Animal health and research

University of Eastern Finland
Lab Animal Centre

Short overview:
- Infections in laboratory animals
- Ways to minimize the risk of outbreaks
- Importance and interpretation of health monitoring results
- Current situation in Lab Animal Centre
- New rules for barrier unit

How we know that our animals are healthy?
- Can’t do research: all animals are dead
- Can’t do research: all animals are ill
- Can’t do research: all animals are seropositive

Diseases can be:
- Infectious diseases
  - presence of pathogenic microbial agents
  - viruses
  - bacteria
  - fungi
  - protozoa
  - parasites
  - aberrant proteins (prions)
- Genetic modification
- Non-infectious diseases
  - poor welfare
  - nutritional deficiencies
  - housing conditions etc
  - heredity

Avoid diseases!
- Human
- Animals
- Food, water, air
- Biol. material

Disasters come in many shapes

Disasters come in many shapes
Some are caused by the force of Nature, many by human behaviour!
How Infectious Diseases Spread
There are three ways for diseases to spread between animals (or between animals and people):
- **direct contact**
  - skin diseases
  - sexually transmitted diseases
- **indirect contact through the environment:**
  - Via respiratory tract
  - Through contaminated water or bedding
- **fomites:**
  - inanimate objects, e.g. utensils, contaminated cages, needles, etc., have become carriers of infection

Routes of Shedding
- Organisms can be excreted by a variety of routes:
  - Respiratory tract
    - Sneezing
    - Coughing
  - Gastrointestinal tract
    - Feces
  - Other body fluids
    - Urine
    - Saliva etc

How contagious it is?
Depends on:
- virulence and number of infective particles that an animal is exposed to
- animal, species and strain
- immune system and stress
People
- Restricted access
- Limit traffic
- Protective clothing
- SOP
- Proper handling of animals and processing of materials
- Pets
- No pets of same species

Experimental procedures
- Cell, tissue, fluids
  - May be contaminated by rodent viruses
  - Should be tested
- Procedure rooms
  - Limited traffic
  - Protective clothing, SOPs
  - Desinfection between procedures

Animals
- Obtain from a trusted breeder, with health monitoring results
- Safe transportation
- Quarantine

Conventional vs barrier

Conventional
- Free entrance for researcher
- No control of diseases
- Do not autoclave routinely

Barrier
- Entrance with physical barrier (shower)
- Equipment is autoclaved or sterilized
- Only embryos or SPF animals

Situation in and out of animal house
- Health monitoring gives us historical review
- Reviews describe a situation about 8…10 years
- Be aware!
Different names for conditions

- Specific pathogen free (SPF) or (SPOF)
- Virus antibody free (VAF)
- Caesarian-originated barrier-sustained (COBS)
- Murine pathogen free (MPF)
- Restricted flora (RF)
- Germfree (GF)

Kuopio 2012

- May - BALB/c nude - Taconic from barrier – Staphylococcus aureus; informed in July
- July - NZW rabbits - Harlan – Hillcrestin barrier – Eimeria spp; informed August (sampled on rabbits departue day)
- Sept - BALB/c nude – Harlan isolator – Pseudomonas aeruginosa and Klebsiella spp

Oulu

2008 rats - Streptococcus agalactia – Harlan + Oulu

Current status

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<th>Mice</th>
<th>Rats</th>
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<td>Rats</td>
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<td>H. rodentium S. aureus (Helico. spp, S. aureus)</td>
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<td>Rabbits</td>
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The barrier quarantine program will consist of the following:

- Review of disease surveillance history from the sending institution; health monitoring results should be within last 60 days prior shipment.
- Collection of faeces for direct PCR testing for rodent pathogens.
- Taking swabs for microbiology screening.
- Collection of micro-blood sample for serology or whole animal can be used if it is reasonable.

Quarantine schedule:

- Week 1: Animals are housed in isolator(s).
- Week 2: Collection of faecal pellets 7-10 days after arrival for PCR testing and sending it to Surrey Diagnostic e.g.: Mouse Parvovirus, Murine Norovirus etc. testing. If needed additional test might be required according to the health status of mice.
- Swabs for microbiological testing will be collected from laryngeal area and sent to EVIRA for screening of Pasteurella pneumotropica and Staphylococcus aureus.
- Faecal pellets will be collected and tape test performed for parasitology.
- Week 3-4: After test results, following activities are performed:
  - If tests are negative, animals will be transferred into the barrier unit.
  - If tests are equivocal, animals will remain in quarantine for future testing.
  - If tests are positive for any of the agents tested, animals will be replaced to the other units or humanely euthanized.
Why are healthy animals important?

- Welfare of animals
- Less risk for caretakers and researchers
- Better scientific results
- Infectious diseases are important variable that can have devastating effects on the research program

Genetical predisposition to viral diseases

- Ectomelia virus
- A, CBA, DBA, C3H, BALB/c
- Lactate dehydrogenase virus (paralysis)
- AKR, C58
- Murine hepatitis virus (mortality)
- BALB/c, C57Bl
- Sendai virus (mortality)
- DBA/2J, 129/J
- Theler’s murine encephalomyelitis virus
- CD-1 SJL, (NMRI), DBA/2, SWR

Modulation of oncogenesis

- Oncogenic
- Retroviruses
- Helicobacter spp
- May increase
  - Mycoplasma pulmonis
  - Citrobacter rodentium
- May decrease
  - Salmonella
  - H1 parvovirus

Modulation of breeding

- Rotaviruses
- MHV
- Mycoplasma pulmonis – decreases fertility, may cause purulent processes
- Pathogens passing through placenta
  - Retroviruses
  - LCMV
  - Paroviruses
  - Ectromelia virus
  - Cardioviruses
  - Clostridium piliforme

Most prevalent agents

- Mice and rats - mouse parvovirus and rat parvovirus, both members of the Paroviridae family
- Guinea pigs – Guinea pig cytomegalovirus and parainfluenzavirus

Figure 1. Prevalence of agent-specific serum antibodies in mice.

EDM, mouse rotavirus; MAU, mouse adenovirus; MHV, mouse hepatitis virus; MNV, mouse norovirus; Reo3, reovirus type 3; TMEV, Theler’s murine encephalomyelitis virus
Figure 2. Prevalence of agent-specific serum antibodies in rats.
PVM, pneumonia virus of mice; RCV, rat coronavirus; SDAV, sialodacryoadenitis virus; TMEV, Theiler’s murine encephalomyelitis virus.

Charles River survey
Mice:
- mouse norovirus
- paroviruses
- mouse hepatitis virus
- rotavirus
- Theiler’s murine encephalomyelitis virus
- Helicobacter spp.
- Pasteurella pneumotropica
- pinworms

Rats:
- ‘rat respiratory virus’
- paroviruses
- rat theilovirus
- Helicobacter spp.
- Pneumotropica
- pinworms

Mice in pet shops in Germany
- Helicobacter species (92.9%)
- mouse parvovirus (89.3%)
- mouse hepatitis virus (82.7%)
- Pasteurella pneumotropica (71.4%)
- Syphacia species (57.1%).
- Several microorganisms (e.g. mouse parvovirus, Theiler’s murine encephalomyelitis virus, etc) had considerably higher prevalences than those reported in similar studies on wild mice from North America, Europe or Australia.

Dammann, P; Lab Anim October 2011 vol. 45 no. 4

Wild-caught Norway rats
- rat coronavirus/sialodacryoadenitis virus (91.7%)
- Mycoplasma pulmonis (72.9%)
- cilia-associated respiratory bacillus (52.1%)
- rat parovirus/rat minute virus (29.2%)
- Kilham rat virus (10.4%)
- Tsolan’s H-1 virus (10.4%)
- Sendai virus (4.2%)
- Theiler’s mouse encephalomyelitis virus
- various endoparasites
- Not detected; reovirus and pneumonia virus of mice

Easterbrook JD; Lab Anim. 2008 Jan;42(1)

Manual of Microbiological Monitoring of Laboratory Animals

- http://books.google.com/books?id=CaHuLkp6_GOC&printsec=frontcover&source=gbis_summary_r#PPR1,M1
Implications of infectious agents on the results of animal experiment

- [http://www.utexas.edu/research/arc/misc/GVSOLAS.pdf](http://www.utexas.edu/research/arc/misc/GVSOLAS.pdf)