New technological developments in Health Monitoring of rodent colonies and 3 R’s

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Commonly Recognized Viral and Bacterial Pathogens

- Organisms in black are less likely to cause clinical disease
  - May cause disease in some mice

- Organisms highlighted in red are more likely to cause clinical disease
  - Don’t *always* cause disease
Respiratory pathogens

- Sendai virus
- *Mycoplasma pulmonis*
- CAR bacillus
- Pneumonia virus of mice (immunodeficient only)
- K virus

Skin and joint pathogens

- Ectromelia virus
- *Streptobacillus moniliformis* (zoontotic)
- Fleas, ticks, mites
• **Digestive system pathogens**
  - Mouse cytomegalovirus
  - Mouse thymic virus
  - Mouse hepatitis virus
  - Mouse rotavirus
  - Reovirus 3
  - Mouse adenoviruses
  - *Bacillus piliformis*
  - *Salmonella enteritidis* (zoonotic)
  - *Citrobacter freundii*

• **CNS pathogens**
  - GDVII (Theiler’s virus)
  - Encephalitozoon cuniculi
• Hemopoietic pathogens
  Lymphocytic choriomeningitis virus *(zoonotic)*
  Lactic dehydrogenase – elevating virus

• Pathogens affecting multiple systems
  Minute virus of mice
  Polyoma virus *(immunodeficient only)*
  Hantaviruses *(zoonotic)*
Factors Affecting Ease of Eradication

- **Organisms that are most difficult to eradicate include those that exhibit two or more of the following characteristics**
  - Spread very easily and/or rapidly
  - May be shed for long periods of time by immunocompetent animals
  - May persistent for long periods of time in the environment
  - May present diagnostic challenges

- **Organisms that are easiest to eradicate typically**:
  - Spread slowly and/or only by direct contact
  - Are quickly eliminated by immunocompetent* animals
  - Are rapidly inactivated under normal environmental conditions
  - Are reliably detected using standard diagnostic tests

* NOTE: Infections, and shedding, may persist far longer in immune compromised or deficient animals
Most Difficult to Eradicate

- Hantavirus
- K virus
- Lymphocytic choriomeningitis virus
- Minute virus of mice
- Mouse hepatitis virus
- Mouse parvovirus
- Mouse rotavirus
- Polyoma virus
- Sendai virus
Moderately Difficult to Eradicate

• *Corynebacterium* (Note: may be difficult to eradicate once established in a population)
• Ectromelia virus
• GDVII (Theiler’s) virus
• Mouse adenovirus
• Reovirus 3
• *Clostridium piliforme*
• *Mycoplasma arthritidis*
• *Mycoplasma pulmonis*
• *Salmonella*
Least Difficult to Eradicate

- Lactic dehydrogenase elevating virus
- Mouse cytomegalovirus
- Mouse thymic virus
- CAR bacillus
- *Citrobacter rodentium* (moderate?)
- *Streptobacillus moniliformis*
- Pneumonia virus of mice
Least Difficult to Eradicate

- Lactic dehydrogenase elevating virus
- Mouse cytomegalovirus
- Mouse thymic virus
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- *Citrobacter rodentium* (moderate?)
- *Streptobacillus moniliformis*
- Pneumonia virus of mice
Mouse Adapted
Opportunistic Pathogens
Mouse Norovirus

• Recently recognized virus of laboratory mice
  – Considered an opportunist by some, pathogen by others

• Asymptomatic infections in most animals
  – Mild transient inflammation of liver and spleen (red pulp hypertrophy and white pulp activation)
  – Tropism for macrophages and dendritic cells

• Virus can persist up to 8 weeks in spleen, mesenteric lymph nodes, jejunum
  – Persistent infection in severely immunodeficient mice
Clinical Disease Due to MNV

• Seen only in mice with deficiencies of the innate immune response, specifically those lacking intact interferon signaling pathways due to a lack of type I and/or type II IFN receptors or the STAT-1 molecule
  – Severe pneumonia and destruction of splenic and liver tissues
  – Significant mortality among affected animals
  – Exclude from these mice

Deficiencies of the acquired immune response, even severe immune deficiencies, do not predispose to disease
**Pneumocystis murina**

- A genus of fungal organisms affecting many species of animals
  - Different *Pneumocystis* species infect different animals
  - *P. murina* infects mice

- No disease in immunocompetent mice
  - Adults clear infections within 3 weeks
  - May take up to 6 weeks in mice infected as neonates

- Pathogenic for severely immunodeficient or immune-suppressed mice
  - Pneumonia progresses to death if not treated
  - Exclude from these mice
Helicobacter

- Over 25 species, many of which persistently colonize mouse GI as commensals

- Most species asymptomatic in most mice - may complicate studies of GI/liver
  - *H. hepaticus* may cause hepatitis, IBD, liver/lower bowel cancer in susceptible strains (A, BALB/c, C3H, SJL, immunodeficient)
  - *H. bilis* may cause typhlitis/hepatitis in immunodeficient, rarely immunocompetent strains
  - Pathogenicity of others not established

- Consider excluding *H. hepaticus* and *H. bilis*, esp from susceptible colonies
Pasteurella

Many commensal species infecting mice, most with low pathogenic potential

- *P. pneumotropica* complex has higher pathogenic potential
  - Highest in immunodeficient mice and as co-pathogen
  - CBA/J and C3H/He also ↑ ?susceptibility

- Possible pneumonia, conjunctivitis, panophthalmitis, dacryoadenitis, otitis, mastitis, inflammation/ abscesses of GU tract

- Consider excluding, esp from susceptible strains
Corynebacterium

- Many species are considered normal flora of skin and MM in humans and other animals
- *C. bovis* and *C. kutscheri* may cause disease in mice – consider excluding, esp from susceptible strains
- *C. bovis* - usually transient colonization of skin
  - Nude mice more prone hyperkeratotic dermatitis
  - Occasional mild disease in haired, severely immunodeficient mice and hairless mice
- *C. kutscheri* – usually asymptomatic colonization of GI
  - Clinical disease possible, esp in BALB/c, A/J, CBA, immunodeficient & stressed mice
  - Internal abscesses, septic arthritis, lymphadenopathy
Opportunists Carried by Humans or Widespread in Environment
Beta-hemolytic *Streptococcus*

- Hardy facultative anaerobic bacterium

- Non-hemolytic commensal strains colonize the mouth/nose, GI tract and genital mucosa

- Virulent $\beta$-hemolytic strains most likely to cause disease in mice
  - Also carried by many clinically healthy mice and humans
  - Produce a variety of secreted proteins, incl. exotoxins that have immunomodulatory effects as superantigens
Strep Health Effects

• Most commonly associated with strains of Lancefield’s group B (serotype)

• Syndromes include meningoencephalitis, pyelonephritis, myocarditis, metritis, hepatitis, pneumonia, dermatitis

• Susceptibility to disease increased with stress
  – No difference related to age or immune status
  – DBA/2 more sensitive than most mice

• Ideally, focus on exclusion of more pathogenic strains
  – Most important to exclude if mice will be stressed (e.g., surgery, irradiation)
Many species of hardy gram positive bacteria
   - Commonly colonize the skin, MM, and GI tract of humans and animals

Pathogenicity varies with Staph species and host factors
   - *S. aureus* (1°), *S. xylosus* (2°) most often associated with disease in mice; others occasionally

Possible disease problems
   - Superficial and deep cutaneous abscesses; dermatitis, esp in BL/6 and other black mice
   - Preputial gland abscesses
   - Retrobulbar cellulitis and abscesses
**Staphyloccoccus**

- Many species of hardy gram positive bacteria
  - Commonly colonize the skin, MM, and GI tract of humans and animals

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Most Susceptible to Staph Disease

- Very young, aged, stressed mice
- Sensitive strains - BALB/c, DBA/2, C57BL/6

Exclusion – esp. S. aureus and S. xylosus – most important if using:
  - Severely immunodeficient, nude
  - Specific immune deficiencies, e.g.,
    - Cybb knockout (lacks phagocyte superoxide production)
    - Nos2 knockout (lacks cytokine-inducible nitric oxide synthase)
    - C3H/He (homozygous for the defective LPS response allele Tlr4Lps-d)
    - Also Tlr4 knockouts
Pseudomonas

• Abundant in soil, water, sewage, agricultural products
  – Not indigenous flora of mice, but commonly found
  – Normally found in human GI and skin

• Health effects –1° immunodeficient or immunosuppressed
  – Upper respiratory disease, otitis media and/or interna, septicemia with hemorrhage & necrosis in multiple organs

• Consider excluding if using: immunodeficient or immunosuppressed animals (irradiated, cyclophosphamide tx, experimental injury, etc); diabetic mice; C3H/He
Proteus

• Ubiquitous in nature (soil, water, sewage) and found in upper respiratory tract and GI of many species, incl. mice

• Health effects
  – Urinary tract infections, including pyelonephritis, most common
  – Systemic disease in severely immunodeficient mice

• Consider excluding if using sensitive strains
C3H/He, Cybb knockout, diabetic, or severely immunodeficient mice
Klebsiella

• Normal inhabitant of human and animal GI; ubiquitous in water, sewage, soil, wood products, grain and other plants

• Rarely associated with disease in mice
  – Host factors and concurrent disease conditions critical determinants of pathogenicity
  – Disease possible if host defenses compromised due to stressful experimental manipulations (surgery, irradiation)

• Recommend excluding if using C3H/He mice
Escherichia coli

• Common commensal of the GI tract of mice and many other species, including humans

• Most strains of *E. coli* are nonpathogenic
  – Some strains may cause disease in immunodeficient mice
  – Diarrhea, pneumonia, UTI, meningitis, septicemia

• No evidence of pathenogenicity in immunocompetent mice

• Consider excluding if using severely immunodeficient mice