INFECTIOUS AGENT EXCLUSION LIST FOR RATS

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Specific examples of interference to research caused by infectious agent exposure are viewable at http://www.lal.org.uk/pdffiles/GVSOLAS.pdf.

I. DNA VIRAL DISEASES

PARVOVIRUS

Etiology: 3 major antigenic groups represented by Kilham's rat virus (KRV or RV), Toolan's H-1, rat parvovirus (RPV, formerly ROPV, rat orphan parvovirus); conserved nonstructural proteins so IFA for serodetection; small, single strand DNA, nonenveloped.
Transmission: oronasal, fomites, transplacental, transmammary; shedding in urine, feces, milk, oropharaynx; common; relatively resistant, remain infectious at room temperature.
Clinical: KRV/RV most pathogenic, perhaps only strain that causes disease following natural exposure (H-1 and RPV are nonpathogenic); experimental neonatal exposure predilection for primordial cells of cerebellar cortex, periventricular region, hepatocytes, endothelial cells, bone marrow; no intestinal mucosal lesions as in other species; brain, liver, and testes affected.
Pathology: multiple foci of hemorrhage in cerebrum and cerebellum with malacia, testes and epidydmis with coagulative necrosis, liver with focal necrosis; damaged endothelial cells and megakaryocytes; neonates with cerebellar hypoplasia, hepatitis, jaundice; abortion, fetal resorption, infertility; scrotal hemorrhage, peritesticular fibrinous exudation.
Significance: inapparent enzootic common; contaminate transplantable tumors, cell lines, viral stocks.

II. RNA VIRAL DISEASES

A. CORONAVIRUS

RCV/SDAV

Etiology: Rat Coronavirus, numerous strains, varied virulence; sialodacryoadenitis virus (SDAV), Parker's rat coronavirus (PRC) initial isolate.
Transmission: nasal secretions and saliva.
Clinical: subclinical to high morbidity, no mortality; sniffling, blepharospasm, epiphora, intermandibular swelling, chromodacryorrhea porphyrin-containing encrustation around eye; megaloglobus, hyphema, corneal ulcers.
Pathology: sialodacryoadenitis of parotid and submandibular salivary, and infraorbital, exorbital, and Harderian lacrimal glands with coagulation necrosis of ductal and acinar epithelial cells with effacement of normal architecture and squamous metaplasia, mononuclear cell infiltration; hyperplastic cervical lymph nodes; regeneration of acinar and ductal structures within 4 weeks; necrotizing rhinitis, tracheitis, bronchitis, alveolitis possible, but transient.
Ddx:. nasal/ocular discharge associated with mycoplasma, Sendai, PVM; subcutaneous edema of head with *Pseudomonaus aeruginosa*; chromodacryorrhea is not diagnostic (porphyrin from Harderian glands) but also caused by high environmental ammonia, stress.
Significance: periodic outbreaks with high morbidity; permanent ocular damage; co-pathogen with *Mycoplasma pulmonis*, CAR bacillus; EGF depletion.

B. PARAMYXOVIRUS

PVM

Etiology: *Pneumovirus*, pneumonia virus of mice (PVM).
Transmission: common enzootic infections; affinity for respiratory epithelium and endothelium; wide host range including mice, hamsters, guinea pigs, gerbils.
Clinical: nasal, ocular discharge.
Pathology: multifocal, nonsuppurative vasculitis and interstitial pneumonitis with necrosis; prominent perivascular mononuclear cell infiltrates, and BALT hyperplasia.
Ddx:.Sendai, SDAV.
Significance: respiratory pathogen; copathogen with *Mycoplasma pulmonis*; interspecies transmission possible; more commonly a cause of morbidity in immunocompetent rats than mice, perhaps in part due to high degree of BALT hyperplasia.

SENDAI VIRUS

Etiology: *Parainfluenza 1*, (Sendai, Japan).

Transmission:

Helicobacter colis – individual report of ulcerative typhlitis in nudes; also *H. trogontum* as potential gastrointestinal pathogen.

Lawsonia intracellularis – emerging enteric pathogen; wide host range.

B. GRAM NEGATIVE RESPIRATORY

BORDETELLA
Etiology: *Bordetella bronchiseptica*.
Transmission: aerosol; colonizes apices of respiratory epithelium; uncommon opportunistic pathogen; common upper respiratory inhabitant of guinea pig (and important primary pathogen) and rabbit (potential copathogen).
Clinical: nasal discharge.
Pathology: suppurative rhinitis, anteroventral suppurative bronchopneumonia with consolidation.
Dx:.readily culturable small blue-gray colonies of motile bacillus.
Significance: uncommon, opportunistic, secondary co-pathogen with concurrent infections of *Mycoplasma pulmonis*, PVM, Sendai, or coronavirus.

CAR BACILLUS
Etiology: Cilia-Associated Respiratory (CAR) Bacillus; filamentous, argyrophilic bacillus with gliding motility; difficult to culture; survives freezing & thawing.
Transmission: contact, infected dams, contaminated bedding; colonizes respiratory ciliated epithelium; wide host range including mice, rabbits, cattle, pigs.
Pathology: chronic suppurative bronchitis and bronchiolitis with marked peribronchiolar leukocytic infiltration; mucopurulent bronchopneumonia progressing to bronchiectasis; Warthin-Starry staining shows numerous slender bacilli inserted along apices of ciliated respiratory epithelium.
Ddx:. experimental intranasal inoculation results in lesions similar to *Mycoplasma pulmonis*, but natural respiratory disease usually mixed infection.
Significance: primary or secondary pathogen; importance and prevalence developing and require further study.

MYCOPLASMOSIS
Etiology: *Mycoplasma pulomonis*, only clinically significant *Mycoplasma,* lacks cell wall, fastidious, requires selective media; chronic respiratory disease (CRD), murine respiratory mycoplasmosis (MRM);

CORYNEBACTERIUM
Etiology: *Corynebacterium kutscheri*, gram-positive, diphtheroid bacillus with “Chinese letter” configurations *in situ.*
Transmission: inapparent infection oropharynx, cervical lymph nodes; mice, rats, and guinea pigs;
Clinical: exacerbated by immunosuppression or concomitant disease; hematogenous spread to lungs , kidneys, liver; chromodacryorrhea, mucopurulent nasal discharge, respiratory distress.
Pathology: raised, pale, coalescing foci of pulmonary suppuration; also kidney and liver; multifocal coagulation to caseous necrosis with neutrophillic infiltration not associated with airways; “Chinese letter” amorphous basophilic bacterial colonies; lymphoid hyperplasia.
Dx: carriers detected by oropharyngeal washes or cervical lymph node cultures.
Significance: inapparent carriers.

STAPHYLOCOCCUS
Etiology: *Staphylococcus aureus*, coagulase positive.
Transmission: present on skin of clinically normal carriers.
Clinical: ulcerative dermatitits, self-trauma, males, frequently shoulder, head, neck and ears.
Pathology: sharply demarcated ulcerative dermatitis with epidermal coagulation necrosis and discrete colonies of coccoid bacteria in overlying necrotic debris.
Ddx:.bite wounds, mycotic infection, rarely epitheliotropic lymphoid tumors (mycosis fungoides).
Significance: sporadic, males.

STREPTOCOCCUS
Etiology: *Streptococcus pneumoniae*, diplococcus.
Transmission: carried in the nasoturbinates & tympanic bullae of clinically normal rats; polysaccharide capsule resists phagocytosis; activates alternate complement cascade.
Clinical: asymptomatic; adolescents, serosanguinous to mucopurulent nasal discharge, rhinitis, conjunctivitis, vestibular signs; acute primary disease or secondary infections.
Pathology: fibrinopurulent polyserositis, pleuritis, peritonitis, pericarditis, periorchitis, meningitis; suppurative otitis media and rhinitis; fibrinopurulent bronchopneumonia; embolism.
Ddx:.*Corynbacterium,Salmonella, Pseudomonas, Pasteurella*; impression smears with encapsulated diplococci; alpha hemolysis on 5% blood agar.
Significance: acute systemic disease; mortality; potential zoonosis; mice can become infected, but unlike rats rarely develop disease.

D. OTHER BACTERIAL INFECTIONS

PSEUDOMONAS
Etiology: *Pseudomonas aeruginosa*, gram-negative bacillus.
Transmission: sipper tubes; water; fomites, ungloved hands; grows at room temperature; asymptomatic carriers 5-20%; predisposing factors that produce neutropenia.
Clinical: dyspnea, high mortality.
Pathology: acute coagulation necrosis with suppuration, and obliteration of pulmonary architecture; abscessation of lung, spleen, kidney; thromboembolism, vegetative endocarditis (catheter sequellae); visceral ecchymoses.
Ddx: *Corynebacterium, Pasteurella, Salmonella, Mycoplasma*; identifiable with Brown and Brenn tissue gram stain; Kosher’s citrate medium.
Significance: important cause of disease, mortality.

Enterococcus faecium-durans-2 – single report; sucklings, enteritis, diarrhea; high morbidity & mortality.

Erysipelas rhusiopathiae – single report; fibrinopurulent polyarthritis, endocarditis, myocarditis.

Hemobartonella muris – historical, uncommon; transmitted by *Polyplax spinulosa*; extra-erythrocytic parasite; inapparent, splenomegaly, reticulocytosis.

Klebsiella pneumonia – fecal isolate, normal animals; rare,

Streptobacillus moniliformis – gram-negative peomorphic filamentous rod; commensal, nasopharynx; opportunistic respiratory pathogen in concert with CAR bacillus or *Mycoplasma*; wound abscessation; potential zoonosis – rat bite fever, Haverill fever; *Spirillum minus* also a cause of rat bite fever in feral rats.

Idiopathic – Eosinophillic Granulomatous Pneumonia in Brown Norway Rats – eosinophillic-rich granulomatous pneumonitis; perhaps, inadvertent allergen exposure; Brown Norway model of asthma pathogenesis – readily develop increased bronchiolar responsiveness and elevated IgE postexposure to allergens.

IV. MYCOTIC INFECTIONS

DERMATOPHYTOSIS
Etiology: *Trichophyton mentagrophytes*.
Transmission: asymptomatic carriers, fomites; relatively rare florid skin infections;
Clinical: neck, back, base of tail, patchy hair loss, raised erythematous, pustular dermatitis.
Pathology: hyperkeratotic, hyperplastic dermatitis with folliculitis; arthrospores in hair shaft, PAS or methenamine silver stains.
Dx:.skin scrapings in 10% KOH.