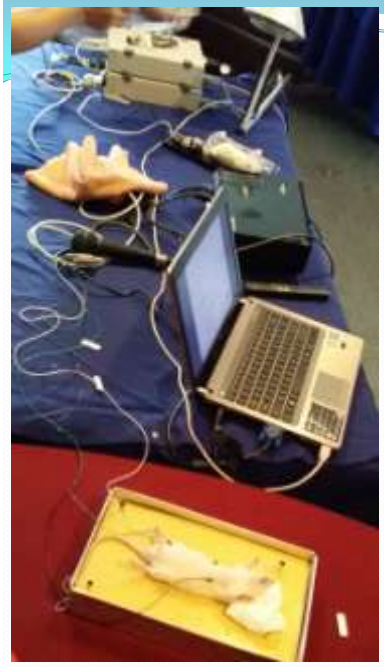
Figure 21.19 Lateral tail vein. (Photo: T.P. Rooymans.)

Figure 21.22 Administration of substances via stomach/oesophageal tube. (Photo: T.P. Rooymans.)

Figure 21.20 Lateral saphenous vein. (Photo: T.P. Rooymans.)



Interaperitoneal injection. (Photo: T.P. Rooymans.)



(a)

(c)

(b)

Blood sampling procedures. (a) Ear vessels. (b, c) Saphenous vein.

(a)

(b)

Figure 27.7 Administration techniques. (a) Intramuscular injection into the hindlimb of a guinea pig. (b) Oral gavage via gastric tube. A mouth gag prevents the guinea pig from biting into the tube.

re 28.4 Collection of blood from the ear vein of a rabbit.

Figure 21.23 Subcutaneous injection under the skin of the neck. (Photo: T.P. Rooymans.)

RULE OF THUMB:

- 10% of the animal's weight is blood.
- The maximum amount of blood that can be collected is 10% of the blood volume of the animal.
- Or 1% of the body weight of the animal.

ANIMAL CARE AND USE STATEMENT (Protocol Review Form)

- Should be accomplished as part of the research proposal – research can only proceed once this is approved
- Explains in full detail all aspects of the research that involves animals
- Makes sure all groups know what they will be doing before the actual conduct of the research

ANIMAL CARE AND USE STATEMENT (Protocol Review Form)

I. PROCEDURE(S) OR TITLE OF RESEARCH/STUDY
II. PURPOSE / OBJECTIVES
III. DURATION OR TIMEFRAME
- excluding quarantine but including conditioning time
IV. RESPONSIBLE PERSON / PRINCIPAL INVESTIGATOR
- Name/s and qualifiction
V. BACKGROUND AND SIGNIFICANCE OF PROCEDURE OR RESEARCH
- Include biomedical characteristics of the animals that are essential to the research & indicate related studies with the proposed animal model

ANIMAL CARE AND USE STATEMENT (Protocol Review Form)

VI. DESCRIPTION OF METHODOLOGIES / EXPERIMENTAL DESIGN

A. Species and type of animal
B. Source of animals
C. Reason/basis for selecting animal species
D. Sex, age and number of animals (justify number)
E. Quarantine and/or conditioning process
F. Animal care procedures
   - Cage type, # of animals per cage
   - Cleaning method
   - Room temp., humidity, ventilation, lighting
   - Diet, feeding and watering method

ANIMAL CARE AND USE STATEMENT (Protocol Review Form)

G. Experimental or animal manipulation methods
   - General description (including conditioning method)
   - Dosing method
   - Expected outcome, effects, adverse side effects
   - Specimen or biological agent (frequency, volume, route, and method of restraint)
   - Animal examination procedures
   - Use of anesthetics
   - Surgical procedures
   - Euthanasia
H. Is there a non-animal model applicable? If so, provide reasons for not using it.

ANIMAL CARE AND USE STATEMENT (Protocol Review Form)

- It is expected that the study will be conducted according to the approved protocol
- Obtain approval from the IACUC prior to making any changes affecting the protocol

REFERENCES

- PALAS Code of Practice for the Care and Use of Laboratory Animals in the Philippines
- Guide for the Care and Use of Laboratory Animals
- The UFAW handbook on The Care and Management of Laboratory and Other Research Animals

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