INFECTIOUS AGENT EXCLUSION LIST FOR MICE

Division of Comparative Medicine

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

A. ADENOVIRUS

MOUSE ADENOVIRUS-1

Etiology: MAV-1 (FL), nonenveloped, polytropic.

Transmission: urine, feces, nasal secretions.

Clinical: naturally asymptomatic; experimentally fatal, multisystemic, prolonged viruria.

Pathology: thymic involution; foci of endothelial and epithelial necrosis with hemorrhage, and type A intranuclear inclusions in renal tubules, adrenal cortex, also spleen, intestine, brain, salivary glands, myocardium.

Ddx:.polyoma virus, cytomegalovirus.

Significance: rare multisystemic infection, neonatal encephalitis, SCID or nude enteritis; model for adrenal necrosis.

MOUSE ADENOVIRUS-2

Etiology: MAV-2 (K87), nonenveloped, enterotropic.

Transmission: feces.

Clinical: none, enterotropic, runting in sucklings, recover.

Pathology: runting may occur; intranuclear inclusions in small intestinal and cecal mucosal epithelium. Dx: antiserum to MAV-2 reacts with MAV-1, use MAV-2 antigen in serological tests; intranuclear intestinal inclusions are pathognomonic.

Significance: moderate prevalence, rare suckling runting.

B. HERPESVIRUS

MOUSE THYMIC VIRUS Etiology:

Clinical: neonatal or immunocompromised mice, viremic, dissemination to pulmonary vascular bed results in sudden onset of dyspnea, death; none in mice >18 days, resistance.

Pathology: intranuclear inclusions in vascular endothelium of jejunum, ileum, lung, liver; pulmonary congestion, edema, hemorrhage, atelectasis, alveolar septal thickening.

Ddx: MAV-1, MCMV, or polyoma virus-associated multisystemic infection with intranuclear inclusions. Significance: low natural prevalence.

POLYOMAVIRUS

Etiology: Polyomavirus, Papovavirus; "many tumors", especially salivary gland tumors, experimentally develop in neonates <24 hours old parenterally administered high titers of oncogenic strains of virus, similar to SV40, BK and JC viruses.

Transmission: intranasal urine, environmentally stable, but inefficient transmission can be broken by husbandry practices.

Clinical: natural infection rare; neonatal inoculation of nasal mucosa to submandibular salivary gland to lung, then dissemination especially kidney with high mortality; persists in lungs and kidneys; cleared in older mice; nude mice develop multisystemic wasting, paralysis associated with demyelination progressive multifocal

leukoencephalopathy, and vertebral tumors; tumors of uterus and bone.

Pathology: nude mice develop multifocal inflammation and necrosis, tumor formation; multiple tissues affected including bronchial, renal pelvic, ureteral epithelium; oligodendroglia with demyelination, intranuclear inclusions. Ddx: nude wasting – MHV, Pneumocystis carinii, Sendai, PVM; intranuclear inclusions – K virus, adenovirus, MCMV.

Significance: minimal, rare, contamination of transplantable tumors; prevalence may increase with use of polyoma middle T (Py V-MT) transgene.

D23.IyARVORUS

Significance:

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D. CORONAVIRUS

MOUSE HEPATITIS VIRUS Etiology:

Pathology: variable, genotype dependent; includes neoplasia, but most MuLV sequences are not oncogenic, instead encode strain-specific characteristics, e.g., demyelination (with LDV in C58 and AKR), dilute color (DBA), hairlessness (HR); endogenous proviruses given gene designations, e.g., AKR mice endogenous proviruses are designated akv-1, akv-2, akv-3, etc.; restriction genes e.g., fv-1, fv-4 and receptors influence evolution of recombinant pathogenic isolates, in addition, numerous intracisternal A particles (IAP), virus-like 30s RNA sequences (VL30), murine retrovirus-related DNA sequences (MuRRS), tRNA glutathione-like sequences (GLN), murine repeated virus sequences on Y chromosome (MuRVY), early transposons (ET).

MMTV

Etiology: Mouse mammary tumor viruses; exogenous MMTV-S, (standard), "milk factor", Bittner agent; 100% all mice harbor multiple copies of endogenous MMTV except perhaps "Lake Casitas" mice.

Transmission: MMTV-S in milk, saliva, semen, eliminated by fostering, intentionally maintained in model strains (C3H/HeJ, C3H/HeOuJ); 0-4 copies of endogenous provirus transmitted genetically, given gene designations (Mtv-1, -2, -8, etc.).

Clinical: MMTV-S associated mammary tumors; varied reintegration consequence; e.g., Mtv-29 functions as a super-antigen in SJL mice, stimulates T-cell cytokine expression, resulting in B-cell lymphoma; thymic lymphoma in GR mice.

Pathology: mammary neoplasia (C3H) or B-cell lymphoproliferative disease (SJL) or thymic lymphoma (GR) depending on strain; does not rely on recombinatorial events for oncogenesis, but instead direct insertional activation of proto-oncogenes.

HANTAVIRUS – zoonotic hazard; aerosol, contact with infected urine; no clinical disease in rats; also naturally infects Peromyscus mice; 2 major lineages, (HFRS) Hemorrhagic Fever and Renal Syndrome in humans with fever, thrombocytopenia, myalgia, headache, petechiae, retroperitoneal and renal hemorrhage; (HPS) Hantavirus Pulmonary Syndrome in humans with fever, pulmonary edema, shock; Bunyviridae.

III. BACTERIAL DISEASES

CITROBACTER COLONIC HYPERPLASIA

Etiology: Citrobacter rodentium, cocc-bacillus, (formerly C. freundii, strain 4280), transmissible murine colonic hyperplasia (TMCH).

Transmission: contaminated food, bedding, orofecal, direct, low contagiousness; selectively colonizes surface mucosa of cecum and colon within 4 days; locus of enterocyte attachment and type III secretion system facilitate attachment; translocated intimin receptor; recovered mice are refractory to reinfection; no carrier state.

Clinical: runted, lose weight, sticky, unformed feces; low mortality, often recover within 2 months; permanent rectal prolapse possible.

Pathology: thickened descending colon devoid of feces; marked colonic crypt hyperplasia (Th-1 response, IL-12, IFN, TNF, elevated keratinocyte growth factor), basophilic epithelial cells; inflammation and erosion possible among infants of some strains; hyperplasia followed by excessive goblet cells and cryptal cysts (mucin and cellular debris), normal mucosa within 2 months.

Ddx: MacConkey agar, but in 2-3 weeks can no longer isolate; enteritis in young – rota, reo, MHV, MAV-2; in older mice – Tyzzer's, Salmonella; rectal prolapse - Helicobacter

Significance: rare, no carrier state, transient, low contagiousness, low mortality, runting and rectal prolapse.

ESCHERICIA COLI

Etiology: Escherichia coli, coliform typhlocolitis, common intestinal organism; but atypical, non-lactose fermenting isolate.

Transmission:eodin rec37 sta5.4(o)-088 0 nhin 22 Tc3(w)3.6(o)5.5arcldMtxi(col)0.4(Tw(irc2bholog)-6.2(y)16.nell)6.4(a3.6(o)

Ddx: Tyzzer's, Citrobacter, Helicobacter, Escherichia.

CMDC #109.2 Effective 1/07 Page 7 of 11 Pathology: multifocal necrosis and venous thrombosis with leukocyte infiltration in liver, spleen, Peyer's patches, mesenteric lymph nodes; focal hepatic granulomas as hallmark lesion; intermittent shedding. Ddx: culture mesenteric lymph nodes; Tyzzer's, MHV, ectromelia virus, Helicobacter, Pseudomonaus. Significance: depopulate, interspecies transmission, zoonotic.

OTHER GRAM NEGATIVE INFECTIONS

Pasteurella pneumotropica – gram-negative coccobacillus; commensal, common intestinal and nasopharyngeal isolate from healthy mice; subclinical, often seron

Corynebacterium bovis – "coryneform hyperkeratosis"; diffuse hyperkeratotic dermatitis of nude mice; transmitted by fomites, direct, or topical administrations; asymptomatic transient infection in immunocompetent strains, other nudes like source; high morbidity; orthokeratotic, hyperkeratotic epidermal hyperplasia; ddx: hyperkeratosis-associated with low ambient humidity.

Corynebacterium hoffmani – frequent opportunistic isolate in BALB/c conjunctivitis; ddx: P. pneumotropica.

Staphylococcus aureus – gram-positive, coccoid bacterium, common inhabitant of skin, mucous membranes, nasopharynx, intestine; asymptomatic; nude – periorbital abscess, furunculosis and folliculitis around muzzle, lacrimal & prepucial gland abscesses; B6 – contributes to ulcerative dermatitis, secondary to acariasis; pruritic with self-excoriation; readily identifiable bacteria, botryomycotic granules, Splendore-Hoeppli material, especially

Clinical: Myobia – head, eyelids, neck, shoulders; Myocoptes – all over body, primarily inguinal, abdominal.

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